WHO GUIDELINES ON PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR

WEB ANNEX
Evidence Profiles*

* The main guidelines document is available at:

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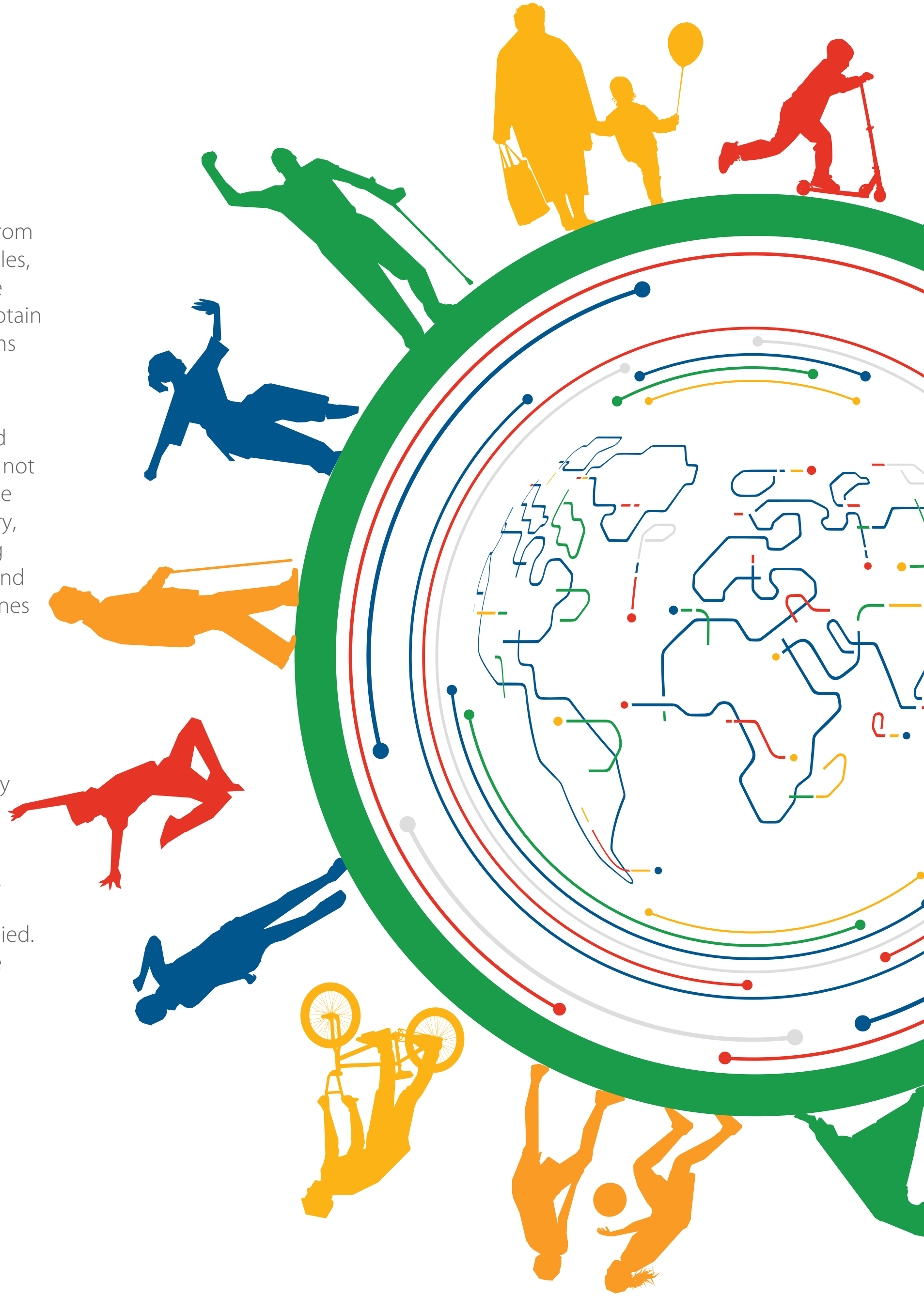

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METHODS

Scope of guideline and questions of interest

The Guideline Development Group (GDG) reviewed the scope of the guideline and agreed on the most relevant PI/ECO (Population, Intervention/Exposure, Comparison, Outcome) questions at their first meeting. The key questions which were addressed for each sub population are summarised below:

What is the association between **physical activity** and health-related outcomes?

a. Is there a dose-response association (volume, duration, frequency, intensity)?
b. Does the association vary by type or domain of physical activity?

What is the association between **sedentary behaviour** and health-related outcomes?

a. Is there a dose-response association (total volume and the frequency, duration and intensity of interruption)?
b. Does the association vary by type and domain of sedentary behaviour?

For each **Population (P)**, the **Exposure (E)** was greater volume, duration, frequency or intensity of physical activity; with as **Comparison(C)** no physical activity or lesser volume, duration, frequency, or intensity of physical activity. The critical and important outcomes for each population are summarised in Table 1 in Annex 1 and the details of each PI/ECO question in the relevant section of Annex 1.

The GDG recommended use of the most recently published relevant systematic reviews to address the PI/ECO questions and requested that the available systematic reviews be updated to reflect the most recent data.

The evidence

The update of the WHO recommendations on physical activity has been conducted by identifying and updating the most recent, relevant umbrella reviews related to the scope of these guidelines. This approach was adopted due to an extensive body of systematic reviews conducted in recent years undertaken to inform the development of a number of national physical activity guidelines. The additional updating of the identified reviews was undertaken to ensure the new WHO guidelines reflect the most recent available data in a rapidly developing field of public health.

Umbrella reviews were selected if they met the following three criteria: (1) the evidence reviews had been conducted according to standard systematic processes that were well documented; (2) the assessment of the certainty of the evidence used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method or an equivalent methodology that was clearly described and documented; and (3) the evidence reviews addressed the populations of interest with no restrictions to country or country income level.

The PI/ECO questions and the critical and important health outcomes were mapped against existing evidence reviews and where needed additional new reviews were commissioned to address gaps. The GDG requested that the evidence reviews be updated, using the same search terms, search languages and databases as the original reviews.

The following evidence reviews were identified as meeting the above three criteria and were chosen for recency and comprehensiveness:

- A systematic review of the literature conducted by Poitras et al., (2016) on the association between physical activity and health indicators in school aged children and youth *(1)* as part of the process for developing the *Canadian 24-Hour Movement Guidelines for Children and Youth (2)*. This review focused only on studies that used objective measurements of physical activity.

  A total of 162 studies were included (204,171 participants from 31 countries) in the review.

- A systematic review of the literature of the association between sedentary behaviour and health indicators in school-aged children conducted by Carson et al., (2016) *(3)* as part of the process for developing the *Canadian 24-Hour Movement Guidelines for Children and Youth (2)*.

  A total of 235 studies (194 unique samples) were included representing 1,657,064 unique participants from 71 different countries.

- A systematic review conducted by Okely et al., (2019) *(4)* undertaken to update Poitras et al., (2016) *(1)* and Carson et al., (2018) *(3)* as part of the development of the 2019 *Australian 24-Hour Movement Guidelines for Children and Young People* (5-17 years) *(5)*.

  This report identified an additional 42 studies on physical activity, 32 on sedentary behaviour published through to July 2918 *(4).*

  The GRADE tables developed from these updates were used as the basis for the commissioned update conducted for WHO.

- The systematic reviews conducted and synthesized as part of the development of the *2019 Canadian Guideline for Physical Activity Throughout Pregnancy (6)*. This consisted of 12 systematic reviews of over 25,000 related studies in English, Spanish and French language on maternal physical activity during pregnancy reporting on maternal, fetal or neonatal morbidity, or fetal mortality outcomes. Seven of these systematic reviews addressed outcomes deemed critical and important by the GDG *(7-13)*.

  The GRADE tables from these evidence reviews were used as the basis for the literature search conducted to update and inform the development of WHO recommendations.

- The scientific report of the Physical Activity Guidelines Advisory Group (PAGAC) *(14)* which provides a summary of a systematic update of evidence on physical activity and sedentary behaviours and health outcomes since 2008 through to 2016 to inform the development of the 2018 *Physical Activity Guidelines for Americans, 2nd Edition (15)*.

  The evidence summarised addressed a total of 38 main research questions and 104 sub-questions selected for their public health relevance. The evidence comprised results from systematic reviews comprising a total of 1,130 articles, which were each abstracted to answer the 38 research questions *(14)*.

The systematic reviews protocols utilized a modified version of “A Measurement Tool to Assess Systematic Reviews” (AMSTAREXBP) to assess the methodological quality of systematic reviews and meta-analyses. Risk of bias, or internal validity, was assessed for each original study using an adapted version of the USDA NEL Bias Assessment Tool (BAT) *(16)*.
The new evidence identified in the updated searches conducted for these WHO guidelines is presented below and links are provided to report and supplementary materials of the PAGAC *(14)*.

Methods for updating the evidence and data extraction

A search for systematic reviews and pooled analyses of cohort studies was conducted for studies published from the date of last searches conducted for each of the included reviews (listed above) up to September 2019 and standardized data extraction protocols, were developed and employed.

To update the searches conducted by Poitras et al., (2016) *(1)*, Carson et al., (2016) *(3)*, and Okely et al., (2019)*(4)* MEDLINE, EMBASE, PsycInfo, and SportDiscus databases were searched to identify reviews that were peer-reviewed, written in English or French. To update the searches conducted by PAGAC *(14)* PubMed, CINAHL and Cochrane databases were searched to identify reviews that were peer-reviewed, written in English.

Searches were performed with no restriction by country or country income status and inclusive of reviews addressing any subjective or objectively measured physical activity or sedentary behaviour. It was decided not to conduct searches in additional languages other than those of the original searches, due to resource constraint and previous experience in the field indicating that these searches yielded very few, if any additional reviews. Reviews that examined an association (based on levels above or below a threshold of physical activity or sedentary behaviour) and also reviews that explored the dose-response relationship between these and health-related outcomes were considered.

An external team of reviewers used the AMSTAR 2 (Assessment of Multiple Systematic Reviews) instrument to rate the credibility of the systematic reviews under consideration for inclusion *(17)*. The AMSTAR 2 tool contains 16 items that relate to the planning and conduct of the review. The overall confidence in the results of each review was rated according to published guidance: a rating of “high” reflects that the review had zero or one noncritical weakness; “moderate” indicates the review was judged to have more than one noncritical weakness; “low” means the review was judged to have one critical flaw with or without noncritical weaknesses or multiple noncritical weaknesses; and “critically low” signifies that more than one critical flaw was present. One reviewer completed the AMSTAR 2 tool for all provisionally included reviews. Reviews that were rated critically low by one reviewer were reviewed by a second reviewer using the same tool. Reviews ultimately rated as critically low were excluded because they were judged to be too unreliable to provide an accurate and comprehensive summary of the available evidence, unless it was the only review available for a particular outcome.

This body of evidence also included pooled cohort studies. An external team of reviewers used the Newcastle-Ottawa Scale to assess the quality of those studies *(18)*. Each study was given a quality rating of good, fair, or poor quality. In general, a good-quality study met all criteria on the Newcastle-Ottawa scale. A fair-quality study did not meet, or it was unclear whether it met at least one criterion, but also had no known important limitations that could invalidate its results. A poor-quality study had a single fatal flaw or multiple important limitations. Poor-quality studies were excluded.

There was an assessment for overlap, recognising potential for duplication of studies in multiple review. Reviews that contained redundant bodies of evidence, overviews-of-reviews and some pooled cohort studies were excluded where other reviews that were more comprehensive and/or recent were identified.

Methods for new reviews

Where gaps in existing evidence were identified, new umbrella reviews were commissioned. Reviews were commissioned to examine:

1. **The relationship between occupational (i.e., work-related) physical activity and health-related outcomes*(19)***; and
2. **The association between leisure-domain physical activity and adverse health outcomes *(20)*.**

For these two new reviews, searches were undertaken using PubMed, SPORTDiscus and Embase from 2009 to December 2019.

3. **The association between physical activity and falls prevention.**

This utilized the 2019 Cochrane Collaboration Systematic Review by Sherrington *(21)*, and updated with evidence published to November 2019.

4. **The association between physical activity and osteoporosis and sarcopenia.**

The search for existing systematic reviews on osteoporosis and sarcopenia was conducted in PubMed for reviews published from 2008 up to November 2019 identified no new reviews and eight new primary studies.

5. **The evidence on associations between physical and health outcomes in people living with HIV.**

A scoping review ascertained the availability of evidence on physical activity and health-related outcomes among people living with HIV to support conducting an umbrella review which was conducted for evidence published up to October 2019 using PubMed, CINAHL and Web of Science and no start date limitation.

Grading the Body of Evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) method was used to rate the certainty of the evidence for each PICO *(22)*. When available, the GRADE “Evidence Profiles” or “Summary of Findings” tables from each review were used as a starting point. If no table was available within the existing systematic reviews, Evidence Profile tables for each population and outcome of interest were constructed.

The GRADE method was used to rate the certainty of the evidence for each PICO *(22)* with the following criteria considered: study design, risk of bias, consistency of effect, indirectness, precision of effect, and other limitations, including publication bias and other factors for upgrading (magnitude of effect, dose-response, and effects of confounders).

Well-conducted longitudinal studies were upgraded to better reflect the certainty in findings regarding associations from such studies.

Studies that evaluated intermediate/indirect outcomes were not necessarily downgraded; the GRADE rating reflects the certainty in effects on those outcomes.

In some cases, the GRADE ratings from existing reviews were modified to ensure consistency in how GRADE methods were applied.

The certainty in the body of evidence for each outcome was assigned based on the following guidance *(23)*:

High :We are very confident that the true effect lies close to that of the estimate of the effect
Moderate: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect
Very low: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Going from evidence to recommendations

The GDG employed the GRADE Evidence to Decisions (EtD) framework for generating question specific recommendations. The EtD framework is a systematic, structured and transparent approach to decision making. The framework uses explicit criteria for generating guideline recommendations considering research evidence, certainty of evidence, and where required, expert opinion and topical knowledge from the perspective of the target audience. The criteria elicit judgments about the balance between the observed evidence of desirable and undesirable outcomes, overall certainty of evidence, relative values of patients for desirable and undesirable outcomes, resource use (cost considerations) where applicable, potential impact on inequities in health, acceptability and feasibility of recommendations.

The GDG considered the body of evidence in totality for each recommendation for all critical and important outcomes. For a particular exposure/intervention and outcome link, studies differed widely in the specific exposure/intervention assessed, outcomes assessed, study design, and analytic methods, resulting in heterogeneity in the available evidence. Therefore, it was not possible to apply the classic GRADE approach to each specific exposure/intervention and outcome link; rather, GRADE was applied for the overall body of evidence addressing each exposure/intervention and outcome link, across study design types and variations in exposure/intervention measurements and analyses. When these factors resulted in concerns regarding the coherence of the evidence (in other words, that the evidence for a particular exposure/intervention and outcome link did not fit together when looked at in different ways), the panel downgraded the certainty of evidence*(24)*.

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A: EVIDENCE ON PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR FOR CHILDREN AND ADOLESCENTS (5 TO UNDER 18 YEARS OF AGE)

Guiding Questions

A1. What is the association between **physical activity** and health-related outcomes?
Is there a dose-response association (volume, duration, frequency, intensity)?
Does the association vary by type or domain of physical activity?
A2. What is the association between **sedentary behaviour** and health-related outcomes?
Is there a dose-response association (total volume and the frequency, duration and intensity of interruption)?
Does the association vary by type and domain of sedentary behaviour?
Inclusion Criteria

Population: Children aged 5 to under 18 years of age
Exposure: Greater volume, duration, frequency or intensity of physical activity; greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour.
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity; lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour.

The GRADE Evidence Profiles developed for the 2019 *Australian 24-Hour Movement Guidelines for Children and Young People (5-17 years)* by Okely et al. *(1)* were used as a basis for this update for children and adolescents, given the rigor in methods and recency in included evidence. The following modifications were made to the GRADE assessments from the Okely update: 1) evidence from observational studies evaluating associations was upgraded one level if the studies were well-conducted longitudinal studies with no serious risk of bias, to better reflect the certainty in findings regarding associations from such studies and 2) evidence from all studies was downgraded one level if there was only one study, due to inability to assess consistency. The development of the Australian guideline utilized the GRADE-ADOLOPMENT approach, leveraging the work done in Canada in the development of their 24-hour guidelines *(2, 3)*. For each PICO, identified systematic reviews were incorporated into the existing Evidence Profiles according to the study designs included in the review. A summary of findings for each review is provided. In cases where the identified systematic reviews suggested differences in the quality assessment (risk of bias, inconsistency, indirectness, imprecision, or other risk of bias) or overall certainty, the evidence profiles were edited accordingly. Additional evidence reviewed for the US Physical Activity Guidelines Advisory Committee report were included in the draft Evidence Profiles to contextualize the overall body of evidence.

Outcomes	Importance
Physical fitness (e.g. cardiorespiratory, motor development, muscular fitness)	Critical
Cardiometabolic health (e.g. blood pressure, dyslipidaemia, glucose, insulin resistance)	Critical
Bone health	Critical
Adiposity	Critical
Adverse effects (e.g. injuries and harms)	Critical
Mental health (e.g. depressive symptoms, self-esteem, anxiety symptoms, ADHD)	Critical
Cognitive outcomes (e.g. academic performance, executive function)	Critical
Prosocial behaviour (e.g. conduct problems, peer relations, social inclusion)	Important
Sleep duration and quality	Important

Evidence identified

Twenty-one reviews were identified (published from 2017 to 2019) that examined the association between physical activity and/or sedentary behaviour and health-related outcomes among children and adolescents *(4-24)*.

Fourteen reviews examined the relationship between physical activity and health-related outcomes, five reviews examined the relationship between sedentary behaviour and health-related outcomes, and two reviews included both physical activity and sedentary behaviour (**Table A.1**). The most commonly reported outcomes in the reviews were measures of adiposity and cardiometabolic health. No reviews were identified that evaluated the association between physical activity and adverse effects, mental health outcomes, or sleep outcomes and no reviews were identified that evaluated the association between sedentary behaviour and physical fitness, adverse effects, cognitive outcomes, or prosocial behaviour.

Furthermore, none of the existing reviews robustly examined whether there was a dose-response association between physical activity or sedentary behaviour and health-related outcomes, whether the association varied by type or domain of physical activity or sedentary behaviour, and whether physical activity modified the effect of sedentary behaviour on mortality.

In most cases, each review was narrowly scoped to look at specific types of physical activity (e.g., high-intensity interval training, school-based physical activity programs) or sedentary behaviour (e.g., objectively-measured sedentary time) and limited inclusion to specific study designs (e.g., only randomized controlled trials).

Few reviews (three) included evidence published into 2019. About half of the reviews included evidence published from database inception through at least 2017; seven reviews searched through 2014, 2015, or 2016 and three reviews did not report search dates. Extracted data for each review is included in **Appendix 1A.**

None of the systematic reviews were rated as having high credibility based on the AMSTAR 2 instrument. Six were rated as having moderate credibility, 10 were rated as having low credibility, and 5 were rated as having critically low credibility. Given concerns regarding the comprehensiveness and the validity of the results presented in reviews rated as having very low credibility, they were not incorporated into the final Evidence Profiles. **Table A.2** presents the ratings for each review according to all the AMSTAR 2 main domains.

Table A.1. Systematic Reviews Assessed

Author, Year	Behaviour		Outcomes									Last search date	# of included studies	AMSTAR 2
	PA	SB	Physical fitness	CM health	Bone health	Adip-osity	AEs	Mental health	Cognitive outcomes	Prosocial behaviour	Sleep duration and quality			
Bea, 2017 *(4)*	X			X								2015	13	Moderate
Belmon, 2019 *(5)*		X									X	Jan 2017	45	Low
Cao, 2019 *(6)*	X		X									Feb 2019	17	Low
Collins, 2018 *(7)*	X					X						June 2017	18	Low
Eddolls, 2017 *(8)*	X			X		X						Sept 2016	13	Low
Errisuriz, 2018 *(9)*	X		X			X						NR	12	Critically Low
Fang, 2019 *(10)*		X				X						May 2019	16	Low
Koedijk, 2017 *(11)*		X			X							Jan 2019	17	Moderate
Krahenbühl, 2018 *(12)*	X				X							2016	21	Critically Low
Lee, 2018 *(13)*	X					X						Jan 2014	27	Critically Low
Marker, 2019 *(14)*		X				X						June 2018	24	Low
Marques, 2018 *(15)*	X								X			2016	51	Moderate
Martin, 2017 *(16)*	X					X			X			Mar 2015	15	Moderate
Miguel-Berges, 2018 *(17)*	X					X						July 2015	36	Low
Mohammadi, 2019 *(18)*	X	X				X						Aug 2017	17	Low
Pozuelo-Carrascosa, 2018 *(19)*	X			X								Feb 2018	19	Moderate
Singh, 2019 *(20)*	X								X	X		Sept 2017	58	Critically Low
Skrede, 2019 *(21)*	X	X		X								April 2018	30	Critically Low
Stanczykiewicz, 2019 *(22)*		X						X				NR	31	Low
Verswijveren, 2018 *(23)*	X			X								2017	29	Moderate
Xue, 2019 *(24)*	X								X			NR	19	Low

Abbreviations: AEs = adverse effects; CM = cardiometabolic; PA = physical activity; SB = sedentary behaviour

Table A.2. Credibility Ratings (AMSTAR 2)

Author, Year	PICO[1]	A priori Methods[2]	Study Design Selection[3]	Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assess-ment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Bea, 2017 *(4)*	Y	N	N	PY	Y	Y	PY	PY	Y	N	N/A	N/A	Y	N	N/A	Y	**Moderate**
Belmon, 2019 *(5)*	Y	N	N	PY	Y	Y	PY	PY	N	N	N/A	N/A	Y	N	N/A	Y	**Low**
Cao, 2019 *(6)*	Y	N	N	PY	Y	Y	PY	Y	N	N	Y	Y	N	Y	Y	Y	**Low**
Collins, 2018 *(7)*	Y	N	N	PY	Y	Y	N	Y	PY	N	Y	Y	Y	Y	Y	Y	**Low**
Eddolls, 2017 *(8)*	Y	N	N	PY	N	N	PY	N	Y	N	N/A	N/A	Y	Y	N/A	Y	**Low**
Errisuriz, 2018 *(9)*	Y	N	N	N	Y	Y	PY	PY	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Fang, 2019 *(10)*	Y	N	N	PY	Y	N	PY	PY	Y	N	N	N	N	Y	Y	Y	**Low**
Koedijk, 2017 *(11)*	Y	N	N	PY	Y	Y	Y	PY	PY	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Krahenbühl, 2018 *(12)*	Y	N	N	PY	N	N	PY	PY	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Lee, 2018 *(13)*	Y	N	N	PY	Y	Y	N	PY	N	N	N/A	N/A	N	Y	N/A	N	**Critically Low**
Marker, 2019 *(14)*	Y	N	N	PY	N	Y	PY	N	N	N	Y	Y	N	Y	Y	Y	**Low**
Marques, 2018 *(15)*	Y	N	N	PY	Y	Y	PY	PY	PY	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Martin, 2017 *(16)*	Y	N	N	PY	Y	N	PY	Y	Y	N	N/A	N/A	Y	N	N/A	N	**Moderate**
Miguel-Berges, 2018 *(17)*	Y	N	N	PY	Y	Y	Y	PY	Y	Y	N/A	N/A	N	N	NA	N	**Low**
Mohammadi, 2019 *(18)*	Y	N	N	PY	Y	Y	PY	PY	PY	N	N/A	N/A	Y	Y	N/A	Y	**Low**
Pozuelo-Carrascosa, 2018 *(19)*	Y	N	N	PY	Y	Y	PY	Y	Y	N	Y	N	Y	Y	Y	Y	**Moderate**
Singh, 2019 *(20)*	Y	N	N	PY	Y	Y	N	PY	PY	N	N/A	N/A	Y	Y	N/A	Y	**Critically Low**
Skrede, 2019 *(21)*	Y	N	N	N	Y	N	PY	PY	N	N	N	N	N	N	N/A	Y	**Critically Low**
Stanczykiewicz, 2019 *(22)*	Y	N	N	Y	Y	Y	PY	Y	PY	N	Y	N	Y	Y	Y	Y	**Low**
Verswijveren, 2018 *(23)*	Y	N	N	PY	Y	Y	PY	PY	PY	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Xue, 2019 *(24)*	Y	N	N	PY	Y	N	PY	Y	PY	N	N	N	N	Y	Y	Y	**Low**

Abbreviations: COI = conflict of interest; N = no; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; CM = cardiometabolic; PA = physical activity; SB = sedentary behaviour; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *(25)*

A.1. Physical Activity

Table A.1.a. Physical fitness and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Physical fitness (e.g., cardiorespiratory, motor development, muscular fitness)
***Importance**: CRITICAL

Black font is from original GRADE Evidence Profiles developed to support the development of the Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	For reference: Summary from PAGAC ***(27)***
The range of mean ages was 6.9 to 16.0 years. Data were collected by RCT, non-randomized intervention trial, cross-sectionally and up to 3.75 years of follow-up. Fitness was assessed as: aerobic fitness (VO2max, VO2peak, CRF), muscular strength, coordination, shoulder mobility and endurance, and flexibility. All outcomes were measured objectively.								
7 RCTs[a] N = 1,483	Serious risk of bias[b]	No serious inconsistency	Serious indirectness[c]	No serious imprecision	None	**Aerobic fitness:** **4 studies** reported a favourable effect of PA interventions on aerobic fitness at post-test (Kriemler et al. 2010; Cohen et al. 2015) and 6-month and 2-year follow-up (Eather et al. 2013; Meyer et al. 2014); **2 studies** reported no effect (Verstraete et al. 2007; Finkelstein et al. 2013).[d] Cao et al. 2019 *(6)* (16 RCTs, 1 NRT; n=563): High-intensity interval training compared with moderate-intensity continuous training had a moderate beneficial effect on cardiorespiratory fitness (SMD = 0.51 [95% CI, 0.33 to 0.69], p<0.01; I^2=0%). No evidence that intervention duration, exercise modality, work and rest ratio, and total bouts modified the effect of high-intensity interval training on cardiorespiratory fitness. **Muscular strength and endurance:** **1 study** reported a favourable effect of PA interventions on upper and lower-body muscular fitness at post-test; these differences were no longer significant after 3 months (Meinhardt et al. 2013); **1 study** reported no effect at post-test (Verstraete et al. 2007); **1 study** reported mixed favourable and null findings at 6-month follow up (Eather et al. 2013). **No reviews reporting strength and endurance outcomes identified.** **Flexibility:**	LOW[e]	15 ESRs Strong evidence demonstrates that, in children and adolescents, higher amounts of physical activity are associated with more favourable status for cardiorespiratory and muscular fitness. **PAGAC Grade: Strong** Strong evidence demonstrates that increased moderate-to-vigorous physical activity increases

						1 study reported no effect at post-test (Verstraete et al. 2007); **1 study** reported a favourable effect of PA on flexibility at 6-month follow-up (Eather et al. 2013). **No reviews reporting flexibility outcomes identified.**		cardiorespiratory fitness and that increased
8 NRTs[f] N = 5,336 **No reviews limited to NRTs identified.**	Serious risk of bias[g]	No serious inconsistency	Serious indirectness[h]	No serious imprecision	None	**Aerobic Fitness:** **1 study** reported no effect of PA intervention on aerobic fitness (Rowland et al. 1996); **4 studies** reported a favourable effect of PA intervention for INT compared with CTRL (Dimitriou et al. 2011; Buchele 2018;Brusseau et al 2016, Chesham et al. 2018); **1 study** reported mixed effects of PA intervention on aerobic fitness across subsamples at post-test (favourable effect for Grade 6 children but not Grade 1 to 5) (Burns et al. 2017); and **1 study** reported no differential effect of PA intervention on aerobic fitness between INT and CTRL, however the intervention group decreased from baseline to post-test (Shore et al. 2014). **Muscular Strength and Endurance:** **1 study** reported a favourable effect of PA intervention on upper-body strength for INT compared with CTRL (Dimitriou et al. 2011); **1 study** reported a favourable effect of PA intervention on endurance, co-ordination and shoulder mobility (Postler et al 2017); and **1 study** reported no differential effect of PA intervention on muscular fitness, however the control group improved upper-body strength from baseline to post-test (Shore et al. 2014). **Flexibility:** **1 study** reported a favourable differential effect of PA intervention for INT compared with CTRL (Dimitriou et al. 2011). **1 study** reported no differential effect of a PA intervention on flexibility, and an increase from baseline to post-test for the intervention group (Shore et al. 2014).	VERY LOW[i]	resistance exercise increases muscular fitness in children and adolescents. **PAGAC Grade: Strong**
2 Longitudinal[j] N = 630 **No reviews including or limited to longitudinal designs identified.**	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[k]	Dose response gradient[l]	**Aerobic fitness:** There was a favourable, dose-response gradient between **VPA** and aerobic fitness, and no association between **LPA** or **MPA** and aerobic fitness in **2 longitudinal studies** (Carson et al. 2013*(28)*; Santos et al. 2018).	LOW[m]	
48 Cross-sectional[n] N = 14,985 **No reviews including or limited to longitudina**	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	**Aerobic fitness:** **Meeting/Not Meeting PA Guidelines (≥60 min/day MVPA):** favourable associations (**3/3 studies;** Ortega et al. 2008; Martinez-Gomez et al. 2010a; Silva et al. 2013). **Total PA:** associations were favourable (**14/18 studies;** Eiberg et al. 2005; Andersen et al. 2006; Ruiz et al. 2006; Butte et al. 2007b; Hands et al. 2009; Schofield et al. 2009; Ruiz et al. 2011; Machado-Rodrigues et al. 2012; Martinez-Gomez et al. 2012; Hjorth et al. 2013; Lambourne et al. 2013; Larouche et al. 2014; Hansen et al. 2014; Saavedra et al. 2014), or mixed	VERY LOW[u]	

l designs identified.						(favourable and null; **4/18 studies;** Rizzo et al. 2007; Dencker et al. 2010; Kristensen et al. 2010; Jimenez-Pavon et al. 2013c).[o] **VPA:** associations were favourable (**11/12 studies;** Gutin et al. 2005a; Ruiz et al. 2006; Rizzo et al. 2007; Butte et al. 2007b; Lohman et al. 2008; Martinez-Gomez et al. 2010a; Kristensen et al. 2010; Ottevaere et al. 2011; Hay et al. 2012; Martinez-Gomez et al. 2012; Jimenez-Pavon et al. 2013c), or mixed (favourable and null; **1/12 studies;** Dencker et al. 2010).[p] **MVPA:** associations were favourable (**14/16 studies;** Eiberg et al. 2005; Gutin et al. 2005a; Ruiz et al. 2006; Butte et al. 2007b; Ortega et al. 2008; Lohman et al. 2008; Martinez-Gomez et al. 2010a; Ruiz et al. 2011; Ottevaere et al. 2011; Machado-Rodrigues et al. 2012; Martinez-Gomez et al. 2012; Hjorth et al. 2013; Silva et al. 2013; Santos et al. 2014), or mixed (favourable in boys, null in girls; **2/16 studies;** Dencker et al. 2010; Jimenez-Pavon et al. 2013c).[q] *Bouts of MVPA* were favourably associated with aerobic fitness in **2/2 studies** (Eiberg et al. 2005; Butte et al. 2007b). **MPA:** associations were favourable (**5/9 studies;** Gutin et al. 2005a; Ruiz et al. 2006; Martinez-Gomez et al. 2010; Dencker et al. 2010; Ottevaere et al. 2011), mixed favourable and null (**2/9 studies;** Rizzo et al. 2007; Butte et al. 2007b), or null (**2/9 studies;** Hay et al. 2012; Martinez-Gomez et al. 2012).[r] **LPA:** associations were favourable (**1/6 studies;** Martinez-Gomez et al. 2010a), mixed favourable and null (**1/6 studies;** Butte et al. 2007b), or null (**4/6 studies;** Dencker et al. 2010; Hay et al. 2012; Machado-Rodrigues et al. 2012; Jimenez-Pavon et al. 2013c). **Muscular Strength and Endurance** **Total PA:** associations were favourable (**2/4 studies;** Martinez-Gomez et al. 2012; Larouche et al. 2014), mixed favourable and null (**1/4 studies;** Hands et al. 2009), or null (**1/4 studies;** Moliner-Urdiales et al. 2010).[s] **VPA:** associations were favourable (**1/2 studies;** Martinez-Gomez et al. 2012), or mixed favourable and null (**1/2 studies;** Moliner-Urdiales et al. 2010). **MVPA:** associations were favourable (**1/3 studies;** Martinez-Gomez et al. 2012), or mixed favourable and null (**2/3 studies;** Moliner-Urdiales et al. 2010; Aggio et al. 2015).[t] **MPA:** null associations (**2/2 studies;** Moliner-Urdiales et al. 2010; Martinez-Gomez et al. 2012). **LPA:** associations were null (**1/2 studies;** Moliner-Urdiales et al. 2010), or mixed null and unfavourable (**1/2 studies;** Aggio et al. 2015). **Flexibility** **Total PA:** associations were mixed favourable and null (**1/2 studies;** Hands et al. 2009) or null (**1/2 studies;** Larouche et al. 2014).		

						MVPA: favourable associations (**1/1 studies;** Aggio et al. 2015). **LPA:** null associations (**1/1 studies;** Aggio et al. 2015).		

Abbreviations: CRF = cardiorespiratory fitness; ESR = existing systematic review; LPA = light physical activity; MVPA = moderate-to-vigorous physical activity; NRT = non-randomized trial; PA = physical activity; RCT = randomized controlled trial; VO_2max = maximal oxygen uptake; VO_2peak = peak oxygen uptake; VPA = vigorous physical activity.

[*] As determined by WHO

[a] Includes **6 RCT studies** (Verstraete et al. 2007; Kriemler et al. 2010; Meinhardt et al. 2013; Finkelstein et al. 2013; Eather et al. 2013; Meyer et al. 2014) from **5 unique samples**. Kriemler et al. 2010 and Meyer et al. 2014 both report data from the KISS Study. Results are reported separately, and participants are only counted once.

[b] Serious risk of bias. Unclear method of randomization for sibling pairs; allocation concealment unlikely; missing pedometer data disproportionately high in controls relative to intervention group (18.1% vs 6.1%), likely due to incentives for wear time offered to the intervention group only; control group wore sealed pedometers while intervention group wore unsealed pedometers; 6-min walk test assessors were not blinded to group assignment (Finkelstein et al. 2013). No allocation concealment, which was likely to contaminate the control group (Meinhardt et al. 2013). Teachers of control group classes were aware of intervention arm but not its content; drop-outs were older and had higher adiposity than adherers and differences likely to be related to outcome of interest (Meyer et al. 2014).

[c] Serious indirectness. Differences in intervention: randomized trials examined various types of physical activity programs and provided indirect evidence bearing on the potential effectiveness of different intensities and durations of physical activity. Indirect comparisons: different durations and intensities of physical activity were not compared.

[d] MVPA (but not total PA) was significantly greater in the intervention vs control group at post-intervention (post 9-month intervention group difference of ~11 min/day) (Kriemler et al. 2010); there was a trend toward higher levels of total PA (but not MVPA) in the intervention vs control group at 3-yr follow-up (Cohen's $d = 0.35$, p=0.06; not significant) (Meyer et al. 2014).

[e] The quality of evidence from randomized studies was downgraded from "high" to "low" due to: (1) a serious risk of bias in three studies that diminished the level of confidence in the observed effects, and (2) serious indirectness of the interventions and the comparisons being assessed.

[f] Includes **1 non-randomized controlled trial** (Shore et al. 2014), **1 community trial** (Dimitriou et al. 2011), and **1 uncontrolled trial** (Rowland et al. 1996).

[g] Serious risk of bias. No inclusion/exclusion criteria established; inadequate reporting of recruitment, allocation concealment, and blinding; large unexplained loss to follow-up (36.5% retention) and unknown if follow-up differed by group allocation (Shore et al. 2014); selective reporting bias: reported use of PACER to measure aerobic fitness but did not report in results (Dimitriou et al. 2011).

[h] Serious indirectness. Differences in intervention: non-randomized trials examined various types of physical activity programs and provided indirect evidence bearing on the potential effectiveness of different intensities and durations of physical activity. Indirect comparisons: different durations and intensities of physical activity were not compared.

[i] The quality of evidence from randomized studies was downgraded from "high" to "low" due to: (1) a serious risk of bias in two studies that diminished the level of confidence in the observed effects, and (2) serious indirectness of the interventions and the comparisons being assessed.

[j] Includes **1 longitudinal study** (Carson et al. 2013).

[k] Serious imprecision. Wide confidence intervals for dose-response trend (Carson et al. 2013).

[l] There was a positive, dose-response gradient between VPA and aerobic fitness (Carson et al. 2013).

[m] The quality of evidence from the longitudinal study was upgraded from "low" to "moderate" due to no serious risk of bias but downgraded from "moderate" to "low" due to imprecision (wide confidence intervals), and because of this limitation was not upgraded for the dose-response trend.

[n] Includes **28 cross-sectional studies** (Eiberg et al. 2005; Gutin et al. 2005a; Andersen et al. 2006; Ruiz et al. 2006; Rizzo et al. 2007; Butte et al. 2007b; Ortega et al. 2008; Lohman et al. 2008; Hands et al. 2009; Schofield et al. 2009; Martinez-Gomez et al. 2010a; Dencker et al. 2010; Kristensen et al. 2010; Moliner-Urdiales et al. 2010; Ruiz et al. 2011; Ottevaere et al. 2011; Hay et al. 2012; Machado-Rodrigues et al. 2012; Martinez-Gomez et al. 2012; Hjorth et al. 2013; Lambourne et al. 2013; Silva et al. 2013; Jimenez-Pavon et al. 2013c; Larouche et al. 2014; Santos et al. 2014; Hansen et al. 2014; Saavedra et al. 2014; Aggio et al. 2015) from **17 unique samples**. **Five studies** report data from the EYHS (Andersen et al. 2006, Ruiz et al. 2006; Ortega et al. 2008; Rizzo et al. 2008; Kristensen et al. 2010); **6 studies** report data from HELENA (Martinez-Gomez et al. 2010a; Moliner-Urdiales et al. 2010; Ottevaere et al. 2011; Ruiz et al. 2011; Martinez-Gomez et al. 2012; Jimenez-Pavon et al. 2013c); **2 studies** report data from the CoSCIS study (Eiberg et al. 2005; Dencker et al. 2010). Data are reported separately, and participants are only counted once.

[o] Positive associations between Total PA and aerobic fitness were found in the total sample (Eiberg et al. 2005; Andersen et al. 2006; Ruiz et al. 2006; Rizzo et al. 2007; Ruiz et al. 2011; Martinez-Gomez et al. 2012), in boys but not girls (Dencker et al. 2010; Jimenez-Pavon et al. 2013c), and in 9-year olds but not 15-year olds (Kristensen et al. 2010).

[p] Dencker et al. (2010) reported a positive association between VPA and aerobic fitness for boys, but not girls.

[q] Positive associations were reported between MVPA and aerobic fitness in the total sample (Eiberg et al. 2005; Martinez-Gomez et al. 2010a; Ruiz et al. 2011; Ottevaere et al. 2011; Martinez-Gomez et al. 2012) , and in boys but not girls in subdivided samples (Dencker et al. 2010; Jimenez-Pavon et al. 2013b).

[r] From the HELENA cohort, Martinez-Gomez et al. (2010a) and Ottevaere et al. (2011) reported positive associations for MPA and aerobic fitness in total sample, Martinez-Gomez et al. (2012) reported a null association, and Jimenez Pavon et al. (2013c) reported a positive association for boys, not girls. From the Viva la Familia study, Butte et al. (2007b) reported positive associations when controlling for BMI z-score but not %FM.

[s] Total PA was positively associated with standing broad jump and not associated with upper body- and other lower body strength and endurance in boys, and not associated with any muscular fitness outcome in girls (Moliner-Urdiales et al. 2010); No correlation with abdominal muscle endurance (curl-ups) or upper body strength, but high tertiles of total PA had better upper body strength (grip strength) (Hands et al. 2009).

[t] MVPA was positively associated with lower body strength but not upper body strength in one study (Aggio et al. 2015), and not associated with upper and lower body strength in boys and girls, with the exception of a positive association for standing broad jump for boys (Moliner-Urdiales et al. 2010).

[u] The quality of evidence from cross-sectional studies remained as "low" as there were no serious concerns about the quality of studies or reasons to rate-up.

Table A.1.b. Cardiometabolic health and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Cardiometabolic health (e.g., blood pressure, dyslipidaemia, glucose, insulin resistance)
*__Importance__: CRITICAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
The range of mean ages was 5.1 to 17.0 years. Data were collected by RCT, non-randomized intervention trial, cross-sectionally and up to 4 years of follow-up. Cardiometabolic biomarkers assessed were: blood pressure (systolic BP, diastolic BP, mean arterial BP, pre-high BP, high BP, hypertension), blood lipids (TG, HDL, LDL, total cholesterol), insulin sensitivity/resistance (HOMA, HOMA-%S; QUICKI, Matsuda index), fasting insulin and glucose, oral glucose tolerance test results (2-hr plasma glucose, AUC I/$G_{t30\ min}$, AUC I/$G_{t120min}$), HbA1c, RPP, inflammatory markers (CRP, IL-6, TNF-α, C3, C4), artery properties (PWV, carotid intima-media thickness, carotid compliance, Young's elastic modules, stiffness index), ALT, cardiac sympathetic-parasympathetic modulation, homocysteine, liver fat & GGT (γ-glutamyl transferase) and composite cardiometabolic risk scores. All outcomes were measured objectively.								
2 RCTs[a] N = 502	No serious risk of bias Serious risk of bias	No serious inconsistency	Serious indirect-ness[b]	No serious imprecision Serious imprecision	None Outcomes were variably reported Limited to laboratory-based PA	The intervention group had larger reductions in **TGs**, **glucose**, and **cardiometabolic disease risk score** and a greater increase in **HDL** vs the control group. **Systolic BP** and **diastolic BP** were not different between groups (Kriemler et al. 2010).[c] There were no differences in **glucose, HDL**, **TG,** or **systolic BP** or **diastolic BP** between the control and intervention groups 3-yr post-intervention (Meyer et al. 2014).[c] Three reviews examined the effectiveness of high-intensity interval training *(8)*, resistance training *(4)*, and school-based PA programs *(19)* versus no intervention on measures of cardiometabolic health. Within all 3 reviews, there was consistent evidence that interventions were associated with better cardiometabolic outcome measures, however; there was varied precision in effect sizes and few individual trials found statistically significant benefit of physical activity across all cardiometabolic outcomes. Eddolls et al. 2017 *(8)* (13 RCTs; n=1,899): High-intensity interval training was associated with improvements in **systolic and diastolic BP** but only 2 of 5 RCTs reporting BP found these improvements to be statistically significantly different from moderate-intensity training or other control groups. Four RCTs examined effects of high-intensity interval training on **glucose** (4 trials), **total cholesterol** (2 trials), **HDL** (3 trials), **LDL** (1 trial), **TG** (3 trials), and **insulin** (1 trial) and all reported improvements (with 3/4 finding differences to be	MODERATE[d]	9 ESRs Moderate evidence indicates that physical activity is positively associated with cardiometabolic health in children and adolescents. **PAGAC Grade: Moderate** Moderate evidence indicates that physical activity is positively associated with cardiometabolic health in children and adolescents in general; the evidence is strong for plasma TG and insulin. **PAGAC Grade: Moderate**

						statistically significant) following high-intensity training vs. moderate-intensity training (6-12 weeks). Bea et al. 2017 *(4)* (13 RCTs; n=1,134): Few studies found statistically significant positive effects of resistance training versus no resistance training on measures of cardiometabolic health. Pozuelo-Carrascosa et al. 2018 *(19)* (19 RCTs; n=11,988): School-based PA programs were associated with statistically significant improvements in **diastolic BP** (ES = -0.21 [95% CI, -0.42 to -0.01]; p=0.4) and **fasting insulin** (ES = -0.12 [95% CI, -0.42 to -0.04]; p=0.03) compared with no physical activity interventions. There was no improvement in **fasting glucose** (ES = -0.06 [95% CI, -1.28 to 0.08]; p=0.085), **systolic BP** (ES = -0.14 [95% CI, -0.31 to 0.03]; p=0.11), **HDL** (ES =- 0.09 [95% CI, -0.05 to 0.23]; p=0.15); **LDL** (ES = -0.23 [95% CI, -0.52 to 0.07]; p=0.13), **TG** (ES = 0.02 [95% CI, 0.11 to 0.15]; p=0.77); or **TC** (ES = -0.03 [95% CI, -0.37 to 0.31]; p=0.86) when comparing school-based PA interventions versus no PA interventions.		
2 NRT[e] N = 71 **No reviews limited to NRTs identified.**	Serious risk of bias[f]	No serious inconsistency	Serious indirect-ness[g]	No serious imprecision	None	There were significant intervention effects on **systolic BP**, **total cholesterol & fasting glucose** (Aires et al. 2015). Aerobic training had no effect on **total cholesterol**, **HDL** or **TG**. In boys, **LDL** decreased during the control weeks prior to the intervention (Rowland et al. 1996).[h]	VERY LOW[i]	
15 Longitudinal [j] **No reviews including or limited to longitudinal designs identified.**	Serious risk of bias[k]	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	***Meeting/Not Meeting Guidelines:*** Changes in *PA guideline adherence* over 2-yr did not influence incidence of **pre-high BP** or **high-BP** (de Moraes et al. 2015).[l] 1 study showed favourable effect with meeting the PA guidelines on BP (deMoraes et al. 2014). ***Total PA:*** **Systolic BP:** null association (**2/2 studies;** Hallal et al. 2011; Knowles et al. 2013); **Diastolic BP:** associations were favourable (**1/2 studies;** Knowles et al. 2013), or mixed (favourable and null; compared with the *least active tercile,* children in the *most active tercile* of PA at age 12 yr. had lower diastolic BP at age 14; no difference between least active and intermediate terciles; **1/1 studies;** Hallal et al. 2011); **Mean arterial BP:** null association (**2/2 studies;** Hjorth et al. 2014a; Macdonald-Wallis et al. 2017); **TG:** null association (**1/1 studies;** Hjorth et al. 2014a); **HDL cholesterol:** favourable association (**1/1 studies;** Hjorth et al. 2014a); 1/1 showed a null association with Blood Lipids (Telford et al. 2015) **HOMA:** associations were null (**1/1 studies;** Hjorth et al. 2014a), or mixed favourable (in boys but not girls at 4-yr follow-up) and null (2-yr follow-up) (Telford et al. 2009); 1/1 showed favourable association with IR (Peplies et al. 2016); **Cardiometabolic disease risk score:** null association (**1/1 studies;** Hjorth et al. 2014a).	LOW[m]	

						VPA: null associations with **systolic BP** (Carson et al. 2013). ***MVPA:*** **Systolic BP:** null association (**1/1 studies;** Knowles et al. 2013); **Diastolic BP:** null association (**1/1 studies;** Knowles et al. 2013); **Mean arterial BP:** null association (**1/1 studies;** Hjorth et al. 2014a); **TG:** null association (**2/2 studies;** Hjorth et al. 2014a, Chinapaw et al. 2018); **HDL cholesterol:** favourable association (**1/1 studies;** Hjorth et al. 2014a); TC:HDLC ratio and composite cardiometabolic risk 1/1 study showed favourable associations (Chinapaw et al. 2018) **HOMA:** null association (**3/3studies;** Hjorth et al. 2014a, Henderson et al. 2016, Chinapaw et al. 2018); **Cardiometabolic disease risk score:** null association (**1/1 studies;** Hjorth et al. 2014a). Liver fat & GGT: favourable association (1/1 Anderson et al. 2016) ***MPA:*** null associations with **systolic BP** (Carson et al. 2013). TG and HOMA-IR favourable association (1/1 Skrede et al.2017) ***LPA:*** null associations with **systolic BP** (Carson et al. 2013).		
47 Cross-sectional[n] N = 27,571	Serious risk of bias[o]	No serious inconsistency	No serious indirect-ness	No serious imprecision	Exposure /outcome gradient[p]	Verswijveren et al. 2018 *(23)*: (4 cross-sectional studies; n=4,294): No included studies examined associations between patterns of LPA, MPA, or VPA and **blood lipids**. Two studies found no evidence of an association between MVPA and MPA and measures of **glucose** metabolism. No evidence of an association between PA bouts and **systolic BP, diastolic BP, large artery compliance, and small artery compliance** was found in 3 studies. Blood Pressure (Systolic BP, Diastolic BP, Mean Arterial BP): ***Meeting/Not Meeting Guidelines:*** **1 study** found that *meeting PA guidelines*[q] was associated with reduced odds of having **high BP**, but no difference in odds of **pre-high BP** or **risk of high** BP (de Moraes et al. 2015). **1 study** found that *meeting PA guidelines*[q] was associated with lower **systolic BP** and **diastolic BP** (Janssen et al. 2013). **1 study** found that *meeting 10,000 steps/day* did not impact the odds of having **high BP** (Schofield et al. 2009). ***Total PA:*** **Hypertension:** favourable dose-response gradient (**1/1 studies;** Mark and Janssen 2008). **Diastolic hypertension:** favourable association (**1/1 studies;** Knowles et al. 2013). **Systolic hypertension:** no association (**1/1 studies;** Knowles et al. 2013). **Systolic BP:** associations were favourable (**3/8 studies;** Andersen et al. 2006; Ekelund et al. 2006; Mark and Janssen 2008), null (**4/8 studies;** Leary et al. 2008; Owen et al. 2010; Knowles et al. 2013; Chaput et al. 2013), or mixed (favourable and null; **1/8 studies;** Hurtig-Wennlof et al. 2007). Mark and Janssen (2008) found a favourable dose-response gradient. **Diastolic BP:** associations were favourable (**6/8 studies;** Andersen et al. 2006; Ekelund et al. 2006; Mark and Janssen 2008; Owen et al. 2010; Knowles et al. 2013; Chaput et al. 2013), null (**1/8 studies;** Leary et al. 2008),	VERY LOW[t]	

						or mixed (favourable and null; **1/8 studies;** Hurtig-Wennlof et al. 2007). Mark and Janssen (2008) found an inverse dose-response gradient. **Mean arterial BP:** null association (**1/1 studies;** Hjorth et al. 2014a). ***VPA:*** **High-normal systolic BP %:** was greatest in the lowest tertile of *VPA* (**1/1 studies;** Hay et al. 2012). **BP Z-score:** no association (**1/1 studies;** Stabelini Neto et al. 2014). ***MVPA:*** **Hypertension:** the likelihood of **hypertension** decreased in a curvilinear manner with *MVPA* (**1/1 studies;** Hjorth et al. 2014a). **BP Z-score:** favourable association (**1/1 studies;** Stabelini Neto et al. 2014). **Systolic BP:** associations were favourable (**4/9 studies;** Holman et al. 2011; Colley et al. 2012; Mendoza et al. 2012; Carson et al. 2013); null (**4/9 studies;** Leary et al. 2008; Hearst et al. 2012; Knowles et al. 2013; Chaput et al. 2013); or mixed (favourable and null; **1/9 studies;** Hurtig-Wennlof et al. 2007). **1 study** found a favourable association between *sporadic MVPA* and **systolic BP** (Holman et al. 2011). **Diastolic BP:** associations were favourable (**1/8 studies;** Chaput et al. 2013); null (**5/8 studies;** Leary et al. 2008; Colley et al. 2012; Mendoza et al. 2012; Hearst et al. 2012; Carson et al. 2013);or mixed (favourable and null; **2/8 studies;** Hurtig-Wennlof et al. 2007; Knowles et al. 2013). **Mean arterial BP:** null association (**1/1 studies;** Hjorth et al. 2014a). ***MPA:*** **BP Z-score:** favourable association (**1/1 studies;** Stabelini Neto et al. 2014). **Systolic BP:** null association (**1/1 studies;** Hay et al. 2012). ***LPA:*** **BP Z-score:** favourable association (**1/1 studies;** Stabelini Neto et al. 2014). **Systolic BP:** null associations (**2/2 studies;** Hay et al. 2012; Carson et al. 2013). **Diastolic BP:** favourable association (**1/1 studies;** Carson et al. 2013). <u>Triglycerides (TG):</u> ***Meeting/Not Meeting Guidelines:*** *meeting PA guidelines*[q] had a null association with fasting **TGs** (**1/1 studies;** Janssen et al. 2013). ***Total PA:*** associations were favourable (**3/7 studies;** Andersen et al. 2006; Ekelund et al. 2006; Owen et al. 2010), null (**2/7 studies;** Chaput et al. 2013; Hjorth et al. 2014a), or mixed (favourable and null; **2/7 studies;** Wennlof et al. 2005; Hurtig-Wennlof et al. 2007). ***VPA:*** null association (**1/1 studies;** Stabelini Neto et al. 2014). ***MVPA:*** associations were favourable (**1/7 studies;** LeBlanc and Janssen 2010) or null (**6/7 studies;** Hurtig-Wennlof et al. 2007; Mendoza et al. 2012; Carson et al. 2013; Chaput et al. 2013; Hjorth et al. 2014a; Stabelini Neto et al. 2014). ***MPA:*** null association (**1/1 studies;** Stabelini Neto et al. 2014).		

						LPA: null associations (**2/2 studies;** Carson et al. 2013; Stabelini Neto et al. 2014). <u>Cholesterol:</u> ***Meeting/Not Meeting Guidelines:*** **HDL cholesterol:** *meeting PA guidelines*[q] was favourably associated with HDL (**1/1 studies;** Janssen et al. 2013). ***Total PA:*** **Total cholesterol:** associations were favourable (**1/2 studies;** Andersen et al. 2006), or mixed (favourable and null; **1/2 studies;** Hurtig-Wennlof et al. 2007). **HDL cholesterol:** associations were favourable (**2/5 studies;** Chaput et al. 2013; Hjorth et al. 2014a) or null (**3/5 studies;** Andersen et al. 2006; Hurtig-Wennlof et al. 2007; Owen et al. 2010). ***VPA:*** **HDL cholesterol:** null associations (**1/1 studies;** Stabelini Neto et al. 2014). ***MVPA:*** **"High risk" cholesterol:** increased *MVPA* was associated with reduced odds (**1/1 studies;** LeBlanc and Janssen 2010). **Total cholesterol:** associations were favourable (**1/3 studies;** Hurtig-Wennlof et al. 2007) or null (**2/3 studies;** Hurtig-Wennlof et al. 2007; Mendoza et al. 2012). **HDL cholesterol:** associations were favourable (**3/7 studies;** Mendoza et al. 2012; Chaput et al. 2013; Hjorth et al. 2014a) or null (**4/7 studies;** Hurtig-Wennlof et al. 2007; Hearst et al. 2012; Carson et al. 2013; Stabelini Neto et al. 2014). **Non-HDL cholesterol:** *MVPA* (total, bouts, sporadic) was favourably associated (**1/1 studies;** Holman et al. 2011). **LDL cholesterol:** null associations (**3/3 studies;** LeBlanc and Janssen 2010; Mendoza et al. 2012; Carson et al. 2013). ***MPA:*** **HDL cholesterol:** null associations (**1/1 studies;** Stabelini Neto et al. 2014). ***LPA:*** **HDL cholesterol:** associations were null (**1/2 studies;** Stabelini Neto et al. 2014) or mixed (favourable and null; **1/2 studies;** Carson et al. 2013). <u>Insulin Resistance:</u> ***Meeting/Not Meeting Guidelines:*** **HOMA:** *meeting PA guidelines*[q] had no impact on **HOMA** (**1/1 studies;** Janssen et al. 2013). ***Total PA:***		

						HOMA: associations were favourable (**5/6 studies;** Andersen et al. 2006; Rizzo et al. 2008; Sardinha et al. 2008; Owen et al. 2010; Hjorth et al. 2014a), or null (**1/6 studies;** Jimenez-Pavon et al. 2013c). **QUICKI:** null association (**1/1 studies;** Jimenez-Pavon et al. 2013c). ***VPA:*** **HOMA:** associations were favourable (**1/2 studies;** Rizzo et al. 2008) or null (**1/2 studies;** Jimenez-Pavon et al. 2013c). **QUICKI:** null association (**1/1 studies;** Jimenez-Pavon et al. 2013c). ***MVPA:*** **HOMA:** associations were favourable (**4/7 studies;** Rizzo et al. 2008; Sardinha et al. 2008; Hjorth et al. 2014a; Henderson et al. 2014), null (**3/7 studies;** Henderson et al. 2012; Carson et al. 2013; Jimenez-Pavon et al. 2013c). **QUICKI:** null association (**1/1 studies;** Jimenez-Pavon et al. 2013c). **Matsuda score:** null association (**1/1 studies;** Henderson et al. 2012). **HOMA-%S:** favourable association (**1/1 studies;** Carson et al. 2013). **OGTT results (**AUC I/G_{t30min} or AUC $I/G_{t120min}$): null associations (**1/1 studies;** Henderson et al. 2014). ***MPA:*** **HOMA:** associations were favourable (**1/2 studies;** Rizzo et al. 2008), or null (**1/2 studies;** Jimenez-Pavon et al. 2013c). **QUICKI:** null association (**1/1 studies;** Jimenez-Pavon et al. 2013c). ***LPA:*** **HOMA:** associations were null (**4/4 studies;** Rizzo et al. 2008; Sardinha et al. 2008; Carson et al. 2013; Jimenez-Pavon et al. 2013c). **QUICKI:** null association (**1/1 studies;** Jimenez-Pavon et al. 2013c). **HOMA-%S:** null association (**1/1 studies;** Carson et al. 2013). <u>Fasting Insulin</u> ***Total PA:*** associations were favourable (**8/11 studies;** Brage et al. 2004a; Andersen et al. 2006; Ekelund et al. 2006; Butte et al. 2007b; Rizzo et al. 2008; Sardinha et al. 2008; Owen et al. 2010; Jimenez-Pavon et al. 2012), null (**1/11 studies;** Jimenez-Pavon et al. 2013c), or mixed (favourable and null) (**2/11 studies;** Wennlof et al. 2005; Hurtig-Wennlof et al. 2007). ***VPA:*** associations were favourable (**2/4 studies;** Rizzo et al. 2008; Jimenez-Pavon et al. 2012), or null (**2/4 studies;** Butte et al. 2007b; Jimenez-Pavon et al. 2013c). ***MVPA:*** associations were favourable (**5/9 studies;** Rizzo et al. 2008; Sardinha et al. 2008; Henderson et al. 2012; Jimenez-Pavon et al. 2012; Carson et al. 2013), null (**2/9 studies;** Mendoza et al. 2012; Jimenez-Pavon et al. 2013c), or mixed (favourable and null **2/9 studies;** Hurtig-Wennlof et al. 2007; Butte et al. 2007b). Butte et al. 2007b found that *5-* but not *10-min bouts of MVPA* were favourably associated with fasting insulin.		

						MPA: associations were favourable (**1/3 studies;** Butte et al. 2007b), null (**1/3 studies;** Jimenez-Pavon et al. 2013c), or mixed (favourable and null; **1/3 studies;** Rizzo et al. 2008). ***LPA:*** associations were favourable (**1/5 studies;** Butte et al. 2007b), or null (**4/5 studies;** Rizzo et al. 2008; Sardinha et al. 2008; Carson et al. 2013; Jimenez-Pavon et al. 2013c). <u>Fasting Glucose</u> ***Total PA:*** associations were favourable (**3/7 studies;** Andersen et al. 2006; Ekelund et al. 2006; Rizzo et al. 2008), null (**3/7 studies;** Brage et al. 2004a; Chaput et al. 2013; Jimenez-Pavon et al. 2013c), or mixed (favourable and null; **1/7 studies;** Hurtig-Wennlof et al. 2007). ***VPA:*** associations were favourable (**1/3 studies;** Rizzo et al. 2008), or null (**2/3 studies;** Jimenez-Pavon et al. 2013c; Stabelini Neto et al. 2014). ***MVPA:*** associations were favourable (**1/8 studies;** Rizzo et al. 2008), null (**6/8 studies;** Owen et al. 2010; Mendoza et al. 2012; Carson et al. 2013; Chaput et al. 2013; Jimenez-Pavon et al. 2013c; Stabelini Neto et al. 2014), or mixed (favourable and null) (**1/8 studies;** Hurtig-Wennlof et al. 2007). **1/1 studies** found no association between *MVPA* and **2-hr plasma glucose** (Carson et al. 2013). ***MPA:*** associations were favourable (**1/3 studies;** Rizzo et al. 2008), or null (**2/3 studies;** Jimenez-Pavon et al. 2013c; Stabelini Neto et al. 2014). ***LPA:*** associations were null (**4/4 studies;** Rizzo et al. 2008; Carson et al. 2013; Jimenez-Pavon et al. 2013c; Stabelini Neto et al. 2014). **1/1 studies** found no association with **2-hr plasma glucose** (Carson et al. 2013). <u>HbA1c</u> ***Total PA:*** null association (**1/1 studies;** Owen et al. 2010). ***MVPA:*** null association (**1/1 studies;** Mendoza et al. 2012). <u>Inflammatory Markers (CRP, TNF-α, IL-6, C3, C4)</u> ***Meeting/Not Meeting Guidelines:*** null association between *meeting PA guidelines*[r] and **CRP** (**1/1 studies;** Loprinzi et al. 2013). ***Total PA:*** **CRP:** null associations (**3/3 studies;** Owen et al. 2010; Martinez-Gomez et al. 2012; Loprinzi et al. 2013). **IL-6, TNF-α, C3** or **C4:** null associations (**1/1 studies;** Martinez-Gomez et al. 2012). ***VPA:*** **CRP**, **IL-6, TNF-α, C3** or **C4:** null associations (**1/1 studies;** Martinez-Gomez et al. 2012). ***MVPA:*** **CRP:** associations were favourable [increasing quartiles of *MVPA (total, bouts, sporadic)* were associated with reduced **CRP** (**1/5 studies;** Holman et al. 2011)], or null (**4/5 studies;** Mendoza et al. 2012; Martinez-Gomez et al.		

						2012; Carson et al. 2013; Loprinzi et al. 2013). *Bouts of MVPA* did not differ across CRP quartiles (**1/1 studies;** Loprinzi et al. 2013). **IL-6, TNF-α, C3** or **C4:** null associations (**1/1 studies;** Martinez-Gomez et al. 2012). ***MPA:*** **CRP**, **IL-6, TNF-α, C3** or **C4:** null associations (**1/1 studies;** Martinez-Gomez et al. 2012). ***LPA:*** **CRP:** null associations (**1/1 studies;** Carson et al. 2013). <u>Alanine amino transferase:</u> ***Total PA*** did not differ by **ALT** status, and % of awake time spent in ***VPA***, ***MPA*** or ***LPA*** did not differ by **ALT** status (**1/1 studies;** Quiros-Tejeira et al. 2007). <u>Artery properties:</u> ***Total PA:*** negative association with **PWV** (**1/1 studies;** Sakuragi et al. 2009); null association with carotid **IMT** (**1/1 studies;** Lamotte et al. 2013). ***VPA:*** null associations with **IMT, carotid compliance, Young's elastic modules,** or **stiffness index** (**1/1 studies;** Ried-Larsen et al. 2013). ***MVPA:*** null associations with **IMT, carotid compliance, Young's elastic modules,** or **stiffness index** (**1/1 studies;** Ried-Larsen et al. 2013). <u>Rate Pressure Product:</u> ***Total PA, VPA***, or ***MPA****:* null associations (**1/1 studies;** Mota et al. 2012). <u>Cardiac sympathetic/parasympathetic modulation:</u> ***MVPA:*** positively associated with one index of **cardiac parasympathetic modulation** (root mean square of successive differences) but not associated with another (high frequency power), and negatively associated with **sympathetic-parasympathetic balance** (**1/1 studies;** Gutin et al. 2005b). <u>Homocysteine</u> ***Total PA, MVPA, VPA*** or ***MPA:*** null associations (**1/1 studies;** Ruiz et al. 2007). <u>Composite Cardiometabolic Disease Risk Score</u> ***Meeting/Not Meeting Guidelines:*** *meeting PA guidelines*[q,s] was associated with reduced **cardiometabolic risk score** (**2/2 studies;** Mendoza et al. 2012; Janssen et al. 2013); achieving 10,000 steps/day was not associated with different odds of having any number of **cardiovascular risk factors** (**1/1 studies;** Schofield et al. 2009). ***Total PA:*** associations were favourable (**3/7 studies;** Brage et al. 2004b; Ekelund et al. 2009; Jimenez-Pavon et al. 2013b), or null (**4/7 studies;** Rizzo et al. 2007; Schofield et al. 2009; Moreira et al. 2011; Hjorth et al. 2014a). **1/1**		

						studies found that *lower mean cadence values* were associated with larger accrued **numbers of risk factors** (Barreira et al. 2013). ***VPA:*** associations were favourable (**1/2 studies;** Jimenez-Pavon et al. 2013b), or null (**1/2 studies;** Stabelini Neto et al. 2014). ***MVPA:*** associations were favourable (**6/8 studies;** Ekelund et al. 2006; Nguyen et al. 2010; Holman et al. 2011; Carson and Janssen 2011; Jimenez-Pavon et al. 2013b; Stabelini Neto et al. 2014), null (**1/8 studies;** Hjorth et al. 2014a), or mixed (favourable and null; **1/8 studies;** Rey-Lopez et al. 2013). **1 study** found that the odds of a high cardiometabolic risk score decreased in a graded dose-response manner across quartiles of *sporadic MVPA* or *bout MVPA,* with similar associations for some individual cardiometabolic disease risk factors (non-HDL cholesterol, CRP, systolic BP) (Holman et al. 2011). ***MPA:*** favourable associations (**2/2 studies;** Jimenez-Pavon et al. 2013b; Stabelini Neto et al. 2014). ***LPA:*** null association (**1/1 studies;** Stabelini Neto et al. 2014**).**		

Abbreviations: ALT = alanine amino transferase; AUC I/G_{t30min} and AUC I/$G_{t120min}$ = area under the curve of the ratio of insulin to glucose at 30 and 120 min post-oral glucose tolerance test; BP = blood pressure; C3 and C4 = complement factors 3 and 4; CRP = C-reactive protein; ES = effect size; HbA1c = glycosylated haemoglobin; HDL = high density lipoprotein cholesterol; HOMA = homeostatic model assessment insulin resistance; HOMA-%S = insulin sensitivity; IL-6 = interleukin-6; IMT = intima media thickness; LDL = low density lipoprotein cholesterol; LPA = light intensity physical activity; MPA = moderate intensity physical activity; MVPA = moderate-to-vigorous physical activity; OGTT = oral glucose tolerance test; PA = physical activity; PWV = pulse wave velocity; QUICKI = quantitative insulin sensitivity check index; RPP = rate-pressure product; sporadic MVPA = <5 consecutive minutes of moderate-to-vigorous physical activity; TG = triglycerides; TNF-α = tumour necrosis factor alpha; VPA = vigorous intensity physical activity.

[*]As determined by WHO

[a] Includes **2 studies** (Kriemler et al. 2010; Meyer et al. 2014) from one cluster randomized controlled trial ("Kinder-und Jugendsportstudie''; KISS). Results are reported separately, and participants are only counted once.

[b] Serious indirectness. Indirect comparisons: different durations and intensities of PA were not compared.

[c] MVPA (but not total PA) was significantly greater in the intervention vs control group at post-intervention (post 9-month intervention group difference of ~11 min/day) (Kriemler et al. 2010); there was a trend toward higher levels of total PA (but not MVPA) in the intervention vs control group at 3-yr follow-up (Cohen's d = 0.35, p=0.06; not significant) (Meyer et al. 2014).

[d] The quality of the evidence from the randomized study was downgraded from "high" to "moderate" due to serious indirectness of the interventions and the comparisons being assessed.

[e] Includes **1 non-randomized intervention study** (Rowland et al. 1996).

[f] Serious risk of bias. PA outside of prescribed intervention was not controlled (e.g. sports teams/recreational programs) or measured, and it is unclear whether activity external to the intervention changed over the course of the study and/or may have influenced the results. Dietary analysis in a subset of non-randomly selected subjects (n=11) showed a decrease in caloric intake in the intervention vs control period (potentially important confounder) (Rowland et al. 1996).

[g] Serious indirectness. Indirect comparisons: different durations and intensities of physical activity were not compared.

[h] Training intensity estimated by HR monitor; mean HR during the training sessions was 174.4, SD = 10 bpm (Rowland et al. 1996).

[i] The quality of the evidence from the non-randomized study was downgraded from "low" to "very low" due to: (1) serious risk of bias in the included study that diminished the level of confidence in the observed effects, and (2) serious indirectness of comparisons.

[j] Includes **7 longitudinal studies** (Telford et al. 2009; Hallal et al. 2011; Telford et al. 2012a; Knowles et al. 2013; Hjorth et al. 2014a; Carson et al. 2014; de Moraes et al. 2015) from **6 unique samples**. **Two studies** reported data from the LOOK study (Telford et al. 2009; Telford et al. 2012a); results are reported separately, and participants are only counted once.

[k] Serious risk of bias. Participants were divided into intervention (community-based healthy lifestyle promotion) and control (no treatment) groups, but possible group-effects were not considered, and all analysis was reported pooled across groups (de Moraes et al. 2015). Sixty-eight percent of participants did not provide valid baseline accelerometer data or did not have complete cardiometabolic risk factor data at baseline and/or follow-up; reasons for missing data were not reported; those lost to follow-up were older, heaver and displayed lower cardiorespiratory fitness than those included at follow-up (Carson et al. 2014). Those included in analysis represent only ~10% of the total cohort (Hallal et al. 2011).

[l] Cut-point for "meeting" PA guidelines was ≥60 min MVPA/day (de Moraes et al. 2015).

[m] The quality of the evidence from longitudinal studies was not upgraded from "low" to "moderate" due to serious risk of bias in three studies that diminished the level of confidence in the observed effects.

[n] Includes **47 cross-sectional studies** (Brage et al. 2004a; Brage et al. 2004b; Wennlof et al. 2005; Gutin et al. 2005b; Andersen et al. 2006; Ekelund et al. 2006; Hurtig-Wennlof et al. 2007; Rizzo et al. 2007; Ruiz et al. 2007; Quiros-Tejeira et al. 2007; Butte et al. 2007b; Rizzo et al. 2008; Sardinha et al. 2008; Leary et al. 2008; Mark and Janssen 2008; Sakuragi et al. 2009; Ekelund et al. 2009; Schofield et al. 2009; Owen et al. 2010; LeBlanc and Janssen 2010; Nguyen et al. 2010; Holman et al. 2011; Carson and Janssen 2011; Moreira et al. 2011; Hay et al. 2012; Mota et al. 2012; Colley et al. 2012; Henderson et al. 2012; Mendoza et al. 2012; Jimenez-Pavon et al. 2012; Martinez-Gomez et al. 2012; Hearst et al. 2012; Barreira et al. 2013; Rey-Lopez et al. 2013; Carson et al. 2013; Janssen et al. 2013; Lamotte et al. 2013; Knowles et al. 2013; Chaput et al. 2013; Ried-Larsen et al. 2013; Loprinzi et al. 2013; Jimenez-Pavon et al. 2013b; Jimenez-Pavon et al. 2013c; Hjorth et al. 2014a; Stabelini Neto et al. 2014; Henderson et al. 2014; de Moraes et al. 2015) from **20 unique samples**. **Two studies** reported data from the CHMS (Colley et al. 2012; Janssen et al. 2013); **12 studies** reported data from the EYHS (Brage et al. 2004a; Brage et al. 2004b; Wennlof et al. 2005; Andersen et al. 2006; Ekelund et al. 2006; Hurtig-Wennlof et al. 2007; Rizzo et al. 2007; Ruiz et al. 2007; Rizzo et al. 2008; Sardinha et al. 2008; Ekelund et al. 2009; Ried-Larsen et al. 2013); **5 studies** reported data from

HELENA (Jimenez-Pavon et al. 2012; Martinez-Gomez et al. 2012; Rey-Lopez et al. 2013; Lamotte et al. 2013; Jimenez-Pavon et al. 2013c); **2 studies** reported data from IDEFICS (Jimenez-Pavon et al. 2013b; de Moraes et al. 2015); **8 studies** reported data from NHANES (Mark and Janssen 2008; LeBlanc and Janssen 2010; Holman et al. 2011; Carson and Janssen 2011; Mendoza et al. 2012; Barreira et al. 2013; Carson et al. 2013; Loprinzi et al. 2013); **3 studies** reported data from QUALITY (Henderson et al. 2012; Chaput et al. 2013; Henderson et al. 2014); **2 studies** reported data from Viva la Familia (Quiros-Tejeira et al. 2007; Butte et al. 2007b); results are reported separately and participants are only counted once.

[o] Serious risk of bias. Participants were divided into intervention (community-based healthy lifestyle promotion) and control (no treatment) groups, but possible group-effects were not considered, and all analysis was reported pooled across groups (de Moraes et al. 2015). Many studies had a large amount of missing data, or did not report sufficient information to determine the proportion of missing data (Gutin et al. 2005b; Andersen et al. 2006; Hurtig-Wennlof et al. 2007; Rizzo et al. 2007; Rizzo et al. 2008; Mark and Janssen 2008; Ekelund et al. 2009; LeBlanc and Janssen 2010; Holman et al. 2011; Carson and Janssen 2011; Mota et al. 2012; Mendoza et al. 2012; Carson et al. 2013; Janssen et al. 2013; Ried-Larsen et al. 2013; Jimenez-Pavon et al. 2013b; Stabelini Neto et al. 2014). Possible detection bias as participants were retained if they provided PA data for at least 1-7 days; 68% provided at least 5 days of PA data and at 32% provided 1-4 days; PA levels were slightly higher in those with fewer days of PA data; MVPA and LPA were recorded but not reported (Owen et al. 2010). Participants with missing data differed from those included in the analysis on some outcome measures (Andersen et al. 2006; Jimenez-Pavon et al. 2013c). Potential failure to adjust for relevant confounders (Barreira et al. 2013). No information provided regarding criteria for valid exposure measurement; possible detection bias (Quiros-Tejeira et al. 2007). Possible selective reporting bias (systolic BP reported in absence of diastolic BP); not possible to discern which potentially important confounders were included in the analyses (Hay et al. 2012). Possible detection bias; participants were excluded from the study if they did not wear the pedometer for >4 hours in total over the full 4 days of data collection (Schofield et al. 2009).

[p] Exposure/outcome gradients were observed in **4 studies** (Andersen et al. 2006; Mark and Janssen 2008; Holman et al. 2011; Hay et al. 2012) from **3 unique samples**.

[q] Cut-point for "meeting" PA guidelines was ≥ 60 min MVPA/day (Janssen et al. 2013; de Moraes et al. 2015).

[r] Cut-point for "meeting" PA guidelines was ≥ 60 min of at least moderate intensity PA, daily (1 min bouts) (Loprinzi et al. 2013).

[s] Cut-point for "meeting" PA guidelines was ≥ 60 min MVPA/day on 5 of 7 days (Mendoza et al. 2012).

[t] The quality of evidence from cross-sectional studies was downgraded from "low" to "very low" due to serious risk of bias in 24 studies that diminished the level of confidence in the observed effects.

Table A.1.c. Bone health and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Bone health
***Importance**: CRITICAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
The range of mean ages was 5.2 to 17.7 years. Data were collected by RCT, cross-sectionally, and up to 12 years of follow-up. Measures included: BMD, BMC, scanned area, cross-sectional area, total skeletal area, section modulus, bone stress index, femur and tibia bone strength index, strength-strain index, polar moment of inertia, cross-sectional moment of inertia, periosteal and endosteal circumference, cortical thickness, cortical BMC, cortical bone area, BMD ratios (femoral neck to trochanter, femoral neck to intertrochanter, trochanter to intertrochanter). All outcomes were measured objectively by DXA or peripheral quantitative CT.								
2 RCTs[a] N = 73 **No eligible reviews identified.**	No serious risk of bias	No serious inconsistency	Serious indirect-ness[b]	No serious imprecision	None	In both groups, **BMD** increased more during periods of physical training than during periods of no physical training (Gutin et al. 1999).	MODERATE[c]	10 ESRs Strong evidence demonstrates that children and youth who are more physically active than their peers have higher bone mass, improved bone structure, and greater bone strength. **PAGAC Grade: Strong**.
7 Longitudinal[d] N = 948 **No eligible reviews identified.**	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	*Total PA* **1 study** reported that baseline *total PA* predicted follow-up **BMC** at the **hip, trochanter, spine** and **whole body** in *boys* and at the **trochanter** and **whole body** in *girls* (data not shown). **Total PA** explained 1-2% of the variability in **BMC** (Janz et al. 2006). Children who maintained **high levels of PA** over the 3-yr period (≥50th percentile) accrued, on average, 14% more **trochanteric BMC** and 5% more **whole-body BMC** relative to peers maintaining **low levels of PA** (<50th percentile) (Janz et al. 2006). **1 study** found that spending a higher proportion of total PA in MPA-VPA relative to LPA was favourably associated with **BMC, BMD** and **bone area** (Heidemann et al. 2013). *VPA* **Hip** and **spine BMC:** mixed (favourable and null) associations (**2/2 studies;** Janz et al. 2014a; Francis et al. 2014). *MVPA*	MODERATE[e]	

						Whole body, spine and **hip BMC:** mixed (favourable and null) associations (**3/3 studies;** Janz et al. 2010; Francis et al. 2014; Janz et al. 2014b); **Hip BMD:** mixed (favourable and null) associations (**1/1 studies;** Janz et al. 2014b). **Femoral neck cross-sectional area** and **section modulus:** mixed (favourable and null) associations (**2/2 studies;** Janz et al. 2007; Janz et al. 2014b); **Measures of bone strength** (**bone stress index** and **polar moment of inertia**): mixed (favourable and null) associations (**1/1 studies;** Janz et al. 2014b).		
14 Cross-sectional[f] N = 6,520 **No eligible reviews identified.**	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	*Meeting/Not Meeting Guidelines (≥60 min/day MVPA)* **1 study** reported that meeting guidelines had no association with **BMC** (whole body, hip, lumbar spine, trochanter, intertrochanter, femoral) (Gracia-Marco et al. 2011a). **1 study** reported that meeting guidelines had mixed favourable, null, and unfavourable associations with **BMC** of at least 1 anatomical region (**whole body, upper limb, lower limb)** (Gracia-Marco et al. 2011b). **1 study** reported that meeting guidelines had mixed favourable (girls) and null (boys) associations (**lumbar spine**) or null associations (**whole body, hip, trochanter, intertrochanter** or **femoral neck**) with **BMD** (Gracia-Marco et al. 2011a). *Total PA* *Total PA and BMC:* **Whole body BMC:** associations were favourable (**1/2 studies;** Gracia-Marco et al. 2012), or mixed (favourable in boys, null in girls; **1/2 studies**; Janz et al. 2001); **Hip BMC:** favourable associations (**2/2 studies;** Janz et al. 2001; Gracia-Marco et al. 2012); **Spine BMC:** favourable association (**1/1 studies;** Janz et al. 2001). *Total PA and BMD:* **Whole body BMD:** null associations (**1/1 studies;** Janz et al. 2001); **Hip BMD:** favourable associations (**1/1 studies;** Janz et al. 2001); **Spine BMD:** mixed (null in boys, favourable in girls) associations (**1/1 studies;** Janz et al. 2001); **Calcaneal** and **distal forearm BMD:** favourable associations (**1/1 studies;** Hasselstrom et al. 2007). *Total PA and Area and strength:* **Total skeletal area:** favourable associations (**1/1 studies;** Janz et al. 2001). **Femur** and **tibia strength index/strength-strain index:** mixed (favourable and null) associations (**1/1 studies;** Farr et al. 2011). *VPA* *VPA and BMC:* **Whole body BMC:** associations were favourable (**1/1 studies;** Tobias et al. 2007) or mixed (favourable in boys, null in girls; **1/1 studies;** Janz et al. 2001); **Whole body BMC adjusted for bone area:** null associations (**1/1 studies;** Tobias et al. 2007);	LOW[g]	

						Hip BMC: favourable associations (**2/2 studies;** Janz et al. 2001 and 2014a); **Spine BMC:** associations were favourable (**2/3 studies;** Janz et al. 2001 and 2014a) or null (**1/3 studies;** Francis et al. 2014). **Upper limb *absolute* BMC:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Lower limb *absolute* BMC:** null associations (**1/1 studies;** Tobias et al. 2007); **Upper** and **lower limb *areal* BMC:** null associations (**1/1 studies;** Tobias et al. 2007); **Cortical BMC:** favourable associations (**1/1 studies**; Sayers et al. 2011). *VPA and BMD:* **Whole body BMD:** associations were favourable (**1/2 studies;** Tobias et al. 2007) or null (**1/2 studies**; Janz et al. 2001); **Whole body *areal* BMD:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Hip BMD:** favourable associations (**1/1 studies;** Janz et al. 2001); **Spine BMD:** mixed (null in boys, favourable in girls) associations (**1/1 studies;** Janz et al. 2001); **Calcaneal** and **distal forearm:** favourable associations (**1/1 studies;** Hasselstrom et al. 2007); **Upper limb *absolute*** or ***areal* BMD:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Lower limb *absolute*** or ***areal* BMD:** null associations (**1/1 studies;** Tobias et al. 2007); **Femoral neck, trochanter** and **intertrochanter BMD:** favourable associations (**1/1 studies;** Cardadeiro et al. 2012); **Cortical BMD:** unfavourable associations (**1/1 studies;** Sayers et al. 2011); **BMD ratios:** null (femoral neck to intertrochanter, trochanter to intertrochanter) or mixed (null in boys, negative in girls; femoral neck to intertrochanter) associations (**1/1 studies;** Cardadeiro et al. 2012). *VPA and Area and strength:* **Total skeletal area:** favourable association (**1/1 studies;** Janz et al. 2001); **Cortical bone area:** favourable association (**1/1 studies;** Sayers et al. 2011); **Periosteal circumference of the tibia:** positive association (**1/1 studies;** Sayers et al. 2011); **Endosteal circumference of the tibia:** negative association (**1/1 studies;** Sayers et al. 2011); **Cross-sectional area** and **section modulus** of **narrow neck, intertrochantic** and **shaft** regions of **femur:** favourable associations (**1/1 studies;** Janz et al. 2004). <u>*MVPA*</u> *MVPA and BMC:* **Whole body BMC:** mixed (favourable and null) associations (**1/1 studies;** Janz et al. 2008); **Hip BMC:** favourable associations (**2/2 studies;** Janz et al. 2008; Janz et al. 2014a); **Spine BMC:** mixed (favourable in boys, null in girls) associations (**2/3 studies;** Janz et al. 2008; Janz et al. 2014a), or null associations (**1/3 study;** Francis et al. 2014).		

						MVPA and BMD: **Femoral neck, trochanter** and **intertrochanter BMD:** null associations (**1/1 studies;** Cardadeiro et al. 2012); **BMD ratios:** null (femoral neck to trochanter, trochanter to intertrochanter) or mixed (null in boys, positive in girls; femoral neck to intertrochanter) associations (**1/1 studies;** Cardadeiro et al. 2012). <u>*MPA*</u> *MPA and BMC:* **Whole body *absolute* or *areal* BMC:** favourable associations (**1 /1 studies;** Tobias et al. 2007); **Upper limb *absolute* or *areal* BMC:** null associations (**1/1 studies;** Tobias et al. 2007); **Lower limb *absolute* or *areal* BMC:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Cortical BMC:** null associations (**1/1 studies**; Sayers et al. 2011). *MPA and BMD:* **Whole body *absolute* or *areal* BMD:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Upper limb *absolute* or *areal* BMD:** null associations (**1/1 studies;** Tobias et al. 2007); **Lower limb *absolute* or *areal* BMD:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Femoral neck, trochanter, intertrochanter BMD:** null associations (**1/1 studies;** Cardadeiro et al. 2012); **Cortical BMD:** null associations (**1/1 studies;** Sayers et al. 2011); **BMD ratios:** null (femoral neck to trochanter, femoral neck to intertrochanter, trochanter to intertrochanter; **1/1 studies;** Cardadeiro et al. 2012). *MPA and Area and strength:* **Cortical bone area:** favourable association (**1/1 studies;** Sayers et al. 2011); **Periosteal** and **endosteal circumference of the tibia:** null associations (**1/1 studies;** Sayers et al. 2011); **Cross-sectional area** of **femoral shaft:** favourable associations (**1/1 studies;** Janz et al. 2004); **Section modulus** of **femoral shaft:** mixed (null in boys, favourable in girls) associations (**1/1 studies;** Janz et al. 2004); **Cross-sectional area** and **section modulus** of **narrow neck** and **intertrochantic** regions of **femur:** mixed (null in boys, favourable in girls) associations (**1/1 studies;** Janz et al. 2004). <u>*LPA*</u> *LPA and BMC:* **Whole body *absolute* or *areal* BMC:** null associations (**1/1 studies**; Tobias et al. 2007); **Upper** or **lower limb *absolute* BMC:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Upper** or **lower limb *areal* BMC:** null associations (**1/1 studies;** Tobias et al. 2007); **Cortical BMC:** null associations (**1/1 studies**; Sayers et al. 2011).		

						LPA and BMD: **Whole body BMD:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Whole body *areal* BMD:** null associations (**1/1 studies;** Tobias et al. 2007); **Upper** and **lower limb *absolute* or *areal* BMD:** favourable associations (**1/1 studies;** Tobias et al. 2007); **Cortical BMD:** unfavourable association (**1/1 studies;** Sayers et al. 2011). *LPA and Area and strength:* **Cortical bone area:** null association (**1/1 studies**; Sayers et al. 2011); **Periosteal circumference of the tibia:** positive association (**1/1 studies;** Sayers et al. 2011); **Endosteal circumference of the tibia:** null association (**1/1 studies;** Sayers et al. 2011). *Other (impact measured by g-band)* **1/1 studies** (Deere et al. 2012) found both favourable (higher impacts) and null (lower impacts) associations between impact and **BMD** (femoral neck, hip), **hip structure** (femoral neck width, cross-sectional area, cortical thickness) and **predicted strength** (cross-sectional moment of inertia). A dose-response gradient was found for higher impact activity and **BMD** (femoral neck, total hip).		

Abbreviations: BMC = bone mineral content; BMD = bone mineral density; CSA = cross sectional area; CT = computer tomography; DXA = dual-energy x-ray absorptiometry; LPA = light intensity physical activity; MPA = moderate physical activity; MVPA = moderate-and-vigorous physical activity; PA = physical activity; VPA = vigorous physical activity.

[*] As determined by WHO

[a] Includes **1 randomized-controlled trial** (Gutin et al. 1999).

[b] Serious indirectness. Differences in intervention: the RCT examined a training program that provided indirect evidence bearing on the potential effectiveness of different intensities and durations of PA. Indirect comparisons: different durations and intensities of PA were not compared.

[c] The quality of the evidence from the randomized study was downgraded from “high” to “moderate” due to serious indirectness of the intervention being assessed.

[d] Includes **7 longitudinal studies** (Janz et al. 2006; Janz et al. 2007; Janz et al. 2010; Heidemann et al. 2013; Francis et al. 2014; Janz et al. 2014a; Janz et al. 2014b) from **2 unique samples**. **Six studies** reported data from the Iowa Bone Development Study (Janz et al. 2006; Janz et al. 2007; Janz et al. 2010; Francis et al. 2014; Janz et al. 2014a; Janz et al. 2014b) and **1 study** reported data from the CHAMPS study sample (Heidemann et al. 2013). Results are reported separately, and participants are only counted once.

[e] The quality of evidence from longitudinal studies was upgraded from “low” to “moderate” due to no serious risk of bias.

[f] Includes **14 cross-sectional studies** (Janz et al. 2001; Janz et al. 2004; Hasselstrom et al. 2007; Tobias et al. 2007; Janz et al. 2008; Sayers et al. 2011; Farr et al. 2011; Gracia-Marco et al. 2011a; Gracia-Marco et al. 2011b; Cardadeiro et al. 2012; Gracia-Marco et al. 2012; Deere et al. 2012; Francis et al. 2014; Janz et al. 2014a), from **6 unique samples**. **Five** studies reported data from the Iowa Bone Development Study (Janz et al. 2001; Janz et al. 2004; Janz et al. 2008; Francis et al. 2014; Janz et al. 2014a), **3 studies** from the ALSPAC (Tobias et al. 2007; Sayers et al. 2011; Deere et al. 2012), **3 studies** from HELENA (Gracia-Marco et al. 2011a; Gracia-Marco et al. 2011b; Gracia-Marco et al. 2012), and **1 study** from each of CoSCIS (Hasselstrom et al. 2007), EYHS (Cardadeiro et al. 2012), and Jump-In: Building Better Bones (Farr et al. 2011). Results are reported separately, and participants are only counted once.

[g] The quality of the evidence from cross-sectional studies remained rated as “low” as there were no serious limitations across studies or reasons to upgrade.

Table A.1.d. Adiposity/body composition and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Adiposity/Body composition
***Importance**: CRITICAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design No. of participants	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**[a]	**Certainty**	**US PAGAC evidence *(27)***
The range of mean ages was 6.9 to 12 years. Data were collected by RCT, non-randomized intervention trial, cross-sectionally and up to 3 years of follow-up. Body composition markers were: BMI (absolute, percentile, Z-score, conditional Z-score velocity), weight status (CDC, IOTF or WHO cut-points), sum of SF, body mass, WC, %BF, FM, FM index, FFM, FFM index, ponderal index, and trunk fat. Outcomes were measured objectively in all but one instance.								
9 RCTs[b] n=3,957	Serious risk of bias[c]	No serious inconsistency	Serious indirect-ness[d]	No serious imprecision Serious imprecision	New systematic reviews were limited to specific physical activity interventions (laboratory-based HIIT, classroom-based active learning, resistance training)	Collins et al. 2018 *(7)* (18 RCTs; n=1,153): Significant, small effect sizes were identified comparing resistance training interventions vs. no resistance training for %BF (Hedges' g = 0.215 [95% CI, 0.059 to 0.371], p = 0.007) and SF thickness (Hedges' g = 0.274 [95% CI, 0.066 to 0.483, p = 0.01) but were not significant for BMI, FFM, FM, lean mass, or WC. Eddolls et al. 2017 *(8)* (13 RCTs; n=1,899): No consistent evidence of an effect of HIIT vs. moderate-intensity PA on changes in body composition as measured by BMI, %BF, or FFM, although most trials found a general trend of greater changes in body composition in high- vs. moderate-intensity groups. Martin et al. 2017 *(16)*: (2 RCTs, 1 NRT; n=6,980): All 3 studies reported small effect sizes with **2/3 studies** reporting no difference in BMI between classroom-based physical activity interventions vs. no intervention. **2/9 studies** reported improved adiposity for intervention vs control at post-test (Gutin et al. 1999; Eather et al. 2013); **4/9 studies** reported mixed favourable and null findings (Verstraete et al. 2007; Kriemler et al. 2010; Ford et al. 2013, Harrington et al 2018). **2/9 studies** had no intervention effects (Finkelstein et al. 2013, Drummy et al. 2016); **1/9 studies** reported that significant favourable effects in Kriemler et al. 2010 were null at 3 year follow up (Meyer et al. 2014). Favourable effects for %BF, but not FM, remained at 15-week follow up for Ford et al. 2013.[e]	LOW[f]	10 ESRs Strong evidence demonstrates that higher levels of physical activity are associated with smaller increases in weight and adiposity during childhood and adolescence. **PAGAC Grade: Strong**
11 NRT[g] n=4,552	Serious risk of bias[h]	No serious inconsistency	Serious of indirect-ness[i]	No serious imprecision	NR	**6/11 studies** reported null effects of PA intervention on adiposity outcomes (Rowland et al. 1996; Pangrazi et al. 2003; Williams and Warrington 2011; Huang et al. 2012; Duncan et al. 2012, Aires et al. 2015).	VERY LOW[j]	

No reviews limited to NRTs identified.						**4/11 studies** reported significant effects of PA intervention on adiposity outcomes (Benjamin Neelon et al. 2015, Postler et al. 2017, Brusseau et al. 2016) **1/11 studies** reported lower odds of overweight/obesity halfway through (1 year) a school/afterschool-based **total PA** intervention program, at post-test (2 years) and at 2-year follow-up (Sigmundova and Sigmund 2012).		
19 Longitudinal [k] n=28,141	Serious risk of bias[l]	No serious inconsistency	No serious indirect-ness	No serious imprecision	NR	Miguel-Berges et al. 2018 *(17)*: (6 longitudinal studies; n=1,834): All studies found a negative relationship between pedometer-measured PA and measures of BMI or WC, with only 2 of 6 studies reporting these associations to be statistically significant. ***Total PA:*** **1/8 studies** reported favourable associations (Janz et al. 2005); **3/8 studies** reported mixed favourable and null associations (Riddoch et al. 2009; White and Jago 2012, Griffiths et al. 2016); **4/8 studies** reported null associations (Butte et al. 2007a; Basterfield et al. 2012; Hjorth et al. 2014a; Hjorth et al. 2014b). ***VPA:*** **3/4 studies** reported favourable associations (total and bouts, Janz et al. 2005; dose-response trend, Carson et al. 2014, Hamer et al 2018); **1/4 studies** reported null associations (Butte et al. 2007a). ***MVPA:*** **5/10 studies** reported favourable associations (Janz et al. 2009; Mitchell et al. 2013, Augustin et al 2017,Chinapaw et al. 2018, Henderson et al. 2016); **2/10 studies** reported mixed favourable and null associations (Riddoch et al. 2009; Hjorth et al. 2014b); **3/10 studies** reported null associations (Stevens et al. 2007; Hallal et al. 2012; Hjorth et al. 2014a). ***MPA:*** **2/2 studies** reported null associations (total and bouts, Janz et al. 2005; Butte et al. 2007a). ***LPA:*** **2/3 studies** reported null associations (Butte et al. 2007a; Treuth et al. 2009); **1/3 studies** reported an unfavourable association, with evidence of dose-response gradient (Carson et al. 2014). **FFM** ***Total PA:*** **1/1 studies** reported mixed favourable and null associations (Stevens et al. 2004).	LOW[m]	
48 Cross-sectional[n] n=57,696	Serious risk of bias[o]	Serious inconsistency[p]	No serious indirect-ness	No serious imprecision	NR	Miguel-Berges et al. 2018 *(17)*: (30 cross-sectional studies; n=19,006): Most studies (24/30) found a statistically significant association between higher levels of pedometer-measured PA and lower adiposity, as measured by BMI and WC. Mohammadi et al. 2019 *(18)*: (10 cross-sectional studies; n=NR): **4/7 studies** found significant associations between **total** PA and weight status, BMI, %BF, and WC among Malaysian adolescents whereas 3/**7 studies** found null results.	VERY LOW[q]	

						Meeting/Not Meeting Guidelines (≥60 min/day MVPA): **2/3 studies** reported favourable associations (Steele et al. 2009; Martinez-Gomez et al. 2010b); **1/3 studies** reported null associations (Mendoza et al. 2012). ***Total PA:*** **9/22 studies** reported favourable associations (Duncan et al. 2008; Riddoch et al. 2009; Steele et al. 2009; Ferrar and Olds 2010; Owen et al. 2010; Belcher et al. 2010; Mark and Janssen 2011; Ekstedt et al. 2013; Manios et al. 2013). **8/22 studies** reported mixed favourable and null associations (Andersen et al. 2006; Duncan et al. 2006; Ness et al. 2007; Ortega et al. 2007; Dollman et al. 2010; Ruiz et al. 2011; Tudor-Locke et al. 2011; Jimenez-Pavon et al. 2013c). **3/22 studies** reported null associations (Ekelund et al. 2006; Hands et al. 2009; Martinez-Gomez et al. 2012). **1/22 studies** reported mixed favourable, null, and unfavourable associations (Jimenez-Pavon et al. 2013a). **1/22 studies** reported mixed null and unfavourable associations (Hands and Parker 2008). ***VPA:*** **10/15 studies** reported favourable associations (Ekelund et al. 2004; Lohman et al. 2006; Steele et al. 2009; Martinez-Gomez et al. 2010b; Mark and Janssen 2011; Sayers et al. 2011; Chung et al. 2012; Martinez-Gomez et al. 2012; Jimenez-Pavon et al. 2013a; Katzmarzyk et al. 2015b). **4/15 studies** reported mixed favourable and null associations (Ortega et al. 2007; Kelly et al. 2010; Belcher et al. 2010; Jimenez-Pavon et al. 2013c). **1/15 studies** reported mixed null and unfavourable associations (Ortega et al. 2010). ***MVPA:*** **20/30 studies** reported favourable associations (Ekelund et al. 2004; Lohman et al. 2006; Ness et al. 2007; Stevens et al. 2007; Mark and Janssen 2009; Riddoch et al. 2009; Steele et al. 2009; Belcher et al. 2010; Martinez-Gomez et al. 2010b; Holman et al. 2011; Grydeland et al. 2012; Lawman et al. 2012; Carson et al. 2013; Ekstedt et al. 2013; Jimenez-Pavon et al. 2013a; Taverno Ross et al. 2013; daSilva et al. 2014; Young et al. 2014; Katzmarzyk et al. 2015a; Katzmarzyk et al. 2015b). **6/30 studies** reported mixed favourable and null associations (Kelly et al. 2010; Peart et al. 2011; Ruiz et al. 2011; Mendoza et al. 2012; St George et al. 2013; Jimenez-Pavon et al. 2013c). **3/30 studies** reported null associations (Hurtig-Wennlof et al. 2007; Ortega et al. 2007; Martinez-Gomez et al. 2012). **1/30 studies** reported mixed null and unfavourable associations (Ortega et al. 2010). **2 studies** examined *sporadic MVPA* (i.e. 1-4 min bouts) and associations were favourable (Mark and Janssen 2009; Holman et al. 2011).		

						3 studies examined *bouts of MVPA* and associations were favourable (**2/3 studies;** Holman et al. 2011; da Silva et al. 2014) or mixed (favourable and null; **1/3 studies;** Mark and Janssen 2009). ***MPA:*** **2/10 studies** reported favourable associations (Mark and Janssen 2011; Chung et al. 2012). **2/10 studies** reported mixed favourable and null associations (Belcher et al. 2010; Jimenez-Pavon et al. 2013c). **5/10 studies** reported null associations (Ortega et al. 2007; Steele et al. 2009; Sayers et al. 2011; Martinez-Gomez et al. 2012; Jimenez-Pavon et al. 2013a). **1/10 studies** reported mixed null and unfavourable associations (Ortega et al. 2010). **No studies** reported only unfavourable associations. ***LPA :*** **1/9 studies** reported favourable associations (Mark and Janssen 2011). **2/9 studies** reported mixed favourable and null associations (Treuth et al. 2009; Kwon et al. 2011). **3/9 studies** reported null associations (Ekelund et al. 2004; Sayers et al. 2011; Carson et al. 2013). **3/9 studies** reported mixed null and unfavourable associations (Steele et al. 2009; Jimenez-Pavon et al. 2013a; Jimenez-Pavon et al. 2013c). **<u>FFM</u>** **Total PA:** **1/2 studies** reported favourable associations (Ness et al. 2007); **1/2 studies** reported mixed favourable and null associations (Jimenez-Pavon et al. 2013a). **VPA :** **2/4 studies** reported favourable associations (Jimenez-Pavon et al. 2013a; Sayers et al. 2011); **2/4 studies** reported mixed null and unfavourable associations (Lohman et al. 2006; Lohman et al. 2008). **MVPA:** **1/4 studies** reported null associations (Jimenez-Pavon et al. 2013a); **3/4 studies** reported mixed null and unfavourable associations (Lohman et al. 2006; Lohman et al. 2008; Taverno Ross et al. 2013). **MPA:** **2/2 studies** reported null associations (Jimenez-Pavon et al. 2013a; Sayers et al. 2011). **LPA:** **1/2 studies** reported favourable associations (Sayers et al. 2011); **1/2 studies** reported mixed unfavourable (boys) and null (girls) associations (Jimenez-Pavon et al. 2013a).		

Abbreviations: %BF = percent body fat; BMI = body mass index; CTRL = control group; FFM = fat free mass; FM = fat mass; HITT = high-intensity interval training; INT = intervention group; LPA = light physical activity; MPA = moderate physical activity; MVPA = moderate-to-vigorous physical activity; NR = not reported; RCT = randomized controlled trial; SF = skinfold; WC = waist circumference.

[*] As determined by WHO

[a] Summary of findings are absolute effects in relation to adiposity-specific indicators unless otherwise stated (i.e. in relation to FFM).

[b] Includes **6 RCT studies** (Verstraete et al. 2007; Kriemler et al. 2010; Finkelstein et al. 2013; Eather et al. 2013; Ford et al. 2013; Meyer et al. 2014) from **5** unique samples, and **1 modified randomized crossover study** (Gutin et al. 1999). Kriemler et al. 2010 and Meyer et al. 2014 both report data from the KISS study. Results are reported separately, and participants are only counted once.

[c] Serious risk of bias. Performance bias: Randomization was reported, but the method by which sibling pairs were further randomized beyond the initial randomization was not described and it is plausible that siblings discussed and detected group assignment (Finkelstein et al. 2013). Detection bias: 6 min walk test assessors were not blinded to group assignment; pedometers were open for INT, but sealed for CTRL, which could have influenced the outcome; missing pedometer data were disproportionately high in controls relative to intervention group (18.1% vs 6.1%), likely due to incentives for wear time offered to the intervention group only (Finkelstein et al. 2013). Selective reporting: %BF from BodPod was not available at follow up and reasons were not described. Many analyses were only reported for sub-samples with no explanation. Sequence generation: unclear how the subsample of children who had objective PA measures was selected (Ford et al. 2013).

[d] Serious indirectness. Differences in intervention: studies examined various types of physical activity programs and provided indirect evidence bearing on the potential effectiveness of different intensities and durations of physical activity. Indirect comparisons: different durations and intensities of physical activity were not compared within individual studies.

[e] MVPA (but not total PA) was significantly greater in the intervention vs control group at post-intervention (post 9-month intervention group difference of ~11 min/day) (Kriemler et al. 2010); there was a trend toward higher levels of total PA (but not MVPA) in the intervention vs control group at 3-yr follow-up (Cohen's *d* = 0.35, p=0.06; not significant) (Meyer et al. 2014).

[f] The quality of the evidence from randomized studies was downgraded from "high" to "low" due to: (1) a serious risk of bias in two studies that diminished the level of confidence in the observed effects, and (2) serious indirectness of the interventions and the comparisons being assessed.

[g] Includes **3 non-randomized controlled intervention studies** (Pangrazi et al. 2003; Williams and Warrington 2011; Sigmundova and Sigmund 2012) and **3 single group intervention studies** (Rowland et al. 1996; Duncan et al. 2012; Huang et al. 2012).

[h] Serious risk of bias. Allocation concealment: Group assignment was based on completion of intervention or drop-out, with drop-outs serving as CTRL. Attrition bias: the large amount of missing data was likely related to the outcome of interest (Williams and Warrington 2011). Other source of bias: there was no CTRL group (Duncan et al. 2012; Huang et al. 2012). Attrition bias: Analysis did not control for clustering by class order/number and change scores were not compared with a reference group (Huang et al. 2012). Allocation concealment was not described. Performance bias: no blinding attempted. Other sources of bias: The authors reported implausibly large effect sizes for the intervention (i.e., a reduction in the proportion of obesity to 0% in INT, while the proportion doubled in CTRL) (Sigmundova and Sigmund 2012). Incomplete outcome data: dietary analysis showed there was a small increase in caloric intake in INT compared to CTRL that was not controlled for in analysis (Rowland et al. 1996).

[i] Serious indirectness. Differences in intervention: Studies examined various types of physical activity programs and provided indirect evidence bearing on the potential effectiveness of different intensities and durations of physical activity. Indirect comparisons: different durations and intensities of physical activity were not compared within individual studies.

[j] The quality of evidence from non-randomized intervention studies was downgraded from "low" to "very low" due to: (1) a serious risk of bias in four studies that diminished the level of confidence in the observed effects, and (2) serious indirectness of the interventions and the comparisons being assessed.

[k] Includes **14 longitudinal studies** (Stevens et al. 2004; Janz et al. 2005; Stevens et al. 2007; Butte et al. 2007a; Janz et al. 2009; Riddoch et al. 2009; Treuth et al. 2009; Basterfield et al. 2012; Hallal et al. 2012; White and Jago 2012; Mitchell et al. 2013; Carson et al. 2014; Hjorth et al. 2014a; Hjorth et al. 2014b) from **11 unique samples**; Janz et al. 2005 and 2009 reported data from the Iowa Bone Development Study; Stevens et al. 2007 and Treuth et al. 2009 reported data from the TAAG study; Hjorth et al. 2014a and 2014b reported data from the OPUS study. Results are presented separately, and participants are only counted once.

[l] Serious risk of bias. Authors reported significance at p<0.10. It is unclear if data from the univariate or multivariate models are reported. Loss to follow-up not examined by fat mass index (Basterfield et al. 2012). Enrolment protocol was not adequately described. Adiposity outcomes were reportedly estimated using a "previously validated equation", however in the validation study BMI was a better predictor of BF than the new equation. In the overweight group, baseline PA was a significant predictor of fat mass and fat-free mass, but not %BF; this is concerning as %BF is a function of fat mass and fat-free mass (Stevens et al. 2004). Sixty-eight percent of participants did not provide valid baseline accelerometer data or did not have complete cardiometabolic risk factor data (which included WC) at baseline and/or follow-up; reasons for missing data were not provided. Those lost to follow-up were older, heavier and displayed lower cardiorespiratory fitness levels than completers. Conditional BMI Z-score velocity was validated with infants as cited, however the validity and reliability with children and youth are unknown (Carson et al. 2014). Reasons for exclusions are not adequately reported (Hallal et al. 2012). Reasons for missing outcome data not clear (Riddoch et al. 2009). Only the subset that gained weight was included in the analysis (n=798 out of n=879), which may have affected the associations reported (Butte et al. 2007a).

[m] The quality of evidence from longitudinal studies was not upgraded from "low" to "moderate" due to serious risk of bias.

[n] Includes **48 studies** (Ekelund et al. 2004; Andersen et al. 2006; Duncan et al. 2006; Ekelund et al. 2006; Lohman et al. 2006; Ness et al. 2007; Ortega et al. 2007; Stevens et al. 2007; Hurtig-Wennlof et al. 2007; Duncan et al. 2008; Hands and Parker 2008; Lohman et al. 2008; Hands et al. 2009; Mark and Janssen 2009; Riddoch et al. 2009; Steele et al. 2009; Treuth et al. 2009; Ferrar and Olds 2010; Martinez-Gomez et al. 2010b; Owen et al. 2010; Ortega et al. 2010; Dollman et al. 2010; Kelly et al. 2010; Belcher et al. 2010; Peart et al. 2011; Holman et al. 2011; Kwon et al. 2011; Mark and Janssen 2011; Tudor-Locke et al. 2011; Ruiz et al. 2011; Sayers et al. 2011; Chung et al. 2012; Grydeland et al. 2012; Lawman et al. 2012; Martinez-Gomez et al. 2012; Mendoza et al. 2012; Barreira et al. 2013; Carson et al. 2013; Ekstedt et al. 2013; St George et al. 2013; Taverno Ross et al. 2013; Manios et al. 2013; Jimenez-Pavon et al. 2013a; Jimenez-Pavon et al. 2013c; da Silva et al. 2014; Young et al. 2014; Katzmarzyk et al. 2015a; Katzmarzyk et al. 2015b) from **19 unique samples**. **Two studies** reported data from the Western Australia Child and Adolescent PA and Nutrition Survey 2003 (Hands and Parker 2008 and Hands et al. 2009); **9 studies** reported data from NHANES (Belcher et al. 2010; Holman et al. 2011; Chung et al. 2012; Barreira et al. 2013; Carson et al. 2013; Mark and Janssen 2009 and 2011; Mendoza et al. 2012 and Peart et al. 2011); **2 studies** reported data from the ACT Trial (Lawman et al. 2012 and St George et al. 2013); **6 studies** reported data from the EYHS (Andersen et al. 2006; Ortega et al. 2007; Ortega et al. 2010; Ekelund et al. 2004 and 2006; and Hurtig-Wennlof et al. 2007); **2 studies** reported data from ISCOLE (Katzmarzyk et al. 2015a and 2015b); **3 studies** reported data from ALSPAC (Ness et al. 2007; Riddoch et al. 2009 and Sayers et al. 2011); **2 studies** reported data from the Australian National Children's Nutrition and PA survey (Ferrar and Olds 2010 and Dollman et al. 2010); **6 studies** reported data from TAAG (Stevens et al. 2007; Treuth et al. 2009; Kelly et al. 2010; Young et al. 2014; and Lohman et al. 2006 and 2008); **4 studies** reported data from HELENA (Ruiz et al. 2011; Martinez-Gomez et al. 2010b and 2012; and Jimenez-Pavon et al. 2013a); Duncan et al. 2006 and 2008 were from the same sample; results are reported separately and participants are only counted once.

[o] Serious risk of bias. Potential confounders were not controlled for (da Silva et al. 2014; Katzmarzyk et al. 2015b). Reasons for missing PA and BMI data were not reported (daSilva et al. 2014). The amount of missing data/exclusions and reasons were not reported (Hurtig-Wennlof et al. 2007; Duncan et al. 2008). Risk of detection bias as participants were retained if they provided PA data for at least 1 to 7 days; 68% provided at least 5 days of PA data and 32% provided 1-4 days. PA levels were slightly higher in those with fewer days of PA data. MVPA and LPA were recorded but not reported (Owen et al. 2010). Reasons for missing data were not explained (Steele et al. 2009). Participants with missing PA data differed on some outcome measures (Andersen et al. 2006). BMI z-score was measured and analysed for males and females 5-12 yr. and collected but not reported for 13-16 yr. olds (Dollman et al. 2010). Parent-estimated height and weight were used (Tudor-Locke et al. 2011). Thirty percent of adiposity data were missing without explanation (Jimenez-Pavon et al. 2013c). A large proportion of data were missing with no explanation (Ruiz et al. 2011; Sayers et al. 2011; Taverno Ross et al. 2013). FFM and FM were estimated using an equation developed specifically for the study, however a methods paper showed the equation did not perform satisfactorily or meet the criteria for cross-validation (Taverno Ross et al. 2013). Validity and reliability of outcome measure is unknown and a reference for the equation is not provided (Young et al. 2014).
[p] Serious inconsistency. Findings for LPA were highly inconsistent. Findings for other intensities of PA consistently reported null or favourable associations between PA and adiposity outcomes. Consistency for other measures was not an issue, with consistency and strength of findings explained by varied outcome measurement and intensity of PA (stronger associations for higher intensities of PA and more precise measures of adiposity).
[q] The quality of evidence from cross-sectional studies was downgraded from “low” to “very low” due to: (1) serious risk of bias in 14 studies that diminished the level of confidence in the observed effects and (2) serious unexplained inconsistency in the findings for LPA.

Table A.1.e. Adverse effects and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Adverse effects
*__Importance__: CRITICAL
Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
The range of mean ages was 10 to 15 years. Data were collected longitudinally which up to 19 months of follow-up. Measures included spinal pain occurrences. Outcomes were measured subjectively (self-report) or objectively (clinical examination and audit of linked medical records).								
2 Longitudinal [a] n=2,101 **No eligible reviews identified.**	Serious risk of bias	Serious inconsistency	No serious indirect-ness	No serious imprecision	None	*Total PA* **1/2 studies** reported unfavourable association with **diagnosed** or **traumatic spinal pain** (Franz et al. 2017). **1/2 studies** reported null associations with **self-reported number of spinal pain sites** and **frequency of spinal pain** (Aartun et al. 2016). *LPA* **1 study** reported unfavourable association between *% time in LPA* with **self-reported spinal pain** (Franz et al. 2017) *MPA* **1 study** reported null associations between *% time in MPA* with **self-reported** or **diagnosed spinal pain** (Franz et al. 2017). *MVPA* 1 study reported null associations between *total MVPA* or *meeting at least 1 hour/d of MVPA* with **self-reported number of spinal pain sites** and **frequency of spinal pain** (Aartun et al. 2016). *VPA* **1/2 studies** reported unfavourable associations between *% time in VPA* with **diagnosed or traumatic spinal pain** (Franz et al. 2017); **1/2 studies** reported null associations between *total VPA* with **self-reported number of spinal pain sites** and **frequency of spinal pain** (Aartun et al. 2016).	VERY LOW[b]	Outcome not included

Abbreviations: LPA = light intensity physical activity; MPA = moderate physical activity; MVPA = moderate-and-vigorous physical activity; PA = physical activity; VPA = vigorous physical activity.

[*]As determined by WHO
[a] Includes **2 longitudinal studies** (Aartun et al. 2016; Franz et al. 2017).
[b] The quality of evidence from longitudinal studies was not upgraded from “low” to “moderate” due to serious risk of bias and was downgraded from “low” to “very low” due to inconsistency across studies.

Table A.1.f. Mental health and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Mental health (e.g., depressive symptoms, self-esteem, anxiety symptoms, ADHD)
***Importance**: CRITCAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
The range of mean ages was 12.0 to 16.9 years. Data were collected cross-sectionally and with 3-year follow-up. Psychological distress was assessed as depressed mood by self-reported MFQ, depressive symptoms by self-reported short-MFQ and CES-D and MDD by face-to-face interview using sections of the Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version.								
1 Longitudinal [a] n=736 **No eligible reviews identified.**	No serious risk of bias	Unable to assess	No serious indirect-ness	No serious imprecision	None	No association between baseline **MVPA** or **PAEE** and **depressed mood** or **Major Depressive Disorder** at follow-up (Toseeb et al. 2014).	LOW[b]	5 ESRs Insufficient evidence is available to determine the relationship between physical activity and anxiety among youth. **PAGAC Grade: Not assignable**. 4 ESRs, 1 review of reviews Strong evidence demonstrates that physical activity reduces the risk of experiencing depression. **PAGAC Grade: Strong.** Strong evidence demonstrates that physical activity interventions reduce
4 Cross-sectional[c] n=10,641 **No eligible reviews identified.**	No serious risk of bias	Serious inconsistency[d]	No serious indirect-ness	No serious imprecision	None	***Total PA:*** associations were null (**2/3 studies;** Johnson et al. 2008; Toseeb et al. 2014), or mixed (null and favourable) depending on if assignment to tertiles adjusted for total PA or adjusted for %time in MVPA (**1/3 studies;** Wiles et al. 2012). ***VPA:*** null associations (**1/1 studies;** Johnson et al. 2008). ***MVPA:*** associations were favourable (**1/4 studies;** Wiles et al. 2012), null (**2/4 studies;** Johnson et al. 2008; Toseeb et al. 2014), or mixed (null and unfavourable; **1/4 studies;** Young et al. 2014). ***LPA:*** null associations (**1/1 studies;** Johnson et al. 2008).	VERY LOW[e]	

								depressive symptoms in individuals with and without major depression across the lifespan. **PAGAG Grade: Strong**.

Abbreviations: CES-D = Center for Epidemiological Studies-Depression Scale; MDD = Major Depressive Disorder; MFQ = Mood and Feelings Questionnaire; MVPA = moderate to vigorous physical activity; PA = physical activity; PAEE = physical activity energy expenditure.

[*] As determined by WHO

[a] Includes **1 longitudinal study** (Toseeb et al. 2014).

[b] The overall quality of evidence from longitudinal studies was upgraded from “low” to “moderate” due to no serious risk of bias but downgraded to “low” due to inability to assess consistency (1 study).

[c] Includes **4 cross-sectional studies** (Johnson et al. 2008; Wiles et al. 2012; Toseeb et al. 2014; Young et al. 2014) from **3 unique samples**. **Two studies** (Johnson et al. 2008; Young et al. 2014) report data from the TAAG study. Results are reported separately and participants are only counted once.

[d] Serious inconsistency. Inconsistency is related to the associations between MVPA and depressive symptoms/depressed mood; favourable, null and unfavourable associations were reported in four studies, with no clear reason for differences (Johnson et al. 2008; Wiles et al. 2012; Toseeb et al. 2014; Young et al. 2014).

[e] The quality of evidence from cross-sectional studies was downgraded from “low” to “very low” due to unexplained inconsistency among the findings.

Table A.1.g. Cognitive outcomes and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Cognitive outcomes (e.g., academic performance, executive function)
*__Importance__: CRITCAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
The range of mean ages was 7.8 to 16.9 years. Data were collected by RCT, non-randomized intervention trial, cross-sectionally and up to ~~5~~ 6 years of follow-up. Cognitive Development / Academic Achievement were assessed by: WIAT-III, TEA-Ch, CDR, computerized cognitive assessment system, d2 Test of Attention, Letter Digit Substitution Test, BAS, Trail Making Test, Stroop Color and Word Test, Verbal Fluency Test, WISC-IV, WAI, OSPAN, The Tower of London, school records and GPA, and state or national level standardized tests. Mathematics Engagement was assessed using School Engagement Measure. On-task Behaviour was assessed through systematic direct observation. All outcomes were measured objectively.								
4 RCTs n=2,847	Serious risk of bias	No serious inconsistency	Serious indirect-ness	No serious imprecision	Possibility of publication bias Most trials did not address higher level EF measures	Xue et al. 2018 *(24)* (19 RCTs; n = 5,038): Exercise interventions with multiple sessions per week for 6 weeks or longer were associated with greater change in overall EF (SMD 0.20 [95% I, 0.09 to 0.30], *p*<0.05), inhibitory control (SMD 0.26 [95% CI, 0.08 to 0.45], *p*<0.01), working memory (SMD 0.10 [95% CI, -0.05 to 0.25], *p*<0.02), and cognitive flexibility (SMD 0.14 [95% CI, -0.03 to 0.31], *p*<0.04) compared with no exercise interventions. There was no evidence of an effect on planning. Effects of exercise interventions was comparatively larger on populations with higher versus lower BMIs. Martin et al. 2017 *(16)*: (3 RCTs, 2 NRTs; n=2,204): Mixed effects of classroom-based PA vs. no PA on measures of learning, reasoning, math, reading, fluid intelligence social studies, and math, science, and English. __**On-task behaviour**__ **3 studies** found positive effects of PA intervention on on-task behaviour (Bartholomew et al. 2018; Riley et al. 2016; Grieco et al. 2016). __**Cognition**__ **1 study** found no difference between PA intervention and control groups for **content recall** (Norris et al. 2015). __**Academic achievement**__ **1 study** found no change on **mathematical test performance** following the PA intervention (Riley et al. 2016).	MODERATE[m]	9 ESRs Moderate evidence indicates an effect of both acute and long-term moderate-to-vigorous physical activity interventions on brain, cognition, and academic outcomes (e.g., school performance, psychometric profile of memory and executive function) in preadolescent children ages 5 to 13 years. **PAGAC Grade: Moderate.** Insufficient evidence is available to determine whether a relationship

5 NRTs[a] n=547	Serious risk of bias[b]	No serious inconsistency	Serious indirect-ness[c]	No serious imprecision	NR	**<u>On-task behaviour</u>** **2/3 studies** showed positive effects of PA intervention on **on-task behaviour** (Goh 2017; Mullender-Wijnsma et al. 2015); **1/3 studies** showed no effects of PA intervention **on on-task behaviour** (Wilson et al. 2016). **<u>Cognition</u>** **2 studies** showed no effects of PA intervention on **sustained attention** or executive function text performance (**processing speed, selective attention**) (Wilson et al. 2016; van den Berg et al. 2016). **<u>Academic Achievement</u>** **GPA** increased in both groups, but there were no between-group differences (Shore et al. 2014).[d]	VERY LOW[e]	exists between moderate-to-vigorous physical activity and cognition in adolescents ages 14 to 18 years. **PAGAC Grade: Not assignable.**
9 Longitudinal[f] n=15,460 **No reviews limited to longitudinal studies identified.**	Serious risk of bias[g]	No serious inconsistency	No serious indirect-ness	No serious imprecision	NR	**<u>Academic Achievement</u>** **School Grades** *%MVPA* at age 11 yr was favourably associated with **English** (but not **Math** or **Science**), and with academic attainment at age 13 and 16 in boys and girls (association also significant for **Science** in girls at age 16 yr) (Booth et al. 2014). **1 study** found null association between *MVPA* and **Grade based points** (Corder et al. 2015). **Standardized tests** 1 study found *PA index* was favourably associated with **writing** score, but not **reading** or **numeracy** (Telford et al. 2012b). **1 study** found that changes in *MVPA* had mixed favourable (in girls) and null (in boys) associations with changes in **NAPLAN test scores** (Owen et al. 2018). **1 study** found null associations between *total PA (cpm)* or *% time in MVPA* with **numeracy, reading** and **English** (Aadland et al. 2017). **<u>Cognition</u>** **Executive function tests (CDR):** **1 study** found no association between *total PA* or *% time in MVPA* at age 11 yr and test speed or accuracy at age 13. In boys, *%MVPA* (adjusted for total PA) was favourably associated with accuracy, but not speed. In girls, no association with speed or accuracy (Booth et al. 2013). **1 study** found no associations between *total PA (cpm)* or *% time in MVPA* with **inhibition, working memory** and **cognitive flexibility** (Aadland et al. 2017). **1 study** found unfavourable associations between *LPA* and **verbal reasoning** and **verbal knowledge**, while mixed unfavourable and null associations for *MVPA* (Aggio et al. 2016). **1 study** found mixed unfavourable (in girls) and null (in boys) associations between *LPA* and **fluid intelligence**; and mixed unfavourable (in boys) and null (in girls) associations between *VPA* and **inhibitions** (Wickel et al. 2017). **1 study** found null associations between *LPA* with **inhibition** and **working memory**, between *MPA or MVPA* **with inhibition, working memory** and **fluid intelligence**; and between *VPA* with **working memory** and **intelligence** (Wickel et al. 2017)	LOW[h]	

						<u>**Mathematics Engagement**</u> **1 study** found that changes in *MVPA* had null association with changes in **mathematics engagement** (Owen et al. 2018a). **1 study** found null associations between *LPA, MPA, VPA* and *MVPA* with **mathematics engagement**. (Owen et al. 2018b) **1 study** found mixed favourable associations between *MPA* and **cognitive engagement**, and null associations with **behavioural, emotional and overall school engagement**. (Owen et al. 2018b)		
6 Cross-sectional[i] n=11,996	Serious risk of bias[j]	Serious inconsistency[k]	No serious indirect-ness	No serious imprecision		Marques et al. 2016 *(15)* (41 cross-sectional studies, 2 RCTs, and 8 longitudinal studies; n = NR): There was no consistent evidence of a relationship between objectively-measured PA and academic outcomes (**4/11 studies** found statistically significant positive association; **1/11 study** found an inverse relationship; **6/11 studies** reported no relationship). **12/18 studies** reported statistically significant associations between self-reported PA and academic measures and **6/18 studies** found no relationship. <u>**Academic Achievement**</u> **Standardized tests** **Total PA** **2/2 studies** reported no association between *total PA* and WIAT-III (Lambourne et al. 2013; Hansen et al. 2014). **MPA, MVPA, VPA** **1/3 studies** reported mixed unfavourable and null associations between *MVPA* and **state Math test** performance with inconsistencies occurring across samples (Young et al. 2014). **1/3 studies** reported mixed favourable and null associations, with *%MVPA* favourably associated with **English** (but not **Math** or **Science**) scores in boys, and **English** and **Science** (but not **Math**) scores in girls (Booth et al. 2014). **School Grades** **1/3 studies** found *MPA, MVPA* and *VPA* were unfavourably associated with **Math** and **Language scores,** and **GPA** (Esteban-Cornejo et al. 2014). <u>**Cognition**</u> **Total PA and MVPA** **Executive function tests (TEA-Ch, CDR)** **1/1 studies** reported mixed null and favourable associations between *total PA* or *%MVPA* and **test speed and accuracy** (Booth et al. 2013).	VERY LOW[l]	

Note: CDR = Cognitive Drug Research; EF = executive function; GPA = grade point average; MPA = moderate intensity physical activity; MVPA = moderate-to-vigorous physical activity; NR = not reported; NRT = non-randomized trial; PA = physical activity; SMD = standardized mean difference; TEA-Ch = Test of Everyday Attention for Children; VPA = vigorous intensity physical activity; WIAT-III = Weschsler Individual Achievement Test of oral language, written language and mathematics-Third Edition.

[*] As determined by WHO

[a] Includes **1 non-randomized trial** (Shore et al. 2014).

[b] Serious risk of bias. No inclusion/exclusion criteria established; inadequate reporting of recruitment, allocation concealment, and blinding; large unexplained loss to follow-up (36.5% retention) and unknown if follow-up differed by group allocation (Shore et al. 2014).

[c] Serious indirectness. Differences in intervention: studies examined PE class content and provided indirect evidence bearing on the potential effectiveness of different intensities and durations of PA. Indirect comparisons: different durations and intensities of PA were not compared within individual studies.

[d] The intervention group increased steps/day (baseline to post-intervention: 9692 to 12307) more than the control group (9420 to 10608) (Shore et al. 2014).

[e] The quality of evidence from the non-randomized study was downgraded from "low" to "very low" due to: (1) a serious risk of bias that diminished the level of confidence in the observed effects, and (2) serious indirectness of the intervention and the comparison being assessed.

[f] Includes **3 longitudinal studies** (Telford et al. 2012b; Booth et al. 2013; Booth et al. 2014) from **2 unique samples**. **Two studies** reported data from the ALSPAC sample (Booth et al. 2013; Booth et al. 2014); results are reported separately, and participants are only counted once.
[g] Serious risk of bias. Validity and reliability of outcomes unknown (Telford et al. 2012b; Booth et al. 2013; Booth et al. 2014).
[h] The quality of evidence from the longitudinal studies was not upgraded from "low" to "moderate" due to serious risk of bias.
[i] Includes **6 cross-sectional studies** (Lambourne et al. 2013; Booth et al. 2013; Esteban-Cornejo et al. 2014; Young et al. 2014; Booth et al. 2014; Hansen et al. 2014) from **5 unique samples**. **Two studies** reported data from the ALSPAC sample (Booth et al. 2013; Booth et al. 2014); results are reported separately, and participants are only counted once.
[j] Serious risk of bias. Valid PA data missing for 41.5% of the sample (Hansen et al. 2014). Validity and reliability of outcomes unknown (Booth et al. 2013 and 2014; Esteban-Cornejo et al. 2014; Young et al. 2014).
[k] Serious inconsistency. **Two studies** found unfavourable associations [between PA (MPA, MVPA, VPA) and GPA (Esteban-Cornejo et al. 2014), and between MVPA and state Math test performance (Young et al. 2014)], **2 studies** found no associations [between total PA and WIAT-III (Lambourne et al. 2013; Hansen et al. 2014)], and **2 studies** found no or favourable associations [between PA (total, %MVPA) and executive function tests (Booth et al. 2013); and between %MVPA and national English, Math and Science test scores (Booth et al. 2014)].
[l] The quality of evidence from cross-sectional studies was downgraded from "low" to "very low" due to: (1) a serious risk of bias in five studies that diminished the level of confidence in the observed effects, and (2) large unexplained inconsistency among the findings.
[m] The quality of evidence from the RCT was downgraded from "high" to "moderate" due to: (1) a serious risk of bias that diminished the level of confidence in the observed effects, and (2) serious indirectness of the intervention and the comparison being assessed.

Table A.1.h. Prosocial behaviour and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Prosocial behaviour (e.g., conduct problems, peer relations, social inclusion)
***Importance**: IMPORTANT

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
The range of mean age was 6.0 to 11.15 years; data were collected by RCT, non-randomized intervention trials, cross-sectionally and up to 4 years of follow-up. Prosocial behaviour conduct problems and peer problems were assessed via the Strengths and Difficulties Questionnaire, Effort and time on task were assessed via the Classroom Behaviour and Assets Scale, Social acceptance was assessed via Harter's Self-perception Profile for Children and time in play and social skills were assessed via The Social Skills Improvement System Rating Scale and The Pictorial Scale of Perceived Competence and Social Acceptance for Young Children. All outcomes were measured objectively.								
1 RCT[a] n=226 **No eligible reviews identified.**	Serious risk of bias	Unable to assess	No serious indirect-ness	No serious imprecision	None	There was no effect of MVPA on time in play and social skills (Bundy et al. 2017).	LOW[f]	Outcome not included
1 NRT[b] n=1,322 **No eligible reviews identified.**	Serious risk of bias	Unable to assess	No serious indirect-ness	No serious imprecision	None	There were positive effects of MVPA on effort and time on task (Carlson et al. 2015)	VERY LOW[g]	
1 Longitudinal[c] n=7,704 **No eligible reviews identified.**	Serious risk of bias	Unable to assess	No serious indirect-ness	No serious imprecision	None	PA associated with fewer peer problems. MVPA– unfavourable association with conduct hyperactivity problems (boys & girls) & conduct problems (boys only) (Ahn et al. 2018)	VERY LOW[h]	

1 Cross-sectional[d] n=652 **No eligible reviews identified.**	Serious risk of bias[e]	Unable to assess	No serious indirect-ness	No serious imprecision	None	There was no association between *total PA* and **prosocial behaviour**, **peer problems**, **social acceptance** or **conduct problems** for boys or girls (Sebire et al. 2011). *MVPA* was favourably correlated with **peer problems** and **social acceptance** (in boys, not girls). *MVPA* was favourably associated with **prosocial behaviour** (in girls, not boys). *MVPA* was not associated with **conduct problems** in boys or girls.	VERY LOW[i]	

Abbreviations: MVPA = moderate-to-vigorous physical activity; PA = physical activity

[*]As determined by WHO

[a] Includes **1 RCT study** (Bundy et al. 2017)

[b] Includes **1 NRT study** (Carlson et al. 2015)

[c] Includes **1 longitudinal study** (Ahn et al. 2018)

[d] Includes **1 cross-sectional study** (Sebire et al. 2011).

[e] Serious risk of bias. Complete data for only 66% of participants; no indication that data were missing at random. Internal consistency of the scales was questionable (alpha = 0.60 to 0.66).

[f] The quality of evidence from this RCT was downgraded from “high” to “low” due to a serious risk of bias that diminished the level of confidence in the observed effects and because inconsistency could not be assessed (1 study).

[g] The quality of evidence from this NRT was downgraded from “low” to “very low” due to a serious risk of bias that diminished the level of confidence in the observed effects and because inconsistency could not be assessed (1 study).

[h] The quality of evidence from this longitudinal study could not be upgraded from “low” to “moderate” due to serious risk of bias that diminished the level of confidence in the observed effects and was downgraded from “low” to “very low” because inconsistency could not be assessed (1 study).

[i] The quality of evidence from this cross-sectional study was downgraded from “low” to “very low” due to a serious risk of bias that diminished the level of confidence in the observed effects and because inconsistency could not be assessed (1 study).

Table A.1.I. Sleep duration and quality and physical activity, children and adolescents

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Sleep duration and quality
***Importance**: IMPORTANT

No GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years)*(26)* and no systematic reviews identified by WHO.

A.2. Sedentary Behaviour

Table A.2.a. Physical fitness and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Physical fitness (e.g., cardiorespiratory, motor development, muscular fitness)
***Importance**: CRITICAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
Mean baseline age ranged between 6.7 and 17.7 years; where mean age was not reported, baseline age ranged from 6 to 18.5 years. Data were collected from longitudinal (n=3) and cross-sectional (n=18) study designs with up to 2 year follow up. Fitness was assessed as CFR (Andersen test, PACER, AMIS 2001 Cardiopulmonary Function test, FITNESSGRAM 20 m shuttle-run, submaximal cycle ergometer test, 3 minute step test, Leger shuttle run, Physical Work Capacity 170 test); flexibility (EUROFIT test, Dordel-Koch test, Motorik-Modeule, FITNESSGRAM); muscular strength/endurance (EUROFIT test, Dordel-Koch test, hand grip strength, Motorik-Modeule, FITNESSGRAM); power (EUROFIT test, Dordel-Koch test). All outcomes were measured objectively.								
3 Longitudinal [a] n = 4,327 **No eligible reviews identified.**	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	Dose-response gradient [b]	**<u>CRF</u>** For prospective findings, higher sedentary behaviour was associated with lower fitness for: 1) <u>Accelerometer-derived sedentary time</u> - *1/1 study*. 2) <u>Screen time</u> - *3/3 studies.*	MODERATE [f]	Outcome not included
18 Cross-sectional [c] n = 55,636 [e] **No eligible reviews identified.**	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	Exposure/outcome gradient [d]	**<u>CRF</u>** Higher sedentary behaviour was associated with lower fitness for: 1) <u>Accelerometer-derived sedentary time</u> - *2/5 studies* (only in females for 1 study). 2) <u>Screen time</u> - *3/3 studies.* 3) <u>TV</u> - 3/3 studies (only in females for 1 study). 4) <u>Video game</u> - *2/2 studies* (only for males on weekdays in 1 study). 5) <u>Computer</u> - *0/1 study.* *6) <u>Total sedentary behaviour</u> – 1/1 study.* **<u>Muscular Strength/Endurance</u>** Higher sedentary behaviour was associated with lower fitness for: 1) <u>Accelerometer-derived sedentary time</u> - *0/1 study.*	MODERATE [g]	

						2) Screen time - *2/2 studies.* 3) TV - *1/3 studies* (not for grip strength in 1 study). 4) Computer - *2/2 studies* (not for strength of arm in 1 study). 5) Video game - *0/2 studies.* **Flexibility** Higher sedentary behaviour was associated with lower fitness for: 1) Accelerometer-derived sedentary time - *0/1 study.* 2) Screen time - *1/1 study.* 3) Computer - *1/1 study.* **Other** Higher sedentary behaviour was associated with lower fitness for: 1) Accelerometer-derived sedentary time and peak expiratory flow - *0/1 study.* 2) Screen time and overall fitness score - *1/1 study.* 3) TV and overall fitness score - *1/1 study.* 4) TV and higher resting HR - *1/1 study.*		

Abbreviations: CRF = cardiorespiratory fitness; HR = heart rate; TV = television viewing.

[*]As determined by WHO
[a]Includes 3 longitudinal studies *(29-31)*.
[b]A dose-response gradient of higher screen time with lower fitness was observed in 1 longitudinal study *(31)*.
[c]Includes 18 cross sectional study *(32-49)*.
[d]A gradient of higher accelerometer-derived sedentary time, screen time, or TV with lower fitness was observed in 7 cross-sectional studies *(33, 36, 39, 41, 44, 46, 47)*.
[e]Two studies used the German Health Interview and Examination Survey for Children and Adolescents *(41, 44)*.
[f]The quality of evidence for longitudinal studies was upgraded to “moderate” from “low” due to no serious risk of bias.
[g]The quality of evidence for cross-sectional studies was upgraded to “moderate” from “low” due to an exposure/outcome gradient.

Table A.2.b. Cardiometabolic health and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Cardiometabolic health (e.g., blood pressure, dyslipidaemia, glucose, insulin resistance)
***Importance**: CRITICAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
Mean baseline age ranged between 6.7 and 16.7 years; where mean age was not reported, baseline age ranged from 5 to 19 years. Data were collected by longitudinal (n=6) and cross-sectional (n=25) study designs with up to 27 years follow up. Metabolic syndrome/cardiovascular disease risk factors were assessed as SBP, DBP, mean arterial BP, HbA1c, HOMA-IR, TG, HDL, TC/HDL ratio, metabolic syndrome risk score, insulin, glucose, non-HDL, resting heart rate, LDL, CRP, Matsuda insulin sensitivity, HOMA2-%B, OGTT-derived measures of insulin secretion (AUC I/G$_{t30\ min}$ and AUC I G$_{t120min}$), total cholesterol, apolipoprotein A1, apolipoprotein-B100, lipoprotein(a), adiponectin, leptin, VLDL TG, VLDL cholesterol, and HDL TG. All outcomes were measured objectively.								
12 Longitudinal [a] n = 23,834 **No eligible reviews identified.**	Serious risk of bias[b]	Serious inconsistency[c]	No serious indirect-ness	No serious imprecision	Dose-respons e gradient [d]	**<u>Clustered Risk Score</u>** Higher sedentary behaviour was associated with a higher clustered risk score for: 1) <u>Accelerometer-derived sedentary time</u> - *1/3 study.* 2) <u>Screen time</u> - *4/5 studies.* 3) <u>TV</u> - 2/2 studies. 4) <u>Computer</u> - *0/1 study.* **<u>BP</u>** Higher sedentary behaviour was associated with higher blood pressure for: 1) <u>Accelerometer-derived sedentary time</u> - *0/1 study.* 2) <u>Screen time</u> - *2/5 studies.* 3) <u>TV</u> - *1/3 studies.* 4) <u>Computer</u> - *2/2 studies (not for SBP in 2 studies).* 5) <u>Video games</u> - *0/1 studies.* **<u>Cholesterol</u>** Higher sedentary behaviour was associated with lower cholesterol for: 1) <u>Accelerometer-derived sedentary time</u> - *1/1 study (for HDL in 1 study).* 2) <u>Screen time</u> - 0/3 *studies.* 3) <u>TV</u> - *1/2 studies (for HDL in 1 study).* 4) <u>Computer</u> - *0/1 study.* **<u>Insulin</u>** Higher sedentary behaviour was associated with higher insulin for: 1) <u>Screen time</u> - *1/1 study.*	LOW[e]	<u>4 ESRs</u> Limited evidence suggests that greater time spent in sedentary behaviour is related to poorer cardiometabolic health; the evidence is somewhat stronger for television viewing or screen time than for total sedentary time. **PAGAC Grade: Limited.**

						2) TV - 1/1 study. 3) Computer - 1/1 study. **TG, HOMA-IR, Glucose, Other** Sedentary behaviour was not associated with other individual risk factors for the majority of studies.		
25 Cross-sectional[f] n = 69,342[j] **No eligible reviews identified.**	Serious risk of bias[g]	Serious inconsistency[h]	No serious indirect-ness	No serious imprecision	Exposure/outcome gradient[i]	**Clustered Risk Score** Higher sedentary behaviour was associated with a higher clustered risk score for: 1) Accelerometer-derived sedentary time - *1/3 studies.* 2) Long accelerometer-derived sedentary bouts (≥5 min) - *0/2 studies.* 3) Screen time - *3/3 studies* (only in females for 1 study). 4) TV - *6/10 studies* (only for females in 1 study). 5) Computer - *1/6 studies* (only for males in 1 study). 6) Video game - *1/3 studies* (only for males and weekends in 1 study). 7) Total sedentary behaviour – 0/2 studies. 8) Resting - *1/1 studies.* Higher sedentary behaviour was associated with a lower clustered risk score for: 1) Accelerometer-derived sedentary breaks - *1/2 studies.* 2) Short accelerometer-derived sedentary bouts (1-4 min) - *1/1 study.* **BP** Higher sedentary behaviour was associated with a higher BP for: 1) Accelerometer-derived sedentary time - *0/5 studies.* 2) Accelerometer-derived sedentary bouts - *0/2 studies.* 3) Accelerometer-derived sedentary breaks - 0/2 studies. 4) Screen time - *2/5 studies* (not for SBP in 1 study). 5) TV - *5/8 studies* (only males in 1 study and not for SBP in 1 study). 6) Computer - *1/6 studies.* 7) Video games - *1/3 studies* (not for SBP or mean atrial pressure in 1 study). 8) Total sedentary time - *0/2 studies.* Higher sedentary behaviour was associated with a lower BP for: 1) Reading - *1/2 studies.* 2) Homework - *1/1 study* (not for DBP or mean atrial pressure in 1 study). **Cholesterol** Higher sedentary behaviour was associated with a lower cholesterol for: 1) Accelerometer-derived sedentary time - *0/5 studies* 2) Accelerometer-derived sedentary bouts and breaks - *0/3 studies.* 3) Screen time - *1/4 studies (for HDL in 1 study).* 4) TV - *3/7 studies* (1 study was for non-HDL and 2 studies were HDL, no association with LDL in 2 studies or total cholesterol in 1 study). 5) Computer - *1/4 studies* (for HDL in 1 study, only in males for 1 study) 6) Video games - *0/1 study* 7) Total sedentary behaviour – 0/2 studies Higher sedentary behaviour was associated with a higher cholesterol for: 1) Listening to music - *1/1 study* (for HDL in 1 study).	VERY LOW[k]	

						TG, HOMA-IR, Insulin, Glucose, CRP, Other Sedentary behaviour was not associated with other individual risk factors for the majority of studies.		

Abbreviations: TV = television viewing; HDL = high-density lipoprotein cholesterol; LDL = low-density lipoprotein cholesterol; VLDL, very low-density lipoprotein cholesterol, TG = triglycerides; SBP = systolic blood pressure; DBP = diastolic blood pressure; BP = blood pressure; HOMA-IR = homeostatic model assessment of insulin resistance; CRP = C-reactive protein; OGTT= Oral glucose tolerance test; HbA1c= glycated haemoglobin; TC=total cholesterol; AUC I = Area under the curve of insulin; min = minutes.

[*]As determined by WHO

[a]Includes 12 longitudinal studies *(50-55)*.

[b]Out of the 5 studies that used a subjective measure of sedentary behaviour, information on psychometric properties of the sedentary behaviour survey items were not provided.

[c]Mixed results observed. No serious inconsistency for screen time.

[d]A dose response gradient for higher screen time, sedentary time with higher cardiometabolic risk was observed for ~~5~~8 studies *(50, 52-55)*.

[e]The quality of evidence for longitudinal studies could not be upgraded from "low" due to serious risk of bias, was downgraded to "very low" due to serious inconsistency but upgraded to "low" due to a dose-response effect.

[f]Includes 25 cross-sectional studies *(40, 41, 56-78)*.

[g]Out of the 21 studies that used a subjective measure of sedentary behaviour, information on psychometric properties of the sedentary behaviour items were only provided in 6 studies *(41, 65, 71-74)*. One study did not report psychometric properties *(58)* but used the same sample of another study where psychometric properties were reported *(71)*.

[h]Mixed results observed.

[i]A gradient for higher TV, screen time, video games, computer, sedentary bouts, sedentary breaks, sedentary time with higher cardiometabolic risk was observed for 6 studies *(56, 58, 64, 74, 75, 78)* and lower risk for 2 studies *(59, 71)*.

[j]4 studies used data from the Quebec Adiposity and Lifestyle Investigation in Youth study *(58, 66, 67, 71)* and 2 studies used data from the German Health Interview and Examination Survey for Children and Adolescents study *(41, 57)*.

[k] The quality of evidence for cross-sectional studies was downgraded to "very low" from "low" due to serious risk of bias and serious inconsistency.

Table A.2.c. Bone health and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Bone health
*__Importance__: CRITICAL

Bone health outcomes not reviewed in Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years) *(26)*. Red font denotes information from WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design No. of participants	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence *(27)***
Mean age ranged between 2 and 24 years; most studies among school-aged children. Sedentary time was objectively measured by wearable monitors/accelerometers in 9/17 studies. SB was classified as <100 counts per minutes in all studies. Eight studies used only questionnaires to assess the type of SB including questions about average daily engagement in sedentary patterns such as time spent watching TV or using computers.								
17 obser-vational studies[a] n = NR	Serious risk of bias[b]	No serious inconsistency	No serious indirect-ness	Serious imprecision	Not all studies adjusted for MVPA in analyses	Koedijk et al. 2017 *(11)*: **Lower extremity bone outcomes:** Consistent evidence of a negative association between objectively measured total sedentary time and lower extremity bone outcomes in school-aged children, independent of MVPA. **Lumbar spine bone outcomes:** No association observed between objectively measured total sedentary time and lumbar spine bone outcomes. **Total body bone outcomes:** Consistent evidence of no association between objectively measured total sedentary time and total body bone outcomes in school-aged children.	VERY LOW[c]	4 prospective cohort studies Limited evidence suggests that sedentary behaviour is not related to bone health in children and adolescents. **PAGAC Grade: Limited.**

Abbreviations: MVPA = moderate-to-vigorous intensity physical activity; NR = not reported; SB = sedentary behaviour

[*] As determined by WHO
[a] Nine cross-sectional studies, six longitudinal prospective cohort studies, one longitudinal retrospective cohort study, and one case-control study.
[b] Only 3 of 17 studies were rated as high quality.
[c] The quality of evidence from observational studies could not be upgraded from “low” to “moderate” as there were serious limitations across studies and was downgraded from “low” to “very low” due to serious imprecision.

Table A.2.d. Adiposity/body composition and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Adiposity/Body composition
***Importance**: CRITICAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
Mean baseline age ranged between 5.0 and 16.7 years; where mean age was not reported, baseline age ranged from 3 to 19 years and grades 5 to 12. Data were collected by longitudinal (n=32), case-control (n=5), and cross-sectional (n=125) design with up to 12 years follow-up. Body composition was assessed as BMI (objectively measured, self-report, parental-report), BMI z-score (objectively measured, self-reported), BMI percentiles (objectively measured, self-reported), overweight and obesity (objectively measured, self-report, parental-report; International Obesity Task Force, Centre for Disease Control and Prevention, World Health Organization, other country-specific percentiles), WHtR (objectively measured), WHR (objectively measured), fat mass (TANITA bioelectric impedance, duel-energy x-ray absorptiometry, Lunar Prodigy DEXA scanner), WC (objectively measured), WC z-score (objectively measured), sum of skinfolds (objectively measured), % body fat (objectively measured), and overfat (slaughter equation).								
45 Longitudinal [a] n = 102,934[d]	Serious risk of bias[b]	No serious inconsistency	No serious indirect-ness	No serious imprecision	Dose-response gradient [c]	Among *prospective findings*, higher sedentary behaviour was associated with unfavourable body composition for: 1) Accelerometer-derived sedentary time – *5/18 studies* (1 study found higher waist circumference at follow-up was associated with higher sedentary time at baseline). 2) Accelerometer-derived breaks - *0/2 study*. 3) Screen time - *15/17 studies* (only for 6 and 10 yr. old's in 1 study, only in males for 1 study, not for waist circumference in 1 study). 4) TV - *15/18 studies* (only for females in 1 study, not for movie viewing in 1 study, not for movie viewing in males in 1 study, only for males and not for body fatness, waist circumference and skinfold thickness for males in 1 study). 5) Computer - *3/5 studies* (only for females in 1 study, not for waist circumference in 2 studies, not for body fatness, hip circumference, and BMI in 1 study). 6) Video game - *0/2 studies*. 7) Total sedentary behaviour - *0/1 study*. 8) Weekend internet use – 1/1 study Higher sedentary behaviour was associated with better body composition 1) Accelerometer-derived sedentary time – *1/9 studies* (Higher total or uninterrupted SB (exposure and change) were associated with better body composition).	MODERATE[e]	8 ESRs Limited evidence suggests that greater time spent in sedentary behaviour is related to higher weight status or adiposity in children and adolescents; the evidence is somewhat stronger for television viewing or screen time than for total sedentary time. **PAGAC Grade: Limited.**

						2) Accelerometer-derived breaks - *1/2 study*. (Fragmentation findings were inconsistent – less fragmentation was beneficial overall (7-15y), but more fragmentation was beneficial between 9-12y		
5 Case-control[f] n = 4,748	No serious risk of bias	No serious inconsistency	No serious indirectn-ess	No serious imprecision	None.	Higher sedentary behaviour was associated with being overweight/obese (case group) for: 1) Screen time - *4/4 studies.* 2) TV - *2/2 studies (*only for weekends in 1 study*).* 3) Computer - *0/2 studies.*	LOW	
125 Cross-sectional[g] n = 1,386,706[j]	Serious risk of bias[h]	No serious inconsistency	No serious indirect-ness	No serious imprecision	Exposur e/outco me gradient[i]	Fang et al. 2019 *(10)* (14 cross-sectional studies, 2 longitudinal studies, 1 case-control study; n = 45,381): Total screen time ≥2 hours/day was positively associated with childhood overweight/obesity compared with total screen time <2 hours/day (OR = 1.67 [95% CI, 1.48 to 1.88]). Marker et al. 2019 *(14)* (20 cross-sectional studies; n = 36,119)[m]: No statistically significant association between sedentary video gaming and body mass among children (correlation = 0.09 [95% CI, -0.07 to 0.25]) or adolescents (correlation = 0.01 [95% CI, -0.21 to 0.23]). Mohammadi et al. 2019 *(18)*: (2 cross-sectional studies; n=NR): **1/2 studies** found no association between screen time and BMI z-score; **1/2 studies** found a negative association between self-reported sedentary activities and risk of obesity among girls. Higher sedentary behaviour was associated with unfavourable body composition for: 1) Accelerometer-derived sedentary time - *3/18* studies (only after 3pm on weekdays for males in 1 study). 2) Long accelerometer-derived sedentary bouts (≥5 min) - *3/4 studies* (Only 5-9 minute bouts on weekdays and weekends only and in low MVPA group for only 5-9 minute and 10-19 minute bout on total days and weekends only in 1 study, Only 10-14 minute bouts for only BMI z-score and in males only in 1 study, and only at least 40 minutes (waist circumference only) in 11-14 yr old males after 3pm on weekdays and only at least 80 minutes for males only in 1 study). 3) Short accelerometer-derived sedentary bouts (1-4 minute) - *1/2 studies* (only for the weekend in 1 study). 4) Screen time - *26/36 studies* (only for males in 3 studies, not for urban participants in 1 study, not for certain ethnic groups in 1 study). 5) TV - *58/71 studies* (only for participates aged 4-8 yr in 1 study, only for males in 4 studies, only for females in 3 studies, only for weekdays in 1 study, only 12-18 yr old males for 1 study, not for BMI z-score in 1 study). 6) Computer - 7*/30 studies* (only for females in 2 studies). 7) Video game - 3*/20 studies* (only for weekends in 1 study and only for females in 1 study). 8) Total sedentary behaviour -*3/4 studies* (not for WC in 1 study, only in 1 sample and only for 6-11 yr olds in 1 study). 9) Homework - *3/7 studies* (only for males in 1 study, only in 6-11 yr old males in 1 study) 10) Quiet time - *1/1 study* (only for males in 1 study) Higher sedentary behaviour was associated with favourable body composition for:	VERY LOW[k]	

						1) Accelerometer-derived sedentary time - *1/18 studies*. 2) Accelerometer-derived sedentary breaks - *2/4 studies* (only 11-14 yr old males after 3pm on weekdays in 1 study). 3) Short accelerometer-derived sedentary bouts (1-4 min) - *1/2 studies* (1-4 minute bouts in 1 study). 4) Long accelerometer-derived sedentary bouts (≥5 min) - *1/4 studies* (only for girls and only for WC in 1 study). 5) Screen time - *1/36 studies* 6) Computer - *2/30* studies (only for 1hr/day in 1 study, not for sum of skinfolds in 1 study). 7) Reading - *1/2 studies* (only for low group in 1 study) 8) Non-screen time - *1/1 study*.		
1 NRT[l]	Serious risk of bias	No serious inconsistency	No serious indirect-ness	Serious imprecision	None	No effect for total sitting (during class school or whole day). Effect for sitting in long bouts (>10 min) and number of sit-to-stand transitions. No effect for BMIz/WCz.	VERY LOW[e]	

Abbreviations: WHtR = waist to height ratio; WHR = waist to hip ratio; WC = waist circumference; BMI = body mass index; min= minutes; OR = odds ratio

[*]As determined by WHO
[a]Includes 45 longitudinal studies *(50, 51, 53, 54, 61, 79-105)*; Allen et al. 2016; Barrense-Dias et al. 2016; Collings et al. 2015; Griffiths et al. 2016; Janz et al. 2017; Mann et al. 2017; Marques et al. 2016; Oellingrath et al. 2016; Sluijs et al. 2016; Tanaka et al. 2018; Wheaton et al. 2015; Skrede et al. 2017; Dong et al. 2017)
[b]Out of the 26 studies that used a subjective measure of sedentary behaviour, only 7 studies mention psychometric properties for the sedentary behaviour items *(85, 88, 94, 96, 99, 100, 102)*.
[c]Dose response gradient was observed for higher TV, sedentary time, screen time, computer with unfavourable body composition in 14 studies *(50, 51, 53, 81, 88-90, 93, 95-97, 99, 100, 102)*.
[d]Two studies used the Longitudinal Study of Australian Children *(84, 89)*.
[e]The quality of evidence for longitudinal studies could not be upgraded from “low” to “moderate” due to serious risk of bias but was upgraded to “moderate” due to a dose-response.
[f]Includes 5 case-control studies *(106-110)*.
[g]Includes 125 cross-sectional studies *(32, 37, 40, 42, 45, 49, 56, 59, 60, 63, 71, 78, 89, 111-222)*.
[h] Out of 108 studies that used a subjective measure of sedentary behaviour only 33 studies mentioned psychometric properties for the sedentary behaviour items *(49, 85, 88, 94, 96, 99, 100, 102, 106-109, 114, 120, 126, 128, 145-148, 152, 154, 168, 179-181, 183, 186, 191, 192, 197, 209, 210)*.
[i] A gradient for higher TV, video games, sedentary bouts, sedentary breaks, screen time, studying with unfavourable body composition was observed in 30 studies *(60, 71, 78, 122, 126, 128, 129, 138, 149, 152, 156, 159, 171, 173-177, 183, 185, 189, 194, 195, 197, 203-205, 208, 212, 221)*.
[j]Two studies used the Gateshead Millenium Study *(80, 81)*. Two studies used the optimal well-being, development and health for Danish children through a health New Nordic Diet school meal study *(54, 86)*. Three studies used the Longitudinal Study of Australian Children *(89, 123, 124)*. Three studies used the China Health and Nutrition Survey *(200, 220, 221)*. Three studies used the Quebec Adiposity and Lifestyle Investigator in Youth study *(71, 132, 157)*. Two studies used the 2007-2009 Canadian Health Measures Survey *(60, 135)*. Three studies used the International Study of Childhood Obesity, Lifestyle and the Environment *(133, 168, 169)*. Two studies used the 2003/04 and 2005/06 National Health and Nutrition Examination Survey *(78, 192)*. Two studies used the Alimentación y Valoración del Estado Nutricional de los Adolescentes study *(45, 182)*]. Two studies used the Arab Teens Lifestyle Study *(111, 112)*.
[k]The quality of evidence for cross-sectional studies was downgraded to “very low” from “low” due to serious risk of bias.
[l]Includes one non-RCT (Allen et al. 2016)
[m] 15/20 studies were among children or adolescents.

Table A.2.e. Adverse effects and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Adverse effects
***Importance**: CRITICAL

No GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years)*(26)* and no systematic reviews identified by WHO.

Table A.2.f. Mental health and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Mental health (e.g., depressive symptoms, self-esteem, anxiety symptoms, ADHD)
*__Importance__: CRITCAL

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
Self-esteem								
Mean age ranged between 9.87 and 16.4 years; where mean age was not reported, age ranged from 12 to 19 years and grades 3 to 5. Data were collected by cross-sectional design (n=10). Self-esteem was assessed as overall/global/general and social self-esteem (Rosenberg Self-Esteem scale, Culture Free Self Esteem Inventories for Children, Marsh's Physical Self-Description questionnaire; Harter Self-Perception Profile for Children questionnaire, Harter's Self-Competence scale); general self-efficacy (Rosenberg's Self-Efficacy scale and Schwarzer's Generalized Self-Efficacy scale); offline and online social self-efficacy (Self-Efficacy Questionnaire for Children and Self-Efficacy scale); academic, social, physical appearance, athletic, and behavioural self-concept (Harter's Self-Competence scale, Rosenberg's Self-Esteem scale, Marsh's Physical Self-Description questionnaire). All measures were assessed through a self-reported questionnaire. Some studies modified the scales.								
10 Cross-ectional[a] n = 82,919	Serious risk of bias[b]	Serious inconsistency[c]	No serious indirect-ness	No serious imprecision	Exposure/Outcome Gradient[d]	Stanczykiewicz et al. 2019 *(22)* (k=8; n = NR)[h]: **5/8 studies** found statistically significant association between SB and anxiety symptoms, although results were inconsistent across measures of SB within studies. Overall, the estimated average effect was not statistically significant (r = 0.05 [95% CI, -0.01 to 0.11], p = 0.085). Higher sedentary behaviour was associated with lower self-esteem for: 1) Accelerometer-derived sedentary time – *0/2 studies.* 2) Accelerometer-derived sedentary bouts – *0/1 study.* 3) Accelerometer-derived sedentary breaks – *0/1 study.* 4) Screen time – *2/2 studies* (not physical self-concept in 1 study). 5) TV – *2/4 studies.* 6) Computer – *3/5 studies* (one for females only in 1 study, not for online game in 1 study, not for physical concept in 1 study. 7) Video games – *¼ studies* (only in self-concept and self-esteem in 1 study). Higher sedentary behaviour was associated with higher self-esteem for: 1) Computer – *1/5 studies* (only for self-concept in 1 study) 2) Video games – *¼ studies* (only for online self-efficacy for 1 study) 3) cell phone – *2/2 studies* (not for global self-esteem in 1 study and only for social self-concept in 1 study).	VERY LOW[e]	Outcome not included

1 Longitudinal [f] n = 519	Serious risk of bias	Unable to assess	No serious indirect-ness	No serious imprecision	None	In boys, higher sedentary behaviour is associated with lower self-esteem (0/1) 1) Other Screen time (computers, video game consoles mobile devices) (1/1) 2) TV (0/1) In girls, higher sedentary behaviour was associated with higher self-esteem. 1) Other Screen time (computers, video game consoles mobile devices) (0/1) 2) TV (1/1)	VERY LOW[i]	
Psychological distress								
Mean age ranged between 13.54 and 18.43 years; where mean age was not reported, age ranged from 6 to 15 years. Data were collected by longitudinal design (n=6). Psychological Distress was assessed using different methods. Anxiety was assessed using the Self-Rating Anxiety Scale (SAS). Depression was assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) and the Mood and Feelings Questionnaire (MFQ). Psychopathological symptoms were measured using the Multidimensional Sub-health Questionnaire of Adolescents (MSQA). Psychopathological symptoms were measured using the Multidimensional Sub-health Questionnaire of Adolescents (MSQA).								
6 Longitudinal [g] n = 7,417	Serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	Higher sedentary behaviour associated with higher levels of psychological distress 1) Accelerometer-derived sedentary time – 0/2 studies 2) Screen time – 4/4 studies 3) Computer use for homework – 0/1 study 4) TV – 0/1 study	LOW[j]	

[*]As determined by WHO
[a]Includes 10 cross-sectional studies *(125, 212, 223-230)*.
[b]Of the nine studies that used a subjective measure of sedentary behaviour, only one study *(229)* reported psychometric properties for the items.
[c]Mixed findings were observed.
[d]A gradient for higher screen time and TV with lower self-esteem was observed in 3 studies *(212, 228, 230)*.
[e] The quality of evidence for cross-sectional studies was downgraded to "very low" from "low" due to serious risk of bias and serious inconsistent
[f] Includes one longitudinal study (Braig et al. 2018).
[g] Includes 6 longitudinal studies (Sund et al. 2011; Hume et al. 2011; Gunnell et al. 2016; Wu et al. 2016; Zahl et al. 2017; Babic et al. 2017).
[h] Review included studies among children, adolescents, and adults. Only 8 of 31 total included studies were among children or adolescents.
[i]The quality of evidence for the longitudinal study could not be upgraded from "low" to "moderate" due to serious risk of bias and was downgraded from "low" to "very low" due to inability to assess consistency (1 study).
[j]The quality of evidence for the longitudinal studies could not be upgraded from "low" to "moderate" due to serious risk of bias.

Table A.2.g. Cognitive outcomes and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Cognitive outcomes (e.g., academic performance, executive function)
*__Importance__: CRITCAL

Black font is from original GRADE Evidence Profiles for academic achievement from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
Mean baseline age ranged between 12.0 and 16.9 years; where mean age was not reported, baseline age ranged from 6 to 18 years and grades 9 to 12. Data were collected by longitudinal (n=4) and cross-sectional (n=12) study designs with up to 2 years follow up. Academic achievement was assessed as school/academic performance (self- and proxy-report by interview, questionnaire and Child Behaviour Checklist); grades/grade point average (self- and proxy-report by interview or questionnaire, objectively measured) standardized test scores (National Center for Education Statistics, the National Assessment Program for Literacy and Numeracy); and Reading and Mathematics skills (Wide Range Achievement Test, Revision 3).								
10 Longitudinal [a] n = 33,703 **No eligible reviews identified.**	Serious risk of bias[b]	Serious inconsistency	No serious indirect-ness	No serious imprecision	Dose response gradient [c]	Among *longitudinal findings*, higher sedentary behaviour was associated with lower academic achievement for: 1) Total screen time – 2/2 studies 2) TV - *3/6 studies* (weekdays only for one study). 3) Video games - *2/6 studies.* 4) Computer - *1/2 study.* 5) Non-school sedentary time excluding TV – 1/1 studies 6) Mobile Phone – 0/1 study Among longitudinal findings, higher sedentary behaviour was associated with higher academic achievement for: - Accelerometer – derived sedentary time – 2/2 studies 1) Reading - *2/3 studies.* 2) Homework outside of school *-2/2 study.*	LOW[d]	Outcome not included
12 Cross-sectional[e] n = 14,887 **No eligible reviews identified.**	Serious risk of bias[f]	Serious inconsistency	No serious indirect-ness	No serious imprecision	Exposure/outcome gradient [h]	Higher sedentary behaviour was associated with lower academic achievement for: 1) TV - *1/6 studies* (only for males in 1 study). 2) Video games - *3/6 studies (for GPA only in 1 study).* 3) Computer - *1/4 study.* 4) Total sedentary behaviour - 1/2 studies 5) Cell phone - *0/2 studies* Higher sedentary behaviour was associated with higher academic achievement for: 1) Computer - *1/4 studies.*	VERY LOW[i]	

						2) <u>Total sedentary behaviour</u> - *1/2 studies* (before school only for 1 study). Due to heterogeneity in the measurement of sedentary behaviour and academic achievement a meta-analysis was not possible.		

[*]As determined by WHO
[a]Includes ~~4~~ 10 longitudinal studies *(231-234)*.
[b]No studies provided information on psychometric properties of the sedentary behaviour items.
[c]A dose-response gradient for higher TV/accelerometer derived sedentary time and lower academic achievement or reading and homework with higher academic achievement was observed in ~~2~~ 4 studies *(231, 233)*; Aggio et al. 2016; Wickel et al. 2017).
[d]The quality of evidence for longitudinal studies could not be upgraded from “low” to “moderate” due to serious risk of bias and was downgraded to “very low” from “low” due to serious inconsistency but upgraded to “low” from “very low” due to a dose response gradient.
[e]Includes 12 cross-sectional study *(224, 226, 235-244)*.
[f]Apart from 3 studies *(236, 240, 242)* information on psychometric properties of the sedentary behaviour items were not provided.
[g]Mixed findings were observed.
[h]A gradient for higher video games and computer use with lower academic achievement was observed in 2 studies *(224, 239)*.
[i]The quality of evidence for cross-sectional studies was downgraded to “very low” from “low” due to serious risk of bias and serious inconsistency.

Table A.2.h. Prosocial behaviour and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Prosocial behaviour (e.g., conduct problems, peer relations, social inclusion)
*__Importance__: IMPORTANT

Black font is from original GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years).*(26)* Red font denotes additions based on WHO update using review of existing systematic reviews.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
Mean baseline age ranged between 5 and 14 years; where mean age was not reported, baseline age ranged from 4 to 18 years and grades 6 to 10. One study did not report age or grade, rather that the sample was male guidance school students. Data were collected by randomized controlled trial (n=1), cross-over trial (n=1), longitudinal (n=10), and cross-sectional (n=12) study designs with up to 21 years follow up. Behavioural conduct/pro-social behaviour was assessed as ADHD symptoms (parent- and teacher-reported ADHD-IV Rating Scale, parental reported Strengths and Difficulties Questionnaire), time on task (direct observation), conduct problems (parent-reported Strength and Difficulties Questionnaire), peer relationship problems (parental-reported Strength and Difficulties Questionnaire), pro-social behaviour (parental-reported Strengths and Difficulties Questionnaire), criminal conviction (computer system), antisocial personality (modified Diagnostic Interview Schedule, self-reported Negative Life Events instrument), personality traits (self-reported Multidimensional Personality Questionnaire), behavioural problems (parental-reported Behavioural Problems Index, parental-reported 11-item symptomology checklist, self-reported Achenbach's Youth Questionnaire), aggression/violence (teacher-reported, self-report questionnaire, self-reported Buss and Perry's Aggression Questionnaire, parental-reported Child Behavior Checklist, self-reported State-Trait Anger and the Anger Expression Scale), attention/inattention/hyperactivity problems (teacher-reported questionnaire, self- and parental-reported Child Behavior Checklist, parental-reported Strength and Difficulties Questionnaire, self-reported ADHD symptoms scale, parental-reported ADHD Rating Scale-IV and parent and child attention symptomology checklist), impulsiveness (self-reported Barratt Impulsiveness Scale - II), serious and covert conduct (self-report questionnaire), bullying perpetration (self-reported Kidscape Questionnaire), social problem/withdrawn/delinquent behaviour (parental reported Child Behavior Checklist).								
1 Randomized controlled Trial[a] n = 202 **No eligible reviews identified.**	No serious risk of bias	Unable to assess	Serious indirectness[b]	No serious imprecision	None	Smaller decrease in unfavourable measures of behavioural conduct/pro-social behaviour for the sedentary art group compared to the physical activity group for: 1) Non-Screen time - *1/1 study* (not for parental- or teacher-reported hyperactivity/impulsivity, oppositional behaviour, moodiness, behaviour toward peers, and reputation with peers and not for teacher-reported inattention).	LOW[c]	Outcome not included
1 Cross-over Trial[d] n = 96 **No eligible reviews identified.**	No serious risk of bias	Unable to assess	No serious indirectness	No serious imprecision	None	Unfavourable measures of behavioural conduct/pro-social behaviour for the sedentary group compared to the physical activity group for: 1) Non-Screen time - *1/1 study* (only for 10-minute exercise break group).	VERY LOW[e]	

14 Longitudinal[f] n = 43,784 **No eligible reviews identified.**	Serious risk of bias[g]	No serious inconsistency	No serious indirect-ness	No serious imprecision	Dose-respons e gradient[h]	For *longitudinal findings*, higher sedentary behaviour was associated with unfavourable measures of behavioural conduct/pro-social behaviour for: 1) Screen time --*4/4 studies* (not for emotional symptoms, hyperactivity/inattention, peer relationship problems or pro-social behaviour in 1 study). 2) TV - *5/6 studies* (not for violent conviction by age 26yr in 1 study, not for emotional symptoms, hyperactivity/ inattention, peer relationship problems, or pro-social behaviour for 1 study, only in females for 1 study). 3) Video games - *6/9 studies* (not for serious or covert conduct problems in 1 study). For longitudinal findings, higher sedentary behaviour was associated with favourable measures of behavioural conduct/pro-social behaviour for: 1) Computer - *1/2 studies* (only in females for 1 study).	LOW[i]	
12 Cross-sectional[j] n = 95,287 **No eligible reviews identified.**	Serious risk of bias[k]	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	Higher sedentary behaviour was associated with unfavourable measures of behavioural conduct/pro-social behaviour for: 1) Screen time - *1/3 studies*. 2) TV - *4/6 studies* (not for withdrawn in 1 study, not for parental-reported attention problems, or antisocial personality in 1 study). 3) Computer - *3/5 studies* (not for anger in and anger control in 1 study). 4) Video game - *3/4 studies* (not for behavioural problems or attention problems in 4 to 8 and 13 to 18 yr olds in 1 study, not for parental-reported attention problems, or antisocial personality in 1 study). 5) Higher tech time - *1/1 study each* (not for behavioural problems in 4 to 8 yr olds or attention and behavioural problems for 9 to 12 yr olds).	VERY LOW[l]	

Abbreviations: ADHD = attention deficit/hyperactivity disorder; TV = television viewing.

[*]As determined by WHO
[a]Includes 1 randomized controlled trial *(245)*.
[b]It is unclear if children were engaging in sedentary time during the whole before school period and whether the art class was just replacing other sedentary time.
[c]The quality of evidence for the randomized controlled trial was downgraded to “low” from “high” due to serious indirectness and inability to assess inconsistency (1 study).
[d]Includes 1 cross-over trial *(246)*.
[e]The quality of evidence for the cross-over trial was downgraded to “very low” from “low” due to inability to assess consistency (1 study).
[f]Includes 14 longitudinal studies *(79, 232, 247-254)*; Allen et al. 2015; Roser et al. 2016; Chaelin et al. 2018; Wu et al. 2018).
[g]Apart from 2 studies *(247, 249)* information on psychometric properties of the sedentary behaviour items were not provided.
[h]A dose-response gradient was for higher TV, screen time, computer, and video games with unfavourable behavioural conduct/pro-social behaviour was observed in ~~6~~9 studies *(232, 249-253)*; Allen et al. 2015; Wu et al. 2018; Chaeli et al. 2018).
[i]The quality of evidence for the longitudinal studies was not upgraded from “low” to “moderate” due to serious risk of bias but was upgraded to “moderate” from “low” for dose-response gradient.
[i]Includes 12 cross-sectional studies *(41, 125, 236, 240, 255-262)*.
[j]Apart from 4 studies *(41, 236, 240, 260)* information on psychometric properties of the sedentary behaviour items were not provided.
[k]Two studies used the German Health Interview and Examination Survey for Children and Adolescents *(41, 262)*.
[l]The quality of evidence for cross-sectional studies was downgraded to “very low” from “low” due to serious risk of bias.

Table A.2.i. Sleep duration and quality and sedentary behaviour, children and adolescents

Questions: What is the association between **sedentary behaviour** and health-related outcomes? Is there a dose response association (total volume and the frequency, duration and intensity of interruption)? Does the association vary by type and domain of sedentary behaviour?
Population: Children aged 5-under 18 years of age
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour
Outcome: Sleep duration and quality
***Importance**: IMPORTANT

No GRADE Evidence Profiles from Australian 24-Hour Movement Guidelines for Children (5-12 years) and Young People (12-17 years)*(26)* and no systematic reviews identified by WHO.

	Quality Assessment							
No. of studies/ Study design **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(27)*
8 Longitudinal studies n = NR	Serious risk of bias[a]	No serious inconsistency	Serious indirect-tness[b]	Could not be determined [c]	None	Belmon et al. 2019 *(5)* (45 longitudinal studies; n=NR)[d]: **4/4 studies** found that more screen time was associated with shorter sleep duration and **5/5 studies** found that more TV watching was associated with shorter sleep duration. **2/2 studies** reported no association between computer use/gaming and sleep duration. **1/1 study** found no association between screen time and sleep quality or sleep timing.	VERY LOW[e]	Outcome not included

Abbreviations: NR = not reported; SB = sedentary behaviour; TV = television

[*]As determined by WHO
[a] Serious risk of bias. All included studies were rated as low quality.
[b] Serious indirectness. Measures of SB were limited to screen time and TV watching
[c] Precision unable to be determined based on data reported in review.
[d] Review included 45 total studies examining the correlates of sleep behaviour in children and adolescents. 8/45 studies examined the association between SB and sleep.
[e] The quality of evidence from longitudinal studies was not upgraded from “low” to “moderate” due to serious risk of bias and was downgraded to “very low” from “low” due to serious indirectness and inability to determine imprecision.

APPENDIX 1A. DATA EXTRACTIONS

<table>
<tr><td colspan="2">SR/MA
Citation: Bea JW, Blew RM et al. Resistance training effects on metabolic function among youth: A systematic review. Ped Exerc Sci 2017;29(3):297-315.</td></tr>
<tr><td>Purpose: To evaluate the relationship between resistance training and metabolic function in youth.</td><td rowspan="5">Abstract:
Purpose: This systematic review evaluates the relationship between resistance training and metabolic function in youth.
Methods: PubMed, Embase, Cochrane Library, Web of Science, CINAHL, and ClinicalTrials.gov were searched for articles that: (1) studied children; (2) included resistance training; (3) were randomized interventions; and (4) reported markers of metabolic function. The selected studies were analyzed using the Cochrane Risk-of-Bias Tool.
Results: Thirteen articles met inclusion criteria. Mean age ranged from 12.2–16.9 years, but most were limited to high school (N=11) and overweight/obese (N=12). Sample sizes (N= 22–304), session duration (40–60min), and intervention length (8–52 wks) varied. Exercise frequency was typically 2–3 d/wk. Resistance training was metabolically beneficial compared to control or resistance plus aerobic training in 5 studies overall and 3 out of the 4 studies with the fewest threats to bias (P≤ 0.05); each was accompanied by beneficial changes in body composition, but only one study adjusted for change in body composition.
Conclusions: Limited evidence suggests that resistance training may positively affect metabolic parameters in youth. Well-controlled resistance training interventions of varying doses are needed to definitively determine whether resistance training can mitigate metabolic dysfunction in youth and whether training benefits on metabolic parameters are independent of body composition changes.</td></tr>
<tr><td>Timeframe: Inception - 2015</td></tr>
<tr><td>Total # studies included: 13</td></tr>
<tr><td>Other details Evidence was from randomized trials only.</td></tr>
<tr><td>Outcomes addressed:
Cardiometabolic health: metabolic syndrome, insulin resistance, or any component of their definitions</td></tr>
</table>

SR/MA: Systematic review **Citation:** Belmon LS, van Stralen MM, Busch V, Harmsen IA, Chinapaw MJM. What are the determinants of children's sleep behaviour? A systematic review of longitudinal studies. Sleep Medicine Reviews 2019;43:60-70.	
Purpose: Review the longitudinal evidence on determinants of children's sleep behaviour	**Abstract:** **BACKGROUND:** Aim of the review is to systematically review the longitudinal evidence on determinants of children's sleep behaviour. **DATA SOURCES:** Systematic search of PubMed, PsychInfo and Web of Science for papers published until January 2017 with additional hand searching of papers found in reference lists. **STUDY SELECTION**: Papers were required to have a longitudinal design and include potential determinants of sleep behaviour (duration, quality and timing) and include participants aged 4-12 years of age. Papers had to be published in English. **DATA EXTRACTION**: Two independent reviewers screened all titles and abstracts. Full papers were extracted by one researcher and checked by another with discrepancies resolved by consensus. Study quality was assed using a 13-item scale devised by one of the authors. Data for each question of interest were combined to provide an overall assessment of the quality of evidence, which was interpreted as strong, moderate or insufficient to draw conclusions. **DATA SYNTHESIS:** Forty-five studies were identified and of these 12 were classed as "high quality". The team found strong evidence for child age being associated with sleep duration. There was moderate strength evidence for an association between screen-time, past sleep behaviour and a difficult temperament being potential determinants of sleep duration. There was moderate evidence for a negative association between weekend schedule and sleep timing. There was insufficient evidence for the determinants of sleep quality. **LIMITATIONS**: Study limited to healthy children. Cannot assess causation in samples. **CONCLUSIONS:** Age associated with sleep duration and some evidence that screen-time, past sleep duration and temperament associated with sleep duration. There was a lack of high quality evidence to fully assess the key research questions suggesting that more evidence is needed in this area.
Timeframe: Papers published up to Jan 2017.	
Total # studies included: 45	
Other details: The relevance of the review to the research question is unclear as it focusses on the determinants of sleep behaviours not the associations between sleep behaviour and health outcomes or health outcomes and physical activity.	
Outcomes addressed: Sleep duration, sleep quality and sleep timing.	

<table>
<tr><td colspan="2">SR/MA
Citation: Cao M, Quan M, Zhuang J. Effect of high-intensity interval training versus moderate-intensity continuous training on cardiorespiratory fitness in children and adolescents: a meta-analysis. Int J Environ Res Public Health 2019;16:1533.</td></tr>
<tr><td>Purpose: To compare the effects between high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) on cardiorespiratory fitness in children and adolescents.</td><td rowspan="5">Abstract:
Enhancing cardiorespiratory fitness (CRF) can lead to substantial health benefits. Comparisons between high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) on CRF for children and adolescents are inconsistent and inconclusive. The objective of this study
was to perform a meta-analysis to compare the effects between HIIT and MICT on CRF in children and adolescents. We searched MEDLINE, PubMed, Web of Science, and Google Scholar to identify relevant articles. The standardized mean differences (SMD) and 95% confidence intervals (95% CI)
were calculated to determine the pooled effect size of HIIT and MICT on CRF. A total of 563 subjects from 17 studies (18 effects) were identified. The pooled effect size was 0.51 (95% CI = 0.33–0.69) comparing HIIT to MICT. Moreover, intervention duration, exercise modality, work and rest ratio,
and total bouts did not significantly modify the effect of HIIT on CRF. It is concluded that compared with endurance training, HIIT has greater improvements on cardiorespiratory fitness among children and adolescents.</td></tr>
<tr><td>Timeframe: Inception – February 2019</td></tr>
<tr><td>Total # studies included: 17</td></tr>
<tr><td>Other details:
RCTs or controlled trials only.</td></tr>
<tr><td>Outcomes addressed:
Cardiorespiratory fitness</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Collins H, Fawker S et al. The effect of resistance training interventions on weight status in youth: a meta-analysis. Sports Medicine Open 2018;4:41.</td></tr>
<tr><td>Purpose: To examine the effect of resistance training interventions on weight status in youth.</td><td rowspan="5">Abstract:
Background: There has been a rise in research into obesity prevention and treatment programmes in youth, including the effectiveness of resistance-based exercise. The purpose of this meta-analysis was to examine the effect of resistance training interventions on weight status in youth.
Methods: Meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and was registered on PROSPERO (registration number CRD42016038365). Eligible studies were from English language peer-reviewed published articles. Searches were conducted in seven databases between May 2016 and June 2017. Studies were included that examined the effect of resistance training on weight status in youth, with participants of school age (5–18 years).
Results: There were 24 complete sets of data from 18 controlled trials (CTs) which explored 8 outcomes related to weight status. Significant, small effect sizes were identified for body fat% (Hedges' g = 0.215, 95% CI 0.059 to 0.371, P = 0.007) and skinfolds (Hedges' g = 0.274, 95% CI 0.066 to 0.483, P = 0.01). Effect sizes were not significant for: body mass (Hedges' g = 0.043, 95% CI − 0.103 to 0.189, P = 0.564), body mass index (Hedges' g = 0.024, 95% CI − 0.205 to 0.253, P = 0.838), fat-free mass (Hedges' g = 0.073, 95% CI − 0.169 to 0.316, P = 0.554), fat mass (Hedges' g = 0.180, 95% CI − 0.090 to 0.451, P = 0.192), lean mass (Hedges' g = 0.089, 95% CI − 0.122 to 0.301, P = 0.408) or waist circumference (Hedges' g = 0.209, 95% CI − 0.075 to 0.494, P = 0.149).
Conclusions: The results of this meta-analysis suggest that an isolated resistance training intervention may have an effect on weight status in youth. Overall, more quality research should be undertaken to investigate the impact of resistance training in youth as it could have a role to play in the treatment and prevention of obesity.</td></tr>
<tr><td>Timeframe: Inception - June 2017</td></tr>
<tr><td>Total # studies included: 18 (24 datasets)</td></tr>
<tr><td>Other details Evidence was from controlled trials only.</td></tr>
<tr><td>Outcomes addressed: Adiposity and weight status</td></tr>
</table>

SR/MA **Citation:** Eddolls WT, McNarry MA, Stratton G, Winn CO, Mackintosh KA. High-intensity interval training interventions in children and adolescents: A systematic review. Sports Medicine. 2017; 1;47(11):2363-74.	
Purpose: Assess impact of HIIT interventions on health outcomes in young people	**Abstract:** **Background**: Whilst there is increasing interest in the efficacy of high-intensity interval training in children and adolescents as a time-effective method of eliciting health benefits, there remains little consensus within the literature regarding the most effective means for delivering a high- intensity interval training intervention. Given the global health issues surrounding childhood obesity and associated health implications, the identification of effective intervention strategies is imperative. **Objectives:** The aim of this review was to examine high-intensity interval training as a means of influencing key health parameters and to elucidate the most effective high-intensity interval training protocol. **Methods:** Studies were included if they: (1) studied healthy children and/or adolescents (aged 5–18 years); (2) prescribed an intervention that was deemed high intensity; and (3) reported health-related outcome measures. **Results:** A total of 2092 studies were initially retrieved from four databases. Studies that were deemed to meet the criteria were downloaded in their entirety and independently assessed for relevance by two authors using the pre-determined criteria. From this, 13 studies were deemed suitable. This review found that high-intensity interval training in children and adolescents is a time-effective method of improving cardiovascular disease biomarkers, but evidence regarding other health-related measures is more equivocal. Running-based sessions, at an intensity of 90% heart rate maximum/100–130% maximal aerobic velocity, two to three times a week and with a minimum intervention duration of 7 weeks, elicit the greatest improvements in participant health. **Conclusion:** While high-intensity interval training improves cardiovascular disease biomarkers, and the evidence supports the effectiveness of running-based sessions, as outlined above, further recommendations as to optimal exercise duration and rest intervals remain ambiguous owing to the paucity of literature and the methodological limitations of studies presently available.
Timeframe: Inception to 09/2016	
Total # studies included: 13	
Other details (e.g. definitions used, exclusions etc): Only healthy (non-clinical) samples, and only interventional (not observational) research.	
Outcomes addressed: All were eligible. However, results only found CVD outcomes; including BMI, Blood Pressure and various biomarkers of cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood triglycerides, and insulin.	

Systematic Review **Citation:** Errisuriz VL, Golaszewski NM, Born K, Bartholomew JB. Systematic Review of Physical Education-Based Physical Activity Interventions Among Elementary School Children. J Prim Prev 2018;39(3):303–27.	
Purpose: To systematically review studies examining PE interventions designed to impact PA, fitness, and/or body composition; and to make recommendations for new research directions based upon these findings.	**Abstract:** Physical education (PE)-based interventions are a popular method to target children's physical activity (PA) and fitness; however, little is known about their effectiveness or what factors lead to successful interventions. This paper: (1) systematically reviews studies examining PE interventions designed to impact PA, fitness, and/or body composition; and (2) makes recommendations for new research directions based upon these findings. Our systematic review was limited to experimental and quasi-experimental studies conducted in elementary schools. We conducted literature searches using predetermined keywords in 3 databases, identified a total of 4964 potentially relevant studies, and screened their abstracts and full texts for eligibility. This resulted in 12 relevant studies. We used criteria established by Downs and Black (1998) to assess each study's methodological quality. PE interventions consistently showed increases in moderate-to-vigorous PA or vigorous PA during PE class but were less consistent in impacting leisure-time PA. PE interventions affected body composition differentially, depending on the assessment used (i.e., body mass index or skinfold thickness). Half of the studies assessing fitness did not show a significant impact; however, those that did were designed to influence fitness outcomes. Few studies assessed psychosocial determinants regarding PA, and no study demonstrated significant impacts on constructs other than knowledge. Interventions often contained multiple components (e.g., diet, family) implemented alongside PE interventions. Identifying effective intervention components was difficult due to lack of process evaluation. We identify the need for future research to use more objective and accurate PA measurements and adiposity, incorporate measurement of psychological constructs, expand interventions' theoretical basis, and include strong process evaluation.
Timeframe: Not reported.	
Total # studies included: 12	
Author-stated inclusion criteria: The study must have tested an intervention (i.e., a deliberate attempt to change usual teaching practice in PE) with the intention of increasing PA or fitness. Only studies utilizing experimental or quasi-experimental methods. Only elementary (or primary) schools.	
Outcomes addressed: Physical activity, physical fitness and body composition	
Populations analysed: Children, adolescents and young adults	**Author-stated funding source:** No funding source used.

<table>
<tr><td colspan="2">SR/MA
Citation: Fang K, Mu M et al. Screen time and childhood overweight/obesity: A systematic review and meta-analysis. Child Care Health Dev. 2019;45:744-753.</td></tr>
<tr><td>Purpose: To estimate the relationship between screen time and overweight/obesity in children.</td><td rowspan="5">Abstract:
Background: Controlling childhood overweight/obesity would help early prevention on children from getting chronic noncommunicable diseases, exposing to screen for long periods may increase the risk of overweight/obesity due to lack of physical activity and tend to intake too much energy, and the relationship between screen time and overweight/obesity is inconsistent. Thus, the object of the present study was to estimate the relationship between screen time and overweight/obesity in children (<18 years) by systematically review prevalence studies.
Methods: We collected data from relevant studies published up to May 2019 using predefined inclusion/exclusion criteria. And all the literatures were searched in PubMed, ScienceDirect, Embase, and Web of Science.
Results: A total of 16 studies met the criteria and were included in the meta-analysis. When compared with the screen time <2 hr/day, an increased overweight/obesity risk among children was shown in the screen time ≥2 hr/day (OR = 1.67; 95% CI [1.48, 1.88], P < .0001). The subgroup analysis showed a positive association between the different types of screen time and overweight/obesity among children.
Conclusion: Based on our study, increasing screen time could be a risk factor for being overweight/obesity in children and adolescents.</td></tr>
<tr><td>Timeframe: Inception – May 2019</td></tr>
<tr><td>Total # studies included: 16</td></tr>
<tr><td>Other details:
Evidence from cohort study, case–control or cross-sectional study designs. Screen time was categorized as <2 and ≥2 hr/day.</td></tr>
<tr><td>Outcomes addressed:
adiposity (overweight/obesity)</td></tr>
</table>

SR/MA **Citation:** Koedijk JB, Rijswijk et al. Sedentary behaviour and bone health in children, adolescents and young adults: a systematic review. *Osteoporos Int* 2017;28:2507-2519.	
Purpose: To examine the association between SB and bone health in children, adolescents and young adults.	**Abstract:** Sedentary behaviour (SB) is increasing in Western societies and some studies suggest a deleterious effect of SB on bone. The aim of this systematic review was to examine the association between SB and bone health in children, adolescents and young adults. Electronic databases (PubMed, MEDLINE, PsycINFO and Science Citation Index) were searched for relevant articles up to January 9, 2017. Studies were included when results on bone health (e.g. strength, mass and structure) and either subjectively (questionnaires) or objectively (accelerometry) measured SB were reported in healthy participants ≤24 years. Two reviewers independently screened titles and abstracts for eligibility, rated methodological quality and extracted data. Seventeen observational studies were included. Several studies that used DXA or quantitative ultrasound suggested that objectively measured SB was negatively associated with lower extremity bone outcomes, such as femoral neck bone mineral density. The magnitude of this negative association was small and independent of moderate-to-vigorous physical activity. In contrast to the lower extremities, there was insufficient evidence for an association of lumbar spine bone outcomes with objectively measured SB. In high-quality studies that used DXA, no association was observed between objectively measured SB and total body bone outcomes. In studies using questionnaires, none of these relationships were observed. Well-designed longitudinal studies, objectively measuring SB, are needed to further unravel the effect of SB, physical activity and their interaction on bone health.
Timeframe: Inception – Jan. 2019	
Total # studies included: 17	
Other details There were no restrictions placed on study design.	
Outcomes addressed: Bone health	

<table>
<tr><td colspan="2">SR/MA
Citation: Krahenbühl T, Guimarães RF et al. Bone geometry and physical activity in children and adolescents: systematic review. Rev Paul Pediatr. 2018;36(2):230-237.</td></tr>
<tr><td>Purpose: To examine the influence of physical activity and/or sports on bone geometry in children and adolescents.</td><td rowspan="5">Abstract:
Objective: To perform a systematic review on the practice of physical activity and/or sports in health and its influence on bone geometry of healthy children and adolescents.
Data source: The method used as reference was the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Databases searched for articles published from 2006 to 2016, with “Bone geometry” AND (Sport* OR Exercise* OR “Physical Activity”) as descriptors, were PubMed, BIREME/LILACS and SciELO.
Data syntheses: After the selection, 21 articles were included. Most studies stated that practice of physical activity and/or sports was beneficial for bone geometry and bone mineral density. Only two studies presented values of bone parameters for control individuals better than those of swimmers. Physical activities and sports studied were: gymnastics (n=7), rhythmic gymnastics (n=2), tennis (n=1), soccer (n=3), capoeira (n=1), swimming (n=4), cycling (n=0), jumping activities (n=2), studies relating physical activity with isokinetic peak torque (n=1), physical activity measured by questionnaire (n=4), and additional physical education classes (n=2).
Conclusions: Among the sports and physical activities found, gymnastics, soccer, and more intense physical activity assessed by questionnaires were mentioned along with better results in bone geometry compared to the absence of physical activity, whereas swimming and jumping exercises did not influence it. Therefore, sports activities with weight bearing and those practiced more frequently and intensively are beneficial for bone geometry.</td></tr>
<tr><td>Timeframe: 2006 until 2016</td></tr>
<tr><td>Total # studies included: 21</td></tr>
<tr><td>Other details:
Evidence from observational studies only (13 cross-sectional and 8 longitudinal studies).</td></tr>
<tr><td>Outcomes addressed:
Bone geometry</td></tr>
</table>

SR/MA: Systematic review	
Citation: Lee, Pope and Gao. The role of Youth Sports in promoting children's physical activity and preventing pediatric obesity: A systematic review. Behavioural Medicine 2018;44(1):62-76.	
Purpose: Examine the impact of youth sports participation on daily physical activity and paediatric obesity in children aged 6 to 19. **Timeframe:** Up to Jan 2014 **Total # studies included:** 27 **Other details** Majority of the studies used single item assessments of sports participation. Limited information about frequency, intensity etc. It is a narrative synthesis and no pooling of data across studies. Although study quality is assessed the link between study quality and interpretation is unclear. **Outcomes addressed:** Physical activity (MVPA) and obesity status which was defined as BMI, body fat percentage, and waist circumference.	**Abstract:** **BACKGROUND:** Aim of the paper was to examine the impact of youth sports participation on daily physical activity and pediatric obesity in children aged 6 to 19. **DATA SOURCES:** English-language studies in Web of Science, Academic Search Premier, Google Scholar, Pub Med, PsychInfo and ERIC were searched for studies published up to January 2014 with additional hand searching of papers found in reference lists. **STUDY SELECTION**: Studies had to include children <19 years of age and examine association between sport participation, and physical activity related outcomes [(adherence to PA guidelines, leisure time physical activity, total energy expenditure, time in MVPA and/or obesity related outcomes (BMI, body fat percentage, skinfold and or obesity related outcomes)]. Studies that combined PE with after-school sports and studies targeting participants with disabilities were excluded. **DATA EXTRACTION**: Data extracted by one reviewer and verified by another. Discrepancies resolved by consensus. Quality of study findings and methodology were assessed using a 9-item checklist that had been developed by the team. **DATA SYNTHESIS:** Twenty-seven articles were found with samples ranging from 21 to 71,854. Of the included studied 16 focused on adolescents only. A total of 17 studies examined associated between youth sport and physical activity and of these 15 showed that greater amounts and frequency of engagement in organized youth sport were associated with physical activity in youth or later in adolescence. From the 7 studies, 7 presented odds ratios to quantify the magnitude of the sports participation and PA relationship and these ranged from 17.4 (95% CI = 1.13 to 2.67) to 13.2 (95% CI = 9.4 to 18.7). In the studies that investigated the relationship of school-based sports and physical activity sports-based participants were more likely to engage in MVPA (OR = 3.21 [95% CI = 2.95 to 3.49] than non-participants. Seventeen studies examined the association between youth sports participation and obesity status with sample sizes from 21 to 12,188 and age ranges from 6 to 19 years of age. Evidence for an association between sports participation and obesity were mixed and inconsistent. **LIMITATIONS**: The majority of the studies had self-reported measures of physical activity (only 7 used accelerometers or pedometers). Most of the sport participation surveys used a single item and did not assess frequency, duration or type of participation. **CONCLUSION:** Participating in youth sports is positively associated with MVPA and there is some evidence that these associations persist into later adolescence and adulthood. There is inconsistent evidence of an association between youth sports participation and indicators of obesity related outcomes.

<table>
<tr><td colspan="2">Systematic Review
Citation: Marker C, Gnambs T, Appel M. Exploring the myth of the chubby gamer: A meta-analysis on sedentary video gaming and body mass. Soc Sci Med [Internet]. 2019 Jun 9;(September 2018):112325. Available from: https://doi.org/10.1016/j.socscimed.2019.05.030.</td></tr>
<tr><td>Purpose: To provide an estimate of the average effect size of the relationship between sedentary video gaming and body mass and to provide additional evidence on processes (i.e., displacement effect of physical activity by video gaming time)</td><td rowspan="5">Abstract:
RATIONALE: High body mass and obesity are frequently linked to the use of sedentary media, like television (TV) or non-active video games. Empirical evidence regarding video gaming, however, has been mixed, and theoretical considerations explaining a relationship between general screen time and body mass may not generalize to non-active video gaming.
OBJECTIVE: The current meta-analysis had two main goals. First, we wanted to provide an estimate of the average effect size of the relationship between sedentary video gaming and body mass. In doing so we acknowledged several context variables to gauge the stability of the average effect. Second, to provide additional evidence on processes, we tested the displacement effect of physical activity by video gaming time with the help of a meta-analytic structural equation model (MASEM).
METHOD: Published and unpublished studies were identified through keyword searches in different databases and references in relevant reports were inspected for further studies. We present a random-effects, three-level meta-analysis based on 20 studies (total N = 38,097) with 32 effect sizes.
RESULTS: The analyses revealed a small positive relationship between non-active video game use and body mass, $\hat{\rho}$=.09, 95% CI [0.03, 0.14], indicating that they shared less than 1% in variance. The studies showed significant heterogeneity, Q (31) = 593.03, $p < .001$, I2 = 95.13. Moderator analyses revealed that the relationship was more pronounced for adults, $\hat{\rho}$=.22, 95% CI [0.04, 0.40], as compared to adolescents, $\hat{\rho}$=.01, 95% CI [-0.21, 0.23], or children, $\hat{\rho}$=.09, 95% CI [-0.07, 0.25]. Meta-analytic structural equation modeling found little evidence for a displacement of physical activity through time spent on video gaming.
CONCLUSION: These results do not corroborate the assumption of a strong link between video gaming and body mass as respective associations are small and primarily observed among adults.</td></tr>
<tr><td>Timeframe: Inception – June 2018</td></tr>
<tr><td>Total # studies included: 24</td></tr>
<tr><td>Author's definition of sedentary video gaming:
The authors focus on time and frequency of video gaming only for sedentary (non-active) video games. They exclude studies focused on active video games.</td></tr>
<tr><td>Outcomes addressed: Body mass</td></tr>
<tr><td>Populations analysed: Children, adolescents and young adults</td><td>Author-stated funding source: This work was supported by the German Science Foundation (DFG) Grant AP 207/2-1 awarded to Markus Appel</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA: Systematic review
Citation: Marques A, Santos DA, Hillman CH, Sardinha LB. How does academic achievement relate to cardiorespiratory fitness, self-reported physical activity and objectively reported physical activity: a systematic review in children and adolescents aged 6-18 years. Br J Sports Med (in press).</td></tr>
<tr><td>Purpose: Review evidence of the association between objective and self-reported physical activity and cardiorespiratory fitness with academic achievement</td><td rowspan="5">Abstract:
BACKGROUND: Aim of the study was to systematically review the evidence from 2000 to 2016 of an association between objective and self-reported physical activity and cardiorespiratory fitness with academic achievement in children and adolescents.
DATA SOURCES: Systematic review of Embase, ERIC, PubMed, PsychINFO, SPORTdiscus and Web of Science. Studies published in English, Spanish or Portuguese were eligible if published from 2000 to 2016.
STUDY SELECTION: Studies had to include children or adolescents aged 6-18, had to have school grade or standardised test as an outcome and assess either self-reported or objectively assessed physical activity or cardiorespiratory fitness. Cross-sectional, longitudinal and intervention (trials) were eligible. Studies with a sample of less than 30 participants were excluded.
DATA EXTRACTION: Titles and abstracts reviewed by two assessors. Full text articles reviewed by same individuals. Discrepancies resolved by consensus. Study quality assessed using the “Quality Assessment Tool for Quantitative Studies”.
DATA SYNTHESIS: Fifty-one articles were identified and of these 41 were cross-sectional, 8 longitudinal and 2 intervention. In half of the studies the outcome variable was student marks at school and the other was standardised test scores. There were 11 studies that included objective assessments of physical activity and academic achievement. There was inconsistent evidence. There were 18 studies that used self-reported assessments of physical activity and of these 12 reported a positive association between physical activity and academic achievement. The 28 studies that assessed the relationship between cardio-respiratory fitness and academic achievement reported a general positive association with high fitness associated with higher academic achievement (but direction of causation unclear).
LIMITATIONS: Narrative synthesis. Studies were not ranked based on size. Grades from teachers are not standardised and can be open to bias making comparisons across schools challenging.
CONCLUSIONS: Overall findings support a positive association between self-reported physical activity plus cardio-respiratory fitness and academic achievement. Objectively measured physical activity was inconsistently associated with academic achievement. Physical activity DOES NOT have a detrimental effect on academic achievement.</td></tr>
<tr><td>Timeframe: 2000 to 2016</td></tr>
<tr><td>Total # studies included: 51</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Studies with less than 30 participants excluded. English, Spanish and Portuguese language studies only.</td></tr>
<tr><td>Outcomes addressed:

School grade (teacher assessed) or standardised test score.</td></tr>
</table>

SR/MA **Citation:** Martin R, Murtagh EM. Effect of active lessons on physical activity, academic, and health outcomes: a systematic review. Research Quarterly for Exercise and Sport 2017;88(2):149-68.	
Purpose: Examine the benefits of PA interventions integrated within school lessons, for learning, PA and health outcomes	**Abstract:** **Purpose:** The purpose of this study was to conduct a systematic review of classroom-based physical activity interventions that integrate academic content and assess the effectiveness of the interventions on physical activity, learning, facilitators of learning, and health outcomes. **Method:** Six electronic databases (ERIC, PubMed, Google Scholar, Science Direct, Cochrane Library, and EMBASE) and reference lists were searched for English-language articles, published January 1990 through March 2015, reporting classroom-based interventions that deliberately taught academic content using physically active teaching methods for at least 1 week duration, with physical activity, health, learning, or facilitators-of-learning outcomes. Two authors reviewed full-text articles. Data were extracted onto an Excel spreadsheet, and authors were contacted to confirm accuracy of the information presented. **Results:** Fifteen studies met the inclusion criteria. Six studies reporting on physical activity levels were found to have medium-to-large effect sizes. All 4 studies reporting learning outcomes showed positive effects of intervention lessons. Teachers and students were pleased with the programs, and enhanced on-task behaviour was identified (n = 3). Positive effects were also reported on students' body mass index levels (n = 3). **Conclusions:** Physically active academic lessons increase physical activity levels and may benefit learning and health outcomes. Both students and teachers positively received and enjoyed these teaching methods. These findings emphasize the need for such interventions to contribute toward public health policy.
Timeframe: 01/1990 – 03/2015	
Total # studies included: 15	
Other details (e.g. definitions used, exclusions etc): All classroom-based PA interventions which reported on PA outcomes, health outcomes, or learning-related outcomes.	
Outcomes addressed: Physical activity levels, Learning outcomes, Teacher and Student satisfaction with classroom-based PA, and BMI.	

<table>
<tr><td colspan="2">SR/MA
Citation: Miguel-Berges ML, Reilly JJ et al. Associations between pedometer-determined physical activity and adiposity in children and adolescents: systematic review. Clin J Sport Med. 2018;28:64-75.</td></tr>
<tr><td>Purpose: To examine the evidence on the associations between pedometer-determined physical activity and adiposity.</td><td rowspan="5">Abstract:
Objective: The present review sought to examine the evidence on the associations between pedometer-determined physical activity and adiposity. Design: Of 304 potentially eligible articles, 36 were included. A search for observational studies was carried out using Cochrane Library (CENTRAL), the OVID (MEDLINE, Embase, and PsycINFO), EBSCOhost (Sportdiscus), and PEDro database from their commencement to July 2015. Of 304 potentially eligible articles, 36 were included.
Results: Most studies (30/36; 83%) were cross sectional and all used proxies for adiposity, such as body mass index (BMI) or BMI z-score as the outcome
measure. Few studies (2/36; 6%) focused on preschool children. There was consistent evidence of negative associations between walking and adiposity; significant negative associations were observed in 72% (26/36) of studies overall.
Conclusions: The present review supports the hypothesis that higher levels of walking are protective against child and adolescent obesity. However,
prospective longitudinal studies are warranted; there is a need for more research on younger children and for more “dose-response” evidence.</td></tr>
<tr><td>Timeframe: Inception – July 2015</td></tr>
<tr><td>Total # studies included: 36</td></tr>
<tr><td>Other details:
Evidence from observational studies only (83% cross-sectional studies).</td></tr>
<tr><td>Outcomes addressed:
Adiposity</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA: Systematic review
Citation: Mohammadi S, Jalaludin MY, Su TT, Dahlui M, Mohamed MNA and Majid HA. Dietary and physical activity patterns related to cardiometabolic health among Malaysian adolescents: a systematic review. BMC Public Health 2019;19:251</td></tr>
<tr><td>Purpose: Examine the review of the associations in observational and intervention studies of the association between diet, physical activity and cardiometabolic risk factors in Malaysian adolescents.</td><td rowspan="5">Abstract:
BACKGROUND: Systematic review of the associations in observational and intervention studies of the association between diet, physical activity and cardiometabolic risk factors in Malaysian adolescents. (As diet is not related to the current research question data have not been abstracted below).
DATA SOURCES: Systematic search of PubMed, Science Direct, Cochrane Review and Web of Science until 31st August 2017.
STUDY SELECTION: Observation and intervention studies that included Malaysian adolescents age 13-18. Studies had to include physical activity (including sedentary) or diet as an outcome.
DATA EXTRACTION: Titles, abstracts and papers were independently screened by two assessors. Disagreements discussed and resolved by two further authors. Risk of bias assessed using a modified Newcastle-Ottawa scale.
DATA SYNTHESIS: Seventeen studies (16 cross-sectional and one intervention) were found. All 17 studies were classed as poor quality. Physical activity was assessed in ten studies all of which used the Physical Activity Questionnaire for Older children. Seven studies examined the link between physical activity and cardiometabolic health. Three found no evidence of associations. Three studies reported associations between physical activity and weight status, three found associations with BMI, two with percentage of body fat and one with waist circumference. Two studies reported that the mean physical activity score was higher of underweight and normal weight participants when compared to overweight and obese adolescents. There was equivocal evidence of an association between physical activity intensity and cardiometabolic health. Two studies assessed sedentary behaviour. One study reported an association between sedentary time and BMI while the other found no association.
LIMITATIONS: Self-report measures of physical activity. Poor study quality.
CONCLUSIONS: Weak evidence of an association between physical activity and indicators of cardiometabolic health (all indicators of adiposity).</td></tr>
<tr><td>Timeframe: Up to August 2017.</td></tr>
<tr><td>Total # studies included: 17</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
The bulk of the review focusses on dietary factors not summarised as out of scope.

The sample is limited to studies conducted in Malaysia.

Inconsistencies in how results are summarised (i.e. refers to objective measures when it appears ass assessments of physical activity are self-reported).</td></tr>
<tr><td>Outcomes addressed:
BMI and Body weight

Although the title talks about cardiometabolic health the outcomes are all indicators of body mass (BMI and body weight).</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Pozuelo-Carrascosa DP, Cavero-Redondo I, Herraiz-Adillo A et al. School-Based Exercise Programs and Cardiometabolic Risk Factors: A Meta-analysis. Pediatrics. 2018;142(5):e20181033</td></tr>
<tr><td>Purpose: To provide a comprehensive synthesis of the effectiveness of school-based PA
interventions on cardiometabolic risk factors in children</td><td rowspan="5">Abstract:
CONTEXT: The effects of school-based physical activity (PA) programs on different cardiometabolic risk factors and the most appropriate features of PA programs to achieve maximum effectiveness are unclear.
OBJECTIVE: To provide a comprehensive synthesis of the effectiveness of school-based PA interventions on cardiometabolic risk factors in children.
DATA SOURCES: We identified studies from database inception to February 22, 2018.
STUDY SELECTION: We selected studies that were focused on examining the effect of school-based PA interventions on cardiometabolic risk factors in children.
DATA EXTRACTION: Random-effects models were used to calculate the pooled effect size (ES) for the included cardiometabolic risk factors (waist circumference [WC], triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, systolic blood pressure and diastolic blood pressure (DBP), and fasting insulin and glucose).
RESULTS: Nineteen randomized controlled trials (which included 11 988 children aged 3–12 years) were included in the meta-analysis. School-based PA programs were associated with a significant small improvement in WC (ES = −0.14; 95% confidence interval [CI]: −0.22 to −0.07; P < .001), DBP (ES = −0.21; 95% CI: −0.42 to −0.01; P = .040), and fasting insulin (ES = −0.12; 95% CI: −0.20 to −0.04; P = .003).
LIMITATIONS: Authors of few studies described the implementation conditions of their interventions in detail, and compliance rates were lacking in most studies. In addition, results by sex were provided in a small number of studies.
CONCLUSIONS: School-based PA interventions improve some cardiometabolic risk factors in children, such as WC, DBP, and fasting insulin.</td></tr>
<tr><td>Timeframe: Inception until February 22 2018</td></tr>
<tr><td>Total # studies included: 19</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
All studies were RCT</td></tr>
<tr><td>Outcomes addressed:
Cardio-metabolic risk factors (waist circumference, triglycerides, total cholesterol, LDL cholesterol, blood pressure, insulin and glucose)</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Singh AS, Saliasi E, van den Berg V, et al. Effects of physical activity interventions on cognitive and academic performance in children and adolescents: a novel combination of a systematic review and recommendations from an expert panel. Br J Sports Med 2019;53:640-47</td></tr>
<tr><td>Purpose: To summarise the current evidence on the effects of physical activity (PA) interventions on cognitive and academic performance in children, and formulate research priorities and recommendations.</td><td rowspan="5">Abstract:
Objective To summarise the current evidence on the effects of physical activity (PA) interventions on cognitive and academic performance in children, and formulate research priorities and recommendations.
Design Systematic review (following PRISMA guidelines) with a methodological quality assessment and an international expert panel. We based the evaluation of the consistency of the scientific evidence on the findings reported in studies rated as of high methodological quality.
Data sources PubMed, PsycINFO, Cochrane Central, Web of Science, ERIC, and SPORTDiscus.
Eligibility criteria for selecting studies PA intervention studies in children with at least one cognitive or academic performance assessment.
Results Eleven (19%) of 58 included intervention studies received a high-quality rating for methodological quality: four assessed effects of PA interventions on cognitive performance, six assessed effects on academic performance, and one on both. All high-quality studies contrasted the effects of additional/adapted PA activities with regular curriculum activities. For cognitive performance 10 of 21 (48%) constructs analysed showed statistically significant beneficial intervention effects of PA, while for academic performance, 15 of 25 (60%) analyses found a significant beneficial effect of PA. Across all five studies assessing PA effects on mathematics, beneficial effects were reported in six out of seven (86%) outcomes. Experts put forward 46 research questions. The most pressing research priority cluster concerned the causality of the relationship between PA and cognitive/academic performance. The remaining clusters pertained to PA characteristics, moderators and mechanisms governing the ’PA–performance’ relationship and miscellaneous topics.
Conclusion There is currently inconclusive evidence for the beneficial effects of PA interventions on cognitive and overall academic performance in children. We conclude that there is strong evidence for beneficial effects of PA on maths performance. The expert panel confirmed that more ’high-quality’ research is warranted. By prioritising the most important research questions and formulating recommendations we aim to guide researchers in generating high-quality evidence. Our recommendations focus on adequate control groups and sample size, the use of valid and reliable measurement instruments for physical activity and cognitive performance, measurement of compliance and data analysis.</td></tr>
<tr><td>Timeframe: Until September 2017</td></tr>
<tr><td>Total # studies included: 58</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) 11 studies with high quality selected for evidence synthesis.
No adverse effects of PA on any outcome.</td></tr>
<tr><td>Outcomes addressed: At least one cognitive or academic performance</td></tr>
</table>

SR/MA **Citation:** Skrede T, Steene-Johannessen et al. The prospective association between objectively measured sedentary time, moderate-to-vigorous physical activity and cardiometabolic risk factors in youth: a systematic review and meta-analysis. *Obes Rev* 2019;20:55-74.	
Purpose: To summarize the evidence on a prospective relationship between objectively measured sedentary time, MVPA and cardiometabolic health indicators in youth.	**Abstract:** Sedentary time and moderate-to-vigorous physical activity (MVPA) may be uniquely related to cardiometabolic health. Excessive sedentary time is suggested as an independent cardiometabolic risk factor, while MVPA is favourably associated with cardiometabolic health. This systematic review and meta-analysis summarizes the evidence on a prospective relationship between objectively measured sedentary time, MVPA and cardiometabolic health indicators in youth. PubMed, Embase, CINAHL, PhyscINFO and SPORTDiscus were systematically searched from January 2000 until April 2018. Studies were included if sedentary time and physical activity were measured objectively and examined associations with body mass index, waist circumference, triglycerides, high-density lipoprotein, insulin, blood pressure or the clustering of these cardiometabolic risk factors. We identified 30 studies, of which 21 were of high quality. No evidence was found for an association between sedentary time and cardiometabolic outcomes. The association between MVPA and individual cardiometabolic risk factors was inconsistent. The meta-analysis for prospective studies found a small but significant effect size between MVPA at baseline and clustered cardiometabolic risk at follow-up (ES –0.014 [95% CI, 0.024 to 0.004]).We conclude that there is no prospective association between sedentary time and cardiometabolic health, while MVPA is beneficially associated with cardiometabolic health in youth.
Timeframe: Jan. 2000 – April 2018	
Total # studies included: 30	
Other details Evidence was from prospective studies only.	
Outcomes addressed: Cardiometabolic health	

<table>
<tr><td colspan="2">SR/MA
Citation: Stanczykiewicz B, Banik A, Knoll N et al. Sedentary behaviors and anxiety among children, adolescents and adults: a systematic review and meta-analysis. BMC Public Health. 2019;9:459</td></tr>
<tr><td>Purpose: summarize the evidence for the SB--anxiety relationship.
(1) synthesize the associations between SB and anxiety symptoms and (2) examine if SB-anxiety associations are moderated by the age group (children/adolescents vs. adults), participants’ health status (general population vs. people with a chronic physical or mental illness).</td><td rowspan="5">Abstract:
Background: Although the number of studies examining the relationships between sedentary behaviors (SB) and anxiety is growing, an overarching evidence, taking into account children, adolescents, and adults as well as different types of SB and different categories of anxiety outcomes, is still missing. Thus, this systematic review and meta-analysis aimed at obtaining a comprehensive overview of existing evidence.
Methods: A search in the following databases: PsycINFO, PsycARTICLES, Academic Search Complete, ERIC, HealthSource: Nursing/Academic Edition and MEDLINE, resulted in k = 31 original studies included in the systematic review (total N = 99,192) and k = 17 (total N = 27,443) included in the meta-analysis. Main inclusion criteria referred to testing the SB--anxiety relationship, the quality score (above the threshold of 65%), and the language of publications English). The study was following the PRISMA statement and was registered at PROSPERO (CRD42017068517).
Results: Both the systematic review and meta-analysis indicated that overall average effects were small: higher levels of symptoms of anxiety were associated with higher levels of SB (weighted r = .093, 95% CI [.055, .130], p < .001). Moderator analyses indicated that trends for stronger effects were observed among adults, compared to children/ adolescents (p = .085).
Conclusions: Further longitudinal studies are necessary to elucidate the predictive direction of the anxiety—SB relationship and to clarify whether the effects depend on the type of anxiety indicators.</td></tr>
<tr><td>Timeframe:</td></tr>
<tr><td>Total # studies included: 31</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Most studies were x-sectional. Seven prospective and 3 RCT included</td></tr>
<tr><td>Outcomes addressed:
Anxiety</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Verswijveren SJMM, Lamb KE, Bell LA et al. Associations between activity patterns and
cardio-metabolic risk factors in children and adolescents: A systematic review. PLOS One 2018; 13(8): e0201947.</td></tr>
<tr><td>Purpose: To synthesise the evidence concerning associations between activity patterns and cardio-metabolic risk factors in children and adolescents aged 5±19 years.</td><td rowspan="5">Abstract:
Introduction
Total volumes of physical activity and sedentary behaviour have been associated with cardio-metabolic risk profiles; however, little research has examined whether patterns of activity (e.g., prolonged bouts, frequency of breaks in sitting) impact cardio-metabolic risk. The aim of this review was to synthesise the evidence concerning associations between activity patterns and cardio-metabolic risk factors in children and adolescents aged 5±19 years.
Materials and methods
A systematic search of seven databases was completed in October 2017. Included studies were required to report associations between objectively-measured activity patterns and cardio-metabolic risk factors in children and/or adolescents, and be published between 1980 and 2017. At least two researchers independently screened each study, extracted data, and undertook risk of bias assessments.
Results
From the 15,947 articles identified, 29 were included in this review. Twenty-four studies were observational (cross-sectional and/or longitudinal); five were experimental. Ten studies examined physical activity patterns, whilst 19 studies examined sedentary patterns. Only one study examined both physical activity and sedentary time patterns. Considerable variation in definitions of activity patterns made it impossible to identify which activity patterns were most beneficial to children's and adolescents' cardio-metabolic health. However, potential insights and current research gaps were identified.
Discussion and conclusion
A consensus on how to define activity patterns is needed in order to determine which activity patterns are associated with children's and adolescents' cardio-metabolic risk. This will inform future research on the impact of activity patterns on children's and adolescents' short- and longer-term health.</td></tr>
<tr><td>Timeframe: 1980 to 2017</td></tr>
<tr><td>Total # studies included: 29</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Device-measured PA and sedentary patterns. 24 observational (76% x-sectional) and five interventions</td></tr>
<tr><td>Outcomes addressed:
Cardio-metabolic risk factors (i.e., adiposity, blood lipids, inflammatory biomarkers, endothelial function biomarkers, blood glucose, vascular health, fitness, or summary cardio-metabolic scores)</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-Analysis
Citation: Xue Y, Yang Y, Huang T. Effects of chronic exercise interventions on executive function among children and adolescents: a systematic review with meta-analysis. Br J Sports Med. 2019 Feb 8;(1):1–9.</td></tr>
<tr><td>Purpose: To synthesise randomised controlled trials (RCTs) regarding the effects of chronic exercise interventions on different domain-specific executive functions (EFs) among children and adolescents.</td><td rowspan="5">Abstract:
OBJECTIVE: To synthesise randomised controlled trials (RCTs) regarding the effects of chronic exercise interventions on different domain-specific executive functions (EFs) among children and adolescents.
DESIGN: Systematic review with meta-analysis.
DATA SOURCES: PsycINFO, PubMed, SPORTDiscus, Academic Search Premier, Embase and Web of Science were searched.
ELIGIBILITY CRITERIA FOR SELECTING STUDIES: RCTs or cluster RCT design, which employ chronic exercise interventions and target healthy children (age 6-12 years) and adolescents (age 13-17 years). We defined chronic exercise as physical activity (PA) which consists of multiple exercise sessions per week and lasts for an extended period of time (typically over 6 weeks).
RESULTS: We included 19 studies, with a total of 5038 participants. The results showed that chronic exercise interventions improved overall EFs (standardised mean difference (SMD)=0.20, 95% CI 0.09 to 0.30, $p<0.05$) and inhibitory control (SMD=0.26, 95% CI 0.08 to 0.45, $P<0.05$). In meta regression, higher body mass index was associated with greater improvements in overall EFs performance (β=0.03, 95% CI 0.0002 to 0.06, $p<0.05$), whereas age and exercise duration were not. In subgroup analysis by intervention modality, sports and PA programme (SMD=0.21, 95% CI 0.12 to 0.31, $p<0.05$) and curricular PA (SMD=0.39, 95% CI 0.08 to 0.69, $p<0.05$) improved overall EFs performance, but integrated PA did not (SMD=0.02, 95% CI -0.05 to 0.09, $p>0.05$). Interventions with a session length < 90 minutes improved overall EFs performance (SMD=0.24, 95%CI 0.10 to 0.39, $p=0.02$), but session length ≥ 90 minutes did not (SMD=0.05, 95%CI -0.03 to 0.14). No other moderator was found to have an effect.
CONCLUSIONS: Despite small effect sizes, chronic exercise interventions, implemented in curricular or sports and PA programme settings, might be a promising way to promote multiple aspects of executive functions, especially inhibitory control.</td></tr>
<tr><td>Timeframe: Not reported.</td></tr>
<tr><td>Total # studies included: 19</td></tr>
<tr><td>Author’s Definition of chronic exercise:
Physical activity which consists of multiple exercise sessions per week and lasts for an extended period of time (typically over 6 weeks).</td></tr>
<tr><td>Outcomes addressed:
Executive function (i.e., cognition flexibility, inhibitory control, working memory and planning)</td></tr>
<tr><td>Populations analysed:
children and adolescents</td><td>Author-stated funding source: TH was supported by Shanghai Pujiang Program (16PJC052) and the research project from General Administration of Sport of China (2017B044).</td></tr>
</table>

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B1: EVIDENCE ON PHYSICAL ACTIVITY FOR ADULTS (18 TO UNDER 65 YEARS OF AGE)

Guiding Questions

B1. What is the association between **physical activity** and health-related outcomes?

a. Is there a dose response association (volume, duration, frequency, intensity)?
b. Does the association vary by type or domain of physical activity?

Inclusion Criteria

Population: Adults 18 years of age and older
Exposure: Greater volume, duration, frequency or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity.

Outcomes	Importance
All-cause and cause-specific mortality	Critical
Incidence of CVD	Critical
Incidence of cancer	Critical
Incidence of Type 2 Diabetes	Critical
Adiposity/Prevention of weight gain/Body composition	Critical
Mental health outcomes (e.g. depressive symptoms, anxiety symptoms)	Critical
Cognitive outcomes (e.g. dementia, cognition)	Critical
Adverse events	Critical
Sleep duration and quality	Important
Incidence of hypertension	Important
Health-related quality of life	Important

Abbreviations: CVD = cardiovascular disease; NA = not applicable; PA = physical activity

Evidence identified

Seventy-five reviews (published from 2017 to 2019) were initially identified that examined the association between physical activity and health-related outcomes among adults *(1-75)*. However, 35 reviews were excluded from further evaluation given the study design, populations, exposures, or outcomes that were out-of-scope or other concerns regarding the quality or relevance of the review. **Table B1.1** presents the reviews that were excluded and their reason for exclusion.

Table B1.2 presents the ratings for each remaining review according to all the AMSTAR 2 main domains. In general, the included reviews had many limitations in their design, execution, and reporting. Only two systematic reviews were rated as having high credibility based on the AMSTAR 2 instrument. Fifteen were rated as having moderate credibility, 11 were rated as having low credibility, and the remaining 9 were rated as having critically low credibility. Given concerns regarding the comprehensiveness and the validity of the results presented in reviews rated as having critically low credibility, they were not incorporated into the final Evidence Profiles. All 3 pooled cohort studies were rated as good quality according to the Newcastle-Ottawa Scale (**Table B1.3**).

Table B1.4 lists the 28 reviews and 3 pooled cohort studies that were included in the evidence profiles by outcome. Most of the included reviews searched for evidence through 2016 or 2017; very few reviews searched for evidence into 2018 or 2019. As a result, very few individual studies represented within the reviews were published in 2018 or 2019. Most reviews had narrow foci in terms of study designs, exposures (limited to specific types of physical activity), and outcomes. Extracted data for each included review is presented in **Appendix 2.**

Table B1.1. Excluded Systematic Reviews, with Reasons for Exclusion

Author, Year	Reason for Exclusion	Rationale
Al Tunaiji 2019 *(1)*	Design	Includes no studies published after 2017
Amirfaiz 2019 *(3)*	Outcome	Outcome (metabolic syndrome) out of scope
Banno 2018 *(5)*	Population	Review limited to persons with insomnia; not generalizable
Coenen 2018 *(16)*	Exposure	Occupational physical activity
Colpani 2018 *(17)*	Exposure	Any lifestyle factor, not physical activity independently
Del Pozo-Cruz 2018 *(18)*	Exposure	Replacing sedentary time
Fernandes 2018 *(22)*	Exposure	Acute exercise only
Flahr 2018 *(23)*	Population	Review limited to studies of shift workers; not generalizable
Fuezeki 2017 *(24)*	Design	Analysis of NHANES data only
Guo 2017 *(27)*	Exposure	Any cardiovascular health metric
Halloway 2017 *(28)*	Outcome	MRI brain imaging
Herold 2019 *(30)*	Outcome	Required measures of functional or structural brain changes
Hussenoeder 2018 *(32)*	Design	Overview-of-reviews
Igarashi 2018a *(33)*	Outcome	Continuous blood pressure
Igarashi 2018b *(34)*	Outcome	Continuous blood pressure
Jiang 2017 *(35)*	Population	Review limited to persons with insomnia; not generalizable
Lewis 2018 *(37)*	Outcome	Outcome (zeitebers/circadian system time cues) out of scope
Lipnicki 2019 *(38)*	Design	Not a systematic review
Liu 2018 *(40)*	Design	Pooled data from Asia consortium; study is included in the review by Blond *(11)*
Lopez-Valenciano 2019 *(41)*	Outcome	Continuous blood pressure
Loprinzi 2018a *(44)*	Exercise	Acute exercise
Loprinzi 2018c *(42)*	Population	Most studies conducted with rodents
Lowe 2019 *(45)*	Population	Review limited to persons with insomnia; not generalizable
Murphy 2019 *(48)*	Outcome	Continuous blood pressure

Nordengen 2019 *(49)*	Outcome	Continuous blood pressure
Oja 2018 *(52)*	Outcome	Continuous blood pressure
Origua Rios 2017 *(53)*	Outcome	Results not presented by study nor in format amendable to GRADE evaluation
Prince 2019 *(56)*	Relevance	Aim is to examine the prevalence of different types of PA according to various occupational types
Shepherd-Banigan 2017 *(62)*	Relevance	Only 3 new trials identified that examined the effects of yoga on the incidence of hot flashes among peri- and post-menopausal women
Smart 2019 *(64)*	Outcome	Continuous blood pressure
Stringhini 2017 *(67)*	Design	Not a systematic review
Viana 2019 *(71)*	Quality	Statement of concern published by journal to alert readers of uncertainty about the weight and significance reported by authors
Wang 2019 *(72)*	Population	Review limited to persons with active sleep disturbances or insomnia; not generalizable
Wewege 2018 *(74)*	Redundancy	Review by Andreato 2018 is more recent, more comprehensive, and better quality and includes all included studies by Wewege; similar results were found with both reviews.
Zhang 2018 *(75)*	Outcome	Continuous blood pressure

Table B1.2. Credibility Ratings (based on AMSTAR 2 *(76)*)

Author, Year	PICO[1]	Apriori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Amagasa 2018 *(2)*	Y	Y	N	PY	N	Y	PY	Y	N	N	N/A	N/A	N	Y	N/A	Y	**Low**
Andreato 2019 *(4)*	Y	PY	N	PY	Y	Y	PY	Y	Y	N	Y	N	Y	Y	N	Y	**Moderate**
Barredo 2017 *(6)*	N	N	N	N	N	Y	N	N	PY	N	N/A	N/A	N	N	N/A	N	**Critically Low**
Baumeister 2019 *(7)*	Y	N	N	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Behrens 2019 *(8)*	Y	PY	N	PY	Y	Y	PY	PY	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**
Benke 2018 *(9)*	Y	PY	N	PY	N	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Binkley 2019 *(10)*	N	N	N	N	N	N	N	Y	Y	N	N/A	N/A	N	N	N/A	N	**Critically Low**
Blond 2019 *(11)*	Y	PY	N	PY	Y	N	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Boyer 2019 *(12)*	Y	N	N	N	N	N	N	Y	Y	N	Y	Y	Y	N	Y	N	**Low**
Brasure 2018 *(13)*	Y	Y	Y	PY	Y	Y	Y	Y	Y	N	N/A	N/A	Y	Y	N/A	Y	**High**
Chastin 2019 *(14)*	Y	Y	Y	PY	Y	Y	N	Y	PY	N	Y	Y	N	N	Y	Y	**Moderate**
Cocchiara 2019 *(15)*	N	N	N	PY	Y	Y	N	N	Y	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Dinu 2019 *(19)*	Y	N	N	PY	Y	Y	PY	PY	Y	N	N	Y	Y	Y	N	Y	**Low**
Ekelund 2019 *(20)*	Y	PY	N	PY	N	Y	PY	Y	Y	N	Y	N	N	N	Y	Y	**Moderate**
Engeroff 2018 *(21)*	Y	N	N	PY	Y	Y	PY	Y	PY	N	N/A	N/A	Y	N	N/A	Y	**Moderate**
Gordon 2017 *(26)*	Y	PY	N	PY	N	N	PY	PY	PY	N	Y	Y	Y	Y	Y	Y	**Low**
Gordon 2018 *(25)*	Y	PY	N	PY	N	Y	N	PY	PY	N	Y	Y	Y	Y	Y	N	**Low**
Hart 2019 *(29)*	Y	N	N	N	Y	Y	N	PY	PY	N	Y	Y	Y	Y	Y	Y	**Critically Low**
Hidayat 2019 *(31)*	Y	PY	N	PY	Y	Y	PY	N	N	N	Y	N	N	Y	Y	Y	**Critically Low**
Kovacevic 2018 *(36)*	Y	PY	N	Y	Y	N	PY	Y	PY	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Liu 2019 *(39)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	N	**Moderate**
Loprinzi 2018 *(43)*	Y	N	N	PY	N	N	N	PY	N	N	N/A	N/A	N	Y	N/A	Y	**Critically Low**
Maillard 2018 *(46)*	N	N	N	PY	N	N	PY	N	N	N	N	N	N	Y	N	Y	**Critically Low**

Author, Year	PICO[1]	Apriori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Martinez-Dominguez 2018 *(47)*	Y	PY	N	PY	N	N	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Northey 2018 *(50)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Paudel 2019 *(54)*	Y	Y	N	PY	Y	Y	PY	PY	PY	N	N	Y	Y	Y	Y	Y	**Low**
Perez-Lopez 2017 *(55)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	Y	N	N	Y	Y	Y	**Moderate**
Rathore 2017 *(57)*	Y	N	Y	PY	N	N	N	Y	Y	N	Y	Y	Y	Y	N	Y	**Low**
Robbins 2019 *(58)*	Y	PY	N	PY	Y	Y	PY	PY	PY	N	N/A	N/A	N	Y	N/A	Y	**Low**
Saeidifard 2019 *(59)*	Y	N	N	PY	Y	Y	PY	Y	Y	N	N	N	N	N	N	Y	**Critically Low**
Schuch 2018 *(61)*	Y	PY	Y	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	**High**
Schuch 2019 *(60)*	Y	PY	Y	PY	Y	Y	Y	Y	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**
Stanmore 2017 *(66)*	Y	N	N	PY	Y	N	N	Y	Y	N	Y	Y	Y	Y	Y	Y	**Low**
Stutz 2019 *(68)*	Y	PY	N	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Su 2019 *(69)*	Y	PY	N	PY	Y	N	PY	PY	N	N	Y	N	N	Y	Y	Y	**Critically Low**
Sultana 2019 *(70)*	Y	N	N	PY	Y	Y	N	Y	PY	N	Y	N	Y	Y	Y	Y	**Low**
Wang 2017 *(73)*	Y	N	Y	PY	N	Y	N	Y	Y	N	Y	N	Y	Y	N	N	**Low**

Abbreviations: COI = conflict of interest; N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.

Table B1.3. Quality Ratings of Included Pooled Cohort Studies (based on Newcastle-Ottawa scale *(77)*)

Author, Year	Represen-tativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertain-ment of exposure	Outcome of interest was not present at start of study	**Bias in selection of the exposed cohort**	Comparability of cohorts on the basis of the design or analysis	**Bias due to con-founding**	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow-up of cohorts	**Bias due to outcome ascertain-ment**	Quality Rating
O'Donovan 2017 *(51)*	Truly representative of the target populations of the corresponding countries	Drawn from the same community as the exposed cohort	Structured interview	Yes	**Low**	Controlled foo age, sex, smoking, total cholesterol, SBP, BMI, longstanding illness, and SES	**Low**	Record linkage	Yes	No statement	**Low**	Good
Siahpush 2019 *(63)*	Truly representative of the civilian noninstitutional population of the US	Drawn from the same community as the exposed cohort	Structured interview	Yes	**Low**	Controlled for BMI, alcohol consumption, presence of chronic condition, sex, age, poverty status, education, home ownership, marital status, race/ethnicity, nativity, and survey year	**Low**	Record linkage	Yes	Subjects lost to follow up unlikely to introduce bias	**Low**	Good
Stamatakis 2017 *(65)*	Truly representative of the target populations of the corresponding countries	Drawn from the same community as the exposed cohort	Structured interview	Yes	**Low**	Analysis controlled for BMI, age, educational attainment, presence of long-standing illness, weekly frequency of alcohol consumption, smoking habits, psychological distress/depression, number of servings	**Low**	Record linkage	Yes	No statement	**Low**	Good

						of fruit and vegetables						

Table B1.4. Systematic Reviews Assessed, by Author

	Outcomes												
Author, Year	**All-cause mortality**	**CVD mortality**	**Incidence of CVD**	**Incidence of cancer**	**Incidence of Type 2 Diabetes**	**Adiposity-related outcomes**	**Mental health-related outcomes**	**Cognitive function**	**Sleep**	**Incidence of HYP**	**Health-related QOL**	**Last Search Date**	**Credibility/ Quality**
Amagasa 2018 *(2)*	X					X	X	X				Jan-2017	Low
Andreato 2019 *(4)*						X						May-2018	Moderate
Barredo 2017 *(6)*											X	Nov-2015	Critically Low
Baumeister 2019 *(7)*				X								Aug-2018	Moderate
Behrens 2019 *(8)*				X								Mar-2018	Moderate
Benke 2018 *(9)*				X								July-2017	Moderate
Binkley 2019 *(10)*						X					X	Jan-2015	Critically Low
Blond 2019 *(11)*	X	X										Mar-2019	Moderate
Boyer 2019 *(12)*					X							Jun-2016	Low
Brasure 2018 *(13)*								X				Jul-2017	High
Chastin 2019 *(14)*	X					X						Feb-2018	Moderate
Cocchiara 2019 *(15)*							X		X			Feb-2017	Critically Low
Dinu 2019 *(19)*	X	X	X		X							Feb-2018	Low
Ekelund 2019 *(20)*	X											Jul-2018	Moderate
Engeroff 2018 *(21)*								X				Nov-2017	Moderate
Gordon 2017 *(26)*							X					Feb-2017	Low
Gordon 2018 *(25)*							X					Aug-2017	Low

Hart 2019 *(29)*											X	Dec-2017	Critically Low
Hidayat 2019 *(31)*												Jul-2018	Critically Low
Kovacevic 2018 *(36)*									X			Jun-2016	Moderate
Liu 2019 *(39)*												Aug-2018	Moderate
Loprinzi 2018 *(43)*								X				Sep-2017	Critically Low
Maillard 2018 *(46)*						X						Jul-2017	Critically Low
Martinez-Dominguez 2018 *(47)*							X					Jul-2017	Moderate
	Outcomes												
Author, Year	**All-cause mortality**	**CVD mortality**	**Incidence of CVD**	**Incidence of cancer**	**Incidence of Type 2 Diabetes**	**Adiposity-related outcomes**	**Mental health-related outcomes**	**Cognitive function**	**Sleep**	**Incidence of HYP**	**Health-related QOL**	**Last Search Date**	**Credibility/ Quality**
Northey 2018 *(50)*								X				Nov-2016	Moderate
O'Donovan 2017[a] *(51)*	X	X										NA	Good quality
Paudel 2019 *(54)*					X	X				X		Mar-2018	Low
Perez-Lopez 2017 *(55)*							X		X		X	Jun-2017	Low
Rathore 2017 *(57)*								X				Dec-2016	Low
Robbins 2019 *(58)*									X			Sep-2018	Low
Saeidifard 2019 *(59)*	X	X	X									Sep-2017	Critically Low
Schuch 2018 *(61)*							X					Oct-2017	High
Schuch 2019 *(60)*							X					Oct-2018	Moderate
Siahpush 2019[a] *(63)*	X	X										NA	Good quality

Stamatakis 2017[a] *(65)*	X	X									NA	Good quality
Stanmore 2017 *(66)*							X				Jan-2017	Low
Stutz 2019 *(68)*								X			Jun-2017	Moderate
Su 2019 *(69)*					X						Jul-2018	Critically Low
Sultana 2019 *(70)*					X						Jun-2019	Low
Wang 2017 *(73)*										X	Jan-2015	Low

[a] Not a systematic review. Pooled cohort analysis.

B. ADULTS

B.1. Physical Activity

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: Adults 18 years of age and older
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity

Table B.1.a. All-cause mortality: Association between physical activity and all-cause mortality among adults (in alphabetical order by author)

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**
		Risk of bias	**Inconsistency**	**Indirectness†**	**Imprecis-ion**	**Other**		
Amagasa 2018 *(2)* Low	4 cohort studies N=17,133	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	All four cohort studies used data from NHANES 2003 to 2004 and 2005 to 2006; age range 50 to 80 years and compared replacing SB with LPA (3/4 studies) or quintiles of LPA (1/4 study). 3/4 studies reported **replacing 30-60 min of SB with LPA** was associated with lower **all-cause mortality** risk after adjustment for MVPA (HR range, 0.80 to 0.88 [95% CI range, 0.73 to 0.92]). 1/4 only found an effect among women with low MVPA when comparing modest to high levels of LPA vs. very low LPA.	MODERATE[a]

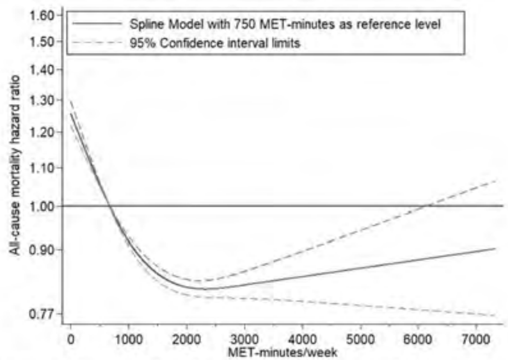
Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness†	Impreci-sion	Other		
Blond 2019 *(11)* Moderate	48 prospective cohort studies N=NR	No serious risk of bias	Serious inconsistency	No serious indirect-ness	No serious imprecision	Dose--response relationship	Five studies used accelerometers to measure PA while all other studies used self-reported PA. Eight measures included occupational PA. Most studies focused on MVPA or leisure-time PA. A curvilinear relationship was found between **<u>total PA</u>** and **all-cause mortality** (*p* non-linearity <0.001). Compared with 750 MET min/week, those participating in 2000 MET min/week (4 hrs/week) had a statistically significantly lower risk of all-cause mortality (HR = 0.82 [95% CI, 0.81 to 0.84]) with an ARD = -16 deaths per 10,000 person years [95% CI, -17 to -14 deaths). Other comparisons presented below.  Figure 2 Dose–response relationship between physical activity and all cause mortality. Dose–response relation between metabolic equivalent of task (MET) min/week (with 750 MET min/week as the reference) and mortality risk estimated with restricted cubic spline regression and generalised least square trend estimation for summarised dose–response data.	MODERATE[b]

Table 1 Mortality HRs with 750 metabolic equivalent of task (MET) min/week as reference and estimated absolute rate differences per 10 000 person years

MET min/week		0	500	1000	2000	3000	4000	5000	6000
Running (5 mph)[*]		0 hour/week	1 hour/week	2 hours/week	4 hours/week	6 hours/week	8 hours/week	10 hours/week	12 hours/week
All cause mortality	Studies	30	35	33	34	17	5	2	3
	Participants[†]	812 489	984 339	358 878	465 615	225 616	78 220	4436	97 856
	PY[†]	10 324 343	9 532 179	4 007 856	5 235 839	1 910 230	689 649	65 073	48,6671
	Total cases[†]	47 141	104 927	36 201	43 861	12 342	3684	246	2962
	HR (95% CI)	1.26 (1.22 to 1.29)	1.06 (1.05 to 1.06)	0.92 (0.91 to 0.93)	0.82 (0.81 to 0.84)	0.83 (0.80 to 0.85)	0.84 (0.79 to 0.90)	0.86 (0.78 to 0.94)	0.88 (0.78 to 0.99)
	ARD (95% CI)[‡]	23 (19 to 25)	5 (4 to 5)	−7 (−8 to −6)	−16 (−17 to −14)	−15 (−18 to −13)	−14 (−18 to −8)	−12 (−19 to −5)	−11 (−19 to −1)

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness†	Imprecision	Other		
Chastin 2019 *(14)* Moderate	12 prospective cohort studies N=127,724	No serious risk of bias	Serious inconsistency	Serious indirect-ness	No serious imprecision	None	Studies compared **high vs. low levels of physical activity** (as defined by each study, and inconsistent between studies). Of the 5/12 prospective cohort studies that were pooled two studies used self-report of light PA whereas 3 studies used accelerometer-measured light PA. Light PA was defined variably including 100-2019 counts/min, 100-1040 counts/min, using Freedson cutpoints, MET>1.5 – 2.99, or self-report light activity (e.g., very easy). Most studies were among adults ≥50 years. A pooled analysis of 5 studies reporting all-cause mortality found a statistically significant reduced risk of **all-cause mortality** for the highest vs. lowest levels of **light intensity physical activity** (HR = 0.71 [95% CI 0.62 to 0.83], 5 studies).	LOW[c]
Dinu 2019 *(19)* Low	11 prospective cohort studies N=231,259	No serious risk of bias	Serious inconsistency	Serious indirect-ness	No serious imprecision	None	All studies evaluated the effects of **active commuting** (cycling 5 studies, walking 3 studies, mixed mode 3 studies) on health outcomes. Exposure levels of active commuting were variably reported as minutes spent walking or cycling for transportation per day, as dichotomized variables (yes or no), or as METs with the reference category as no active commuting in most studies. Follow-up ranged from 4 to 25 years. Persons engaged in **active commuting** had a significantly lower risk of **all-cause mortality** compared with those participating in no active commuting (RR = 0.92 [95% CI 0.85 to 0.98], 11 studies). When the 3 studies that had the largest estimates of effects were removed from the analysis, the heterogeneity was reduced (I^2 of 67% to 11%) and the direction of effect changed (RR = 1.00 [95% CI, 0.96 and 1.04], 8 studies).	LOW[d]

<table>
<tr><th rowspan="2">Systematic review evidence

Review credibility</th><th rowspan="2">No. of studies/ Study design

No. of participants</th><th colspan="5">Quality Assessment</th><th rowspan="2">Description of evidence

Summary of findings</th><th rowspan="2">Certainty</th></tr>
<tr><th>Risk of bias</th><th>Inconsistency</th><th>Indirectness†</th><th>Imprecision</th><th>Other</th></tr>
<tr><td>Ekelund 2019 (20)

Moderate</td><td>8 prospective cohort studies

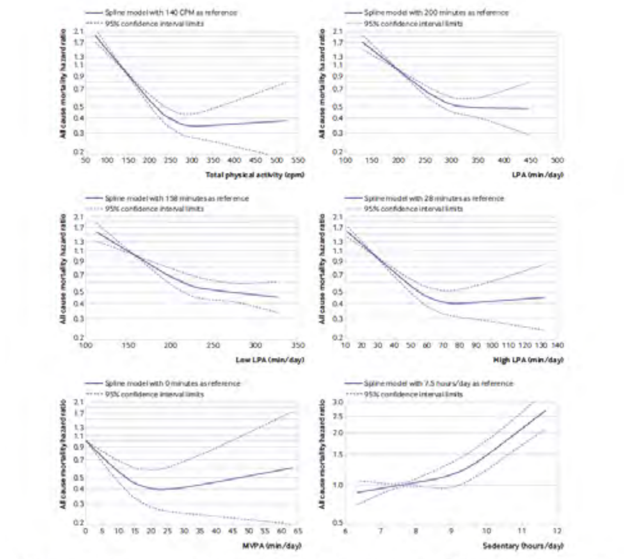
N=36,383</td><td>No serious risk of bias</td><td>No serious inconsistency</td><td>No serious indirect-ness</td><td>No serious imprecision</td><td>Dose--response relationship</td><td>Harmonized meta-analysis from eight prospective cohort studies, including data from 3 large surveillance systems and 2 from unpublished data. Mean age in studies was 63 years with median follow-up of 5.8 years (range 3 to 14.5 years). All 8 studies used accelerometers to measure PA and SB; exposure variables differed within each study including total volume of PA (cpm), min/day spend in intensity-specific variables (sedentary <u><</u>100 cpm, light 101-1951 cpm, moderate to vigorous <u>></u>1952 cpm, vigorous <u>></u>5725 cpm), bouts of MVPA (10 or more minutes of consecutive readings <u>></u>1952 cpm). Data was categorized into quartiles with the least active quartile as the referent.

Compared with the lowest levels of PA, <u>any level of PA regardless of intensity</u> (i.e., total PA) was associated with a lower risk of mortality. The magnitude of risk for increasing quarter of total PA was least active (referent, 1.00), 2^{nd} quarter (adjusted HR = 0.48 [95% CI, 0.43 to 0.54]), 3^{rd} quarter (adjusted HR = 0.34 [95% CI, 0.26 to 0.45]), and 4^{th} quarter (adjusted HR = 0.27 [95% CI, 0.23 to 0.32]). Higher levels of <u>light intensity PA, low light intensity PA, and high light intensity PA</u> were also significantly associated with reduced risk of death during follow-up as was <u>MVPA</u> (including when controlling for SB time) (table below).

Table 2 | Meta-analysis for associations between total physical activity, intensities of physical activity or sedentary time by quarters and all cause mortality
<table>
<tr><th rowspan="2">Variables</th><th colspan="4">Hazard ratios (95% CI) for all cause mortality*; No of participants; No of deaths</th></tr>
<tr><th>First quarter (least active)</th><th>Second quarter</th><th>Third quarter</th><th>Fourth quarter (most active)</th></tr>
<tr><td>Model B†</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Total physical activity (cpm)</td><td>1 (ref) (n=9096; 1187)</td><td>0.48 (0.43 to 0.54) (n=9105, 483)</td><td>0.34 (0.26 to 0.45) (n=9096, 265)</td><td>0.27 (0.23 to 0.32) (n=9086, 214)</td></tr>
<tr><td>Physical activity intensity</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Light (min/d)</td><td>1 (ref) (n=9073; 1089)</td><td>0.60 (0.54 to 0.68) (n=9101; 511)</td><td>0.44 (0.38 to 0.51) (n=9090; 320)</td><td>0.38 (0.28 to 0.51) (n=9119; 229)</td></tr>
<tr><td>Low light (min/d)</td><td>1 (ref) (n=9066; 1010)</td><td>0.66 (0.56 to 0.77) (n=9106; 518)</td><td>0.47 (0.38 to 0.58) (n=9112; 353)</td><td>0.42 (0.34 to 0.52) (n=9099; 268)</td></tr>
<tr><td>High light (min/d)</td><td>1 (ref) (n=9054; 1159)</td><td>0.55 (0.49 to 0.63) (n=9120; 483)</td><td>0.38 (0.30 to 0.48) (n=9088; 278)</td><td>0.37 (0.32 to 0.46) (n=9113; 229)</td></tr>
<tr><td>Moderate to vigorous (min/d)</td><td>1 (ref) (n=9002; 1139)</td><td>0.64 (0.55 to 0.74) (n=9153; 468)</td><td>0.55 (0.40 to 0.74) (n=9123; 305)</td><td>0.52 (0.43 to 0.61) (n=9105; 237)</td></tr>
<tr><td>Sedentary (min/d)</td><td>1 (ref) (n=9102; 327)</td><td>1.28 (1.09 to 1.51) n=9105; 417)</td><td>1.71 (1.36 to 2.15) (n=9096; 562)</td><td>2.63 (1.94 to 3.56) (n=9080; 843)</td></tr>
</table>
cpm=counts per minute.
Model A adjusted for sex (when applicable), age, and wear time (n=36852, 2304 deaths). Model B adjusted for sex (when applicable), age, body mass index, socioeconomic position, and wear time (n=36383, 2149 deaths). Model C additionally adjusted for covariates listed in table 1 (n=35932, 2047 deaths).
*By Cox regression.
†Moderate-to-vigorous physical activity and sedentary time are mutually adjusted.

Differences in min/day between the referent (least active) and 2^{nd} quarter were broadly equal to 60 min/day of light intensity PA, 35 min/day of low light intensity PA, 25 min/day of high light intensity PA, and 5 min/day of MPVA.

A non-linear, dose-response association was found between all exposure variables and mortality (p<0.02 for all exposure variables) (figure below). The maximal risk reduction for total PA was observed at about 300 cpm (adjusted HR = 0.34 [95% CI 0.27 to 0.43]). Maximal risk reductions for light intensity PA was ~375 min/day, low light intensity PA at ~325 min/day, high light intensity PA at ~80 min/day, and MVPA at ~24 min/day. No further risk reductions occurred with higher levels of activity except for low light intensity PA where the risk appeared to reduce further.</td><td>HIGH[e]</td></tr>
</table>

							 Fig 2 | Dose-response associations between total physical activity (top left), light intensity physical activity (LPA) (top right), low LPA (middle left), high LPA (middle right), moderate-to-vigorous intensity physical activity (MVPA) (bottom left), and sedentary time (bottom right, data from REGARDS (Reasons for Geographic and Racial Differences in Stroke)[8] and FHS (Women's Health Study)[12] are only included for MVPA) and all cause mortality. Modelling performed using restricted cubic splines with knots at 25th, 50th, and 75th centiles of exposure specific distribution from medians of quarters (least to most active). The exposure reference is set as the median of the medians in the reference group (least active) (see supplementary table 3). Knot locations are available in supplementary table 8. cpm=counts per minute	
O'Donovan 2017[f] *(51)* Good quality[g]	Pooled cohort analysis N=37,059	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	Compared with those who **met PA guidelines[h]** and whose HDL-C was normal, all-cause mortality risk was elevated in those who did not meet PA guidelines and whose HDL-C was normal (adjusted HR = 1.37 [95% CI, 1.16 to 1.61]) and in those who did not meet PA guidelines and whose HDL-C was low (adjusted HR = 1.65 [95% CI 1.37 to 1.98]).	MODERATE[i]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness†	Imprecision	Other		
Siahpush 2019[j] *(63)* Good quality[g]	Pooled cohort analysis N=68,706	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	Smokers who reported **meeting aerobic and strengthening PA guidelines**[h] had significantly lower risk of all-cause mortality (adjusted HR = 0.71 [95% CI, 0.62 to 0.81]) than those not meeting either recommendation as did those meeting aerobic PA recommendations (adjusted HR = 0.81 [95% CI 0.75 to 0.88]) versus those not meeting either recommendation. There was no association between all-cause mortality and meeting strength recommendations (and not aerobic PA recommendations) vs. meeting neither recommendation (HR = 0.90 [95% CI, -.76 to 1.07]).	MODERATE[i]
Stamatakis 2018[k] *(65)* Good quality[g]	Pooled cohort analysis N=80,306	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	Dose-response relationship[l]	Adherence to both **aerobic and strengthening PA guidelines**[h] vs. not adhering to either (adjusted HR = 0.71 [95% CI 0.57 to 0.87]) and adherence to the strength exercise guideline[m] vs. not adhering (HR = 0.80 [95% CI, 0.70 to 0.91]) was associated with significantly reduced risk of all-cause mortality Additionally, participation in any strength-promoting exercise vs. no strength-promoting exercise (adjusted HR = 0.77 [95% CI, 0.69 to 0.87]), as well as own-body-weight strength activities vs. none and gym-based strength activities vs. none were associated with a significantly reduced risk of all-cause mortality.	MODERATE[n]

Abbreviations: ARD = absolute rate difference; CI = confidence interval; cpm = counts per minute; HDL-C = high-density lipoprotein cholesterol; HR = hazards ratio; LPA = light physical activity; MET =metabolic equivalent of task; min = minutes; MVPA = moderate-to-vigorous intensity PA; NR = not reported; PA = physical activity; RR = risk ratio; SB = sedentary behaviour

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence upgraded given no serious limitations in included evidence
[b] Certainty of evidence upgraded given no serious risk of bias of included studies and evidence of dose-response relationship; however, serious inconsistency (high between study variance, I^2>77%) present
[c] Certainty of evidence not upgraded given serious inconsistency in effects between studies and statistical heterogeneity and indirectness in comparisons of exposures
[d] Certainty of evidence not upgraded given serious risk of bias (not appropriately adjusting for confounding), serious inconsistency (heterogeneity) and indirectness in comparisons of exposures
[e] Certainty of evidence upgraded given no serious limitations in the body of evidence, individual participant-level data meta-analysis, and evidence of a dose response relationship
[f] Not a systematic review. Pooled analysis of nine cohorts of the Health Survey for England and the Scottish Health Survey and linked to the British National Health Service Central Registry for data on mortality
[g] Quality rated based on the Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses *(77)*
[h] 150 min/week of moderate-intensity leisure time PA, or at least 75 min/week of vigorous-intensity leisure-time PA, or an equivalent combination and performing strengthening exercises >2 times/week
[i] Certainty of evidence upgraded given no serious limitations in included evidence
[j] Not a systematic review. Pooled analysis of 1998-2009 National Health Index Survey and linked National Death Index
[k] Not a systematic review. Pooled analysis of 11 cohorts of the Health Survey for England and the Scottish Health Survey and linked to the British National Health Service Central Registry for data on mortality
[l] There was evidence of a trend for greater reduced risk for all-cause mortality when comparing high, low, and no weekly volume of any strength exercise and own-body-weight strength activity

[m] Performing strengthening exercises $\geq$2 times/week
[n] Certainty of evidence upgraded given no serious limitations in included evidence; some evidence of dose-response relationship but not judged to warrant further upgrading

Table B.1.b. CVD mortality: Association between physical activity and CVD mortality among adults (in alphabetical order by author)

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment Risk of bias	Inconsistency	Indirectness†	Imprecision	Other	Description of evidence Summary of findings	Certainty
Blond 2019 *(11)* Moderate	48 prospective cohort studies N=NR	No serious risk of bias	Serious inconsistency	No serious indirect-tness	No serious imprecision	Possible publication bias Evidence of a dose-response relationship	Five studies used accelerometers to measure PA while all other studies used self-reported PA. Eight measures included occupational PA. Most studies focused on MVPA or leisure-time PA. An inverse relationship was found between **PA** and **CVD mortality** (*p* non-linearity <0.001). The mortality risk was lower for all PA levels above the recommended level compared with the recommended level (750 MET min/week). Compared with 750 MET min/week, those participating in 2000 MET min/week (4 hrs/week) had a statistically significantly lower risk of all-cause mortality (HR = 0.81 [95% CI, 0.77 to 0.85]) with an ARD = -5 deaths per 10,000 person years [95% CI, -6 to -4 deaths).	MODERATE[a]

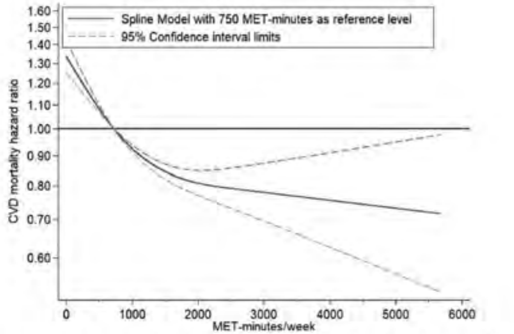


Figure 3 Dose–response relationship between physical activity and cardiovascular disease (CVD) mortality. Dose–response relation b metabolic equivalent of task (MET) min/week (with 750 MET min/week as the reference) and mortality risk estimated with restricted cu regression and generalised least square trend estimation for summarised dose–response data.

Table 1 Mortality HRs with 750 metabolic equivalent of task (MET) min/week as reference and estimated absolute rate differences per 10(person years

MET min/week		0	500	1000	2000	3000	4000	5000	6000
Running (5 mph)*		0 hour/week	1 hour/week	2 hours/week	4 hours/week	6 hours/week	8 hours/week	10 hours/week	12 hou
CVD mortality	Studies	15	18	18	17	8	2	2	NA
	Participants†	579 901	986 340	279 319	286 717	111 007	19 489	5488	NA
	PY†	7 721 115	9 761 494	3 860 943	3 796 251	1 165 769	274 344	65 089	NA
	Total cases†	12 318	30 196	8618	8661	3258	486	87	NA
	HR (95% CI)	1.34 (1.26 to 1.42)	1.08 (1.07 to 1.10)	0.93 (0.91 to 0.94)	0.81 (0.77 to 0.85)	0.78 (0.69 to 0.87)	0.75 (0.63 to 0.91)	0.73 (0.56 to 0.95)	NA
	ARD (95% CI)‡	8 (6 to 10)	2 (2 to 2)	−2 (−2 to −1)	−5 (−6 to −4)	−5 (−8 to −3)	−6 (−9 to −2)	−7 (−11 to −1)	NA

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
Dinu 2019 *(19)* Low	9 prospective cohort studies N=177,239	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	All studies evaluated the effects of mixed mode (cycling and/or walking) active commuting on health outcomes. Exposure levels of active commuting were variably reported as minutes spent walking or cycling for transportation per day, as dichotomized variables (yes or no), or as METs with the reference category as no active commuting in most studies. Follow-up ranged from 4 to 25 years. There was no significant association between **active commuting** and **CVD mortality** compared with those participating in no active commuting (RR = 0.94 [95% CI 0.85 to 1.05], 9 studies).	LOW[b]
O'Donovan 2017[c] *(51)* Good quality[d]	9 cohort studies N=37,059	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision	None	Compared with those who met PA guidelines[e] and whose HDL-C was normal, CVD mortality risk was not significantly elevated in those who did not meet PA guidelines and whose HDL-C was normal (adjusted HR = 1.11 [95% CI, 0.82 to 1.52]); CVD mortality risk was elevated among those who did not meet PA guidelines and whose HDL-C was low (adjusted HR = 1.63 [95% CI 1.16 to 2.27]) compared with those meeting recommendations and with normal HDL-C.	LOW[f]
Siahpush 2019[g] *(63)* Good quality[d]	Pooled cohort analysis N=68,706	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	Smokers who reported meeting aerobic and strengthening PA guidelines[h] (adjusted HR = 0.54 [95% CI, 0.39 to 0.76]), those meeting only aerobic PA guidelines (adjusted HR = 0.85 [95% CI 0.72 to 0.99]), and those meeting only strengthening exercise guidelines (HR = 0.63 [95% CI 0.43 to 0.93]) had significantly lower risk of CVD mortality than those not meeting both recommendations.	MODERATE[i]
Stamatakis 2018[j] *(65)* Good quality[d]	Pooled cohort analysis N=80,306	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	There was no association between participation in any strength exercises vs. no participation (adjusted HR = 0.88 [95% CI, 0.71 to 1.08]) or meeting vs. not meeting the strength exercise guideline[k] (adjusted HR = 0.92 [95% CI 0.72 to 1.12]) and CVD mortality, including analysis limited to own-bodyweight exercises and gym-based exercises.	MODERATE[l]

Abbreviations: ARD = absolute rate difference; CI = confidence interval; CVD = cardiovascular disease; HDL-C = high-density lipoprotein cholesterol; HR = hazards ratio; MET =metabolic equivalent of task; min = minutes; MVPA = moderate-to-vigorous intensity physical activity; NR = not reported; RR = risk ratio; SB = sedentary behaviour

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence upgraded given no serious risk of bias of included studies and evidence of dose-response relationship; however, serious inconsistency (high between study variance, I^2>77%) present; possible small studies effects/publication bias not judged as sufficient to warrant additional downgrading
[b] Certainty of evidence not upgraded given serious risk of bias (not appropriately adjusting for confounding) and indirectness in comparisons of exposures
[c] Not a systematic review. Pooled analysis of 9 population-based cohorts
[d] Quality rated based on the Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses *(77)*
[e] 150 min/week of moderate-intensity leisure time PA, or at least 75 min/week of vigorous-intensity leisure-time PA, or any combination of moderate- and vigorous-intensity PA equivalent to at least 7.5 MET-h/week
[f] Certainty of evidence not upgraded given imprecision in estimates of effects (wide confidence interval representing range in results)
[g] Not a systematic review. Pooled analysis of 1998-2009 National Health Index Survey and linked National Death Index
[h] 150 min/week of moderate-intensity leisure time PA, or at least 75 min/week of vigorous-intensity leisure-time PA, or an equivalent combination and performing strengthening exercises >2 times/week

[i] Certainty of evidence upgraded given no serious limitations in included evidence
[j] Not a systematic review. Pooled analysis of 11 cohorts of the Health Survey for England and the Scottish Health Survey and linked to the British National Health Service Central Registry for data on mortality
[k] Performing strengthening exercises $\geq$2 times/week
[l] Certainty of evidence upgraded given no serious limitations in included evidence and evidence of dose-response relationship

Table B.1.c. CVD incidence: Association between physical activity and CVD incidence among adults (in alphabetical order by author)

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**
		Risk of bias	**Inconsistency**	**Indirectness†**	**Imprecision**	**Other**		
Dinu 2019 *(19)* Low	5 prospective cohort studies N=183,872	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	All studies evaluated the effects of mixed mode (cycling and/or walking) active commuting on health outcomes. Exposure levels of active commuting were variably reported as minutes spent walking or cycling for transportation per day, as dichotomized variables (yes or no), or as METs with the reference category as no active commuting in most studies. Follow-up ranged from 4 to 25 years. Persons engaged in **active commuting** had a significantly lower risk of **CVD incidence** (coronary heart disease, stroke and heart failure) compared with those participating in no active commuting (RR = 0.91 [95% CI 0.83 to 0.99], 5 studies).	LOW[a]

Abbreviations: CI = confidence interval; CVD = cardiovascular disease; MET = metabolic equivalents of task; PA = physical activity; RR = risk ratio

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not upgraded given serious risk of bias (not appropriately adjusting for confounding) and indirectness in comparisons of exposures

Table B.1.d. Cancer incidence: Association between physical activity and cancer incidence among adults (in alphabetical order by author)

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**
		Risk of bias	**Inconsistency**	**Indirectness †**	**Imprecision**	**Other**		
Baumeister 2019 *(7)* Moderate	14 prospective cohort studies N=2.39 million (2,738 cases)	No serious risk of bias	Serious inconsistency	No serious indirectness	No serious imprecision	None	Examination of the relationship between self-reported PA and liver cancer. Mean follow-up was 11.6 years (range 6-20 years); median age=45 years (range 20 to 93 years) at baseline. PA was significantly inversely associated with **liver cancer risk**, comparing high levels of PA to low levels of PA (HR = 075 [95% CI, 0.63 to 0.89]).	LOW[a]
Behrens 2019 *(8)* Moderate	3 prospective cohort studies (N=12,605 cases), 5 case-control studies (N=1,295 cases)	Serious risk of bias[b]	No serious inconsistency	No serious indirectness	No serious imprecision[c]	None	Studies examined the relationship between PA and melanoma risk. Most studies examined recreational PA. Cohort studies revealed a statistically significant positive association between high versus low physical activity and **melanoma risk** (RR= 1.27 [95% CI, 1.16 to 1.40]) whereas case-control studies yielded a statistically non-significant inverse risk estimate for physical activity and melanoma (RR = 0.85 [95% CI = 0.63–1.14]).	LOW[d]
Benke 2019 *(9)* Moderate	48 prospective cohort studies, 24 case-control studies (N=151,748 cases)	No serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	Possible publication bias	Evaluation of the association between physical activity and risk of prostate cancer. Mean age was 61 years and all studies used self-reported PA. There was no significant association between PA and **total prostate cancer incidence** when comparing the highest level of PA to the lowest (RR=0.99 [95% CI, 0.94 to 1.04], 50 studies). There was no difference in effects when stratifying by study design (cohort vs. case-control). The corresponding RRs for advanced and non-advanced **prostate cancer incidence** were 0.92 (95% CI, 0.80 to 1.06) and 0.95 (95% CI, 0.85 to 1.07), respectively.	VERY LOW[e]
Liu 2019 *(39)* Moderate	20 prospective cohort studies (N=31,807 cases)	No serious risk of bias	Serious inconsistency	No serious indirectness	No serious imprecision	Possible publication bias	There was a significant inverse relationship found between PA and **lung cancer** when comparing higher to lower levels of PA. Compared with low levels of PA, the pooled RR was 0.83 [95% CI, 0.77 to 0.90]). Smokers with a high level of PA were associated with a 10% lower risk for lung cancer (RR = 0.90 [95% CI: 0.84, 0.97], while the association was not significant among non-smokers (RR= 0.95 [95% CI: 0.88, 1.03].	VERY LOW[f]

Abbreviations: CI = confidence interval; HR = hazards ratio; MET = metabolic equivalents of task; PA = physical activity; RR = risk ratio

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not upgraded given serious inconsistency (direction and magnitude of effects of individual studies and I2>60%)
[b] With the exception of one case-control study, none of the studies controlled for sun sensitivity or sun exposure on an individual level, in addition to other sources of potential bias

[c] No serious imprecision evident for cohort studies; serious imprecision for estimate of effect among case-control studies
[d] Certainty of evidence not upgraded given serious risk of bias
[e] Certainty of evidence downgraded given serious inconsistency (direction and magnitude of effects and I^2>70%), serious imprecision (upper and lower limits of the confidence intervals included both benefit and harm), and possible publication bias
[f] Certainty of evidence downgraded given serious inconsistency (direction and magnitude of effects and I^2>70%) and possible publication bias

Table B.1.e. Type 2 diabetes incidence: Association between physical activity and Type 2 diabetes incidence among adults

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**
		Risk of bias	**Inconsistency**	**Indirectness†**	**Imprecision**	**Other**		
Boyer 2019 *(12)* Low	27 prospective cohort studies N=1,150, 574	No serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Studies examined the relationship between PA and type 2 diabetes in specific racial/ethnicity groups. Duration of follow-up ranged from 2 to 28 years. Method of diabetes ascertainment ranged considerably including medical records, reports of medication or insulin use, OGT tests, FBG, or self-report. A reduced risk of **developing diabetes** was found when comparing the **highest vs. lowest levels of PA** among non-Hispanic whites (RR = 0.71 [95% CI 0.60 to 0.85], 8 studies, n=238,719), Asians (RR = 0.76 [95% CI 0.67 to 0.85], 16 studies, n=928,319), Hispanics (RR = 0.74 [95% CI, 0.64 to 0.84], 3 studies, n=10,817), and American Indians (RR = 0.73 [95% CI 0.60 to 0.88], 4 studies, n=7,022). The effect among non-Hispanic blacks was not statistically significant (RR = 0.91 [95% CI 0.76 to 1.08], 5 studies, n=30,452).	VERY LOW[a]
Dinu 2019 *(19)* Low	4 prospective cohort studies N=102,077	Serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	None	All studies evaluated the effects of mixed mode (cycling and/or walking) active commuting on health outcomes. Exposure levels of active commuting were variably reported as minutes spent walking or cycling for transportation per day, as dichotomized variables (yes or no), or as METs with the reference category as no active commuting in most studies. Follow-up ranged from 4 to 25 years. There was no significant association between **active commuting** and **diabetes incidence** compared with those participating in no active commuting (RR = 0.0.78 [95% CI 0.60 to 1.03], 4 studies).	VERY LOW[b]
Paudel 2019 *(54)* Low	3 cross sectional studies N=14,902	Serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Examination of the association between PA and incidence of T2D among South Asian adults. All 3 studies found no association between total PA and T2D.	VERY LOW[c]

Abbreviations: CI = confidence interval; FBG = fasting blood glucose; OGT = oral glucose tolerance; PA = physical activity; NR = not reported; RR = risk ratio; T2D = type 2 diabetes

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious inconsistency in direction of effects, serious indirectness in comparisons, and serious imprecision in pooled estimates of effects
[b] Certainty of evidence downgraded given serious risk of bias (not appropriately adjusting for confounding), serious inconsistency in effects between studies and statistical heterogeneity and indirectness in comparisons of exposures
[c] Certainty of evidence rated as very low according to authors given serious risk of bias and serious imprecision. Serious indirectness is also present given variability in comparisons

Table B.1.e. Adiposity-related outcomes: Association between physical activity and measures of adiposity among adults, by comparison and author

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment Risk of bias	 Inconsistency	 Indirectness †	 Imprecision	 Other	Description of evidence Summary of findings	Certainty
Walking								
Paudel 2019 *(54)* Low	3 cross sectional studies N=435	Serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Examination of the association between PA and measures of adiposity among South Asian adults. One study reported a protective association with walking and **BF%, FMI, and FFMI**, one study reported no association between walking with BMI, WC and FMI but found significant associations between cycling and BMI, BW, WC, and fat mass, and the last study found no association between increasing levels of walking and BMI or WC.	VERY LOW[a]
Light-intensity PA								
Amagasa 2018 *(2)* Low	14 cross-sectional studies 1 cohort study N=20,552	No serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	None	**LIPA** was found to have a favourable association with **WC** in 8/12 cross-sectional studies and an inconsistent association with **BMI** in 4/10 cross-sectional studies. One cohort study found that women in the highest tertiles of LIPA time had **lower fat mass, BF%, and central fat** at 1 year compared with women in lowest and middle tertiles of LPA; no significant effects were found in **fat-free mass, BW, BMI, and WC**.	VERY LOW[b]
Chastin 2019 *(14)* Moderate	4 RCTs or CCTs 17 cross-sectional studies 1 prospective cohort N=NR	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Studies evaluated the association between **LIPA** (as defined by each study, and inconsistent between studies) and adiposity measures. 2/4 trials reported significant effects on measures of **fat mass** or **BF%**. Cross-sectional studies showed "consistent reports across studies on the association between time spent in LIPA and adiposity markers; but the reported effect sizes were small and consistently stronger with increased absolute intensity of LIPA." One cohort study showed a small decrease in **BW** to be associated with increased time spent in LIPA.	VERY LOW[c]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
High-intensity interval training								
Andreato 2019 *(4)*[d] Moderate	48 RCTs or pre-post studies N=1,222	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	Dose-response relationship[e]	Studies evaluated the association between **HIIT vs. MICT vs. controls** on anthropometric variables among adults with overweight or obesity. Mean follow-up was 10 weeks (range 2 to 24 weeks). In most studies, HIIT was performed 3 times per week; 30 studies evaluated cycling and 18 evaluation running/walking. Compared with no exercise control groups, HIIT was significantly associated with decreased **body mass** (MD = -1.45 kg [95% CI -1.85 to -1.05 k], n=1,168), **BMI** (MD = -0.44 kg/m^2 [95% CI -0.59 to -0.30], n=990), **WC** (MD = -2.3 cm [95% CI, -3.1 to -1.4], n=671), and **BF%** (MD = -1.29% [95% CI -1.70 to -0.87], n=833). When comparing HIIT vs. MICT protocols that had similar energy expenditures or workloads, HIIT was associated with greater reduction in **body mass** than MICT (MD = -0.41 kg [95% CI -0.79 to -0.023); but there were no other differences between HIIT and MICT with similar protocols on **BMI, WC, or BF%.**	LOW[f]
Sultana 2019 *(70)* Low	21 RCTs N=NR	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Studies evaluated the association between **low-volume HIIT** (<500 MET-min/week) performed for at least 4 weeks for a minimum of 2 days/week vs. a non-exercising control or MICT and measures of body composition. Most studies recruited adults with overweight or obesity, mean age ranged from 19 to 70 years. Exercise interventions ranged from 4 to 16 weeks, with most taking place for 12 weeks with exercise sessions performed 2 to 5 days/week. No significant association was found between low-volume HIIT vs. non-exercising control groups for measures of **total body fat mass** (ES = -0.129 [95% CI, -0.468 to 0.210], 6 studies), **BF%** (ES = -0.063 [95% CI, -0.383 to 0.257], 7 studies), and **lean body mass** (ES = 0.050 [95% CI, -0.250 to 0.351], 8 studies) or between low-volume HIIT vs. MICT on **total body fat mass** (ES =-0.021 [95% CI, -0.272 to 0.231], 6 studies), **BF%** (ES = 0.005 [95% CI, -0.294 to 0.304], 7 studies) or **lean body mass** (ES = 0.030 [95% CI, -0.167 to 0.266], 11 studies).	VERY LOW[g]

Abbreviations: ARD = absolute rate difference; BF% = percent body fat; BMI = body mass index; BW = body weight; CCT = controlled clinical trial; CI = confidence interval; cm = centimeters; DXA = dual-energy X-ray absorptiometry; ES = effect size; FMI = fat mass index; FFMI = fat-free mass index; HIIT = high-intensity interval training; HR = hazards ratio; kg = kilograms; LIPA = light-intensity physical activity; m = meters; MET =metabolic equivalent of task; MetS = metabolic syndrome; MICT = moderate-intensity continuous training; min = minutes; MVPA = moderate-to-vigorous intensity PA; NAFLD = non-alcoholic fatty liver disease; NR = not reported; PCOS = polycystic ovary syndrome; RCT = randomized controlled trial; RR = risk ratio; SB = sedentary behaviour; SIT = sprint interval training; WC = waist circumference

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence rated as very low according to authors given serious risk of bias and serious imprecision. Serious indirectness is also present given variability in comparisons
[b] Certainty of evidence not upgraded
[c] Certainty of evidence not upgraded given serious indirectness in comparisons of exposures and lack of detailed results, with most evidence from cross-sectional studies and inconsistency across RCTs and nonrandomized intervention studies

[d] Review by Wewege 2017 *(74)* included overlapping evidence and found consistent effects of HIIT vs. MICT on measures of adiposity among adults with overweight or obesity.
[e] A significant association was found between number of sessions and greater reductions in body mass
[f] Certainty of evidence downgraded given serious risk of bias of all included studies, including lack of control for participants' diets and total PA and serious indirectness given variability of exercise protocols and comparisons; review did not report results of RCTs separately (10 studies were 'adequately randomized')
[g] Certainty of evidence downgraded given serious risk of bias of all included studies, serious indirectness given variability of exercise protocols and comparisons, and serious imprecision in estimates of effect within individual studies and pooled effect sizes

Table B.1.f. Mental health outcomes: Association between physical activity and measures of mental health among adults, by comparison and author

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**
		Risk of bias	**Inconsistency**	**Indirect-ness†**	**Imprecision**	**Other**		
Higher vs. lower or no PA								
Amagasa 2018 *(2)* Low	1 cross-sectional study 1 cohort study N=2,254	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	One cross-sectional study found that **higher vs. lower LPA** was associated with a lower risk of **psychological distress**. One cohort study for older adults in Taiwan showed that higher vs. lower LPA was associated with three dimensions of **well-being**: psychological, learning and growth, and social well-being.	VERY LOW[a]
Martinez-Dominguez 2018 *(47)* Moderate	10 RCTs N=1,463	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision	None	Studies evaluated the effects of **exercise interventions that were at least 6 weeks in duration** vs. no exercise control groups reporting symptoms of anxiety among middle-aged and older women (mean age range, 54 to 78 years). Exercise interventions lasting 12 weeks to 4 months were associated with reduced **symptoms of anxiety** vs. no exercise control groups among women (SMD = -0.42 [95% CI, -0.81 to -0.02], 8 RCTs); however, no significant association was seen between exercise interventions lasting 6 to 14 months) and symptoms of anxiety among women (SMD = -0.03 [95% CI, -0.18 to 0.13], 7 RCTs).	MODERATE[b]
Perez-Lopez 2017 *(55)* Moderate	11 RCTs N=1,943	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	Studies evaluated the effects of **exercise interventions that were at least 6 weeks in duration** vs. no exercise control groups reporting symptoms of depression among middle-aged and older women (mean age range, 44 to 66 years). Exercise interventions lasting 12 weeks to 4 months were associated with reduced **symptoms of depression** vs. no exercise control groups among women (SMD = -0.44 [95% CI, -0.69 to -0.18], 5 RCTs) as were exercise interventions lasting 6 to 14 months (SMD = -0.29 [95% CI, -0.49 to -0.09], 6 RCTs).	HIGH[c]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirect-ness†	Imprecision	Other		
Schuch 2018 *(61)* High	49 prospective cohort studies N=266,939	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Possible publication bias	Studies examined the prospective relationship between **PA** and incident depression. All but one study relied on self-reported PA. Average follow-up was 7.4 years. Compared with those with low levels of PA, adults with high levels of PA had lower odds of **developing depression** (adjusted OR = 0.78 [95% CI, 0.70 to 0.87] as did older adults with high levels of PA (adjusted OR = 0.79 [95% CI, 0.72 to 0.86]).	MODERATE[d]
Schuch 2019 *(60)* Moderate	13 prospective cohort studies N=75,831	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Possible publication bias	Studies examined the prospective relationship between **PA** and incident depression. All studies relied on self-reported PA. Average follow-up was 3.5 years. Compared with those with low levels of PA, adults with high levels of PA had lower odds of **developing anxiety** (adjusted OR = 0.81 [95% CI, 0.69 to 0.95].	MODERATE[d]
Resistance training								
Gordon 2017 *(26)* Low	16 RCTs N=922	No serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	None	Studies evaluated the effect of **resistance training** vs. a non-active control group on measures of symptoms of anxiety. Participants were mean age 43 years. Anxiety symptoms were the primary outcomes in 9/16 studies; most frequently reported measure of anxiety was the State-Trait Anxiety Inventory. Mean intervention length was 11 weeks and intervention frequency ranged from 2 to 5 days/week. Resistance training was found to be associated with significantly reduce **symptoms of anxiety** vs. non-active control groups (ES = 0.31 [95% CI, 0.17 to 0.44]); larger effects were seen among studies of healthy samples (ES = 0.50 [95% CI, 0.22 to 0.78]) vs. those with a physical or mental illness (ES = 0.19 [95% CI, 0.06 to 0.31]), although confidence intervals overlapped between groups. Effect sizes did not significantly vary according to other population, intervention, or study characteristics. No significant difference was found between studies examining resistance training vs. aerobic exercise training.	LOW[e]
Gordon 2018 *(25)* Low	33 RCTs N=1,877	No serious risk of bias[f]	Serious inconsistency	No serious indirectness	Serious imprecision	Possible publication bias	Studies evaluated the effect of **resistance training** vs. a non-active control group on measures of symptoms of depression. Participants were mean age 52 years. Depressive symptoms were the primary outcomes in 18/33 studies; most frequently reported measure of anxiety was the Beck Depression Inventory. Mean intervention length was 16 weeks and intervention frequency ranged from 2 to 7 days/week with 3 days/week the most common intensity. Resistance training was found to be associated with significantly reduce **symptoms of depression** vs. non-active control groups (ES = 0.66 [95% CI, 0.48 to 0.83]). No significant difference was found between studies examining resistance training vs. aerobic exercise training.	VERY LOW[g]

Abbreviations: CI = confidence interval; ES = effect size; OR = odds ratio; PA = physical activity; RCT = randomized controlled trial; SMD = standardized mean difference

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not upgraded given indirectness in exposure of interest (LPA only)
[b] Certainty of evidence downgraded given serious imprecision in study-specific and pooled estimates of effects
[c] Certainty of evidence downgraded given some evidence of inconsistency (range of effects) and indirectness in outcome measures
[d] Certainty of evidence upgraded given no major limitations in body of evidence; possible small studies effect not judged to warrant downgrading
[e] Certainty of evidence downgraded given serious inconsistency in direction of effects and serious imprecision in effect estimates indicating potential benefit or harm. Furthermore, pooled estimates include multiple estimates per study for different measures
[f] Effects were significantly smaller when outcome assessment was blinded compared with when outcome assessment was not blinded
[g] Certainty of evidence downgraded given serious inconsistency in direction of effects, serious imprecision in effect estimates, and presence of small studies effect. Furthermore, pooled estimates include multiple estimates per study for different measures

Table B.1.g. Cognitive function outcomes: Association between physical activity and measures of cognitive function among adults

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**
		Risk of bias	**Inconsistency**	**Indirect-ness†**	**Imprecision**	**Other**		
Amagasa 2018 *(2)* Low	2 cross-sectional studies N=435	No serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	None	Two cross-sectional studies among older adults (mean age 64 and 65 years) that studied objectively measured LPA (as a continuous measure or vs. replacing 30 min of SB with LPA. One study found that LPA was significantly associated with higher **cognitive functioning** whereas the other study found no associations between LPA and **spatial working memory and task switching**.	VERY LOW[a]
Brasure 2018 *(13)* High	14 RCTs N=2,824	No serious risk of bias[b]	Serious inconsistency	Serious indirectness	Serious imprecision	None	**Multicomponent physical activity interventions** (including flexibility, strength, balance, endurance, and aerobic training) were tested in 4 trials (n=1,885). All trials included older adults aged >60 years without cognitive impairment and represented mostly white women. A wide range of neuropsychological tests were used to assess **cognitive function**; only 3/25 comparisons showed a statistically significant benefits with multicomponent PA interventions compared with attention controls, including one trial that report no difference in the **incidence of MCI or dementia** between groups at 2 years. Six trials (n=531) tested **aerobic training** vs. attention controls in healthy older adults. One study found that older adults in the aerobic exercise group were significantly less likely to receive a **dementia diagnosis** at 18 months; 11/35 comparisons showed statistically significant benefit on **measures of cognitive function** whereas 24/35 showed no statistically significant difference between groups. Three trials **examined resistance training** vs. usual care among frail, older adults. No trial reported diagnostic outcomes; less than a third of comparisons favoured the interventions on measures of e**xecutive function, attention and processing speed, and memory**. One small trial tested **tai chi** vs. attention control in older adults aged 60-79 years; 1/2 outcomes for **executive function, attention, and processing speed** showed a significant benefit.	LOW[c]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirect-ness†	Imprecision	Other		
Engeroff 2018 *(21)* Moderate	9 cross-sectional studies 14 longitudinal N=11,707	No serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Most PA was self-reported using questionnaires not previously validated, and all measures of PA were different between studies. All studies measured cognitive function among older adults aged >60 years. There was an inconsistent association between **MVPA** and **global cognitive function**; 3/4 longitudinal studies showed no association between lifetime PA and MMSE scores whereas 1/4 longitudinal study found showed a beneficial association between levels of PA at age 74 years and MMSE scores at age 84 years. Most cross-sectional studies found no association between PA and measures of global cognitive function. There was mixed evidence on the relationship between PA and the specific cognitive domains of **executive function and memory,** but no evidence of an association with **attention or working memory.**	VERY LOW[d]
Northey 2018 *(50)* Moderate	39 RCTs N=NR	Serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	None	Studies evaluated relationship between **PA interventions of at least 4 weeks** and cognitive function measures among adults aged 50 years and older. Interventions included aerobic exercise (18 studies), resistance training (13 studies), multicomponent training (10 studies), tai chi (4 studies) and yoga (2 studies). A multi-level analysis combining multiple measures of cognitive per study (333 dependent effect sizes in 36 studies) found a significant effect of physical activity interventions vs. no PA on measures of cognition (SMD = 0.29 [95% CI 0.17 to 0.41]).	MODERATE[e]
Rathrore 2017 *(57)* Low	15 RCTs N=1,315	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Highly heterogenous studies including sample populations (7 studies among youth 5-17-years, 3 studies among adults 18-64 years, and 5 studies among older adults >65 years. Seven studies evaluated acute PA (1 session) whereas eight studies evaluated chronic PA (more than 1 PA sessions from 4 weeks to 6 months). Review was limited to **working memory performance**. 10/15 studies reported a statistically significant improvement in **working memory performance** among those in a **physical activity intervention** vs. no PA. Chronic PA interventions (ES = 0.27 [95% CI, 0.12 to 0.42], 8 RCTS, n=1,139) were significantly associated with improvements in working memory performance in pooled analysis compared with no exercise. There was no association between acute PA interventions vs. no PA on working memory (ES = -0.15 [95% CI, -0.33 to -0.63], 7 RCTs, n=1,098).	LOW[f]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirect-ness†	Imprecision	Other		
Stanmore 2017 *(66)* Low	17 RCTs N=926	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Mean age 69 years (range = 17-85 years), six studies were among clinical samples among patients with Parkinson's , MCI, sub-acute stroke, or schizophrenia and one study was among healthy adolescents. All interventions used active video games/exergames that lasted an average of 10 weeks (range = 4-24 weeks) with an average of 3.2 sessions per week for 15-60 min of exercise per session. **Exergames** were significantly associated with improved **global cognitive function** vs. no exergame control conditions in pooled analysis (ES = 0.436 [95% CI 0.18 to 0.69], 17 RCTs, n=926). Results were consistent when stratified by type of control group (attention controls only, PA intervention controls), population (clinical, non-clinical, and older adults only), and length of intervention (<12 weeks, ≥12 weeks). Statistically significant effects were also seen for individual domains of cognitive function including **executive function, task-switching, inhibitory control, and attentional processing speed**; but were not found for **working memory, reasoning, verbal learning and memory, spatial learning and memory, and language.**	VERY LOW[g]

Abbreviations: CI = confidence interval; ES = effect size; LPA = light physical activity; MCI = mild cognitive impairment; MMSE = mini-mental state exam; NR = not reported; PA = physical activity; RCT = randomized clinical trial; SB = sedentary behaviour

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not upgraded
[b] Review was limited to studies with low to moderate risk of bias, although review authors notes a medium rating for study limitations
[c] Strength of evidence rated as Low by review authors for multicomponent physical activity interventions given indirectness in outcome measures, unknown consistency, and imprecision. All other interventions were rated as having Insufficient strength of evidence given limited data.
[d] Certainty of evidence downgraded given serious inconsistency in measures of effects within and between studies and across domain-specific measures of cognition, serious indirectness in measures of physical activity and cognitive function, and serious imprecision (wide confidence interval)
[e] Certainty of evidence assigned by review authors as Moderate owing to the level of uncertainty across each domain of the risk of bias tool
[f] Certainty of evidence related to chronic (>1 session) PA interventions; downgraded due to serious indirectness in outcome measures and serious imprecision of effects in individual trials and pooled effect
[g] Certainty of evidence downgraded given serious risk of bias in included evidence, serious inconsistency (I^2>60% in all pooled analysis), serious indirectness (heterogeneous comparisons and outcome measures), and serious imprecision in effect estimates

Table B.1.h. Adverse events

Methods:

This umbrella review was a-priori registered in PROSPERO. The PROSPERO registration number is not known yet, but will be added to this review as soon as it has been received (). This umbrella review synthesized and combined relevant data from systematic reviews or meta-analyses, in order to inform the WHO in their development of Guidelines for PA.

Inclusion and exclusion criteria:

Peer-reviewed reviews were eligible for inclusion in this umbrella review if they met all of the following inclusion criteria:
A measure of LTPA was reported;
An assessment of a relevant adverse health outcome was reported, examples of which are described below;
Full-text systematic reviews were available, based on more than one paper (preferably containing meta-analyses), describing studies with an intervention-based, cross-sectional or longitudinal design.

Reviews were excluded if:
They covered samples of elite or professional sports persons only (including paid, sponsored, and/or scholarship athletes);
In case of mixed samples of non-elite and elite athletes: data regarding the non-elite samples could not be extracted separately;
They focused on a clinical population, which cannot be generalized to the general population;
They had falls as a risk or adverse event, with a focus on the elderly population (this outcome is considered by another WHO review);
They were published in a language other than English.

Population-Exposure-Control-Outcome

The WHO Guideline Development Group decided to use PECO (Population-Exposure-Control-Outcome) questions to define the scope of their guidelines.

Population: Adults 18 years of age and older
Exposure: Duration, frequency and/or intensity of LTPA (dose of LTPA), or a composite score reflecting total volume of LTPA
Comparison: No LTPA, or LTPA of a lesser duration, frequency and/or intensity, or composite score of total volume of LTPA
Outcomes: Adverse health effects (especially injury, osteoarthritis, erectile dysfunction, and exposure to air pollution)

Search and Selection

In order to identify relevant evidence, a search for existing systematic reviews (preferably with meta-analyses) was conducted. The following databases were searched for systematic reviews that met the inclusion criteria: PubMed, SPORTDiscus, and Embase. Systematic searches were conducted in December 2019, limited from 2009 onwards (since this was an update of the WHO guidelines from 2009 *(78)*) and contained the following sets of key terms: harms and injuries, physical activity, and publication type. The full search strategy can be found in Supplementary file 3. Snowball searches by screening reference lists of included studies and by consultation experts were used, to identify additional reviews that were not found in the three databases mentioned above. Final search results were exported to Endnote reference manager and the final counts were captured in a PRISMA flow diagram *(79)*.

Study Selection

Two reviewers (BC and ML) assessed the title and abstract of each identified study in a first selection round, assessing the in- or exclusion criteria for each article as described above. This was done blinded in the Rayyan web app *(80)*. If no consensus could be reached, conflicts between the independent reviewers were resolved in a consensus meeting, with the help of a third reviewer (EV).

Full Text Search Selection
After obtaining full text articles, two researchers (BC and ML) performed a full text screening of the remaining studies after the initial study selection. If the inclusion criteria were met, the systematic review was included in the subsequent assessments. This was done blinded in the Rayyan web app also *(80)*. Any conflicts were resolved with the help of the third reviewer (EV). The final numbers were updated in a final version of the PRISMA flow diagram, as part of the final report.

Assessing Bias in Systematic Reviews
The included systematic reviews were assessed for quality using the AMSTAR 2 (i.e. A Measurement Tool To Assess Systematic Reviews) *(81)*. This is a 16-point assessment tool for assessing the methodological quality of systematic reviews. AMSTAR 2 has a good inter-rater agreement, test-retest reliability, and content validity. The rating values are High, Moderate, Low, and Critically Low. The cut-off values of properly addressing each of the 16 points were 100%, ≥75%, ≥50%, and below 50%, respectively. One reviewer (ML) assessed the risk of bias of the studies included. A second reviewer (BC) reviewed the initial assessment and in case of disagreement, consensus was reached through discussion. If a review was rated Critically Low, this review was excluded since it was judged that the review outcome would not provide an accurate summary of the available evidence.

Outcome-specific AMSTAR 2 summary rating of the included systematic reviews

Author, Year	PECO[1]	A priori Methods[2]	Study Design Selection[3]	Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assess-ment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Injury																	
Borel, 2019 *(82)*	Y	PY	N	PY	PY	PY	PY	N	Y	N	PY	PY	PY	Y	Y	PY	**Low**
Damsted, 2018 *(83)*	Y	N	PY	Y	PY	PY	PY	Y	Y	N	N/A	N/A	N/A	N/A	N/A	PY	**Low**
Johnston, 2018 *(84)*	PY	Y	PY	Y	PY	PY	PY	Y	Y	Y	N/A	N/A	N/A	N/A	N/A	PY	**Low**
Lopes, 2012 *(85)*	Y	N	Y	Y	PY	N	PY	PY	Y	Y	N/A	N/A	N/A	N/A	N/A	Y	**Low**
Neubauer, 2016 *(86)*	PY	N	N	PY	PY	N	N	N	N	N	N/A	N/A	N/A	N/A	N/A	PY	**Critically Low**
Nielsen, 2012 *(87)*	Y	N	PY	Y	PY	N	Y	PY	Y	N	N/A	N/A	N/A	N/A	N/A	N	**Low**
Qu, 2014 *(88)*	Y	N	PY	PY	Y	PY	N	Y	PY	Y	PY	PY	N	N	Y	Y	**Low**
Saragiotto, 2014 *(89)*	PY	N	Y	PY	PY	PY	PY	PY	Y	Y	N/A	N/A	N/A	N/A	N/A	Y	**Low**
Sobhani, 2013 *(90)*	PY	N	N	Y	Y	N	Y	Y	Y	Y	N/A	N/A	N/A	N/A	N/A	PY	**Low**
Tonoli, 2010 *(91)*	PY	N	N	PY	N	N	N	N	PY	N	N/A	N/A	N/A	N/A	N/A	N	**Critically Low**
Van der Worp, 2015 *(92)*	PY	N	PY	Y	PY	Y	N	Y	Y	Y	N/A	N/A	N/A	N/A	N/A	Y	**Low**
Videbaek, 2015 *(93)*	PY	N	PY	Y	PY	N	PY	PY	Y	Y	PY	Y	Y	Y	PY	Y	**Low**
Osteoarthritis																	
Alentorn-Geli, 2017 *(94)*	PY	N	PY	Y	PY	PY	PY	Y	Y	Y	Y	N	PY	Y	N	PY	**Low**
Timmins, 2017 *(95)*	Y	Y	PY	Y	PY	PY	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Moderate**
Erectile Dysfunction																	
Sommer, 2016 *(96)*	PY	N	N	N	N	N	N	PY	N	N	N/A	N/A	N/A	N/A	N/A	PY	**Critically Low**

Abbreviations: COI = conflict of interest; N = no; PECO = population, exposure, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PECO?

[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

[3] Did the review authors explain their selection of the study designs for inclusion in the review?

[4] Did the review authors use a comprehensive literature search strategy?

[5] Did the review authors perform study selection in duplicate?

[6] Did the review authors perform data extraction in duplicate?

[7] Did the review authors provide a list of excluded studies and justify the exclusions?

[8] Did the review authors describe the included studies in adequate detail?

[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

[10] Did the review authors report on the sources of funding for the studies included in the review?

[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?

[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *(81)* For each Yes, 1.0 point was given, and for each Partial Yes, 0.5 points was given. The total sum was then divided by the number of questions answered (i.e. 11 or 16). The rating ranges were described in the Methods above.

Supplementary file 2. GRADE: Grading the body of evidence

Injury

Population: Adults 18 years of age and older
Exposure: Duration, frequency and/or intensity of LTPA, or a composite score reflecting total volume of LTPA
Comparison: No LTPA, or LTPA of a lesser duration, frequency and/or intensity, or composite score of total volume of LTPA.
Outcome: Adverse health outcomes (especially injury, osteoarthritis, erectile dysfunction, and exposure to pollution)

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Prevalence of injuries in Brazilian recreational street runners: meta-analysis (Borel et al., 2019) *(82)*									

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
23[a]	20 cross-sectional 3 prospective cohort	Serious[b]	Not serious	Not serious	Not serious	None	**Adverse health outcomes** The pooled prevalence of injuries was 36.5% (95% CI 30.8-42.5%). Based on a total population of 3,786 runners. Injury prevalence were given by location and type: • knee injury: 32.9% (95% CI 26.7-39.6%). • ankle injury: 17.7% (95% CI 11.2-26.9%). • hip injury: 13.3% (95% CI 6.9-24.1%). • muscle injuries (including strains and contractures): 27.9% (95% CI 18.2-40.1%). • The prevalence of ligament injuries (e.g. sprains and dislocations): 27.8% (95% CI 19.4-38.1%). • inflammatory lesions (i.e. plantar fasciitis, tendinitis, synovitis, bursitis, and medial tibial stress syndrome): 26.5% (95% CI 14.9-40.1%). • bone injuries (i.e. fracture, chondromalacia patella and bone oedema): 5.6% (95% CI 1.8-16.3%). The following LTPA exposure relationships were reported: • six studies showed a relationship between running distance of 20km or more per week and the occurrence of injury. • five studies showed a relationship between running experience of more than five years and the occurrence of injury. • four studies showed a relationship between a training frequency > 3 days/week and the occurrence of injury. **Dose-response relationship** No effects to report, due to heterogeneity no meta-analysis was performed and hence no ORs or RRs were provided. **Type of LTPA** No effects to report, while only one type of LTPA (i.e. running) was included in the review.	Moderate[rr]	CRITICAL

Is there evidence for an association between changes in training load and running-related injuries? A systematic review (Damsted et al., 2018) *(83)*

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
4	1 randomized controlled trial[c] 1 cross-sectional[d] 2 prospective cohort[e]	Serious[f]	Serious[g]	Not serious	Not serious	None	**Adverse health outcomes** The following LTPA exposure relationships were reported: • 2 out of 4 reviews found an association between sudden increases in training load (>30%) and an increased risk of running-related injury: i.e. increasing the weekly running distance by more than 30% compared to a less than 10% change in the previous week Evidence from two studies defined sudden increases in training load as: • Changing one or more of the running variables (velocity, distance, , frequency, or volume) compared with the non-injured runners • The mean difference between the increase in the running distance the week before the onset of an injury and the average weekly increase during other weeks was found to be 86% **Dose-response relationship** No effects to report, due to heterogeneity no meta-analysis was performed and hence no ORs or RRs were provided. **Type of LTPA** No effects to report, only one type of LTPA (i.e. running) was included in the review.	Low[ss]	CRITICAL
The associations between training load and baseline characteristics on musculoskeletal injury and pain in endurance sport populations: a systematic review (Johnston et al., 2018) *(84)*									
10	10 prospective cohorts[h]	Serious[i]	Serious[j]	Serious[k]	Not serious	None	**Adverse health outcomes** No effects to report; this review only looked at dose-response relationships. **Dose-response relationship** • medium effect size association between high total training distances per week/month (not specified in the review) and increased rate of injury and/or pain • medium effect size association between low training frequency (<2 sessions/week) and increased rate of injury and/or pain. • large effect size association between short training duration (<2 hours/week) and increased rate of injury and/or pain; however, this finding may be less applicable given that recreational endurance participation was defined by some studies as a training frequency of three to six training sessions/week *(97, 98)* and training duration of two to four hours/week *(99)*. Definitions of the effect sizes: • Small: OR ≥ 1.5 or RR ≥ 2 • Medium: OR ≥ 2 or RR ≥ 3 • Large: OR ≥ 3 or RR ≥ 4 **Type of LTPA** Running and Triathlon as LTPA were included in the review.	Very Low[tt]	CRITICAL

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
What are the main running-related musculoskeletal injuries? A systematic review (Lopes et al., 2012) *(85)*									
8	2 prospective cohorts[l] 1 clinical trial[m] 2 retrospective cohorts[n] 3 cross-sectional[o]	Serious[p]	Serious[q]	Not serious	Not serious	Electronic searches were conducted only in the main databases related to the sports injuries field	**Adverse health outcomes** • Prevalence and incidence numbers based on a total population of 3,500 runners • The highest incident rate of running-related musculoskeletal injury (RRMIs) was found for patellar tendinopathy (22.7%) • The most prevalent general RRMI was found for plantar fasciitis (17.5%) • The most prevalent RRMI during ultra-marathon races was found for ankle dorsi-flexors tendinopathy (29.6%). • The most frequently general RRMIs reported were: 1) medial tibial stress syndrome (incidence rate ranging from 13.6% to 20.0%; prevalence rate of 9.5%) 2) Achilles tendinopathy (incidence rate ranging from 9.1% to 10.9%; prevalence rate ranging from 6.2% to 9.5%) 3) plantar fasciitis (incidence rate ranging from 4.5% to 10.0%; prevalence rate ranging from 5.2% to 17.5%) • For RRMIs sustained during ultra-marathon races, the most frequently reported injuries were: 1) Achilles tendinopathy (prevalence rate ranging from 2.0%to 18.5%) 2) Patellofemoral syndrome (prevalence rate ranging from 7.4% to 15.6%) **Dose-response relationship** No effects to report; this review only looked at the adverse health outcomes. **Type of LTPA** No effects to report; only one type of LTPA (i.e. running) was included in the review.	Low[uu]	CRITICAL
Stress fractures of the femoral neck: a review (Neubauer et al., 2016) *(86)*									

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
							Due to **Critically Low** rating on the AMSTAR 2 scale, this systematic review did **NOT** qualify for assessing the GRADE evidence.		CRITICAL

Training errors and running related injuries: a systematic review (Nielsen et al., 2012) *(87)*

28	7 Retrospective cohort[r] 12 Prospective cohort[s] 6 Case-control[t] 3 Randomized controlled trial[u]	Serious[v]	Serious[w]	Not serious	Not serious	None	**Adverse health outcomes** • In several studies, an increased risk, relative risk, or odds ratio for sustaining an RRI was reported when the weekly running frequency increased: persons running 6-7 times per week had the highest risk of RRI. • Based on the studies reviewed, it was not possible to identify which training errors were related to running related injuries. **Dose-response relationship** No effects to report, due to heterogeneity no meta-analysis was performed and hence no ORs or RRs were provided. **Type of LTPA** No effects to report; only one type of LTPA was included in the review.	Low[vv]	CRITICAL

Association between physical activity and risk of fracture (Qu et al., 2014) *(88)*

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
15	15 Prospective Cohort[x]	Serious[y]	Serious[z]	Not serious	Not serious	None	**Adverse health outcomes** • In the meta-analysis, the participants (total of 1,235,768) with the highest category of LTPA had an approximately 29% lower risk of total fractures compared to those in the lowest category, with 95% CIs of 0.63–0.80 (p<0.01) and moderate heterogeneity across studies (p=0.0, I^2=74.2%). • The analysis for subtypes of fracture showed a statistically significant inverse relationship between higher category of LTPA and risk of hip or wrist fracture (39% and 28% lower risk, respectively): i.e. among individuals in the highest category of LTPA, compared to those in the lowest category (95% CIs were 0.54–0.69 and 0.49–0.96, respectively, all p<0.01). • The association between LTPA and vertebral fracture risk was not statistically significant (RR, 0.87; 95% CI, 0.72–1.03; p<0.01). • Regarding age: the stratified analysis found an RR of 0.76 (95% CI, 0.60-0.91; p=0.52; I^2= 85.0%) for adults <62 years old. **Dose-response relationship** The review did not conduct a dose-response analysis, the existence of a dose-response relationship between LTPA and fracture risk remains unknown. **Type of LTPA** No effects to report; the review did not specify the type of LTPA in their high vs. low or moderate vs. sedentary comparisons.	Low[ww]	CRITICAL

What are the main risk factors for running-related injuries? (Saragiotto et al., 2014) *(89)*

9	9 Prospective Cohort[aa]	Serious[bb]	Serious[cc]	Not serious	Not serious	Even though the electronic search was conducted in the main databases related to the sports-injuries field, it is possible that eligible articles have been published in journals not indexed in any of the searched databases.	**Adverse health outcomes** No effects to report; this review only looked at risk factors for adverse health outcomes. Two of the five studies that investigated weekly distance as a risk factor identified that training for more than 64 km a week was a risk factor for lower extremity injuries. **Dose-response relationship** No effects to report, due to heterogeneity no meta-analysis was performed and hence no ORs or RRs were provided. **Type of LTPA** No effects to report; only one type of LTPA was included in the review.	Low[xx]	CRITICAL

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Epidemiology of ankle and foot overuse injuries in sports: a systematic review (Sobhani et al., 2013) *(90)*									
6	4 Prospective cohort[dd] 2 Cross-sectional[ee]	Serious[ff]	Serious[gg]	Serious[hh]	None	None	**Adverse health outcomes** The highest incidences of ankle and foot injury, expressed per 1000 athletes per season, were reported for: • sports dance (ballet), 338.5 (95% CI: 283.2-401.4) • running, 250.0 (95% CI: 100.5-515.1), • gymnastics, 188.7 (95% CI: 90.5-347.0) **Dose-response relationship** No effects to report, due to heterogeneity no meta-analysis was performed and hence no ORs or RRs were provided. **Type of LTPA** No effects to report; multiple sports were included in the review, but all summarizing conclusions were based on elite sports.	Very Low[yy]	CRITICAL
Incidence, risk factors and prevention of running related injuries in long-distance running: a systematic review (Tonoli et al., 2010) *(91)*									
							Due to **Critically Low** rating on the AMSTAR 2 scale, this systematic review did **NOT** qualify for assessing the GRADE evidence.		CRITICAL
Injuries in runners: a systematic review on risk factors and sex differences (van der Worp et al., 2015) *(92)*									

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
13	11 Prospective cohort[ii] 2 Retrospective cohort[jj]	Serious[kk]	Serious[ll]	Serious[mm]	Not Serious	Selection & Publication bias[kk]	**Adverse health outcomes** This review only looked at risk factors for adverse health outcomes. Factors that increased the risk of running-related injuries in women were: • older age: not specified • previous participation in non-axial sports (e.g. cycling, swimming, etc.) • participating last year in a marathon • running on concrete surface • longer weekly running distance (> 48–63.8 km) • wearing the same running shoes for > 4 to 6 months Men were at greater risk of running-related injuries if they had: • restarted running • history of previous injuries • running experience of 0–2 years • weekly running distance between 32–47.8 km • weekly running distance more than 64 km per week **Dose-response relationship** No effects to report, due to heterogeneity no meta-analysis was performed and hence no ORs or RRs were provided. **Type of LTPA** No effects to report; only one type of LTPA (i.e. running) was included in the review.	Very Low[zz]	CRITICAL

Incidence of Running-Related injuries per 1000 h of running in different types of runners: a systematic review and meta-analysis (Videbaek et al., 2015) *(93)*

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
12	7 Prospective cohort[nn] 5 Randomized controlled trials[oo]	Serious[pp]	Serious[qq]	Not Serious	Not Serious	None	**Adverse health outcomes** The weighted estimates showed that novice runners faced a significantly greater injury rate of 17.8 (95 % CI 16.7–19.1; population of 2,480) than recreational runners, who sustained 7.7 (95 % CI 6.9–8.7; population of 946) running-related injuries per 1000 hours of running. The weighted estimate showed an injury incidence for all types of runners combined of 1.07 (95 % CI 1.01–1.13) per 1000 km of running. (Based on a total population of 2,248 runners). **Dose-response relationship** No effects to report; the meta-analysis only looked at the adverse health outcomes relationship. **Type of LTPA** No effects to report; only one type of LTPA (i.e. running) was included in the review.	Low[aaa]	CRITICAL

PA = physical activity; OR = odds ratio; CI = confidence interval; RRMI = running-related musculoskeletal injury; RRI = running-related injury; RR = relative risk;

a: Authors did not provide breakdown of the cross-sectional and prospective cohort studies. Abiko et al., 2017; Araujo et al., 2015; Campos et al., 2016; Fernandes et al., 2014; Ferreira et al., 2012; Hespanhol Junior et al., 2012; Hespanhol Junior et al., 2013; Hino et al., 2009; Ishida et al., 2013; Lopes et al., 2011; Oliveira et al., 2012; Oliveira EGA, Santos-Filho SD, 2018; Pazin et al., 2008; Pileggi et al., 2010; Purim et al., 2014; Rangel et al., 2016; Rios et al., 2017; Rolim et al. 2015; Salicio et al., 2017; Saragiotto et al., 2016; Souza et al., 2014; Yamato et al., 2011
b: Most studies did not use a standard definition of injury. The limitations of the study include the moderate quality of evidence, use of self-administered questionnaires that can lead to memory bias, and lack of standard collected information, thus compromising a more detailed interpretation of the data.
c: Buist et al., 2008
d: Cantidio Ferreira et al., 2012
e: Nielsen et al., 2013; Nielsen et al., 2014
f: Among the non-randomized studies, the most frequent reasons for decreased quality scores were: low external validity, a follow-up period shorter than 12 weeks, and lack of reporting a measure of association, while the risk of bias was more related to the absence of blinding procedures in the included randomized trial.
g: Due to the heterogeneity observed in the study designs, the runners' profiles, as well as the methods used for data collection and analysis of changes in training load, comparison of the results of the four studies included in the present systematic review must be performed with caution.
h: Bovens et al., 1989; Hein et al., 2014; Hespanhol Junior et al., 2013; Lysholm and Wiklander, 1987; Malisoux et al., 2015; Nielsen et al., 2013; Nielsen et al., 2014; Taunton et al., 2003; van Middelkoop et al., 2007; Zwingenberger et al., 2014
i: There was variability in definitions of injury and/or pain, external training load, baseline assessments, data collection and statistical analysis.
j: No heterogeneity I^2 tests were performed or provided.
k: The generalizability of results should be considered given that nine studies involved a recreational ESP whereas three involved an elite ESP.
l: Lysholm, Wiklander, 1987; Pileggi et al., 2010
m: Jakobsen et al., 1994
n: Jacobs, Berson, 1986; McKean et al., 2006
o: Fallon 1996; Hutson 1984; Scheer, Murray, 2011
p: (Outcome) Although most of the studies have a clear definition of RRMIs the definitions always differ between studies. In terms of the participants, only one study performed a random sample

selection and two studies sampled the entire target population of runners. There are only three prospective studies that could enable the assessment of the loss to a follow-up criterion, and all of them fulfilled this criterion, which indicated a lower risk of bias in these studies.
q: No heterogeneity I^2 tests were performed or provided.
r: Koplan 1982; Koplan 1995; Marti 1988a; Marti 1988b; McKean 2006; Valliant 1981; Wen 1997
s: Bovens 1989; Fields 1990; Hootman 2002; Kelsey 2007; Lysholm 1987; Macera 1989; Middelkoop 2008; Pollock 1977; Satterthwaite 1999; Taunton 2003; Walter 1989; Wen 1998
t: Colbert 2000; Duffey 2000; McCrory 1999; Messier 1995; Messier 1991; Messier 1988
u: Buist 2008; Jakobsen 1994; Mechelen 1993
v: The types of participants (novice, recreational, and elite), and the injury definition used varied considerably between the studies.
w: No heterogeneity I^2 tests were performed or provided.
x: Mussolino et al., 1998; Hoidrup et al., 2001; Lau et al., 2001; Feskanich et al., 2002; Roy et al., 2003; Samelson et al., 2006; Thorpe et al., 2006; Michaelsson et al., 2007; Robbins et al., 2007; Appleby et al., 2008; Lee et al., 2010; Trimpou et al., 2010; Armstron et al., 2011; Nikander et al., 2011; Morseth et al., 2012
y: The quality of individual studies varied; some of these may have had limited adjustments for potential statistical confounders. The classification of the quantity of physical activity is difficult to evaluate, a fact that inevitably weakens the strength of the identified association. Differences in methodology between studies may also introduce heterogeneities.
z: Most of the I^2 estimates calculated in this meta-analysis were assessed as moderate. The overall I^2 value of 74.2% is considered as substantial.
aa: Bredeweg et al., 2012; Pileggi et al., 2010; Buist et al., 2009; Lun et al., 2004; Taunton et al., 2003; Wen et al., 1998; Fields et al., 1990; Macera et al., 1989; Walter et al., 1989
bb: The inconsistencies among studies complicate inter-study comparisons and prevent us from confirming the relationship between all risk factors and running injuries. In addition, relatively few prospective studies were identified in this review, reducing the overall ability to detect risk factors.
cc: We found a great heterogeneity of statistical methods between studies, which prevented us from performing a meta-analysis. No heterogeneity I^2 tests were performed or provided.
dd: Dannenberg et al., 1996; Olsen et al., 2006; Seil et al., 1998; van Ginckel et al., 2009
ee: Weiss 1985; Tuffery 1989
ff: Methodological information was missing or provided poorly in most studies. Lack of adequate description of population characteristics, sampling method, and participation rate makes it impossible to generalize results to relevant populations.
gg: Due to the heterogeneity across studies in terms of population characteristics, overuse definitions, assessment tools and sampling methods, data pooling and a meta-analysis were not possible. No heterogeneity I^2 tests were performed or provided.
hh: Incidence and Prevalence rates ranged considerably across studies.
ii: Thijs et al., 2011; Buist et al., 2010; Buist et al., 2010; Hesar et al., 2009; van Ginckel et al., 2009; van Middelkoop et al., 2008; Thijs et al., 2008; Lun et al., 2004; Taunton et al., 2003; Wen et al., 1998; Macera et al., 1989
jj: McKean et al., 2006; Wen et al., 1997
kk: By our inclusion criteria (e.g. long-distance runners recreational and/or competitive) for selecting the original studies, a broad spectrum in the type of runners (novice, track and field, etc.) was selected. Although we performed an extensive literature search, it is likely that both selection and publication bias influenced the results.
ll: The heterogeneity in study populations, in operationalization of both outcomes and risk factors, and time to follow-up prevented us from following a formal meta-analytical approach. No heterogeneity I^2 tests were performed or provided.
mm: Indirect comparisons = A point of concern is that many of the included studies did not clearly describe the participation rate of the target group, which limits the generalizability of findings.
nn: Bovens et al., 1989; Buist et al., 2010; Nielsen et al., 2013; Malisoux et al., 2015; Wen et al., 1998; Krabak et al., 2011; Lysholm et al., 1987
oo: Bredeweg et al., 2012; Buist et al., 2008; Jakobsen et al., 1994; Theisen et al., 2014; van Mechelen et al., 1993
pp: The definition of injury varies considerably across studies. Second, runners from the included studies were classified into four groups according to the type of runner, enabling relevant intergroup comparison. Third, the method of gathering data on exposure time may be questionable. Further, some studies specified the premise that the same runner was included and was contributing exposure time, if running was resumed after an injury occurrence (e.g. the can contribute two injuries from one individual).
qq: No heterogeneity I^2 tests were performed or provided.
rr: Certainty was downgraded from High to Moderate because of serious risk of bias.
ss: Certainty was downgraded from High to Low because of serious risk of bias and inconsistency.
tt: Certainty was downgraded from High to Very Low because of serious risk of bias, inconsistency, and indirectness.
uu: Certainty was downgraded from High to Low because of serious risk of bias and inconsistency.
vv: Certainty was downgraded from High to Low because of serious risk of bias and inconsistency.
ww: Certainty was downgraded from High to Low because of serious risk of bias and inconsistency.

xx: Certainty was downgraded from High to Low because of serious risk of bias and inconsistency.
yy: Certainty was downgraded from High to Very Low because of serious risk of bias, inconsistency, and indirectness.
zz: Certainty was downgraded from High to Very Low because of serious risk of bias, inconsistency, and indirectness.
aaa: Certainty was downgraded from High to Low because of serious risk of bias and inconsistency.

Osteoarthritis

Population: Adults 18 years of age and older
Exposure: Duration, frequency and/or intensity of LTPA, or a composite score reflecting total volume of LTPA
Comparison: No LTPA, or LTPA of a lesser duration, frequency and/or intensity, or composite score of total volume of LTPA.
Outcome: Adverse health outcomes (especially injury, osteoarthritis, erectile dysfunction, and exposure to pollution)

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
The association of recreational and competitive running with hip and knee osteoarthritis: a systematic review and meta-analysis (Alentorn-Geli et al., 2017) *(94)*									

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
25	13 case-control[a] 5 cross-sectional[b] 7 prospective cohort[c]	Serious[d]	Serious[e]	Serious[f]	Not serious	None	**Adverse health outcomes** • Compared with the control group, recreational runners had a significantly lower association with hip and/or knee OA (OR 0.66; 95% CI 0.57-0.76; I^2 50%) and knee OA alone (OR 0.72; 95% CI 0.63-0.83; I^2 0%) in the overall population and in males (OR 0.78; 95% CI 0.68-0.89; I^2 0%; and OR 0.7; 95% CI 0.5-0.97; I^2 0% respectively). • Compared with the control group, female recreational runners had a lower association with hip and/or knee OA (OR 0.54; 95% CI 0.41-0.71; I^2 43%). • In fact, running at recreational level was even found to have a protective effect on hip and/or knee OA. • It was also not possible to demonstrate the confounding effect of associated risk factors (age, gender, weight, occupational workload and previous injury) on the risk of OA in runners. **Dose-response relationship** Compared with the control group, individuals with exposure to running of less than 15 years had a lower association with hip and/or knee OA in: • the overall population (OR 0.6; 95% CI 0.49-0.73; I^2 47%) • males (OR 0.79; 95% CI 0.68-0.91; I^2 0%) • females (OR 0.52; 95% CI 0.47-0.57; I^2 0%) **Type of LTPA** No effects to report; the meta-analysis pooled running and orienteering (e.g. runners that use a topographical map to navigate from point A to point B at speed in unfamiliar terrain) populations at the recreational level, but did not analyze these separately.	Very Low[n]	CRITICAL

Running and knee osteoarthritis: a systematic review and meta-analysis (Timmins et al., 2017) *(95)*

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
10	4 case-control[g] 1 ambispective cohort[h] 2 prospective cohort[i] 3 retrospective cohort[j]	Serious[k]	Serious[l]	Serious[m]	Not serious	None	**Adverse health outcomes** The combined odds ratio of undergoing knee surgery due to OA was 0.46 (95% CI 0.30-0.71) in runners or orienteers when compared with non-runners. The I^2 was 0%, with 95% CI 0% to 73%. From this evidence, it is not possible to conclude whether running was associated with a diagnosis of knee OA, and studies offered differing conclusions.[p] **Dose-response relationship** No effects to report; this review only looked at the adverse health outcomes relationship for OA. **Type of LTPA** No effects to report; the meta-analysis pooled running and orienteering populations, but did not analyze these separately.	Very Low[o]	CRITICAL

PA = physical activity; OA = osteoarthritis; OR = odds ratio; CI = confidence interval

a: Oahaghin et al., 2009; Kettunen et al., 1999; Kohatsu and Schurman, 1990; Lau et al., 2000; Lo et al., 2016; Manninen et al., 2001; Marti et al., 1989; Puranen et al., 1975; Sohn and Micheli, 1985; Spector et al., 1996; Wingard et al., 1993; Wingard et al., 1998; Vrezas et al., 2010
b: Konradsen et al., 1990; Lane et al., 1986; Panush et al., 1986; Puranen et al., 1975; Williams 2013
c: Chakravarty et al., 2008; Cheng et al., 2000; Kujala et al., 1994; Kujala et al., 1999; Lane et al., 1993; Lane et al., 1998; Panush et al., 1995
d: The assessment of the risk of bias was conducted using a tool not specifically designed for observational, etiologic association studies and the use of other appraisal tools might therefore provide different insights. 16/25 studies scored High risk on the type of bias detection.
e: Due to high between-studies heterogeneity (high I^2 statistic), the random-effects model, which can inappropriately weight smaller studies in some instances, was necessary. 30-60% (as captured in summary of effects) may be considered moderate.
f: In some studies, the runners were also exposed to other types of sport (i.e. tennis), the runners included some individuals performing only walking exercise, or involved orienteering running.
g: Kohatsu, 1990; Sandmark, 1999; Manninen, 2001; Thelin, 2006
h: Panush, 1986
i: Lane, 1986; Felson, 2007
j: de Carvalho, 1977; Muhlbauer, 2000; Mosher, 2010
k: Gray literature was not included in the eligibility criteria. As a result, the findings of this review may reflect publication bias. The meta-analysis included only a small number of studies, with odds ratios that represent unadjusted proportions (i.e., odds were not adjusted for confounding factors). Given the nature of observational studies, only low- to moderate-quality evidence could be expected. However, the assessment of potential bias undertaken in this review indicated that many studies would be downgraded to low or very low quality.
l: Although the I^2 indicated low heterogeneity, the upper 95% CI of the I^2 is high (73%), and the pooled estimate should be interpreted with caution.
m: The populations under investigation are not the same. The outcomes are differently defined in these studies.
n: Certainty rated from High to Very Low because of serious risk of bias, inconsistency, and indirectness.
o: Certainty rated from High to Very Low because of serious risk of bias, inconsistency, and indirectness.
p: The review considered 5 different outcomes related to knee OA: diagnosis of knee OA, radiographic and imaging markers, arthroplasty for knee OA, knee pain, and knee-associated disability. Due to heterogeneity of outcome definition and measurement of studies, only 1 meta-analysis was appropriate: This combined the case-control studies that identified cases of knee surgery due to OA. Hence overall, there was no conclusion to be made on the relationship between running and knee OA as a long-term adverse health outcome.

Erectile Dysfunction

Population: Adults 18 years of age and older
Exposure: Duration, frequency and/or intensity of LTPA, or a composite score reflecting total volume of LTPA
Comparison: No LTPA, or LTPA of a lesser duration, frequency and/or intensity, or composite score of total volume of LTPA.
Outcome: Adverse health outcomes (especially injury, osteoarthritis, erectile dysfunction, and exposure to pollution)

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Bicycle riding and erectile dysfunction: a review (Sommer et al., 2010) *(96)*									
							Due to **Critically Low** rating on the AMSTAR 2 scale, this systematic review did **NOT** qualify for assessing the GRADE evidence.		HIGH

LTPA = leisure-time physical activity

Exposure to Air Pollution

Population: Adults 18 years of age and older
Exposure: Duration, frequency and/or intensity of LTPA, or a composite score reflecting total volume of LTPA
Comparison: No LTPA, or LTPA of a lesser duration, frequency and/or intensity, or composite score of total volume of LTPA.
Outcome: Adverse health outcomes (especially injury, osteoarthritis, erectile dysfunction, and exposure to air pollution)

Certainty assessment							Summary Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
N/A									
							No Systematic Reviews were found in relation to the Exposure to air Pollution outcome for assessing the GRADE evidence.		LOW

LTPA = leisure-time physical activity

Table B.1.i. Sleep outcomes: Association between physical activity and sleep outcomes among adults

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	**Inconsistency**	**Indirectness†**	**Imprecision**	**Other**		
Kovacevic 2018 *(36)* Moderate	10 RCTS N=NR	Serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	None	Studies evaluated the effects of **resistance training** vs. no intervention or other exercise intervention on sleep outcomes. Seven studies compared resistance training with a non-exercise control group and 3 studies compared the effects of aerobic exercise plus resistance training vs. aerobic exercise alone. Variability in study populations included those with mental health symptoms or diagnoses, older adults, nursing home residents, and adults with co-morbid health conditions (fibromyalgia, heart failure and sleep apnoea, breast cancer), mean age was 58 years. 1/3 studies found a significant effect of resistance training vs. no exercise on subjective measures of **sleep quantity**; 5/7 studies reported significant improvement in subjective measures of **sleep quality**. In studies comparing aerobic exercise plus resistance training vs. aerobic exercise alone, 1/1 study found no effect on **sleep quantity**. 2/2 studies found no effect on objective measures of **sleep quality** whereas 1/1 study found a significant effect on subjective measures of sleep quality.	LOW[a]
Perez-Lopez 2017 *(55)* Moderate	3 RCTs N=469	No serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Studies evaluated the effects of **exercise interventions that were at least 6 weeks in duration** vs. no exercise control groups reporting symptoms of insomnia among middle-aged and older women. Exercise interventions were associated with reduced **symptoms of insomnia** vs. no exercise control groups among women (SMD = -0.52 [95% CI, -1.02 to -0.02], 3 RCTs).	LOW[b]
Robbins 2019 *(58)* Low	5 pre-post studies N=NR	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Studies evaluated the effects of **any workplace intervention**, including PA or yoga, on measures of sleep. 1/5 studies found a significant improvement in self-reported **sleep quality** following a yoga intervention; no studies reported significant improvement in self-reported **sleep quantity** following the intervention.	VERY LOW[c]

Stutz 2019 *(68)* Moderate	23 crossover studies N=275	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Studies evaluated the effects of **one single session of exercise close to usual bedtime** (less than 4 hours before usual bedtime) on various measures of sleep. All studies enrolled healthy or good sleepers, except one study that enrolled adults with self-reported sleep difficulties. Adults included sedentary individuals as well as trained athletes. Most interventions were cycling or running, with an average duration of 87 minutes. Compared with no-exercise, one session of PA ending 12 minutes to 4 hours before bedtime significantly increased **REM latency and slow-wave sleep, and decreased stage 1 sleep. N**o effects were found for **SOL, TST, SE, WASO, stage 2, 3, and 4 sleep, REM sleep, or subjective sleep quality.**	VERY LOW[d]

Abbreviations: CI = confidence interval; NR = not reported PA = physical activity; RCT = randomized controlled trial; REM = rapid eye movement; SE = sleep efficiency; SMD = standardized mean difference; SOL = sleep onset latency; TST = total sleep time; WASO = wake after sleep onset

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious risk of bias, serious inconsistency of effects(direction and significance of effects highly variable), and serious indirectness in measures, interventions, and variability in populations
[b] Certainty of evidence downgraded given serious inconsistency (I^2=81%), serious indirectness in outcome measure, and imprecision in estimate of effect
[c] Certainty of evidence downgraded given serious risk of bias and serious indirectness in measures of sleep as well as interventions
[d] Certainty of evidence downgraded given serious risk of bias, serious inconsistency within and between studies in measures of sleep, serious indirectness in measures of sleep as well as interventions, and serious imprecision in estimates of effects

Table B.1.j. Incidence of hypertension: Association between physical activity and incidence of hypertension among adults

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness†	Imprecision	Other		
Paudel 2019 *(54)* Low	5 cross sectional studies N=10,344	Serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Examination of the association between **PA** and **incident hypertension** among South Asian adults. Two studies found lower odds of hypertension among those with mild or moderate levels of PA compared with a sedentary group and higher (≥30 hrs/week) vs. lower (<10 hrs/week) of walking. One study found the prevalence of hypertension was lower among persons with moderate levels of occupational PA whereas another study found no association between levels of occupational PA and hypertension. One study saw higher prevalence of hypertension among those with low vs. high levels of total PA.	VERY LOW[a]

Abbreviations: hrs = hours; PA = physical activity

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence rated as very low according to authors given serious risk of bias and serious imprecision. Serious indirectness is also present given variability in comparisons

Table B.1.k. Health-related quality of life: Association between physical activity and measures of HRQOL among adults

See the Supplementary materials for description of evidence of US PAGAC by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**
		Risk of bias	**Inconsistency**	**Indirectness†**	**Imprecision**	**Other**		
Perez-Lopez 2017 *(55)* Moderate	3 RCTs N=189	No serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Studies evaluated the effects of **exercise interventions that were at least 6 weeks in duration** vs. no exercise control groups reporting symptoms of depression among middle-aged and older women. Exercise interventions was not associated with reduced **measures of quality of life** vs. no exercise control groups among women (SMD = -0.27 [95% CI, -1.08 to 0.54], 3 RCTs).	LOW[a]
Wang 2017 Low	4 RCTs N=314	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Evaluation of **Tai Chi** exercise in perimenopausal women on measures of the SF-36. Studies represented women aged 45 and older; most with low bone mass or osteopenia. There was no consistent effect of Tai Chi vs. no Tai Chi across all 8 subscales on the SF-36.	MODERATE[b]

Abbreviations: CI = confidence interval; RCT = randomized clinical trial; SF-36 = short-form 36 quality-of-life instrument; SMD = standardized mean difference

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious inconsistency (I^2=85%), serious indirectness in outcome measure, and imprecision in estimate of effect

[b] Certainty of evidence downgraded given serious indirectness in measures of effect (subscales vs. domain-specific measures of SF-36)

Table B.1.I. Occupational physical activity domain

Methods:
An umbrella review (i.e. a review of reviews) was performed. This review had been a-priori registered in PROSPERO (id. 163090). This umbrella review synthesized and combined relevant data from systematic reviews or meta-analyses.

Inclusion and exclusion criteria:
Reviews were eligible for inclusion in this umbrella review if they met all of the following criteria:
- contained a quantitative assessment of OPA, possibly in combination with LTPA and/or transport-related PA;
- contained an assessment of one or more health-related outcomes (as described in more detail below);
- was published as a full-text systematic review (with meta-analyses, if available) in a peer-reviewed journal;
- described at least 2 studies with either one of the following study designs: intervention studies (such as [randomized]-controlled trials) or longitudinal [prospective or retrospective] observational design studies).

Reviews were excluded if they:
- measured total PA, LTPA or transport-related PA only, or in combination and did not specify the OPA domain;
- focused on sedentary behaviour only (rather than PA);
- focused only on biomechanical (i.e. ergonomic) physical work exposures, rather than energetic (occupational) PA;
- focused on a specific (clinical) population (such as specific samples of people with underlying diseases or pregnant woman);
- published in a language other than English.

Population-Exposure-Control-Outcome
The WHO Guideline Development Group decided for the scope of their guidelines to use PECO (Population-Exposure-Control-Outcome) search questions.
- Population: Adults (aged 18-64 years).
- Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
- Comparison: No OPA, OPA of shorter duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
- Outcomes: Outcomes considered critical or important, according to the WHO PA guidelines committee: all-cause mortality, diabetes mellitus type 2, cancer, osteoarthritis, mental health outcomes, adiposity/(prevention of) body weight gain, cognitive outcomes, sleep duration of quality, hypertension, health-related quality of life.

Search and selection
In order to identify relevant evidence, a search for existing systematic reviews or meta-analyses was conducted. The following databases were searched: Pubmed, Web of Science, Embase and Sportdiscus. The full search strategy can be found in Supplementary material 1. Systematic searches were conducted in December 2019. Searches contained the following keywords: occupational physical activity, systematic reviews, and meta-analyses. The searches were not restricted by publication date. Final search results were exported into Endnote reference manager. To identify additional reviews not found in the database search mentioned above snowball searching was used, by screening reference lists of included articles, and experts in the field were consulted.

Study selection

Two reviewers screened the title and abstract of each reference (BC and ML), following the in- or exclusion criteria for each of the reviews. Discrepancies between the two independent reviewers were resolved in a consensus meeting. In case of no agreement, a third reviewer was consulted (PC). This was done blinded in the online application Rayyan *(100)*. Two reviewers did a full text screening for in- and exclusion criteria (BC and ML). Discrepancies were resolved with the help of the third reviewer (PC).

Assessing Bias in systematic reviews

The included systematic reviews were assed using AMSTAR 2 *(76)* (A Measurement Tool to Assess Systematic Reviews), which is a 16-point assessment tool for the assessment of the methodological quality of systematic reviews. AMSTAR 2 has good inter-rater agreement, test-retest reliability and content validity *(101)*. Each item was rated High, Moderate, Low or Critically Low. The cut-off values were 100%, ≥75%, ≥50%, and below 50%, respectively. Two reviewers used the tool to assess the risk of bias in the included reviews. If rated Critically Low, the review was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence.

Criterion-specific AMSTAR 2 credibility rating, over-all rating score, overall rating, for each included review. See supplementary material 7 for all considerations.

Author, Year	PECO[1]	A-priori Methods[2]	Study Design Selection[3]	Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assess-ment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Rating score[17]	Overall Rating[18]
Samitz 2011	Yes	No	Yes	Yes	PY	PY	Yes	Yes	No	Yes	Yes	Yes	No	PY	Yes	Yes	**0.71**	**Low**
Coenen 2018	Yes	Yes	Yes	Yes	PY	PY	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	**0.78**	**Moderate**
Wendel Vos 2004	Yes	No	PY	No	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	**0.59**	**Low**
Jian Li 2013	Yes	No	Yes	PY	No	No	No	Yes	No	No	PY	No	No	No	PY	Yes	**0.34**	**Critically low**
Sattelmair 2011	Yes	No	Yes	PY	PY	PY	PY	Yes	No	Yes	Yes	No	No	no	Yes	Yes	**0.56**	**Low**
Wolin 2009	Yes	No	Yes	PY	PY	No	No	PY	No	No	PY	PY	PY	PY	Yes	No	**0.41**	**Critically low**
Mahmood, 2017	Yes	Yes	Yes	PY	PY	PY	PY	Yes	No	No	Yes	No	No	PY	Yes	Yes	**0.59**	**Low**
Boyle 2012	Yes	No	Yes	PY	PY	PY	PY	Yes	Yes	Yes	Yes	Yes	Yes	PY	Yes	Yes	**0.78**	**Moderate**
Samad 2005	Yes	No	Yes	PY	No	No	No	Yes	No	No	Yes	No	No	No	No	No	**0.28**	**Critically low**
Robsahm 2013	Yes	No	Yes	PY	No	No	No	Yes	PY	No	Yes	Yes	Yes	Yes	No	Yes	**0.56**	**Low**
Wu Y, 2013	Yes	No	Yes	PY	PY	PY	No	Yes	No	No	Yes	No	No	Yes	Yes	PY	**0.5**	**Low**
Pizot 2016	Yes	No	Yes	PY	PY	No	No	Yes	No	Yes	No	no	No	Yes	Yes	Yes	**0.5**	**Low**
Chen X 2019	Yes	No	Yes	PY	PY	PY	No	Yes	Yes	Yes	Yes	N/A	N/A	Yes	Yes	Yes	**0.75**	**Moderate**
Voskuil 2007	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	No	No	PY	Yes	No	**0.53**	**Low**
Schmid 2015	Yes	No	Yes	PY	No	PY	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	**0.69**	**Low**
Vermaete 2013	Yes	No	Yes	PY	No	Yes	PY	Yes	Yes	Yes	Yes	No	No	PY	No	Yes	**0.56**	**Low**
Singh 2014	Yes	Yes	Yes	PY	Yes	PY	No	Yes	Yes	Yes	Yes	Yes	PY	PY	Yes	Yes	**0.75**	**Moderate**
Psaltopoulou 2015	Yes	No	Yes	PY	PY	PY	PY	Yes	Yes	No	Yes	No	No	PY	Yes	Yes	**0.81**	**Moderate**
Chen Y 2014	Yes	No	Yes	PY	PY	PY	PY	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	**0.69**	**Low**
Behrens 2014	Yes	No	Yes	Yes	No	No	No	Yes	Yes	No	Yes	Yes	PY	PY	No	No	**0.5**	**Low**
Behrens, 2013	Yes	no	Yes	Yes	No	No	PY	Yes	Yes	No	Yes	Yes	No	Yes	Yes	no	**0.59**	**Low**
Shephard 2016	Yes	No	Yes	PY	No	No	No	Yes	No	Yes	N/A	N/A	N/A	N/A	N/A	Yes	**0.5**	**Low**
Krstev 2019	Yes	No	Yes	PY	No	no	PY	Yes	no	Yes	NO	No	No	PY	no	Yes	**0.41**	**Critically low**

Benke, 2018	Yes	No	Yes	PY	No	PY	PY	Yes	Yes	Yes	Yes	Yes	No	PY	Yes	Yes	**0.69**	**Low**
Shephard, 2017	Yes	No	Yes	PY	No	No	No	Yes	No	Yes	N/A	N/A	N/A	N/A	No	Yes	**0.5**	**Low**
Liu 2011	Yes	No	Yes	Yes	No	Yes	PY	Yes	Yes	Yes	Yes	Yes	Yes	PY	Yes	Yes	**0.81**	**Moderate**
O Rorke, 2010	Yes	No	Yes	Yes	PY	PY	No	No	No	Yes	Yes	No	No	PY	Yes	No	**0.41**	**Critically low**
Bao 2008	Yes	No	Yes	PY	No	No	PY	Yes	No	Yes	Yes	No	PY	No	Yes	Yes	**0.53**	**Low**
Keimling 2014	Yes	No	Yes	PY	PY	No	PY	Yes	No	No	Yes	No	No	Yes	Yes	No	**0.47**	**Critically low**
Aune 2015	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	PY	PY	Yes	Yes	Yes	**0.75**	**Moderate**
McWilliams 2011	Yes	No	Yes	Yes	No	PY	PY	Yes	Yes	Yes	No	No	No	No	No	Yes	**0.5**	**Low**
Gignac 2019	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	N/A	N/A	N/A	N/A	No	no	**0.58**	**Low**
Palmer 2012	Yes	No	No	PY	No	No	No	Yes	Yes	Yes	N/A	N/A	No	No	No	no	**0.32**	**Critically low**
White 2017	Yes	Yes	Yes	Yes	Yes	Yes	PY	Yes	Yes	Yes	Yes	PY	Yes	PY	PY	Yes	**0.88**	**Moderate**
Yang B, 2018	Yes	No	Yes	PY	PY	No	No	Yes	No	PY	Yes	No	No	Yes	Yes	No	**0.5**	**Low**
Huai 2013	Yes	No	Yes	PY	No	PY	PY	Yes	Yes	Yes	Yes	No	No	Yes	Yes	no	**0.59**	**Low**

Abbreviations: COI = conflict of interest; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] This score is based on the following calculation (Yes=1point, PY=0.5 point). Take the total amount of points and divide these the number of questions answered.
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both *(76)*.

1.0. All-cause mortality

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: All-cause mortality.

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Domains of physical activity and all-cause mortality: systematic review and dose–response meta-analysis of cohort studies (Samitz, G. 2012)*(102)* 82412/17069 (no of participants/deaths)									
6[a]	Prospective studies	Serious[c]	Serious[d]	Not serious	Not serious	None	This review compared highest with lowest PA levels in the association with mortality. **OPA** Associations were found for OPA (RR=0.83; 95% CI 0.71–0.97) OPA: 4 studies in men; (RR=0.94; 95% CI 0.75-1.19) 90,8% I^2 OPA: 3 studies in women: (RR=0.66; 95% CI 0.49-0.89) 89% I^2 **LTPA:** The strongest associations between PA and mortality were observed for LTPA (RR 0.74; 95% CI 0.70–0.77),	Low[i]	Critically
Do highly physically active workers die early? A systematic review with meta-analysis of data from 193 696 participants. (Coenen, 2018)*(103)*									

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
17[b]	Prospective cohort studies	Serious[e]	Serious[f]	Not serious	Not serious[g]	Some risk of publication bias [h]	This review compared workers with high level of OPA with low level of OPA in association with mortality: **OPA:** Pooled results showed that male workers with high level OPA had a statistically significant higher mortality risk than those engaging in low level OPA (HR 1.18, 95% CI 1.05 to 1.34, I2 =76%) A non-significant tendency for an inverse association was found among women (HR=0.90; 95% CI 0.80 to 1.01), I2 =0%). **LTPA:** LTPA not assessed in this review	Low[j]	Critically

a: Eaton 1995; Andersen 2000; Yu 2003; Barengo 2004; Lissner 1996; Besson 2008

b: Petersen 2012; Hu G 2014; Clays 2014; Harari 2015; Richard 2015; Etemadi; 2014; Menotti 2006; Chau 2015; Holtermann 2012; Holtermann 2010; Stender 1993; Wanner 2014; Holtermann 2011; Turi 2017; Huerta 2016; Krause 2017

c: Serious: We can't rule out residual confounding; The assessment of physical activity at baseline only, may also have introduced bias, particularly in studies of longer duration

d: Serious risk of inconsistency: high heterogeneity in the studies. Different results for men and women.

e: Serious: Possible conservative misclassification bias, leading to an underestimation of the magnitude of the association/ Studies included in this review were based only on self-reports of occupational PA

f: Serious risk of inconsistency: there was considerable heterogeneity in our pooled study findings, with up to 77% heterogeneity in the main findings.

g: We decided not to rate down for serious imprecision because the men did not include the 1.0 in their analysis. And the most studies were in the male population.

h: We do not rate down because only some risk is detected: Some risk of publication bias with under-publication of negative and underpowered results.

i: rated down from high to low because of serious risk of bias and serious inconsistency

j: rated down from high to low because of serious risk of bias and serious inconsistency

2.0. Cardio-vascular disease

2.1. Stroke

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Cardio-vascular disease.

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity and stroke. A meta-analysis of observational data. (Wendel-Vos 2004) *(104)*									
11[a]	Cohort studies	Serious [c]	Serious[d]	Not serious	Not serious	None	This review compared three groups (active, moderately active and inactive) **OPA:** People who were physically active at work were at lower risk of ischaemic stroke compared with both physically inactive (RR = 0.57, 95% CI: 0.43, 0.77) and moderately physically active (RR = 0.77, 95% CI: 0.60, 0.98) people at the workplace. For total stroke these numbers were not significant (RR=0.74, 95% 0.49-1.12) and (RR= 0.92, 95% 0.92-1.24) **LTPA:** People who were active in their leisure time were at lower risk of ischaemic stroke compared with inactive (RR= 0.79. 95% 0.69-0.91) and moderately active (RR=0.84, 95% 0.63-1.11). For total stroke these numbers were (RR=0.78, 95% 0.71-0.85) and (RR=0.95, 95% 0.68- 1.32)	Low[f]	Critically

Physical activity and risk of cardiovascular disease: What does the new epidemiological evidence show? (Li J. 2013) *(105)* **Overall CVD risks/ Coronary heart disease/stroke/unclassified CVD**

This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence. (AMSTAR2 rating)

2.2. Coronary Heart Disease

Dose Response Between Physical Activity and Risk of Coronary Heart Disease (Sattelmair 2011) *(106)* **Coronary Heart Disease.**

4[b]	Cohort studies	Serious[e]	Not Serious	Not serious	Not serious	None	This review compared the highest to the categories of PA for each type of PA using random effects pooled RRs. **OPA :** OPA was associated with a reduction (RR=0.84, 95% CI; 0.79-0.90) risk of CHD. 3 out of 4 studies were based on men (RR=0.87, CI 95% 0.81-0.99). Heterogeneity (I^2) was 0% **LTPA:** The pooled risk among all studies that assessed LTPA indicated a risk reduction (RR, 0.74; 95% CI, 0.69-0.78) in Coronary Heart Disease.	Moderate[g]	Critically

a: Okada 1976; Paffenbarger 1978; Salonen 1982; Menotti 1990; Haheim 1996; Gillum 1996; Nakayama 1997; Evenson 1999

b: Eaton 1995; Rosengren 1997; Hu 2007; Virkkunen 2007.

c: Serious; The definitions of high, moderate, and low levels of physical activity varied substantially among studies. In the meta-analysis the degree of adjustment variables varied from study to study

d: Serious; High heterogeneity

e: Serious; primary source of potential residual confounding is likely to stem from confounding variables that were either unmeasured or insufficiently measured in the individual studies themselves. For instance, dietary intake was rarely assessed in the studies reviewed.

f: certainty downgraded from high to low because of serious risk of bias and serious inconsistency

g: certainty downgraded form high to moderate because of serious risk of bias

3.0. Cancer

3.1. Colon cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Colon cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity and colon cancer prevention: a meta-analysis (Wolin, 2009) *(107)*									

This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence (AMSTAR2 rating)

Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: A systematic review and meta analyses (Mahmood, 2017) *(108)*

15[a]	5 Cohort studies 10 case control	Serious[d]	Not serious	Not serious	Not serious	none	This review compared the highest vs the lowest category of PA. **OPA**: OPA was inversely associated with risk of colon cancer (RR=0.74, 95% CI: 0.67-0.82). The OPA association was stronger for men than for women, but sex also explained little of the heterogeneity. **Dose response:** From the dose-response analyses, the pooled RR per 210 MET h/week was RR=0.89, 95% CI: 0.85- 0.93) **LTPA:** LTPA was inversely associated with risk of colon cancer(RR=0.80 ,95% CI: 0.71-0.89) The LTPA association was stronger for men than for women, but sex also explained little of the heterogeneity.	Moderate[h]	Critically

Physical Activity and Risks of Proximal and Distal Colon Cancers: A Systematic Review and Meta-analysis (Boyle, 2012) *(109)*

10[b]	6 cohort studies 4 case control	Serious[e]	Serious[f]	Not serious	Not serious	none	This review compared the highest and lowest category of PA that were used for the main results. **OPA:** OPA was inversely related with proximal colon cancer (RR= 0.72; 95% CI: 0.61-0.85) and distal colon cancer (RR= 0.75, 95% CI: 0.63-0.88). **LTPA:** LTPA was inversely related with proximal colon cancer (RR=0.84, 95% CI: 0.76-0.92) and distal colon cancer (RR=0.74, 95% CI: 0.66-0.83)	Low[i]	Critically

A **meta-analysis of the association of physical activity with reduced risk of colorectal cancer (Samad, 2005)** *(110)*

This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence (AMSTAR2 rating)

Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies (Robsahm. 2013) *(111)*

5[c]	Cohort studies	Serious[g]	Not serious	Not serious	Not serious	none	This review compared the most physically active vs those who were the least physically active. **OPA:** OPA was inversely related with proximal colon cancer; (RR=0.59, 95% CI: 0.53-0.66) OPA activity was inversely related with distal colon cancer (RR=0.61, 95% CI: 0.53-0.70) **LTPA:** LTPA was inversely related with proximal colon cancer: (RR=0.53, 95% CI: 0.44-0.64) LTPA was inversely related with distal colon (RR=0.40, 95% CI: 0.30-0.53)	Moderate[j]	Critically

a: Cohort studies 5; Morati, 2008; Larsson 2006; Colbert 2001; Thune 1996; Boyle 2011; Case control 10: Parent 2011; Isomura 2006; Kato 1990; Arbman 1993; Markowitz 1992; Zhang 2006; Hou 2004; White 1996; Brownson 1991; Slattery 1990.

b: 6 cohort studies: Boyle 2011; Colbert 2001; Freidenreich 2006; Howard 2008; Larsson 2000; Maradi 2008. 4 case control studies; Isomura 2006; Levi 1999; Brownson 1989; Vena 1985.

c: Gerhardsson et al., 1986; Thune and Lund, 1996; Friedenreich et al., 2006; Larsson et al., 2006; Moradi et al., 2008

d: Serious; Variable methods were used to measure the extent of physical activity in occupations, ranging from enquiring about the years spent in active jobs to asking whether the jobs involved light activity only (i.e. occasional walking) or doing heavy manual labour. There was considerable variation between studies with regard to adjustment for confounding, which may have affected estimates of the associations between domain-specific physical activity/sedentary behaviour and colon and rectal cancer risk, and therefore upon our results

e: Serious: our results do not provide any information about the duration, frequency, intensity, or timing of physical activity required to optimally reduce the risk of colon cancer

f: Serious: Although we found low statistical heterogeneity in the primary meta-analysis and in the subgroup analyses, as with most meta-analyses of observational studies, the included studies were conducted on different population groups, and the measurement and categorization of the exposure (physical activity) was highly heterogeneous.

g: Moreover, it is difficult to measure the level of physical activity in a valid and reliable way, and it is particularly difficult to assess the lifetime level of activity

h: certainty downgraded from high to moderate because of serious risk of bias

i: certainty downgraded from high to low because of serious risk of bias and inconsistency

j: certainty downgraded from high to moderate because of serious risk of bias

3.2. Rectal cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Rectal cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: A systematic review and meta-analysis (Mahmood, 2017) *(108)*									
12[a]	5 cohort 7 case control	Serious[c]	Not serious	Not serious	Not serious	none	This review compared the highest versus the lowest category of PA. **OPA:** OPA was inversely associated with rectal cancer risk (RR= 0.88, 95% CI: 0.79, 0.98). Low heterogeneity for rectal cancer. **LTPA:** A weak association was observed with rectal cancer: (RR= 0.87, 95% CI: 0.75, 1.01)	Moderate[e]	Critically
Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies (Robsahm. 2013) *(111)*									
3[b]	Cohort studies	Very serious[d]	Not serious	Not serious	Not serious	none	This review compared those in the highest PA level compared with those least active **OPA:** An inverse association was observed between OPA and the risk of rectum cancer (RR=0.80, 95% CI: 0.72-0.89) **LTPA:** An inverse association was observed between LTPA and the risk of rectal cancer (RR=0.66, 95% CI: 0.55-0.79)	Low[f]	Critically

a: Cohort studies 5; Morati, 2008; Larsson 2006; Colbert 2001; Thune 1996; Boyle 2011. Case control 7 studies; Parent 2011; Isomura 2006; Kato 1990; Arbman 1993; Markowitz 1992; Longnecker 1995; Slattery 2003

b: Friedenreich 2006; Larsson 2006; Moradi 2008.

c: Serious; Variable methods were used to measure the extent of physical activity in occupations, ranging from enquiring about the years spent in active jobs to asking whether the jobs involved light activity only (i.e. occasional walking) or doing heavy manual labour. There was considerable variation between studies with regard to adjustment for confounding, which may have affected estimates of the associations between domain-specific physical activity/sedentary behaviour and colon and rectal cancer risk, and therefore upon our results.

d: Moreover, it is difficult to measure the level of physical activity in a valid and reliable way, and it is particularly difficult to assess the lifetime level of activity. There were only three studies included in the review.

e: Certainty rated from high to moderate because of serious risk of bias

f: Certainty rated from high to low because of very serious risk of bias

3.3. Breast cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Breast cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Physical activity and risk of breast cancer: a meta-analysis of prospective studies (Wu Y, 2013) *(112)*									
7[a]	Cohort studies	Serious[d]	Not serious[e]	Not serious	Not serious	none	This review compared to the highest versus lowest categories of PA. **OPA:** An inverse association was observed between OPA and the risk of breast cancer risk **(**RR = 0.90, 95 % CI = 0.83–0.97) **LTPA:** An inverse association was observed between LTPA and the risk of breast cancer risk (RR= 0.89, 95% CI = 0.85-0.92)	Low[h]	Critically
Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of prospective studies (Pizot, 2015) *(113)*									
11[b]	Cohort studies	Serious[f]	Not serious	Not serious	Not serious	none	They compared the highest versus lowest level of PA. **OPA:** An inverse association was observed between OPA and the risk of breast cancer (RR=0.88, 95% CI= 0.82-0.95) **LTPA:** An inverse association was observed between LTPA and the risk of breast cancer (RR= 0.87, 95% CI=0.84-0.91)	Moderate[i]	Critically
Physical Activity and Risk of Breast Cancer: A Meta-Analysis of 38 Cohort Studies in 45 Study Reports (Chen, 2019) *(114)*									

6[c]	Cohort studies	Serious[g]	Not serious	Not serious	Not serious	None	The highest category compared with that of the lowest category of PA **OPA:** OPA was related with a significantly lower risk of breast cancer (ORR 0.91; 95% CI: 0.84-0.99) **LTPA:** LTPA was related with a significantly lower risk of breast cancer (ORR 0.88; 95% CI: 0.85- 0.91)	Moderate[j]	Critically

a: Thune 1997; Moradi 2002; Rintala 2002; Pronk 2011; steindorf 2012; Luoto 2000; Mertens 2006

b: Steenland 1995; Thune 1997; Moradi 1999; Dirx 2001 ; Moradi 2002; Rintala 2002; Rintala 2003; Mertens 2006; George 2010; Pronk 2011; Steindorf 2013;

c: Steindorf 2012; Mertens 2006; Rintala 2003; Moradi 2002; Luoto 2000, Thune 1997.

d: Serious; First, a wide range of definitions of physical activity have been used in previous studies as they have not uniformly assessed all types of physical activity (i.e., occupational, household, and recreational), the dose of activity (frequency, intensity, and duration), or all time periods in life when activity was performed. There are unmeasured confounders.

e: No Serious inconsistency for OPA: 46.1%. But the overall between-study heterogeneity is common in meta-analysis because of diversity in design quality, population stratification, characteristics of the sample, non-comparable measurement of physical activity, variation of the covariates, doses, and lengths of follow up:

f: Serious; Different measurements of Occupational physical activity, different methods of confounding.

g: Serious; first, PA was more likely to be ascertained using self-administered questionnaires, which are prone to misreporting. Second, we did not have individual-level data for study participants

h: Certainty was downgraded from high to low because of serious risk of bias and serious inconsistency

i: Certainty was downgraded from high to moderate because of serious risk of bias.

j: Certainty was downgraded from high to moderate because of serious risk of bias.

3.4. Endometrial cancer.

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Endometrial cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical Activity and Endometrial Cancer Risk, a Systematic Review of Current Evidence (Voskuil, 2007) *(115)*									
4 [a]	Cohort studies	Serious[d]	Serious[e]	Not serious	Serious	None[f]	All four studies that assessed both total PA and LTPA found that the association with endometrial cancer risk was stronger for total PA than for LTPA. Overall, the evidence was less consistent for OPA than for total PA and LTPA. In two of four studies that assessed OPA, a decreased risk of endometrial cancer was found in women in the highest versus the lowest category of OPA (e.g., manual/standing work versus sedentary work)	Very low[h]	Critically
10[b]	Case control studies	Serious[d]	Serious[e]	Not serious	Not serious	None[f]	Effect estimates of eight case-control studies that reported on OPA and that included 95% CIs (summary OR, 0.80; 95% CI, 0.66-0.96). Six of 10 studies reporting on OPA found a decreased risk of endometrial cancer. Two of these studies also showed some evidence for a dose-response effect; however, no P values were reported	Very low[i]	Critically

A systematic review and meta-analysis of physical activity and endometrial cancer risk (Schmid. 2015) *(116)*.

19[c]	7 Cohort 12 Case control	Serious[g]	Not serious	Not serious	Not serious	none	This review compared high versus low levels of PA. **OPA:** OPA resulted in summary (RR= 0.81; 95 % CI 0.75–0.87) in risk reduction for endometrial cancer. **LTPA:** LTPA resulted in summary risk reduction for endometrial cancer (RR= 0.84; 95% CI 0.78-0.91).	Moderate[J]	Critically

a: Pukkala 1993; Moradi 1998; Furberg and Thune 2003; Friberg 2006

b: Sturgeon 1993; Shu 1993; Levi 1993; Zheng 1993; Dosemeci 1993; Kalandid 1996; Olson 1997; Goodman 1997; Moradi 2000; Matthews 2005

c: Kalandidi 1996; Furberg and Thune 2003; John 2010, Levi 1993; Sturgeon 1993; Moradi 1998; Moradi 2000; Soll-Johanning 2004; Robsahm 2010; Friedenreich 2010; Tavani 2009; Matthews 2005; Freindenreich 2007; Weiderpass 2001; Friberg 2006; Gierach 2009

d: Serious; the number of high-quality prospective cohort studies is still limited. Most studies on occupational activity used crude methods for exposure assessment (i.e., job title) and a large number of women were not, or only shortly, engaged in paid employment. This may have resulted in errors in the measurement of physical activity and consequently risk estimation for risk of endometrial cancer. Several issues have not receiver sufficient attention in the epidemiologic studies thus far. Some studies have used very rough assessments of physical activity, without specifically taking into account the frequency, duration, and intensity of physical activities, and the different periods in life during which activity patterns may have changed. In addition, the association of physical activity and premenopausal endometrial cancer risk has been insufficiently studied. Future epidemiologic studies will need to address these issues to specify the association between physical activity and endometrial cancer risk.

e:Serious risk of inconsistency; We assessed statistical heterogeneity across studies using a formal test and found statistical evidence for heterogeneity for total, leisure time, and occupational activities combined, both in cohort and case-control studies.

f: Rated down for imprecision because no meta-analysis was conducted, and because of conflicting results.

g: Serious; A further potential limitation is that a determination of the precise nature of the association between physical activity and endometrial cancer may have been hampered by the heterogeneous measures of physical activity and associated misclassification of the exposure across studies.

h:Certainty is downgraded from high to low because of serious risk of bias and serious inconsistency and imprecision

i: Certainty is downgraded from high to low because of serious risk of bias and serious inconsistency and imprecision

j: Certainty is downgraded from high to moderate because of serious risk of bias

3.5. Lymphoma (Hodgkin and non-Hodgkin)

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Lymphoma (Hodgkin and non-Hodgkin.

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Physical Activity and Risk of Lymphoma: A Meta-Analysis (Vermaete, 2013) *(117)*									
5[a]	4 case control 1 cohort	Serious [b]	Not serious	Not serious	Serious imprecision[c]	None	This review compared the highest vs the lowest PA level **OPA:** The meta analysis showed no significant relationship between OPA (fixed effects model) and the risk of lymphoma (OR= 0.98; 95% CI: 0.80– 1.21;) **LTPA:** The random effects meta-analysis showed no significant relationship between recreational PA on the risk of lymphoma (pooled OR = 0.86; 95% CI 0.73–1.02)	Low[d]	Critically

a: Brownson 1991; Zahm 1999; Cerhen 2005; Parent 2011; Van Velthoven 2010.

b: Serious: The level of evidence generated by case control studies is considerably less than that by prospective cohort studies, according to the Centre for Evidence-Based Medicine. Some studies were of low quality, especially regarding the assessment of physical activity. Remarkable differences were found in the definitions of the "highest activity level." For example, in the study of Van Veldhoven and colleagues, the highest activity level was defined as 45.74 MET-hours/week or more, whereas the highest activity level was defined as 17.5 MET-hours/week or more in 2 other studies.

c: Rated down for imprecision because of the 95% CI overlap of no effect (i.e. CI included RR of 1.0)

d: Certainty downgraded from high to low because of serious risk of bias and serious imprecision

3.6. Gastric cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Gastric cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Physical activity is associated with reduced risk of gastric cancer: A systematic review and meta-analysis (Singh 2014). *(118)*									
6[a]	2 cohort 4 Case-control	Serious[f]	Serious[g]	Not serious	Serious[n]	None	This review compared the most physically active people vs. the least physically active people **OPA:** An not significant inverse relationship between OPA and gastric cancer risk was found (OR =0.90; 95% CI; 0.69–1.18) **LTPA:** A significant inverse relationship between LTPA and gastric cancer risk was found (OR=0.82; 95% CI; 0.72-0.94)	Very Low[p]	Critically

Physical Activity and Gastric Cancer Risk: A Systematic Review and Meta-Analysis (Psaltopoulou 2016) *(119)*

2[b]	Cohort studies	Very serious[h]	Serious[i]	Not serious	Serious[n]	none	This review compared the highest level of PA vs. those at the lowest level **OPA:** A not significant inverse relationship between OPA and gastric cancer was found. Combined cohort and case control effect estimates were (RR=0.89, 95% CI; 0.62-1.27). OPA and gastric cancer; (RR=1.25, 95% CI; 0.67-2.33) (2 cohort studies) **LTPA:** LTPA showed a total not significant effect of (RR=0.88, 95% CI; 0.76-1.02) (Cohort and case control combined LTPA and gastric cancer: (RR=0.92, 95% CI; 0.74-1.15) (7 cohort studies)	Very Low[q]	Critically
3[c]	Case control	Very serious[h]	Serious[i]	Not serious	Not serious	none	**OPA:** OPA and gastric cancer; (RR=0.72, 95% CI; 0.55-0.93) **LTPA:** LTPA and gastric cancer: (RR=0.86; 95% CI; 0.69-1.07) 9 case control)	Very low[r]	Critically

Physical Activity and Risks of Esophageal and Gastric Cancers: A Meta-Analysis (Chen, 2014) *(120)*

6[d]	3 cohort studies 3 case-control	Serious[j]	Serious[k]	Not serious	Not serious	Publication bias[o]	This review compared the highest vs the lowest categories of PA. **OPA:** Studies investigating the effects of OPA showed a significant effect (RR=0.79, 95% CI; 0.65-0.95) indicating a inverse relationship with gastric cancer. **LTPA:** LTPA (RR=0.89, 95% CI ; 0.74-1.06) was also inversely related with gastric cancer (not significant).	Very low[s]	Critically

The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis (Behrens, 2014) *(121)*

7[e]	4 cohort 3 case control	Serious[l]	Serious[m]	Not serious	Serious[n]	none	This review compared the highest versus lowest PA **OPA:** High levels **of** OPA statistically non-significant inverse relations to gastric cancer (RR=0.84, 95% CI; 0.70-1.02) **LTPA:** High levels of LTPA showed statistically significant inverse relationship with gastric cancer (RR=0.80, 95% CI; 0.73-0.89)	Very low[t]	Critically

a: Cohort studies; Huerta 2010; Severson 1989. Case-Control studies; Brownson 1991; Dosemeci 1993; Vigen 2006; Parent; 2011

b: Huerta 2010; Severson 1989.

c: Parent 2011; Suwanrunguang 2008 ; Vigen 2006

d: Cohort; Huerta 2010; Severson 1989; Brownson 1991. Case control; Dosemici 1993; Parent 2011; Suwanrungguang 2008.

e: Huerta 2010; Severson 1989; Brownson 1991; Dosemici 1993; Parent 2011; Suwanrungruang 2008; Vigen 2006

f: Serious; Despite adjusting for numerous covariates, it is not possible to eliminate the potential of residual confounding. Socioeconomic status interacts with both exposure (level of physical activity) and outcome (risk of gastric cancer, through H. pylori infection), and may have contributed to unmeasured confounding

g: Serious: This heterogeneity could be related to methodologic differences on the measurement of physical activity on the individual studies.

h: Very serious; self-reporting regarding the ascertainment of exposure prevailed not only in case– control but also in cohort studies; therefore, methodological differences may be responsible for the heterogeneity reported in our meta-analysis/ Adjustment for meaningful confounders, such as socioeconomic status, outdoor activities, and H. pylori infection, which was referred only in one study was not present in most studies. Only three studies included in this analyses

i: Serious because of a High heterogeneity

j: Serious; Potential confounding factors were not adjusted for in the included studies

k: Serious; High heterogeneity

l: Serious; a potential limitation of the present meta-analysis. That a causal relation for the observed inverse association between physical activity and gastroesophageal cancer could not be established because no intervention study was available for inclusion.

m: Serious; There is no test for heterogeneity for occupational activity.

n: Rated down for imprecision because of the 95% CI overlap of no effect (i.e. CI included RR of 1.0)

o: There was some evidence of publication bias in the primary meta-analysis. Visual inspection of the funnel plots revealed a small degree of asymmetry

p: Rated from high to very low because of serious risk of bias, serious inconsistency and serious imprecision

q: Rated from high to very low because of serious risk of bias, serious inconsistency and serious imprecision

r: Rated from high to very low because of very serious risk of bias and serious inconsistency

s: Rated from high to very low because of serious risk of bias, serious inconsistency and serious imprecision

t: Rated from high to very low because of serious risk of bias, serious inconsistency and serious imprecision

3.7. Esophageal cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Esophagael cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical Activity and Risks of Esophageal and Gastric Cancers: A Meta-Analysis (Chen, 2014) *(120)*									
The relation between OPA and EC could not be conducted because of considerable heterogeneity, so no combined risk estimate was obtained. This may have been because of the small number of studies were evaluated here.									
The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis (Behrens, 2014) *(121)*									
6[b]	4 cohort 2 Case control	Serious[f]	Serious[g]	Not serious	Serious[h]	none	This review was comparing highest versus lowest PA level. **OPA** No statistically significant relationship was observed between OPA and esophageal cancer (RR=0.91, 95% CI; 0.46, 1.81) **LTPA:** LTPA was associated with statistically significant reduction of the risk for esophageal cancer (RR=0.72, 95% CI; 0.63-0.83)	Very low [j]	Critically

a: Huerta 2010; Brownson 1991; Dar 2013; Etemadi 2012; Parent 2011; Vigen 2006.

b: Serious; potential limitation of the present meta-analysis. That a causal relation for the observed inverse association between physical activity and gastroesophageal cancer could not be established because no intervention study was available for inclusion.

c: Serious; There is not tested for heterogeneity for occupational activity.

d: Rated down for imprecision because of the 95% CI overlap of no effect (i.e. CI included RR of 1.0)

e: Certainty is downgraded from high to very low because of serious risk of bias, serious inconsistency, publication bias and serious imprecision

f: Certainty is downgraded from high to very low because of serious risk of bias, inconsistency and imprecision

3.8. Renal cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Renal cancer.

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
The association between physical activity and renal cancer: systematic review and meta-analysis (Behrens, 2013) *(122)*									
11[a]	6 cohort studies 5 case control	Serious[d]	Not serious	Not serious	Serious[f]	None	This review compared the high vs low levels of PA. **OPA:** The effects of OPA showed a not significant reduction in renal cancer risk (RR=0.91, 95% CI; 0.79, 1.04) $I^2$21%) **LTPA:** The effects of LTPA showed a not significant reduction in renal cancer risk **(RR=**0.88, 95% CI; 0.77, 1.00).	Low[g]	Critically
Can habitual physical activity contribute to reducing the health burden of renal cancer? (Shephard, 2016) *(123)*									
7[b]	Cohort	Serious[e]	Not serious	Not serious	Serious[f]	None	In 7 occupational studies, the average risk renal cancer was for physically active individuals 0.88 (No CI reported) , but omitting one study without co-variates, the risk ratio rose to 0.98 (No CI reported). 2/7 studies showed a significant decrease in relationship between OPA and the risk for renal cancer. 5/7 showed no significant decrease in risk reduction	Low[h]	Critically

7[c]	Case control	Serious[e]	Not serious	Not serious	Serious[f]	none	The weighted average for the occupational studies was 0.98 (No CI reported) , or 0.99 (No CI reported) when omitting 3 studies with limited co-variates; 3/7 a non-significant reduction in the risk for renal cancer 1/7 only stated 'no effect' 1/7 a non-significant increase 2/7 a significant decrease in the risk for renal cancer.	Low[i]	Critically

a: 5 Case controlt; Brownson 1991; Goodman 1986; Mellengaard 1995; Parent 2011; Tavani 2007. Cohort 6; Bergstrom 1999; Bergstrom 2001; Mahabir 2004; Moore 2008; Van Dijk 2004; Washio 2005.

b: Bergstrom 1991; Bergstrom 2001; Mahabir 2004; Moore 2008; Van Dijk 2004; Washio 2005.

c: Brownson 1991; Goodman 1986; Mellengaard 1995; Parent 2011; Tavani 2007

d: One limitation of this meta-analysis is the large variation in the underlying studies regarding their definitions of exposure to physical activity – ranging from 'physically very active' to '5 h of vigorous physical activity per week or more'.

Similarly, the definitions of physical activity referent groups ranged from 'not physically active' to 'o5 h of vigorous physical activity per week'.

e: Moreover, measurements of physical activity have often been weak, and some samples have included very few individuals who were vigorously active, either at work or in their leisure hours

f: Rated down for imprecision because of the 95% CI overlap of no effect (i.e. CI included RR of 1.0)

g: downgraded from high to low because of serious risk of bias and serious imprecision

h: downgraded from high to low because of serious risk of bias and serious imprecision

i: downgraded from high to low because of serious risk of bias and serious imprecision

3.9. Prostate cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Prostate cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Occupational Risk factors for prostate cancer; A meta-analyses (Krstev, 2019) *(124)*									
This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence. (AMSTAR2 rating)									
Physical activity in relation to risk of prostate cancer: A systematic review and meta-analysis (Benke, 2018) *(9)*									
28[a]	Prospective studies	Serious[f]	Serious[g]	Not serious	Not serious	none	This study is comparing the highest versus the lowest level of overall PA **OPA:** A not significant inverse relationship between OPA and total PCa (prostate cancer) risk was observed (RR=0.91, 95% CI 0.82-1.01) (28 studies) A statistically significant inverse relationship between long-term (>10 years, 13 studies) OPA and total PCa was observed (RR=0.83, 95% CI 0.71–0.98) Evaluated by cancer subtype, an inverse association with long term OPA was noted for nonadvanced/non-aggressive PCa (RR=0.51, 95% CI; 0.37–0.71) (2 studies) **LTPA:** The relationship between Recreational physical activity and total PCA was (RR=1.03, 95% CI; 1.00-1.06)	Low[m]	Critically

Physical activity and prostate cancer: An updated review (Shephard, 2017) *(125)*

19[b]	Cross sectional and prospective cohort	Serious[h]	Serious[i]	Not serious	Serious[j]	None	A total of seven analyses found no effect of OPA. Six analyses identified a possible trend favoring the more active workers Six analyses demonstrated a significantly lower risk of prostate cancer in the most active and/or the least well-educated individuals.	Very low[n]	Critically
16[c]	Case control studies	Serious[h]	Serious[i]	Not serious	Serious[j]	None	1 study found a large adverse effect, 5 studies found a statistically non-significant negative trend. These studies showed a trend to a benefit of 16-40% for those with heavy work. Seven studies showed a significant benefit to those with the most active employment. One found a large benefit. In the remaining six, benefits were larger than suggested by the cross-sectional and cohort studies (33–64% for the active categories).	Very low[o]	Critically

Does physical activity reduce the risk of prostate cancer? A systematic review and meta-analysis. (Liu 2011) *(126)*

9[d]	Cohort	Serious[k]	Not serious	Not serious	Not serious	none	This review compared the highest versus lowest level of PA **OPA** OPA was significantly related with a reduced risk of PCa (RR: 0.81; 95% CI, 0.73–0.91). (Case control+ Cohort) OPA in cohort studies: (RR: 0.91; 95% CI, 0.87–0.95) The higher quality OPA studies reported a lower reduced risk (RR: 0.86, 95%CI 0.87-0.94) than the lower quality OPA studies (RR: 0.75, 95% CI: 0.61-0.94). **LTPA:** LTPA was related with a non-significant reduced risk of PCa: (RR: 0.95; 95%CI 0.89-1.00) In cohort studies LTPA was related with a significantly reduced risk (RR=0.95, 95% CI: 0.89-1.00)	Moderate[p]	Critically
18[e]	Case control	Serious[k]	Serious [l]	Not serious	Not serious	none	**OPA**: OPA case-control studies showed a significantly reduced PCa risk (OR: 0.73; 95% CI, 0.62–0.87) **LTPA:** LTPA case control studies showed a reduced not significant PCA risk: (OR= 0.98, 95% CI: 0.85-1.14)	Low[q]	Critically

a: contains information of 26 prospective studies: Bairati (2000), Strom (2008), Parent (2011), Krishnadasan (2008), Lagiou (2008), Orsini (2009), Pierotti (2005), Le Marchand (1991), Thune (1994), Grotta (2015), Wiklund (2008), Lund Hameid (2006), Friedenreich (2004), Norman (2002), Villeneuve (1999), Johnsen (2009), Hrafnkelsdottir (2015), Zeegers (2005), Putnam (2000), Nilsen (2000), Sormunen (2014), Doolan (2014), Hartman (1998), Le Marchand (1991), Lacey (2001), Illic (1996), Hosseini (2010)

b: Vidardottir 2008; Hartman 1998; Johnsen 2009; Lund-Nielsen 2000; Paffenbarger 1987; Putnam 2000; Severson 1989; Zegger 2005; Albanes 1989; Grotta 2015; Harvei and Kravdal 1997; Hrafnkelsdottir 2015; Hsing 1994; Thune and Lund 1994; Norman 2002; Orsini 2009; Clarke and Whittemore 2000; Parent 2011; Vena 1987.

c: Illic 1996; Doolan 2014; Hosseini 2010; Lacey 2001; Sass-Kortak 2007; Friedenreich 2004; Lagiou 2008; Le Marchand 1991; Wiklund 2008; Bairati 2000; Brownson 1991; Dosemeci 1993; Krishnadasan 2008; Pierotti 2005; Strom 2008; Villeneuve 1999

d: Johnson (2009), Orsini (2009), Lund (2006) Zeegers (2005), Norman (2002), Lund (2000), Putnam (2000), Hartman (1998), Severson (1989)

e: Parent (2011), Mostafa (2010), Wiklund (2008), Krishnadasan (2008), Lagiou (2008) Strom (2008), Darlington (2007), Sass-Kortsak (2007), Pierotti (2005), Friedenreich (2004), Lacey (2001), Bairati (2000) , Andersonn (1996), Illic (1996), Dosemeci (1993), Brownson (1991), Le Marchand (1991) He (1988)

f: However, our findings must be interpreted with caution. First,our result on long-term OPA and total PCa incidence appeared to be affected by individual studies, rendering the previous inverse association statistically non-significant. but most long-term OPA studies used job titles to assess OPA which may have introduced some degree of misclassification in our meta-analysis.

g: Serious inconsistency due to a high inconsistency h: Moreover, in terms of occupational activity, relatively few investigators have co-varied their findings for exposure to toxic chemicals, and often there has been an incomplete allowance for socioeconomic and dietary differences between those engaged in sedentary and physically demanding work.

i: Serious inconsistency; this is the reason why no meta-analysis is performed.

j: Serious imprecision because a meta-analysis could not be performed.

k: Measurement of OPA varied, and another potential limitation is the residual confounding factors that were not adjusted for in the included studies, which may have affected the results.

l: First, we observed some significant between-study heterogeneity across all of the included studies

m: Certainty downgraded from high to low because of serious risk of bias and inconsistency

n: Certainty downgraded from high to very low because of serious risk of bias and inconsistency and imprecision

o: Certainty downgraded from high to very low because of serious risk of bias and inconsistency and imprecision

p: Certainty downgraded from high to moderate because of serious risk of bias

q: Certainty downgraded from high to low because of serious risk of bias and inconsistency

3.10. Pancreatic cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Pancreatic cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			

Can physical activity modulate pancreatic cancer risk? a systematic review and meta-analysis (O'Rorke, 2010) *(127)*

This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence. (AMSTAR2 rating)

Physical activity and pancreatic cancer risk: A systematic review (Bao, 2008) *(128)*

3[a]	Cohort	Very serious[b]	Not serious	Not serious	Not serious	none	This review compared the highest versus the lowest category of physical activity. **OPA:** OPA was reported in three prospective studies (25, 26, 32). The individual relative risks ranged from 0.63 to 0.88, and the pooled relative risk was (RR=0.75 95% CI, 0.58-0.96) **LTPA:** LTPA was inversely related with pancreatic cancer (RR=0.94, 95% CI, 0.84-1.05)	Low[c]	Critically

a: Berrington de Gonzalez 2006; Isaksson 2002; Stoltenberg-Solomon 2002

b: In addition, the observed association could be due to unmeasured confounding. However, the confounding may exist in both directions: on one hand, individuals who have medical conditions such as diabetes are ordinarily excluded from employment as manual laborers, and on the other hand, physically demanding occupations are usually associated with harmful occupational exposures, lower social economic status, and unhealthy lifestyles such as smoking and drinking. The inverse association between occupational physical activity and pancreatic cancer should be interpreted with caution because it was based on only three studies.

c: Certainty downgraded from high to low because of very serious risk of bias

3.10.

3.11. Bladder cancer

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: bladder cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

The association between physical activity and bladder cancer: Systematic review and meta-analysis (Keimling 2014) ***(129)***

This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence. (AMSTAR2 rating)

4.0. Diabetes Mellitus type 2

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Diabetes type 2

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis (Aune, 2015) *(130)*									
3[a]	Cohort studies	Very serious[a]	Not serious	Not serious	Not serious	None	This review compared the high versus the low levels of PA. **OPA** A high level of OPA was significantly related with a reduced diabetes type 2 risk (RR=0.85, 95%CI 0.79-0.92). **LTPA:** A high level of LTPA was significantly related with a reduced diabetes type 2 risk (RR=0.74, 95% CI: 0.70-0.79)	Low[c]	Critically

a: Hu G 2003; Chien 2009; Steinbrecher 2012

b: It is possible that the observed inverse association between physical activity and risk of type 2 diabetes risk was influenced by unmeasured or residual confounding. The inverse association between occupational physical activity and pancreatic cancer should be interpreted with caution because it was based on only three studies.

c: Rated from high to low because of very serious risk of bias.

5.0. Osteoarthritis

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Osteoarthritis

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Occupational risk factors for osteoarthritis of the knee: a meta-analysis (McWilliams 2011) *(131)*									
8[a]	2 cohort 3 cross sectional 3 case control	Serious[c]	Serious[d]	Not serious	Not serious	Publication bias[e]	Heavy or manual work (546.853 subjects) was associated with knee osteoarthritis (OR=1.45, 95% CI; 1.20-1.76) **Cohort studies;** 1 study non-significant increase 1 study non-significant decrease **Case-control;** 3 study significant increase **Cross sectional;** 1 study non-significant decrease 1 study non-significant increase 1 study significant increase	Very low[i]	Critically
Men and women's occupational activities and the risk of developing osteoarthritis of the knee, hip or hands: A systematic review and recommendations for future research (Gignac, 2019) *(132)*									

11[b]	6 cohort 2 case control 3 cross sectional	Serious[f]	Serious[g]	Not serious	Serious[h]	None	Cumulative physical workloads were associated with a moderate level of evidence for an hip OA among men. Heavy physical demands yielding mixed evidence for knee OA. mixed evidence for cumulative physical loads and sitting, standing and walking being associated with hip OA. Evidence was also mixed for physically demanding work related to developing OA in multiple joints.	Very low[j]	Critically

Occupational activities and osteoarthritis of the knee (Palmer, 2012) ***(133)***

This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence. (AMSTAR2 rating)

a: Toivanen 2010; Kohatsu 1990; Elsner 1996; Yoshimura 2006; Riyazi 2008; Andrianakos 2006; Fernandez-Lopez 2008; Kim 2010.

b: Ezzat 2013; Toivanen 2010; Apold 2014; Felson 1991; Karkkainen 2013; Kujala 1995; Sahlstrom 1997; Vingard 1991; Olsen 1994; Ratzlaff 2012; Rubak 2014.

c: Early adult life is thought to be important for the development of OA, but recall of activities in the past maybe biased or inaccurate. The differences in measurement could contribute to variability, although the current job is likely to be similar to the longest-held job for many subjects.

d: High heterogeneity has been observer (I^2 80.9)

e: There appears to be a strong likelihood of publication bias within the literature for occupation and knee OA

f: Our quality appraisal identified several constraints and limitations to study designs and measurement. Most research utilized case-control or cross-sectional designs with few longitudinal studies and no interventions. There is potential for recall bias across all methods of collecting work history, which is a limitation of most of the studies reviewed.

g: Serious risk of inconsistency; heterogeneity has been described.

h: Serious risk of imprecision; No RR-OR reported, no CI reported.

i: : Rated from high to very low because of serious risk of bias, inconsistency and publication bias

j: Rated from high to very low because of serious risk of bias, serious inconsistency and serious imprecision

6.0. Mental Health

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Osteoarthritis

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Domain-Specific Physical Activity and Mental Health: A Meta-analysis (White, 2017) *(134)*									
13[a]	12 cross sectional 1 cohort[b]	Serious[c]	Serious[d]	Not serious	Serious[e]	none	**OPA:** work-related PA had a weak positive relationship with mental ill-health among adults (r=0.10, 95% CI: 0.04-0.16) Work-related PA had a weak positive relationship with mental health among adults (r=0.02, 95% CI; -0.09-0.12) **LTPA:** LTPA had a negative relationship with mental ill-health (r=-0.11, 95% CI; -0.16- -0.06) LTPA had a positive relationship with mental health (r=0.13, 95% CI; 0.08-0.18)	Very low[e]	Critically

a: Bogaert 2014, Cerin 2009, Im 2014, Jurakic 2010; Kull 2012; Lin 2008; McKercher 2013; Mutric 2007; Pedisic 2015; Purakom 2013; Teychenne 2008; Teychenne 2010; Humpreys 2013.

b: 9 studies investigated the relation between Work-PA and Mental-ill Health, 5 studies were investigated on the relation between Work related-PA and Mental Health.

c: Self-determined motivation may also explain some of adolescents / Mostly, 98% of the included studies were observational, the majority of which were cross-sectional. As cross-sectional studies cannot infer causality, the study designs of the included studies are a limitation

d: Although work-related PA was positively associated with mental health there was a significant high heterogeneity

e: Certainty downgraded from high to very low because of serious risk of bias and serious inconsistency and serious imprecision.

7.0. Sleep quality and/or duration

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Sleep quality/and or duration

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Association between insomnia and job stress: a meta-analysis (Yang, 2018) *(135)*									
7[a]	4 cross sectional 3 prospective	Serious [b]	Serious[c]	Not serious	Serious[d]	Strong association	**OPA**: The odds ratio for the relationship between heavy workload was and insomnia (OR= 2.76; 95%CI: 1.71-4.45) suggesting that a higher workload is related to and increased risk of insomnia symptoms in this populations **LTPA:** LTPA was not assessed in this study.	Low[e]	Important

a: Tachibana 1998; Akerstedt 2002; Linton 2004; Ota A 2005; Ota A 2009; Akerstedt 2012; Yoshioka 2013.

b: We considered that measurements made with those questionnaires did not provide such good quality as the standard scales, which may enhance the risk of bias.

c: High heterogeneity

d: Serious imprecision due to the broad confidence intervals.

e: Certainty downgraded from high to very low because of serious risk of bias, inconsistency and imprecision. Certainty upgraded from very low to low because of a strong association (RR >2.0)

8.0. Hypertension

Population: Adults (aged 18-64 years)
Exposure: Duration, frequency and/or intensity of OPA, or a compositional score reflecting total volume of OPA.
Comparison: No OPA, or a lesser duration, frequency and/or intensity, no or a smaller compositional score of total volume of OPA.
Outcome: Hypertension

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical Activity and Risk of Hypertension A Meta-Analysis of Prospective Cohort Studies (Huai, 2013) ***(136)***									
5[a]	Cohort studies	Serious[b]	Not serious	Not serious	Serious[c]	none	In this study the lowest category was defined as low-level PA (reference group), the highest category as high-level PA, all categories in between were pooled to represent moderate-level PA **OPA:** The pooled result showed that the relationship between high-level OPA and risk of hypertension was statistically not significant (RR, 0.93; 95% CI, 0.81–1.08). Result showed that the relationship between moderate-level OPA and risk of hypertension was not significant (RR, 0.96; 95% CI, 0.87–1.06). **LTPA:** The overall result showed that high-level LTPA was related with a significant decreased risk of hypertension compared with the reference group with low-level LTPA (RR, 0.81; 95% CI, 0.76–0.85).	Low[d]	Important

a: Camoes 2020; Pouliou 2012; Gu 2007; Barengo 2005; Pereira 1999; Juntunen 2003.

b: In addition, the association between RPA and decreased risk of hypertension in this meta-analysis might be confounded by various factors

c: Rated down for imprecision because of the 95% CI overlap of no effect (i.e. CI included RR of 1.0)

d: Certainty is downgraded from high to low because of serious risk of bias and imprecision.

9.0. Abbreviation list

PA	Physical Activity
OPA	Occupational Physical Activity
LTPA	Leisure Time Physical Acitivty
RR	Risk Ratio
CI	Confidence interval
HR	Hazard Ratio
CHD	Coronary Heart Disease
MET	Metabolic equivalent of task
OR	Odds Ratio
OA	Osteoarthritis
ORR	Overall Relative Risk

DATA EXTRACTIONS OF INCLUDED EVIDENCE (IN ALPHABETICAL ORDER BY AUTHOR)

<table>
<tr><td colspan="2">SR/MA
Citation: Amagasa, S., Machida, M., Fukushima, N., Kikuchi, H., Takamiya, T., Odagiri, Y., & Inoue, S. (2018). Is objectively measured light-intensity physical activity associated with health outcomes after adjustment for moderate-to-vigorous physical activity in adults? A systematic review. International Journal of Behavioral Nutrition and Physical Activity, 15(1), 65.</td></tr>
<tr><td>Purpose: to systematically examine associations of objectively assessed LPA and health outcomes after adjustment for MVPA in adults</td><td rowspan="5">Abstract:
Background: An increasing number of studies have demonstrated that light-intensity physical activity (LPA) confers health benefits after adjustment for moderate-to-vigorous physical activity (MVPA). The purpose of this systematic review was to summarize existing epidemiological evidence on associations of objectively measured LPA with health outcomes in adults.
Methods: This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We searched on PubMed, Web of Science, CINAL, and Cochrane Library for articles analysing the association between objectively determined LPA and health outcomes that were published up to January 2017. Data were extracted regarding authors, publication year, country of survey, study setting, number of participants, study design, physical activity (PA) assessment (type of accelerometer and intensity), health outcomes, confounders, and results (summary measures and association). A coding system was used to summarize the results.
Results: Of the 3254 studies identified, 24 cross-sectional and 6 longitudinal studies were included in this review. Most of the studies targeted the Western population. LPA was inversely associated with all-cause mortality risk and associated favorably with some cardiometabolic risk factors including waist circumference, triglyceride levels, insulin, and presence of metabolic syndrome. Only a small amount of data were available on mental health and cognitive function.
Conclusions: LPA appears to be beneficially associated with important health outcomes after adjustment for MVPA in the adult population. Although current global PA guidelines recommend only MVPA, promoting LPA may confer additional health benefits.</td></tr>
<tr><td>Timeframe: inception to February 2, 2017</td></tr>
<tr><td>Total # studies included: 30</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) objectively measured LPA</td></tr>
<tr><td>Outcomes addressed: health outcomes & ACM</td></tr>
</table>

SR/MA	
Citation: Andreato LV, Esteves JV, Coimbra DR, Moraes AJ, de Carvalho T. The influence of high-intensity interval training on anthropometric variables of adults with overweight or obesity: a systematic review and network meta-analysis. Obesity reviews. 2019 Jan;20(1):142-55; https://doi-org.ezproxy1.library.usyd.edu.au/10.1111/obr.12766	
Purpose: to evaluate the influence of HIIT on anthropometric variables of adults afflicted with overweight or obesity	**Abstract:** Objective The goal of this study was to evaluate the influence of high-intensity interval training (HIIT) on anthropometric variables in adults afflicted with overweight or obesity and to compare the effects with those of moderate-intensity continuous training. Methods A computer literature search was performed for HIIT intervention studies that evaluated anthropometric variables in adults afflicted with overweight or obesity. Results Of the 857 articles retrieved in the electronic search, 48 met the inclusion criteria. The analyses demonstrated that HIIT was effective in decreasing body mass (−1.45 kg [95% CI: −1.85 to −1.05 kg]), body mass index (−0.44 kg m−2 [95% CI: −0.59 to −0.30 kg m−2]), waist circumference (−2.3 cm [95% CI: −3.1 to −1.4 cm]), waist/hip ratio (−0.01 [95% CI: −0.02 to −0.00]), body fat percentage (−1.29% [95% CI: −1.70% to −0.87%]) and abdominal visceral fat area (−6.83 cm2 [95% CI: −11.95 to −1.71 cm2]). When considering equalization between the two methods (energy expenditure or workload matched), no differences were found in any measure except body mass (for which HIIT was superior). Conclusions High-intensity interval training and moderate-intensity continuous training results were similar, particularly when equalization between the two methods was considered. Thus, HIIT can be used as a secondary method for the treatment of obesity in adults.
Timeframe: inception to May 2018	
Total # studies included: 48 intervention study (10 RCT, 38 n-RCT)	
Other details (e.g. definitions used, exclusions etc) also compared with moderate-intensity continuous training	
Outcomes addressed: body mass, BMI, waist circumference, waist/hip ratio or body composition	

SR/MA **Citation:** Baumeister SE, Leitzmann MF, Linseisen J, Schlesinger S. Physical Activity and the Risk of Liver Cancer: A Systematic Review and Meta-Analysis of Prospective Studies and a Bias Analysis. JNCI J Natl Cancer Inst (2019) 111(11): djz111.	
Purpose: The aim of this study was to synthesize prospective observational studies on the association of physical activity and liver cancer risk by means of a systematic review and meta-analysis. **Timeframe:** Inception to Jan 23 2019 **Total # studies included:** 14 cohort studies **Other details (e.g. definitions used, exclusions etc)** Self-reported PA by type **Outcomes addressed:** Liver	**Abstract:** Background: Physical inactivity is an established risk factor for several cancers of the digestive system and female reproductive organs, but the evidence for liver cancers is less conclusive. Methods: The aim of this study was to synthesize prospective observational studies on the association of physical activity and liver cancer risk by means of a systematic review and meta-analysis. We searched Medline, Embase, and Scopus from inception to January 2019 for prospective studies investigating the association of physical activity and liver cancer risk. We calculated mean hazard ratios (HRs) and 95% confidence intervals (CIs) using a random-effects model. We quantified the extent to which an unmeasured confounder or an unaccounted selection variable could shift the mean hazard ratio to the null. Results: Fourteen prospective studies, including 2738 liver cancers, were included in the systematic review and meta-analysis. The mean hazard ratio for high compared with low physical activity was 0.75 (95% CI=0.63 to 0.89; 95% prediction interval=0.52 to 1.07; I2=64.2%).We estimated that 67.6% (95% CI=56.6% to 78.5%) of all true effect estimates would have a hazard ratio less than 0.8. Bias analysis suggested than an unobserved confounder would have to be associated with a 1.99-fold increase in the risk of physical activity or liver cancer to explain away the observed mean hazard ratio. An unaccounted for selection variable would have to be related to exposure and endpoint with a relative risk of 1.58 to explain away the mean hazard ratio. Conclusions: Physical activity is inversely related to the risk of liver cancer. Further studies with objectively measured physical activity and quasi-experimental designs addressing confounding are needed.
Populations Analyzed: Adults	**Author-Stated Funding Source:** No funding received for this paper.

SR/MA **Citation:** Behrens G, Niedermaier T, Berneburg M, Schmid D, Leitzmann MF. Physical activity, cardiorespiratory fitness and risk of cutaneous malignant melanoma: Systematic review and meta analysis. PLoS ONE 2018; 13(10): e0206087. https://doi. org/10.1371/journal.pone.0206087	
Purpose:	**Abstract:**
Timeframe: Inception to March 29, 2018	**Background** Numerous epidemiologic studies have examined the relation of physical activity or cardiorespiratory fitness to risk of cutaneous melanoma but the available evidence has not yet been quantified in a systematic review and meta-analysis.
Total # studies included: 21 cohort studies	**Methods** Following the preferred reporting items for systematic reviews and meta-analyses (PRISMA), we identified 3 cohort studies (N = 12,605 cases) and 5 case-control studies (N = 1,295 cases) of physical activity and melanoma incidence, and one cohort study (N = 49 cases) of cardiorespiratory fitness and melanoma risk.
Other details (e.g. definitions used, exclusions etc) Self-reported PA by type	**Results** Cohort studies revealed a statistically significant positive association between high versus low physical activity and melanoma risk (RR = 1.27, 95% CI = 1.16–1.40). In contrast, case control studies yielded a statistically non-significant inverse risk estimate for physical activity and melanoma (RR = 0.85, 95% CI = 0.63–1.14; P-difference = 0.02). The only available cohort study of cardiorespiratory fitness and melanoma risk reported a positive but statistically not significant association between the two (RR = 2.19, 95% CI = 0.99–4.96). Potential confounding by ultraviolet (UV) radiation-related risk factors was a major concern in cohort but not case-control studies.
Outcomes addressed: Melanoma	**Conclusions** It appears plausible that the positive relation of physical activity and cardiorespiratory fitness to melanoma observed in cohort studies is due to residual confounding by UV radiation related risk factors.
Populations Analyzed: Adults	**Author-Stated Funding Source:** No funding received for this paper.

<table>
<tr><td colspan="2">SR/MA
Citation: Benke IN, Leitzmann MF, Behrens, G, Schmid D. Physical activity in relation to risk of prostate cancer: a systematic review and meta-analysis. Annals of Oncology 2018; 29: 1154–1179, doi:10.1093/annonc/mdy073</td></tr>
<tr><td>Purpose: This study aims to quantitatively summarize observational studies relating physical activity (PA) to PCa incidence and mortality.</td><td rowspan="5">Abstract:
Background: Prostate cancer (PCa) is one of the most common cancers among men, yet little is known about its modifiable risk and protective factors. This study aims to quantitatively summarize observational studies relating physical activity (PA) to PCa incidence and mortality.
Materials and methods: Published articles pertaining to PA and PCa incidence and mortality were retrieved in July 2017 using the Medline and EMBASE databases. The literature review yielded 48 cohort studies and 24 case–control studies with a total of 151 748 PCa cases. The mean age of the study participants at baseline was 61 years.
Results: In random-effects models, comparing the highest versus the lowest level of overall PA showed a summary relative risk (RR) estimate for total PCa incidence close to the null [RR=0.99, 95% confidence interval (CI)=0.94–1.04]. The corresponding RRs for advanced and non-advanced PCa were 0.92 (95% CI=0.80–1.06) and 0.95 (95% CI=0.85–1.07), respectively. We noted a statistically significant inverse association between long-term occupational activity and total PCa (RR=0.83, 95% CI=0.71–0.98, n studies=13), although that finding became statistically non-significant when individual studies were removed from the analysis. When evaluated by cancer subtype, an inverse association with long-term occupational activity was noted for nonadvanced/ non-aggressive PCa (RR=0.51, 95% CI=0.37–0.71, n studies=2) and regular recreational activity was inversely related to advanced/aggressive PCa (RR=0.75, 95% CI=0.60–0.95, n studies=2), although these observations are based on a low number of studies. Moreover, PA after diagnosis was related to reduced risk of PCa mortality among survivors of PCa (summary RR based on four studies=0.69, 95% CI=0.55–0.85).
Conclusions: Whether PA protects against PCa remains elusive. Further investigation taking into account the complex clinical and pathologic nature of PCa is needed to clarify the PA and PCa incidence relation. Moreover, future studies are needed to confirm whether PA after diagnosis reduces risk of PCa mortality.</td></tr>
<tr><td>Timeframe: Inception to July 2017</td></tr>
<tr><td>Total # studies included: 48 cohort studies and 24 case-control studies</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Self-reported PA by type, timing and dose</td></tr>
<tr><td>Outcomes addressed: Prostate cancer</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: No funding received for this paper.</td></tr>
</table>

SR/MA **Citation:** Blond K, Brinkløv CF, Ried-Larsen M, Crippa A, Grøntved A. Association of high amounts of physical activity with mortality risk: a systematic review and meta-analysis. British journal of sports medicine. 2019;bjsports-2018.	
Purpose: To clarify if there is a greater all cause and cause specific mortality risk associated with high levels of physical activity above the recommended amounts.	**Abstract:** Objectives To systematically review and analyse studies of high amounts of physical activity and mortality risk in the general population. Eligibility criteria Inclusion criteria related to follow-up (minimum 2 years), outcome (mortality from all causes, cancer, cardiovascular disease (CVD) or coronary heart disease), exposure (eg, a category of >1000 metabolic equivalent of task (MET) min/week), study design (prospective cohort, nested case control or case-cohort) and reports of cases and person years of exposure categories. Information sources Systematic searches were conducted in Embase and Pubmed from database inception to 2 March 2019. Risk of bias The quality of the studies was assessed with the Newcastle–Ottawa scale. Included studies From 31 368 studies identified, 48 were included. Two authors independently extracted outcome estimates and assessed study quality. Synthesis of results We estimated hazard ratios (HRs) using random effect restricted cubic spline dose–response meta-analyses. Compared with the recommended level of physical activity (750 MET min/ week), mortality risk was lower at physical activity levels exceeding the recommendations, at least until 5000 MET min/week for all-cause mortality (HR=0.86, 95%CI 0.78 to 0.94) and for CVD mortality (HR=0.73, 95%CI 0.56 to 0.95). Strengths and limitations of evidence The strengths of this study include the detailed dose– response analyses, inclusion of 48 studies and examination of sources of heterogeneity. The limitations include the observational nature of the included studies and the inaccurate estimations of amount of physical activity. Interpretation Compared with the recommended level, mortality risk was lower at physical activity levels well above the recommended target range. Further, there was no threshold beyond which lifespan was compromised. Registration PROSPERO CRD42017055727
Timeframe: inception to 2 March 2019	
Total # studies included: 48	
Other details (e.g. definitions used, exclusions etc) MET min/week	
Outcomes addressed: mortality from all causes and cardiovascular disease (CVD)	

<table>
<tr><td colspan="2">Meta-analysis
Citation: Boyer W.R., Churilla J.R., Ehrlich S.F., Crouter S.E., Hornbuckle L.M., Fitzhugh E.C. Protective role of physical activity on type 2 diabetes:Analysis of effect modification by race–ethnicity, Journal of Diabetes; 2018, 10166–178</td></tr>
<tr><td>Purpose: to compile the evidence from prospective cohort studies on potential effect modification of the aerobic PA and T2D risk relationship by race–ethnic groups; a second analysis was conducted to assess the overall effect of meeting the 2008 DHHS moderate-intensity aerobic PA recommend-ation on T2D risk.</td><td rowspan="4">Abstract:
Background: It is well known physical activity (PA) plays a role in the prevention of type 2 diabetes (T2D). However, the extent to which PA may affect
T2D risk among different race–ethnic groups is unknown. Therefore, the aim of the present study was to systematically examine the effect modification of race–ethnicity on PA and T2D.

Methods: The PubMed and Embase databases were systematically searched through June 2016. Study assessment for inclusion was conducted in three phases: title review (n = 13 022), abstract review (n = 2200), and full text review (n = 265). In all, 27 studies met the inclusion criteria and were used in the analysis. Relative risks (RRs) and 95% confidence intervals (CIs) were extracted and analyzed using Comprehensive Meta-Analysis software. All analyses used a random-effects model.

Results: A significant protective summary RR, comparing the most active group with the least active PA group, was found for non-Hispanic White (RR 0.71, 95% CI 0.60–0.85), Asians (RR 0.76, 95% CI 0.67–0.85), Hispanics (RR 0.75, 95% CI 0.64–0.89), and American Indians (RR 0.73, 95% CI 0.60–0.88). The summary effect for non-Hispanic Blacks (RR 0.91, 95% CI 0.76–1.08) was not significant.

Conclusions: The results of the present study indicate that PA (comparing most to least active groups) provides significant protection from T2D, with the exception of non-Hispanic Blacks. The results also indicate a need for race–ethnicity-specific reporting of RRs in prospective cohort studies that incorporate multi-ethnic samples.</td></tr>
<tr><td>Timeframe: Inception through June 2016</td></tr>
<tr><td>Total # studies included: 27</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc): assessed aerobic based PA; published or available in English; prospective cohort studies; assessed and reported the race–ethnicity specific relative risks (RR) for T2D; adjusted risk estimates for age; and allowed for the determination of a</td></tr>
</table>

most versus least physically active group	
Outcomes addressed: Race–ethnicity specific relative risks (RR) for T2D;	
Population analysed: Adults (age ≥18 years) at the time of follow-up	**Author-Stated Funding Source:** None declared.

<table>
<tr><td colspan="2">Systematic review
Citation: Brasure M, Desai P, Davila H, Nelson VA, Calvert C, Jutkowitz E, et al. Physical activity interventions in preventing cognitive decline and alzheimer-type dementia a systematic review. Ann Intern Med. 2018;168(1):30–8.</td></tr>
<tr><td>Purpose: To assess the effectiveness of physical activity interventions in slowing cognitive decline and delaying the onset of cognitive impairment and dementia in adults without diagnosed cognitive impairments</td><td rowspan="5">Abstract:
BACKGROUND: The prevalence of cognitive impairment and dementia is expected to increase dramatically as the population ages, creating burdens on families and health care systems.
PURPOSE: To assess the effectiveness of physical activity interventions in slowing cognitive decline and delaying the onset of cognitive impairment and dementia in adults without diagnosed cognitive impairments.
DATA SOURCES: Several electronic databases from January 2009 to July 2017 and bibliographies of systematic reviews.
STUDY SELECTION: Trials published in English that lasted 6 months or longer, enrolled adults without clinically diagnosed cognitive impairments, and compared cognitive and dementia outcomes between physical activity interventions and inactive controls.
DATA EXTRACTION: Extraction by 1 reviewer and confirmed by a second; dual-reviewer assessment of risk of bias; consensus determination of strength of evidence.
DATA SYNTHESIS: Of 32 eligible trials, 16 with low to moderate risk of bias compared a physical activity intervention with an inactive control. Most trials had 6-month follow-up; a few had 1- or 2-year follow-up. Evidence was insufficient to draw conclusions about the effectiveness of aerobic training, resistance training, or tai chi for improving cognition. Low-strength evidence showed that multicomponent physical activity interventions had no effect on cognitive function. Low-strength evidence showed that a multidomain intervention comprising physical activity, diet, and cognitive training improved several cognitive outcomes. Evidence regarding effects on dementia prevention was insufficient for all physical activity interventions.
LIMITATION: Heterogeneous interventions and cognitive test measures, small and underpowered studies, and inability to assess the clinical significance of cognitive test outcomes.
CONCLUSION: Evidence that short-term, single-component physical activity interventions promote cognitive function and prevent cognitive decline or dementia in older adults is largely insufficient. A multidomain intervention showed a delay in cognitive decline (low-strength evidence).</td></tr>
<tr><td>Timeframe: January 2009 – July 2017</td></tr>
<tr><td>Total # studies included: 32</td></tr>
<tr><td>Author-stated inclusion criteria:
We included randomized controlled trials of physical activity interventions with any sample size and large (n > 500) prospective quasi-experimental cohort studies with comparator groups if they enrolled adults without diagnosed cognitive impairments, had follow-up of at least 6 months, were published in English, and reported 1 of our preselected primary or intermediate outcomes. We excluded trials enrolling pure subgroups of patients with major medical conditions or conditions that may explain changes in cognitive function (namely stroke, Parkinson disease, cancer, and traumatic brain injury).</td></tr>
<tr><td>Outcomes addressed:</td></tr>
</table>

Main: Mild cognitive impairment or dementia **Other:** cognitive function (executive function, attention, processing speed and memory	
Populations analysed: adults without diagnosed cognitive impairments	**Author-stated funding source:** This review was funded by the National Institute on Aging and AHRQ. These agencies and members of the National Academies Committee on Preventing Dementia and Cognitive Impairment helped refine the scope and reviewed a draft report of findings. The authors are solely responsible for the content preparation, writing of the manuscript, and decision to submit the manuscript for publication.

<table>
<tr><td colspan="2">SR/MA
Citation: Chastin, S. F., De Craemer, M., De Cocker, K., Powell, L., Van Cauwenberg, J., Dall, P., ... & Stamatakis, E. (2019). How does light-intensity physical activity associate with adult cardiometabolic health and mortality? Systematic review with meta-analysis of experimental and observational studies. Br J Sports Med, 53(6), 370-376.</td></tr>
<tr><td>Purpose: to synthesise evidence from observational and experimental studies and to quantify the effect of LIPA on acute and long-term cardiometabolic health through meta-analysis.</td><td rowspan="5">Abstract:
Aim To assess the relationship between time spent in light physical activity and cardiometabolic health and mortality in adults.
Design Systematic review and meta-analysis.
Data sources Searches in Medline, Embase, PsycInfo, CINAHL and three rounds of hand searches. Eligibility criteria for selecting studies Experimental (including acute mechanistic studies and physical activity intervention programme) and observational studies (excluding case and case–control studies) conducted in adults (aged ≥18 years) published in English before February 2018 and reporting on the relationship between light physical activity (<3 metabolic equivalents) and cardiometabolic health outcomes or all-cause mortality. Study appraisal and synthesis Study quality appraisal with QUALSYST tool and random effects inverse variance meta-analysis.
Results Seventy-two studies were eligible including 27 experimental studies (and 45 observational studies). Mechanistic experimental studies showed that short but frequent bouts of light-intensity activity throughout the day reduced postprandial glucose (−17.5%; 95% CI −26.2 to −8.7) and insulin (−25.1%; 95% CI −31.8 to –18.3) levels compared with continuous sitting, but there was very limited evidence for it affecting other cardiometabolic markers. Three light physical activity programme intervention studies (n ranging from 12 to 58) reduced adiposity, improved blood pressure and lipidaemia; the programmes consisted of activity of >150 min/week for at least 12 weeks. Six out of eight prospective observational studies that were entered in the meta-analysis reported that more time spent in daily light activity reduced risk of all-cause mortality (pooled HR 0.71; 95% CI 0.62 to 0.83).
Conclusions Light-intensity physical activity could play a role in improving adult cardiometabolic health and reducing mortality risk. Frequent short bouts of light activity improve glycaemic control. Nevertheless, the modest volume of the prospective epidemiological evidence base and the moderate consistency between observational and laboratory evidence inhibits definitive conclusions.</td></tr>
<tr><td>Timeframe: from inception to February 2018</td></tr>
<tr><td>Total # studies included: 31 (8 for ACM)</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) light physical activity (<3 metabolic equivalents)</td></tr>
<tr><td>Outcomes addressed: cardiometabolic health outcomes or all-cause mortality</td></tr>
</table>

SR/MA **Citation:** Dinu, M., Pagliai, G., Macchi, C., & Sofi, F. (2019). Active commuting and multiple health outcomes: a systematic review and meta-analysis. *Sports Medicine*, *49*(3), 437-452.	
Purpose: To evaluate the relationship between active commuting and all-cause mortality, cardiovascular disease, cancer and diabetes.	**Abstract:** Background Active commuting is associated with greater physical activity, but there is no consensus on the actual beneficial effects of this type of physical activity on health outcomes. Objective To examine the association between active commuting and risk of all-cause mortality, incidence and mortality from cardiovascular diseases, cancer and diabetes through meta-analysis. Methods A comprehensive search of MEDLINE, Embase, Google Scholar, Web of Science, The Cochrane Library, Transport Research International Documentation database, and reference lists of included articles was conducted. Only prospective cohort studies were included. Results Twenty-three prospective studies including 531,333 participants were included. Participants who engaged in active commuting had a significantly lower risk of all-cause mortality [relative risk (RR) 0.92, 95% CI 0.85–0.98] and cardiovascular disease incidence (RR 0.91; 95% CI 0.83–0.99). There was no association between active commuting and cardiovascular disease mortality and cancer. Participants who engaged in active commuting had a 30% reduced risk of diabetes (RR 0.70; 95% CI 0.61–0.80) in three studies after removal of an outlying study that affected the heterogeneity of the results. Subgroup analyses suggested a significant risk reduction (− 24%) of all-cause mortality (RR 0.76; 95% CI 0.63–0.94) and cancer mortality (− 25%; RR 0.75; 95% CI 0.59–0.895) among cycling commuters. Conclusion People who engaged in active commuting had a significantly reduced risk of all-cause mortality, cardiovascular disease incidence and diabetes.
Timeframe: MEDLINE (source: PubMed, 1966 to February 2018), Embase (1980 to February 2018)	
Total # studies included: 23	
Other details (e.g. definitions used, exclusions etc) only prospective cohort studies included	
Outcomes addressed: all-cause mortality, cardiovascular disease, cancer and diabetes	

<table>
<tr><td colspan="2">SR/MA
Citation: Ekelund, U., Tarp, J., Steene-Johannessen, J., Hansen, B. H., Jefferis, B., Fagerland, M. W., ... & Larson, M. G. (2019). Dose-response associations between accelerometry measured physical activity and sedentary time and all-cause mortality: systematic review and harmonised meta-analysis. bmj, 366, l4570.</td></tr>
<tr><td>Purpose: to examine the association between accelerometer measured physical activity and sedentary time and all cause mortality</td><td rowspan="4">Abstract:
Objective To examine the dose-response associations between accelerometer assessed total physical activity, different intensities of physical activity, and sedentary time and all-cause mortality. Design Systematic review and harmonised meta-analysis. Data sources PubMed, PsycINFO, Embase, Web of Science, Sport Discus from inception to 31 July 2018. Eligibility criteria Prospective cohort studies assessing physical activity and sedentary time by accelerometry and associations with all-cause mortality and reported effect estimates as hazard ratios, odds ratios, or relative risks with 95% confidence intervals. Data extraction and analysis Guidelines for meta-analyses and systematic reviews for observational studies and PRISMA guidelines were followed. Two authors independently screened the titles and abstracts. One author performed a full text review and another extracted the data. Two authors independently assessed the risk of bias. Individual level participant data were harmonised and analysed at study level. Data on physical activity were categorised by quarters at study level, and study specific associations with all-cause mortality were analysed using Cox proportional hazards regression analyses. Study specific results were summarised using random effects meta-analysis. Main outcome measure All-cause</td></tr>
<tr><td>Timeframe: from inception to 31 July 2018</td></tr>
<tr><td>Total # studies included: 8</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) prospective cohort studies that assessed sedentary time and physical activity by accelerometry</td></tr>
</table>

Outcomes addressed: all cause mortality	mortality. Results 39 studies were retrieved for full text review; 10 were eligible for inclusion, three were excluded owing to harmonisation challenges (eg, wrist placement of the accelerometer), and one study did not participate. Two additional studies with unpublished mortality data were also included. Thus, individual level data from eight studies (n=36383; mean age 62.6 years; 72.8% women), with median follow-up of 5.8 years (range 3.0-14.5 years) and 2149 (5.9%) deaths were analysed. Any physical activity, regardless of intensity, was associated with lower risk of mortality, with a non-linear dose-response. Hazards ratios for mortality were 1.00 (referent) in the first quarter (least active), 0.48 (95% confidence interval 0.43 to 0.54) in the second quarter, 0.34 (0.26 to 0.45) in the third quarter, and 0.27 (0.23 to 0.32) in the fourth quarter (most active). Corresponding hazards ratios for light physical activity were 1.00, 0.60 (0.54 to 0.68), 0.44 (0.38 to 0.51), and 0.38 (0.28 to 0.51), and for moderate-to-vigorous physical activity were 1.00, 0.64 (0.55 to 0.74), 0.55 (0.40 to 0.74), and 0.52 (0.43 to 0.61). For sedentary time, hazards ratios were 1.00 (referent; least sedentary), 1.28 (1.09 to 1.51), 1.71 (1.36 to 2.15), and 2.63 (1.94 to 3.56). Conclusion Higher levels of total physical activity, at any intensity, and less time spent sedentary, are associated with substantially reduced risk for premature mortality, with evidence of a non-linear dose-response pattern in middle aged and older adults.

<table>
<tr><td colspan="2">Systematic review
Citation: Engeroff T, Ingmann T, Banzer W. Physical Activity Throughout the Adult Life Span and Domain-Specific Cognitive Function in Old Age: A Systematic Review of Cross-Sectional and Longitudinal Data. Sport Med. 2018;48(6):1405–36.</td></tr>
<tr><td>Purpose: To study associations between adherence to leisure PA during adulthood and domain-specific cognitive function in old age.</td><td rowspan="4">Abstract:
BACKGROUND: A growing body of literature suggests that physical activity might alleviate the age-related neurodegeneration and decline of cognitive function. However, most of this evidence is based on data investigating the association of exercise interventions or current physical activity behaviour with cognitive function in elderly subjects.
OBJECTIVE: We performed a systematic review and hypothesize that physical activity during the adult life span is connected with maintained domain-specific cognitive functions during late adulthood defined as age 60+ years.
METHODS: We performed a systematic literature search up to November 2017 in PubMed, Web of Science, and Google Scholar without language limitations for studies analyzing the association of leisure physical activity during the adult life span (age 18+ years) and domain-specific cognitive functions in older adults (age 60+ years).</td></tr>
<tr><td>Timeframe: Inception – November 2017</td></tr>
<tr><td>Total # studies included: 23</td></tr>
<tr><td>Author-stated inclusion criteria:
To be included in our analysis, studies had to assess (1) leisure PA during a time point or time span of adulthood (age 18? years), and (2) cognitive function during a time point or time span of old age, defined as a sample mean age of 60?years (either in the overall sample or a subsample analysis). To define long-term effects, C 10</td></tr>
</table>

years should separate at least one time point of leisure PA behaviour and cognitive function assessment. Participants (either the overall sample or a subsample that was analyzed separately) should have no cognitive impairments or mental illnesses. **Author-stated leisure time physical activity definition:** Leisure PA included all activities that people participated in during their free time and that were not work related and did not involve life maintenance tasks such as housecleaning.	RESULTS: The literature review yielded 14,294 articles and after applying inclusion and exclusion criteria, nine cross-sectional and 14 longitudinal studies were included. Moderate- and vigorous-intensity leisure physical activity was associated with global cognitive function and specific cognitive domains including executive functions and memory but not attention or working memory. Most studies assessed mid- to late-adulthood physical activity, thus information concerning the influence of young adult life-span physical activity is currently lacking. CONCLUSIONS: Observational evidence that moderate- and vigorous-intensity leisure physical activity is beneficially associated with maintained cognitive functions during old age is accumulating. Further studies are necessary to confirm a causal link by assessing objective physical activity data and the decline of cognitive functions at multiple time points during old age.
Outcomes addressed: Cognitive function was defined as an assessment/ outcome that indicates the performance or decline in (1) a definable cognitive domain, or (2) multiple cognitive domains, or (3) overall/global cognitive function.	
Populations analysed: adults without diagnosed cognitive impairments	**Author-stated funding source:** No sources of funding were used to assist in the preparation of this article.

<table>
<tr><td colspan="2">Meta-analysis
Citation: Gordon B., McDowell C., Lyons M., Herring M., The Effects of Resistance Exercise Training on Anxiety: A Meta-Analysis and Meta-Regression Analysis of Randomized Controlled Trials. Sports Med. 2017); 47:2521–2532.</td></tr>
<tr><td>Purpose: To estimate the population effect size for resistance exercise training (RET) effects on anxiety

Timeframe: From inception to February 20

Total # studies included: 16

Other details (e.g. definitions used, exclusions etc): RCTs to either a RET intervention or a non-active control condition, and an anxiety outcome measured at baseline and at mid- and/or post-intervention

Outcomes addressed: Anxiety measured using: Profile of mood states-tension, Hopkins symptom checklist, State-Trait Anxiety Inventory, Mental Health Functioning Index-Anxiety, Hospital Anxiety and Depression Scales, Depression, Anxiety and Stress Scale-21, Brunel Mood Scale-Tension, Generalized Anxiety Disorder</td><td>Abstract:

Background: The salutary effects of resistance exercise training (RET) are well established, including increased strength and function; however, less is known regarding the effects of RET on mental health outcomes. Aerobic exercise has well-documented positive effects on anxiety, but a quantitative synthesis of RET effects on anxiety is needed. Objectives: To estimate the population effect size for resistance exercise training (RET) effects on anxiety and to determine whether variables of logical, theoretical, and/or prior empirical relation to anxiety moderate the overall effect. Methods: Thirty-one effects were derived from 16 articles published before February 2017, located using Google Scholar, MEDLINE, PsycINFO, PubMed, and Web of Science. Trials involved 922 participants (mean age = 43 ± 21 years, 68% female/32% male) and included both randomization to RET (n = 486) or a non-active control condition (n = 436), and a validated anxiety outcome measured at baseline, mid-, and/or post-intervention. Hedges' d effect sizes were computed and random effects models were used for all analyses. Meta-regression quantified the extent to which participant and trial characteristics moderated the mean effect. Results: RET significantly reduced anxiety symptoms (Δ = 0.31, 95% CI 0.17-0.44; z = 4.43; p < 0.001). Significant heterogeneity was not indicated (Q (30) = 40.5, p > 0.09; I = 28.3%, 95% CI 10.17-42.81); sampling error accounted for 77.7% of observed variance. Larger effects were found among healthy participants (Δ = 0.50, 95% CI 0.22-0.78) compared to participants with a physical or mental illness (Δ = 0.19, 95% CI 0.06-0.31, z = 2.16, p < 0.04). Effect sizes did not significantly vary according to sex (β = −0.31), age (β = −0.10), control condition (β = 0.08), program length (β = 0.07), session duration (β = 0.08), frequency (β = −0.10), intensity (β = −0.18), anxiety recall time frame (β = 0.21), or whether strength significantly improved (β = 0.19) (all p ≥ 0.06). Conclusions: RET significantly improves anxiety symptoms among both healthy participants and participants with a physical or mental illness. Improvements were not moderated by sex, or based on features of RET. Future trials should compare RET to other empirically-supported therapies for anxiety.</td></tr>
<tr><td>Population analysed: All ages, including children and adolescents, patient groups, older adults and some with mental health concerns.</td><td>Author-Stated Funding Source: No sources of funding were used to assist in the conduct of this analysis or the preparation of this article.</td></tr>
</table>

Meta-analysis **Citation:** Gordon B.R., McDowell C.P., Hallgren M., Meyer M., Lyon M., Herring M.P. Association of Efficacy of Resistance Exercise Training With Depressive Symptoms: Meta-analysis and Meta-regression Analysis of Randomized Clinical Trials. *JAMA Psychiatry.* 2018;75(6):566-576.	
Purpose: To estimate the association of efficacy of resistive exercise training (RET) with depressive symptoms.	**Abstract:** **Importance:** The physical benefits of resistance exercise training (RET) are well documented, but less is known regarding the association of RET with mental health outcomes. To date, no quantitative synthesis of the antidepressant effects of RET has been conducted. **Objectives:** To estimate the association of efficacy of RET with depressive symptoms and determine the extent to which logical, theoretical, and/or prior empirical variables are associated with depressive symptoms and whether the association of efficacy of RET with depressive symptoms accounts for variability in the overall effect size. **Data Sources:** Articles published before August 2017, located using Google Scholar, MEDLINE, PsycINFO, PubMed, and Web of Science. Study Selection: Randomized clinical trials included randomization to RET (n = 947) or a nonactive control condition (n = 930). **Data Extraction and Synthesis**: Hedges d effect sizes were computed and random-effects models were used for all analyses. Meta-regression was conducted to quantify the potential moderating influence of participant and trial characteristics. **Main Outcomes and Measures:** Randomized clinical trials used validated measures of depressive symptoms assessed at baseline and mid-intervention and/or postintervention. Four primary moderators were selected a priori to provide focused research hypotheses about variation in effect size: total volume of prescribed RET, whether participants were healthy or physically or mentally ill, whether or not allocation and/or assessment were blinded, and whether or not the RET intervention resulted in a significant improvement in strength. **Results:** Fifty-four effects were derived from 33 randomized clinical trials involving 1877 participants. **Resistance exercise training was associated with a significant reduction in depressive symptoms with a moderate-sized mean effect of 0.66 (95% CI, 0.48-0.83; z = 7.35; P < .001).** Significant heterogeneity was indicated (total Q = 216.92, df = 53; P < .001; I2 = 76.0% [95% CI, 72.7%-79.0%]), and sampling error accounted for 32.9% of observed variance. The number needed to treat was 4. Total volume of prescribed RET, participant health status, and strength improvements were not significantly associated with the antidepressant effect of RET. However, smaller reductions in depressive symptoms were derived from randomized clinical trials with blinded allocation and/or assessment. **Conclusions and Relevance:** Resistance exercise training significantly reduced depressive symptoms among adults regardless of health status, total prescribed volume of RET, or significant improvements in strength. Better-quality randomized clinical trials blinding both allocation and assessment and comparing RET with other empirically supported treatments for depressive symptoms are needed.
Timeframe: Published before August 2017	
Total # studies included: 33	
Other details (e.g. definitions used, exclusions etc): Peer-reviewed publication, clinical trials, randomized allocation to either an RET intervention or a nonactive control condition, and a validated self-report or clinician-rated measure of depressive symptoms assessed at baseline and at mid-intervention and/or postintervention. No multi-component studies included. Interventions ranged between 6 and 52 weeks.	
Outcomes addressed: Measures of depressive symptoms using: Beck Depression Inventory; Brunel Mood Scale Cardiac Depression Scale; Center for Epidemiologic Studies Depression Scale, Depression Adjective Checklist, Depression, Anxiety and Stress Scale; GDS, Geriatric Depression Scale, Hospital Anxiety and Depression Scale, Hamilton Rating Scale for Depression, Major Depression Inventory, Mental Health Functioning Index, Profile of Mood States, Hopkins Symptom Checklist	

Population analysed: Adults what were either older, or were overweight or obese, or may have had some or other medical condition (T2DM, Cancer, Fibromyalgia etc), and one study with law enforcement officers and one study with participants with major depressive disorder	**Author-Stated Funding Source:** None reported.

SR/MA **Citation:** Hidayat K, Zhou H-J, Shi B-M. Influence of physical activity at a young age and lifetime physical activity on the risks of 3 obesity-related cancers: systematic review and meta-analysis of observational studies. Nutrition Reviews 2019 doi: 10.1093/nutrit/nuz024	
Purpose: The present systematic review and meta-analysis of observational studies was performed in accordance with the MOOSE guidelines to determine whether physical activity at a young age and lifetime physical activity may lower the risks of breast cancer, colon cancer, and endometrial cancer. **Timeframe:** Inception to July 2019 **Total # studies included:** 80 **Other details (e.g. definitions used, exclusions etc)** Self-reported PA by type **Outcomes addressed:** Breast, colon, endometrial cancer	**Abstract:** Context: Excess weight has been linked to increased risks of 13 types of cancers. Physical activity is a non-nutritional modifiable lifestyle factor that is not only crucial for weight control but is also known to regulate hormones and metabolic pathways that may contribute to carcinogenesis. There is solid evidence that being physically active during middle and late adulthood lowers the risks of 3 obesity-related cancers, namely breast cancer, colon cancer, and endometrial cancer. However, the associations between physical activity at a young age (childhood, adolescence, and young adulthood; age 5 to _30 yr) and lifetime physical activity and the risks of breast cancer, colon cancer, and endometrial cancer are less defined. Objective: The present systematic review and meta-analysis of observational studies was performed in accordance with the MOOSE guidelines to determine whether physical activity at a young age and lifetime physical activity may lower the risks of breast cancer, colon cancer, and endometrial cancer. Data sources: The PubMed and Web of Science databases were searched for relevant observational studies published from inception to July 2018. Study selection: Observational studies (prospective cohort, case cohort, nested case-control, historical cohort, and case-control) were considered relevant if they investigated the association between physical activity at a young age or lifetime physical activity and the risks of developing selected cancers. Data extraction: A random-effects meta-analysis was performed to generate the summary relative risk (RR) with 95%CI for the highest vs the lowest category of physical activity of any type. Results: Eighty publications were included in the present meta-analysis. Higher physical activity at a young age was associated with lower risks of breast cancer (RR 0.81, 95%CI 0.76, 0.87) and colon cancer (RR 0.67, 95%CI 0.50, 0.88). Similarly, lifetime physical activity was inversely associated with the risks of breast cancer (RR 0.79, 95%CI 0.72, 0.86) and colon cancer (RR 0.75, 95%CI 0.69, 0.82). For breast cancer, menopausal status did not appear to modify the observed inverse association. The benefit with respect to endometrial cancer risk reduction was only observed with higher lifetime physical activity (RR 0.77, 95%CI 0.67, 0.88), not with higher physical activity at a young age (RR 0.89, 95%CI 0.73, 1.07). Conclusions: Being physically active over a lifetime, starting from early childhood, may lower the risks of developing breast cancer, colon cancer, and endometrial cancer.
Populations Analyzed: Adults	**Author-Stated Funding Source:** This study was supported by grants from Suzhou Science and Technology Bureau (No. SYS201741).

SR/MA **Citation:** Kovacevic A, Mavros Y, Heisz JJ, Singh MA. The effect of resistance exercise on sleep: a systematic review of randomized controlled trials. Sleep medicine reviews. 2018 Jun 1;39:52-68. https://doi-org.ezproxy1.library.usyd.edu.au/10.1016/j.smrv.2017.07.002	
Purpose: to review the effects of acute and chronic resistance exercise on sleep quantity and quality.	**Abstract:** Impaired sleep quality and quantity are associated with future morbidity and mortality. Exercise may be an effective non-pharmacological intervention to improve sleep, however, little is known on the effect of resistance exercise. Thus, we performed a systematic review of the literature to determine the acute and chronic effects of resistance exercise on sleep quantity and quality. Thirteen studies were included. Chronic resistance exercise improves all aspects of sleep, with the greatest benefit for sleep quality. These benefits of isolated resistance exercise are attenuated when resistance exercise is combined with aerobic exercise and compared to aerobic exercise alone. However, the acute effects of resistance exercise on sleep remain poorly studied and inconsistent. In addition to the sleep benefits, resistance exercise training improves anxiety and depression. These results suggest that resistance exercise may be an effective intervention to improve sleep quality. Further research is needed to better understand the effects of acute resistance exercise on sleep, the physiological mechanisms underlying changes in sleep, the changes in sleep architecture with chronic resistance exercise, as well its efficacy in clinical cohorts who commonly experience sleep disturbance. Future studies should also examine time-of-day and dose–response effects to determine the optimal exercise prescription for sleep benefits.
Timeframe: inception to 20 June 2016	
Total # studies included: 13	
Other details (e.g. definitions used, exclusions etc) RCT or randomized crossover trial.	
Outcomes addressed: sleep, wakefulness, daytime drowsiness, use of sleep remedies	

<table>
<tr><td colspan="2">SR/MA
Citation: Liu Y, Li Y, Bai Y-P, Fan X-X. Association Between Physical Activity and Lower Risk of Lung Cancer: A Meta-Analysis of Cohort Studies. Front. Oncol. 2019; 9:5. doi: 10.3389/fonc.2019.00005</td></tr>
<tr><td>Purpose: We aimed to investigate the relationship between physical activity and risk of lung cancer in men and women, as well as other high-risk populations such as cigarette smokers.</td><td rowspan="5">Abstract: Background: Epidemiological evidences regarding the association between physical activity and the risk of lung cancer are still controversial.
Objectives: We aimed to investigate the relationship between physical activity and risk of lung cancer in men and women, as well as other high-risk populations such as cigarette smokers.
Methods: We conducted a meta-analysis of cohort studies to evaluate the association between physical activity and risk of lung cancer. Relevant studies were identified by searching PubMed and Web of Knowledge through August 2018. Study-specific relative risk (RR) with 95% confidence interval (CI) were pooled using random effect model when significant heterogeneity was detected.
Results: Twenty cohort studies with a total of 2,965,811 participants and 31,807 lung cancer cases were included. There was an inverse association between the physical activity and risk of lung cancer. Compared with the low level of physical activity, the pooled RR was 0.83 (95%CI: 0.77, 0.90), with significant heterogeneity ($I2$ = 62.6%, P heterogeneity < 0.001). The corresponding pooled RRs were 0.90 (95%CI: 0.82, 0.99) for women and 0.81 (95%CI: 0.73, 0.90) for men. Smokers with a high level of physical activity were associated with a 10% lower risk for lung cancer (RR = 0.90, 95% CI: 0.84, 0.97), while the association was not significant among non-smokers (RR = 0.95, 95% CI: 0.88, 1.03). Subgroups analysis stratified by whether the studies adjusted for smoking intensity and durations yielded the same magnitude of RR. However, the RR for subgroups without adjustment for dietary factors was 0.74 (95%CI: 0.71, 0.77), which was significantly lower than that with dietary factors adjusted (RR = 0.89, 95%CI: 0.84, 0.95).
Conclusions: Increased physical activity might be associated with lower risk of
lung cancer. Such inverse association was identified among smokers rather than non-smokers. Large interventional studies are expected to further verify these findings.</td></tr>
<tr><td>Timeframe: Inception to August 2018</td></tr>
<tr><td>Total # studies included: 21 cohort studies</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Self-reported PA by type</td></tr>
<tr><td>Outcomes addressed: Lung</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: No funding received for this paper.</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-analysis
Citation: S. J. Martínez-Domínguez, H. Lajusticia, P. Chedraui, F. R. Pérez-López & for the Health Outcomes and Systematic Analyses (HOUSSAY) Project (2018) The effect of programmed exercise over anxiety symptoms in midlife and older women: a meta-analysis of randomized controlled trials, Climacteric, 21:2, 123-131,</td></tr>
<tr><td>Purpose: To evaluate the effect of programmed exercise, for at least 6 weeks, as compared to no intervention over mild
or low to moderate anxiety symptoms on anxiety symptoms (AS) in mid-aged and older women.</td><td rowspan="5">We aimed to perform a systematic review and meta-analysis in order to clarify the effect of programmed exercise over mild-to-moderate anxiety symptoms (ASs) in midlife and older women. A structured search of PubMed, Medline, Web of Science, Scopus, Embase, Cochrane Library, Scielo, and the US, UK and Australian Clinical Trials databases (from inception through July 27, 2017) was performed, with no language restriction using the following terms: 'anxiety', 'anxiety symptoms', 'exercise', 'physical activity', 'menopause', and 'randomized controlled trial' (RCTs) in mid-aged and older women. We assessed RCTs that compared the effect of exercise for at least 6 weeks versus no intervention over ASs as outcome (as defined by trial authors). Exercise was classified according to duration as 'mid-term exercise intervention' (MTEI; for 12 weeks to 4 months), and 'long-term exercise intervention' (LTEI; for 6-14 months). Mean +/- standard deviations of changes for ASs, as assessed with different questionnaires, were extracted to calculate Hedges' g and then used as effect size for meta-analyses. Standardized mean differences (SMDs) of ASs after intervention were pooled using a random-effects model. Ten publications were included for analysis related to 1463 midlife and older women (minimum age 54.2 +/- 3.5 and maximum age 77.6 +/- 5.4 years). Eight MTEIs were associated with a significant reduction of ASs (SMD = -0.42; 95% CI -0.81 to -0.02) as compared to controls. There was no reduction of ASs in seven LTEIs (SMD = -0.03; 95% CI -0.18 to 0.13). It can be concluded that MTEIs of low-to-moderate intensity seem to improve mild-moderate ASs in midlife and older women.

(*Low intensity more effective than moderate intensity)</td></tr>
<tr><td>Timeframe: From inception through July 27,
2017</td></tr>
<tr><td>Total # studies included: 10</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc): RCTs only; Programmed exercise was classified according to duration as ‘midterm exercise intervention’ (MTEI; from 12 weeks to 4 months) or ‘long-term exercise intervention’ (LTEI; from 6 to 14 months). Exercise intensity was classified as low (walking, yoga, and progressive exercise) or moderate (aerobic exercise and cardiovascular training).</td></tr>
<tr><td>Outcomes addressed: AS measured with standard instrument including: Beck Depression Inventory. State-Trait Anxiety Inventory, Brief Symptom Inventory, Women’s Health Questionnaire, Hospital Anxiety and Depression Scale, Generalized Anxiety Disorder Questionnaire, Depression, Anxiety and Stress Scale.</td></tr>
<tr><td>Population analysed: Otherwise healthy women aged 40 or more</td><td>Author-Stated Funding Source: None</td></tr>
</table>

Meta-analysis **Citation:** Northey JM, Cherbuin N, Pumpa KL, Smee DJ, Rattray B. Exercise interventions for cognitive function in adults older than 50: A systematic review with meta-Analysis. Br J Sports Med. 2018;52(3):154–60.	
Purpose: To determine if physical exercise is effective in improving cognitive function in middle to older adults. **Timeframe:** Inception – November 2016 **Total # studies included:** 43 **Author-stated inclusion criteria:** Studies were included from the initial search if they strictly met the following criteria: (1) studies of community dwelling men or women aged 50 years or older. Because criteria for diagnosing cognitive ability (eg, the presence of mild cognitive impairment (MCI)) differ between studies and prior reviews,8 there were no limitations on baseline cognitive status. However, studies which included clinical samples with other neurological (eg, stroke) or mental illnesses (eg, depression) were excluded. (2) A structured exercise programme of any mode, duration, frequency or intensity. Exercise programmes that were not explicitly stated as fully supervised, or of <4 weeks, were excluded. Studies must have allowed the isolated effects of exercise to be measured. (3) A control group could include no contact, waiting list, attention control, sham exercise or alternative active treatment. (4) At least one outcome measure of cognition, measured at baseline and follow-up by any validated neuropsychological test of cognition. (5) The study design was strictly limited to RCTs. (6) A trial must have been published in a peer-reviewed journal. **Outcomes addressed:** Cognition	**Abstract:** BACKGROUND: Physical exercise is seen as a promising intervention to prevent or delay cognitive decline in individuals aged 50 years and older, yet the evidence from reviews is not conclusive. OBJECTIVES: To determine if physical exercise is effective in improving cognitive function in this population. DESIGN: Systematic review with multilevel meta-analysis. DATA SOURCES: Electronic databases Medline (PubMed), EMBASE (Scopus), PsychINFO and CENTRAL (Cochrane) from inception to November 2016. ELIGIBILITY CRITERIA: Randomised controlled trials of physical exercise interventions in community-dwelling adults older than 50 years, with an outcome measure of cognitive function. RESULTS: The search returned 12 820 records, of which 39 studies were included in the systematic review. Analysis of 333 dependent effect sizes from 36 studies showed that physical exercise improved cognitive function (0.29; 95% CI 0.17 to 0.41; p<0.01). Interventions of aerobic exercise, resistance training, multicomponent training and tai chi, all had significant point estimates. When exercise prescription was examined, a duration of 45-60 min per session and at least moderate intensity, were associated with benefits to cognition. The results of the meta-analysis were consistent and independent of the cognitive domain tested or the cognitive status of the participants. CONCLUSIONS: Physical exercise improved cognitive function in the over 50s, regardless of the cognitive status of participants. To improve cognitive function, this meta-analysis provides clinicians with evidence to recommend that patients obtain both aerobic and resistance exercise of at least moderate intensity on as many days of the week as feasible, in line with current exercise guidelines.
Populations analysed: middle to older adults (>50 years)	**Author-stated funding source:** No funding source stated.

<table>
<tr><td colspan="2">SR/MA
Citation: O'Donovan, G., Stensel, D., Hamer, M., & Stamatakis, E. (2017). The association between leisure-time physical activity, low HDL-cholesterol and mortality in a pooled analysis of nine population-based cohorts. European journal of epidemiology, 32(7), 559-566.</td></tr>
<tr><td>Purpose: to investigate associations between leisure-time physical activity, low HDL-C and mortality in a pooled analysis of nine population-based cohorts in Britain.</td><td rowspan="5">Abstract:
The objective of this study was to investigate associations between leisure-time physical activity, low high-density lipoprotein cholesterol (HDL-C) and mortality. Self-reported leisure-time physical activity, HDL-C concentration, and mortality were assessed in 37,059 adults in Health Survey for England and Scottish Health Survey. Meeting physical activity guidelines was defined as C150 min wk-1 of moderate-intensity activity, C75 min wk-1 of vigorous-intensity activity, or equivalent combinations. Low HDL-C was defined as \1.03 mmol L-1 . Cox proportional hazard models were adjusted for age, sex, smoking, total cholesterol, systolic blood pressure, body mass index, longstanding illness, and socioeconomic status. There were 2250 deaths during 326,016 person-years of follow-up. Compared with those who met physical activity guidelines and whose HDL-C was normal (reference group), all-cause mortality risk was not elevated in those who met physical activity guidelines and whose HDL-C concentration was low (hazard ratio: 1.07; 95% confidence interval: 0.75, 1.53). Compared with the reference group, all-cause mortality risk was elevated in those who did not meet physical activity guidelines and whose HDL-C was normal (1.37; 1.16, 1.61), and in those who did not meet physical activity guidelines and whose HDL-C was low (1.65; 1.37, 1.98). Cardiovascular disease mortality hazard ratios were similar, although confidence intervals were wider. There was no statistically significant evidence of biological interaction between physical inactivity and low HDL-C. This novel study supports the notion that leisure-time physical activity be recommended in those with low HDL-C concentration who may be resistant to the HDL-raising effect of exercise training</td></tr>
<tr><td>Timeframe: -</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) frequency and duration of participation in domestic physical activity (light and heavy housework, gardening, and do-it-yourself tasks); frequency, duration and pace of walking (slow, average, brisk, or fast); and participation in sports and exercises using a prompt card showing 10 main groups, including cycling, swimming, running, football, rugby, tennis, and squash.</td></tr>
<tr><td>Outcomes addressed: HDL-cholesterol, ACM, CVD mortality</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Paudel S, Owen AJ, Owusu-Addo E, Smith BJ. Physical activity participation and the risk of chronic diseases among South Asian adults: a systematic review and meta-analysis. Scientific reports. 2019;9(1):9771.</td></tr>
<tr><td>Purpose: To systematically review published, peer-reviewed literature to identify the association between PA domains (total, transport, household, occupational and leisure) and selected chronic diseases and their markers and provide summary estimates of the strength of associations among South Asian adults 40 years or older.</td><td rowspan="5">Abstract: South Asia specific reviews on the role of physical activity (PA) domains on chronic disease prevention are lacking. This study aimed to systematically review published literature to identify the association between PA domains and chronic diseases and to provide summary estimates of the strength of association. Nine electronic databases were searched using the predefined inclusion criteria which included population (South Asian adults 40 years or older), exposure (PA or sedentary behaviour) and outcome (type 2 diabetes mellitus, breast cancer, colorectal cancer, coronary heart disease, stroke, vascular disease and musculoskeletal diseases and their markers). A random-effects meta-analysis was carried out for cardiometabolic outcomes whereas narrative synthesis was completed for other outcome variables. Inactive or less active South Asian adults were at 31% higher risk of being hypertensive. Likewise, the risk of cardiometabolic outcomes was 1.34 times higher among inactive adults. Household PA was found to have a protective effect on breast cancer risk. Total and leisure time PA had a protective effect on osteoporosis among males and females respectively. Contemporary studies with a longitudinal design, representative samples, valid and reliable assessment of different domains are needed to establish the role of PA in chronic disease prevention in the region.</td></tr>
<tr><td>Timeframe: between January 2000 and March 2018</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Routine PA</td></tr>
<tr><td>Outcomes addressed: Chronic diseases, musculoskeletal diseases</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-analysis
Citation: Perez-Lopez F.R., Martinez-Dominguez S.J., Lajusticia H., Chedraui P.Effects of programmed exercise on depressive symptoms in midlife and older women: A meta-analysis of randomized controlled trials. Maturitas. 2017; 106; 38–47.</td></tr>
<tr><td>Purpose: To determine the effect of programmed exercise, for at least 6 weeks, as compared to no intervention over mild to moderate depressive symptoms in midaged and older women (> 40 years).</td><td rowspan="5">Abstract:

Objective: To perform a systematic review and meta-analysis to clarify the effect of programmed exercise on depressive symptoms (DSs) in midlife and older women.

Methods: We carried out a structured search of PubMed-Medline, Web of Science, Scopus, Embase, Cochrane Library and Scielo, from database inception through June 29, 2017, without language restriction. The search included the following terms: depression", "depressive symptoms", "exercise", "physical activity", "menopause", and "randomized controlled trial" (RCTs) in midlife and older women. The US, UK and Australian Clinical Trials databases were also searched. We assessed randomized controlled trials (RCTs) that compared the effect of exercise for at least 6 weeks versus no intervention on DSs as the outcome (as defined by trial authors). Exercise was classified according to duration as "mid-term exercise intervention" (MTEI; lasting for 12 weeks to 4 months), and "long-term exercise intervention" (LTEI; lasting for 6-12 months). Mean changes (+/-standard deviations) in DSs, as assessed with different questionnaires, were extracted to calculate Hedges' g and then used as the effect size for meta-analysis. Standardized mean differences (SMDs) of DSs after intervention were pooled using a random-effects model.

Results: Eleven publications were included for analysis related to 1943 midlife and older women (age range 44-55 years minimum to 65.5+/-4.0 maximum), none of whom was using a hormone therapy. Seven MTEIs were associated with a significant reduction in DSs (SMD=-0.44; 95% CI -0.69, -0.18; p=0.0008) compared with controls. The reduction in DSs was also significant in six LTEIs (SMD=- 0.29; 95% CI -0.49; -0.09; p=0.005). Heterogeneity of effects among studies was moderate to high. Less perceived stress and insomnia (after exercise) were also found as secondary outcomes.

Conclusion: Exercise of low to moderate intensity reduces depressive symptoms in midlife and older women.</td></tr>
<tr><td>Timeframe: From inception through June 29, 2017,</td></tr>
<tr><td>Total # studies included: 11</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc): RCTs in otherwise healthy women (>40 yrs); no significant differences regarding rate of anxiety or severity at baseline between intervention and control groups; program of exercise for at least 6 weeks; controls defined as women who did not participate in the exercise program.</td></tr>
<tr><td>Outcomes addressed: Depression measured with any of the following surveys: Beck Depression Inventory, Patient Health Questionnaire, Women's Health Questionnaire, Brief Symptom Inventory, Geriatric Depressed Scale.</td></tr>
<tr><td>Population analysed: Otherwise healthy women aged 40 or more</td><td>Author-Stated Funding Source: No funding was received.</td></tr>
</table>

Meta-analysis
Citation: Rathore A, Lom B. The effects of chronic and acute physical activity on working memory performance in healthy participants: A systematic review with meta-analysis of randomized controlled trials. Syst Rev. 2017;6(1):1–16.

Purpose: to evaluate and synthesize randomized controlled trial studies that investigated the effects of both chronic and acute PA on working memory performance (WMP) in physically and cognitively healthy individuals.

Timeframe: August 2009 – December 2016

Total # studies included: 8

Author-stated inclusion criteria:
1- Population: the sample population was identified as cognitively and physically healthy via validated diagnostic tools.
2- Intervention: PA defined as “any bodily movement produced by skeletal muscles that result in energy expenditure” [40]. Acute PA interventions were identified as those with a single PA session while chronic PA interventions were defined as those with more than one PA session. Furthermore, PA was the purposefully selected term as it incorporates a broader spectrum of interventions that otherwise could be excluded under the term “exercise.” Thus, “physical activity” was expected to capture conventional forms of activity, such as cardiovascular exercise and resistance training, but also less conventional forms, such as yoga. Finally, no limitations were imposed based upon modality, dose, intensity, or supervision, but dual-task interventions or self-reported interventions were excluded due to confounding factors noted in previous research [33].
3- Comparator: any kind of control group was eligible, including no treatment, waitlist, health education, sham exercise, or sedentary treatment.
4- Outcome: validated WMP cognitive assessment tools, according to a specific categorization described below.
5- Study design: randomized controlled trials, including cluster-RCTs, crossover-RCTs that are full-length studies published in peer-reviewed, English language journals.

Outcomes addressed:
Working memory performance

Abstract:
BACKGROUND: Understanding how physical activity (PA) influences cognitive function in populations with cognitive impairments, such as dementia, is an increasingly studied topic yielding numerous published systematic reviews. In contrast, however, there appears to be less interest in examining associations between PA and cognition in cognitively healthy individuals. Therefore, the objective of this review was to evaluate and synthesize randomized controlled trial (RCT) studies that investigated the effects of both chronic and acute PA on working memory performance (WMP) in physically and cognitively healthy individuals.
METHODS: Following the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines, a systematic review of studies published between August 2009 and December 2016 was performed on RCTs investigating the effects of chronic and acute PA on WMP with healthy participants as the sample populations. Searches were conducted in Annual Reviews, ProQuest, PsycARTICLES, PsycINFO, PubMed, and Web of Science. Main inclusion criteria stipulated (1) healthy sample populations, (2) PA interventions, (3) WMP as an outcome, and (4) RCT designs. Descriptive statistics included cohort and intervention characteristics and a risk of bias assessment. Analytical statistics included meta-analyses and moderation analyses.
RESULTS: From 7345 non-duplicates, 15 studies (eight chronic PA and seven acute PA studies) met the inclusion criteria and were evaluated. Overall, there was noticeable variance between both cohort and intervention characteristics. Sample populations ranged from primary school children to retirement community members with PA ranging from cycling to yoga. The majority of studies were characterized by "low" or "unclear" risk of selection, performance, detection, attrition, reporting, or other biases. Meta-analysis of chronic PA revealed a significant, small effect size while analysis of acute PA revealed a non-significant, trivial result. Age and intensity were significant moderators while allocation concealment, blinding, and intervention length were not.
CONCLUSIONS: Chronic PA can significantly improve WMP while acute PA cannot. The limiting factors for acute PA studies point to the diversity of working memory instruments utilized, unequal sample sizes between studies, and the sample age groups. Large-scale, high-quality RCTs are needed in order to provide generalizable and more powerful analysis between PA and WMP in a systematic approach.

Populations analysed: Healthy adults

Author-stated funding source: This work was not supported by specific funding.

<table>
<tr><td colspan="2">SR/MA
Citation: Robbins R, Jackson CL, Underwood P, Vieira D, Jean-Louis G, Buxton OM. Employee Sleep and Workplace Health Promotion: A Systematic Review. American Journal of Health Promotion. 2019 Apr 7:0890117119841407. https://doi-org.ezproxy1.library.usyd.edu.au/10.1177/0890117119841407</td></tr>
<tr><td>Purpose: to examine workplace-based employee health interventions that measure sleep duration as an outcome.</td><td rowspan="5">Abstract:
Objective:
Workplace-based employee health promotion programs often target weight loss or physical activity, yet there is growing attention to sleep as it affects employee health and performance. The goal of this review is to systematically examine workplace-based employee health interventions that measure sleep duration as an outcome.
Data Source:
We conducted systematic searches in PubMed, Web of Knowledge, EMBASE, Scopus, and PsycINFO (n = 6177 records).
Study Inclusion and Exclusion Criteria:
To be included in this systematic review, studies must include (1) individuals aged >18 years, (2) a worker health-related intervention, (3) an employee population, and (4) sleep duration as a primary or secondary outcome.
Results:
Twenty studies met criteria. Mean health promotion program duration was 2.0 months (standard deviation [SD] = 1.3), and mean follow-up was 5.6 months (SD = 6.5). The mean sample size of 395 employees (SD = 700.8) had a mean age of 41.5 years (SD = 5.2). Measures of sleep duration included self-report from a general questionnaire (n = 12, 66.6%), self-report based on Pittsburgh Sleep Quality Index (n = 4, 22.2%), and self-report and actigraphy combined (n = 5, 27.7%). Studies most commonly included sleep hygiene (35.0%), yoga (25.0%), physical activity (10.0%), and cognitive–behavioural therapy for insomnia (10.0%) interventions. Across the interventions, 9 different behaviour change techniques (BCTs) were utilized; the majority of interventions used 3 or fewer BCTs, while 1 intervention utilized 4 BCTs. Study quality, on average, was 68.9% (SD = 11.1). Half of the studies found workplace-based health promotion program exposure was associated with a desired increase in mean nightly sleep duration (n = 10, 50.0%).
Conclusions:
Our study findings suggest health promotion programs may be helpful for increasing employee sleep duration and subsequent daytime performance.</td></tr>
<tr><td>Timeframe: inception to 1 Sep 2018</td></tr>
<tr><td>Total # studies included: 20</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) any intervention studies, adult employees</td></tr>
<tr><td>Outcomes addressed: sleep duration, PSQI</td></tr>
</table>

<table>
<tr><td colspan="2">Meta-analysis
Citation: Schuch F.B., Vancampfort D., Firth J., Rosenbaum S., Ward P.B., Silva E.S., Hallgren M., Ponce De Leon A., Dunn A.L., Deslandes A.C., Fleck M.P., Carvalho A.F., Stubbs B. Physical Activity and Incident Depression: A Meta-Analysis of Prospective Cohort Studies. Am J Psychiatry, 2018; 175:631–648.</td></tr>
<tr><td>Purpose: To determine the prospective relationship between physical activity and incident depression and explored potential moderators</td><td rowspan="5">Abstract:

Objective: The authors examined the prospective relationship between physical activity and incident depression and explored potential moderators.

Method: Prospective cohort studies evaluating incident depression were searched from database inception through Oct. 18, 2017, on PubMed, PsycINFO, Embase, and SPORTDiscus. Demographic and clinical data, data on physical activity and depression assessments, and odds ratios, relative risks, and hazard ratios with 95% confidence intervals were extracted. Random-effects meta-analyses were conducted, and the potential sources of heterogeneity were explored. Methodological quality was assessed using the Newcastle-Ottawa Scale.

Results: A total of 49 unique prospective studies (N=266,939; median proportion of males across studies, 47%) were followed up for 1,837,794 person-years. Compared with people with low levels of physical activity, those with high levels had lower odds of developing depression (adjusted odds ratio=0.83, 95% CI=0.79, 0.88; I(2)=0.00). Furthermore, physical activity had a protective effect against the emergence of depression in youths (adjusted odds ratio=0.90, 95% CI=0.83, 0.98), in adults (adjusted odds ratio=0.78, 95% CI=0.70, 0.87), and in elderly persons (adjusted odds ratio=0.79, 95% CI=0.72, 0.86). Protective effects against depression were found across geographical regions, with adjusted odds ratios ranging from 0.65 to 0.84 in Asia, Europe, North America, and Oceania, and against increased incidence of positive screen for depressive symptoms (adjusted odds ratio=0.84, 95% CI=0.79, 0.89) or major depression diagnosis (adjusted odds ratio=0.86, 95% CI=0.75, 0.98). No moderators were identified. Results were consistent for unadjusted odds ratios and for adjusted and unadjusted relative risks/hazard ratios. Overall study quality was moderate to high (Newcastle-Ottawa Scale score, 6.3). Although significant publication bias was found, adjusting for this did not change the magnitude of the associations.

Conclusions: Available evidence supports the notion that physical activity can confer protection against the emergence of depression regardless of age and geographical region.</td></tr>
<tr><td>Timeframe: From inception through Oct. 18, 2017,</td></tr>
<tr><td>Total # studies included: 49</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc): Prospective design with at least 1 year of follow-up; physical activity was measured with a self-report questionnaire, such as the International Physical Activity Questionnaire (IPAQ) or objective physical activity measures (e.g., accelerometers). Physical activity was defined as any bodily movement produced by skeletal muscles and requiring energy expenditure</td></tr>
<tr><td>Outcomes addressed: Depression measured with standardised instruments or through diagnostic interview or physician diagnosis</td></tr>
<tr><td>Population analysed: Adults any age who were free of depression or depressive symptoms at baseline</td><td>Author-Stated Funding Source: None reported.</td></tr>
</table>

Meta-analysis **Citation:** Schuch F.B., Stubbs B., Meyer J., Heissel A., Zech P., Vancampfort D., Rosenbaum S., Deenik J., Firth J., Ward P.B., Carvalho A.F., Hiles S.A., Physical activity protects from incident anxiety: A meta-analysis of prospective cohort studies. *Depress Anxiety*. 2019;1-13.	
Purpose: To examine the prospective relationship between PA and incident anxiety and explore potential moderators.	**Abstract:** **Background**: Prospective cohorts have suggested that physical activity (PA) can decrease the risk of incident anxiety. However, no meta-analysis has been conducted. AIMS: To examine the prospective relationship between PA and incident anxiety and explore potential moderators. **Methods**: Searches were conducted on major databases from inception to October 10, 2018 for prospective studies (at least 1 year of follow-up) that calculated the odds ratio (OR) of incident anxiety in people with high PA against people with low PA. Methodological quality was assessed using the Newcastle-Ottawa Scale (NOS). A random-effects meta-analysis was conducted and heterogeneity was explored using subgroup and meta-regression analysis. **Results**: Across 14 cohorts of 13 unique prospective studies (N = 75,831, median males = 50.1%) followed for 357,424 person-years, **people with high self-reported PA (versus low PA) were at reduced odds of developing anxiety (adjusted odds ratio [AOR] = 0.74; 95% confidence level [95% CI] = 0.62, 0.88; crude OR = 0.80; 95% CI = 0.69, 0.92).** High self-reported PA was protective against the emergence of agoraphobia (AOR = 0.42; 95% CI = 0.18, 0.98) and posttraumatic stress disorder (AOR = 0.57; 95% CI = 0.39, 0.85). The protective effects for anxiety were evident in Asia (AOR = 0.31; 95% CI = 0.10, 0.96) and Europe (AOR = 0.82; 95% CI = 0.69, 0.97); for children/adolescents (AOR = 0.52; 95% CI = 0.29, 0.90) and adults (AOR = 0.81; 95% CI = 0.69, 0.95). Results remained robust when adjusting for confounding factors. Overall study quality was moderate to high (mean NOS = 6.7 out of 9). **Conclusion**: Evidence supports the notion that self-reported PA can confer protection against the emergence of anxiety regardless of demographic factors. In particular, higher PA levels protects from agoraphobia and posttraumatic disorder.
Timeframe: From inception to October 10, 2018	
Total # studies included: 13	
Other details (e.g. definitions used, exclusions etc): Measured PA with a self-report questionnaire such as the IPAQ or any objective PA measures (e.g., pedometers and accelerometers). Only evaluations of high versus low PA, using any criterion, were eligible; used a prospective cohort study design with a follow-up period of 1 year or longer.	
Outcomes addressed: Incident (new cases from baseline to follow-up) anxiety as the outcome, namely increased anxiety symptoms identified via established anxiety screening instruments (e.g., Hospital Anxiety and Depression Scale and Beck Anxiety Scale; Beck, Ward or anxiety disorders, diagnosed using structured or semi-structured diagnostic interviews (e.g. instruments using Diagnostic and Statistical Manual (DSM) for Mental Disorders or International Classification of Disease criteria, including PTSD).	
Population analysed: Participants of any age, free from anxiety at baseline	**Author-Stated Funding Source:** Health Education England and the National Institute for Health Research HEE NIHR ICA Program Clinical Lectureship, Grant/Award Number: ICA-CL-2017-03-001; Maudsley Charity; the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care South London at King's College Hospital NHS Foundation Trust; AstraZeneca grant; Blackmores Institute Fellowship

<table>
<tr><td colspan="2">SR/MA
Citation: Siahpush, M., Levan, T. D., Nguyen, M. N., Grimm, B. L., Ramos, A. K., Michaud, T. L., & Johansson, P. L. (2019). The Association of Physical Activity and Mortality Risk Reduction Among Smokers: Results From 1998–2009 National Health Interview Surveys–National Death Index Linkage. Journal of Physical Activity and Health, 16(10), 865-871.</td></tr>
<tr><td>Purpose: to investigate this association in relation to all-cause, cardiovascular disease, cancer, and respiratory disease mortality in the United States using data from the 1998–2009 National Health Interview Survey (NHIS), which have been linked to the National Death Index (NDI).</td><td rowspan="5">Abstract:
Background: The mortality benefits of meeting the US federal guidelines for physical activity, which includes recommendations for both aerobic and muscle-strengthening activities, have never been examined among smokers. Our aim was to investigate the association between reporting to meet the guidelines and all-cause, cancer, cardiovascular disease, and respiratory disease mortality among smokers. Methods: We pooled data from the 1998–2009 National Health Interview Survey, which were linked to records in the National Death Index (n = 68,706). Hazard ratios (HR) were computed to estimate the effect of meeting the physical activity guidelines on mortality. Results: Smokers who reported meeting the guidelines for physical activity had 29% lower risk of all-cause mortality (HR: 0.71; 95% confidence interval [CI], 0.62–0.81), 46% lower risk of mortality from cardiovascular disease (HR: 0.54; 95% CI, 0.39–0.76), and 26% lower risk of mortality from cancer (HR: 0.74; 95% CI, 0.59–0.93), compared with those who reported meeting neither the aerobic nor the muscle-strengthening recommendations of the guidelines. Meeting the aerobic recommendation of the guidelines was associated with a 42% decline in that risk (HR: 0.58; 95% CI, 0.44–0.77). Conclusion: Smokers who adhere to physical activity guidelines show a significant reduction in mortality</td></tr>
<tr><td>Timeframe: 1998–2009</td></tr>
<tr><td>Total # studies included: 12</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) the length of time of moderate or vigorous aerobic physical activity in minutes per week</td></tr>
<tr><td>Outcomes addressed: ACM, CVD mortality, ca mortality, respiratory diseases mortality</td></tr>
</table>

SR/MA
Citation: Stamatakis, E., Lee, I. M., Bennie, J., Freeston, J., Hamer, M., O'Donovan, G., ... & Mavros, Y. (2017). Does strength-promoting exercise confer unique health benefits? A pooled analysis of data on 11 population cohorts with all-cause, cancer, and cardiovascular mortality endpoints. American journal of epidemiology, 187(5), 1102-1112.

Purpose: to examine the associations between SPE and all-cause, CVD, and cancer mortality and to compare the SPE and aerobic activity guidelines in terms of their associations with mortality outcomes.	**Abstract:** Public health guidance includes recommendations to engage in strength-promoting exercise (SPE), but there is little evidence on its links with mortality. Using data from the Health Survey for England and the Scottish Health Survey from 1994–2008, we examined the associations between SPE (gym-based and own-body-weight strength activities) and all-cause, cancer, and cardiovascular disease mortality. Multivariable-adjusted Cox regression was used to examine the associations between SPE (any, low-/high-volume, and adherence to the SPE guideline (≥2 sessions/ week)) and mortality. The core sample comprised 80,306 adults aged ≥30 years, corresponding to 5,763 any-cause deaths (736,463 person-years). Following exclusions for prevalent disease/events occurring in the first 24 months, participation in any SPE was favourably associated with all-cause (hazard ratio (HR) = 0.77, 95% confidence interval (CI): 0.69, 0.87) and cancer (HR = 0.69, 95% CI: 0.56, 0.86) mortality. Adhering only to the SPE guideline was associated with all-cause (HR = 0.79, 95% CI: 0.66, 0.94) and cancer (HR = 0.66, 95% CI: 0.48, 0.92) mortality; adhering only to the aerobic activity guideline (equivalent to 150 minutes/week of moderate-intensity activity) was associated with all-cause (HR = 0.84, 95% CI: 0.78, 0.90) and cardiovascular disease (HR = 0.78, 95% CI: 0.68, 0.90) mortality. Adherence to both guidelines was associated with all-cause (HR = 0.71, 95% CI: 0.57, 0.87) and cancer (HR = 0.70, 95% CI: 0.50, 0.98) mortality. Our results support promoting adherence to the strength exercise guidelines over and above the generic physical activity targets.
Timeframe: -	
Total # studies included: The Health Survey for England and the Scottish Health Survey	
Other details (e.g. definitions used, exclusions etc) Physical activity was assessed using a questionnaire that inquired about participation in sports and exercises during the 4 weeks prior to the interview. Participants were shown a card (see the Web with 10 exercise groupings, including working out at a gym/weight training/exercise biking, which we labeled "gym-based" SPE, and exercises such as press-ups and sit-ups, which we labeled "own-body-weight" SPE.	
Outcomes addressed: all-cause mortality, cardiovascular disease mortality, and cancer mortality	

<table>
<tr><td colspan="2">Meta-analysis
Citation: Stanmore E, Stubbs B, Vancampfort D, de Bruin ED, Firth J. The effect of active video games on cognitive functioning in clinical and non-clinical populations: A meta-analysis of randomized controlled trials. Neurosci Biobehav Rev [Internet]. 2017;78(March):34–43.</td></tr>
<tr><td>Purpose: to establish effects of exergames on overall cognition and specific cognitive domains in clinical and non-clinical populations.<hr>Timeframe: Inception – January 2017<hr>Total # studies included: 17<hr>Author-stated inclusion criteria:
Only English-language research articles published in peer-reviewed
journals were included. No restrictions were placed on populations studied or sample type. Eligible studies were randomized controlled trials (RCTs) which compared the effects of exergame interventions to non-exergame control conditions on performance in untrained cognitive tasks (i.e. performance in cognitive tasks which varied from those directly practiced within the exergame itself). This includes clinically-validated measures of global cognition, or specific tests of individual domains of cognitive functioning. Studies which combined exergaming with other therapeutic aspects were also eligible for inclusion, provided that (a) the exergame was identified as a primary component of a multi-modal intervention, and (b) the intervention dedicated as much/more time to the exergame component as any other aspect of the intervention. Single-session studies which examined acute effects of exergames on cognitive functioning were excluded from this review.
Author-stated exergame definition:
exergames were defined as any video game for which required upper- or lower-body physical activity for user interaction.<hr>Outcomes addressed:
Cognitive functioning</td>
<td>Abstract:
Physically-active video games ('exergames') have recently gained popularity for leisure and entertainment purposes. Using exergames to combine physical activity and cognitively-demanding tasks may offer a novel strategy to improve cognitive functioning. Therefore, this systematic review and meta-analysis was performed to establish effects of exergames on overall cognition and specific cognitive domains in clinical and non-clinical populations. We identified 17 eligible RCTs with cognitive outcome data for 926 participants. Random-effects meta-analyses found exergames significantly improved global cognition (g=0.436, 95% CI=0.18-0.69, p=0.001). Significant effects still existed when excluding waitlist-only controlled studies, and when comparing to physical activity interventions. Furthermore, benefits of exergames where observed for both healthy older adults and clinical populations with conditions associated with neurocognitive impairments (all p<0.05). Domain-specific analyses found exergames improved executive functions, attentional processing and visuospatial skills. The findings present the first meta-analytic evidence for effects of exergames on cognition. Future research must establish which patient/treatment factors influence efficacy of exergames, and explore neurobiological mechanisms of action.</td></tr>
<tr><td>Populations analysed: No criteria on populations (clinical and non-clinical).</td><td>Author-stated funding source: No funding source stated.</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Stutz J, Eiholzer R, Spengler CM. Effects of evening exercise on sleep in healthy participants: A systematic review and meta-analysis. Sports Medicine. 2019 Feb 14;49(2):269-87. https://doi-org.ezproxy1.library.usyd.edu.au/10.1007/s40279-018-1015-0</td></tr>
<tr><td>Purpose: to investigate the extent to which evening exercise affects sleep and whether variables such as exercise intensity or duration modify the response.</td><td rowspan="5">Abstract:
Background
Current recommendations advise against exercising in the evening because of potential adverse effects on sleep.
Objectives
The aim of this systematic review was to investigate the extent to which evening exercise affects sleep and whether variables such as exercise intensity or duration modify the response.
Methods
A systematic search was performed in PubMed, Cochrane, EMBASE, PsycINFO, and CINAHL databases. Studies evaluating sleep after a single session of evening physical exercise compared to a no-exercise control in healthy adults were included. All analyses are based on random effect models.
Results
The search yielded 11,717 references, of which 23 were included. Compared to control, evening exercise significantly increased rapid eye movement latency (+ 7.7 min; p = 0.032) and slow-wave sleep (+ 1.3 percentage points [pp]; p = 0.041), while it decreased stage 1 sleep (− 0.9 pp; p = 0.001). Moderator analyses revealed that a higher temperature at bedtime was associated with lower sleep efficiency (SE) (b = − 11.6 pp; p = 0.020) and more wake after sleep onset (WASO; b = + 37.6 min; p = 0.0495). A higher level of physical stress (exercise intensity relative to baseline physical activity) was associated with lower SE (− 3.2 pp; p = 0.036) and more WASO (+ 21.9 min; p = 0.044). Compared to cycling, running was associated with less WASO (− 12.7 min; p = 0.037). All significant moderating effects disappeared after removal of one study.
Conclusion
Overall, the studies reviewed here do not support the hypothesis that evening exercise negatively affects sleep, in fact rather the opposite. However, sleep-onset latency, total sleep time, and SE might be impaired after vigorous exercise ending ≤ 1 h before bedtime.</td></tr>
<tr><td>Timeframe: inception to 8 Aug 2018</td></tr>
<tr><td>Total # studies included: 23</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) any language, healthy adult, any study with non-exercise control group.</td></tr>
<tr><td>Outcomes addressed: sleep onset latency, rem latency, total sleep time, sleep efficiency, time awake after sleep onset, awakenings, stage 1–4 sleep, slow-wave sleep, rem sleep, fragmentation index, subjective score of sleep quality</td></tr>
</table>

Meta-analysis **Citation:** Sultana RN, Sabag A, Keating SE, Johnson NA. The Effect of Low-Volume High-Intensity Interval Training (HIIT) on Body Composition and Cardiorespiratory Fitness: A Systematic Review and Meta-Analysis. *Sports Med.* 2019 Nov;49(11):1687-1721.	
Purpose: to examine the effect of low-volume HIIT versus a non-exercising control & mod intensity continuous training (MICT) on body composition and cardio-respiratory fitness in normal weight, overweight and obese adults **Timeframe:** from inception to June 2019 **Total # studies included:** 47 **Other details (e.g. definitions used, exclusions etc): R**egular exercise training intervention (≥ 4 weeks), a minimum of 2 days/week. Training needed to involve a low-volume HIIT or SIT protocol and a non-exercising control, or MICT intervention **Outcomes addressed:** change in adiposity as fat mass (kg) or body fat (%), change in lean body mass (kg) or cardiorespiratory fitness measured as maximal or peak oxygen uptake (L/min or mL/kg/min). Only studies that used DXA, BIA or ADP to measure composition were included.	**Abstract:** **Background**: Evidence for the efficacy of low-volume high-intensity interval training (HIIT) for the modulation of body composition is unclear. **Objectives**: We examined the effect of low-volume HIIT versus a non-exercising control and moderate-intensity continuous training (MICT) on body composition and cardiorespiratory fitness in normal weight, overweight and obese adults. We evaluated the impact of low-volume HIIT (HIIT interventions where the total amount of exercise performed during training was ≤ 500 metabolic equivalent minutes per week [MET-min/week]) compared to a non-exercising control and MICT. **Methods**: A database search was conducted in PubMed (MEDLINE), EMBASE, CINAHL, Web of Science, SPORTDiscus and Scopus from the earliest record to June 2019 for studies (randomised controlled trials and non-randomised controlled trials) with exercise training interventions with a minimum 4-week duration. Meta-analyses were conducted for between-group (low-volume HIIT vs. non-exercising control and low-volume HIIT vs. MICT) comparisons for change in total body fat mass (kg),body fat percentage (%), lean body mass (kg) and cardiorespiratory fitness. **Results**: From 11,485 relevant records, 47 studies were included. No difference was found between low-volume HIIT and a non-exercising control on total body fat mass (kg) (effect size [ES]: - 0.129, 95% confidence interval [CI] - 0.468 to 0.210; p = 0.455), body fat (%) (ES: - 0.063, 95% CI - 0.383 to 0.257; p = 0.700) and lean body mass (kg) (ES: 0.050, 95% CI - 0.250 to 0.351; p = 0.744), or between low-volume HIIT and MICT on total body fat mass (kg) (ES: - 0.021, 95% CI- 0.272 to 0.231; p = 0.872), body fat (%) (ES: 0.005, 95% CI - 0.294 to 0.304;p = 0.974) and lean body mass (kg) (ES: 0.030, 95% CI - 0.167 to 0.266;p = 0.768). However, low-volume HIIT significantly improved cardiorespiratory fitness compared with a non-exercising control (p < 0.001) and MICT (p = 0.017). **Conclusion**: **These data suggest that low-volume HIIT is inefficient for the modulation of total body fat mass or total body fat percentage in comparison with a non-exercise control and MICT.** A novel finding of our meta-analysis was that there appears to be no significant effect of low-volume HIIT on lean body mass when compared with a non-exercising control, and while most studies tended to favour improvement in lean body mass with low-volume HIIT versus MICT, this was not significant. However, despite its lower training volume, low-volume HIIT induces greater improvements in cardiorespiratory fitness than a non-exercising control and MICT in normal weight, overweight and obese adults. Low-volume HIIT, therefore, appears to be a time-efficient treatment for increasing fitness, but not for the improvement of body composition.
Population analysed: Normal-weight, overweight and/or obese adult participants (18 years or older), who were physically active and inactive, and of any health status	**Author-Stated Funding Source:** No funding source

<table>
<tr><td colspan="2">Meta-analysis
Citation: Wang Y., Shan W., Li Q., Yang N., Shan W. Tai Chi Exercise for the Quality of Life in a Perimenopausal Women Organization: A Systematic Review. Worldviews on Evidence-Based Nursing, 2017; 14:4, 294–305.</td></tr>
<tr><td>Purpose: This systematic review and meta-analysis aimed to summarize and analyze the effectiveness of NW interventions on the physical fitness, the body composition, and the quality of life in the elderly population.</td><td rowspan="5">Abstract:

Background: Improvement of the quality of life in perimenopausal women has recently become an important global health issue. Extensive research reports provide evidence of Tai Chi for the quality of life, but no systematic review has individually investigated Tai Chi as a main intervention on the quality of life in perimenopausal women.

Objective: To assess clinical evidence of Tai Chi for the quality of life in perimenopausal women.

Methods: Studies related to the effect of Tai Chi on the quality of life in perimenopausal women in the databases of China and abroad were searched. RevMan version 5.2 software was used, and the Medical Outcomes Study 36-item short form health survey (SF-36) and bone mineral density (BMD) were selected as evaluation indices.

Results: Five trials were included. The results of this study showed that Tai Chi had a significant effect on bodily pain, general health, vitality, mental health of SF-36, and the spine dimension of BMD, as supported by the following data: bodily pain (Standard Mean Difference [SMD] =–3.63; 95% confidence interval [CI] [–6.62, –0.64]; p = .02); general health (SMD=−5.08; 95% CI [−7.60, –2.56]; p < .0001); vitality (SMD=−5.67; 95% CI [–8.54, –2.81], p = .0001); mental health (SMD = −2.51; 95% CI [–4.82, –0.20], p = .03); and spine dimension of BMD (SMD = −0.06; 95% CI [–0.10, –0.01]; p = .01). However, Tai Chi had no effect on physical function, emotional health, social function, role–physical of SF-36, and the hip dimension of BMD, as supported by the following data: physical function (SMD = –1.79; 95% CI [–5.15, 1.57]; p = .30); emotional health (SMD=−2.90; 95% CI [–7.23, 1.43], p = .19]; social function (SMD=−2.23, 95% CI [–5.08, 0.61], p = 0.12; role–physical (SMD = − 1.18; 95% CI [–4.84, 2.47], p = .53; and hip dimension of BMD (SMD = −0.01; 95% CI [–0.03, 0.01]; p = .31).

Linking Evidence to Action: This systematic review found significant evidence for Tai Chi improving bodily pain, general health, vitality, mental health of SF–36, and the spine dimension of BMD in patients with perimenopausal syndrome. Findings suggest that Tai Chi might be recommended as effective and safe adjuvant treatment for patients with perimenopausal syndrome. More high-quality randomized controlled trials are urgently needed to confirm these results.</td></tr>
<tr><td>Timeframe: from inception to before
January 4, 2015</td></tr>
<tr><td>Total # studies included: 5</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
RCTs in English or Chinese comparing Tai Chi
with controls were included, whether they entailed allocation concealment or blinding or not.</td></tr>
<tr><td>Outcomes addressed: Medical Outcomes Study 36-item short form health survey (SF-36) was used to assess overall health-related quality of life. It consists of eight dimensions of health: physical function, bodily pain, general health, vitality, mental health,
social function, role-physical, and emotional health</td></tr>
</table>

Population analysed: Women meeting diagnostic criteria of perimenopausal syndrome who (a) did not have any uncontrolled medical conditions or physical conditions that would preclude them from participating in an exercise program and (b) had not received HRT in the previous 3 months.	**Author-Stated Funding Source:** None stated.

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B2: EVIDENCE ON SEDENTARY BEHAVIOUR FOR ADULTS (18 YEARS OF AGE AND OLDER)

Guiding Questions

B2. What is the association between **sedentary behaviour** and health-related outcomes?

a. Is there a dose response association (total volume, frequency, **duration**, and intensity of interruptions)?
b. Does the association vary by type and domain of sedentary behaviour?
c. Does physical activity modify the effect of sedentary behaviour on mortality?

Inclusion Criteria

Population: Adults 18 years of age and older
Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour
Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour

Outcomes	Importance
All-cause and cause-specific mortality	Critical
Incidence of cardiovascular disease	Critical
Incidence of cancer (site-specific)	Critical
Incidence of Type 2 Diabetes	Critical
Adiposity/Prevention of weight gain/Body composition	Critical
Mental health outcomes (e.g. depressive symptoms, anxiety symptoms)	Important
Cognitive outcomes (e.g. dementia, cognition)	Important
Physical function (e.g., physical strength, fitness)	Important
Musculoskeletal health (e.g., pain)	Important
Sleep duration and quality	Important
Health-related quality of life	Important

Evidence identified

Twenty-two studies (published from 2017 to 2019) were initially identified that examined the association between sedentary behaviour and health-related outcomes among adults (1-22). Five review were subsequently excluded from further evaluation given the study design or exposures that were out-of-scope. **Table B2.1** presents the reviews that were excluded and their reason for exclusion.

Table B2.1. Excluded Systematic Reviews, with Reasons for Exclusion

Author, Year	Reason for Exclusion	Rationale
Al Tunaiji 2019 *(2)*	Exposure	Examines relationship between lack of MVPA and CVD incidence
Baumeister 2019 *(4)*	Exposure	Examines relationship between PA and liver cancer
Chastin 2017 *(7)*	Exposure	Examines relationship between light-intensity PA and health outcomes
Friedenreich 2019 *(11)*	Design	Modelling study; underlying risk estimates not based on full systematic review methodology
Fuzeki 2017 *(12)*	Design	Analysis of NHANES data only

Table B2.2 presents the ratings for each remaining review according to all the AMSTAR 2 main domains. In general, the included reviews were of moderate credibility. One review was rated as having high credibility, 9 were rated as having moderate credibility, 3 were rated as having low credibility, and the remaining 4 were rated as having critically low credibility. Given concerns regarding the comprehensiveness and the validity of the results presented in reviews rated as having critically low credibility, they were not incorporated into the final Evidence Profiles. A total of 13 reviews were included in the Evidence Profiles below.

Table B2.3 lists the 17 reviews that were assessed by outcome. A de novo search for important outcomes, that were not included in the PAGAC report was not conducted due to resource constraints. Evidence Profiles for these outcomes, therefore, are not included in this report. Extracted data for each included review is presented in **Appendix A.**

Table B2.2. Credibility Ratings (based on AMSTAR 2 *(23)*)

Author, Year	PICO[1]	Apriori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Ahmad 2017 *(1)*	Y	PY	N	PY	Y	Y	Y	PY	PY	N	N/A	N/A	Y	Y	N/A	N	**Moderate**
Bailey 2019 *(3)*	Y	PY	N	PY	Y	Y	PY	PY	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**
Berger 2019 *(5)*	Y	PY	N	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Chan 2019 *(6)*	Y	PY	N	PY	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
del Pozo-Cruz 2018 *(8)*	Y	PY	N	PY	Y	N	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Ekelund 2018 *(9)*	Y	Y	N	PY	N	Y	PY	Y	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**
Ekelund 2019 *(10)*	Y	PY	N	PY	N	Y	PY	Y	Y	N	Y	N	N	N	Y	Y	**Moderate**
Ku 2018 *(13)*	Y	N	Y	PY	N	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	**Moderate**
Ku 2019 *(14)*	Y	N	Y	PY	N	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	**Moderate**
Lee 2019 *(15)*	N	N	N	PY	N	N	PY	Y	Y	N	N	N	N	Y	Y	Y	**Critically Low**
Ma 2018 *(16)*	N	N	N	PY	Y	Y	N	N	N	N	N	N	N	N	Y	N	**Critically Low**
Mahmood 2017 *(17)*	Y	PY	N	PY	Y	Y	PY	Y	N	N	Y	N	N	Y	Y	Y	**Low**
Mañas 2017 *(18)*	Y	N	N	PY	Y	N	PY	Y	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Patterson 2018 *(19)*	Y	N	N	PY	N	Y	PY	Y	PY	N	Y	Y	N	Y	Y	Y	**Low**
Shepard 2017 *(20)*	Y	N	N	N	N	N	N	Y	N	N	N/A	N/A	N	N	N/A	N	**Critically Low**
Wang 2018 *(21)*	Y	Y	Y	Y	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	**High**
Xu 2019 *(22)*	Y	PY	N	N	N	N	N	Y	N	N	Y	N	N	Y	N	Y	**Low**

Abbreviations: COI = conflict of interest; N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.

Table B2.3. Systematic Reviews Assessed, by Author

	Outcomes													
Author, Year	**ACM**	**Cause-specific mortality**	**CVD**	**Cancer**	**Diabetes**	**Adip-osity**	**Mental health outcomes**	**Cognitive outcomes**	**Physical function**	**Musculo-skeletal health**	**Sleep**	**HRQOL**	**Last Search Date**	**AMSTAR 2**
Ahmad 2017 *(1)*			X		X	X							Dec 2016	Moderate
Bailey 2019 *(3)*			X		X								Feb 2019	Moderate
Berger 2019 *(5)*		Prostate		Prostate									Jan 2019	Moderate
Chan 2019 *(6)*				Breast									Apr 2017	Moderate
del Pozo-Cruz 2018 *(8)*	X		X		X	X							Dec 2016	Moderate
Ekelund 2018[a] *(9)*		CVD, Cancer											Oct 2015	Moderate
Ekelund 2019 *(10)*	X												Jul 2018	Moderate
Ku 2018 *(13)*	X												Jan 2018	Moderate
Ku 2019 *(14)*	X												Mar 2019	Moderate
Lee 2019 *(15)*				Ovarian									Dec 2017	Critically Low
Ma 2018 *(16)*				Colorectal									Feb 2017	Critically Low
Mahmood 2017 *(17)*				Colorectal									Dec 2015	Low
Mañas 2017 *(18)*	X[b]												Oct 2016	Critically Low
Patterson 2018 *(19)*	X	CVD, Cancer			X								Sep 2016	Low
Shepard 2017 *(20)*				Bladder									Jun 2016	Critically Low
Wang 2018 *(21)*				Colorectal									Sep 2018	High
Xu 2019[c] *(22)*	X												May 2018	Low

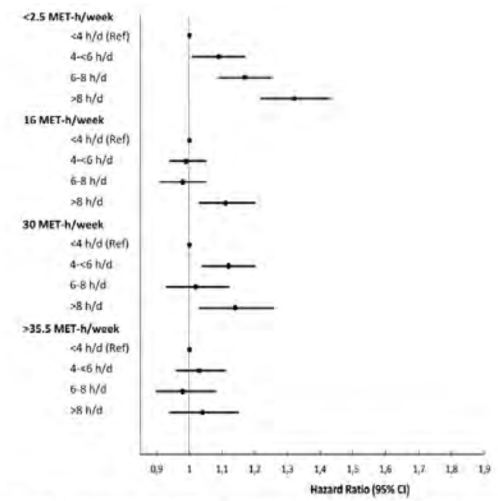
[a] Secondary data analysis of 2016 review
[b] Not included for this outcome given better quality reviews reporting this outcome [c] Individual participant data meta-analysis

B.2. Sedentary Behaviour

Table B.2.a. All-cause and cause-specific mortality: Association between sedentary behaviour and all-cause mortality among adults (in alphabetical order by author)

See the Supplementary materials for description of evidence of US PAGAC *(24)* by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	**Inconsistency**	**Indirectness †**	**Imprecision**	**Other**		
Berger 2019 *(5)* Moderate	3 prospective cohort studies N=277,763	Serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	None	Most studies used self-report sedentary behaviour (one study combined self-report and job title assignment). Mean follow-up was not reported. No significant association was found between high versus low ST and risk of **prostate cancer-related mortality** (RR = 1.14 [95% CI 0.94 to 1.38], 3 studies).	VERY LOW[a]
del Pozo-Cruz *(8)* Moderate	3 prospective cohort studies N=12,108	No serious risk of bias	Serious inconsistency[b]	No serious indirectness	Serious imprecision[b]	None	Included adults aged mean age ranged 49 to 61 years; mean follow-up time not reported. All studies used accelerometers to measure ST with <100 cpm (from the vertical axis of the accelerometer) used to define ST. The review reported that all 3 studies found that replacing 30 minutes of ST with LIPA or MVPA was associated with significantly lower risk of **all-cause mortality**. One study found that replacing ST with LIPA also had a significant beneficial association with risks of **CVD-** and **cancer-**related mortality and that "MPVA had an even better significant association with risks of mortality from **any cause** and **CVD.**" "Hazards ratios ranged from 0.80 to 0.87 for LIPA and from 0.19 to 0.51 for MVPA", no data given by study including variance for effect estimates.	LOW[c]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
Ekelund 2018 *(9)* Moderate	11 prospective cohort studies N=888,327	No serious risk of bias	NA[d]	No serious indirectness	No serious impression	Dose-response relationship[e]	Secondary data analysis of 2016 review on the relationship between sitting time and all-cause mortality. Sitting time was categorized into four groups (0 to <4 hrs/day, 4 to < 6 hrs/day, 6-8 hrs/day, and >8 hrs/day) and TV-viewing time into four groups (<1 hr/day, 1-2 hrs/day, 3-4 hrs/day, and >5 hrs/day). Nine studies had data on the relationship between **sitting time** and **CVD mortality** (n=850,060; median follow-up 10.2 years). A significant dose-response relationship was found between sitting time and CVD mortality for the lowest quartile of PA (<2.5 MET-hrs/week): the HR for CVD mortality was 1.32 (p for trend <0.001, 95% CI only reported in figure) for those who sat for more than 8 hrs/day compared with the reference group (<4 hrs/day). There was no clear dose-response association in any of the other quartiles of PA, but significantly increased hazards were observed in those with sitting time <8 hrs/day vs. <4 hrs/day for those in the 2nd quartile (16 MET-hrs/week) (HR = 1.11 [95% CI, 1.03 to 1.20]) and 3rd quartile (30 MET-hrs/week) (HR = 1.14 [95% CI, 1.03 to 1.26]) of PA. There was no increased risk for CVD mortality in the most active quartile of PA (>35.5 MET-hrs/week) in any category of sitting time.  **Figure 1** Meta-analysis of the stratified associations between sitting time (n=850 060; 25 703 deaths) and CVD mortality. The reference categories are the groups with <4 hour/day of sitting or <1 hour/day of TV-viewing for all quartiles of physical activity. Median upper boundary for Q1–Q3 and lower boundary for Q4 in MET-hour/week. The equivalent amount of time spent in moderate intensity activity are ≈5 min/day (Q1); 25–35 min/day (Q2); 50–65 min/day (Q3) and 60–75 min/day (Q4).	HIGH[f]

Five studies had data on the relationship between **TV-viewing time** and **CVD mortality** (n=458,127, median follow-up 8.5 years). Patterns were similar with those seen for sitting time. In the 'inactive' group (lowest PA quartile, <2.5 MET-hrs/week) the hazard of CVD mortality was 1.59 (95% CI only shown in figure) in those who watched TV for >5 hrs/day compared with those who watched TV for <1 hr/day) (p for trend <0.001). For the other quartiles of PA, the hazard estimates were only significantly increased in the 2nd quartile (HR=1.28, 95% CI not reported) and 3rd quartile (HR=1.41, 95% CI not reported) of PA when comparing >5 hrs/day of TV time vs. <1 hr/day of TV time. There was no increased risk of CVD mortality in the most active quartile of PA for any level of TV viewing time.

Eight studies (n=777,696, median follow-up 11.5 years) had data on the relationship between **sitting time** and **cancer mortality**. There was no clear dose response relationship between sitting time and cancer risk by level of PA. In both the lowest quartile of PA (<2.5 MET-hrs/week) and the 2nd quartile of PA (16 MET-hrs/week), there was a significantly higher risk of cancer mortality in the highest sitting category (>8 hrs/day) vs. lowest (<4 hrs/day) (HR=1.21 [95% CI, 1.14 to 1.29] for the lowest PA quartile and HR=1.08 [95% CI, 1.00 to 1.15] for the 2nd PA quartile).

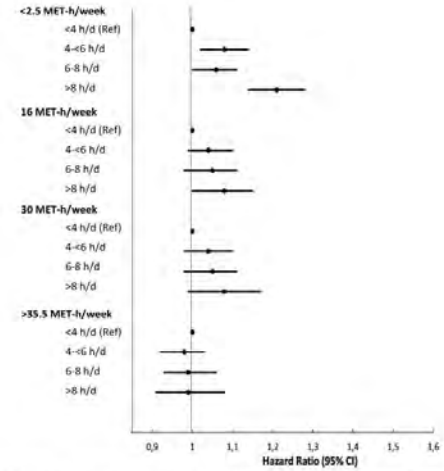


Figure 3 Meta-analysis of the stratified associations between sitting time (n=777 696; 30 851 deaths) and *cancer mortality*. The reference categories are the groups with <4 hour/day of sitting or <1 hour/day of TV viewing for all quartiles of physical activity. Median upper boundary for Q1–Q3 and lower boundary for Q4 in MET-hour/week. The equivalent amount of time spent in moderate intensity activity are ≈5 min/day (Q1); 25–35 min/day (Q2); 50–65 min/day (Q3) and 60–75 min/day (Q4).

Five studies (n=458,091 median follow-up=8.5 years) had data on the relationship between **TV-viewing time** and **cancer mortality**. There was no significantly increased risk of cancer mortality by TV time among those in the inactive or most active PA quartiles, but there was a significantly increased hazards in the 2nd PA quartile (HR=1.18 [95% CI, 1.04 to 1.34) and 3rd PA quartile (HR=1.29 [95% CI, 1.10 to 1.51]) when comparing TV viewing time of >5 hrs/day vs. <1 hr/day.

<table>
<tr><th rowspan="2">Systematic review evidence

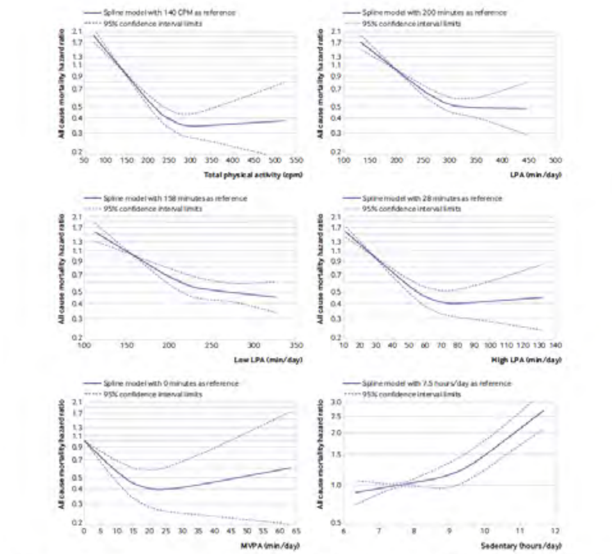
Review credibility</th><th rowspan="2">No. of studies/ Study design

No. of participants</th><th colspan="5">Quality Assessment</th><th rowspan="2">Description of evidence

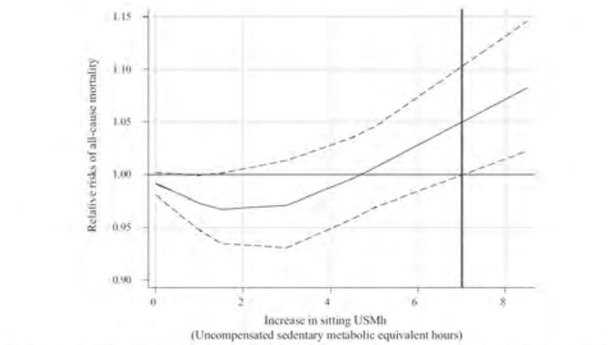
Summary of findings</th><th rowspan="2">Certainty</th></tr>
<tr><th>Risk of bias</th><th>Inconsistency</th><th>Indirectness †</th><th>Imprecision</th><th>Other</th></tr>
<tr>
<td>Ekelund 2019 (10)

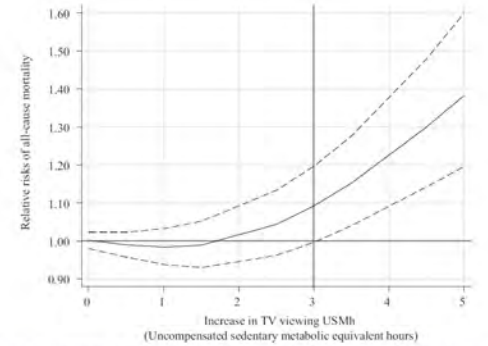
Moderate</td>
<td>8 prospective cohort studies

N=36,383</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Dose--response relationship</td>
<td>
Harmonized meta-analysis from eight prospective cohort studies, including data from 3 large surveillance systems and 2 from unpublished data. Mean age in studies was 63 years with median follow-up of 5.8 years (range 3 to 14.5 years). All 8 studies used accelerometers to measure ST (sedentary ≤100 cpm). Data was categorized into quartiles with the least active quartile as the referent.
Increasing time spent in sedentary behaviour was significantly associated with all-cause mortality. Hazard ratios for increasing quarters of ST were 1.28 (95% CI, 1.09 to 1.51) for the 2^{nd} quartile, 1.71 (95% CI, 1.36 to 2.15) for the 3^{rd} quartile, and 2.63 (95% CI, 1.94 to 3.56) for the highest quartile of ST, after adjustment for potential confounders including time spent in MVPA (table below).
Table 2 | Meta-analysis for associations between total physical activity, intensities of physical activity or sedentary time by quarters and all cause mortality
<table>
<tr><th rowspan="2">Variables</th><th colspan="4">Hazard ratios (95% CI) for all cause mortality*; No of participants; No of deaths</th></tr>
<tr><th>First quarter (least active)</th><th>Second quarter</th><th>Third quarter</th><th>Fourth quarter (most active)</th></tr>
<tr><td>Model B†</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Total physical activity (cpm)</td><td>1 (ref) (n=9096; 1187)</td><td>0.48 (0.43 to 0.54) (n=9105, 483)</td><td>0.34 (0.26 to 0.45) (n=9096, 265)</td><td>0.27 (0.23 to 0.32) (n=9086, 214)</td></tr>
<tr><td>Physical activity intensity</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Light (min/d)</td><td>1 (ref) (n=9073; 1089)</td><td>0.60 (0.54 to 0.68) (n=9101; 511)</td><td>0.44 (0.38 to 0.51) (n=9090; 320)</td><td>0.38 (0.28 to 0.51) (n=9119; 229)</td></tr>
<tr><td>Low light (min/d)</td><td>1 (ref) (n=9066; 1010)</td><td>0.66 (0.56 to 0.77) (n=9106; 518)</td><td>0.47 (0.38 to 0.58) (n=9112; 353)</td><td>0.42 (0.34 to 0.52) (n=9099; 268)</td></tr>
<tr><td>High light (min/d)</td><td>1 (ref) (n=9054; 1159)</td><td>0.55 (0.49 to 0.63) (n=9120; 483)</td><td>0.38 (0.30 to 0.48) (n=9088; 278)</td><td>0.37 (0.32 to 0.46) (n=9113; 229)</td></tr>
<tr><td>Moderate to vigorous (min/d)</td><td>1 (ref) (n=9002; 1139)</td><td>0.64 (0.55 to 0.74) (n=9153; 468)</td><td>0.55 (0.40 to 0.74) (n=9123; 305)</td><td>0.52 (0.43 to 0.61) (n=9105; 237)</td></tr>
<tr><td>Sedentary (min/d)</td><td>1 (ref) (n=9102; 327)</td><td>1.28 (1.09 to 1.51) n=9105; 417)</td><td>1.71 (1.36 to 2.15) (n=9096; 562)</td><td>2.63 (1.94 to 3.56) (n=9080; 843)</td></tr>
</table>
cpm=counts per minute.
Model A adjusted for sex (when applicable), age, and wear time (n=36852, 2304 deaths). Model B adjusted for sex (when applicable), age, body mass index, socioeconomic position, and wear time (n=36383, 2149 deaths). Model C additionally adjusted for covariates listed in table 1 (n=35932, 2047 deaths).
*By Cox regression.
†Moderate-to-vigorous physical activity and sedentary time are mutually adjusted.
Differences in min/day between the referent (least sedentary) and 2^{nd} quarter were broadly equal to 70 min/day of sedentary time.
The dose-response relationship between ST and mortality increased gradually from about 7.5 to 9 hrs/day and were more pronounced at >9.5 hrs/day (see figure below).
</td>
<td>HIGH[g]</td>
</tr>
</table>

							 Fig 2 | Dose-response associations between total physical activity (top left), light intensity physical activity (LPA) (top right), low LPA (middle left), high LPA (middle right), moderate-to-vigorous intensity physical activity (MVPA) (bottom left), and sedentary time (bottom right, data from REGARDS (Reasons for Geographic and Racial Differences in Stroke)[8] and FHS (Women's Health Study)[12] are only included for MVPA) and all cause mortality. Modelling performed using restricted cubic splines with knots at 25th, 50th, and 75th centiles of exposure specific distribution from medians of quarters (least to most active). The exposure reference is set as the median of the medians in the reference group (least active) (see supplementary table 3). Knot locations are available in supplementary table 8. cpm=counts per minute	
Ku 2018 *(13)* Moderate	19 prospective cohort studies N=1,250,482	No serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	Potential overlap in 6 of 7 studies of device-based measures	Analysis of the relationship between sedentary time and **all-cause mortality** in adults. Mean follow-up was 7.8 years (range 2.8 to 15.7 years). Mean age of participants ranged from 40 to 64 years. 12/19 included subjective measures of sedentary time and 7/19 used objective device-based measures. Cut-off points for categories of sedentary time were inconsistent across studies. A linear dose-response relationship was found between daily sedentary time and risk (log-linear) of **all-cause mortality**. A significant relationship was found when limited to both subjective measures (regression coefficient = 0.03 [SE, 0.01], p<0.01) and device-based measures (regression coefficient = 0.09 [SE, 0.03], p<0.01). The regression line and upper and lower 95% CI bounds showed that increased hazards of all-cause death became significant when total sedentary time exceeded approximately 7.5 hrs/day (7 hrs/day when looking at only subjective measures and 9 hrs/day when looking only at objective measures). Studies with longer follow-ups had weaker associations between daily sedentary time and mortality risks.	LOW[h]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
Ku 2019 *(14)* Moderate	11 prospective cohort studies N=36,341	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Potential overlap in 3 of 11 studies	Analysis of the relationship between sedentary time and all-cause mortality in older adults (≥65 years). Mean follow-up was 7.8 years (range 2.3 to 14.2 years). Mean age of participants ranged from 67 to 79 years. All studies used accelerometers to measure ST; 6 studies defined ST as <100 counts/min, 2 studies defined ST as <200 counts/min, 1 used <50 counts/min, and 2 studies did not report the cut point used to define ST. There was no significant dose-response association between ST and **all-cause mortality** among older adults (regression coefficient = 0.04 [SE, 0.03], p=0.15). Removing 3 studies that did not adjust for accelerometer wear time resulted in a significant dose response relationship between ST and all-cause mortality (regression coefficient = 0.08 [SE, 0.03], p=0.02). Within this model, the regression line and upper and lower 95% CI bounds showed that increased hazards of (log-transformed) all-cause death became significant when total sedentary time exceeded approximately 9 hrs/day.	MODERATE[i]
Patterson 2018 *(19)* Low	34 prospective cohort studies N=1,331,468	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean follow-up was 8.9 years (range, 2 to 31 years). Most studies assessed sedentary behaviour via self-report, 3 included objective measurement via accelerometer. Categories used by the study authors to define levels of sedentary behaviour varied considerably across studies. For **total sitting time**, the PA-adjusted relationship was not significantly linear for **all-cause mortality** or **CVD mortality.** In PA-adjusted analysis, the RR was 1.01 (95% CI 1.00 to 1.01) for each additional hr/day below 8 hrs/day and 1.04 (95% CI, 1.03 to 1.05) for each hr/day above 8 hr/day for **all-cause mortality**. For **CVD mortality** the adjusted RR per 1 hr/day was 1.01 (95% CI, 0.99 to 1.02) when total exposure was ≤6 hrs/day and RR=1.04 (95% CI, 1.03 to 1.04) when >6 hrs/day. For **cancer mortality**, the adjusted RR was 1.01 (95% CI, 1.00 to 1.02) with no evidence of non-linearity.	MODERATE[i]

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
Xu 2019[j] *(22)* Low	7 prospective cohort studies N=284,161	No[d]	No[d]	No[d]	No[d]	Dose-response relationship Does not include all available and eligible cohort studies Does not account for LIPA	Examination of the relationship between sedentary activity and all-cause mortality according to PA level using individual participant level data. All measures of ST and PA were self-reported. Mean follow-up ranged from 6.6 to 13.7 years. Sedentary activity was defined by a measure that takes into account both time spent in specific activities and the intensity of those activities by computing a "net uncompensated sedentary behaviour metabolic equivalent hours" (USMh) (where USMh = [MET x hr on SB] – [MET x hr on MVPA]). Data from 5 cohort studies (n=258,688) were pooled to examine the relationship between **sitting** and **all-cause mortality**. The predicted dose-response RRs of sitting were 0.97 (95% CI, 0.95 to 1.00) at 1 USMh, 0.97 (95% CI, 0.93 to 1.01) at 3 USMh, 1.01 (95% CI, 0.97 to 1.05) at 5 USMh, 1.05 (95% CI, 1.00 to 1.10) at 7 USMH, and 1.08 (95% CI, 1.02 to 1.15) at 8.5 USMh. The threshold for risk started to 7 USMh, and on average, between 0 and the maximum of 8.5 USMh of 8.5 hrs, the increase in mortality was 1% (RR=1.01 [95% CI, 1.00 to 1.02]).  Fig. 1. Increase in sitting (USMh) and risk of all-cause mortality. The solid line is the nonlinear prediction of the risk and the dotted lines indicate the 95% confidence interval. The threshold is 7 USMh. USMh indicates the *uncompensated sedentary metabolic equivalent hours*. For example, for people with no reported physical activity at all, the threshold (7 USMh/d) is reached after sitting 7 hours/d. If there was a 4-MET activity for 30 minutes/d, then this threshold (7 USMh/d) would only be reached after 9 hours of sitting per day. Data from 4 cohort studies (n=156,593) were pooled to examine the relationship between **TV viewing** and **all-cause mortality.** The predicted dose-specific RRs of TV viewing were 0.98 (95% CI, 0.94 to 1.03) at 1 USMH, 1.09 (95% CI, 1.00 to 1.20) at 3 USMh, and 1.38 (95% CI, 1.20 to 1.60) at 5 USMh. The threshold for risk started at 3 USMh and the average increase in risk of death between 0 and the maximum value of 5 USMh was an increase of 7% (RR 1.07 [95% CI, 1.04 to 1.10]).	LOW[k]

								 Fig. 2. Increases in TV viewing (USMh) and risk of all-cause mortality. The solid line is the nonlinear prediction of the risk and the dotted lines indicate the 95% confidence interval. The threshold is 3 USMh/d. USMh indicates the *uncompensated sedentary metabolic equivalent hours*. For example, for people with no reported physical activity at all, the threshold (3 USMh/d) is reached after watching TV 3 hours/d. If there was a 4-MET activity for 30 minutes/d, then this threshold (3 USMh/d) would only be reached after 4 hours of TV viewing per day.	

Abbreviations: CI = confidence interval; cpm = counts per minute; CVD = cardiovascular disease; HR = hazard ratio; hrs =hours; min = minutes; LIPA = light intensity physical activity; MET = metabolic equivalents of task; MVPA = moderate-to-vigorous intensity physical activity; NA = not assessed; PA = physical activity; RR = risk ratio; SE = standard error; ST = sedentary time; USMh = net uncompensated sedentary behaviour metabolic equivalent hours

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not upgraded given serious risk of bias of most studies (generally lack of adjustment for potential confounding variables) and downgraded due to serious inconsistency in direction of effects and high statistical heterogeneity
[b] Unable to assess given data presented in article and supplemental material (i.e., qualitative results only, no effect estimates or measures of variance)
[c] Certainty of evidence not upgraded given unknown consistency and precision of effects
[d] Not able to assess given data presented in article and supplemental materials
[e] For the relationship between sitting time and CVD mortality and TV-viewing time and CVD mortality only. No dose response relationship was found according to level of PA for cancer mortality.
[f] Certainty of evidence upgraded given no serious limitations of included evidence and indication of dose-response relationship
[g] Certainty of evidence upgraded given no serious limitations in the body of evidence, individual participant-level data meta-analysis, and evidence of a dose response relationship
[h] Certainty of evidence not upgraded given serious inconsistency in pooled effects and serious indirectness given the variability in measurement and cut points defining sedentary time
[i] Certainty of evidence upgraded given no major study limitations. The potential overlap in study populations was not judged as being significant enough to warrant downgrading.
[j] Individual participant data meta-analysis
[k] Certainty of evidence not upgraded here given lack of detail about individual studies; however, all data comes from existing systematic reviews that serve as the basis for several secondary data analysis presented in this evidence profile. Main limitation is that it does not include all available and eligible cohort studies that could have contributed to this analysis.

Table B.2.b. CVD incidence: Association between sedentary behaviour and CVD incidence among adults (in alphabetical order by author)
See the Supplementary materials for description of evidence of US PAGAC *(24)* by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
Ahmad 2017 *(1)* Moderate	22 reviews and 1 case-control study N=655	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	One case-control study found a significantly higher risk of MI among those self-reporting >215 min/day of ST vs. <70 min/day of ST (RR=1.58 [95% CI, 1.05 to 2.36]). There was no difference in MI risk among those reporting >130-214 min/day of ST vs. <70 min/day (RR = 0.96 [95% CI, 0.64 and 1.44]).	VERY LOW[a]
Bailey 2019 *(3)* Moderate	5 prospective cohort studies N=224,414	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean age of sample ranged from 44 to 64 years and mean follow-up ranged from 2.7 to 13 years. All studies used a single-item self-report measure of total daily sitting time; cutpoints for categories of sitting time were not consistent across studies (range for highest sitting category was >7.1 hrs to 16 hs/day and range for the lowest sitting category was <4 hrs to <8 hrs/day). All studies but one adjusted for physical activity. Higher total daily sitting time was associated with significantly increased risk of CVD when not adjusted for PA levels (HR = 1.29 [95% CI, 1.27 to 1.30]; the risk was attenuated but remained significant with adjustment for PA (HR = 1.14 [95% CI, 1.04 to 1.23]).	MODERATE[b]

Abbreviations: CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; hrs = hours; MI = myocardial infarction; min = minutes; PA =physical activity; RR = risk ratio

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious indirectness in measures of sedentary behaviour and serious imprecision in measures of effects
[b] Certainty of evidence upgraded given no significant study limitations

Table B.2.c. Cancer incidence: Association between sedentary behaviour and cancer incidence among adults (in alphabetical order by author)
See the Supplementary materials for description of evidence of US PAGAC *(24)* by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
Berger 2019 *(5)* Moderate	12 prospective cohort studies N=671,852	Serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	None	Most studies used self-report sedentary behaviour (one study combined self-report and job title assignment). Mean follow-up time was not reported. There was no association between high versus low ST and risk of incident **prostate cancer** (RR = 1.07 [95% CI 0.99 and 1.16], 11 studies).	VERY LOW[a]
Chan 2019 *(6)* Moderate	6 prospective cohort studies N=285,295	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Increased total sitting time was not associated with **premenopausal breast cancer** (RR = 1.04 [95% CI, 0.83 to 1.32], 2 studies, n=1,290) but was associated with **postmenopausal breast cancer** (RR = 1.20 [95% CI, 1.00 to 1.44], 4 studies, n=4,704). No significant associations were found between sitting watching TV or sitting at work and either pre- or post-menopausal breast cancer.	VERY LOW[b]
Mahmood 2017 *(17)* Low	4 prospective cohort studies N=1,709,572 4 case-control studies N=2,463	NR	No serious inconsistency	Serious indirectness	No serious imprecision	None	Six studies investigated occupational sedentary behaviour and two studies assessed recreational sedentary behaviour. Sedentary behaviour ascertained based on job title or measured via self-report. The pooled RR for the highest vs. lowest category of occupational sitting time for **colon cancer** was 1.44 (95% CI, 1.28 to 1.62). No significant association was found between occupational sitting time and **rectal cancer** (RR = 1.02 [95% CI, 0.82 to 1.28]). Two studies evaluated the association between self-reported recreational TV time (hrs/day): 1 study found that watching TV for more than 9 hrs/day (compared with less than 3 hrs/day) was associated with significantly increased risk of **colon cancer** in men (RR = 1.56 [95% CI 1.11 to 1.20]) and women (RR = 1.45 [95% CI, 0.99 and 2.13]) and the other found an association between TV time $\geq$2 hrs/day vs. <1.14 hrs/day and **colon cancer** in both men and women (RR = 2.22 [95% CI, 1.23 to 4.17]).	LOW[c]
Wang 2018 *(21)* High	3 cross-sectional studies N=56,412	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	All 3 studies used self-reported measures of SB; one study included overall SB, two studies reported recreational SB (including one limited to TV viewing only), and one study also included transport-related SB. Categorization of SB was highly variable between studies Age ranged from 40 to 74 years in all 3 studies. None of the 3 studies reported statistically significant associations between time spent in SB and **any colorectal neoplasia** or **advanced colorectal neoplasia;** however, the pooled result suggested a significant increased risk of advanced colorectal neoplasia with higher levels of SB (RR = 1.24 [95% CI, 1.04 to 1.49], 3 studies).	VERY LOW[d]

Abbreviations: CI = confidence interval; hrs = hours; NR = not reported; RR = risk ratio; SB = sedentary behaviour; TV = television

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not upgraded given serious risk of bias of most studies (generally lack of adjustment for potential confounding variables) and due to serious inconsistency in direction of effects and high statistical heterogeneity
[b] Certainty of evidence not upgraded given serious risk of bias of most studies (generally lack of adjustment for potential confounding variables) and due to serious inconsistency and imprecision in direction and magnitude of effects
[c] Certainty of evidence not upgraded given lack of risk-of-bias assessment of individual studies and indirectness in measures of sedentary behaviour
[d] Certainty of evidence downgraded given serious risk of bias of all included studies and serious indirectness in measures of sedentary behaviour

Table B.2.d. Type 2 diabetes incidence: Association between sedentary behaviour and Type 2 diabetes incidence among adults (in alphabetical order by author)

See the Supplementary materials for description of evidence of US PAGAC *(24)* by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	Inconsistency	Indirectness †	Imprecision	Other		
Ahmad 2017 *(1)* Moderate	1 prospective cohort, 1 case-control, 2 cross-sectional N=158,964	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	All four studies suggested that greater **sedentary time** is associated with higher prevalence of diabetes. The one prospective cohort study (n=1,376) found an 84% increased risk for developing diabetes in the highest quartile of TV and sitting time. One cross-sectional study (n=617) found that the odds of diabetes was 43% (OR = 1.43 [95% CI, 0.72 to 2.82]) greater in those sitting ≥185 min/day vs. <185 min/day and were over four times greater (OR = 4.23 [95% CI 2.13 to 8.41]) in those watching ≥85 min/day or TV compared to those with <85 min/day. One cross-sectional (n=156,316) and one case-control study (n=655) reported higher proportions of diabetes among those watching TV almost every day (vs. those watching TV once a week or less) and those in sedentary activities longer than 215 min/day (vs. ≤70 min/day), respectively.	VERY LOW[a]
Bailey 2019 *(3)* Moderate	5 prospective cohort studies N=4,575	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean age of sample ranged from 44 to 64 years and mean follow-up ranged from 2.7 to 13 years. All studies used a single-item self-report measure of total daily sitting time; cutpoints for categories of sitting time were not consistent across studies (range for highest sitting category was ≥7.1 hrs to 16 hs/day and range for the lowest sitting category was <4 hrs to <8 hrs/day). All studies but one adjusted for physical activity. Higher **total daily sitting time** was associated with significantly increased risk of diabetes when not adjusted for PA levels (HR = 1.13 [95% CI, 1.04 to 1.22] and with adjustment for PA (HR = 1.11 [95% CI, 1.01 to 1.19]).	MODERATE[b]
Patterson 2018 *(19)* Low	11 prospective cohort studies N=400,292	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean follow-up was 8.9 years (range, 2 to 31 years). Most studies assessed sedentary behaviour via self-report, 3 included objective measurement via accelerometer. Categories used by the study authors to define levels of sedentary behaviour varied considerably across studies. Increased **total sitting time** and **TV viewing** (linear RR for a 1 hr/day increase in sedentary behaviour) was associated with an increased risk of diabetes (total sitting time: RR=1.10 [95% CI, 1.00 to 1.01], 4 studies and TV viewing time: RR=1.09 [95% CI, 1.07 to 1.12], 6 studies) after adjustment for level of PA, but there was no evidence of a significant linear association.	MODERATE[b]

Abbreviations: CI = confidence interval; hrs = hours; min = minutes; NR = not reported; OR = odds ratio; PA = physical activity; RR = risk ratio; ST = sedentary time; TV = television

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious indirectness in measures of sedentary behaviour and serious imprecision in measures of effects
[b] Certainty of evidence upgraded given no significant study limitations

Table B.2.e. Adiposity: Association between sedentary behaviour and measures of adiposity among adults (in alphabetical order by author)

See the Supplementary materials for description of evidence of US PAGAC *(24)* by outcome

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment** **Risk of bias**	**Inconsistency**	**Indirectness †**	**Imprecision**	**Other**	**Description of evidence** **Summary of findings**	**Certainty**
Ahmad 2017 *(1)* Moderate	1 prospective cohort, 1 case-control, 13 cross-sectional studies N=13,395	Serious risk of bias	No serious inconsistency	Serious indirectness[a]	Serious imprecision[a]	None	13/15 studies reported that higher amounts of ST were significantly associated with **BMI**; 2/15 reported no significant association. Data by study not presented.	VERY LOW[b]
del Pozo-Cruz *(8)* Moderate	6 cross-sectional studies N=4,774	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	None	All studies used accelerometers to measure ST; cut points for defining ST varied across studies, with <100 cpm when only data from the vertical axis of the accelerometer were used or <200 cpm when data from the vector axis of the accelerometer were used. Reallocation of 30 minutes of ST with LIPA was significantly associated with lower **waist circumference** (regression coefficient = -0.57 [95% CI, -0.86 to -0.27], 5 studies) but not **BMI** (regression coefficient = -0.010 [95% CI -0.385 to 0.365], 6 studies). Reallocation of 30 minutes of ST with MVPA was significantly associated with **waist circumference** (regression coefficient = -2.955 [95% CI, -3.878 to -2.032], 5 studies) and **BMI** (regression coefficient = -0.921 [95% CI, -1.31 to -0.531], 6 studies). After removing one study that was contributing to the statistical heterogeneity of the pooled analysis, the result was no longer statistically significant for the relationship between replacing ST with MVPA and BMI.	VERY LOW[c]

Abbreviations: BMI = body mass index; CI = confidence interval; hrs = hours; min = minutes; NA = not assessed; OR = odds ratio; RR = risk ratio; ST = sedentary time; TV = television

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious indirectness in measures of sedentary behaviour and serious imprecision in measures of effects
[b] Certainty of evidence downgraded given serious risk of bias; majority of evidence from cross-sectional studies
[c] Certainty of evidence downgraded given serious risk of bias of all included studies and serious inconsistency and imprecision in measures of effects between studies and outcomes

APPENDIX A. DATA EXTRACTIONS OF INCLUDED EVIDENCE (IN ALPHABETICAL ORDER BY AUTHOR)

<table>
<tr><td colspan="2">SR/MA
Citation: Ahmad S, Shanmugasegaram S, Walker KL, Prince SA. Examining sedentary time as a risk factor for cardiometabolic diseases and their markers in South Asian adults: a systematic review. Int J Public Health. 2017 May;62(4):503-515</td></tr>
<tr><td>Purpose: To systematically review the literature to determine whether sedentary time was associated with cardiometabolic diseases and their risk factors among South Asian adults.</td><td rowspan="5">Abstract:
OBJECTIVES:
The objective was to systematically review the literature to determine whether sedentary time was associated with cardiometabolic diseases and their risk factors among South Asian adults.
METHODS:
Six electronic databases were searched to identify all studies that examined the association between sedentary time and cardiometabolic diseases (e.g., diabetes, cardiovascular disease) and their risk factors [e.g., body mass index (BMI), waist circumference (WC), lipids, blood pressure (BP), glucose] among South Asian adults. Two independent reviewers performed abstract/full-text screening, data abstraction, and quality assessments.
RESULTS:
Searching identified 1757 potential articles; 22 were used in the analysis. Greater sedentary time was associated with an increased likelihood of diabetes (n = 5), higher BMI (n = 13), WC (n = 3), BP (n = 2), and glucose (n = 4). Thirteen out of 22 studies were of higher quality.
CONCLUSION:
Results identified a trend whereby greater sedentary time was associated with an increased risk for diabetes, and several other cardiometabolic risk factors among South Asian adults. High quality studies are needed to identify whether risk factors are independent of physical activity levels to inform culturally-specific interventions for South Asians.</td></tr>
<tr><td>Timeframe: N/A</td></tr>
<tr><td>Total # studies included: 22 (one prospective study on incident diabetes)</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) studies in South East Asian adults included. Results from one prospective study indicating 84% higher risk for developing diabetes in top vs bottom quartile for sedentary time. No dose-response and no meta-analysis</td></tr>
<tr><td>Outcomes addressed: Type 2 diabetes and CVD risk factors</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Bailey DP, Hewson DJ, Champion RB, Sayegh SM. Sitting time and risk of cardiovascular disease and diabetes: a systematic review and meta-analysis. American journal of preventive medicine. 2019 Aug 1.</td></tr>
<tr><td>Purpose: Sitting time and CVD and Diabetes</td><td rowspan="3">Abstract: Context: Whether physical activity attenuates the association of total daily sitting time with cardiovascular disease and diabetes incidence is unclear. This systematic review and meta-analysis examined the association of total daily sitting time with cardiovascular disease and diabetes with and without adjustment for physical activity.
Evidence acquisition: PubMed, Web of Science, BASE, MEDLINE, Academic Search Elite, and ScienceDirect were searched for prospective studies, published between January 1, 1989, and February 15, 2019, examining the association of total daily sitting time with cardiovascular disease or diabetes outcomes. Data extraction and study quality assessments were conducted by 2 independent reviewers. Pooled hazard ratios (HRs) were calculated using a fixed-effects model. The quality assessment and meta-analysis procedures were completed in 2018.
Evidence synthesis: Nine studies with 448,285 participants were included. A higher total daily sitting time was associated with a significantly increased risk of cardiovascular disease (HR=1.29, 95% CI=1.27, 1.30, p<0.001) and diabetes (HR=1.13, 95% CI=1.04, 1.22, p<0.001) incidence when not adjusted for physical activity. The increased risk for diabetes was unaffected when adjusting for physical activity (HR=1.11, 95% CI=1.01, 1.19, p<0.001). For cardiovascular disease, the increased risk was attenuated but remained significant (HR=1.14, 95% CI=1.04, 1.23, p<0.001).
Conclusions: Higher levels of total daily sitting time are associated with an increased risk of cardiovascular disease and diabetes, independent of physical activity. Reductions in total daily sitting may be recommended in public health guidelines.</td></tr>
<tr><td>Timeframe: Jan 1989 to Feb 2019</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td><td></td></tr>
<tr><td>Outcomes addressed:
Incidence of CVD
Incidence of Diabetes</td><td></td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Berger FF, Leitzmann MF, Hillreiner A, Sedlmeier AM, Prokopidi-Danisch ME, Burger M, Jochem C. Sedentary Behaviour and Prostate Cancer: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. Cancer Prev Res (Phila). 2019 Oct;12(10):675-688. doi: 10.1158/1940-6207.CAPR-19-0271. Epub 2019 Jul 30. PMID: 31362941.</td></tr>
<tr><td>Purpose: To examine sedentary behaviour and total, advanced, and fatal prostate cancer with particular attention paid to aggressive prostate cancer because obesity (a correlate of SB) is linked to advanced prostate cancer only.</td><td rowspan="5">Abstract: Prostate cancer is the second most common cancer in men worldwide, and sedentary behaviour is widespread, yet reviews and meta-analyses summarizing the role of sedentary behaviour as a potential risk factor for prostate cancer are scarce. We searched PubMed, Web of Science, and Cochrane databases for relevant articles up to January 2019. We pooled maximally adjusted risk estimates in a random effects model and performed meta-regression meta-analysis, assessed heterogeneity and publication bias using I^2, funnel plots, Egger's and Begg's tests, and conducted sensitivity analyses and influence diagnostics. Data from 12 prospective cohort studies including a total of 30,810 prostate cancer cases were analyzed. We found no statistically significant association between high versus low sedentary behaviour and prostate cancer incidence (relative risk (RR)=1.07, 95% confidence interval (CI)=0.99-1.16, P=0.10). We noted that adjustment for body mass index (BMI) modified the relation of sedentary behaviour to prostate cancer, particularly aggressive cancer. Sedentary behaviour was related to a statistically significant increased risk of aggressive prostate cancer in analyses not adjusted for BMI (RR=1.21, 95% CI=1.03-1.43), whereas no association was apparent in BMI-adjusted analyses (RR=0.98, 95% CI=0.90-1.07), and the difference between those summary risk estimates was statistically significant (P(difference)=0.02). Sedentary behaviour is not independently associated with prostate cancer. However, prolonged sedentary behaviour may be related to increased risk of aggressive prostate cancer through a mechanism involving obesity. This finding represents a potentially important step towards considering sedentary behaviour as a modifiable behavioural risk factor for aggressive prostate cancer.</td></tr>
<tr><td>Timeframe: Inception to January 2019</td></tr>
<tr><td>Total # studies included: 12</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Inclusion criteria included use of total daily sitting time or sedentary behaviours during occupation, leisure time, or transportation as exposure variables.</td></tr>
<tr><td>Outcomes addressed: Incidence of total prostate cancer and aggressive prostate cancer (the latter includes prostate cancer mortality)</td></tr>
</table>

SR/MA **Citation:** Chan DS, Abar L, Cariolou M, Nanu N, Greenwood DC, Bandera EV, McTiernan A, Norat T. World Cancer Research Fund International: Continuous Update Project—systematic literature review and meta-analysis of observational cohort studies on physical activity, sedentary behavior, adiposity, and weight change and breast cancer risk. Cancer Causes & Control. 2019 Aug 30:1-8.	
Purpose: Incidence of breast cancer	**Abstract:** Purpose The purpose of the present study was to systematically review the complex associations between energy balance related factors and breast cancer risk, for which previous evidence has suggested different associations in the life course of women and by hormone receptor (HR) status of the tumour. Methods Relevant publications on adulthood physical activity, sedentary behaviour, body mass index (BMI), waist and hip circumferences, waist-to-hip ratio, and weight change and pre- and postmenopausal breast cancer risk were identified in PubMed up to 30 April 2017. Random-effects meta-analyses were conducted to summarize the relative risks across studies. Results One hundred and twenty-six observational cohort studies comprising over 22,900 premenopausal and 103,000 postmenopausal breast cancer cases were meta-analyzed. Higher physical activity was inversely associated with both pre- and postmenopausal breast cancers, whereas increased sitting time was positively associated with postmenopausal breast cancer. Although higher early adult BMI (ages 18–30 years) was inversely associated with pre- and postmenopausal breast cancers, adult weight gain and greater body adiposity increased breast cancer risk in postmenopausal women, and the increased risk was evident for HR+ but not HR− breast cancers, and among never but not current users of postmenopausal hormones. The evidence was less consistent in premenopausal women. There were no associations with adult weight gain, inverse associations with adult BMI (study baseline) and hip circumference, and non-significant associations with waist circumference and waist-to-hip ratio that were reverted to positive associations on average in studies accounting for BMI. No significant associations were observed for HR-defined premenopausal breast cancers. Conclusion Better understanding on the impact of these factors on pre- and postmenopausal breast cancers and their subtypes along the life course is needed.
Timeframe: inception to Apr 2017	
Total # studies included: 126	
Other details (e.g. definitions used, exclusions etc) mixture of physical activity, sedentary, and diet studies	
Outcomes addressed: Incidence of breast cancer	

MA **Citation:** Del Pozo-Cruz J, García-Hermoso A, Alfonso-Rosa RM, Alvarez-Barbosa F, Owen N, Chastin S, Del Pozo-Cruz B. Replacing Sedentary Time: Meta-analysis of Objective-Assessment Studies. Am J Prev Med. 2018 Sep;55(3):395-402. doi: 10.1016/j.amepre.2018.04.042. PMID: 30122216.	
Purpose: To examine replacing time spent sedentary with physical activity in relation to cardiometabolic risk markers and all-cause mortality using device-based measurement.	**Abstract:** Context: The aim was to summarize estimates of the potential benefits for cardiometabolic risk markers and all-cause mortality of replacing time spent in sedentary behaviours with light-intensity physical activity or with moderate to vigorous physical activity, from studies using device-based measurement. Evidence acquisition: Four databases covering the period up to December 2016 were searched and analyzed (February 2017). Data were extracted by two independent reviewers. For the meta- analyses, the estimated regression coefficients (b) and 95% Cis were analyzed for BMI, waist circumference, and high-density lipoprotein cholesterol. Pooled relative rate and 95% CIs were calculated for fasting glucose, fasting insulin, and homeostatic model assessment-insulin resistance values. Hazard ratios were extracted from studies of all-cause mortality risk. Evidence synthesis: Ten studies (with 17,390 participants) met the inclusion criteria. Reallocation of 30 minutes of sedentary time to light-intensity physical activity was associated with reductions in waist circumference, fasting insulin, and all-cause mortality risk; and with an increase in high-density lipoprotein cholesterol. Reallocating 30 minutes of sedentary time to moderate to vigorous physical activity was associated with reductions in BMI, waist circumference, fasting glucose, fasting insulin, and all-cause mortality (not pooled) and with an increase in high-density lipoprotein cholesterol. Conclusions: Replacing sedentary time with either light-intensity physical activity or moderate to vigorous physical activity may be beneficial, but when sedentary time is replaced with moderate to vigorous physical activity, the predicted impacts are stronger and apparent for a broader range of risk markers. These findings point to potential benefits of replacing sedentary time with light-intensity physical activity, which may benefit those less able to tolerate or accommodate higher-intensity activities, including many older adults.
Timeframe: Inception to December 2016.	
Total # studies included: 10	
Other details (e.g. definitions used, exclusions etc) Inclusion criteria: reported objective measure of activity and sedentary behaviour; used isotemporal models of the effects of replacing sedentary behaviour with LIPA or MVPA on at least one cardiometabolic factor or mortality.	
Outcomes addressed: BMI, waist circumference, fasting glucose, fasting insulin, high-density lipoprotein, and all-cause mortality.	

SR/MA

Citation: Ekelund U, Tarp J, Steene-Johannessen J, Hansen BH, Jefferis B, Fagerland MW, Whincup P, Diaz KM, Hooker SP, Chernofsky A, Larson MG. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. bmj. 2019 Aug 21;366:l4570. https://doi.org/10.1136/bmj.l4570

Purpose: to examine the association between accelerometer measured physical activity and sedentary time and all-cause mortality.	**Abstract:** Objective: To examine the dose-response associations between accelerometer assessed total physical activity, different intensities of physical activity, and sedentary time and all cause mortality. Design: Systematic review and harmonised meta-analysis. Data sources: PubMed, PsycINFO, Embase, Web of Science, Sport Discus from inception to 31 July 2018. Eligibility criteria: Prospective cohort studies assessing physical activity and sedentary time by accelerometry and associations with all cause mortality and reported effect estimates as hazard ratios, odds ratios, or relative risks with 95% confidence intervals. Data extraction and analysis Guidelines for meta-analyses and systematic reviews for observational studies and PRISMA guidelines were followed. Two authors independently screened the titles and abstracts. One author performed a full text review and another extracted the data. Two authors independently assessed the risk of bias. Individual level participant data were harmonised and analysed at study level. Data on physical activity were categorised by quarters at study level, and study specific associations with all cause mortality were analysed using Cox proportional hazards regression analyses. Study specific results were summarised using random effects meta-analysis. Main outcome measure: All-cause mortality. Results: 39 studies were retrieved for full text review; 10 were eligible for inclusion, three were excluded owing to harmonisation challenges (e.g., wrist placement of the accelerometer), and one study did not participate. Two additional studies with unpublished mortality data were also included. Thus, individual level data from eight studies (n=36 383; mean age 62.6 years; 72.8% women), with median follow-up of 5.8 years (range 3.0-14.5 years) and 2149 (5.9%) deaths were analysed. Any physical activity, regardless of intensity, was associated with lower risk of mortality, with a non-linear dose-response. Hazards ratios for mortality were 1.00 (referent) in the first quarter (least active), 0.48 (95% confidence interval 0.43 to 0.54) in the second quarter, 0.34 (0.26 to 0.45) in the third quarter, and 0.27 (0.23 to 0.32) in the fourth quarter (most active). Corresponding hazards ratios for light physical activity were 1.00, 0.60 (0.54 to 0.68), 0.44 (0.38 to 0.51), and 0.38 (0.28 to 0.51), and for moderate-to-vigorous physical activity were 1.00, 0.64 (0.55 to 0.74), 0.55 (0.40 to 0.74), and 0.52 (0.43 to 0.61). For sedentary time, hazards ratios were 1.00 (referent; least sedentary), 1.28 (1.09 to 1.51), 1.71 (1.36 to 2.15), and 2.63 (1.94 to 3.56). Conclusion Higher levels of total physical activity, at any intensity, and less time spent sedentary, are associated with substantially reduced risk for premature mortality, with evidence of a non-linear dose-response pattern in middle aged and older adults.

SR/MA

Citation: Ekelund U, Brown WJ, Steene-Johannessen J, Fagerland MW, Owen N, Powell KE, Bauman AE, Lee IM. Do the associations of sedentary behaviour with cardiovascular disease mortality and cancer mortality differ by physical activity level? A systematic review and harmonised meta-analysis of data from 850 060 participants. British Journal of Sports Medicine. 2019 Jul 1;53(14):886-94. https://doi.org/10.1136/bjsports-2017-098963

Purpose: to examine whether these modifying effects of physical activity exist for relationships between sitting and cause-specific mortality

Timeframe: inception to 10 Nov 2014

Total # studies included: 14 prospective cohort studies

Other details (e.g. definitions used, exclusions etc) In the end, only subjective measures were included. Sitting exposures distinguished sitting time or TV time.

Outcomes addressed: CVD mortality, cancer mortality

Abstract:
Objective To examine whether the associations between sedentary behaviours (i.e., daily sitting/TV viewing time) and mortality from cardiovascular disease (CVD) and cancer differ by different levels of physical activity (PA).
Design Harmonised meta-analysis of prospective cohort studies. Data on exposure variables were harmonised according to a predefined protocol and categorised into four groups for sedentary behaviours and into quartiles of PA (MET-hour/week).
Data sources PubMed, PsycINFO, Embase, Web of Science, Sport Discus and Scopus.
Eligibility criteria for selecting studies Individual level data on both sedentary behaviours and PA and reported effect estimates for CVD or cancer mortality.
Results Nine studies (n=850 060; deaths=25 730) and eight studies (n=777 696; deaths=30 851) provided data on sitting time and CVD and cancer mortality, respectively. Five studies had data on TV-viewing time and CVD (n=458 127; deaths=13 230) and cancer (n=458 091; deaths=16 430) mortality. A dose–response association between sitting time (9%–32% higher risk; p for trend <0.001) and TV time (3%–59% higher risk; p for trend <0.001) with CVD mortality was observed in the 'inactive', lowest quartile of PA. Associations were less consistent in the second and third quartiles of PA, and there was no increased risk for CVD mortality with increasing sedentary behaviours in the most active quartile. Associations between sedentary behaviours and cancer mortality were generally weaker; 6%–21% higher risk with longer sitting time observed only in the lowest quartile of PA.
Conclusion PA modifies the associations between sedentary behaviours and CVD and cancer mortality. These findings emphasise the importance of higher volumes of moderate and vigorous activity to reduce, or even eliminate these risks, especially for those who sit a lot in their daily lives.

SR/MA **Citation:** Ku PW, Steptoe A, Liao Y, Hsueh MC, Chen LJ. A cut-off of daily sedentary time and all-cause mortality in adults: a meta-regression analysis involving more than 1 million participants. BMC medicine. 2018 Dec;16(1):74. https://doi.org/10.1186/s12916-018-1062-2	
Purpose: to explore the cut-off duration associated with elevating the risk of all-cause mortality. **Timeframe:** inception to 31 Jan 2018 **Total # studies included: 19 cohort studies** **Other details (e.g. definitions used, exclusions etc)** included only with PA adjustment. **Outcomes addressed:** all-cause mortality	**Abstract:** Background: The appropriate limit to the amount of daily sedentary time (ST) required to minimize mortality is uncertain. This meta-analysis aimed to quantify the dose-response association between daily ST and all-cause mortality and to explore the cut-off point above which health is impaired in adults aged 18–64 years old. We also examined whether there are differences between studies using self-report ST and those with device-based ST. Methods: Prospective cohort studies providing effect estimates of daily ST (exposure) on all-cause mortality (outcome) were identified via MEDLINE, PubMed, Scopus, Web of Science, and Google Scholar databases until January 2018. Dose-response relationships between daily ST and all-cause mortality were examined using random-effects meta-regression models. Results: Based on the pooled data for more than 1 million participants from 19 studies, the results showed a log-linear dose-response association between daily ST and all-cause mortality. Overall, more time spent in sedentary behaviours is associated with increased mortality risks. However, the method of measuring ST moderated the association between daily ST and mortality risk ($p < 0.05$). The cut-off of daily ST in studies with self-report ST was 7 h/day in comparison with 9 h/day for those with device-based ST. Conclusions: Higher amounts of daily ST are log-linearly associated with increased risk of all-cause mortality in adults. On the basis of a limited number of studies using device-based measures, the findings suggest that it may be appropriate to encourage adults to engage in less sedentary behaviours, with fewer than 9 h a day being relevant for all-cause mortality

SR/MA **Citation:** Ku PW, Steptoe A, Liao Y, Hsueh MC, Chen LJ. A Threshold of Objectively-Assessed Daily Sedentary Time for All-Cause Mortality in Older Adults: A Meta-Regression of Prospective Cohort Studies. Journal of clinical medicine. 2019 Apr;8(4):564.https://doi.org/10.3390/jcm8040564	
Purpose: to explore the dose-response relationship between daily ST and all-cause mortality in older adults.	**Abstract:** Background: This meta-analysis aimed to estimate the shape of the dose-response association between objectively-assessed daily sedentary time (ST) and all-cause mortality, and to explore whether there is a threshold of ST above which there is an increase in mortality risk in older adults. Methods: Searches for prospective cohort studies providing effect estimates of daily ST (exposure) on all-cause mortality (outcome) were undertaken in five databases up to 31 March 2019. A random-effects meta-regression model was conducted to quantify the dose-response relationship between daily ST and all-cause mortality. Sensitivity analyses were also performed to test the stability of the results. Results: Our analysis of pooled data from 11 eligible studies did not reveal a consistent shape of association between ST and mortality. After excluding three studies with potential confounding bias, there was a log-linear dose-response relationship between daily ST and all-cause mortality. Overall, higher amounts of time spent in sedentary behaviours were associated with elevated mortality risks in older adults. Visual assessments of dose-response relationships based on meta-regression analyses indicated that increased mortality risks became significant when total ST exceeded approximately 9 h/day. Conclusions: Based on a limited number of studies, this meta-analysis provides a starting point for considering a cut-off daily sedentary time, suggesting older adults spend less time in daily sitting.
Timeframe: inception to 31 March 2019	
Total # studies included: 11 cohort studies	
Other details (e.g. definitions used, exclusions etc) healthy aged 65 or above; included only with device-based measures.	
Outcomes addressed: all-cause mortality	

<table>
<tr><td colspan="2">SR/MA
Citation:
S. Mahmood; R. J. MacInnis; D. R. English; A. Karahalios; B. M. Lynch. Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: a systematic review and meta-analysis. Int J Epidemiol. 2017 Dec 1;46(6):1797-1813.</td></tr>
<tr><td>Purpose: to examine the associations between physical activity, sedentary behaviour and the risk of colon and rectal cancers separately for occupational, recreational,
transport and household domains</td><td rowspan="5">Abstract:
Background: Physical activity is associated with reduced risk of colorectal cancer, but most epidemiological studies have focused on occupational and recreational physical activity. The evidence for other domains of activity, and for sedentary behaviour, is limited. Methods: Medline, Embase and Web of Science were searched from inception to December 2015 for studies examining domain-specific physical activity or sedentary behaviour and the risk of colon and/or rectal cancer. We extracted maximally adjusted relative risks (RRs) except when RRs not adjusted for body mass index, were also presented. We used random-effects meta-analysis to compute pooled RRs comparing the highest versus the lowest level of exposure. We used meta-regression to assess sources of heterogeneity in estimates. Results: We identified 17 cohort and 21 case-control studies, of which 17 had occupational data, 23 had recreational data, three each had data on transport and household physical activity domains, and 6 studies had data on occupational sedentary behaviour. The pooled relative risks (RRs) for colon cancer were 0.74 (95% confidence interval (CI): 0.67, 0.82) for occupational activity, 0.80 (95% CI: 0.71, 0.89) for recreational activity, 0.66 (95% CI: 0.45, 0.98) for transport-related physical activity, 0.85 (95% CI: 0.71, 1.02) for household physical activity, and 1.44 (95% CI: 1.28, 1.62) for occupational sedentary behaviour. For rectal cancer, the pooled RRs were 0.88 (95% CI: 0.79, 0.98) for occupational activity, 0.87 (95% CI: 0.75, 1.01) for recreational activity, 0.88 (95% CI: 0.70, 1.12) for transport-related physical activity, 1.01 (95% CI: 0.80, 1.27) for household physical activity, and 1.02 (95% CI: 0.82, 1.28) for occupational sedentary behaviour. Conclusions: In addition to increasing occupational and recreational physical activity, promoting physical activity during transport and reducing sedentary behaviour in the workplace may also be useful colorectal cancer prevention strategies.</td></tr>
<tr><td>Timeframe: Inception to 31 December 2015</td></tr>
<tr><td>Total # studies included:
38 (6 studies on occupational sedentary behaviours)</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Cohort and case-control studies included that specifically examined domain specific behaviours; Six studies of interest for sedentary behaviour; data reported as comparing the highest vs lowest category. No dose-response</td></tr>
<tr><td>Outcomes addressed:
Colorectal cancer</td></tr>
</table>

<table>
<tr><td colspan="2">SR & MA
Citation: Patterson R, McNamara E, Tainio M, de Sá TH, Smith AD, Sharp SJ, Edwards P, Woodcock J, Brage S, Wijndaele K. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur J Epidemiol. 2018 Sep;33(9):811-829. doi: 10.1007/s10654-018-0380-1. Epub 2018 Mar 28. PMID: 29589226.</td></tr>
<tr><td>Purpose: To examine the relation of sedentary behaviour to all-cause mortality, cardiovascular disease mortality and cancer mortality, and incident type 2 diabetes</td><td rowspan="5">Abstract: Purpose: To estimate the strength and shape of the dose–response relationship between sedentary behaviour and all-cause,
cardiovascular disease (CVD) and cancer mortality, and incident type 2 diabetes (T2D), adjusted for physical activity (PA). Data Sources: Pubmed, Web of Knowledge, Medline, Embase, Cochrane Library and Google Scholar (through September-2016); reference lists. Study Selection: Prospective studies reporting associations between total daily sedentary time or TV viewing time, and C one outcome of interest. Data Extraction: Two independent reviewers extracted data, study quality was assessed; corresponding authors were approached where needed. Data Synthesis: Thirty-four studies (1,331,468 unique participants; good study quality) covering 8 exposure-outcome combinations were included. For total sedentary behaviour, the PA-adjusted relationship was non-linear for all-cause mortality (RR per 1 h/day: were 1.01 (1.00–1.01) B 8 h/day; 1.04 (1.03–1.05)[8 h/day of exposure), and for CVD mortality (1.01 (0.99–1.02) B 6 h/day; 1.04 (1.03–1.04)[6 h/day). The association was linear (1.01 (1.00–1.01)) with T2D and non-significant with cancer mortality. Stronger PA-adjusted associations were found for TV viewing (h/day); non-linear for all-cause mortality (1.03 (1.01–1.04) B 3.5 h/day; 1.06 (1.05–1.08)[3.5 h/day) and for CVD mortality (1.02 (0.99–1.04) B 4 h/day; 1.08 (1.05–1.12)[4 h/day). Associations with cancer mortality (1.03 (1.02–1.04)) and T2D were linear (1.09 (1.07–1.12)). Conclusions: Independent of PA, total sitting and TV viewing time are associated with greater risk for several major chronic disease outcomes. For all-cause and CVD mortality, a threshold of 6–8 h/day of total sitting and 3–4 h/day of TV viewing was identified, above which the risk is increased.</td></tr>
<tr><td>Timeframe: Inception to September 2016</td></tr>
<tr><td>Total # studies included: 34</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Analyses of dose–response associations and for different types of sedentary behaviour. Also, dose–response curves with
and without adjustment for PA were compared. In addition, PAFs were calculated.</td></tr>
<tr><td>Outcomes addressed: All-cause mortality, cardiovascular disease mortality, cancer mortality, and type 2 diabetes incidence.</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation:
J. Wang; L. Huang; Y. Gao; Y. Wang; S. Chen; J. Huang; W. Zheng; P. Bao; Y. Gong; Y. Zhang; M. Wang; M. C. S. Wong.
Physically active individuals have a 23% lower risk of any colorectal neoplasia and a 27% lower risk of advanced colorectal neoplasia than their non-active counterparts: systematic review and meta-analysis of observational studies. Br J Sports Med Epub ahead of print: [please include Day Month Year]. doi:10.1136/bjsports-2018-100350</td></tr>
<tr><td>Purpose: Examine the associations between physical activity (PA), sedentary behaviour (SB) and risk of colorectal neoplasia (CN).</td><td rowspan="5">Abstract:
BACKGROUND: Few studies have examined the associations between physical activity (PA), sedentary behaviour (SB) and risk of colorectal neoplasia (CN). METHODS: We systematically searched Medline, Embase, PsyInfo, Cochrane and other sources from their inception to 30 September 2018 for cohort, case-control and cross-sectional studies that evaluated these associations in asymptomatic, average-risk subjects. Random-effect models were used to estimate relative risks (RRs) of any-type CN, advanced CN, and non-advanced CN, respectively, in individuals with the highest versus the lowest level of PA and SB. Dose-response analyses and subgroup analyses were conducted. The I(2) statistic was used to examine heterogeneity among studies. RESULTS: We identified 32 observational studies, including 17 cross-sectional studies, 10 case-control studies and five longitudinal studies. PA (highest vs lowest) was inversely associated with risk for any-type CN (n=23 studies) and advanced CN (n=15 studies), with a RR of 0.77 (95% CI=0.71 to 0.83, I(2)=57.5%) and 0.73 (95% CI=0.63 to 0.82, I(2)=45.5%), respectively. There was no association between PA and non-advanced CN (n=5 studies). There was an as association between PA and any-type CN in both sexes, and also for the distal colon. We found no dose-response relationship between PA and any-type or advanced CN. Based on three studies identified, SB time (longest vs shortest) was associated with an increased risk of advanced CN (RR=1.24, 95% CI 1.04 to 1.49, I(2)=14.4%). No publication bias was detected by Begg's test. CONCLUSION: We report a 23% lower relative risk of any type of CN and a 27% lower risk of advanced CN in people with the highest level of PA compared with those in the lowest.</td></tr>
<tr><td>Timeframe: Inception to 30 September 2018</td></tr>
<tr><td>Total # studies included: 32 including 17 cross-sectional studies, 10 case-control studies and five longitudinal studies (3 studies on sedentary)</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Three studies reported data on sedentary behaviours and colorectal neoplasia (potential for overlap between two of these studies derived from the same cohort). meta-analysis of three studies. Comparator unclear and no dose-response reported</td></tr>
<tr><td>Outcomes addressed: colorectal neoplasia</td></tr>
</table>

<table>
<tr><td colspan="2">Harmonized MA
Citation: Xu C, Furuya-Kanamori L, Liu Y, Færch K, Aadahl M, A Seguin R, LaCroix A, Basterra-Gortari FJ, Dunstan DW, Owen N, Doi SAR. Sedentary Behavior, Physical Activity, and All-Cause Mortality: Dose-Response and Intensity Weighted Time-Use Meta-analysis. J Am Med Dir Assoc. 2019 Oct;20(10):1206-1212.e3. doi: 10.1016/j.jamda.2019.05.001. Epub 2019 Jul 2. PMID: 31272857.</td></tr>
<tr><td>Purpose: To examine whether sedentary behaviour-related mortality risk can be offset by MVPA considered in a time-use fashion.</td><td rowspan="5">Abstract: Objectives: Previous studies have placed those with excessive sedentary behavior at increased risk of all-cause mortality. There is evidence of interdependency of sedentary behaviour with physical activity, and its elucidation will have implications for guidelines and practice. This study investigated if sedentary behaviour-related mortality risk can be offset by moderate- to vigorous-intensity physical activity (MVPA) considered in a time-use fashion. Design: PubMed was searched (from its inception till May 2018) for studies or meta-analyses that used data harmonized for MVPA. Of the 17 data-custodians located, 7 provided data on sitting time or TV viewing time, or both. A dose-response meta-analysis modelling log relative risks of all-cause mortality against uncompensated sedentary behaviour metabolic equivalent hours (USMh) was run using the robust error meta-regression method. (Registration: CRD42017062439) Setting: Individual subject data held by data custodians on this topic. Participants: General adults. Measurements: Sedentary time, MVPA. Results: Five harmonized cohorts of sitting time (258,688 participants) and 4 of TV viewing time (156,593 participants) demonstrated that sedentary behaviour was significantly associated with mortality, but this risk was attenuated with increasing energy expenditure through MVPA modelled in a time-use fashion.
The average increment in mortality per USMh spent on sitting was 1% [relative risk (RR) 1.01, 95% confidence interval (CI) 1.00, 1.02; P=.01] and that per USMh spent on TV viewing was 7% (RR 1.07, 95% CI 1.04, 1.10; P < .001). The thresholds for risk started at 7 USMh for sitting and 3 USMh for TV viewing. Conclusions/Implications: Our findings suggest that overall daily sitting time energy expenditure of 7 MET-hours (or TV viewing of 3 MET-hours) in excess of that expended on MVPA is independently related to all-cause mortality. These findings support the view that sitting is strongly influenced by consideration of concurrent MVPA in its impact on adverse health consequences and that the USMh is a more practical metric of sedentary behaviour.</td></tr>
<tr><td>Timeframe: Inception to May 2018</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Use of harmonized data from the authors of the cohort studies included in the 2016 Lancet meta-analysis by Ekelund et al.</td></tr>
<tr><td>Outcomes addressed: Total mortality</td></tr>
</table>

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C1: EVIDENCE ON PHYSICAL ACTIVITY FOR OLDER ADULTS (OVER 64 YEARS OF AGE)

Guiding Questions

C1. What is the association between **physical activity** and health-related outcomes?

a. Is there a dose response association (volume, duration, frequency, intensity)?
b. Does the association vary by type or domain of physical activity?

Inclusion Criteria

Population: Adults over 64 years of age
Exposure: Greater volume, duration, frequency or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity

Outcomes	Importance
Falls and fall-related injuries	Critical
Functional ability (e.g., frailty (sarcopenia), balance, strength, mobility, gait speed, activities of daily living)	Critical
Osteoporosis	Critical
Psychosocial outcomes (e.g., social isolation, social participation)	Important

Evidence identified

Twenty-one reviews (published from 2017 to 2019) were initially identified that examined the association between physical activity and health-related outcomes among older adults *(1-21)*. Six reviews were subsequently excluded from further evaluation given the study design, populations, exposures, or outcomes that were out-of-scope. **Table C1.1** presents the reviews that were excluded and their reason for exclusion.

In general, these reviews were of moderate quality based on the AMSTAR 2 instrument. One review was rated as having high credibility, 7 were rated as having moderate credibility, 3 were rated as having low credibility, and the remaining 4 reviews were rated as having critically low credibility. Given concerns regarding the comprehensiveness and the validity of the results presented in these reviews, they were not incorporated into the final Evidence Profiles. **Table C1.2** presents the ratings for each review according to all the AMSTAR 2 main domains.

Table C1.1. Excluded Systematic Reviews, with Reasons for Exclusion

Author, Year	Reason for Exclusion	Rationale
Dillon 2018 *(7)*	Population	Review limited to older adults with visual impairment
Gordt 2017 *(9)*	Exposure	Exposure not applicable (wearable sensor balance and gait training)
Hart 2019 *(10)*	Outcome	Outcome not applicable (health-related quality of life subscale)
Kauppi 2017 *(12)*	Relevance	Cohort study that addresses the association between social network size (exposure) and levels of health risk behaviours (outcome)
Vancampfort 2019 *(20)*	Design	Cross-sectional study
Yoshimura 2017 *(21)*	Population, Exposure	Population limited to adults with sarcopenia; only one included study was an exercise-only intervention

After appropriate exclusions, 2 reviews were included that reported falls-related injuries, 8 reviews were included that reported a measure of physical function (variably defined), and one review was included that measured social support (and was included in the outcome of social isolation) (**Table C1.3**). Only one review searched for evidence through 2019; several of the reviews only searched through 2014 or 2015. Extracted data for each included review is presented in **Appendix A.** A link to the summary of the U.S. Physical Activity Guidelines evidence relevant to these subgroups is provided in the Evidence Profiles.

Table C1.2. Credibility Ratings (based on AMSTAR 2 *(22)*)

Author, Year	PICO[1]	Apriori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Binkley 2019 *(1)*	Y	N	Y	PY	Y	N	PY	PY	PY	N	N/A	N/A	N	N	N/A	N	**Critically Low**
Bruderer-Hofstetter 2018 *(2)*	Y	PY	N	PY	Y	Y	PY	Y	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**
Bueno de Souza 2018 *(3)*	Y	PY	N	PY	Y	N	PY	Y	Y	N	Y	N	Y	Y	N	Y	**Low**
Burton 2019 *(4)*	Y	N	N	PY	Y	N	PY	PY	Y	N	Y	Y	Y	Y	N	Y	**Critically Low**
da Rosa Orssatto 2019 *(5)*	Y	PY	N	PY	Y	N	Y	PY	PY	N	Y	N	Y	Y	Y	Y	**Moderate**
de Souto Barreto 2018 *(6)*	Y	Y	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	N	**Moderate**
Falck 2019 *(8)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	N	Y	Y	Y	Y	Y	**Critically Low**
Hita-Contreras 2018 *(11)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	Y	N	N	Y	Y	Y	**Low**
Kidd 2019 *(13)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Labott 2019 *(14)*	Y	PY	N	PY	Y	N	PY	PY	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**
Lindsay Smith 2017 *(15)*	Y	PY	N	PY	Y	Y	PY	PY	PY	N	N/A	N/A	Y	N	N/A	Y	**Moderate**
McMullan 2018 *(16)*	N	PY	N	PY	Y	Y	Y	PY	Y	N	N	Y	Y	Y	Y	Y	**Critically Low**
Sherrington 2019 *(17)*	Y	Y	N	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**High**
Sivaramakrishnan 2019 *(18)*	Y	Y	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Taylor 2018 *(19)*	Y	N	N	PY	Y	N	PY	PY	Y	N	Y	Y	Y	Y	N	Y	**Low**

Abbreviations: COI = conflict of interest; N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?

[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.

Table C1.3. Systematic Reviews Assessed, by Author

Author, Year	Outcomes			Last Search Date	# of included studies	AMSTAR 2
	Falls-related Injuries	Physical Function	Social Isolation			
Binkley 2019 *(1)*	X	X		Jan 2015	15	Critically Low
Bruderer-Hofstetter 2018 *(2)*		X		May 2017	17	Moderate
Bueno de Souza 2018 *(3)*		X		Mar 2017	9	Low
Burton 2019 *(4)*		X		Aug 2018	18	Critically Low
da Rosa Orssatto 2019 *(5)*		X		Jan 2019	14	Moderate
de Souto Barreto 2018 *(6)*	X			Mar 2018	40	Moderate
Falck 2019 *(8)*		X		Nov 2018	44	Critically Low
Hita-Contreras 2018 *(11)*		X		Apr 2018	7	Low
Kidd 2019 *(13)*		X		Mar 2017	10	Moderate
Labott 2019 *(14)*		X		Dec 2018	24	Moderate
Lindsay Smith 2017 *(15)*			X	Aug 2014	27	Moderate
McMullan 2018 *(16)*		X		Jul 2016	30	Critically Low
Sherrington 2019 *(17)*	X			May 2018	108	High
Sivaramakrishnan 2019 *(18)*		X		Sep 2017	16	Moderate
Taylor 2018 *(19)*		X		Apr 2015	18	Low

C. Older Adults

C.1. Physical Activity

Table C.1.a. Falls-related Injuries*: Association between physical activity and falls-related injuries among older adults (in alphabetical order by author)

See the Supplementary materials for description of evidence that informed the US PAGAC by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment Risk of bias	Inconsistency	Indirectness †	Imprecision	Other	Description of evidence Summary of findings	Certainty
de Souto Barreto 2018 *(6)* Moderate	12 RCTs N=4,972	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	Trials evaluated the effect of <u>moderate-intensity, multicomponent balance exercise interventions</u> of at least 1 year in duration vs. non-exercise control groups. Nine trials reported the **number of injurious fallers**, with 370 of 2,192 (16.9%) and 471 of 2,289 (20.6%) injurious fallers in the exercise and control groups, respectively. A significant reduced risk of becoming an injurious faller was seen among those in the exercise group vs. control group (RR = 0.74 [95% CI, 0.62 to 0.88]0, 9 trials, n=4,481, I^2=40%). Three additional trials reported no cases of injurious falls in either group.	HIGH[a]
	23 RCTs N=9,701	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	Trials evaluated the effect of <u>moderate-intensity, multicomponent balance exercise interventions</u> of at least 1 year in duration vs. non-exercise control groups. Nineteen trials reported the **number of people experiencing a fracture**, with 221 of 4,138 (5.3%) and 270 of 4,272 (6.3%) people in the exercise vs. control groups, respectively, experiencing a fracture. The pooled result showed no significant association between the exercise intervention and risk of fracture (RR = 0.84 [95% CI, 0.71 to 1.00], 19 trials, n=8,410, I^2=0%). Three additional trials reported no cases of fractures in other groups and one trial was not included in the analysis given low compliance to the intervention.	HIGH[a]
Sherrington 2019 *(17)* High	11 RCTs 5 RCTs 2 RCTs	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision	Possible publication bias	Included trials examined the effect of an <u>exercise intervention</u> on the risk of falls or fall-related injuries among adults aged 60 years and older. Exercise may reduce the **number of people experiencing one or more fall-related fractures** (RR = 0.73 [95% CI 0.56 to 0.95], 10 trials; n=4047) (follow-up range 4 to 42 months) and the **number of people experiencing one or more falls requiring medical attention** (RR = 0.61, 95% CI 0.47 to 0.79; 5 trials; n=1019 participants) (follow-up range 3 to 42 months). Exercise interventions that were classified as being primarily gait, balance, coordination or functional task training may reduce the number of people experiencing **one or more fall-related fractures** by 56% compared with control (RR 0.44 [95% CI 0.25 to 0.76]; 7 studies, n=2139) whereas the effect of resistance exercises vs. control was uncertain (RR = 0.97 [95% CI 0.14 to 6.49], 1 trial, n=73). The effect of exercise on the **number of people who experience one or more falls requiring hospital admission** is unclear (RR = 0.78 [95% CI 0.51 to 1.18], 2 trials; n=1705).	LOW[b]

Abbreviations: CI = confidence interval; RCT = randomized clinical trial; RR = risk ratio

* Outcome limited to fall-related injuries (e.g., number of injurious falls or fallers, number of fractures or people experiencing a fracture); number of falls or fallers not included given separate review being conducted to inform this question
† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not downgraded given no serious limitations
[b] Certainty of evidence assigned by review authors using GRADE criteria. For fall-related fracture: Downgraded by two levels due to imprecision (few events and wide CI due to small sample size), and risk of publication bias (likelihood of reporting fractures only if there was a treatment effect; with some indication on viewing the funnel plot). For the number of people experiencing one or more falls requiring medical attention: Downgraded by two levels due to imprecision and the high probability of publication bias (only 5 of 89 RCTs included in the review reported the outcome). Not downgraded for risk of bias as results were essentially unchanged with removal of the trials at a high risk of bias in one or more items. Evidence on falls requiring hospitalization was downgraded to VERY LOW due to imprecision (low event rate and wide confidence intervals) and because most of the 81 studies included in the review for this comparison do not contribute to the outcome and was further downgraded the evidence by one level for risk of bias because the evidence was dominated by one trial that was at high risk of bias in one or more items.

Table C.1.b. Physical Function: Association between physical activity and physical function among older adults (in alphabetical order by author)

See the Supplementary materials for description of evidence that informed the US PAGAC by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	**Inconsistency**	**Indirectness †**	**Imprecision**	**Other**		
Bruderer-Hofstetter 2018 *(2)* Moderate	17 RCTs N = 1,758	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	Possible publication bias	Included evidence evaluated the effect of multicomponent interventions (combining cognitive training and physical exercise) on IADL performance and/or physical capacity (e.g., muscle strength) compared with active control interventions or no interventions among community dwelling older adults aged >55 years. Six studies included adults with MCI or subjective cognitive decline and 11 studies included adults with normal cognition. Overall mean age was 71.4 years. Four studies (three among adults with MCI and one in those with NC) reported no difference in **IADLs** between those in the multicomponent interventions vs. control conditions. In participants with MCI, one study found multicomponent interventions to be superior to physical exercise alone on one measure of **cardiorespiratory fitness** and one other study found multicomponent interventions to be superior to physical exercise alone on **balance.** Among adults with NC, there was inconsistent results for measures of **cardiorespiratory fitness, muscle strength, flexibility, and balance.**	VERY LOW[a]
Bueno de Souza 2018 *(3)* Low	9 RCTs N=516	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Evidence evaluated effects of mat Pilates on measures of physical functional performance among older adults (mean age = 68.5 years). Pilates training varied from 4 to 24 weeks from 2-4 times/week. Meta-analysis indicated a significant effect of mat Pilates on **dynamic balance** (SMD = 1.10 [95% CI, 0.29 to 1.90], 6 trials), **muscle strength** (SMD = 1.13 [95% CI, 0.30 to 1.96], 5 trials), **flexibility** (SMD = 1.22 [95% CI, 0.39 to 2.04], 3 trials) and **cardiorespiratory fitness** (SMD = 1.48 [95% CI, 0.42 to 2.54], 3 trials) compared with no intervention control groups.	LOW[b]
da Rosa Orssatto 2019 *(5)* Moderate	15 RCTs N=593	Serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	Possible publication bias	Studies evaluated the effects of resistance training performed with fast - intentional velocity vs. moderate velocity on measures of functional capacity among older adults (mean age range = 64 to 82 years). Measures of functional capacity were highly variable and included the SPPB, timed up and go test, 30-s char stand, 5-times chair stand, short walk tests, long walk tests, and stair climb tests. Training frequency ranged from 1 to 3 sessions per week with intervention duration ranging from 6 to 36 weeks. Meta-analysis of 14 trials combining different function capacity tests indicated that fast-intended velocity resistance training may be superior compared with moderate-velocity resistance training for **general functional capacity** improvements (SMD = 0.41 [95% CI 0.18 to 0.65], 14 trials) and **SPPB** (SMD = 0.52 [95% CI 0.10 to 0.94]), 5 trials). No difference was seen between fast- and moderate-velocity resistance training on measures of time up and go, 30-s chair stand test, 5-times chair stand, stair climb, short walk or long walk measures.	VERY LOW[c]

Hita-Contreras 2018 *(11)* Low	7 RCTs N=558	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Trials evaluated the effect of exercise interventions (with or without dietary supplementation) on measures of adiposity and physical performance among older adults with sarcopenic obesity (mean age range, 67 to 81 years). Exercise interventions included aerobic exercise (3 studies), combined aerobic and resistance training (3 studies), and whole body electro-myostimulation (1 study). Four interventions also included dietary supplementation. Duration of interventions ranged from 8 to 26 weeks. Physical function was measured by grip strength (5 trials) or gait speed (5 trials). Exercise alone was significantly associated with improvement in **grip strength** (MD = 1.67 kg [95% CI 0.09 to 3.24) and **gait speed** (MD = 0.11 m/s [95% CI, 0.05 to 0.18]).	MODERATE[d]
Kidd 2019 *(13)* Moderate	4 RCTs N=907	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Studies evaluated the effect of physical activity interventions[e] on measures of physical performance among pre-frail and frail adults (mean age range 79 to 84 years). Interventions differed considerably and included weekly group physical activity classes in primary care, a mobility plan following hip surgery (2 studies), and tai chi vs. standard physiotherapy for older adults at risk for falls). Measures of frailty and physical performance were also highly variable. The primary care PA study reported significant improvements on measures of the **Barthel index, rapid gait test, stand up test, balance, gait speed, and lower body strength**. The two studies that evaluated mobility immediately post-hip surgery found that those receiving the intervention (vs. standard physiotherapy) had significantly greater **upright time, number of upright events, "better physical performance," and 4 min gait speed and better gait characteristics**. The tai chi trial experienced considerable drop-out in both groups and so results were not presented.	LOW[f]
Labott 2019 *(14)* Moderate	24 RCTs N=3,018	No serious risk of bias	No serous inconsistency	Serious indirectness	No serious imprecision	None	Review evaluated the effect of exercise training on **handgrip strength** in healthy, community-dwelling older adults (mean aged 73 years). Training types included aquatic exercise, walking, flexibility, TRX-training, home-trainer exercise, strength training in different forms, training on a vibration platform, dance Tai Chi, exergames balance training, calisthenics, and multidimensional training regimes. Most interventions lasted 8 to 15 weeks (range 4 weeks to 36 months). Pooled results showed small effects for **handgrip strength** in favour of the exercise training groups compared with control groups (SMD = 0.28 [95% CI 0.13 to 0.44]).	MODERATE[g]
Sivaramakrishnan 2019 *(18)* Moderate	17 RCTs N=967	No serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Included evidence evaluation the effects of yoga vs. active or inactive controls on measures of physical function among older adults (mean age range 61 to 84 years). Eight types of yoga were tested. The meta-analysis revealed significant effects favouring the yoga group for the following physical function outcomes compared with inactive controls: **balance** (ES = 0.7, 95% CI 0.19 to 1.22, 7 trials), **lower limb strength** (ES = 0.45, 95% CI 0.22 to 0.68, 7 trials), and **lower body flexibility** (ES = 0.50, 95% CI 0.30 to 0.69, 7 trials) compared to inactive controls. No significant difference between yoga and inactive controls was found for body composition (ES = 0.16, 95% CI -0.06 to 0.38), upper body flexibility (ES = 0.28, 95% CI -0.02 to 0.58) or walking speed (ES = 0.38, 95% CI -0.02 to 0.78). Compared with active controls, there was a significant effect favouring yoga for **lower limb strength** (ES = 0.49, 95% CI 0.10 to 0.88, 3	LOW[h]

							trials) and **lower body flexibility** (ES = 0.28, 95% CI 0.01 to 0.54, 3 trials). No significant difference between yoga and active controls was found for balance (ES = 0.32, 95% CI -0.02 to 0.66), mobility (ES = 0.31, 95% CI -0.25 to 0.87) or walking speed (ES = − 0.29, 95% CI -0.79 to 0.22).	
Taylor 2018 *(19)* Low	18 RCTs N=765	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Review evaluated the effect of active video games on measures of physical performance or balance among older adults (mean age 76 years). Except for one trial, all interventions were supervised. Measures of physical performance/mobility and balance varied across studies. A meta-analysis of **timed up and go scores** comparing active video games vs. conventional exercise or no intervention found no significant difference between groups (MD = -2.29 [95% CI, -5.20 to 0.64], 6 trials, n=206) whereas a significant association between active video games and **30-second chair stand scores** was found (MD = 3.99 [95% CI, 1.92 to 6.05], 4 trials, n=188). Measures of **balance** were highly variable, and results were inconsistent within trials and between trials.	VERY LOW[i]

Abbreviations: CI = confidence interval; ES = effect size (Hedges' g); IADL = instrumental activities of daily living; m/s = meters per second; MCI = mild cognitive impairment; min = minutes; NC = normal cognition; RCT = randomized clinical trial; SPPB = short physical performance battery test; SMD = standardized mean difference

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence rated by review authors using GRADE methodology. The quality of evidence was rated as very low for the outcomes of IADL performance and physical capacity among adults with MCI and NC due to study limitations, inconsistency, indirectness, imprecision, and possible publication bias
[b] Certainty of evidence downgraded due to serious imprecision in estimates of effects **(**95% CI crossed the line of no effect, and was wide, such that interpretation of the data would be different if the true effect were at one end of the CI or the other) and indirectness
[c] Certainty of evidence downgraded due to serious risk of bias, serious imprecision in estimates of effect, and possible publication bias
[d] Certainty of evidence downgraded due to serious imprecision in estimates of effects
[e] Review also included evidence on nutrition interventions and physical activity plus nutrition interventions. The summary of evidence is limited to the physical activity only interventions.
[f] Certainty of evidence downgraded given serious risk of bias of all studies and serious indirectness in the applicability and heterogeneity of the comparisons and outcomes
[g] Certainty of evidence downgraded given serious indirectness in heterogeneity of intervention and directness of outcome measures
[h] Certainty of evidence downgraded given serious inconsistency for most outcomes (I^2>70%) and serious imprecision in most effect estimates
[i] Certainty of evidence downgraded given serious risk of bias (unclear selection bias and high risk of performance bias), serious inconsistency (in direction and magnitude of effects within and between studies), and serious imprecision in effect estimates

Table C.1.c. Social Isolation: Association between physical activity and social isolation among older adults (in alphabetical order by author)

See the Supplementary materials for description of evidence that informed the US PAGAC by outcome

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty
		Risk of bias	**Inconsistency**	**Indirectness †**	**Imprecision**	**Other**		
Lindsay Smith 2017 *(15)* Moderate	22 cross-sectional studies, 3 prospective cohort studies, 2 RCTs N=	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	None	Included evidence examined the association between physical activity and **social support** among community dwelling older adults aged 60 years and older. 21/27 studies examined the association between social support and PA and 6/27 examined the association between loneliness and PA. 23/27 studies relied on self-reported PA and 4/27 used objectively-measured PA. The scales used to measure social support and loneliness varied greatly across studies. **13/21** studies reported significant positive associations between PA levels and general social support or PA-specific social support; 1/21 studies reported a negative association and 7/21 reported no association. 4/6 studies reported a significant association between high level of loneliness and lower levels of PA.	VERY LOW[a]

Abbreviations: PA = physical activity; RCT = randomized clinical trial

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious risk of bias in most included studies, serious inconsistency in strength of association, and imprecision in estimates of effects

Table C.1.d. Falls prevention

Information sources and search

The present report updates the searches performed in the 2019 Cochrane Review*(17)*, with this review extending studies published up to 7 November 2019. This review extended the searches performed up to February 2012 in the 2012 Cochrane Review*(23)*. We searched: the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (2 May 2018 to 7 November 2019); the Cochrane Central Register of Controlled Trials. (CENTRAL) (Cochrane Register of Studies Online) (2018 Issue 1 to 7 November 2019); MEDLINE (including Epub Ahead of Print, In-Process & Other Non-Indexed Citations and MEDLINE Daily) (start 2018 to 7 November 2019); Embase (start 2018 to 7 November 2019); the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (May 2018 to 7 November 2019); and the Physiotherapy Evidence Database (PEDro) (2018 to 2019), using tailored search strategies. We did not apply any language restrictions. In MEDLINE, we combined subject-specific search terms with the sensitivity- and precision-maximising version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials.*(24)* The search strategies for CENTRAL, MEDLINE, Embase, CINAHL and PEDro are shown in Appendix 1). We also searched the World Health Organisation International Clinical Trials Registry Platform (WHO ICTRP) and ClinicalTrials.gov for ongoing and recently completed trials (November 2019) (see Appendix 1). We checked reference lists of other systematic reviews as well as contacting researchers in the field to assist in the identification of ongoing and recently completed trials.

Study selection

Independent reviewers (NF, WK) screened the title, abstract and descriptors of identified studies for possible inclusion. From the full text, these review authors independently assessed potentially eligible trials for inclusion and resolved any disagreement through discussion with a third author. We contacted authors for additional information as necessary.

Data collection process

Pairs of reviewers (CS, NF, WK) independently extracted data using a pretested data extraction form (based on the one used in the Cochrane Review*(25)*). Disagreement was resolved by consensus or third party adjudication. Review authors were not blinded to authors and sources. Review authors did not assess their own trials.

Data items

Full details of data extracted (excluding the nine new trials included in this update) are shown in Sherrington 2019. The present publication focuses on the primary outcome, the rate of falls. We grouped similar exercise interventions using the fall prevention classification system (taxonomy) developed by the Prevention of Falls Network Europe (ProFaNE)*(26)*. For simplicity the ProFaNE category gait, balance, co-ordination or functional task training was referred to as balance and functional exercises.

Risk of bias and certainty of evidence

One review author (NF) assessed risk of bias using Cochrane's Risk of bias tool as described in the Cochrane Handbook*(27)*. We constructed and visually inspected funnel plots. We used The Grading of Recommendations Assessment, Development and Evaluation **(**GRADE) approach to assess the quality of evidence*(28)*; we assessed the certainty of the evidence as 'high', 'moderate', 'low' or 'very low' depending on the presence and extent of five factors: risk of bias; inconsistency of effect; indirectness; imprecision; and publication bias. We prepared 'Summary of finding' tables. We used standardised qualitative statements to describe the different combinations of effect size and the certainty of evidence*(29)*.

Rate of falls outcome (falls per person-years) for types of exercise

Type of exercise	Follow-up range	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
		Assumed risk	Corresponding risk				
Exercise[a] (all types) versus control[b] (e.g. usual activities)	3 to 30 months	Control	Exercise (all types)	Rate ratio 0.77 (0.71 to 0.83) [d]	14.306 (64 RCTs)	High[e]	Overall, there is a reduction of 23%(95%CI 17% to 29%) in the number of falls Guide to the data: If 1000 people were followed over 1 year, the number of falls in the overall population would be 655 (95% CI 604 to 706) compared with 850 in the group receiving usual care or attention control. In the unselected population, the corresponding data are 466 (95%CI 430 to 503) compared with 605 in the group receiving usual care or attention control. In the selected higher-risk population, the corresponding data are 993 (95%CI 915 to 1071) compared with 1290 in the control group
		All studies population					
		850 per 1000[c]	655 per 1000 (604 to 706)				
		Not selected for high risk population					
		605 per 1000 [c]	466 per 1000 (430 to 503)				
		Selected for high risk population					
		1290 per 1000 [c]	993 per 1000 (915 to 1071)				
Balance, and functional exercises[f] versus control[b] (e.g. usual activities)	3 to 30 months	Control	Exercise (gait, balance, and functional training)	Rate ratio 0.76 (0.70 to 0.82)	7989 (39 RCTs)	High[h]	Overall, there is a reduction of 24% (95%CI 18% to 30%) in the number of falls Guide to the data based on the all-studies estimate. If 1000 people were followed over 1 year, the number of falls would be 646 (95% CI 595 to 689) compared with 850 in the group receiving usual care or attention control
		All studies population					
		850 per 1000 [g]	646 per 1000 (595 to 689)				
		Specific exercise population					
		865 per 1000 [g]	657 per 1000 (606 to 709)				
Resistance exercises[i] versus control[b] (e.g. usual activities)	4 to 12 months	Control	Exercise (resistance training)	Rate ratio 1.14 (0.67 to 1.97)	327 (5 RCTs)	Very low[k]	The evidence is of very low certainty, hence we are uncertain of the findings of an increase of 14% (95% CI 33% reduction to 97% increase) in the number of falls
		All studies population					

		850 per 1000 [j]	969 per 1000 (570 to 1675)				Guide to the data based on the all-studies estimate. If 1000 people were followed over 1 year, the number of falls would be 969 (95% CI 570 to 1675) compared with 850 in the group receiving usual care or attention control
		Specific exercise population					
		630 per 1000 [j]	719 per 1000 (423 to 1242)				
3D (Tai Chi) exercise[l] versus control[b] (e.g. usual activities)	6 to 17 months	Control	Exercise (3D (Tai Chi))	Rate ratio 0.77 (0.61 to 0.97)	3169 (9 RCTs)	Moderate[n]	Overall, there is probably be a reduction of 23% (95% CI 3% to 39%) in the number of falls Guide to the data based on the all-studies estimate. If 1000 people were followed over 1 year, the number of falls is probably 655 (95% CI 519 to 825) compared with 850 in the group receiving usual care or attention control
		All studies population					
		850 per 1000 [m]	655 per 1000 (519 to 825)				
		Specific exercise population					
		1290 per 1000 [m]	993 per 1000 (787 to 1251)				
3D (dance) exercise[o] versus control[b] (e.g. usual activities)	12 months	Control	Exercise (3D [dance])	Rate ratio 1.34 (0.98 to 1.83)	522 (1 RCT)	Very low[q]	The evidence is of very low certainty, hence we are uncertain of the findings of an increase of 34% (95% CI 2% reduction to 83% increase) in the number of falls Guide to the data based on the all-studies estimate If 1000 people were followed over 1 year, the number of falls may be 1139 (95% CI 833 to 1556) compared with 850 in the group receiving usual care or attention control
		All studies population					
		850 per 1000 [p]	1139 per 1000 (833 to 1556)				
		Specific exercise population					
		800 per 1000 [p]	1072 per 1000 (784 to 1464)				
General physical activity (including walking) training[r] versus control[b] (e.g. usual activities)	12 to 24 months	Control	Exercise (general physical activity [including walking])	Rate ratio 1.14 (0.66 to 1.97)	441 (2 RCTs)	Very low[t]	The evidence is of very low certainty, hence we are uncertain of the findings of an increase of 14% (95% CI 34% reduction to 97% increase) in the number of falls Guide to the data based on the all-studies estimate If 1000 people were followed over 1 year, the number of falls may be 969 (95% CI 561 to 1675) compared with 850 in the group receiving usual care or attention control
		All studies population					
		850 per 1000 [s]	969 per 1000 (561 to 1675)				
		Specific exercise population					
		670 per 1000 [s]	764 per 1000 (443 to 1320)				

Multiple categories of exercise (often including, as primary interventions: gait, balance, and functional (task) training plus resistance training[u] versus control[b] (e.g. usual activities)	2 to 25 months	Control	Exercise (multiple types (including, as primary interventions: gait, balance, and functional (task) training plus resistance training))	Rate ratio 0.72 (0.56 to 0.93)[r]	2283 (15 RCTs)	Moderate[w]	Overall, there is probably a reduction of 28% (95% CI 7% to 44%) in the number of falls Guide to the data based on the all-studies estimate If 1000 people were followed over 1 year, the number of falls would probably be 612 (95%CI 476 to 791) compared with 850 in the group receiving usual care or attention control
		All studies population					
		850 per 1000[v]	612 per 1000 (476 to 791)				
		Specific exercise population					
		1205 per 1000 [v]	868 per 1000 (675 to 791)				

CI: confidence interval

[a] Exercise is a physical activity that is planned, structured and repetitive and aims to improve or maintain physical fitness. There is a wide range of possible types of exercise, and exercise programmes of ten include one or more types of exercise. We categorised exercise based on the Prevention of Falls Network Europe (ProFaNE) taxonomy that classifies exercise type as: i) gait, balance, and functional training; ii) strength/ resistance (including power); iii) flexibility; iv) three- dimensional (3D) exercise (e.g. Tai Chi, Qigong, dance); v) general physical activity; vi) endurance; and vii) other kind of exercises. The taxonomy allows for more than one type of exercise to be delivered within a programme.
[b] A control intervention is one that is not thought to reduce falls, such as general health education, social visits, very gentle exercise, or 'sham' exercise not expected to impact on falls.
[c] The all-studies population risk was based on the number of events and the number of participants in the control group for this outcome over the 64 RCTs. We calculated the risk in the control group using the median falls per person-year for the subgroups of trials for which a) an increased risk of falls was not an inclusion criterion (32 RCTs, 6434 participants), or b) increased risk of falls was an inclusion criterion (32 RCTs, 7872 participants).
[d] Subgroup analysis found no difference based on whether risk of falls was an inclusion criterion or not (test for subgroup differences: Chi2 = 0.1, df = 1, P = 0.75, I^2 = 0%).
[e] There was no downgrading, including for risk of bias, as results were essentially unchanged with removal of the trials with a high risk of bias on one or more items.
[f] Using Prevention of Falls Network Europe (ProFaNE) taxonomy, gait, balance, and functional training is: gait training = specific correction of walking technique, and changes of pace, level and direction; balance training = transferring bodyweight from one part of the body to another or challenging specific aspects of the balance systems; functional training = functional activities, based on the concept of task specificity. Training is assessment-based, tailored and progressed. Exercise programs included in this analysis contained a single primary exercise category (gait, balance, and functional training); these exercise programs may also include secondary categories of exercise.

[g] The all-studies population risk was based on the number of events and the number of participants in the control group for this outcome over the 64 all-exercise types RCTs. The specific exercise population risk was based on the number of events and the number of participants in the control group for this outcome over the 39 RCTs.
[h] We did not downgrade for risk of bias, as results were essentially unchanged with the removal of the trials with a high risk of bias in one or more items.
[i] Using Prevention of Falls Network Europe (ProFaNE) taxonomy, resistance training is any type of weight training (contraction of muscles against resistance to induce a training effect in the muscular system). Resistance is applied by body weight or external resistance. Training is assessment-based, tailored and progressed. Exercise programmes included in this analysis had resistance training as the single primary exercise category; these exercise programmes may also include secondary categories of exercise.
[j] The all-studies population risk was based on the number of events and the number of participants in the control group for this outcome over the 64 all-exercise types RCTs. The specific exercise population risk was based on the number of events and the number of participants in the control group for this outcome over the 5 RCTs.
[k] Downgraded by three levels due to risk of inconsistency (there was substantial heterogeneity ($I^2 = 67\%$)), imprecision (wide CI due to small sample size), and risk of bias (removing studies with high risk of bias in one or more items had a marked impact on results).
[l] Using Prevention of Falls Network Europe (ProFaNE) taxonomy, 3D (Tai Chi) training uses upright posture, specific weight transferences and movements of the head and gaze, during constant movement in a fluid, repetitive, controlled manner through three spatial planes. Exercise programmes included in this analysis had 3D (Tai Chi) training as the single primary exercise category; these exercise programmes may also include secondary categories of exercise.
[m] The all-studies population risk was based on the number of events and the number of participants in the control group for this outcome over the 64 all-exercise types RCTs. The specific exercise population risk was based on the number of events and the number of participants in the control group for this outcome over the nine RCTs.
[n] Downgraded by one level due to inconsistency (there was substantial heterogeneity ($I^2 = 83\%$). There was no downgrading for risk of bias, as results were essentially unchanged with removal of the trials with a high risk of bias on one or more items.
[o] Using Prevention of Falls Network Europe (ProFaNE) taxonomy, 3D (dance) training uses dynamic movement qualities, patterns and speeds whilst engaged in constant movement in a fluid, repetitive, controlled manner through three spatial planes. Exercise programmes included in this analysis had 3D (dance) training as the single primary exercise category; these exercise programmes may also include secondary categories of exercise.
[p] The all-studies population risk was based on the number of events and the number of participants in the control group for this outcome over the 64 all-exercise types RCTs. The specific exercise population risk was based on the number of events and the number of participants in the control group for this outcome in the sole RCT.
[q] Graded very low due to serious imprecision (only one cluster-RCT, with a wide CI due to small sample size).
[r] Using Prevention of Falls Network Europe (ProFaNE) taxonomy, physical activity is any movement of the body, produced by skeletal muscle, that causes energy expenditure to be substantially increased. Recommendations regarding intensity, frequency and duration are required in order to increase performance. Exercise programmes included in this analysis had general physical activity (including walking) training as the single primary exercise category; these exercise programmes may also include secondary categories of exercise.
[s] The all-studies population risk was based on the number of events and the number of participants in the control group for this outcome over the 64 all-exercise types RCTs. The specific exercise population risk was based on the number of events and the number of participants in the control group for this outcome in the two RCTs.
[t] Downgraded by three levels due to inconsistency (there was substantial heterogeneity ($I^2 = 67\%$)), imprecision (wide CI), and risk of bias (removing studies with high risk of bias on one or more items had a marked impact on results).
[u] Exercise programmes included in this analysis had more than one primary exercise category. We categorised exercise based on the Prevention of Falls Network Europe (ProFaNE) taxonomy that classifies exercise type as: i) gait, balance, and functional (task) training; ii) strength/ resistance (including power); iii) flexibility; iv) three-dimensional (3D) exercise (e.g. Tai Chi, Qigong, dance); v) general physical activity; vi) endurance; and vii) other kind of exercises. The programmes of ten included, as the primary intervention, gait, balance, and functional (task) training plus resistance training. The exercise programmes may also include secondary categories of exercise.
[v] The all-studies population risk was based on the number of events and the number of participants in the control group for this outcome over the 64 all-exercise types RCTs. The specific exercise population risk was based on the number of events and the number of participants in the control group for this outcome over the 15 RCTs.
[w] Downgraded by one level due to inconsistency (there was substantial heterogeneity ($I^2 = 71\%$)). We did not downgrade for risk of bias, as results were essentially unchanged with removal of the trials at a high risk of bias in one or more items

Table C.1.e. Sarcopenia

Search and selection strategy
A search for existing systematic reviews was conducted in PubMed for reviews published from 2008 up to November 2019 (Appendix 2).

Two reviewers independently screened titles and abstracts of potential systematic reviews. Where there was uncertainty about the eligibility of a study, the full text was retrieved. Two independent reviewers read full-texts and assessed eligibility criteria using an electronic screening form. Disagreements regarding the eligibility of studies were resolved through discussion and, when necessary, with the help of a third reviewer.

Since we did not find any eligible systematic reviews, we identified reviews that included potentially eligible studies and screened all included studies against our questions. We included individual studies (instead of reviews).

One reviewer extracted information into standardised forms and a second reviewer checked all data. We extracted all outcome measures relevant to sarcopenia and frailty reported by the studies that were included. We selected the most commonly reported outcomes across the included studies to provide an overview of the evidence.

Physical activity classification
We used the Prevention of Falls Network Europe (ProFANE) taxonomy to classify the physical activity and exercise programmes in the included studies (Appendix 3).*(30)* The programmes were classified as primarily involving the following exercise categories: (i) gait, balance, coordination and functional task training (referred to as 'balance and functional exercises' for simplicity); (ii) strength/resistance training (including power training, using resistance so referred to as 'resistance exercises'); (iii) flexibility; (iv) three-dimensional (3D) exercise (with Tai Chi or dance subcategories); (iv) general physical activity (walking programmes); (v) endurance; (vi) overall physical activity; (vii) other.

Grading the body of evidence
Using the GRADE framework, we examined the quality of primary research and assessed the overall quality of evidence in terms of presence and extent of five factors: risk of bias, inconsistency, imprecision, indirectness and publication bias. Details on the criteria used to apply the GRADE approach are provided in Appendix 4. We also undertook random-effects meta-analyses to summarise the effects of physical activity where there was more than one study.

The relationship between physical activity and frailty/sarcopenia prevention in older people

No. of studies	Design	Quality assessment					No. of participants	Summary	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
The association between physical activity and frailty prevention									
Only 1 RCT investigated the association between physical activity and frailty prevention. The follow-up length was 12 months. Frailty outcome was defined as the presence of three or more Fried criteria: (1) unintentional weight loss, (2) exhaustion, (3) low physical activity, (4) slow walking speed, and (5) poor grip strength.									
1	RCT[a]	Serious risk of bias[b]	No serious inconsistency	No serious indirectness	Serious imprecision[e]	None	133	Physical activity interventions may prevent frailty.[f]	Low[g]
The association between physical activity and sarcopenia prevention									
Only 1 longitudinal study investigated the association between physical activity and sarcopenia prevention. The follow-up length was 48 months. Sarcopenia was defined as low muscle mass, low muscle strength and/or low physical performance.									
1	Longitudinal study[h]	No serious risk of bias[i]	No serious inconsistency[j]	No serious indirectness[d]	Serious imprecision[k]	None	4,000	We are uncertain whether physical activity prevents sarcopenia.	Very low[m]
Exercise vs control on frailty-related outcomes									
A total of 4 RCTS investigated the effects of physical activity on frailty-related outcomes. The frailty-related outcomes were: (1) muscle mass measured with leg press with 1RM method, isokinetic dynamometer and hand dynamometer; (2) physical function measured with 6-m, 10-m and 12-m walk , Timed up and go and Short Physical performance Battery test (SPPB); (3) muscle mass measured with dual-energy x-ray absorptiometry (DXA).									
4	RCTs[n]	Serious risk of bias[o]	No serious inconsistency[p]	No serious indirectness[q]	Serious imprecision[r]	None	326	16/18 comparisons showed a positive effect for physical activity, 1/18 showed a neutral effect, and 1/18 showed negative effect for physical activity for frailty-related outcome. Physical activity interventions may prevent frailty-related outcomes.[s]	Low[t]
Exercise vs control on sarcopenia-related outcomes									
A total of 2 RCTs investigated the effects of physical activity on sarcopenia-related outcomes. The sarcopenia-related outcomes were: (1) muscle strength measured with isokinetic dynamometer; (2) muscle mass measured with dual-energy x-ray absorptiometry (DXA).									
2	RCTs[u]	Serious risk of bias[v]	No serious inconsistency[w]	No serious indirectness[q]	Serious imprecision[x]	None	204	All studies (4/4) showed a positive effect for physical activity on sarcopenia-related outcomes Physical activity interventions may prevent sarcopenia-related outcomes.[y]	Low[z]

[a] Includes 1 RCT*(31)*
[b] We downgraded the evidence by one level as the study had a PEDro score <6/10
[e] The single included study had a total of 133 participants analysed. Therefore, we downgraded the evidence.
[f] The effects for the study can be found in Table 3.
[g] Quality of the evidence was downgraded from high to low because of serious risk of bias and serious imprecision.
[h] Includes 1 longitudinal study*(32)*
[i] We did not downgrade the evidence as the study was at low risk of bias
[j] Not applicable.
[k] We downgraded the evidence as there was only one included study.
[l] The effects for the study can be found in Table 4.
[m] Quality of the evidence was downgraded from low to very low because of serious imprecision.

[n] Includes 4 RCTs.*(33-36)*
[o] We downgraded the evidence by one level as 3/4 studies (75%) had a PEDro score <6/10.
[p] We did not downgrade the evidence due to heterogeneity of included studies as most comparisons (16/18 comparisons) showed a positive effect.
[q] Since we only included similar studies in terms of population, intervention, comparator and outcome, we did not downgrade the evidence based on this criterion.
[r] The 4 included studies had a total of 326 participants analysed. Therefore, we downgraded the evidence.
[s] The effects for each individual study can be found in Table 5.
[t] Quality of the evidence was downgraded from high to low because of serious risk of bias and serious imprecision.
[u] Includes 2 RCTs.*(37, 38)*
[v] We downgraded the evidence by one level as 1/2 studies (50%) had a PEDro score <6/10.
[w] We did not downgrade the evidence due to heterogeneity of included studies as all comparisons (4/4 comparisons) showed a positive effect.
[x] The 2 RCTs had a total of 204 participants analysed. Therefore, we downgraded the evidence.
[y] The effects for each individual study can be found in Table 6.
[z] Quality of the evidence was downgraded from high to low because of serious risk of bias and serious imprecision.

Appendix A. Data Extractions of Included Reviews

<table>
<tr><td colspan="2">SR/MA
Citation: Binkley HM, Rudd LE. Head-Out Aquatic Exercise for Generally Healthy Postmenopausal Women: A Systematic Review. Journal of Physical Activity and Health, 2019, 16, 76-97. Journal of Physical Activity and Health, 2019, 16, 76-97</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Background: Aquatic exercise (AE) is a method for exercise and rehabilitation to enhance function for various clients.
Objectives: Investigate the effects of head-out AE interventions on the physiological and psychological outcomes of healthy postmenopausal women of age 50–70 years. Search Strategies: Databases searched included Scopus, ScienceDirect, ResearchGate, PubMed/MEDLINE, PEDro, CINAHL, The Cochrane Library, Nursing & Allied Health Collection: Comprehensive, JSTOR, and OTSeeker.com, through January 2015. Search Criteria: Randomized controlled trial and quasi-randomized controlled trial studies. Data Collection and Analysis: Two researchers scanned studies based on inclusion and exclusion criteria. Studies included were critically appraised using the Physiotherapy Evidence Database scale (PEDro scale). Results: A total of 15 studies including postmenopausal women and head-out AE intervention were reviewed. Considerable variation existed in the interventions and assessments. Outcome measures showed anthropometric measures (body mass index, circumference, skinfolds, and body fat) were inconclusive; upper and lower body strength improved; flexibility improved; all functional movements (short-distance walk, long-distance walk/run, power, agility, balance and falls) improved; bone density improved; biochemical and hormonal variables were inconclusive; and quality of life outcomes improved. Conclusions: Head-out AE appears to be an effective training and conditioning method for postmenopausal women to improve strength, flexibility, functional movements, bone density, and quality of life.</td></tr>
<tr><td>Search Dates:
Jan 1989 – Jan 2015</td></tr>
<tr><td>Total # studies included: 15</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
strength, flexibility, functional variables</td></tr>
</table>

SR/MA **Citation:** Bruderer-Hofstetter M, Rausch-Osthoff A, Mechtry A, Munzer T, Niedermann K. Effective multicomponent interventions in comparison to active control and no interventions on physical capacity, cognitive function and instrumental activities of daily living in elderly people with and without mild impaired cognition – A systematic review and network meta-analysis. Ageing Research Reviews 45 (2018) 1–14. doi.org/10.1016/j.arr.2018.04.002	
Purpose:	**Abstract:** Multicomponent interventions (MCT) combine physical exercises and cognitive training and seem to be most effective in improving cognition in elderly people. However, literature is inconclusive if MCTs are superior to active comparison interventions, if delivery modes matter, and if people can transfer achieved effects to instrumental activities of daily living (IADL). This network meta-analysis aimed to a) identify MCTs that were effective on physical capacity and/or cognitive function and able to transfer these effects into IADL in elderly people with normal cognition (NC) and mild cognitive impairment (MCI); b) provide a rating on the best interventions per outcome; c) evaluate MCTs' mode of delivery. Eligible studies were randomized controlled trials comparing MCTs to active comparison or no treatments. Six studies in participants with MCI (n=1088) and eleven studies in participants with NC (n=670) were included. Five effective MCTs that were superior to physical exercises or cognitive training alone in improving physical capacity and/or cognitive function were detected, however none of these MCTs improved IADL. In people with NC MCTs performed separately or simultaneously were effective. However, in people with MCI MCTs performed separately were more effective. A framework needs to be developed to better understand the mediating effects of physical capacity and cognitive function on IADL and to design MCTs that effectively improve IADL.
Last Search Date: May 2017	
Total # studies included: 17	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: IADL, and/or physical capacity (e.g. CRF; balance; flexibility; muscle strength) and/or cognitive function	

SR/MA **Citation:** Bueno de Souza RO, Marcon LF, Arruda ASF, Pontes Junior FL, Melo RC. Effects of Mat Pilates on Physical Functional Performance of Older Adults: A Meta-analysis of Randomized Controlled Trials. Am J Phys Med Rehabil 2018;97:414–425. DOI: 10.1097/PHM.0000000000000883	
Purpose:	**Abstract:** **Objective**: The present meta-analysis aimed to examine evidence from randomized controlled trials to determine the effects of mat Pilates on measures of physical functional performance in the older population. **Design**: A search was conducted in the MEDLINE/PubMed, Scopus, Scielo, and PEDro databases between February and March 2017. Only randomized controlled trials that were written in English, included subjects aged 60 yrs who used mat Pilates exercises, included a comparison (control) group, and reported performance-based measures of physical function (balance, flexibility, muscle strength, and cardiorespiratory fitness) were included. The methodological quality of the studies was analyzed according to the PEDro scale and the best-evidence synthesis. The meta-analysis was conducted with the Review Manager 5.3 software. **Results**: The search retrieved 518 articles, nine of which fulfilled the inclusion criteria. High methodological quality was found in five of these studies. Meta-analysis indicated a large effect of mat Pilates on dynamic balance (standardized mean difference = 1.10, 95% confidence interval = 0.29–1.90), muscle strength (standardized mean difference = 1.13, 95% confidence interval = 0.30–1.96), flexibility (standardized mean difference = 1.22, 95% confidence interval = 0.39–2.04), and cardiorespiratory fitness (standardized mean difference = 1.48, 95% confidence interval = 0.42–2.54) of elderly subjects. **Conclusions**: There is evidence that mat Pilates improves dynamic balance, lower limb strength, hip and lower back flexibility, and cardiovascular endurance in elderly individuals. Furthermore, high-quality studies are necessary to clarify the effects of mat Pilates on other physical functional measurements among older adults.
Search Dates: January 2011 – March 2017	
Total # studies included: 9	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Performance-based measure of physical function (balance, flexibility, muscle strength, and cardiorespiratory fitness)	

SR/MA	
Citation: Burton E, Farrier K, Gavin R, Johnson S, Horgan NF, Warters A, Hill KD. Physical activity programs for older people in the community receiving home care services: systematic review and meta-analysis. Clin Interv Aging. 2019 Jun 6;14:1045-1064. doi: 10.2147/CIA.S205019.	
Purpose:	**Abstract:** The proportion of older adults is increasing around the world and most wish to live in their home until they die. To achieve this, many will require services in the home to remain living independently. To maintain function (i.e., strength, balance, and endurance), physical activity needs to be undertaken on a regular basis, and is essential as a person ages. Unfortunately, as people age there is a tendency to reduce activity levels, which often leads to loss of function and frailty, and the need for home care services. This updated systematic review includes a mix of study methodologies and meta-analysis, and investigated the effectiveness of physical activity/exercise interventions for older adults receiving home care services. Eighteen studies including ten randomized controlled trials meeting the selection criteria were identified. Many of the studies were multi-factorial interventions with the majority reporting aims beyond solely trying to improve the physical function of home care clients. The meta-analysis showed limited evidence for effectiveness of physical activity for older adults receiving home care services. Future exercise/physical activity studies working with home care populations should consider focusing solely on physical improvements, and need to include a process evaluation of the intervention to gain a better understanding of the association between adherence to the exercise program and other factors influencing effectiveness.
Search Date: Oct 2012 – Aug 2018	
Total # studies included: 18	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: mobility, endurance, strength, balance (TUG, sit-to-stand five time, grip strength, and walking speed)	

<table>
<tr><td colspan="2">SR/MA
Citation: da Rosa Orssatto LB, de la Tocha Freitas C, Shield AJ, Silveira Pinto R, Trajano GS. Effects of resistance training concentric velocity on older adults' functional capacity: A systematic review and meta-analysis of randomised trials. Experimental Gerontology 127 (2019) 110731. https://doi.org/10.1016/j.exger.2019.110731</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Reduced levels of functional capacity in older adults are related to lower quality of life, frailty, and sarcopenia, and can increase risk of falling, fractures and hospitalisation. Resistance training is an effective method to attenuate age-related functional declines. Based on the findings that muscle power and explosive strength are strongly associated with functional performance in older adults, it has been suggested that fast-intended-velocity resistance training may elicit greater improvements in functional capacity when compared to moderate-velocity resistance training. However, currently, there is no high-quality systematic review and meta-analysis supporting this assertion. The present study compared the magnitude of functional capacity improvements following resistance training performed with fast-intentional velocity versus moderate velocity. Pubmed, Scopus, and Web of Science databases were searched from inception to January 2019. The following eligibility criteria for selecting studies was adopted: Participants aged ≥60 years; resistance training based intervention for lower limbs performed solely with slow to moderate concentric velocity (≥2 s for each concentric phase) or solely with the intention of maximising velocity (i.e., as fast as possible); and at least one functional test for lower limbs, with pre- and post-intervention measurements. When studies employed multiple functional tests, a single (pooled) standardised mean difference was calculated and presented as combined functional capacity. In addition, functional tests were grouped accordingly to their specificity for the sub-groups meta-analyses. Fifteen studies were selected (high quality, n=3; and pre-registered, n=2). The results presented heterogeneity and small studies publication bias, leading to a biased advantage for fast-intended-velocity resistance training (95%CI=0.18, 0.65; I2=45%). Short physical performance battery indicated an advantage for fast-intended velocity resistance training (95%CI=0.10, 0.94; I2=0%). There was no difference for timed up and go (95%CI=−0.07, 0.94; I2=48%), 30-s chair stand (95%CI=−0.24, 1.39; I2=71%), 5-times chair stand (95%CI=−1.63, 1.27; I2=57%) stair climb (95%CI=−1.89, 2.81; I2=0%), short walk (95%CI=−0.99, 0.96; I2=21%) and long walk (95%CI=−0.59, 1.00; I2=0%). These results suggest that there is inconclusive evidence to support the superiority of fast-intended-velocity resistance training to improve functional capacity when compared to moderate-velocity resistance training. These results may have been influenced by the lack of high-quality and pre-registered studies, high heterogeneity, and small-studies publication bias.</td></tr>
<tr><td>Last Search Date: Jan 2019</td></tr>
<tr><td>Total # studies included: 15</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
functional test for lower limbs</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: de Souto Barreto P, Rolland Y, Vellas B, Maltais M. Association of Long-term Exercise Training With Risk of Falls, Fractures, Hospitalizations, and Mortality in Older Adults A Systematic Review and Meta-analysis. JAMA Intern Med. 2019;179(3):394-405. doi:10.1001/jamainternmed.2018.5406</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
IMPORTANCE Long-term exercise benefits on prevalent adverse events in older populations, such as falls, fractures, or hospitalizations, are not yet established or known.
OBJECTIVE To systematically review and investigate the association of long-term exercise interventions (≥1 year) with the risk of falls, injurious falls, multiple falls, fractures,
DATA SOURCES PubMed, Cochrane Central Register of Controlled Trials, SportDiscus, PsychInfo, and Ageline were searched through March 2018. hospitalization, and mortality in older adults.
STUDY SELECTION Exercise randomized clinical trials (RCTs) with intervention length of 1 year or longer, performed among participants 60 years or older.
DATA EXTRACTION AND SYNTHESIS Two raters independently screened articles, abstracted the data, and assessed the risk of bias. Data were combined with risk ratios (RRs) using DerSimonian and Laird's random-effects model (Mantel-Haenszel method).
MAIN OUTCOMES AND MEASURES Six binary outcomes for the risk of falls, injurious falls, multiple falls (≥2 falls), fractures, hospitalization, and mortality.
RESULTS Forty-six studies (22 709 participants) were included in the review and 40 (21 868 participants) in the meta-analyses (mean [SD] age, 73.1 [7.1] years; 15 054 [66.3%] of participants were women). The most used exercise was a multicomponent training (eg, aerobic plus strength plus balance); mean frequency was 3 times per week, about 50 minutes per session, at a moderate intensity. Comparator groups were often active controls. Exercise significantly decreased the risk of falls (n = 20 RCTs; 4420 participants; RR, 0.88; 95%CI, 0.79-0.98) and injurious falls (9 RTCs; 4481 participants; RR, 0.74; 95%CI, 0.62-0.88), and tended to reduce the risk of fractures (19 RTCs; 8410 participants; RR, 0.84; 95%CI, 0.71-1.00; P = .05). Exercise did not significantly diminish the risk of multiple falls (13 RTCs; 3060 participants), hospitalization (12 RTCs; 5639 participants), and mortality (29 RTCs; 11 441 participants). Sensitivity analyses provided similar findings, except the fixed-effect meta-analysis for the risk of fracture, which showed a significant effect favouring exercisers (RR, 0.84; 95%CI, 0.70-1.00; P = .047).Meta-regressions on mortality and falls suggest that 2 to 3 times per week would be the optimal exercise frequency.
CONCLUSIONS AND RELEVANCE Long-term exercise is associated with a reduction in falls, injurious falls, and probably fractures in older adults, including people with cardiometabolic and neurological diseases.</td></tr>
<tr><td>Last Search Date: March 2018</td></tr>
<tr><td>Total # studies included: 46</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: mortality; hospitalization; fallers; fallers with multiple falls; injurious fallers; and fractures</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Dillon L, Clemson L, Ramulu P, Sherrington C & Keay L. A systematic review and meta-analysis of exercise-based falls prevention strategies in adults aged 50+ years with visual impairment. Ophthalmic Physiol Opt 2018; 38: 456–467. https://doi.org/10.1111/opo.12562</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Purpose: To determine the impact of exercise or physical training on falls or physical function in people aged 50+ years with visual impairment, compared with control (no intervention or usual care).
Methods: An updated systematic review of randomised controlled trials, investigating the effect of exercise or physical activity on falls prevention or physical function in adults aged 50+ with visual impairment. Searches of CINAHL, the Cochrane Register of Controlled Trials (CENTRAL), Embase, and Medline were undertaken. Three trials were identified for the period February 2013 to July 2017 and added to the four in the original review.
Results: New trials evaluated yoga, the Otago Exercise Programme in combination with a home safety programme and the Alexander Technique. Meta-analysis of data from two trials (n = 163) indicated a non-statistically significant positive impact of exercise on the Chair Stand Test (WMD _1.85 s, 95% CI _4.65 to 0.96, p = 0.20, I2 22%). In this update, two new trials measured falls so meta-analysis was possible for three trials (n = 539) and revealed no impact on falls (RR 1.05, 95% CI 0.73 to 1.50, p = 0.81, I2 30%).
Discussion: Although exercise or physical training can improve physical function in older adults with visual impairment, and diverse strategies are being evaluated, there are no proven falls prevention strategies. In the few studies available, falls are not consistently reported and more work is required to investigate falls prevention in older adults with visual impairment.</td></tr>
<tr><td>Search Dates:
Feb 2013 – July 2017</td></tr>
<tr><td>Total # studies included: 7</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Physical function as classified by ICF. Timed up and go, functional reach, gait speed, gait kinematics</td></tr>
</table>

SR/MA **Citation:** Falck RS, Davis JC, Best JR, Crockett RA, Liu-Ambrose T. Impact of exercise training on physical and cognitive function among older adults: a systematic review and meta-analysis. Neurobiology of Aging 79 (2019) 119e130. https://doi.org/10.1016/j.neurobiolaging.2019.03.007	
Purpose:	**Abstract:** Exercise plays a key role in healthy aging by promoting both physical and cognitive function. Physical function and cognitive function appear to be interrelated and may share common mechanisms. Thus, exercise-induced improvements in physical function and cognitive function may co-occur and be associated with each other. However, no systematic review has specifically assessed and compared the effects of exercise on both physical function and cognitive function in older adults, and the association between changes in both outcomes after exercise training. Thus, we conducted a systematic review and meta-analysis (N = 48 studies) among older adults (60+ years). These data suggest exercise training has a significant benefit for both physical function (g = 0.39; p < 0.001) and cognitive function (g = 0.24; p < 0.001). At the study level, there was a positive correlation between the size of the exercise-induced effect on physical function and on cognitive function (b ¼ 0.41; p ¼ 0.002). Our results indicate exercise improves both physical and cognitive function, reiterating the notion that exercise is a panacea for aging well.
Search Dates: Jan 1990 – Nov 208	
Total # studies included: 58	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: muscle strength, physical performance	

SR/MA **Citation:** Gordt K, Gerhardy T, Najafi B, Schwenk M. Effects of Wearable Sensor-Based Balance and Gait Training on Balance, Gait, and Functional Performance in Healthy and Patient Populations: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Gerontology 2018;64:74–89. DOI: 10.1159/000481454	
Purpose:	**Abstract:** ***Background:*** Wearable sensors (WS) can accurately measure body motion and provide interactive feedback for supporting motor learning. ***Objective:*** This review aims to summarize current evidence for the effectiveness of WS training for improving balance, gait and functional performance. ***Methods:*** A systematic literature search was performed in PubMed, Cochrane, Web of Science, and CINAHL. Randomized controlled trials (RCTs) using a WS exercise program were included. Study quality was examined by the PEDro scale. Meta-analyses were conducted to estimate the effects of WS balance training on the most frequently reported outcome parameters. ***Results:*** Eight RCTs were included (Parkinson n = 2, stroke n = 1, Parkinson/stroke n = 1, peripheral neuropathy n = 2, frail older adults n = 1, healthy older adults n = 1). The sample size ranged from n = 20 to 40. Three types of training paradigms were used: (1) static steady-state balance training, (2) dynamic steady-state balance training, which includes gait training, and (3) proactive balance training RCTs either used one type of training paradigm (type 2: n = 1, type 3: n = 3) or combined different types of training paradigms within their intervention (type 1 and 2: n = 2; all types: n = 2). The meta-analyses revealed significant overall effects of WS training on static steady-state balance outcomes including mediolateral (eyes open: Hedges' g = 0.82, CI: 0.43–1.21; eyes closed: g = 0.57, CI: 0.14–0.99) and anterior- posterior sway (eyes open: g = 0.55, CI: 0.01–1.10; eyes closed: g = 0.44, CI: 0.02–0.86). No effects on habitual gait speed were found in the meta-analysis (g = –0.19, CI: –0.68 to 0.29). Two RCTs reported significant improvements for selected gait variables including single support time, and fast gait speed. One study identified effects on proactive balance (Alternate Step Test), but no effects were found for the Timed Up and Go test and the Berg Balance Scale. Two studies reported positive results on feasibility and usability. Only one study was performed in an unsupervised setting. ***Conclusion:*** This review provides evidence for a positive effect of WS training on static steady-state balance in studies with usual care controls and studies with conventional balance training controls. Specific gait parameters and proactive balance measures may also be improved by WS training, yet limited evidence is available. Heterogeneous training paradigms, small sample sizes, and short intervention durations limit the validity of our findings. Larger studies are required for estimating the true potential of WS technology.
Search Dates: Jan 2006 – June 2016	
Total # studies included: 8	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: balance, gait, functional capacity	

<table>
<tr><td colspan="2">SR/MA
Citation: Hita-Contreras F, Bueno-Notivol JB, Martinez-Amat A, Cruz-Diaz D, Hernandez AV, Perez-Lopez FR. Effect of exercise alone or combined with dietary supplements on anthropometric and physical performance measures in community-dwelling elderly people with sarcopenic obesity: A meta-analysis of randomized controlled trials Maturitas 116 (2018) 24–35. doi.org/10.1016/j.maturitas.2018.07.007</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Objective: To evaluate the effect of exercise (EXE) alone or exercise combined with dietary supplements (EXESUPPL) on body composition and physical performance in subjects 60 years and older with sarcopenic obesity.
Methods: A systematic review was carried out of studies identified through five search engines up to April 15, 2018. We searched for randomized controlled trials (RCTs) evaluating EXE or EXE-SUPPL in elderly individuals with sarcopenic obesity for at least six weeks. Primary outcomes were percentage of body fat mass, appendicular
skeletal muscle mass, and hand grip strength. Random effects meta-analyses with the inverse variance method were used to evaluate the effects of interventions on outcomes. Effects were expressed as mean differences (MD) and their 95% confidence intervals (CI). Risk of bias was assessed with the Cochrane tool.
Results: Nine papers reporting seven RCTs (with a total of 558 participants) were included in the review. EXE alone and EXE-SUPPL increased grip strength (MD 1.30 kg; 95% CI 0.58–2.01), gait speed (MD 0.05 m/s; 95% CI 0.03–0.07) and appendicular skeletal muscle mass (MD 0.40 kg; 95% CI 0.18–0.63). EXE alone and EXE-SUPPL reduced waist circumference (MD −1,40 cm; 95% CI −1.99 to −0.81), total fat mass (MD −1,77 kg; 95% CI −2.49 to −1.04), and trunk fat mass (MD −0.82 kg; 95% CI −1.22 to −0.42).
Conclusion: EXE alone and EXE-SUPPL improved muscle-related outcomes and reduced fat-related outcomes in subjects with sarcopenic obesity. There is a need for better-designed RCTs with systematic assessment of both different exercise regimes and dietary supplements in sarcopenic obese subjects.</td></tr>
<tr><td>Last Search Date: April 2018</td></tr>
<tr><td>Total # studies included: 7</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Included healthy community-dwelling men and/or women aged 60 years and older with sarcopenic obesity</td></tr>
<tr><td>Outcomes addressed: 1) percentage of body fat; 2) three sarcopenia diagnostic criteria: (i) appendicular skeletal muscle mass (ii) grip strength (iii) gait speed</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Kauppi M, Elovainio M, Stenholm S, Virtanen M, Aalto V, Koskenvuo M, Kivimaki M, Vahtera J. Social networks and patterns of health risk behaviours over two decades: A multi-cohort study. Journal of Psychosomatic Research 99 (2017) 45–58. dx.doi.org/10.1016/j.jpsychores.2017.06.003</td></tr>
<tr><td>Purpose:
Timeframe: N/A
Total # studies included: 3
Other details (e.g. definitions used, exclusions etc)
Outcomes addressed: Social network size</td><td>Abstract:
Objective: To determine the associations between social network size and subsequent long-term health behaviour patterns, as indicated by alcohol use, smoking, and physical activity.
Methods: Repeat data from up to six surveys over a 15- or 20-year follow-up were drawn from the Finnish Public Sector study (Raisio-Turku cohort, n =986; Hospital cohort, n= 7307), and the Health and Social Support study (n= 20,115). Social network size was determined at baseline, and health risk behaviours were assessed using repeated data from baseline and follow-up. We pooled cohort-specific results from repeated-measures log binomial regression with the generalized estimating equations (GEE) method using fixed-effects meta-analysis.
Results: Participants with up to 10 members in their social network at baseline had an unhealthy risk factor profile throughout the follow-up. The pooled relative risks adjusted for age, gender, survey year, chronic conditions and education were 1.15 for heavy alcohol use (95% CI: 1.06–1.24), 1.19 for smoking (95% CI: 1.12–1.27), and 1.25 for low physical activity (95% CI: 1.21–1.29), as compared with those with> 20 members in their social network. These associations appeared to be similar in subgroups stratified according to gender, age and education.
Conclusions: Social network size predicted persistent behaviour-related health risk patterns up to at least two decades.</td></tr>
</table>

SR/MA **Citation:** Kidd T, Mold F, Jones C, Ream E, Grosvenor W, Sund-Levander M, Tingstrom P, Carey N. (2019). What are the most effective interventions to improve physical performance in pre-frail and frail adults? A systematic review of randomised control trials. BMC geriatrics, 19(1), 184. https://doi.org/10.1186/s12877-019-1196-x	
Purpose:	**Abstract:** **Background**: With life expectancy continuing to rise in the United Kingdom there is an increasing public health focus on the maintenance of physical independence among all older adults. Identifying interventions that improve physical outcomes in pre-frail and frail older adults is imperative. **Methods**: A systematic review of the literature 2000 to 2017 following PRISMA guidelines and registered with PROSPERO (no. CRD42016045325). **Results**: Ten RCT trials fulfilled selection criteria and quality appraisal. The study quality was moderate to good. Interventions included physical activity; nutrition, physical activity combined with nutrition. Interventions that incorporated one or more physical activity components significantly improved physical outcomes in pre-frail and/or frail older adults. **Conclusions**: Physical activity interventions are key to maintaining independence in pre-frail and frail older adults. A lack of consensus regarding the definition of frailty, and an absence of core measures to assess this means any attempt to create an optimal intervention will be impeded. This absence may ultimately impact on the ability of older and frail adults to live well and for longer in the community.
Search Dates: Jan 2010 – Dec 2016	
Total # studies included: 10	
Other details (e.g. definitions used, exclusions etc) Studies were excluded if physical performance was only measured using ADL or IADL	
Outcomes addressed: Physical performance related to frailty criteria (e.g. gait speed, grip strength, physical activity levels, mobility, balance, muscle mass, body mass index)	

<table>
<tr><td colspan="2">SR/MA
Citation: Labott BK, Bucht H, Morat M, Morat T, Donath L. Effects of Exercise Training on Handgrip Strength in Older Adults: A Meta-Analytical Review. Gerontology. 2019;65(6):686-698. doi: 10.1159/000501203. Epub 2019 Sep 9. PubMed PMID: 31499496</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Background: Handgrip strength measurements are feasible with older adults and a reliable indicator for vitality, physical function, and several risk factors in the ageing process. Interventions with exercise training induce a variety of strength, balance, and endurance improvements. The pooled transfer effects of exercise training on handgrip strength has not been investigated to date. Thus, the objective of this metanalytical review is to examine the effects of different exercise training on handgrip strength in healthy community dwelling older adults of 60 years or older. Methods: The literature search was conducted in three databases (PubMed, Web of Science, SPORTDiscus) using the following search terms with Boolean conjunctions: (hand grip* OR grip strength OR grip power) AND (sport* OR train* OR exercis* OR strength OR intervention OR endurance OR resistance OR balance OR aerob*) AND (old* OR elder* OR senior*). Nonrandomized and randomized controlled trials with an exercise training and handgrip strength as the outcome parameter were screened. Study quality was independently assessed by two researchers using the PEDro scale. Comparison of handgrip strength between the intervention and control groups was conducted by using the hedges g (including adjustment for small sample sizes), calculating standardized mean differences (SMDs). A random effects inverse-variance model was applied for statistical analysis.
Results: Twenty-four trials (mean PEDro score 5.8 ± 0.9) with a total of 3,018 participants (mean age 73.3 ± 6.0 years) were included. Small but significant effects ($p < 0.001$) on handgrip strength were observed (SMD 0.28, 95% CI 0.13–0.44). Study heterogeneity (I^2 56%) and the funnel shape for publication bias analyses were acceptable.
Conclusions: Meaningful but small transfer effects of a multitude of different training approaches on handgrip strength occurred in healthy community-dwelling older adults. Handgrip strength cannot clearly be recommended to assess general functional performance for all kinds of exercise programs, whereas task-specific training and multimodal training modes seem to provide an appropriate stimulus to also improve handgrip strength.</td></tr>
<tr><td>Last Search Date: November 2018</td></tr>
<tr><td>Total # studies included: 24</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Community-dwelling, healthy older adults</td></tr>
<tr><td>Outcomes addressed:
Handgrip strength</td></tr>
</table>

SR/MA

Citation: Lindsay Smith G, Banting L, Eime R, O'Sullivan G, Van Uffelen JG. (2017). The association between social support and physical activity in older adults: a systematic review. International Journal of Behavioral Nutrition and Physical Activity, 14(1), 56. doi: 10.1186/s12966-017-0509-8

Purpose: **Last Date Searched:** Aug 2014 **Total # studies included:** 27 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** Social support, loneliness	**Abstract:** **Background**: The promotion of active and healthy ageing is becoming increasingly important as the population ages. Physical activity (PA) significantly reduces all-cause mortality and contributes to the prevention of many chronic illnesses. However, the proportion of people globally who are active enough to gain these health benefits is low and decreases with age. Social support (SS) is a social determinant of health that may improve PA in older adults, but the association has not been systematically reviewed. This review had three aims: 1) Systematically review and summarise studies examining the association between SS, or loneliness, and PA in older adults; 2) clarify if specific types of SS are positively associated with PA; and 3) investigate whether the association between SS and PA differs between PA domains. **Methods**: Quantitative studies examining a relationship between SS, or loneliness, and PA levels in healthy, older adults over 60 were identified using MEDLINE, PSYCInfo, SportDiscus, CINAHL and PubMed, and through reference lists of included studies. Quality of these studies was rated. **Results**: This review included 27 papers, of which 22 were cross sectional studies, three were prospective/ longitudinal and two were intervention studies. Overall, the study quality was moderate. Four articles examined the relation of PA with general SS, 17 with SS specific to PA (SSPA), and six with loneliness. The results suggest that there is a positive association between SSPA and PA levels in older adults, especially when it comes from family members. No clear associations were identified between general SS, SSPA from friends, or loneliness and PA levels. When measured separately, leisure time PA (LTPA) was associated with SS in a greater percentage of studies than when a number of PA domains were measured together. **Conclusions**: The evidence surrounding the relationship between SS, or loneliness, and PA in older adults suggests that people with greater SS for PA are more likely to do LTPA, especially when the SS comes from family members. However, high variability in measurement methods used to assess both SS and PA in included studies made it difficult to compare studies.

SR/MA	
Citation: McMullan II, McDonough SM, Tully MA, Cupples M, Casson K, Bunting BP. The association between balance and freeliving physical activity in an older community-dwelling adult population: a systematic review and meta-analysis. BMC Public Health (2018) 18:431. https://doi.org/10.1186/s12889-018-5265-4	
Purpose:	**Abstract:** **Background**: Poor balance is associated with an increased risk of falling, disability and death in older populations. To better inform policies and help reduce the human and economic cost of falls, this novel review explores the effects of free-living physical activity on balance in older (50 years and over) healthy community-dwelling adults. **Methods**: Search methods: CENTRAL, Bone, Joint and Muscle Trauma Group Specialised register and CDSR in the Cochrane Library, MEDLINE, EMBASE, CINAHL, PsychINFO, and AMED were searched from inception to 7th June 2016. Selection criteria: Intervention and observational studies investigating the effects of free-living PA on balance in healthy community-dwelling adults (50 years and older). Data extraction and analysis: Thirty studies were eligible for inclusion. Data extraction and risk of bias assessment were independently carried out by two review authors. Due to the variety of outcome measures used in studies, balance outcomes from observational studies were pooled as standardised mean differences or mean difference where appropriate and 95% confidence intervals, and outcomes from RCTs were synthesised using a best evidence approach. **Results**: Limited evidence provided by a small number of RCTs, and evidence from observational studies of moderate methodological quality, suggest that free-living PA of between one and 21 years' duration improves measures of balance in older healthy community-dwelling adults. Statistical analysis of observational studies found significant effects in favour of more active groups for neuromuscular measures such as gait speed; functionality using Timed Up and Go, Single Leg Stance, and Activities of Balance Confidence Scale; flexibility using the forward reach test; and strength using the isometric knee extension test and ultrasound. A significant effect was also observed for less active groups on a single sensory measure of balance, the knee joint repositioning test. **Conclusion**: There is some evidence that free-living PA is effective in improving balance outcomes in older healthy adults, but future research should include higher quality studies that focus on a consensus of balance measures that are clinically relevant and explore the effects of free-living PA on balance over the longer-term.
Last Search Date: June 2016	
Total # studies included: 30	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Balance, falls, and physical function	

<table>
<tr><td colspan="2">SR/MA
Citation: Sherrington C, Fairhall NJ, Wallbank GK, Tiedemann A, Michaleff ZA, Howard K, Clemson L, Hopewell S, Lamb SE. Exercise for preventing falls in older people living in the community.
Cochrane Database of Systematic Reviews 2019, Issue 1. Art. No.: CD012424. DOI: 10.1002/14651858.CD012424.pub2</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Background: At least one-third of community-dwelling people over 65 years of age fall each year. Exercises that target balance, gait and muscle strength have been found to prevent falls in these people. An up-to-date synthesis of the evidence is important given the major long-term consequences associated with falls and fall-related injuries
Objectives: To assess the effects (benefits and harms) of exercise interventions for preventing falls in older people living in the community.
Search methods: We searched CENTRAL, MEDLINE, Embase, three other databases and two trial registers up to 2 May 2018, together with reference checking and contact with study authors to identify additional studies.
Selection criteria: We included randomised controlled trials (RCTs) evaluating the effects of any form of exercise as a single intervention on falls in people aged 60+ years living in the community. We excluded trials focused on particular conditions, such as stroke.
Data collection and analysis: We used standard methodological procedures expected by Cochrane. Our primary outcome was rate of falls.
Main results: We included 108 RCTs with 23,407 participants living in the community in 25 countries. There were nine cluster-RCTs. On average, participants were 76 years old and 77% were women. Most trials had unclear or high risk of bias for one or more items. Results from four trials focusing on people who had been recently discharged from hospital and from comparisons of different exercises are not described here.</td></tr>
<tr><td>Last Search Date:
May 2018</td></tr>
<tr><td>Total # studies included: 10</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Excluded trials focused on particular conditions, such as stroke.</td></tr>
<tr><td>Outcomes addressed:
Fall-related fractures</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Sivaramakrishnan D, Fitzsimons C, Kelly P, Ludwig K, Mutrie N, Saunders DH, Baker G. (2019). The effects of yoga compared to active and inactive controls on physical function and health related quality of life in older adults-systematic review and meta-analysis of randomised controlled trials. International Journal of Behavioral Nutrition and Physical Activity, 16(1), 33.</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Background: Yoga has been recommended as a muscle strengthening and balance activity in national and global physical activity guidelines. However, the evidence base establishing the effectiveness of yoga in improving physical function and health related quality of life (HRQoL) in an older adult population not recruited on the basis of any specific disease or condition, has not been systematically reviewed. The objective of this study was to synthesise existing evidence on the effects of yoga on physical function and HRQoL in older adults not characterised by any specific clinical condition.
Methods: The following databases were systematically searched in September 2017: MEDLINE, PsycInfo, CINAHL Plus, Scopus, Web of Science, Cochrane Library, EMBASE, SPORTDiscus, AMED and ProQuest Dissertations & Theses Global.
Study inclusion criteria: Older adult participants with mean age of 60 years and above, not recruited on the basis of any specific disease or condition; yoga intervention compared with inactive controls (example: wait-list control, education booklets) or active controls (example: walking, chair aerobics); physical function and HRQoL outcomes; and randomised/cluster randomised controlled trials published in English. A vote counting analysis and meta-analysis with standardised effect sizes (Hedges' g) computed using random effects models were conducted.
Results: A total of 27 records from 22 RCTs were included (17 RCTs assessed physical function and 20 assessed HRQoL). The meta-analysis revealed significant effects (5% level of significance) favouring the yoga group for the following physical function outcomes compared with inactive controls: balance (effect size (ES) = 0.7), lower body flexibility (ES = 0.5), lower limb strength (ES = 0.45); compared with active controls: lower limb strength (ES = 0.49), lower body flexibility (ES = 0.28). For HRQoL, significant effects favouring yoga were found compared to inactive controls for: depression (ES = 0.64), perceived mental health (ES = 0.6), perceived physical health (ES = 0.61), sleep quality (ES = 0.65), and vitality (ES = 0.31); compared to active controls: depression (ES = 0.54).
Conclusion: This review is the first to compare the effects of yoga with active and inactive controls in older adults not characterised by a specific clinical condition. Results indicate that yoga interventions improve multiple physical function and HRQoL outcomes in this population compared to both control conditions. This study provides robust evidence for promoting yoga in physical activity guidelines for older adults as a multimodal activity that improves aspects of fitness like strength, balance and flexibility, as well as mental wellbeing.</td></tr>
<tr><td>Last Search Date: Sept 2017</td></tr>
<tr><td>Total # studies included: 22</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Physical function and/or HRQoL</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Taylor LM, Kerse N, Frakking T, Maddison R. J Geriatr Phys Ther 2018;41:108-123. DOI: 10.1519/JPT.0000000000000078</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Background and Purpose: Participation in regular physical activity is associated with better physical function in older people (> 65 years); however, older people are the least active of all age groups. Exercise-based active video games (AVGs) offer an alternative to traditional exercise programs aimed at maintaining or enhancing physical performance measures in older people. This review systematically evaluated whether AVGs could improve measures of physical performance in older people. Secondary measures of safety, game appeal, and usability were also considered. Methods: Electronic databases were searched for randomized controlled trials published up to April 2015. Included were trials with 2 or more arms that evaluated the effect of AVGs on outcome measures of physical performance in older people. Results: Eighteen randomized controlled trials (n = 765) were included. Most trials limited inclusion to healthy community dwelling older people. With the exception of 1 trial, all AVG programs were supervised. Using meta-analyses, AVGs were found to be more effective than conventional exercise (mean difference [MD], 4.33; 95% confidence intervals [CIs], 2.93- 5.73) or no intervention (MD, 0.73; 95% CI, 0.17-1.29) for improving Berg Balance scores in community-dwelling older people. Active video games were also more effective than control for improving 30-second sit-to-stand scores (MD, 3.99; 95% CI, 1.92-6.05). No significant differences in Timed Up and Go scores were found when AVGs were compared with no intervention or with conventional exercise.
Conclusions: Active video games can improve measures of mobility and balance in older people when used either on their own or as part of an exercise program. It is not yet clear whether AVGs are equally suitable for older people with significant cognitive impairments or balance or mobility limitations. Given the positive findings to date, consideration could be given to further development of age-appropriate AVGs for use by older people with balance or mobility limitations.</td></tr>
<tr><td>Last Search Date: April 2015</td></tr>
<tr><td>Total # studies included: 15</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Trials of AVGs targeting individuals with specifi c conditions (eg, stroke or diabetes) were excluded.</td></tr>
<tr><td>Outcomes addressed:
1) Objectively measured physical performance (ie, balance, mobility or physical performance test batteries), or 2) subjectively measured physical performance (ie, activity or balance confidence questionnaires)</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Vancampfort D, Lara E, Smith L, Rosenbaum S, Firth J, Stubbs B, Hallgren M, Koyanagi A. Physical activity and loneliness among adults aged≥ 50 years in six low-and middle-income countries. International journal of geriatric psychiatry. Int J Geriatr Psychiatry. 2019 Dec;34(12):1855-1864. doi: 10.1002/gps.5202.</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Introduction: Loneliness is widespread and associated with deleterious outcomes in middle-aged and older age people in low- and middle-income countries (LMICs). Physical activity is one potential psychosocial strategy with the potential to reduce loneliness in this population. Thus, the aim of this study was to explore associations between physical activity (PA) and loneliness in middle-aged and older people from six LMICs.
Materials and methods: Data from the Study on Global Ageing and Adult Health (SAGE) were analyzed. Self-reported data on loneliness and PA (as assessed by the Global Physical Activity Questionnaire) were collected. Participants were dichotomized into those who do and do not meet the international recommendation of 150 minutes of moderate to vigorous PA per week. Associations between loneliness and PA were examined using logistic regressions.
Results: Among 34 129 individuals aged 50 years or older, the prevalence of loneliness was higher among those not meeting the PA guidelines in all countries, although this difference was not significant in Mexico and South Africa. After full adjustment, not meeting PA guidelines was positively associated with loneliness in the meta-analysis based on country-wise estimates, with a moderate level of between-country heterogeneity being observed (OR = 1.31; 95% CI, 1.07-1.61; $I2$ = 48.7%). At an individual country level, statistical significance was only reached in Ghana (OR = 1.89; 95% CI = 1.44-2.49).
Discussion: Our data suggest that physical inactivity and loneliness commonly cooccur in adults aged 50 years or older in LMICs overall but that this association differs by country. Longitudinal studies are required to confirm these findings and investigate potential mechanisms that may inform future interventions.</td></tr>
<tr><td>Timeframe:
Survey conducted 2007 to 2010</td></tr>
<tr><td>Total # studies included: 1</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
loneliness</td></tr>
</table>

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D1: EVIDENCE ON PHYSICAL ACTIVITY FOR PREGNANT AND POSTPARTUM WOMEN

Guiding Questions

D1. What is the association between **physical activity** and health-related outcomes?

a. Is there a dose response association (volume, duration, frequency, intensity)?
b. Does the association vary by type or domain or timing (pre-pregnancy, antenatal or postnatal) of physical activity?

Inclusion Criteria

Population: Pregnant women and postpartum mothers
Exposure: Greater volume, duration, frequency or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity

Outcomes	**Importance**
Excessive weight gain	Critical
Gestational diabetes mellitus	Critical
Gestational hypertension/pre-eclampsia	Critical
Mental health (e.g., anxiety symptoms, depressive symptoms, post-partum depression)	Critical
Fetal outcomes (e.g., preterm birth, birthweight)	Critical
Adverse outcomes (e.g., miscarriage, stillbirth)	Critical
Delivery complications	Important

Evidence identified

The GRADE Evidence Profiles (EPs) developed for the *Canadian Guideline for Physical Activity Throughout Pregnancy (1)* were used as a basis for this update, given the rigor in methods and recency in included evidence. The original EPs can be found in the supplemental materials of seven systematic reviews prepared to inform the guideline *(2-8)*. Five additional reviews were conducted to inform the Canadian Guideline but are not included here given the outcomes addressed(i.e., urinary incontinence *(9)*, glucose response *(10)*, fetal heart rate and umbilical and uterine blood flow *(11)*, low back pain, pelvic girdle and lumbopelvic pain *(12)*) and type of exercise (i.e., supine exercise *(13)*).

Given the recency of the systematic reviews that were conducted to inform the Canadian Guideline, we compared the included studies within each of those systematic reviews with that of any new systematic reviews. In cases where the bodies of evidence were entirely overlapping, we only included the Canadian review (exclusions are noted in **Table D1.1**).

Seven reviews that informed the development of the Canadian guideline were included *(2-8)*. Ten additional reviews (published in 2018 or 2019) were identified by the WHO team that examined the association between physical activity and health-related outcomes among pregnant or postpartum women *(14-23)*. Four of these reviews were excluded because they were duplicative and less comprehensive than the reviews that were published to inform the Canadian Guideline *(15, 18, 22, 23)*. One additional review was excluded because it was a review of reviews which included outdated literature *(17)* and another publication was excluded because it was an RCT that updated the point estimate from a 2011 review with their study results *(21)*. **Table D1.1** presents the 6 reviews that were excluded and their reason for exclusion. **Table D1.2** presents the 4 reviews that were included and the outcomes they each reported.

Table D1.3 presents the ratings for each included review according to all the AMSTAR 2 main domains. None of the systematic reviews were rated as having high credibility based on the AMSTAR 2 instrument. Three were rated as having moderate credibility and 1 was rated as having low credibility**.**

Table D1.1. Excluded Systematic Reviews, with Reasons for Exclusion

Author, Year	Reason for Exclusion	Rationale
Bennett 2018 *(15)*	Redundancy	All included evidence is included in reviews by Davenport *(5)*
Farpour-Lambert 2018 *(17)*	Design	Review of reviews
Guo 2018 *(18)*	Redundancy	All included evidence is included in the review by Davenport *(5)*
Nobles 2018 *(21)*	Design	Not a systematic review
Syngelaki 2019 *(22)*	Redundancy	All included evidence is included in reviews by Ruchat *(8)* and Davenport *(5)*
Yu 2018 *(23)*	Redundancy	All included evidence is included in reviews by Davenport *(5)*

Table D1.2. Included Systematic Reviews

Author, Year	Excessive weight gain	GDM	Gestational HYP/ preeclampsia	Mental health outcomes	Fetal outcomes (e.g., preterm birth, birth-weight)	AEs (e.g., miscarriage, stillbirth)	Delivery complications	Last Search Date	# of Included Studies	AMSTAR 2
Beetham 2019 *(14)*	X				X			Nov-2018	15	Moderate
Du 2018 *(16)*	X	X	X		X		X	Apr-2018	13	Low
Mijatovic-Vukas 2018 *(19)*		X						Feb-2017	17	Moderate
Nakamura 2019 *(20)*				X				Oct-2017	21	Moderate

Abbreviations: AE = adverse event; GDM = gestational diabetes mellitus; HYP = hypertension

Table D1.3. Credibility Ratings (AMSTAR 2)

Author, Year	PICO[1]	Apriori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Hetero-geneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Beetham 2019 *(14)*	Y	Y	Y	PY	Y	Y	N	Y	Y	N	Y	Y	N	N	N	Y	**Moderate**
Du 2018 *(16)*	Y	PY	N	PY	Y	Y	N	Y	Y	N	Y	N	N	Y	N	N	**Low**
Mijatovic-Vukas 2018 *(19)*	Y	Y	Y	PY	Y	Y	N	Y	Y	N	Y	N	Y	Y	Y	Y	**Moderate**
Nakamura 2019 *(20)*	Y	PY	N	PY	Y	Y	N	PY	PY	N	Y	N	Y	Y	Y	Y	**Moderate**

Abbreviations: COI = conflict of interest; N = no; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *(24)*

D.1. Physical Activity

Table D.1.a. Excessive weight gain and physical activity, pregnant and postpartum women

Black font is from original GRADE Evidence Profile from the systematic review (Ruchat 2018 *(8)*) to support the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy. Red font denotes additions based on WHO update using review of existing systematic reviews. Two systematic reviews were identified that addressed the relationship between physical activity and excessive weight gain *(14, 16)*.

Quality assessment							№ of participants		Effect		Certainty	Importance
№ of studies* Review (AMSTAR 2 rating)	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**prenatal exercise**	**no exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions and **excessive gestational weight gain**												
15 [a]	randomized trials	serious [b]	not serious	not serious	not serious	none	601/1798 (33.4%)	694/1721 (40.3%)	**OR 0.68** (0.57 to 0.80)	**88 fewer per 1 000** (from 52 fewer to 125 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
							Narrative Synthesis: **Additional data from studies (n=3) included in the pooled estimate** **2/3 studies** reported lower odds of EGWG in the exercise-only intervention group compared to the control group (Barakat, 2016; Ruiz, 2013). **1/3 study** reported no difference in the odds of EGWG between the exercise-only intervention group and control group (Renault, 2015). [d]					
Beetham 2019 *(14)* Moderate 4 randomized trials 3 cohort studies		serious[e]	serious[f]	not serious	serious[g]	none	No significant difference in **maternal weight gain** was apparent for women who engaged in <u>vigorous intensity exercise</u> (MD = − 0.46 kg [95% CI −2.05 to 1.12], n = 1834, k = 7, I^2 = 68.94). Findings were consistent across study design and comparison condition. Two RCTs targeting overweight and obese pregnant women did show a significant reduction in maternal weight gain compared to a control group.				⊕⊕◯◯ LOW	CRITICAL
Du 2018 *(16)* Low 12 randomized trials		not serious	not serious	not serious	not serious	none	<u>Physical activity interventions</u> were associated with reduced **gestational weight gain** in pregnant women who were overweight or obese (MD = -1.14 kg [95% CI -1.67 to -0.62], 12 RCTS, n=1,172, I^2=10%).				⊕⊕⊕⊕ HIGH	CRITICAL
Association between prenatal exercise-only interventions and **postpartum weight retention**												

Quality assessment							№ of participants		Effect		Certainty	Importance
№ of studies* **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**prenatal exercise**	**no exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
3 [d]	randomized trials	serious [b]	not serious	not serious	not serious	none	213	207	-	MD **0.92 lower** (1.84 lower to 0)	⊕⊕⊕◯ MODERATE	CRITICAL
							Narrative summary: **Additional data from studies (n=1) included in the pooled estimate** The study by Seneviratne (2015) reported that in the intervention group, compliance with the exercise protocol (i.e the percentage of prescribed exercised session completed) was associated with maternal postnatal BMI.					

* Unless otherwise stated, all studies are included in the pooled estimate.

Abbreviations: BMI = body mass index; CI = confidence interval; EGWG = excessive gestational weight gain; MD = mean difference; OR: Odds ratio; RCT = randomized clinical trial

[a] Two studies reported data on different subgroups of women. These studies were counted only once.
[b] Serious risk of bias. High risk of performance bias.
[c] Renault 2015 and Renault 2014 reported data from the same RCT and were counted as one study. Data from Renault 2014 were included in the meta-analysis; data from Renault 2015 were reported narratively.
[d] One study reported data on different subgroups of women (postpartum weight retention at 16 weeks and at 12 month). This study was counted only once.
[e] Serious risk of bias. High risk of attrition bias; exposure and control groups pulled from different cohorts; all studies did not control for confounding factors.
[f] Serious inconsistency. Direction and magnitude of effects was highly variable across studies; I^2>50%. However, not downgraded for inconsistency because results were consistent across study designs and comparisons.
[g] Serious imprecision. The 95% CI crossed the line of no effect, and was wide, such that interpretation of the data would be different if the true effect were at one end of the CI or the other.

Table D.1.b. Gestational diabetes mellitus and physical activity, pregnant and postpartum women

Black font is from original GRADE Evidence Profile from the systematic review (Davenport 2018 *(5)*) to support the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy. Red font denotes additions based on WHO update using review of existing systematic reviews. Two systematic reviews were identified that addressed the relationship between physical activity and gestational diabetes *(16, 19)*.

Quality assessment							№ of participants		Effect		Certainty	Importance
№ of studies * Review (AMSTAR 2 rating)	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions/prenatal exercise and **gestational diabetes mellitus**												
26	randomized trials	serious [a]	not serious	not serious	not serious	none	271/3505 (7.7%)	380/3429 (11.1%)	**OR 0.62** (0.52 to 0.75)	**39 fewer per 1 000** (from 25 fewer to 50 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Du 2018 *(16)* Low 10 randomized trials		not serious	not serious	not serious	not serious	none	Physical activity interventions during pregnancy were associated with reduced **risk of GDM** in pregnant women who were overweight or obese (RR = 0.71 [95% CI, 0.57 to 0.89], 10 RCTs, n=1,120; I^2=0%).				⊕⊕⊕⊕ HIGH	CRITICAL
1 [b]	non-randomized studies	serious [c]	serious [d]	not serious	not serious [e]	none	Narrative Summary: In the study by Dyck (1999) (supervised exercise intervention, n=7), 3 women (43%) developed GDM.				⊕◯◯◯ VERY LOW	CRITICAL
14 (pooled estimate of effect [f], n=9; 5 studies synthesized narratively)	cohort studies	serious [g]	not serious	not serious	not serious	none	189/6975 (2.7%)	154/2620 (5.9%)	**OR 0.69** (0.54 to 0.88)	**17 fewer per 1 000** (from 7 fewer to 26 fewer)	⊕◯◯◯ LOW	CRITICAL
							Narrative Synthesis: Five cohort studies were included (n=19,803). 3/5 (n=16,814) reported between 11 to 90% decreased odds of GDM with prenatal physical activity compared to no exercise (Iqbal, 2007; Morkrid, 2014; Chasan-Taber, 2008). 2/5 (n=2989) reported that prenatal physical activity did not affect odds of GDM compared to no physical activity (Currie 2014; Chasan-Taber, 2015). Additional data from Badon (2016b) showed an association between LTPA and GDM. [h]					

Quality assessment							№ of participants		Effect		Certainty	Importance
№ of studies * **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mijatovic-Vukas 2018 *(19)* Moderate 17 cohort studies		serious [p]	not serious	not serious	not serious	none	Physical activity was self-reported in all studies, with 10 studies measuring PA in pre-pregnancy and 9 studies measuring PA in early pregnancy. Overall, physical activity was reported to be protective against developing GDM in 13/17 studies. Engaging in PA before pregnancy was significantly associated with a reduced risk of **GDM** (OR = 0.70 [95% CI, 0.57 to 0.85], 11 studies, I^2=52%) as was engaging in any PA during early pregnancy (OR = 0.79 [95% CI, 0.64 to 0.97], 8 studies, I^2=26%). There was evidence that participating in higher (>15 MET-hr/wk) vs. lower (<15 MET-hr/wk) of LTPA pre-pregnancy was associated with a significantly lower risk of GDM (OR = 0.54 [95% CI, 0.34 o 0.87], 6 studies, I^2=95%) as was participating in 90 min/week of LPTA during pre-pregnancy (OR = 0.54 [95% CI 0.34 to 0.87], 4 studies, I^2=70%).				⊕⊕◯◯ LOW	CRITICAL
7 (pooled estimate of effect, n=4 [i]; 3 studies synthesized narratively)	cross-sectional studies	serious [j]	not serious	not serious	not serious	none	86/3265 (2.6%)	50/2375 (2.1%)	**OR 0.66** (0.45 to 0.97)	**7 fewer per 1 000** (from 1 fewer to 11 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Synthesis: Three cross-sectional studies were included (n=12,189). 2/3 (n=739) reported no association between prenatal physical activity and (Li, 2014; Momeni Javid 2015). 1/3 (n=11,450) showed a decrease in odds of GDM with moderate to high activity compared to low activity (Leng, 2016). Additional data from Oken (2006) showed no effect of any light, moderate or vigorous intensity physical activity on GDM. [k]					
3 [l]	case-control studies	not serious [m]	serious [n]	not serious	serious [o]	none	74/271 (27.3%)	122/376 (32.4%)	**OR 0.63** (0.30 to 1.31)	**92 fewer per 1 000** (from 62 more to 199 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: Nasiri-Amiri (2016) (GDM, n=100; no GDM, n=100) found no association between prenatal physical activity and GDM, no matter the intensity of physical activity.					

* Unless otherwise stated, all studies are included in the pooled estimate.

Abbreviations: CI = confidence interval; GDM = gestational diabetes mellitus; hr = hour; LTPA = leisure-time physical activity; MET = metabolic equivalent of task; OR = odds ratio; PA = physical activity; RCT = randomized clinical trial; RR = risk ratio; wk = week

[a] Serious risk of bias. High risk of performance and attrition bias. Reporting bias was an issue in one study (results were reported narratively).
[b] This study did not include a control group such that it could not be included in the meta-analysis (results were reported narratively).
[c] Serious risk of bias. High risk of performance bias. This study did not include a control group such that it could not be included in the meta-analysis (narrative synthesis only).
[d] Serious inconsistency. Only one study was included.
[e] No serious imprecision; only one study but already downgraded for serious inconsistency for this reason.
[f] Five studies could not be pooled due to incomplete reporting of results; results were reported narratively.
[g] Serious risk of bias. Reporting bias was an issue in 6 studies (2/3 of the sample) (results were reported narratively).
[h] Badon 2016a and Badon 2016b reported data from the same cohort study and were counted as one study. Data from Badon 2016a were included in the meta-analysis; data from Badon 2016b were reported narratively (incomplete reporting of data).
[i] Three studies could not be pooled due to incomplete reporting of results; results were reported narratively.
[j] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of prospective and retrospective physical activity measure). Reporting bias was an issue in 4 studies (3/4 of the sample); results were reported narratively.
[k] Oken (2006) reported data that were included in the meta-analysis and data that were not (incomplete reporting of data; additional data were reported narratively)
[l] One study could not be pooled due to incomplete reporting of results; results were reported narratively.
[m] Reporting bias was an issue in one study (results were reported narratively).
[n] Serious inconsistency. High heterogeneity ($I2 \geq 50\%$).
[o] Serious imprecision. The 95% CI crossed the line of no effect, and was wide, such that interpretation of the data would be different if the true effect were at one end of the CI or the other.
[p] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of prospective and retrospective physical activity measure).

Table D.1.c. Gestational hypertension/pre-eclampsia and physical activity, pregnant and postpartum women

Black font is from original GRADE Evidence Profile from the systematic review (Davenport 2018 *(5)*) to support the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy. Red font denotes additions based on WHO update using review of existing systematic reviews. One systematic review was included that addressed the relationship between physical activity and gestational hypertension and pre-eclampsia *(16)*.

Quality assessment							**№ of participants**		**Effect**		**Certainty**	**Importance**
№ of studies * Review (AMSTAR 2 rating)	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions and **gestational hypertension**												
24 (pooled estimate of effect, n =22 [a,b]; 2 studies synthesized narratively)	randomized trials	not serious [c]	not serious	not serious	not serious	none	61/2627 (2.3%)	105/2689 (3.9%)	**OR 0.61** (0.43 to 0.85)	**15 fewer per 1 000** (from 6 fewer to 22 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
							Narrative Synthesis: Two superiority trials were included (n=107). Yeo (2008) reported that GH incidence was 22 % in women randomized to a walking intervention (n=41) and 40% in those randomized to a stretching intervention (n=38). McAuley (2005) reported 2 cases of GH in both groups of women (aerobic and muscular exercise group [n=14] and muscular exercise group [n=14]).					
Du 2018 *(16)* Low 5 randomized trials		not serious	not serious	not serious	not serious	none	Among pregnant women with overweight or obesity, there was no significant difference in the incidence of **gestational hypertension** between physical activity intervention groups vs. standard antenatal care (RR = 0.63 [95% CI 0.38 to 1.05], 5 RCTs, n=671, I^2=0%).				⊕⊕⊕⊕ HIGH	CRITICAL
2 [d]	non-randomized intervention studies	serious [e]	not serious	not serious	not serious	none	Narrative Synthesis: Two studies were included (n=367). Narendran (2005) reported no difference in GH incidence between women who practiced yoga (n=169) and those who walked (n=166) during pregnancy (p=0.25). O'Connor (2011) reported one case of severe hypertension (among 32 women, 3%) during a strength training intervention (no control group).				⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Certainty	Importance
№ of studies * Review (AMSTAR 2 rating)	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
8 (pooled estimate of effect, n=5 [f]; 3 studies synthesized narratively)	cohort studies	serious [g]	not serious	not serious	serious [h]	none	199/3777 (5.3%)	133/1460 (9.1%)	**OR 0.86** (0.64 to 1.15)	**12 fewer per 1 000** (from 12 more to 31 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Synthesis: Three cohort studies were included (n=76,260). 1/3 (n=1,749) reported 49% lower odds of GH with sports/exercise compared to no exercise (Currie, 2014). 2/3 (n=74,511) found no association between GH and prenatal exercise (Juhl, 2010; Chasan-Taber, 2015). Additional data from Vollebregt (2010) showed no effect of prenatal exercise on GH, regardless of how it was examined (total LTPA vs sport, weekly duration or percentiles). [i]					
5 (pooled estimate of effect, n=4 [j]; 1 study reported narratively)	cross-sectional studies	serious [k]	not serious	not serious	serious [h]	none	107/1575 (6.8%)	80/1090 (7.3%)	**OR 0.89** (0.66 to 1.21)	**8 fewer per 1 000** (from 14 more to 24 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: Martin (2010) reported lower odds of GH in women who were active at least once a week over the last 3 months of their pregnancy compared to those who were (n=3,348).					
4	Case-control studies	serious [l]	serious [m]	not serious	serious [h]	none	9037/20443 (44.2%)	27980/55331 (50.6%)	**OR 0.89** (0.68 to 1.16)	**29 fewer per 1 000** (from 37 more to 95 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Certainty	Importance
№ of studies * Review (AMSTAR 2 rating)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise	No exercise	Relative (95% CI)	Absolute (95% CI)		
							Narrative Summary: Additional data from Marcoux (1989) (n=931) showed no association between LTPA during the first 20 weeks of pregnancy and GH, no matter the way LTPA was examined (hours/week, energy expenditure as kcal/min or kcal/week).[n]					
Association between exercise-only interventions and **preeclampsia**												
16 (pooled estimate of effect, n =15 [o,p]; 1 study reported narratively)	randomized trials	serious [q]	not serious	not serious	not serious	none	34/1719 (2.0%)	49/1603 (3.1%)	**OR 0.59** (0.37 to 0.94)	**12 fewer per 1 000** (from 2 fewer to 19 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
							Narrative Summary: Yeo (2008) reported that PE incidence was 14.6% in women randomized to a walking intervention (n=41) and 2.6% in those randomized to a stretching intervention (n=38).					
Du 2018 *(16)* Low 4 randomized trials		not serious	not serious	not serious	serious [h]	none	Among pregnant women with overweight or obesity, there was no significant difference in the incidence of **preeclampsia** between physical activity intervention groups vs. standard antenatal care (RR = 1.39 [95% CI, 0.66 to 2.93], 4 RCTs, n=596, I^2=0%).				⊕⊕⊕◯ MODERATE	CRITICAL
1 [r]	non-randomized intervention studies	serious [q]	serious [s]	not serious	not serious [t]	none	Narrative Summary: In the study by Dyck (1999) (supervised exercise intervention, n=7), one woman (14%) developed PE.				⊕◯◯◯ VERY LOW	CRITICAL
9 (pooled estimate of effect, n =6; 3 studies	cohort studies	serious [g]	not serious	not serious	not serious	none	1952/51843 (3.8%)	653/15639 (4.2%)	**OR 0.87** (0.78 to 0.97)	**5 fewer per 1 000** (from 1 fewer to 9 fewer)	⊕◯◯◯ LOW	CRITICAL

Quality assessment							№ of participants		Effect		Certainty	Importance
№ of studies * **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
synthesized narratively)							Narrative Synthesis: Three cohort studies were included (n=76,260) 3/3 found no association between prenatal exercise and PE, no matter the intensity or volume of exercise (Currie, 2014; Juhl, 2010; Chasan-Taber, 2015). Additional data from Rudra (2008) and Magnus (2008) indicated lower odds of PE with prenatal physical activity. However, additional data from Vollebregt (2010) showed no association between prenatal exercise and PE. [u]					
2	cross-sectional studies	serious [v]	not serious	not serious	serious [h]	none	45/1595 (2.8%)	32/1107 (2.9%)	**OR 0.64** (0.39 to 1.05)	**10 fewer per 1 000** (from 1 more to 17 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
4	case-control studies	serious [w]	not serious	not serious	not serious	none	409/1464 (27.9%)	310/4154 (7.5%)	**OR 0.75** (0.59 to 0.99)	**18 fewer per 1 000** (from 1 fewer to 29 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: Additional data from Marcoux (1989) (n=931) indicated 47 to 43% lower odds of PE with heavy LTPA compared to light/moderate LTPA. [n]					

* Unless otherwise stated, all studies are included in the pooled estimate.

Abbreviations: CI = confidence interval; GH = gestational hypertension; LTPA = leisure time physical activity; OR = odds ratio., RCT = randomized clinical trial; RR = risk ratio

[a] Two superiority trials could not be pooled due to absence of a no-exercise control group; results were reported narratively.
[b] One study reported no cases of GH (not estimable result) and was not included in the pooled analysis.
[c] No serious risk of bias. Unclear risk of selection bias; it was unknown if allocation concealment was adequate.
[d] The two studies could not be pooled due to absence of a no-exercise control group; results were reported narratively.
[e] Serious risk of bias. High risk of performance bias. Unclear risk of attrition bias; attrition rate is unknown.
[f] Three studies could not be pooled due to incomplete reporting of results; results were reported narratively.
[g] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of prospective and retrospective physical activity measure). Reporting bias was an issue in three studies; results were reported narratively.
[h] Serious imprecision. The 95% CI crossed the line of no effect, and was wide, such that interpretation of the data would be different if the true effect were at one end of the CI or the other.
[i] Vollebregt (2010) reported data that were included in the meta-analysis and data that were not (incomplete reporting of data; additional data were reported narratively).
[j] One study could not be pooled due to incomplete reporting of results; results were reported narratively.
[k] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of prospective and retrospective physical activity measure). Reporting bias was an issue in one study (incomplete reporting of data such that it could not be included in the meta-analysis; results were reported narratively).
[l] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of prospective and retrospective physical activity measure).
[m] Serious inconsistency. High heterogeneity (I2≥50%)
[n] Marcoux (1989) reported data that were included in the meta-analysis and data that were not (incomplete reporting of data; additional data were reported narratively).

[o] One superiority trial could not be pooled due to absence of a no-exercise control group; results were reported narratively.
[p] One study reported no cases of PE (not estimable result) and was not included in the pooled analysis.
[q] Serious risk of bias. High risk of performance bias.
[r] This study could not be included in the meta-analysis due to absence of a no-exercise control group; results were reported narratively.
[s] Serious inconsistency. Only one study was included.
[t] No serious imprecision; only one study but already downgraded for serious inconsistency for this reason.
[u] Rudra (2008), Magnus (2008) and Vollebregt (2010) reported data that were included in the meta-analysis and data that were not (incomplete reporting of data; additional data were reported narratively).
[v] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure).
[w] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of prospective and retrospective physical activity measure).

Table D.1.d. Mental health outcomes and physical activity, pregnant and postpartum women

Black font is from original GRADE Evidence Profile from the systematic review (Davenport 2018 *(3)*) to support the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy. Red font denotes additions based on WHO update using review of existing systematic reviews. One systematic review was identified that addressed the relationship between physical activity and postpartum depression *(20)*.

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**prenatal exercise**	**no exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions and **prenatal depressive symptoms**												
15 (pooled estimate of effect, n =13; 2 studies reported narratively)	randomized trials	serious [a]	not serious	not serious	not serious	none	590	585	-	SMD **0.39 SD lower** (0.51 lower to 0.26 lower)	⊕⊕⊕◯ MODERATE	CRITICAL
							Narrative Synthesis: A superiority RCT comparing yoga (n=51) with non-yoga (n=45) antenatal exercises showed an improvement in depressive symptoms with yoga, but not with other antenatal exercise (Satyapriya 2013). In contrast, one RCT found no influence of prenatal exercise on the severity of depressive symptoms during pregnancy (exercise = 429, control = 426; Gustafsson 2015).					
4	non-randomized intervention studies	serious [b]	serious [c]	not serious	not serious	none	215	205	-	SMD **0.81 lower** (1.14 lower to 0.49 lower)	⊕◯◯◯ VERY LOW	CRITICAL
8 (pooled estimate of effect, n =3; 5 studies	cohort studies	serious [d]	not serious	not serious	serious [e]	none	94	170	-	SMD **0.16 SD lower** (0.47 lower to 0.14 higher)	⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies Review (AMSTAR 2 rating)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prenatal exercise	no exercise	Relative (95% CI)	Absolute (95% CI)		
reported narratively							Narrative Synthesis: Five cohort studies were included (n=5,060). 4/5 (n=4,982) reported a favourable effect of prenatal exercise on depressive symptoms (Gjestland 2013; Demissie 2011; Orr 2006; Downs 2008). 1/5 (n=78) reported no association between depression scores and physical activity (Tendais 2011).					
2 (pooled estimate of effect, n =1; 1 study reported narratively	case-control studies	not serious	serious [f]	not serious	not serious [g]	none	39	17	-	MD **0.2 lower** (0.49 lower to 0.09 higher)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: One case-control study was included (case, n=80; control, n=258) and indicated that women meeting the recommendations for 150 minutes/week of moderate intensity physical activity had similar depressive symptoms when compared to women not meeting the recommendations (OR = 1.94; 95%CI: 0.83, 4.56 adjusted for age, parity, education and pre-pregnancy body mass index. Kolu 2014)					
4 (pooled estimate of effect, n =1; 3 study reported narratively	cross-sectional studies	serious [d]	not serious	not serious	not serious	none	117	86	-	MD **11.26 lower** (14.36 lower to 8.16 lower)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Synthesis: Three cross-sectional studies were included (n=439). 3/3 indicated an inverse association between prenatal physical activity level and prenatal depressive symptoms (Loprinzi 2012; Petrovic 2016; de Wit 2015).					
5	randomized trials	serious [h]	not serious	not serious	not serious	none	32/354 (9.0%)	72/329 (21.9%)	**OR 0.33** (0.21 to 0.53)	**134 fewer per 1 000** (from 90 fewer to 163 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**prenatal exercise**	**no exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions and **prenatal depression**												
1	non-randomized intervention study	serious [i]	serious [f]	not serious	not serious [g]	none	13/50 (26.0%)	41/50 (82.0%)	**OR 0.08** (0.03 to 0.20)	**553 fewer per 1 000** (from 343 fewer to 700 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
1	cohort study	serious [j]	serious [f]	not serious	not serious [g]	none	3/53 (5.7%)	24/127 (18.9%)	**OR 0.26** (0.07 to 0.90)	**132 fewer per 1 000** (from 16 fewer to 173 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
1	cross-sectional study	serious [d]	serious [f]	not serious	not serious [g]	none	Narrative Summary: Bowen (2009) found that women who did at least 20 minutes of exercise per day during pregnancy were less likely to experience prenatal depression (assessed using the Edinburgh Postnatal Depression Scale) than women who exercise occasionally (OR 2.23, 95%CI 1.26, 3.92) or did not exercise during pregnancy (OR 3.18, 95%CI 1.47, 6.87).				⊕◯◯◯ VERY LOW	CRITICAL
Association between exercise-only interventions and **postnatal depressive symptoms**												
4	randomized trials	serious [k]	not serious	not serious	serious [e]	none	537	496	-	SMD **0.01 lower** (0.13 lower to 0.12 higher)	⊕⊕◯◯ LOW	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**prenatal exercise**	**no exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Nakamura 2019 *(20)* Moderate 6 randomized trials 11 cohort studies 4 cross-sectional studies		serious [s]	serious [c]	not serious	not serious	none	17/21 studies were included in meta-analysis (6 trials and 11 observational studies). When all study designs were combined, there was a significant association between physical activity and **postpartum depression scores** (SMD = -0.22 [95% CI, -0.42 to -0.01]), I^2=86.4%). Physical activity interventions showed a significant inverse relationship with PA during pregnancy and symptoms of post-partum depression (MD = -0.58 [95% CI, -1.09 to -0.08], I^2=90.7%). Observational evidence also showed an inverse, but not significant relationship between PA during pregnancy and post-partum depression scores (SMD = -0.07 [95% CI, -0.20 to 0.06], I^2-74.4%).				⊕⊕◯◯ LOW	CRITICAL
3 (pooled estimate of effect, n =2; 1 study reported narratively	non-randomized intervention studies	serious [l]	serious [c]	not serious	serious [e]	none	135	117	-	MD **0.69 lower** (1.91 lower to 0.52 higher)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: One non-randomized intervention including depressed women (intervention, n=34)(Battle 2015) demonstrated that a 10 week yoga intervention had a clinically meaningful decrease in depression severity. Using regression analysis, a dose-response relationship was observed where the more time spent practicing yoga, the greater reduction in depressive symptoms in a given week.					
1	cohort studies	serious [m]	serious [f]	not serious	not serious [g]	none	26	8	-	MD **2.71 lower** (4.93 lower to 0.49 lower)	⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies Review (AMSTAR 2 rating)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prenatal exercise	no exercise	Relative (95% CI)	Absolute (95% CI)		
1	cross-sectional studies	very serious [n]	serious [f]	not serious	not serious [g]	none	Narrative Summary: Data from the North Carolina Pregnancy Risk Assessment Monitoring System 2004-2005 found no significant association between third trimester exercise and postnatal depressive symptoms (Ersek 2009). However, women who were physically active both before pregnancy and during the third trimester of pregnancy had a reduction in severity of depressive symptoms (OR 0.66, 95%CI 0.49, 0.87; after controlling for age and marital status).				⊕◯◯◯ VERY LOW	CRITICAL
Association between exercise-only interventions and **postnatal depression**												
2	randomized trials	serious [k]	not serious	not serious	serious [e]	none	7/417 (1.7%)	13/376 (3.5%)	**OR 0.48** (0.18 to 1.22)	**18 fewer per 1 000** (from 7 more to 28 fewer)	⊕⊕◯◯ LOW	CRITICAL
1	cohort study	serious [o]	serious [f]	not serious	not serious [g]	none	419/26494 (1.6%)	886/44372 (2.0%)	**OR 0.79** (0.70 to 0.89)	**4 fewer per 1 000** (from 2 fewer to 6 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: Additional data from the Danish National Birth Cohort (Strom 2009) could not be included in the meta-analysis. They showed that women had a decreased odds of postpartum depression diagnosis if they were vigorously active (OR 0.81, 95%CI 0.66, 0.99), exercising 2-3 hours per week (OR 0.75, 95% CI 0.58-0.98) or achieving 8-15 MET h/week (OR 0.79, 95%CI 0.63, 0.99 compared to no exercise). All ORs were adjusted for maternal age, parity, pre-pregnancy BMI, alcohol intake, smoking, occupation, education, home ownership, marital status, social support and history of previous depression.					

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies Review (AMSTAR 2 rating)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prenatal exercise	no exercise	Relative (95% CI)	Absolute (95% CI)		
1	case-control study	serious [o]	serious [f]	not serious	not serious [g]	none	Narrative Summary: One case-control study (n=57) (Sexton 2012) reported higher prenatal exercise frequency in women who were likely to be depressed during pregnancy (Beck Depression Index, BDI-II >10) predicted postpartum recovery of depression (OR 1.23, 95%CI 0.08, 0.92).				⊕◯◯◯ VERY LOW	CRITICAL
1	cross-sectional study	serious [o]	serious [f]	not serious	not serious [g]	none	Narrative Summary: One cross-sectional study (n=6,330) (Guida 2012) showed that women who did not exercise during the third trimester of pregnancy were more likely to experience postpartum depression than women who exercised 5 or more days per week (OR 1.36, 95% CI 1.15, 1.62). Exercising 1-4 times per week had no observable effect on postpartum depression (OR 1.10, 95% CI 0.93, 1.32).				⊕◯◯◯ VERY LOW	CRITICAL
Association between exercise-only interventions and **prenatal state anxiety symptoms**												
6 (pooled estimate of effect, n =5; 1 study reported narratively)	randomized trials	serious [p]	not serious	not serious	serious [d]	none	136	140	-	SMD **0.03 SD higher** (0.21 lower to 0.27 higher)	⊕⊕◯◯ LOW	CRITICAL
							Narrative Summary: A superiority RCT comparing yoga (n=51) with non-yoga (n=45) antenatal exercises showed an improvement in state anxiety symptoms with yoga, but not other antenatal exercise (Satyapriya 2013).					
1	non-randomized intervention studies	serious [q]	serious [f]	not serious	not serious [g]	none	Narrative Summary: Beddoe (2009) showed that seven weeks of a mindfulness-based yoga intervention did not reduced state anxiety symptoms, whether the intervention was introduced in 2nd or 3rd trimester of pregnancy (n=16).				⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies Review (AMSTAR 2 rating)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prenatal exercise	no exercise	Relative (95% CI)	Absolute (95% CI)		
1	cohort studies	serious [j]	serious [f]	not serious	not serious [g]	none	38	142	-	SMD **0.36 lower** (0.72 lower to 0)	⊕◯◯◯ VERY LOW	CRITICAL
1	cross-sectional studies	not serious	serious [f]	not serious	not serious [g]	none	117	86	-	SMD **0.82 lower** (1.11 lower to 0.53 lower)	⊕◯◯◯ VERY LOW	CRITICAL
Association between exercise-only interventions and **prenatal trait anxiety symptoms**												
3 (pooled estimate of effect, n =2; 1 study reported narratively)	randomized trials	serious [r]	not serious	not serious	serious [e]	none	49	41	-	SMD **0.21 SD lower** (0.63 lower to 0.2 higher)	⊕⊕◯◯ LOW	CRITICAL
							Narrative Summary: A superiority RCT comparing yoga (n=51) with non-yoga (n=45) antenatal exercises showed an improvement in trait anxiety symptoms with yoga, but not other antenatal exercise (Satyapriya 2013).					
1	non-randomized intervention study	serious [q]	serious [f]	not serious	not serious [g]	none	Narrative Summary: Beddoe (2009) reported that 7 weeks of a mindfulness-based yoga intervention reduced trait anxiety symptoms when the intervention was introduced in the third (but not second trimester) (n=16).				⊕◯◯◯ VERY LOW	CRITICAL
1	cross-sectional study	not serious	serious [f]	not serious	not serious [g]	none	117	86	-	SMD **0.82 SD lower** (1.11 lower to 0.53 lower)	⊕◯◯◯ VERY LOW	CRITICAL
1	case-control study	not serious	serious [f]	not serious	not serious [g]	none	17	39	-	MD **0.19 lower** (0.4 lower to 0.02 higher)	⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies Review (AMSTAR 2 rating)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prenatal exercise	no exercise	Relative (95% CI)	Absolute (95% CI)		
Association between exercise-only interventions and **postnatal State anxiety symptoms**												
1	randomized trial	serious [p]	serious [f]	not serious	not serious [g]	none	39	40	-	SMD **0.01 higher** (0.43 lower to 0.45 higher)	⊕⊕◯◯ LOW	CRITICAL

* Unless otherwise stated, all studies are included in the pooled estimate.

Abbreviations: CI = confidence interval; MD = mean difference; OR = odds ratio; SMD = standardised mean difference;

[a] Serious risk of bias. High risk of performance bias and attrition bias. Unclear risk of selection bias; it was unknown if allocation adequately concealed. Reporting bias was an issue in one study and one study did not have a non-exercise control group (superiority trial); results were reported narratively.
[b] Serious risk of bias. High risk of performance bias (compliance to the intervention not reported; women who did not complete the majority of the intervention [>75%] were excluded) and attrition bias.
[c] Serious inconsistency. High heterogeneity (I2 > 50%).
[d] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure) and reporting bias (incomplete reporting of data in four studies such that they could not be included in the meta-analysis; results were reported narratively).
[e] Serious imprecision. The 95% CI crosses the line of no effect, and is wide, such that the interpretation of the data would be different if the true effect were at one end of the CI or the other.
[f] Serious inconsistency. Only one study was included.
[g] No serious imprecision; only one study but already downgraded for serious inconsistency for this reason.
[h] Serious risk of bias. High risk of attrition bias. Unclear risk of selection bias; it was unknown if allocation was adequately concealed.
[i] Serious risk of bias. High risk of performance and attrition bias (all women who did not complete the majority of the intervention [80%] were excluded). Unclear risk of selection bias; it was unknown if the methods of sequence generation and allocation concealment were adequate.
[j] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure).
[k] Serious risk of bias. High risk of performance bias.
[l] Serious risk of bias. High risk of performance and attrition bias (women who did not complete the majority of the intervention [>75%] were excluded; active and inactive groups made on the basis of compliance to physical activity recommendation at the end of the intervention). Reporting bias was an issue in one study (incomplete reporting of data such that it could not be included in the meta-analysis; results were reported narratively).
[m] Serious risk of bias. High risk of attrition and of other bias (extreme imbalance in baseline data between the groups likely to influence the outcome).
[n] Very serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of retrospective physical activity measure), detection bias (potentially flawed measurement of the outcome; unknown validity of postnatal depression symptoms measure). Reporting bias was an issue in this study (incomplete reporting of data such that it could not be included in the meta-analysis; results were reported narratively).
[o] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure). Reporting bias was an issue in one study (incomplete reporting of data such that it could not be included in the meta-analysis; results were reported narratively).
[p] Serious risk of bias. High risk of performance bias and attrition bias. Unclear risk of selection bias; it was unclear if sequence generation and allocation concealment were adequate.
[q] Serious risk of bias. High risk of performance and attrition bias. This study has no control group such that it could not be included in the meta-analysis; results were reported narratively.
[r] Serious risk of bias. High risk of attrition bias. Unclear risk of selection bias; it was unclear if sequence generation was adequate.
[s] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure), attrition bias, and reporting bias.

Table D.1.e. Fetal health outcomes and physical activity, pregnant and postpartum women

Black font is from original GRADE Evidence Profiles from two systematic reviews (Davenport 2018 *(4)* and Davenport 2019 *(7)*) to support the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy. Red font denotes additions based on WHO update using review of existing systematic reviews. Two systematic reviews were identified that addressed the relationship between physical activity and fetal health outcomes *(14, 16)*.

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prenatal exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions and **birthweight <2500 g**												
17 (pooled estimate of effect; n=15 [a,b]; 2 studies synthesized narratively.	randomized trials	serious [c]	not serious	not serious	serious [d]	none	114/1858 (6.1%)	126/1926 (6.5%)	**OR 0.91** (0.70 to 1.20)	**6 fewer per 1,000** (from 12 more to 19 fewer)	⊕⊕◯◯ LOW	CRITICAL
							Narrative synthesis: Two RCTs were included (Intervention, n=158; Control, n=99) and reported no association between prenatal exercise and birthweight <2500 g (Baciuk et al. 2009; deOliveria et al. 2012). **Additional data from studies (n=3) included in the pooled estimate.** All three studies reported no association between prenatal exercise and birth weight <2500 g (Kasawara et al. 2013; Barakat et al. 2016; Ussher et al. 2015). [e]					
Beetham 2019 *(14)* Moderate 2 randomized trials 2 cohort studies		serious [f]	not serious	not serious	serious [d]	none	There was no significant increase in risk of **LBW (< 2500 g)** (RR = 0.44 [95% CI − 0.83 to 1.7], n = 2454, k = 4, I^2 = 0). Results were consistent with no significant differences when limited by study design (RCT, prospective cohort, or retrospective cohort) or by comparison condition.				⊕⊕◯◯ LOW	CRITICAL
Du 2018 *(16)* Low 6 randomized trials		not serious	not serious	not serious	serious [d]	none	Among pregnant women with overweight or obesity, there was no significant difference in the risk of **SGA** between physical activity intervention groups vs. standard antenatal care (RR = 1.02 [95% CI, 0.54 to 1.92], 6 RCTs, n=863, I^2=13%).				⊕⊕⊕◯ MODERATE	CRITICAL

<table>
<tr><th colspan="7">Quality assessment</th><th colspan="2">№ of participants</th><th colspan="2">Effect</th><th rowspan="2">Quality</th><th rowspan="2">Importance</th></tr>
<tr><th>№ of studies

Review (AMSTAR 2 rating)</th><th>Study design</th><th>Risk of bias</th><th>Inconsistency</th><th>Indirectness</th><th>Imprecision</th><th>Other considerations</th><th>Prenatal exercise</th><th>No exercise</th><th>Relative (95% CI)</th><th>Absolute (95% CI)</th></tr>
<tr><td colspan="13">Association between exercise-only interventions and birth weight < 10th percentile</td></tr>
<tr><td rowspan="2">10 [f]</td><td rowspan="2">randomized trials</td><td rowspan="2">not serious</td><td rowspan="2">not serious</td><td rowspan="2">not serious</td><td rowspan="2">serious [d]</td><td rowspan="2">none</td><td>44/713 (6.2%)</td><td>36/549 (6.6%)</td><td>OR 0.98 (0.61 to 1.57)</td><td>1 fewer per 1,000 (from 25 fewer to 34 more)</td><td rowspan="2">⨁⨁⨁◯ MODERATE</td><td rowspan="2">CRITICAL</td></tr>
<tr><td colspan="4">Additional data from one study included in the pooled analysis. Simmons et al. (2016) did not find a relationship between the odds of having a small for gestational age (<10th percentile) baby at birth. [f, g]</td></tr>
<tr><td colspan="13">Association between exercise-only interventions and birth weight >4000 g</td></tr>
<tr><td rowspan="2">17 (pooled estimate of effect; n=15[h], 2 studies synthesized narratively)</td><td rowspan="2">randomized trials</td><td rowspan="2">not serious [i]</td><td rowspan="2">not serious</td><td rowspan="2">not serious</td><td rowspan="2">not serious</td><td rowspan="2">none</td><td>109/1835 (5.9%)</td><td>151/1835 (8.2%)</td><td>OR 0.61 (0.41 to 0.92)</td><td>30 fewer per 1,000 (from 6 fewer to 47 fewer)</td><td rowspan="2">⨁⨁⨁⨁ HIGH</td><td rowspan="2">CRITICAL</td></tr>
<tr><td colspan="4">Narrative synthesis: Two studies were included (Intervention, n=186; Control, n=121) and reported no relationship between prenatal exercise and birthweight > 4000 g (deOliveria et al. 2012; Oostdam et al. 2012).
Additional data from studies (n=4) included in the pooled estimate. 3/4 studies reported no relationship between prenatal exercise and birthweight >4000 g (Kasawara et al. 2013; Barakat et al. 2013; Tomic et al. 2013). 1/4 studies suggested women who were not active during pregnancy had an increased risk of having a baby >4000g [OR 2.53; CI:1.03,6.20] (Barakat et al. 2016).</td></tr>
<tr><td colspan="2">Du 2018 (16)
Low

7 randomized trials</td><td>not serious</td><td>not serious</td><td>not serious</td><td>serious [d]</td><td>none</td><td colspan="4">Among pregnant women with overweight or obesity, there was no significant difference in the risk of LGA between <u>physical activity intervention</u> groups vs. standard antenatal care (RR = 0.90 [95% CI, 0.65 to 1.25], 7 RCTs, n=961, I^2=0%).</td><td>⨁⨁⨁◯ MODERATE</td><td>CRITICAL</td></tr>
</table>

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prenatal exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions and **birth weight >90th percentile.**												
11	randomized trials	serious [j]	not serious	not serious	serious [d]	none	96/775 (12.4%)	81/632 (12.8%)	**OR 1.00** (0.71 to 1.40)	**0 fewer per 1,000** (from 34 fewer to 43 more)	⊕⊕◯◯ LOW	CRITICAL
							Additional data from one study included in the pooled analysis. Simmons et al. (2016) reported no relationship between the odds of having a large for gestational age (>90th percentile) baby at birth.					
Association between prenatal exercise and **IUGR**												
1	randomized trial	not serious	serious [k]	not serious	not serious [l]	none	12/166 (7.2%)	11/168 (6.5%)	**OR 1.11** (0.48 to 2.60)	**7 more per 1,000** (from 33 fewer to 89 more)	⊕⊕⊕◯ MODERATE	CRITICAL
							Additional data from one study included in the pooled analysis. Tomic et al. (2013) did not find an association between prenatal exercise and IUGR.					
2 (pooled estimate of effect; n=1[f]; 1 study reported narratively)	cohort studies	serious [m]	serious [k]	not serious	not serious [l]	none	76/533 (14.3%)	69/216 (31.9%)	**OR 0.36** (0.25 to 0.53)	**175 fewer per 1,000** (from 120 fewer to 214 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: Rego et al. (2016) (n=1380) did not find an association between prenatal exercise and IUGR.					
1 study reported narratively	Case control study	not serious [n]	serious [k]	not serious	not serious [l]	none	Narrative summary: Takito et al. (2010) (Cases; n=272; Control; n=546) did not find an association between prenatal exercise and IUGR.				⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prenatal exercise**	**No exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions and **preterm birth**												
28 (pooled estimate of effect; n=27 [o, h], 1 study reported narratively)	randomized trials	serious [p]	not serious	not serious	serious [d]	none	168/2680 (6.3%)	145/2603 (5.6%)	**OR 1.12** (0.88 to 1.42)	**6 more per 1,000** (from 6 fewer to 22 more)	⊕⊕◯◯ LOW	CRITICAL
							Narrative summary: One study was included (Intervention, n= 34; Control, n=37) and found no association between prenatal exercise and preterm birth (Cavalcante et al. 2009).					
Beetham 2019 *(14)* Moderate 2 randomized trials 2 cohort studies		serious [t]	not serious	not serious	not serious	none	A small, but significant, reduced risk of **preterm birth** existed in babies of mothers who engaged in <u>vigorous physical activity</u> (RR = − 0.20 [95% CI −0.36 to − 0.03], , n = 3025, k = 4, I^2 = 0); however the effect was not significant when limited to the 2 RCTs (RR = − 0.41 [95% CI − 1.64 to 0.82], n = 312, k = 2) or when using only light intensity exercise as a comparison (RR = − 0.16 [95% CI − 0.32 to 0.01] n = 1644, k = 3).				⊕⊕⊕◯ MODERATE	CRITICAL
Du 2018 *(16)* Low 6 randomized trials		not serious	not serious	not serious	serious [d]	none	Among pregnant women with overweight or obesity, there was no significant difference in the risk of **preterm birth** between <u>physical activity intervention</u> groups vs. standard antenatal care (RR = 1.18 [95% CI, 0.59 to 2.39], 6 RCTs, n=737, I^2=0%).				⊕⊕⊕◯ MODERATE	CRITICAL
Association between exercise-only interventions and **neonatal hypoglycemia**												
1	randomized trials	serious [q]	serious [k]	not serious	not serious [l]	none	4/37 (10.8%)	3/37 (8.1%)	OR 1.37 (0.29 to 6.61)	**27 more per 1,000** (from 56 fewer to 287 more)	⊕⊕◯◯ LOW	CRITICAL
Association between prenatal exercise-only interventions and **congenital anomalies**												
1	randomized trials	serious [r]	serious [k]	not serious	not serious [l]	none	9/346 (2.6%)	6/348 (1.7%)	**OR 1.52** (0.54 to 4.32)	**9 more per 1,000** (from 8 fewer to 53 more)	⊕⊕◯◯ LOW	CRITICAL
1	cohort study	serious [s]	serious [k]	not serious	not serious [l]	none	908/18330 (5.0%)	2832/54942 (5.2%)	OR 0.96 (0.89 to 1.04)	2 fewer per 1,000 (from 2 more to 5 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

Abbreviations: CI = confidence interval; LGA = large for gestational age; OR = odds ratio; RCT = randomized clinical trial; RR = risk ratio; SGA = small for gestational age

[a] Two studies reported no cases of birthweight <2500 g (not estimable result) and are not included in the pooled analysis.

[b] Two studies reported data on different sub-groups of women. These studies were counted only once.
[c] Serious risk of bias. High risk of performance (women who did not complete the majority of the intervention [>75%] were excluded) and attrition bias. Reporting bias was an issue in two studies; results were reported narratively. One study included "other risk" of bias (included women who smoked during pregnancy that may have affected birthweight).
[d] Serious imprecision. The 95% CI crosses the line of no effect, and is wide, such that interpretation of the data would be different if the true effect were at one end of the CI or the other.
[e] All three studies reported data that were included in the meta-analysis and additional data reported narratively. These studies were counted only once.
[f] One study reported data on different sub-groups of women. This study was counted only once.
[g] One study reported data that was included in the meta-analysis and additional data reported narratively. This study was counted only once.
[h] Two studies reported data on different sub-groups of women. These studies were counted only once.
[i] No serious risk of bias. Reporting bias was an issue in 3 studies; results were reported narratively.
[j] Serious risk of bias. High performance risk of bias.
[k] Serious inconsistency. Only one study was included.
[l] No serious imprecision; only one study but already downgraded for serious inconsistency for this reason
[m] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure). Reporting bias was an issue in one study; results were reported narratively.
[n] No serious risk of bias. Reporting bias was an issue in one study; results were reported narratively.
[o] Four studies reported no cases of preterm birth (not estimable result) and are not included in the pooled analysis.
[p] Serious risk of bias. High risk of performance bias (women who did not complete the majority of the intervention [>75%] were excluded). Reporting bias was an issue in one study; results were reported narratively. One study included "other risk" of bias (included women who smoked during pregnancy that may have affected preterm birth).
[q] Serious risk of bias. High risk of performance and attrition bias. Unclear risk of selection bias; it was unknown if sequence was adequately generated.
[r] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure).
[s] Serious risk of bias. High risk of other bias (all women were smokers which may have affected the odds of congenital anomalies).
[t] Serious risk of bias. High risk of performance and attrition bias. Unclear risk of selection bias.

Table D.1.f. Adverse effects and physical activity, pregnant and postpartum women

Black font is from original GRADE Evidence Profile from the systematic review (Davenport 2019 *(2)*) to support the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy. No new systematic reviews were identified that addressed the relationship between physical activity and delivery complications.

<table>
<tr><th colspan="7">Quality assessment</th><th colspan="2">№ of participants</th><th colspan="2">Effect</th><th rowspan="2">Quality</th><th rowspan="2">Importance</th></tr>
<tr><th>№ of studies</th><th>Study design</th><th>Risk of bias</th><th>Inconsistency</th><th>Indirectness</th><th>Imprecision</th><th>Other considerations</th><th>Prenatal exercise</th><th>no exercise</th><th>Relative (95% CI)</th><th>Absolute (95% CI)</th></tr>
<tr><td colspan="13">Association between exercise-only interventions and miscarriage</td></tr>
<tr><td rowspan="2">10 [a]</td><td rowspan="2">randomized trials</td><td rowspan="2">serious [b]</td><td rowspan="2">not serious</td><td rowspan="2">not serious</td><td rowspan="2">serious [c]</td><td rowspan="2">none</td><td>22/1160 (1.9%)</td><td>30/1088 (2.8%)</td><td>OR 0.69 (0.40 to 1.22)</td><td>8 fewer per 1 000 (from 6 more to 16 fewer)</td><td rowspan="2">⊕⊕◯◯ LOW</td><td rowspan="2">CRITICAL</td></tr>
<tr><td colspan="4">Additional data from study included in the pooled estimate. Ussher (2015) indicated no effect of prenatal exercise on the odds of miscarriage after adjustment for recruitment centre [as a stratification factor]. [d]</td></tr>
<tr><td>1</td><td>Non-randomized intervention studies</td><td>not serious</td><td>serious [e]</td><td>not serious</td><td>not serious [f]</td><td>none</td><td>1/33 (3.0%)</td><td>1/61 (1.6%)</td><td>OR 1.88 (0.11 to 30.98)</td><td>14 more per 1 000 (from 15 fewer to 324 more)</td><td>⊕◯◯◯ VERY LOW</td><td>CRITICAL</td></tr>
<tr><td rowspan="2">3 (pooled estimate of effect, n = 2 [g]; 1 study reported narratively)</td><td rowspan="2">cohort studies</td><td rowspan="2">serious [h]</td><td rowspan="2">not serious</td><td rowspan="2">not serious</td><td rowspan="2">serious [c]</td><td rowspan="2">none</td><td>21/621 (3.4%)</td><td>11/244 (4.5%)</td><td>OR 0.60 (0.27 to 1.36)</td><td>18 fewer per 1 000 (from 15 more to 32 fewer)</td><td rowspan="2">⊕◯◯◯ VERY LOW</td><td rowspan="2">CRITICAL</td></tr>
<tr><td colspan="4">Narrative Summary: One cohort study of 92,671 women (Madsen, 2007) found a progressive increase in the odds of miscarriage with increasing exercise volume. Exercising more than 7 hours/week before 18 weeks gestation was associated with a 3.7 higher odds of miscarriage. However, secondary analyses that included only women who were interviewed about exercise habits prior to a miscarriage (approximately 1/3 of the cohort) revealed that the association was no longer significant (Nilsson 2014).</td></tr>
</table>

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prenatal exercise**	**no exercise**	**Relative (95% CI)**	**Absolute (95% CI)**		
2	case-control studies	serious [i]	not serious	not serious	serious [c]	none	Narrative Synthesis: One case-control study (case, n=267; control, n=285; Zhang, 2011) reported a protective dose-response effect of exercise on miscarriage (after adjusted for several potential confounding factors). In contrast, Maconochie (2007) found no association between different levels of exercise compared to rare or no exercise and odds of miscarriage (cases, n=603; controls, n=6116, adjusted for year of conception, maternal age, previous miscarriage and previous live birth).				⊕◯◯◯ VERY LOW	CRITICAL
Association between exercise-only interventions and **stillbirth**												
6	randomized trials	serious [j]	not serious	not serious	serious [c]	none	5/860 (0.6%)	6/791 (0.8%)	**OR 0.79** (0.26 to 2.38)	**2 fewer per 1 000** (from 6 fewer to 10 more)	⊕⊕◯◯ LOW	CRITICAL
							Additional data from study included in the pooled estimate. Ussher (2015) indicated no effect of prenatal exercise on the odds of stillbirth after adjustment for recruitment centre [as a stratification factor]. [d]					
3 [k]	Non-randomized intervention studies	serious [l]	serious [l]	not serious	serious [c]	none	1/47 (2.1%)	1/43 (2.3%)	**OR 1.00** (0.06 to 16.93)	**0 fewer per 1 000** (from 22 fewer to 264 more)	⊕◯◯◯ VERY LOW	CRITICAL
2 (pooled estimate of effect, n = 1 [m]; 1 study reported narratively)	cohort studies	serious [n]	serious [e]	not serious	not serious [f]	none	9/533 (1.7%)	6/216 (2.8%)	**OR 0.72** (0.25 to 2.05)	**8 fewer per 1 000** (from 21 fewer to 28 more)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: One study (n=59,573) found no effect of exercising > once/week on odds of stillbirth compared to no exercise (Magnus, 2008).					
1	cross-sectional studies	serious [o]	serious [e]	not serious	not serious [f]	none	6/839 (0.7%)	33/1718 (1.9%)	**OR 0.37** (0.15 to 0.88)	**12 fewer per 1 000** (from 2 fewer to 16 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prenatal exercise	no exercise	Relative (95% CI)	Absolute (95% CI)		
							Additional data from study included in the pooled estimate. Dumith (2012) reported results that were adjusted for potential confounding factors and found no association between exercise and stillbirth (adjusted for maternal age, marital status, level of schooling, family income, parity, prenatal consultation and twin delivery). [d]					
1	case-control studies	serious [p]	serious [e]	not serious	not serious [f]	none	Narrative Summary: Xu (2014) (n= 620 cases; n=1,240 controls) reported a protective effect of exercising 30 minutes ≥2 times/week compared to not exercising (adjusted for history of miscarriage, previous induced abortion, frequency of night shift, frequent staying up late, regular physical exercise, smoking, and alcohol consumption).				⨁◯◯◯ VERY LOW	CRITICAL

Abbreviations: CI = confidence interval; OR = odds ratio

[a] One study reported no cases of miscarriage (not estimable result) and is not included in the pooled analysis.
[b] Serious risk of bias. High risk of performance bias and other bias (all women who were included in one study were smokers, a risk factor for miscarriage).
[c] Serious imprecision. The 95% CI crosses the line of no effect, and is wide, such that the interpretation of data would be different if the true effect were at one end of the CI or the other.
[d] One study reported data that was included in the meta-analysis and additional data reported narratively. This study was counted only once.
[e] Serious inconsistency. Only one study was included.
[f] No serious imprecision; only one study but already downgraded for serious inconsistency for this reason.
[g] Two studies reported data on different sub-groups of women. These studies were counted only once.
[h] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure). Reporting bias was an issue in one study (incomplete reporting of data; results are reported narratively).
[i] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of retrospective physical activity measure). Reporting bias was an issue in both studies (incomplete reporting of data; results are reported narratively).
[j] Serious risk of bias. High risk of performance bias and other bias (all women who were included in one study were smokers, a risk factor for stillbirth).
[k] Two studies reported no cases of stillbirth (not estimable result) and were not included in the pooled analysis.
[l] Serious inconsistency. OR values were not estimable in 2 studies.
[m] One study included different sub-groups of women. This study was counted only once.
[n] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure). Reporting bias was an issue in one study (incomplete reporting of data; results are reported narratively).
[o] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of prospective and retrospective physical activity measure). Reporting bias was an issue in the study (incomplete reporting of data; additional results are reported narratively).
[p] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of retrospective physical activity measure). Reporting bias was an issue in the study (incomplete reporting of data; results are reported narratively).

Table D.1.g. Delivery complications and physical activity, pregnant and postpartum women

Black font is from original GRADE Evidence Profile from the systematic review (Davenport 2019 *(6)*) to support the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy. One systematic review was included that addressed the relationship between physical activity and risk of caesarean delivery *(16)*.

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies **Review (AMSTAR 2 rating)**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**exercise (acute or chronic)**	**no exercise or different frequency, intensity, duration, volume or type of**	**Relative (95% CI)**	**Absolute (95% CI)**		
Association between exercise-only interventions or prenatal exercise and **preterm/prelabour rupture of membranes**												
2 [a]	randomized trials	not serious [b]	serious [c]	not serious	serious [d]	none	3/99 (3.0%)	3/99 (3.0%)	**OR 1.01** (0.20 to 5.16)	**0 fewer per 1 000** (from 24 fewer to 109 more)	⊕⊕◯◯ LOW	CRITICAL
5 (pooled estimate of effect, n = 4; 1 study reported narratively)	cohort studies	serious [e]	not serious	not serious	serious [d]	none	79/747 (10.6%)	68/830 (8.2%)	**OR 1.13** (0.79 to 1.62)	**10 more per 1 000** (from 16 fewer to 44 more)	⊕◯◯◯ VERY LOW	CRITICAL
							Narrative Summary: No association between weekly minutes of exercise and risk of preterm rupture of membranes (n = 190, Putnam et al. 2013)					
Association between exercise-only interventions and **cesarean section**												
47 (pooled estimate of effect, n = 46; 1 study reported narratively)	randomized trials	not serious [f]	not serious	not serious	not serious	none	892/4006 (22.3%)	965/3994 (24.2%)	**OR 0.91** (0.79 to 1.05)	**17 fewer per 1 000** (from 9 more to 41 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
							Narrative Summary: The superiority exercise- only interventions by Kariminia et al. (2004) reported similar rates of caesarean section between the walking group (n=1255) and the pelvic rocking exercise group (n=1292).					

Du 2018 *(16)* Low 10 randomized trials	not serious	not serious	not serious	serious [d]	none	Among pregnant women with overweight or obesity, there was no significant difference in the incidence of **caesarean delivery** between physical activity intervention groups vs. standard antenatal care (RR = 1.02 [95% CI, 0.87 to 1.20]], 10 RCTs, n=982, I^2=0%).	⊕⊕⊕◯ MODERATE	CRITICAL

Quality assessment							№ of participants		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise (acute or chronic)	no exercise or different frequency, intensity, duration, volume or type of exercise	Relative (95% CI)	Absolute (95% CI)		
Association between prenatal exercise and **caesarean section/instrumental delivery**												
2	cohort studies	serious [g]	not serious	not serious	not serious	none	14/77 (18.2%)	33/67 (49.3%)	**OR 0.19** (0.08 to 0.42)	**337 fewer per 1 000** (from 203 fewer to 420 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
1	cross-sectional study	serious [g]	serious [h]	not serious	not serious [i]	none	355/1773 (20.0%)	406/1989 (20.4%)	**OR 0.98** (0.83 to 1.14)	**3 fewer per 1 000** (from 22 more to 29 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Association between exercise-only interventions and **diastasis recti**												
1	randomized trials	serious [j]	serious [h]	not serious	not serious [i]	none	Narrative Summary: The superiority trial by Banerjee et al. (2013) (n=50) indicated a protective effect of abdominal exercises on diastasis rectus abdominis measured at 3 days postpartum compared to routine antenatal exercise.				⊕⊕◯◯ LOW	CRITICAL
1	non-randomized intervention study	serious [k]	serious [h]	not serious	not serious [i]	none	1/8 (12.5%)	9/10 (90.0%)	OR 0.02 (0.00 to 0.30)	**747 fewer per 1 000** (from -- to 170 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

Abbreviations: CI = confidence interval; MD = mean difference; OR = odds ratio

[a] One study reported no cases of preterm/prelabour rupture of membranes (not estimable result) and were not included in the pooled analysis.
[b] No serious risk of bias. Unclear risk of selection bias; unknown if allocation concealment was adequate.
[c] Serious inconsistency. Heterogeneity was not estimable.
[d] Serious imprecision. The 95% CI crossed the line of no effect, and was wide, such that interpretation of the data would be different if the true effect were at one end of the CI or the other.
[e] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of physical activity measure). Reporting bias was an issue in one study (incomplete reporting of data such that it could not be included in the meta-analysis; results were reported narratively).
[f] No serious risk of bias. Unclear risk of selection bias; it was unknown if allocation concealment was adequate. Reporting bias was an issue in one study (incomplete reporting of data such that it could not be included in the meta-analysis; results were reported narratively).
[g] Serious risk of bias. High risk of performance bias (potentially flawed measurement of the exposure; unknown validity of retrospective physical activity measure).
[h] Serious inconsistency. Only one study was included.
[i] No serious imprecision; only one study but already downgraded for serious inconsistency for this reason.

[j] Serious risk of bias. High risk of performance and attrition bias. Unclear risk of selection bias; it was unknown if sequence generation and allocation concealment were adequate. Reporting bias was an issue in one study (incomplete reporting of data such that it could not be included in the meta-analysis; results were reported narratively).

[k] Serious risk of bias. High risk of performance bias.

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E1: EVIDENCE ON PHYSICAL ACTIVITY FOR ADULTS (NO UPPER AGE LIMIT) LIVING WITH CHRONIC CONDITIONS

Guiding Questions

E1. What is the association between **physical activity** and health-related outcomes?

a. Is there a dose response association (volume, duration, frequency, intensity)?
b. Does the association vary by type or domain of physical activity?

Inclusion Criteria

Population: People living with any of the following conditions:

- Cancer
- Hypertension
- Type 2 diabetes
- HIV

Exposure: Greater volume, duration, frequency or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity

Condition	Outcomes	Importance
Cancer	All-cause mortality	Critical
	Cancer-specific mortality	Critical
	Risk of cancer recurrence or second primary cancer	Critical
Hypertension	Risk of co-morbid conditions	Critical
	Physical function	Critical
	Health-related quality of life	Critical
	Cardiovascular disease progression	Critical
Diabetes	Risk of co-morbid conditions	Critical
	Physical function	Critical
	Health-related quality of life	Critical
	Disease progression	Critical
HIV	Risk of co-morbid conditions	Critical
	Physical function	Critical
	Health-related quality of life	Critical
	Disease progression	Critical
	Adiposity	Critical

Evidence identified

Thirty-six reviews were initially identified (published from 2016 to 2019) that examined the association between physical activity and health-related outcomes among people with chronic conditions (1-36). However, 14 reviews were excluded from further evaluation given populations, exposures, or outcomes that were out-of-scope or given redundancy with another more comprehensive and credible review. **Table E1.1a** presents the reviews that were excluded and their reason for exclusion.

Table E1.1.a. Excluded Systematic Reviews, with Reasons for Exclusion for chronic conditions including cancer, hypertension and Type 2 diabetes

Author, Year	**Reason for Exclusion**	**Rationale**
People living with cancer		
Blond, 2019 *(3)*	Population	Review is among a general unselected adult population, not among those with a history of cancer
Dinu, 2019 *(11)*	Population	Review is among a general unselected adult population, not among those with a history of cancer
Lee, 2019 *(16)*	Population	Review is among a general unselected adult population, not among those with a history of cancer
Liu, 2018 *(37)*	Population	Review is among a general unselected adult population, not among those with a history of cancer
Qui, 2019 *(26)*	Redundancy	Review by Friedenreich 2019 *(12)* includes same evidence base, is more comprehensive, and better quality
Spei, 2019 *(30)*	Redundancy	Review by Friedenreich 2019 *(12)* includes same evidence base, is more comprehensive, and better quality
People with hypertension		
Chen, 2017 *(6)*	Population	Review among adults with coronary artery disease, not among those with hypertension
Wang, 2017 *(32)*	Population	Review among a general unselected adult population, not among those with hypertension
Zhang, 2018 *(35)*	Population	Results not presented separately for those with hypertension
People with type 2 Diabetes		
Anand 2018 *(1)*	Outcome	Primary outcome is diastolic dysfunction
Bhati 2018 *(2)*	Outcome	Outcomes are measures of cardiac autonomic function (heart rate reserve, heart rate variability, baroreflex sensitivity)
Delevatti 2019 *(10)*	Exposure	Comparison of progressive aerobic training vs. non-progressive aerobic training
Jayawardena 2018 *(14)*	Exposure	Direct comparison between yoga and other forms of exercise
Mosalman Haghighi 2018 *(22)*	Outcome	Primary outcome is measures of physical activity

For the commissioned umbrella review on physical activity and health outcomes in persons living with HIV, searches were conducted in three reference databases including: Pubmed, CINAHL and Web of Science. Where available, search strings were based on those used in the Physical Activity Guidelines for Americans 2018, with the following distinctions: publications were limited to systematic reviews, meta-analyses, pooled analyses; with no restrictions on publication year; English language only. The searches were completed between the 12-16 October, 2019.

Initial screening of titles and abstracts was done by two independent reviewers, and where consensus was not reached, a third reviewer was consulted. Records were subsequently excluded where duplicates were found, and also if the articles did not specifically address the PICOS. Finally, 24 full-text articles were also excluded, for example, if they did not include PLWHA, or there was no comparator, or the study was not a systematic review (**Table E1.1.b**).

Table E1.1.b. Excluded Systematic Reviews, for persons living with HIV

Author, Year	Reason for Exclusion	Rationale
People living with HIV		
Bjerk, 2017 *(40)*	Population	Review is among a general unselected adult population, not among those with HIV
Cobbing, 2016 *(41)*	Design	Review is a scoping review
Falco, 2012 *(42)*	Exposure	Review is on nutritional interventions
Field, 2016 *(43)*	Design	Review is a narrative review
Forbes, 2019 *(44)*	Population	Review targets men with a history of prostate cancer, not among those with HIV
Gonçalves, 2017 *(45)*	Population	Review is among a general unselected adult population, not among those with HIV
Ivanyi, 2015 *(46)*	Population/Exposure	Review is on the effects of orthoses, footwear, and walking aids on the walking ability of children and adolescents with spina bifida
Kamitani, 2017 *(47)*	Design	Review is an umbrella review
Kietrys, 2018 *(48)*	Design	The study design is a case series
Koepke, 2018 *(49)*	Population	Review is among people with multiple sclerosis
Kong, 2002 *(50)*	Exposure	Review is on testosterone therapy in HIV wasting syndrome
Larsen, 2019 *(51)*	Population	Review is among a general unselected adult population, not among those with HIV
Lee, 2013 *(52)*	Population	Review is among a general unselected adult population at risk of or with diagnosed cardiovascular diseases, not among those with HIV
Maddocks, 2013 *(53)*	Exposure	Review is on neuromuscular electrical stimulation for muscle weakness in adults with advanced disease
McKay, 2018 *(54)*	Exposure	Review evaluates mobile phone applications for health behaviour change
Moraes, 2018 *(55)*	Exposure	Review evaluates psychoneuroimmunology-based interventions
Nelson, 2014 *(56)*	Population	Review is on the management of osteoarthritis
Omura, 2012 *(57)*	Exposure	Review is on patient experience of haemophilia and HIV
Roeh, 2019 *(58)*	Population	Review is on the effects of exercise training on depressive symptoms in somatically ill patients
Roll, 2018 *(59)*	Population/Design	The study is a concept analysis on the health promotion for people with intellectual disabilities
Russell, 2014 *(60)*	Exposure	Review examines the efficacy of nutritional interventions on soccer skills
Tian, 2013 *(61)*	Population/Exposure	Review is among overweight or obese adults and examines the effects of chromium picolinate supplementation
Vancampfort, 2018 *(62)*	Exposure	Review examines physical activity correlates in people living with HIV/AIDS
Yahiaoui, 2012 *(63)*	Design	Not a systematic review

Included Evidence

In general, these reviews had many limitations in their design, execution, and reporting. None of the systematic reviews were rated as having high credibility based on the AMSTAR 2 instrument. Eleven were rated as having moderate credibility, 5 were rated as having low credibility, and the remaining 6 were rated as having critically low credibility. Given concerns regarding the comprehensiveness and the validity of the results presented in reviews rated as having critically low credibility, they were not incorporated into the final Evidence Profiles. **Table E1.2.a** presents the ratings for each review according to all the AMSTAR 2 main domains.

For the HIV umbrella review, there were 24 studies that were found to be eligible for inclusion in the qualitative synthesis and underwent quality scoring. An independent team of nine reviewers used the AMSTAR2 tool to rate the quality of the final included systematic reviews. Of these 24 reviews, 5 scored critically low on the AMSTAR score, and were excluded from further consideration. Of the remaining 19 reviews, 12 were rated as having high quality, 2 as moderate and 5 as low quality. **Table E1.2.b**. presents the ratings for each review according to all the AMSTAR 2 main domains

After appropriate exclusions, 1 review was included among persons with cancer *(12)*, 2 reviews were included among persons with hypertension *(4, 7)*, and 13 reviews were included among those with diabetes *(5, 8, 13, 15, 19, 20, 25, 27, 29, 31, 33, 34, 36)* (**Table E1.3.a**). None of the reviews included evidence published in 2019; in fact, very few reviews included evidence published in 2017 or 2018. The included bodies of evidence for each review was relatively small ranging from 5 to 39 included studies; one review among persons with a history of cancer included 136 studies. The evidence profiles for these studies are presented in **Table 1.4.** Extracted data for each included review is presented in **Appendix A.** A summary of the U.S. Physical Activity Guidelines evidence relevant to these subgroups is provided in the Evidence Profiles.

For HIV, after appropriate exclusions, 19 reviews were included, representing between 5 and 28 studies. Of these, 13 scored a high AMSTAR2 rating, 2 moderate and 4 low (**Table 1.3.b**). The evidence profiles for these reviews are presented in **Table 1.4** and extracted data for each included review are presented in **Appendix A.**

Table E1.2.a. Credibility Ratings (AMSTAR 2) for systematic reviews on physical activity in persons living with cancer, hypertension and Type 2 diabetes

Author, Year	PICO[1]	A priori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
People living with cancer																	
Friedenreich, 2019 *(12)*	Y	PY	N	PY	Y	N	PY	PY	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**
People living with hypertension																	
Cao, 2019 *(4)*	Y	N	N	PY	Y	Y	PY	PY	Y	N	Y	N	Y	Y	Y	Y	**Moderate**
Costa, 2018 *(7)*	Y	PY	N	PY	Y	Y	PY	Y	PY	N	Y	N	Y	N	N	Y	**Low**
de Sousa, 2017 *(9)*	Y	N	N	PY	Y	Y	N	PY	N	N	N	N	N	N	N	Y	**Critically Low**
People living with Type 2 diabetes																	
Chao 2018 *(5)*	Y	N	N	PY	Y	Y	PY	PY	PY	N	Y	N	Y	Y	Y	Y	**Moderate**
De Nardi 2018 *(8)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	Y	N	Y	Y	N	Y	**Moderate**
Jang 2019 *(13)*	Y	N	N	PY	Y	N	PY	PY	Y	N	Y	N	Y	Y	N	Y	**Low**
Lauche 2018 *(15)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	N	Y	**Moderate**
Lee 2017 *(17)*	Y	N	N	PY	Y	Y	PY	PY	Y	N	Y	N	N	Y	N	Y	**Critically Low**
Liao 2019 *(18)*	Y	N	N	PY	Y	N	PY	PY	PY	N	Y	N	N	N	Y	Y	**Critically Low**
Liu, Zhu, et al. 2019 *(19)*	Y	N	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Liu, Ye, et al. 2019 *(20)*	Y	N	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Meng 2018 *(21)*	Y	N	N	PY	Y	Y	N	PY	N	N	Y	N	Y	Y	Y	Y	**Critically Low**
Pan 2018 *(23)*	Y	PY	N	PY	Y	Y	PY	PY	Y	N	N	N	N	N	N	Y	**Critically Low**
Qui 2017 *(25)*	Y	PY	N	PY	N	Y	PY	PY	Y	N	Y	N	N	Y	Y	Y	**Moderate**

Author, Year	PICO[1]	A priori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Rees 2017 *(27)*	Y	N	N	PY	Y	N	PY	PY	Y	N	Y	N	N	Y	Y	Y	**Low**
Sampath Kumar 2019 *(28)*	Y	PY	N	PY	N	Y	N	PY	N	N	N	N	Y	Y	N	Y	**Critically Low**
Song 2018 *(29)*	Y	Y	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Moderate**
Thind 2017 *(31)*	Y	PY	N	PY	N	Y	PY	PY	N	N	Y	N	Y	Y	Y	Y	**Low**
Xia 2019 *(33)*	Y	N	N	PY	Y	Y	PY	Y	Y	N	Y	N	Y	Y	Y	Y	**Low**
Yu 2018 *(34)*	Y	N	N	PY	Y	Y	PY	PY	PY	N	Y	Y	Y	N	Y	N	**Moderate**
Zhou 2019 *(36)*	Y	N	N	PY	Y	Y	PY	PY	PY	N	Y	Y	Y	Y	Y	Y	**Moderate**

Abbreviations: COI = conflict of interest; N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.

Table E1.2.b. Credibility Ratings (AMSTAR 2) for systematic reviews on physical activity in persons living with HIV

Author, Year	PICO[1]	A priori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
People living with HIV																	
Ibeneme, 2019a *(64)*	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
Ibeneme, 2019b *(65)*	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	N	Y	Y	High
O'Brien, 2017 *(66)*	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	NmAc	NmAc	Y	NmAc	NmAc	Y	High
O'Brien, 2016 *(67)*	Y	Y	N	Y	Y	Y	Y	PY	Y	Y	Y	Y	Y	Y	Y	Y	High
Gomes Neto, 2015 *(68)*	Y	Y	Y	Y	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	High
O'Brien, 2010 *(69)*	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Nixon, 2005 *(70)*	Y	Y	Y	Y	Y	Y	Y	PY	Y	N	Y	Y	Y	Y	Y	Y	High
Bhatta, 2017 *(71)*	Y	Y	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Pedro, 2017 *(72)*	Y	Y	N	PY	Y	Y	Y	Y	Y	N	NmAc	NmAc	Y	NmAc	NmAc	N	High
O'Brien, 2004 *(73)*	Y	Y	N	Y	Y	Y	Y	Y	PY	N	Y	N	Y	N	Y	N	High
O'Brien, 2008 *(74)*	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	High
Zech, 2019 *(75)*	Y	Y	N	Y	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Chaparro, 2018 *(76)*	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Voigt, 2018 *(77)*	Y	PY	N	PY	N	Y	PY	Y	Y	N	NmAc	NmAc	Y	NmAc	NmAc	Y	moderate
Poton, 2017 *(78)*	Y	PY	Y	Y	Y	Y	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	moderate
Gomes Neto, 2013b *(79)*	Y	Y	N	Y	Y	Y	N	Y	Y	N	NmAc	NmAc	Y	NmAc	NmAc	N	Low
Fillipas, 2010 *(80)*	Y	Y	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	N	N	Low
Heissel, 2019 *(81)*	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Low
Quiles, 2019 *(82)*	Y	N	Y	PY	Y	Y	Y	Y	Y	N	NmAc	NmAc	Y	NmAC	NmAC	Y	Low
Nosrat, 2017 *(83)*	Y	PY	Y	Y	N	N	N	Y	N	N	NmAc	NmAc	N	NmAc	NmAc	Y	critically low
Gomes Neto, 2013a *(84)*	Y	PY	Y	Y	Y	Y	N	Y	N	N	NmAc	NmAc	N	NmAc	NmAc	Y	critically low
Lopez, 2015 *(85)*	Y	Y	N	PY	Y	N	PY	PY	N	N	NmAc	NmAc	N	NmAc	NmAc	Y	critically low
Lofgren, 2018 *(86)*	Y	N	N	N	N	N	PY	Y	N	N	NmAc	NmAc	N	NmAc	NmAc	N	critically low
Leyes, 2008 *(87)*	Y	N	Y	N	N	Y	Y	PY	N	N	NmAc	NmAc	N	NmAc	NmAc	**Y**	critically low

Abbreviations: COI = conflict of interest; N = no; NmAC = No meta-analysis conducted; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.

Table E1.3.a. Systematic Reviews Assessed, by chronic condition for cancer, hypertension and Type 2 diabetes

Author, Year	Outcomes							Last Search Date	# of Included Studies	AMSTAR 2 *(38)*
	All-causer mortality	Cancer-specific mortality	Risk of cancer reoccurrence	Risk of comorbid conditions	Physical function	Quality of life	Disease progression			
People living with cancer										
Friedenreich, 2019 *(12)*	X	X						Jul-2018	136	Moderate
People with hypertension										
Cao, 2019 *(4)*						X	X	Jul-2018	14	Moderate
Costa, 2018 *(7)*					X		X	Apr-2017	9	Low
de Sousa, 2017 *(9)*							X	Nov-2016	5	Critically Low
People with type 2 diabetes										
Chao 2018 *(5)*							X	Jun-2016	14	Moderate
De Nardi 2018 *(8)*							X	Jul-2017	7	Moderate
Jang 2019 *(13)*							X	Aug-2017	23	Low
Lauche 2018 *(15)*				X			X	Jan-2017	6	Moderate
Lee 2017 *(17)*					X		X	Nov-2016	10	Critically Low
Liao 2019 *(18)*							X	Jan-2018	20	Critically Low
Liu, Zhu, et al. 2019 *(19)*							X	Apr-2018	13	Moderate
Liu, Ye, et al. 2019 *(20)*							X	Sep-2018	24	Moderate
Meng 2018 *(21)*							X	Jun-2016	21	Critically Low
Pan 2018 *(23)*							X	Apr-2017	37	Critically Low
Qui 2017 *(25)*							X	Oct-2017	9	Moderate
Rees 2017 *(27)*						X	X	Feb-2017	9	Low
Sampath Kumar 2019 *(28)*							X	Jun-2017	11	Critically Low
Song 2018 *(29)*							X	Sep-2017	39	Moderate
Thind 2017 *(31)*							X	Feb-2016	23	Low
Xia 2019 *(33)*							X	Apr-2018	17	Low
Yu 2018 *(34)*						X	X	Dec-2016	20	Moderate
Zhou 2019 *(36)*					X	X	X	Mar-2018	23	Moderate

Table E1.3.b. Systematic Reviews Assessed, by health outcomes for persons living with HIV

Author, Year	Outcomes							Last search date	# of included studies	AMSTAR 2
	HRQOL	Body Composition	Anxiety/ Depression	Fitness and Functional Capacity	Cardio-Metabolic Markers	Viral Load/ CD4+	Cognition			
Ibeneme, 2019a *(64)*				X				Jan 2018	23	high
Ibeneme, 2019b *(65)*	X					X		June 2017	19	high
O'Brien, 2017 *(66)*	X	X		X		X		April 2013	20	high
O'Brien, 2016 *(67)*	X	X	X	X		X		April 2013	24	high
Gomes Neto, 2015 *(68)*	X			X				Aug 2014	7	High
O'Brien, 2010 *(69)*	X	X	X	X		X		June 2009	14	high
Nixon, 2005 *(70)*	X		X	X		X		Aug 2003	10	high
Bhatta, 2017 *(71)*	X							Dec 2015	28	high
Pedro, 2017 *(72)*	X	X		X	X	X		July 2016	5	High
O'Brien, 2004 *(73)*	X		X	X		X		NMR2002	10	high
O'Brien, 2008 *(74)*	X	X		X		X		Nov 2008	10	high
Zech, 2019 *(75)*				X				Aug 2017	27	high
Chaparro, 2018 *(76)*				X				Dec 2017	13	high
Voigt, 2018 *(77)*				X				Not reported	15	moderate
Poton, 2017 *(78)*		X		X		X		June 2016	13	moderate
Gomes Neto, 2013b *(79)*	X			X				Aug 2012	8	low
Fillipas, 2006 *(80)*		X			X			Nov 2009	9	low
Heissel, 2019 *(81)*			X					Feb 2019	10	low
Quiles, 2019 *(82)*					X			Nov 2017	9	low
Nosrat, 2017 *(83)*	X		X					Nov 2016	24	critically low
Gomes Neto, 2013a *(84)*	X	X		X				Aug 2012	29	critically low
Lopez, 2015 *(85)*	X		X	X		X		Nov 2015	18	critically low
Lofgren, 2018 *(86)*			X					Feb2017	18	critically low
Leyes, 2008 *(87)*	X	X		X		X		1996-2008	25	critically low

E.1.4. Physical Activity in adults living with chronic conditions

Table E.1.4.a. People who have been diagnosed with cancer, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People who have been diagnosed with cancer
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: All-cause mortality, cancer-specific mortality, risk of cancer recurrence or second primary cancer

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty	US PAGAC evidence *(39)*
		Risk of bias	Inconsistency	Indirect-ness†	Imprecision	Other			
All-cause mortality									
Friedenreich 2019 *(12)* Moderate	136 RCTs and observational studies[a] N=NR[a]	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Dose-response relationship bewee n prediagnosis PA dose and ACM for breast cancer	Higher **pre-diagnosis** PA was protective for ACM among those with breast (HR = 0.82 [95% CI 0.76 to 0.87], 19 studies), colorectal (HR = 0.80 [95% CI, 0.74 to 0.87], 10 studies), hematologic ((HR = 0.84 [95% CI 0.79 to 0.89], 3 studies), and prostate cancer (HR = 0.89 [95% CI0.82 to 0.98), 2 studies). No statistically significant association between pre-diagnosis PA and ACM was found for esophagus, female reproductive, melanoma, or stomach cancer. Higher **postdiagnosis** PA was protective for ACM following breast cancer (HR = 0.58 [95% CI, 0.58 [95% CI 0.52 to 0.65], 17 studies), childhood cancer (HR = 0.79 [95% CI 0.62 to 1.00], 1 study), colorectal cancer (HR = 0.63 [95% CI 0.050 to 0.78], 10 studies), gynaecologic cancer (HR = 0.66 [95% CI, 0.49 to 0.88], 4 studies), glioma (HR = 0.64 [95% CI 0.46 to 0.91], 1 study), hematologic cancer (HR = 0.60 p95% CI 0.51 to 0.69], 2 studies), kidney cancer (HR = 0.60 [95% CI 0.38 to 0.95], 1 study), lung cancer (HR = 0.76 [95% CI 0.60 to 0.97], 2 studies), prostate cancer (HR = 0.60 [95% CI, 0.46 to 0.79], 5 studies), and stomach cancer (HR = 0.75 [95% CI 0.61 to 0.93], 1 study). No	MODERATE[b]	11 ESRs Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of breast cancer-specific mortality and all-cause mortality in **female breast cancer survivors**. **PAGAC Grade: Moderate** 8 ESRs Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of colorectal cancer-specific mortality and all-cause mortality in **colorectal cancer survivors**. **PAGAC Grade: Moderate.** 2 ESRs Limited evidence suggests an inverse association between highest versus lowest levels of physical activity after diagnosis and all-cause mortality in prostate cancer survivors. **PAGAC Grade: Limited.**

							statistically significant association between postdiagnosis PA and ACM was found was esophagus cancer.		
Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**	**US PAGAC evidence** *(39)*
		Risk of bias	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**			
Cancer-specific mortality									
Friedenreich 2019 *(12)* Moderate	136 RCTs and observational studies N=NR[a]	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Evidecne of small study's effect for postdiagnosis PA and colorectal cancer-specific mortality	Meta-analysis found reduced hazards of mortality for those in the highest vs. lowest levels of **pre-diagnosis** total recreational PA for all cancers combined (cancer-specific mortality (HR = 0.82 [95% CI; 0.79 to 0.86], 33 studies), breast cancer (HR = 0.86 [95% CI, 0.78 to 0.94], 23 studies), colorectal cancer (HR = 0.80 [95% CI, 0.74 to 0.87], 14 studies), hematologic cancer (HR = 0.82 [95% CI 0.76 to 0.90], 6 studies), liver cancer (HR = 0.78 [95% CI 0.66 to 0.92], 3 studies), lung cancer (HR = 0.81 [95% CI 0.75 to 0.87], 5 studies), and stomach cancer (HR = 0.74 [95% CI 0.58 to 0.95], 4 studies). No statistically significant relationship was found between pre-diagnosis PA levels and cancer-specific mortality for bladder, brain, esophagus, gynaecologic, kidney, melanoma, pancreas, or prostate cancer. Meta-analysis found reduced hazards of mortality for those in the highest vs. lowest levels of **postdiagnosis** total recreational PA for all cancers combined (cancer-specific mortality (HR = 0.63 [95% CI 0.53 to 0.75], 4 studies), breast cancer (HR = 0.63 [95% CI 0.50 to 0.75], 13 studies), colorectal cancer (HR = 0.62 [95% CI 0.44 to 0.86], 6 studies), and prostate cancer (HR = 0.70 [95% CI 0.55 to 0.90], 4 studies).	MODERATE[b]	11 ESRs Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of breast cancer-specific mortality and all-cause mortality in female breast cancer survivors. **PAGAC Grade: Moderate** 8 ESRs Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of colorectal cancer-specific mortality and all-cause mortality in colorectal cancer survivors. **PAGAC Grade: Moderate.** 2 ESRs Moderate evidence indicates an inverse association between highest versus lowest levels of physical activity after diagnosis and prostate cancer-specific mortality in prostate cancer survivors. **PAGAC Grade: Moderate.**
Risk of cancer recurrence or second primary cancer									
No systematic review identified									Insufficient evidence is available to determine whether physical activity after diagnosis is associated with risk of breast cancer recurrence or second primary breast cancer. **PAGAC Grade: Not assignable.** Insufficient evidence is available to determine whether physical activity after diagnosis is associated with risk of colorectal cancer recurrence

	or second primary colorectal cancer. **PAGAC Grade: Not assignable.** Insufficient evidence is available on the association between physical activity level and prostate cancer recurrence or progression. **PAGAC Grade: Not assignable.**

Abbreviations: ACM = all-cause mortality; CI = confidence interval; HR = hazards ratio; NR = not reported; PA = physical activity; PAGAC = physical activity guidelines advisory committee

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[s] 136 total studies included; each analysis includes fewer studies
[b] Certainty of evidence downgraded given combination of experimental and observational designs

Table E.1.4.b. People with hypertension, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People with hypertension
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Risk of co-morbid conditions, physical function, health-related QOL, cardiovascular disease progression, cardiovascular mortality

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**	**US PAGAC evidence *(39)***
		Risk of bias	**Inconsistency**	**Indirect-ness†**	**Imprecision**	**Other**			
Risk of co-morbid conditions									
No systematic review identified									Insufficient evidence is available to determine whether a relationship exists between physical activity and risk of co-morbid conditions among adults with hypertension. **PAGAC Grade: Not assignable.**
Physical function									
Costa 2018 *(7)* Low	9 RCTs N=245	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Nine studies compared the effects of HIIT (60% men, mean age 57.8 years, mean BMI 30.6 kg/m^2) versus MICT (49% men, mean age 56.1 years, mean BMI 30.4 kg/m^2) including patients with chronic heart failure, coronary heart disease, MetS, abdominal obesity, and prediabetes on resting BP. Most studies included a 12- to 16-week intervention and were conducted in laboratory settings or cardiac rehabilitation centres under direct supervision. Pooled analyses suggested significant differences in **VO2max** in favour of HIIT interventions (MD 2.13 ml/kg/min [95% CI, 1.00 to 3.27], p<0.01).	HIGH[a]	Insufficient evidence is available to determine whether a relationship exists between physical activity and physical function among adults with hypertension. **PAGAC Grade: Not assignable.**

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty	US PAGAC evidence *(39)*
		Risk of bias	Inconsistency	Indirect-ness†	Imprecision	Other			
Health-related QOL									
Cao 2019 *(4)* Moderate	1 RCT N=103	No serious risk of bias	Serious inconsistency	No serious indirectness	No serious imprecision	None	Mean age of participants was 51 years; exercise intervention was 12 weeks vs. no exercise control group. Significant improvements were observed in the exercise group in all domains of the WHOQoL-BREF (physical health: +23.33, *p*<0.05; psychological health +18.17, *p*<0.05; social relationships; +14.51, *p*<0.05; environment: +11.51, *p*<0.05). The control group also showed improvements in physical health, psychological health, and social relationship domains.	MODERATE[b]	Insufficient evidence is available to determine whether a relationship exists between physical activity and health-related quality of life among adults with hypertension. **PAGAC Grade: Not assignable.**
CVD progression									
Cao 2019 *(4)* Moderate	14 RCTs N=860	No serious risk of bias	Serious inconsistency	No serious indirectness	No serious imprecision	None	Mean age ranged from 40 to 83 years. SBP at baseline ranged from 130.3 to 170.5 mm Hg and DBP at baseline ranged from 67.5 to 95.2 mm Hg. Duration of exercise interventions ranged from 40 minutes to 6 months. Compared with no exercise control groups, **SBP** and **DBP** were significantly reduced in pooled analysis among the exercise groups (SBP MD = -12.26 mm Hg [95% CI, -15.17 to -9.34] *p*<0.05; DBP MD = -6.12 mm Hg [95% CI, -7.76 to -4.48], *p*<0.05). Subgroup analyses found that interventions of shorter duration (with shorter follow-up, <8 weeks) achieved greater reductions in BP than those of longer duration (>12 weeks).	HIGH[c]	15 ESRs Strong evidence demonstrates that physical activity reduces the risk of progression of cardiovascular disease among adults with hypertension. **PAGAC Grade: Strong.** Strong evidence demonstrates that, among adults with hypertension, physical activity reduces the disease progression indicator of blood pressure. **PAGAC Grade: Strong.**
Costa 2018 *(7)* Low	9 RCTs N=245	No serious risk of bias	Serious inconsistency	No serious indirectness	No serious imprecision	None	Nine studies compared the effects of HIIT (60% men, mean age 57.8 years, mean BMI 30.6 kg/m^2) versus MICT (49% men, mean age 56.1 years, mean BMI 30.4 kg/m^2) including patients with chronic heart failure, coronary heart disease, MetS, abdominal obesity, and prediabetes on resting BP. Most studies included a 12- to 16-week intervention and were conducted in laboratory settings or cardiac rehabilitation centres under direct supervision. Pooled analyses found no differences between HITT vs. MICT groups in **SBP** (MD - 0.22 mmHg [CI 95%, - 5.36 to 4.92], *p* = 0.93) or **DBP** (MD - 0.38 mmHg [CI 95%, - 3.31 to 2.54], *p* = 0.74).	MODERATE[d]	

Abbreviations: BMI = body mass index; BP = blood pressure; CI = confidence interval; CVD = cardiovascular disease; DBP = diastolic blood pressure; ESR = existing systematic review; HIIT = high-intensity interval training; kg/m = kilograms per meter; MD = mean difference; MetS = metabolic syndrome mm Hg = millimetres of mercury; MICT = moderate-intensity continuous training; NR = not reported; PAGAC = Physical Activity Guidelines Advisory Committee; QOL = quality-of-life; RCT = randomized clinical trial; SBP = systolic blood pressure

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence not downgraded (certainty graded for **effects** on VO2max)
[b] Certainty of evidence downgraded given serious inconsistency (single study, unable to assess inconsistency)
[c] Certainty of evidence not downgraded
[d] Certainty of evidence downgraded given serious inconsistency (inconsistency in direction of effects across studies)

Table E.1.4.c. People with Type 2 Diabetes, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People with Type 2 Diabetes
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Risk of co-morbid conditions, physical function, health-related QOL, disease progression

Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**	**US PAGAC evidence *(39)***
		Risk of bias	**Inconsistency**	**Indirect-ness†**	**Imprecision**	**Other**			
Risk of co-morbid conditions									
Lauche 2017 *(15)* Moderate	0 RCTs	NA	NA	NA	NA	NA	No trials were identified that examined the effects of Tai Chi/qigong on stroke incidence among those with diabetes.	NA	3 ESRs Strong evidence demonstrates an inverse association between volume of physical activity and risk of cardiovascular mortality among adults with type 2 diabetes. **PAGAC Grade: Strong.**
Physical function									
Zhou 2019 *(36)* Moderate	2 RCTs N=NR	No serious risk of bias	No serious inconsistency	Serious indirect-ness	Serious imprecision	None	Studies evaluated **Tai Chi** among adults with T2D, mean age range 36 to 70 years. Mean sessions of exercise ranged from 15 to 120 min with 2 to 14 sessions per week. Total intervention duration ranged from 4 to 24 weeks. There were no effects of Tai Chi on measures of **balance** compared with controls (MD = 2.17 secs [single-leg stance] [95% CI, -3.29 to 8.71], 2 RCTs).	LOW[b]	1 ESR Insufficient evidence was available to determine the relationship between physical activity and physical function in adults with type 2 diabetes. **PAGAC Grade: Not assignable.**

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty	US PAGAC evidence *(39)*
		Risk of bias	Inconsistency	Indirect-ness	Imprecision	Other			
Health-related QOL									
Rees 2017 *(27)* Moderate	2 pre-post N=40	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	Studies evaluated effect of **aquatic exercise** vs. land-based exercises or no-exercise control groups. No significant differences was found before and after aquatic exercise for the physical function domain (SMD = 0.08 [95% CI, -2.80 to 2.96], 2 studies, n=40) or mental health domain (SMD = -0.36 [95% CI, -2.85 to 2.12], 2 studies, n=40) of the SF-36 or SF-12 forms.	LOW[c]	6 ESRs Insufficient evidence was available to determine the relationship between physical activity and health-related quality of life in adults with type 2 diabetes. **PAGAC Grade: Not assignable.**
Yu 2018 *(34)* Moderate	6 RCTs N=NR	Serious risk of bias	No serious inconsistency	No serious indirect-ness	Serious imprecision	None	Studies evaluated **traditional Chinese exercises** (Tai Chi, Ba duan jin, qigong) for patients with T2D, mean age range 49-70 years. Tai Chi was associated with greater improvements in the physical function domain (MD = 5.92 [95% CI 0.68 to 11.16], 5 RCTs), but not on the mental health domain of the SF-36 form. There was no effect of ba duan jin on QOL as reported by 2 studies.	LOW[d]	
Zhou 2019 *(36)* Moderate	5 RCTs N=NR	No serious risk of bias	Serious inconsistency	No serious indirect-ness	Serious imprecision	None	Studies evaluated **Tai Chi** among adults with T2D, mean age range 36 to 70 years. Mean sessions of exercise ranged from 15 to 120 min with 2 to 14 sessions per week. Total intervention duration ranged from 4 to 24 weeks. Tai Chi was associated with significant improvement in the physical function domain (MD = 7.07 [95% CI, -0.79 to 13.35], 5 RCTs), bodily pain domain (MD = 4.30 [95% CI, 0.83 to 7.77], 5 RCTs), and social function domain (MD = 13.84 [95% CI, 6.22 to 21.47], 5 RCTs) of the SF-36, but not the other 5 components of QOL.	LOW[e]	

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty	US PAGAC evidence *(39)*
		Risk of bias	Inconsistency	Indirect-ness	Imprecision	Other			
Disease progression[a]									
Jang 2019 *(13)* Low	23 RCTs or CCTs N=723	Serious risk of bias	Serious inconsistency	Serious indirect-ness	No serious imprecision	See next colu-mn	Studies compared **any exercise intervention** with no intervention among adults with diabetes in Korea, mean age 60 years. Compared with non-exercise control groups, exercise interventions were associated with a statistically significant difference in **HbA1c** (MD = -0.58% [95% CI, -0.80 to -0.27], 17 studies, n=425) at post-test. Greater reductions in HbA1c seen among those with higher HbA1c values at baseline. Studies of aerobic exercise or combined aerobic exercise and resistance training showed bigger effects on HbA1c than those testing resistance training only. No differences in effects according to exercise duration	VERY LOW[f]	34 ESRs Insufficient evidence was available to determine the relationship between physical activity and indicators of progression of neuropathy, nephropathy, retinopathy, and foot disorders. **PAGAC Grade: Not assignable.** Strong evidence demonstrates an inverse association between aerobic activity, muscle-strengthening activity, and aerobic plus muscle-strengthening activity with risk of progression among adults with type 2 diabetes, as assessed by overall effects of physical activity on four indicators of risk of progression: glycated hemoglobin A1C, blood pressure, body mass index, and lipids. **PAGAC Grade: Strong.** Insufficient evidence was available to determine the relationship between tai chi, qigong, and yoga exercise on four indicators of risk of progression: hemoglobin A1C, blood pressure, body mass index, and lipids. **PAGAC Grade: Not assignable.**
Liu, Ye, et al. 2019 *(20)* Moderate	24 RCTs N=962	No serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	Dose-respon-se effect[g]	Trials compared **resistance training** vs. control groups among persons with T2D (mean age range 45 to 71 years) with interventions ranging from 6 to 52 weeks. Resistance training was associated with greater reduction in **HbA1c** vs. control groups (MD = -0.45 [95% CI, -0.65 to -0.25], 20 trials, n=824). No differences were found in **fasting insulin** or **FBG** measures for all interventions; significant effects were found for high-intensity resistance training vs. control groups on fasting insulin (MD = -4.60 [95% CI, -7.53 to -1.67], 5 trials, n=174).	HIGH[h]	
Song 2018 *(29)* Moderate	39 RCTs N=2,917	No serious risk of bias	Serious inconsistency	No serious indirect-tness	No serious imprecision	None	Studies evaluated **traditional Chinese exercises** (Tai Ji Quan, Qigong, Ba Duan Jin) vs. no exercise intervention with T2D patients aged 41 to 80 years (mean age 59 years). Traditional Chinese exercises were associated with significantly greater reduction of percentage **HbA1c** (MD = -0.67% [95% CI -086% to -0.48%], 35 RCTS, n=2,940) and **FBG** (MD = -0.66 mmol/L [95% CI -0.95 to -0.37], 18 RCTS, n=1,433).	MODERATE[i]	
Systematic review evidence	**No. of studies/ Study design**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**	**US PAGAC evidence *(39)***
		Risk of bias	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**			

Review credibility	No. of participants								
Chao 2018 *(5)* Moderate	14 RCTs N=798	Serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	Evidence of small studies effect	Trials evaluated the effects of **Tai Chi** on markers of diabetes compared with non-exercise or exercise control groups. Mean age ranged from 48-64 years. Interventions ranged from 3 to 7 days/week for 4 to 24 weeks total duration. In pooled analysis, compared with non-exercise control groups, participants in the Tai Chi interventions had statistically significantly lower **FBG** (MD = -1.39 [95% CI, -1.95 to -0.84], 10 trials, n=489), **HbA1c** (MD = -0.73 [95% CI, -95 to -0.52), 7 trials, n=293), and **2hPBG** (MD = -2.07 [95% CI -2.89 to -1.26], 5 trials, n=82).	LOW[j]	
Lauche 2017 *(15)* Moderate	7 RCTs N = 361	Serious risk of bias	No serious inconsistency	No serious indirect-ness	No serious imprecision	None	Studies evaluated the effects of **Tai Chi or qigong** for the treatment of diabetes compared with no intervention, conventional exercise, sham exercise, or resistance training. Intervention duration ranged from 6 weeks to 6 months (median 12 weeks), with median sessions of 2 days/week. Pooled results showed statistically significant benefits of Tai Chi/qigong vs. no exercise control for **FBG** (MD = -8.88 mg/dL [95% CI, -16.73 to -1.03], 2 trials, n=85) and **HOMA** (MD = -2.86% [95% CI, 5.35 to -0.38], 2 trials, n=60). There was no effect on measures of **HbA1c** (MD = -0.46% [95% CI, -0.96 to 0.03), 4 trials, n=161). No differences were found when comparing Tai Chi/qiqong with other forms of exercise.	MODERATE[k]	
Systematic review evidence **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment**					**Description of evidence** **Summary of findings**	**Certainty**	**US PAGAC evidence** ***(39)***
		Risk of bias	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other**			
Xia 2019 *(33)* Low	17 RCTs N=NR	Serious risk of bias	Serious inconsistency	No serious indirect-ness	No serious imprecision	None	Studies evaluated the effects of **Tai Chi** vs. active or non-active control among individuals with T2D. Number of Tai Chi sessions ranged from 36 to 336, with most having 2 to 7 sessions weekly with 30-60 min per session. Tai Chi was associated with a significant effect on **FBG** (SMD = -0.54 [95% CI, -0.91 to -0.16], 13 RCTS, n=616) and **HbA1c** (SMD = -0.68 [95% CI, -1.17 to 0.19], 9 RCTs, n=517).	LOW[l]	
Yu 2018 *(34)* Moderate	22 RCTs 2 CCTs N=NR	Serious risk of bias	Serious inconsistency	No serious indirect-ness	Serious imprecision	None	Studies evaluated **traditional Chinese exercises** (Tai Chi, Ba duan jin, qigong) for patients with T2D, mean age range 49-70 years. Tai Chi practice for at least 150 min/week was associated with lowered **HbA1c** (MD = -1.48 [95%	VERY LOW[m]	

							CI, -2.58% to -0.39%], 6 RCTs) and **FBG** (MD = -1.14 mmol/L [95% CI, -1.78 to -0.50], 6 RCTs). Ba duan jin was significantly associated with **HbA1c** (MD = -0.77 [95% CI -0.97 to -0.56], 12 RCTS) and **FBG** (MD = MD = -0.82 mmol/L [95% CI, -1.005 to -0.59], 12 RCTs).		
Zhou 2019 *(36)* Moderate	23 RCTs N=1,234	No serious risk of bias	Serious inconsistency	No serious indirect-ness	No serious imprecision	None	Studies evaluated **<u>Tai Chi</u>** among adults with T2D, mean age range 36 to 70 years. Mean sessions of exercise ranged from 15 to 120 min with 2 to 14 sessions per week. Total intervention duration ranged from 4 to 24 weeks. Tai Chi was associated with significant improvement in **HbA1c** (MD=-0.88% [95% CI, -1.45 to -0.31], 14 RCTs) and **FBG** (SMD = -0.67 [95% CI, -0.87 to -0.47], 21 RCTs)	MODERATE[n]	

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty	US PAGAC evidence *(39)*
		Risk of bias	Inconsis-tency	Indirectness	Imprecision	Other			
Thind 2017 *(31)* Low	23 RCTs N=2,473	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	None	Studies evaluated the effects of **<u>yoga</u>** on adults with T2D (mean age, 53 years). Median number of yoga sessions was 50 with median duration of each session of 60 minutes. Intervention duration ranged from <1 week to 6 months. Yoga was associated with significant differences in **HbA1c** (ES = 0.36 [95% CI, 0.16 to 0.56], 16 RCTs) and **FBG** (ES = 0.58 [95% CI, 0.40 to 0.76), 20 RCTs) at 8 weeks or longer follow-up.	LOW[m]	
De Nardi *(8)*2018 Moderate	7 RCTs N=184	Serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	Trials comparing effects of **<u>HIIT vs. MICT</u>** in individuals with prediabetes (2 trials, n=64, mean age 52 years) and T2D (5 trials, n=120, mean age 61 years). Duration of interventions ranged from 12 to 16 weeks for trials among persons with T2D and 2 to 4 weeks for trials among persons with prediabetes. No differences were found between HIIT and MICT on measures of **FBG** (MD = 0.11 [95% CI, -0.45 to 0.67], 4 trials, n=82) or **HbA1c** (MD = -0.17 [95% CI -0.36 to 0.02], 5 trials, n=119) among patients with T2D. One study among patients with prediabetes found greater reduction in **FBG** among those in the MICT vs. HIIT groups.	MODERATE[k]	
Liu, Zhu, et al. 2019 *(19)* Moderate	13 RCTs N=345	No serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	None	Trials comparing effects of **<u>HIIT vs. MICT or no intervention</u>** in individuals with T2D. HIIT interventions ranged from 11 to 16 weeks with a median of 3 sessions/week with total training per session ranging from 30 seconds to 4 minutes. Statistically significant greater difference in changes in **HbA1c** among those in HIIT vs. MICT intervention groups (MD = -0.37 [95% CI, -0.55 to -0.19], 10 trials, n=220). No difference was found between HITT and no exercise control groups on HbA1c (MD =-0.39 (-0.81 to 0.02), 3 trials, n=63). No differences were found between HIIT vs. MICT or HIIT vs. non-exercise control groups on measures of **FBG, fasting insulin, or HOMA.**	LOW[o]	

Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Description of evidence Summary of findings	Certainty	US PAGAC evidence *(39)*
		Risk of bias	Inconsis-tency	Indirectness	Imprecision	Other			

Qui 2017 *(25)* Moderate	7 RCTs N=189	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	Patients with type 2 diabetes, mean age 59 years, mean BMI 30.4 kg/m^2. Studies evaluated **HIIT vs. MICT or no-exercise control groups**. Frequency of HITT ranged from 2 to 5 times per week, with total length (maximal exercise plus recovery interval) ranged from 20 to 60 minutes with most intervals lasting 1 to 4 minutes. Intervention duration ranged from 12 to 16 weeks. INT was associated with statistically significantly decreased **HbA1c** by 0.26% (95% CI, -0.46 to -0.07%, 5 RCTs) compared with MICT and by 0.83% (95% CI, -1.39% to -0.27%, 4 RCTs) compared with no-exercise control groups.	HIGH[h]	
Rees 2017 *(27)* Moderate	5 RCTs 4 pre-post N=222	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision	None	Studies evaluated effect of **aquatic exercise** vs. land-based exercises or no-exercise control groups. Most interventions lasted 8-12 weeks. No significant difference was found between land exercise and aquatic exercise on **HbA1c** (MD = -0.02% [95% CI, -0.71 to 0.66], 3 trials, n=83) or **FBG** (MD = -5.06 mg/dL [95% I, -12.32 to 2.21], 5 studies. There was a significant difference between aquatic exercise and no-exercise in **HbA1c** (MD = -0.96% [95% CI -1.87 to -0.05), 2 trials, n=60).	MODERATE[p]	

Abbreviations: 1RM = 1 repetition maximum; 2hPBG = two-hour postprandial blood glucose; BMI = body mass index; CCT = controlled clinical trial; CI = confidence interval; ES = effect size (Hedge's g); FBG = fasting blood glucose; HbA1C = hemoglobin A1c; HIIT = high-intensity interval training; HOMA = Homeostatic model assessment; INT = aerobic interval training; kg/m = kilograms per meter; MD = mean difference; mg/dL = milligrams per decilitre; MICT = moderate-intensity continuous training; NA = not applicable; SF-36 = short-form QOL questionnaire; SMD = standardized mean difference; T2D = type 2 diabetes

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Included measures of glycemic control; did not include measures of other cardiometabolic risk factors (i.e., blood pressures, lipids, adiposity)
[b] Certainty of evidence downgraded given serious indirectness in measures of effect and imprecision in effect estimates
[c] Certainty of evidence upgraded given no major limitations
[d] Certainty of evidence downgraded given serious risk of bias and imprecision in effect estimates (wide confidence intervals ranged from clinically significant to non-clinically significant)
[e] Certainty of evidence downgraded given serious inconsistency and imprecision (very wide confidence intervals)
[f] Certainty of evidence downgraded given serious risk of bias, serious inconsistency (heterogeneity) of effects, and serious indirectness (comparison of measures of HbA1c at post-test only)
[g] High-intensity interventions (intensity between 75% and 100% 1RM) were associated with greater differences in HbA1c vs. low-to-moderate intensity interventions (intensity between 20% and 75% 1RM)
[h] Certainty of evidence not downgraded
[i] Certainty of evidence downgraded given substantial heterogeneity in pooled analysis (I^2>80%)
[j] Certainty of evidence downgraded given serious risk of bias and possible publication bias
[k] Certainty of evidence downgraded given serious risk of bias for most included trials
[l] Certainty of evidence downgraded given serious risk of bias and inconsistency (I^2>70%)
[m] Certainty of evidence downgraded due to inconsistency and imprecision in effect estimates; not downgraded for risk of bias because the review did not assess this
[n] Certainty of evidence downgraded given serious inconsistency (heterogeneity) of effects
[o] As assigned by review authors. Certainty of evidence downgraded due to inconsistency and imprecision
[p] Certainty of evidence downgraded given serious imprecision (wide confidence interval in effect estimates)

Table E.1.4.d. People with HIV, relationship between physical activity and health-related outcomes

Table E.1.4.d.1 Effects of physical activity on health-related quality of life among people living with HIV

Questions: What is the association between physical activity and heath related quality of life (HRQOL? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People living with HIV
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcomes: Health-related quality of life (HRQOL)

Exercise modality	Study	No. of Studies No. of participants	AMSTAR2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsis-tency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	O'Brien, 2016 *(67)*	24 RCTs, N=936	High	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No publication bias	This is the 4th updated systematic review by this group. The Cochrane Collaboration protocol was used to search databases up to April 2013. The review included 24 RCTs that compared aerobic exercise (performed at least 3 times per week for at least 20 min for at least 5 weeks) with no exercise or another intervention, among adults living with HIV. Majority of participants were male (73%), and receiving antiretroviral therapy (19/24). The exercise interventions in which HRQOL was measured (N=9) were all conducted 3 x weekly, at at least 50% VO_2max, or between 6 and 24 weeks, for at least 30 and up to 120 min. Of these, 7 showed statistically significant improvements in HRQOL, with one additional study showing a trend, in the intervention groups compared to control conditions. Two meta-analyses showed statistically significant changes on the subscales of mental health, role-emotional, and physical functioning, role physical, general health, and vitality) in quality of life among exercisers when compared with those who did not exercise. Attrition ranged between 5% and 38%.	HIGH (+ve effect)
	O'Brien, 2010 *(69)*	14 RCTs, N=454	High	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No Serious publication bias	This study searched databases between 1980 and June 2009 and included only RCTs, that compared aerobic exercise interventions (at least 3 times per week, for at least 4 weeks, for at least 20 min) with no aerobic exercise interventions or alternative exercise or treatment modalities, Four studies specifically measured HRQOL (duration ranging from 6 to 24 wks) in exercising vs non-exercising groups and demonstrated significant improvements. No meta-analyses on HRQOL were conducted.	HIGH (+ve effect)
	Nixon, 2005 *(70)*	10 RCTs, N=276	High	Serious risk of bias	Serious inconsistency	No serious imprecision	Serious indirectness	No Serious publication bias	Four of the studies compared changes in HRQOL measured in persons undergoing interventions for aerobic exercise vs. no exercise (6- 15 wks) and demonstrated significant improvements. No meta-analyses on HRQOL were conducted..	LOW (+ve effect)
	O'Brien, 2004 *(73)*	10 RCTs, N=458 HIV+ only participants	high	Serious risk of bias	No Serious inconsistency	No serious imprecision	Serious indirectness	Serious publication bias	Meta-analysis was not possible due to the variety of outcomes used for psychological measures. Results of individual studies (Stringer 1998; Baigis, 2002, Lox et al., 1995), showed improvements in QoL in the exercise intervention groups.	MODERATE (+ve effect)

Resistance Exercise	O'Brien, 2017 *(66)*	20 RCTs, N=764	high	Serious risk of bias	Serious inconsistency	No serious imprecision	Serious indirectness	No Serious publication bias	Five individual studies found improvements in QoL and mood and life satisfaction scores among the exercise intervention groups (Agin 2001; Perez-Moreno 2007; Tiozzo 2011; Ogalha 2011). Bhasin (2000) found no change in HRQOL scores in either the testosterone or combined testosterone and exercise groups. Shevitz (2005) reported no significant change in QoL Adjusted Years within groups but reported the increase was greatest with combined progressive resistance exercise and nutrition compared with nutrition alone. The results are inconsistent.	LOW (inconclusive)
	O'Brien, 2008 *(74)*	10 RCTs, N=332	high	Serious risk of bias	Serious inconsistency	No serious imprecision	Serious indirectness	No Serious publication bias	This study performed a systematic review and meta-analysis using the Cochrane Collaboration guidelines where 14 online databases were searched from 1980 to June 2006. Despite the mixed findings reported, individual studies showed significant enhancements in HRQOL in the exercise intervention group compared to the participants in the whey protein only and whey protein and PRE groups (Agin, 2001). On the other hand, Bhasin, 2000 found no association between changes in HRQOL measures between comparison groups. Shevitz, 2005 reported no significant change in QoL adjusted years within groups. However, the greatest increase was in the combined exercise and nutrition group.	VERY LOW (inconclusive)
Multimodal Exercise	Ibeneme, 2019b *(65)*	19 RCTs, N=661 participants included for QoL.	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No Serious indirectness	No Serious Risk of Publication Bias	The study evaluates the impact of physical (aerobic and resistance) exercises on QoL in PLWHA by conducting a systematic review using the Cochrane Collaboration protocol. Databases were searched up to June 2017, only RCTs investigating the effects of either aerobic, resistance or a combination of both exercise types with a control/other intervention(s) for a period of at least 4 weeks among adults living with HIV, comprising male and female with age range 22–66 years were included. Two meta-analyses across 13 sub-group comparisons were performed. Meta-analysis showed that in all domains of QoL, only role activity limitation due to physical health had a significant effect [5.04 point (95% CI:-8.49, -3.74, p= 0.00001)]. Both studies show a positive effect of combined aerobic and resistance exercise on PLWHA on HAART. Overall, the GRADE evidence for this review was of moderate quality. There was evidence that engaging in moderate-intensity aerobic exercises (55–85% Maximum heart rate-MHR), for 30–60 min, 2-5 times/week for 6–24 weeks significantly improves role activity limitation. This corroborates Mutimura 2008 findings who found significant improvements in the exercise group for psychological, independence, and social relationships (p < 0.001) domains of QoL compared to the non-exercise group. Galantino	HIGH (+ve effect)

									2005 also found an improvement in QoL for participants in the combined exercise group compared to the control group in the overall health perception subscale (p=0.04).	
	Gomes Neto, 2015 *(68)*	7 RCTs, N=386	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No Serious indirectness	No serious publication bias	This study performed a meta-analysis to investigate the effects of a combination of aerobic and resistive exercise (CARE) in HIV-infected patients from the earliest date available to August 2014 for RCTs. There is consistent evidence that exercise is effective in improving QoL. All studies that assessed QoL showed improvements in QoL in the exercise group compared to the control. Ogalha 2011 reported improvements in the general health and vitality domains of HRQOL in the exercise group compared to no exercise (p=0.05). Mutimura 2008 found that psychological independence, social relationships and HIV+HAART-specific domains of HRQOL improved in the exercise group compared to no exercise (p=0.05). Fillipas 2006 also found that the overall health and cognitive function domains of HRQOL improved in the exercise group compared to no exercise (p=0.05). Finally, Rojas 2003 reported improvements in health status, emotional well-being, energy, physical strength and global quality of life compared to no exercise (p=0.05).	HIGH (+ve effect)
	Gomes Neto, 2013b	8 RCTs, N=NR	low	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious risk of publication bias	All studies that assessed HRQOL reported significant improvements in HRQOL in the experimental group compared to the control group. Mutimura 2008 reported that psychological, independence, social relationships, HIV-HAART-specific and QoL domains significantly improved in the exercise group compared to no exercise. Perez-Moreno 2007, although statistical significance was not reached for the combined effect of group and time (p=0.09), QoL significantly increased (p<0.01) in the experimental group, whereas no change was observed in the controls. Fillipas 2006 reported an improvement in overall health and cognitive function subscales of QoL in the experimental group. Rojas 2003 found better improvements in five subscales of QoL than in controls.	MODERATE (+ve effect)
	Bhatta, 2017 *(71)*	28 RCTs, N=4136	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	Of the 28 included studies, only six utilised exercise interventions (Cade, 2010; Fillipas, 2006; Galantino, 2005; Maharaj, 2011; Mutimura, 2008; Ogalha, 2011). The intervention duration ranged from 8 (Galantino, 2005) to 24 weeks (Fillipas, 2006; Mutimura, 2008; Ogalha, 2011) and the follow-up period ranged from 2 (Galantino, 2005) to 6 months (Fillipas, 2006; Mutimura, 2008; Ogalha, 2011). The exercise sessions lasted from 1 hour (Fillipas, 2006; Galantino, 2005; Maharaj, 2011; Ogalha, 2011) to 1 hour and 40 minutes in Cade (2010). Where reported, the mean age ranged from	MODERATE (+ve effect)

									33.6 (Maharaj, 2011) to 45.0 years (Cade, 2010). Only three studies were included in the meta-analyses in the studies that used an exercise intervention (Cade, 2010; Maharaj, 2011; Ogalha, 2011). The studies reported different findings for the different domains of quality of life in the intervention group (QoL). Cade (2010) found no improvement in overall health-related QOL, except for emotional well-being. On the contrary, Fillipas (2006) found improvements in general health, as well as cognitive function and self-efficacy. Maharaj (2011) found significant improvements in the physical and mental components of QOL. Mutimura (2008), on the other hand, found improvements in psychological well-being and social interaction domains of QOL. Galantino (2005) reported some enhancements in the functional domain of QOL. Ogalha (2011) found an improvement in general health, vitality, and mental health domains. In summary, the results of the six studies show us that exercise can improve certain aspects of QOL but not others in PLWH. Thus the results are inconclusive	

Abbreviations: N = no; PICO = population, intervention, comparator, outcome; RCTs = randomised controlled trials

1. O'Brien 2016: First, downgraded by the authors to LOW grade due to RoB due to performance bias and attrition bias (withdrawals of included studies were >15 %), publication bias was suspected, and due to variable heterogeneity on specific meta-analyses of sub scales ranging from (I^2 = 0 to 87 %). It was later upgraded to HIGH due to the evident dose-response relationship.
2. O'Brien 2010: Not downgraded even if RoB is unclear.
3. Nixon, 2005: Downgraded to LOW due to (a) RoB due to attrition bias as a result of high withdrawal rates ranging from 4-76% (b) indirectness which may have been caused by the heterogeneity of outcome measures. There is also inconsistency in the findings.
4. O'Brien, 2004: First downgraded to LOW because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used. The outcome was later upgraded to MODERATE due to the evident dose-response relationship.
5. O'Brien, 2017: LOW due to RoB because of high risk of performance and attrition bias; Inconsistency due to heterogeneity present due to participants' variability in ART, body composition, comorbidity, gender, type and location of intervention and methods of outcome measurement.
6. O'Brien, 2008: Downgraded to VERY LOW because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the Hawthorn effect. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants.
7. Ibeneme 2019b: First graded MODERATE due to RoB due to attrition. This was then upgraded to HIGH due to the evident dose-response relationship.
8. Gomes Neto, 2015: First graded as MODERATE due to RoB because the risk to selective reporting was uncertain and none of the studies described blinding of therapists. This was later upgraded to HIGH due to the evident dose-response relationship evident in the results.
9. Bhatta, 2017: Graded to MODERATE due to serious risk of bias (since none of the included studies reported a strong internal or external validity and quality of evidence) and indirectness. There is also heterogeneity due to differences in target population, exercise interventions, delivery persons, assessment tools, duration of intervention and follow up and study duration. In all included studies, there is evidence of a dose-response relationship for selected QOL domains. The findings of the meta-analysis on the effects of exercise on QOL are also domain-specific (Cade, 2010; Maharaj, 2011; Ogalha, 2011), and overall these results are inconclusive, domain-specific mainly due to the fact that QOL is a multi-dimensional construct.

Table E.1.4.d.2: Effects of physical activity on body composition among people living with HIV

Questions: What is the association between physical activity and body composition? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People living with HIV
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcomes: Body mass index, waist and hip circumference, body fat percentage, lean body mass, fat mass, skeletal muscle mass

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsis-tency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	O'Brien, 2016 *(67)*	24 RCTs, N=936	high	**Body mass index (BMI)**					Results showed no change in BMI of participants for four comparisons in the aerobic or combined aerobic and PRE group compared with non-exercising control; constant aerobic exercise compared with non-exercising control; combined aerobic and PRE exercise group compared with non-exercising control and combined aerobic exercise and diet/nutrition counselling group compared with diet/nutritional counselling group only.	HIGH (no effect)
				No serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No publication bias		
				Lean body mass					Meta-analyses of 3 studies, n=68 showed a significant increase in lean body mass of weighted mean difference 1.75 kg (95% CI 013, 3.37,p=0.03] 4 studies, n=89}) for participants in the aerobic or combined aerobic and PRE group compared with participants in the non-exercising control group. No difference in lean body mass was reported for participants in the combined aerobic and PRE exercise group compared with non-exercising control group.	MODERATE (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Leg muscle area					In 2 studies,(Dolan 2006, Grinspoon 2000,, n=60) which had low heterogeneity at 11%, a significant increase in change in weighted mean difference of 4.79 cm^{2}([95%CI 2.04, 7.54 ,p=0.0007]2 studies, n=60 in leg muscle area among participants in the combined aerobic and PRE group compared with the non-exercising control group.	MODERATE (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Percentage body fat					Meta analyses of 2 studies, n=119 showed a significant decrease of weighted mean of 1.12% body fat[95%CI −2.18, −0.07,p=0.04 was found for participants in the constant aerobic exercise group compared with participants in the non-exercising control group . There was also found a significantly greater decrease in percent body fat of 2.35 % 95%CI−4.20, −0.50,p=0.01]2 studies, n=93] was reported among participants in the combined aerobic exercise and diet or nutrition counselling group compared with diet or nutritional counselling group..	HIGH (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		

									heterogeneity was moderate at 46%, but not significant.	
				Fat mass					There was no change in fat mass for two comparisons of participants in the aerobic or combined aerobic {4 studies, n=102and PRE group compared with non-exercising control, and combined aerobic and PRE exercise group compared with non-exercising control{3 studies,n=81]	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Waist and hip circumference and waist-to-hip ratio					No significant differences were found in waist circumference, hip circumference or waist-to-hip ratio for participants in the aerobic or combined aerobic and PRE group compared with non-exercising control; as well as participants in the constant aerobic versus exercise groups and combined aerobic and PRE exercise groups. Results found a slight increase in waist-to-hip ratio of 0.02 for participants in the combined exercise and diet or nutrition counselling group compared with diet or nutritional counselling group, however, these results were not clinically important.	MODERATE (inconclusive)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
	O'Brien, 2010 *(69)*	14 RCTS, N= 454	high	**BMI**					Age of participants range from 18 – 58 years, about 30 % were female. Nine studies assessed body composition with duration of intervention ranging from 12-24 weeks ,3 times a week for 30-120 mins.. Eleven meta-analyses were completed, of which 4 included the same studies and were duplicates. Results showed no change in BMI (WMD: 0.85kg/cm2, 95% CI: -0.62, 2.31, n=49, *P*=0.26) (Lox 1995, Perna 1999) for participants in the aerobic exercise group compared with participants in the non-exercising control group, and no difference in change in fat mass (WMD: 0.07 kg, 95% CI: -1.22, 1.36, n=60, *P*=0.92) (Grinspoon 2000, Dolan 2006) for participants in the combined aerobic and PRE group compared with the non-exercising control group.	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Hip circumference					No change was reported in hip circumference (WMD: 0.11cm, 95% CI: -0.63, 0.85, n=142, *P*=0.77) (Smith 2001, Mutimura 2008a) for participants in the aerobic exercise groups compared with participants in the non-exercising control groups, as well as participants in the constant aerobic exercise groups compared with the non-exercising control groups.	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No publication bias		

				Waist circumference					Results showed no difference in change in waist circumference (WMD: -3.53cm, 95% CI: -10.25, 3.19, n=142, *P*=0.30) (Smith 2001, Mutimura 2008a) for participants in the aerobic exercise groups compared with participants in the non-exercising control groups, as well as participants in the constant aerobic exercise groups compared with the non-exercising control groups.	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Waist-to hip ratio (WHR)					Results showed no change in waist-to-hip ratio (WMD: -0.51, 95% CI: -1.47, 0.45, n=142, *P*=0.30) (Smith 2001, Mutimura 2008a) for participants in the aerobic exercise groups compared with participants in the non-exercising control groups, as well as participants in the constant aerobic exercise groups compared with the non-exercising control groups.	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Percent body fat					Meta-analyses showed a significant decrease in percent body fat of 1.12% (95% CI: -2.18, -0.07, n=119, *P*=0.04) (Lox 1995, Mutimura 2008a) for participants in the aerobic exercise group compared with participants in the non-exercising control group.	MODERATE (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Leg muscle area					Meta-analysis also showed a significant increase in leg muscle area of 4.79 cm^2 among participants in the combined aerobic and PRE group compared with the non-exercising control group (95% CI: 2.04, 7.54, n=60, *P*=0.0007) (Grinspoon 2000, Dolan 2006).	MODERATE (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
Resistance Exercise	O'Brien, 2017 *(66)*	20 RCTs, N=764	high	**BMI**					Mean age range of participants(men =77%) was 32- 49 years with PA interventions of at least 3 times a week for at least 20 mins ranging from 6-52 weeks. Nineteen of the RCTS assessed body composition. . Sixteen meta-analyses were performed, each for body mass index, lean body mass, fat mass, arm and thigh girth, leg muscle area, and waist circumference. Results demonstrated no change in BMI for three comparisons of participants (i) in the PRE or combined PRE and aerobic exercise group compared with non-exercising control; (ii) combined PRE and aerobic exercise group compared with non-exercising control and (iii) combined PRE (or combined PRE and aerobic exercise) and diet/nutrition counselling group compared with diet/nutritional counselling group.	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		
				Lean body mass					Meta-analyses demonstrated no change in lean body mass for three comparisons of	LOW (no effect)

				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	participants (i) in the PRE or combined PRE and aerobic exercise group compared with non-exercising control; (ii) combined PRE and aerobic exercise group compared with non-exercising control and (iii) combined PRE (or combined PRE and aerobic exercise) and testosterone group compared with the testosterone only group.	
				leg muscle area					Results for leg muscle area results demonstrated a significant increase in change in leg muscle area of 4.79 cm^2 in 2 studies(Dolan 2006]; Grinspoon 2000., n=60 95%CI 2.04, 7.54, p=0.0007among participants in the combined PRE and aerobic exercise group compared with the non-exercising control No difference was found in leg muscle area for participants in the PRE (or combined PRE and aerobic exercise) and testosterone group compared with the testosterone only group.	LOW (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		
				Fat mass					Results demonstrated no change in fat mass for three comparisons of participants (i) in the PRE or combined PRE and aerobic exercise group compared with non-exercising control; (ii) combined PRE and aerobic exercise group compared with non-exercising control, and (iii) combined PRE (or combined PRE and aerobic exercise) and testosterone group compared with	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		
				waist circumference					No significant differences were found in change in waist circumference for participants in the combined PRE and aerobic exercise group compared with no exercise.	LOW (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		
				arm and thigh girth					Results demonstrated a significant increase in change in arm and thigh girth of 7.91 cm among participants in 2 studies (Lox 1995 ; Spence 1990 ,n=46 95% CI 2.18, 13.65, p=0.007)in the PRE group compared with the aerobic exercise group. The point estimate is greater than 5 cm, therefore indicating a potential clinically important greater increase in girth among PRE versus aerobic exercisers. Heterogeneity was present in meta-analysis for arm and thigh girth.	MODERATE (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		

	O'Brien, 2008 *(74)*	10 RCTs, N=332	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	Age of the participants ranges from 18-66 years(women<30%) . PA intervention was at least 3x a week for a from 6-16 weeks. Nine of the 10 studies assessed weight and/or body composition. Six meta-analyses were performed for body composition. Meta-analysis showed a statistically significant and clinically important increase in arm and thigh girth of 7.91cm (95%CI: 2.18, 13.65; p0.007; n46) for participants in the PRE or combined PRE and aerobic exercise intervention group compared to the non-exercising control group. Given that many participants in the individual studies were diagnosed with AIDS-related wasting syndrome, increases in body composition may be interpreted as a favourable outcome. This meta-analysis was statistically significant for heterogeneity (p = 0.08; I^2 = 67.4%) using a random effects model. Reasons for heterogeneity may be attributed to the different methods in which mean arm and thigh girth was measured between studies. The other five meta-analyses for body composition showed no difference among groups.	MODERATE (+ve effect)
	Poton, 2017 *(78)*	13 RCTs, N=291	moderate	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	The mean age of participants in the individual trials was 40.2 ± 4.8 years with PA intervention ranging from 6-24 weeks for at least 3 days a week. Seven of the 13 studies assessed lean body mass with RT intervention ranging from 12-24 weeks for at least 3 days a week. The bias-corrected standardised mean difference (Hedges' g) was used to assess effect size (g) measure to quantify lean body mass after progressive resistance training. In general, there was no change in lean body mass (LBM), with an overall effect size of 0.26 (−0.001 to 0.52; p = 0.051). In addition, there was low heterogeneity for trials investigating lean body mass (I^2 = 0.00; p = 0.88). However, the quality of included studies for lean body mass (score PEDro = 5) was low, which leaves open the possibility that various biases to exist and limit the generalisation of these results	MODERATE (no effect)
Multimodal Exercise	Pedro, 2017 *(72)*	5 RCTs, N=253	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No publication bias	Intervention duration ranged from 12- 24 weeks , 3 days a week for a least 20 mins. All 5 studies assessed body fat percentage. The authors found a decrease in body fat percentage in response to aerobic and concurrent training. There was also a reduction in trunk and limb fat and an increase in lean mass. Furthermore, one	HIGH (+ve effect)

									study showed that body fat percentage decreased after aerobic training. One of the limitation was that authors of this study did not conduct heterogeneity test among the studies together with small sample size. In summary, it might not be possible to conclude that physical training improves body composition; therefore, more studies are needed, using validated methods to investigate the effects of different types of training on body composition in individuals with HIV-associated lipodystrophy.	
	Filippas 2006 *(80)*	9 RCTs, N=469	low	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No publication bias	Mean age of participants in the studies ranged from 18 to 71 years with 41% of them female within RCTs where the interventions were either aerobic, progressive resistance exercises or a combination of the two (at least 2 times a week for at least 20 mins for 6-24 weeks). The results showed that compared to non-exercising controls, aerobic exercise (AE) resulted in decreased body mass index (weighted mean difference [WMD] −1.31; 95% CI, −2.59, −0.03; n=186), triceps skinfold thickness of subcutaneous fat (WMD −1.83 mm; 95% CI, −2.36, −1.30; n=144), total body fat (%) (standardised mean difference [SMD], −0.37; 95% CI, −0.74, −0.01; n=118), waist circumference (SMD −0.74 mm, 95% CI, −1.08, −0.39; n=142), and waist-hip ratio (SMD −0.94; 95% CI, −1.30, −0.58; n=142). Progressive resistive exercise (PRE) resulted in increased body weight (5.09 kg; 95% CI, 2.13, 8.05; n=46) and arm and thigh girth (SMD 1.08 cm; 95% CI, 0.35, 1.82; n=46). Aerobic exercise decreases adiposity and may improve certain lipid subsets. PRE increases body weight and limb girth.	MODERATE (+ve effect)

Abbreviations: PICO = population, intervention, comparator, outcome; RoB = risk of bias; RCTs = randomised controlled trials

1. O'Brien, 2016

- BMI: The authors of the review did not downgrade BMI on the GRADE quality of evidence because this was an objective outcome of interest and publication bias was not suspected.
- Lean body mass: Downgraded to MODERATE due to attrition and performance bias reported in the review
- Leg muscle area: Downgraded to MODERATE due to attrition and performance bias reported in the review
- Percentage body fat: Downgraded to MODERATE due to attrition and performance bias. Upgraded from MODERATE to HIGH due to large magnitude of effect.
- Fat mass: Downgraded to MODERATE due to attrition and performance bias reported in the review.
- Waist and hip circumference and waist-to-hip ratio: Downgraded to MODERATE due to attrition and performance bias reported in the review.

2. O'Brien, 2010

BMI; Hip circumference; waist circumference; waist-to hip ratio; percent body fat, fat mass, leg muscle area: were downgraded to MODERATE due to attrition bias because of high withdrawal rates in most of the studies (>15%) and also because of lack of blinding which may have resulted in performance bias .

3. O'Brien, 2017

- BMI: Graded MODERATE because the authors of the review were moderately confident in the effect estimate of a non-significant increase of 0.40 kg/m^2 for body mass index comparing PRE (or combined PRE and aerobic exercise) with no exercise. The outcome was downgraded on the certainty of evidence because publication bias was suspected and that withdrawal rates among the majority of included studies were >15%.
- Lean body mass; Leg muscle area; Waist circumference: Downgraded to LOW because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention.
- Fat mass: The authors of the review graded the outcome as MODERATE because they were moderately confident with the effect estimate of a non-significant increase of 0.36 kg in fat mass comparing PRE (or combined PRE and aerobic exercise) with non-exercising control. The outcome was downgraded on the certainty of evidence due to incomplete outcome data (withdrawals of included studies were >15%).
- Arm and thigh girth: First downgraded to VERY LOW because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention. Furthermore, heterogeneity was reported in the meta-analyses done for arm and thigh girth. The very low GRADE was then upgraded to MODERATE due to the evident dose-response relationship in the results.

4. O'Brien, 2008: Downgraded to LOW because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the performance bias. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants. The LOW grade was then upgraded to MODERATE due to the evident dose-response relationship evident in the results.

5. Poton 2017: Downgraded to MODERATE due to possible serious RoB as there was no clear description of randomization, concealment of allocation. Also, the quality of included studies for lean body mass (score PEDro = 5) was low, which leaves open the possibility that various biases to exist and limit the generalisation of these results. There was also evidence of indirectness in the review.

6. Pedro, 2017: downgraded to MODERATE due to indirectness which might have been caused by different type of individual indifference studies, and different type of intervention and different type of assessment methods. The MODERATE grade was then upgraded to HIGH due to the evident dose-response relationship evident in the results.

7. Fillipas, 2006: Downgraded to LOW due to serious RoB as there was no clear description of randomization, concealment of allocation and blinding, average of >15% withdrawal rates among the studies that assessed body composition with one of the study having 51% withdrawal rate. There was also evidence of indirectness in the review and a substantial level of heterogeneity for body fat mass and waist to hip ratio. However, due to evidence of a large dose-response relationship, we then upgraded the certainty to MODERATE.

Table E.1.4.d.3: Effects of physical activity on anxiety/depression among people living with HIV

Questions: What is the association between physical activity and anxiety and depression? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People living with HIV
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Symptoms of anxiety or depression

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsis-tency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	O'Brien, 2016 *(67)*	24 RCTs, N=936	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	Mean age ranged from 30 – 45. Males accounted for 73 % of overall participants. Duration of exercise ranged from 5 – 52 weeks, 3 times a week for 20 – 120 min. Of the 24 studies that met the inclusion criteria, only 2 studies were included in a meta-analysis,(N = 65) for anxiety and depression. One meta-analysis was performed and demonstrated a significant improvement in the depression-dejection sub scale of the Profile of Mood States Scale (POMS) by a reduction of 7.68 points for participants in the aerobic exercise intervention group compared with the non-exercising control group. This represents a clinically important improvement in depression-dejection among exercisers compared to non-exercisers.	MODERATE (+ve effect)
	O'Brien, 2010 *(69)*	14 RCTs, N=454	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	Age of participants range from 18 – 58 years, about 30 % were female. Duration of exercise ranged from 5 – 24 weeks, 3 times a week for at least 20 min. Only 2 studies were included in a meta-analysis. One meta-analysis was performed and showed a significant improvement in the depression-dejection subscale of the POMS by a reduction of 7.68 points (95% CI: -13.47, -1.90, n=65, *P*=0.009) for participants in the aerobic exercise intervention group compared with the non-exercising control group (LaPerriere 1990, Smith 2001). This represents a clinically important improvement in depression-dejection among exercisers compared to non-exercisers.	HIGH (+ve effect)

	Nixon, 2005 *(70)*	10 RCTs, N=276	high	Serious risk bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	Age of participants ranged from 10 – 58 years, less than 15 % were females. Duration of exercise ranged from 5-24 weeks, 3 times a week for at least 20 min. Only 2 studies were included in a meta-analysis. Meta-analysis demonstrated a significant improvement in the depression-dejection subscale of the POMS by a reduction of 7.68points (95% CI: -13.47, -1.90, n=65, p=0.009) for participants in the aerobic exercise intervention groups compared to the non-exercising control groups (LaPerriere 1990; Smith 2001). This represents a clinically important improvement in depression-dejection among exercisers compared to non-exercisers. LaPerriere 1990 found higher levels of anxiety and depression in non-exercising controls compared with exercisers. Smith 2001 (or Neidig 2003) found significant improvements in depression for exercisers compared to non-exercisers.	HIGH (+ve effect)
	O'Brien, 2004 *(74)*	10 RCTs, N=458 HIV+ only participants	high	Serious of bias	No serious inconsistency	No serious imprecision	No serious indirectness	Serious publication bias	Age of participants ranged from 18 – 58 years. Duration of exercise ranged from 4 – 24 weeks, 3 times a week for 20 to 60 min. Meta-analysis was not possible for psychological status due to the variety of outcomes used. Results of psychological measures of individual studies showed improvement in anxiety and depression (LaPerriere 1990).	LOW (+ve effect)
Resistance Exercise	No systematic reviews identified									
Multi-modal Exercise	Heissel, 2019 *(81)*	10 RCTs, N=479	low	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	Serious publication bias	Participants were 18 years and older. About 49.6 % were females. Duration of exercise was from 4 – 12 weeks, 2 – 6 times a week for 45 – 60 min. Nine studies investigated depression (n = 194 in the exercise group, n = 201 in the control group). An overall standardized mean difference SMD = −0.84 (95% CI -1.57 to −0.11) in favour of the exercise group was found in the random-effect model for post-intervention values. There was a significant overall effect (Z = 2.27, p = 0.02) of exercise compared to the control group at post-treatment. Statistical heterogeneity was high (I2 = 91%, X2 = 87.82, df = 8, p < 0.001). Five studies investigated anxiety (n = 92 in the exercise group, n = 93 in the control group). An overall standardized mean difference SMD = −1.23	MODERATE (+ve effect)

									(95% CI -2.42 to −0.04) in favour of the exercise group was found in the random-effect model for post-intervention values. There was a significant overall effect (Z = 2.03, p = 0.04) of exercise compared to the control group at post-treatment. Pre-post analysis showed that the SMD difference in the depression post analysis (−0.84) and pre-post analysis (−0.91) was 0.07 favouring the pre-post analysis. A minimal difference in SMD post minus pre-post was found for anxiety (0.04) favouring the pre-post analyses. Therefore, no substantial differences between the results and heterogeneity between post and pre-post analyses exist.	

Abbreviations: PICO = population, intervention, comparator, outcome; RoB = risk of bias; RCTs = randomised controlled trial

1. O'Brien, 2016: Downgraded to MODERATE due to attrition and performance bias.
2. O'Brien, 2010: Not downgraded due to large effect size.
3. Nixon, 2005: Downgraded to MODERATE due to high withdrawal rates amongst the included studies. It was then upgraded to HIGH due to the evident dose-response relationship in the results.
4. O'Brien, 2004: Downgraded to LOW because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used. .
5. Heissel 2019: First rated LOW because of the possibility of risk of bias because, for the 10 studies that were included, five studies were graded as having good methodological quality and low risk of bias and the remaining five studies were rated as low quality studies and high risk of bias. Furthermore, Egger's test showed a publication bias for depression (bias = −8.24 (CI 95% 16.41 to −0.06). No publication bias was found for anxiety (bias = −9.66 (CI 95% -36.97 to 17.64). However, the results showed a considerable and indisputable dose-response relationship for both depression and anxiety even after sensitivity analysis. Thus, the LOW grade was upgraded to MODERATE.

Table E.1.4.d.4: Effects of physical activity on fitness and functional capacity among people living with HIV

Questions: What is the association between physical activity, functional capacity and fitness? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People living with HIV
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Measures of fitness and functional capacity (VO_2max, Exercise time, strength)

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	**Inconsistency**	**Imprecision**	**Indirectness**	**Publication Bias**		
Aerobic Exercise	O'Brien, 2016 *(67)*	24 RCTs, N=936	high	**VO_2max**					The mean age of participants in this study ranged from 30-49 years with 73 % males. Duration of exercise ranged from 6 – 52 weeks, 3 times a week for 20 – 120 min. Six meta-analyses were performed for $\dot{V}O_{2max}$, five of which were significant favouring exercise compared with non-exercise. Meta-analyses showed a significant improvement in $\dot{V}O_{2max}$ of 2.63 mL/kg/min for participants in the aerobic exercise intervention group compared with the non-exercising control group; significant improvement occurred in $\dot{V}O_{2max}$ of 2.40 ml/kg/min for participants in the constant aerobic exercise group compared with the non-exercising control group; significant improvement occurred in $\dot{V}O_{2max}$ of 3.71 ml/kg/min for participants in the combined aerobic and PRE group compared with the non-exercising control group; significant improvement occurred in $\dot{V}O_{2max}$ of 2.87 ml/kg/min for participants in the aerobic or combined aerobic and PRE group compared with non-exercising control group and a trend towards an improvement in $\dot{V}O_{2max}$ of 4.30 mL/kg/min for participants in the heavy-intensity exercise group compared with the moderate-intensity exercise group. No significant difference in $\dot{V}O_{2max}$ was found for participants in the combined aerobic exercise and diet or nutrition counselling group compared with the diet or nutrition	VERY LOW (+ve effect)
				No Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		

									counselling group. All point estimates were greater than 2 mL/kg/min, which suggested a potentially clinically important improvement in $\dot{V}O_{2max}$ among exercisers, and a greater improvement with heavy- versus moderate-intensity exercise.	
				Maximum Heart Rate (HRmax)					Duration of exercise ranged from 12 – 16 weeks, 3 times a week for 45 – 135 min. Three meta-analyses showed a non-significant trend towards a decrease in HR_{max} of −9.81 beats/min, 7.33 beats/min and 4.91 beats/min for participants in the aerobic exercise intervention group compared with the non-exercising control group; aerobic or combined aerobic and PRE group compared with the non-exercising control; and combined aerobic and PRE compared with non-exercising control, respectively.	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Exercise time					Duration of exercise ranged between 20-120-min three times per week for 12-52 weeks. Two meta-analyses showed significant increases in exercise time of 3.29 min for participants in the combined aerobic and PRE group compared with the non-exercising control group; and 2.66 min for participants in the aerobic or combined aerobic and PRE group compared with the non-exercising control group. Point estimates did not reach the 5 min threshold for clinical importance.	HIGH (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Strength					Duration of exercise ranged between 20-120 min three times per week for 12-52 weeks	LOW (+ve effect)

				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	Meta-analyses showed significant improvements in upper and lower body strength as measured by increases in 1-repetition maximum for chest press, and knee flexion; and a non-significant improvement in 1-RM for leg press and knee extension for participants in the combined aerobic and PRE group versus the non-exercising control group. There were significantly greater increases in strength among participants in the PRE group compared with to the aerobic exercise only group for upper and lower body muscle groups. All six-point estimates for upper and lower extremity strength were greater than 2 kg and 5 kg, respectively, indicating a clinically important increase in strength for resistive exercise compared with aerobic exercise.	
	O'Brien, 2010 *(69)*	14 RCTs, N=454	high	**VO_2max**					The age of the participants ranged from 18-58 years and ~70% were males. Participants exercised 30-90 min three times per week for 12-24 weeks Three meta-analyses showed a significant improvement in $\dot{V}O_{2max}$ of 2.63 mL/kg/min for participants in the aerobic exercise intervention group compared with the non-exercising control group (95% CI: 1.19, 4.07, n=276, p=0.0003) (Perna, 1999; Smith, 2001; Stringer, 1998; Baigis, 2002; Mutimura, 2008a); significant improvement occurred in $\dot{V}O_{2max}$ of 2.40 ml/kg/min for participants in the constant aerobic exercise group compared with the non-exercising control group (95% CI: 0.82, 3.99, n=248, p=0.003) (Stringer, 1998; Smith, 2001; Baigis, 2002; Mutimura, 2008a); and a trend towards an improvement in $\dot{V}O_{2max}$ of 4.30 mL/kg/min for participants in the heavy-intensity exercise group compared with the moderate-intensity exercise group (95% CI: 0.61,7.98, n=24, p=0.02). All point estimates were greater than 2 mL/kg/min, which suggested a potentially clinically important improvement in $\dot{V}O_{2max}$ among exercisers, and a greater improvement with heavy- versus moderate-intensity exercise.	HIGH (+ve effect)
				Serious Risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Maximum Heart Rate (HRmax)					Participants exercised 45 min three times per week for 12 weeks One meta-analysis showed a non-significant decrease in HR_{max} of -9.81 beats/min (95% CI: -26.28, 6.67, n=49, p=0.24) for participants in the aerobic exercise intervention group compared with the non-exercising control group (Lox, 1995; Perna, 1999).	HIGH (+ve effect)
				No serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		

				Exercise Time (minutes)					Participants exercised 60-120 min three times per week for 12-16 weeks. One meta-analysis showed a non-significant increase in exercise time of 3.92 minutes (95% CI: -0.63, 8.47, n=62, p=0.09) for participants in the combined aerobic and PRE group compared with the non-exercising control group (Rigsby, 1992; Dolan, 2006).	HIGH (+ve effect)
				No serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Strength					Participants exercised 20-120 min three times per week for 12-16 weeks. Six of the 14 included studies assessed muscle strength (Rigsby, 1992; Lox, 1995; Perna, 1999; Grinspoon, 2000; Driscoll, 2004a; Dolan, 2006). Meta-analysis could not be performed for strength, due to differences in the types of strength outcomes assessed, types of interventions, types of comparison groups, and types of participants; however, individual studies suggested improvements in strength among exercisers compared with non-exercisers.	LOW (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		
	Nixon, 2005 *(70)*	10 RCTs, N=276	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	The age of the participants in this study ranged from 18-58 years and ~70% were males. Participants exercised 30-40 min three times per week for 6-15 weeks. Nine of the 10 included studies reported cardiopulmonary outcomes, six of which compared constant or interval aerobic exercise to non-exercising controls (Baigis, 2002; LaPerriere, 1990; Lox, 1995; Perna, 1999; Smith, 2001; Stringer, 1998). Meta-analysis showed a non-significant improvement in $\dot{V}O_{2max}$ of 1.8 ml/kg/min (95% CI: -0.5, 4.2, n=179, p=0.13) for participants in the aerobic exercise intervention group compared to the non-exercising control group (Baigis, 2002; Perna, 1999; Smith, 2001; Stringer, 1998). The confidence interval demonstrated a positive trend towards improvement in $\dot{V}O_{2max}$ in the exercise group.	MODERATE (+ve effect)
	O'Brien, 2004 *(73)*	10 RCTs, N=458 HIV+ only participants	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	Serious publication bias	The age of the participants in this study ranged from 18-58 years. Participants exercised 30-45 min three times per week for 6-15 weeks. Nine studies assessed cardiopulmonary status (Rigsby, 1992; MacAthur, 1993; Jadad, 1996; Stringer, 1998; Ledergerber, 1999; Perna, 1999; Terry, 1999; Smith, 2001; Baigis, 2002). Significant improvements were found among individual trials of aerobic exercisers when compared with non-exercising controls, but meta-analysis could only be performed using	HIGH (+ve effect)

									$\dot{V}O_{2max}$ due to varying outcomes reported. Three meta-analyses showed non-significant improvement in $\dot{V}O_{2max}$ of 1.84 mL·kg^{-1}·min^{-1} (95% CI:-0.53, 4.20, n=179) for participants in the aerobic exercise intervention group compared with the non-exercising control group; non-significant improvement occurred in $\dot{V}O_{2max}$ of 1.56 mL·kg^{-1} ·min^{-1} (95% CI: -0.94, 4.07, n=151) for participants in the constant exercise group compared with the non-exercising control group, and statistically non-significant improvement occurred in $\dot{V}O_{2max}$ of 4.29 mL·kg^{-1} ·min^{-1} (95% CI: -1.23, 9.82, n=24) for participants in the heavy-intensity aerobic exercise group compared with participants in the moderate-intensity exercise group. This finding reached clinical importance, but not statistical significance.	
Resistance Exercise	Poton, 2017 *(78)*	13 RCTs, N=291	moderate	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	The mean age of the participants (43.1% female) in this study was 40.2 ± 4.8 years. The mean training duration was 14.6 ± 5.3 weeks with a frequency of three times a week. Improvements occurred in muscular strength with resistance exercise with an overall effect size of 1.58 (1.46–1.70; p<0.01; ~35.5%). In addition, the I^2 statistic confirmed high heterogeneity for trials that investigated muscular strength (I^2=66.28; P<0.001).	MODERATE (+ve effect)
	O'Brien, 2008 *(74)*	10 RCTs, N=332	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	The age of the participants in this study ranged from 18-66 years old (<30% females). Participants exercised approximately 20-25 min ranging from 1-5 sets of 4-18 repetitions three times per week for 6-16 weeks. Two studies evaluated sub-maximum heart rate (Lox, 1995; Rigsby, 1992). Meta-analysis showed a non-significant reduction in heart rate of -13.02 beats/minute (95% CI: -26.67, 0.64; p=0.06; n=46) for participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group. The confidence interval indicated a trend towards a clinically important improvement in sub-maximum heart rate among exercisers compared with non-exercisers (10 beats/min). This meta-analysis reported statistical significance for heterogeneity using a random effects model. Heterogeneity was likely attributed to the different exercise interventions between the studies. Two studies measured $\dot{V}O_{2max}$ (Dolan, 2006; Lox, 1995). Meta-analysis showed no difference in $\dot{V}O_{2max}$ among participants in the PRE or combined PRE and	HIGH (+ve effect)

									aerobic exercise group compared to the non-exercising control group. Two studies assessed exercise time (Dolan, 2006; Rigsby, 1992). Meta-analysis showed a non-significant increase in exercise time of 3.92 minutes (95% CI: -0.63, 8.47; p=0.09; n=62) for participants in the combined PRE and aerobic exercise group compared to the non-exercising control group. The confidence interval indicated a trend towards an improvement in exercise time among exercisers compared with non-exercisers. This meta-analysis reported statistical significance for heterogeneity using a random effects model. all studies reported on strength outcomes, but meta-analyses could not be performed due to differences in outcomes and participants; however, nine of the 10 studies suggested improvements in strength among exercisers compared to non-exercisers. Grinspoon (2000) found no significant differences in strength for participants in the combined aerobic and PRE exercise group compared with participants in the non-exercising control group.	
	O'Brien, 2017 *(72)*	20 RCTs, N=764	high	**$VO_{2}max$**					The mean age of the participants ranged from 32 to 49 years (23% were females). Participants exercised 30-120 min three times per week for 12-52 weeks. Two meta-analyses showed a significant and potentially clinically important improvement in $\dot{V}O_{2max}$ of 3.71 mL/kg/min for participants in the aerobic exercise intervention group compared with the non-exercising control group. There was no statistical significance for heterogeneity.	MODERATE (+ve effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		
				HRmax					Participants exercised 20-135 mins three times per week for 12-16 weeks. Two meta-analyses showed no significant difference in HR_{max} for participants in the PRE or combined PRE and aerobic exercise group compared with the non-exercising control; and combined PRE and aerobic exercise group compared with non-exercising control. Heterogeneity was present in both meta-analyses.	LOW (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		
				Exercise time					Participants exercised 20-120 min three times per week for 12-52 weeks. Two meta-	HIGH (+ve effect)

				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	analyses demonstrated a significant increase in exercise time of 3.29 min for participants in the combined PRE and aerobic exercise group compared with the non-exercising control group. The point estimate did not reach the 5 min threshold for clinical importance.	
				Strength					Participants exercised 30-120 mins three times per week for 12-52 weeks Meta-analyses showed that improvements occurred in upper and lower body strength, as determined by increases in 1-repetition maximum for chest press, and knee flexion; and a non-significant trend towards improvement in 1-RM for leg press and knee extension for participants in the combined PRE and aerobic group versus non-exercising control group. Two more meta-analyses were conducted comparing combined exercise and testosterone with testosterone alone. Results indicated a non-significant trend towards increased strength among participants in the combined exercise and testosterone group compared with participants in the testosterone alone group for knee flexion and extension. Five of the six-point estimates for upper and lower extremity strength were greater than 2 kg and 5 kg, respectively, indicating a clinically important increase with exercise compared with non-exercise. Heterogeneity was present in five meta-analyses.	LOW (inconclusive)
				Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias		

Multimodal Exercise	Voigt, 2018 *(77)*	15 RCTs, N=537	moderate	No serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	The age of the participants in this study ranged from 18-73 years old. The duration ranged between 31-120 min 2-4 times a week; intensity ranged from low to vigorous for 6-24 weeks. For aerobic exercise training, Galantino (2005) revealed significant improvements in both cardiovascular (maximum oxygen consumption) and flexibility outcomes. Two studies (Agin, 2001 and Strawford, 1999) also reported significant improvements in strength outcomes in the intervention group compared to those in the control group using progressive resistance training interventions. Seven studies which used combined aerobic and PRT interventions found significant improvement in overall strength, cardiovascular, and flexibility parameters. One study with a combined yoga and meditation, and another study with yoga alone found no changes in functional capacity. In another study that used tai chi exercise intervention revealed significant improvements in both flexibility and cardiovascular outcomes.	HIGH (+ve effect)
	Pedro 2017 *(72)*	5 RCTs, N=253	high	No serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	The age of the participants in this study ranged from 18-60 years old. The duration ranged between 12-24 weeks. Muscular strength increased in response to resistance and concurrent training in three studies (Lindegaard, 2008; Dolan, 2006; Mendes, 2013). Strength also increased slightly in response to aerobic training (Lindegaard, 2008). The $\dot{V}O_{2max}$ increased in response to concurrent training (Dolan, 2006; Mendes, 2013) and aerobic training (Lindegaard, 2008; Mendes, 2013; Terry, 2006), but did not increase in response to resistance training (Lindegaard, 2008).	MODERATE (+ve effect)
	Chaparro 2018 *(76)*	13 RCTs, N=NR	high	No serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	Serious publication bias	The mean age for the control group was 42 ± 5.7 years and for the intervention group 42.9 ± 5.3 years. The duration ranged between 60-120 min 2-3 times a week for 6-24 weeks. Two overall meta-analyses and 34 subgroup analyses showed that change in upper body strength in PLWH from baseline was 18 kg (95% CI: 11.2–24.8, $p<0.001$) favouring the intervention group. Lower body strength also increased by 16.8 kg (95% CI: 13–20.6, $p< 0.001$) favouring the intervention group. Sub-analysis revealed a significant increase in the weight lifted for each muscle group, favouring the intervention group. After long-term exercise, the intervention group showed a	HIGH (+ve effect)

									significant change in upper body strength of 13.7 kg (95% CI: 6–21.5, p<0.001), as well as lower-body strength of 16 kg (95% CI: 11.6–20.4, p<0.001).	
	Gomes Neto, 2015 *(68)*	7 RCTs, N=386	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	The age of the participants in this study ranged from 37-46 years old. The duration ranged between 20-85 min 2-3 times a week for 6-24 weeks. Mendes (2013) and Dolan (2006) found significant improvements in muscle strength of the knee extensors and elbow flexors of 25.06 Kg (95% CI: 10.46, 39.66, n=118) and of 4.44 Kg (95% CI: 1.22, 7.67,n=118), respectively, for participants in the concurrent resistance and aerobic exercise group compared with no exercise group. Five studies (including 318 patients) assessed $\dot{V}O_{2peak}$ as outcome. In the study by Mutimura (2008), VO_{2peak} improved from 4.7 ± 3.9 vs 0.5 ± 0.3 ml/kg per min in the intervention group compared to the control, while the study of Hand (2008), detected an improvement of 21% in $\dot{V}O_{2peak}$ estimated in the exercise group versus no improvement in the control. Similarly, Dolan (2006) observed an improvement (1.5 ± 0.8 vs -2.5 ± 1.6 $mL/kgmin^{-1}$) in VO_{2peak} in the training group compared to the control. However, Ogalha (2011) observed a non- significant improvement (0.6 ± 0.9 vs -0.2 ± 0.7 $mL/kgmin^{-1}$) VO_{2peak} in the training group compared to the control. The mean VO_{2peak} in the analysed studies was 26.8 mL kg-1 min^{-1} at baseline, and it increased to 30.7 mL $kgmin^{-1}$ at the end of the intervention. The meta-analyses showed a significant improvement in VO_{2peak} of 4.48 mL kg-1 min^{-1} (95% CI: 2.95, 6.0, n=318) for participants in the CARE group compared with no exercise group.	HIGH (+ve effect)

	Zech, *2019 (75)*	27 RCTs, N=1294	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	Serious publication bias	The average age was 41.46 ± 5.04 years for the intervention groups and 40.99 ± 5.93 years for the control groups. The duration ranged between 30-120 min 2-5 times a week for 6-26 weeks. Seven main meta-analyses and 45 subgroup analyses found in favour of the exercise group. Statistical heterogeneity was moderate, indicating that there was relatively moderate variation in the effect sizes across trials. For the 6-minute walk test, an overall SMD=0.59 in favour of the exercise group was found. There was a significant overall effect of exercise compared with the control group at post treatment. For maximum heart rate, an overall SMD=-0.38 in favour of the exercise group was found. There was no significant overall effect of exercise compared with the control group. For resting heart rate, an overall SMD=-0.29 was found in favour of the exercise group. There was no significant overall effect of exercise compared with the control group. For systolic blood pressure, an overall SMD=-0.27 in favour of the exercise group was found. There was no significant overall effect of exercise compared with the control group. For diastolic blood pressure, an overall SMD=0.01 in favour of the exercise group was found. There was no significant overall effect of exercise compared with the control group. For maximum power output, an overall SMD=0.80 in favour of the exercise group was found. There was a significant overall effect of exercise compared with the control group at post treatment.	MODERATE (+ve effect)
	Ibeneme, 2019a *(64)*	23 RCTs, N=1073	High	Serious risk of bias	Serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	The age of the participants in this study ranged from 18-65 years old. The duration ranged between 20-60 min 3-5 times per week for a range of 6-16 weeks. Eight studies reported statistically significant improvement in the VO_{2max}/ VO_{2peak} in the post-training period in the intervention group, while two studies reported no significant improvement of the intervention on the stated outcomes. Two other trials reported a significant increase in the mean forced expiratory volume (FEV_1) in the intervention group compared to the control group. Farinatti (2010) observed a significant improvement in the slope/ intercept values for the rate - workload relationship. Furthermore, a total of 13 studies also reported a statistically significant improvement in the cardiopulmonary-related parameters, while two other studies reported no significant	HIGH (+ve effect)

									improvement in the study group. The results of the meta-analysis revealed a significant change in VO_{2max} between the intervention and control groups. Results demonstrated a trend towards an increase in VO_{2max} in subjects in the aerobic exercise and resistance exercise group compared normal activities in the control group that favoured the intervention. There was also a trend towards an increase in $\dot{V}O_{2max}$ in subjects in the aerobic exercise group compared to the normal activities in the control group.	

Abbreviations: PICO = population, intervention, comparator, outcome; RoB = risk of bias; RCTs = randomised controlled trials

1. O'Brien, 2016:
   - VO2max: Downgraded to VERY LOW by the authors of the review due to attrition (withdrawals of included studies >15 %), suspected publication bias, substantial heterogeneity (I2 = 67 %); and because the lower level of the confidence interval did not cross the estimated clinically important change in VO2max (despite the estimate surpassing the author's hypothesized clinically important change in VO2max of 2 ml/kg/min).
   - HRmax: Downgraded to MODERATE due to attrition and performance bias.
   - Exercise time: Downgraded to MODERATE due to attrition and performance bias (inability to blind participants to exercise interventions). This was then upgraded to high due to the evident dose-response relationship in the findings.
   - Strength: The authors of the review downgraded the outcome from HIGH to LOW due to incomplete outcome data (withdrawals of included studies were >15 %), publication bias suspected, and MODERATE to considerate heterogeneity (I2 = 46 % and 88% for chess and leg press, respectively).
2. O'Brien, 2010:
   - VO_{2max}: MODERATE due to heterogeneity in the studies included. This was later upgraded to HIGH due to the evident dose-response relationship in the findings.
   - Maximum Heart Rate (HRmax): HIGH because there is no reason to downgrade.
   - Exercise Time (minutes): HIGH because there is no reason to downgrade.
   - Strength: Downgraded to LOW due to a higher magnitude of indirectness.

3. O'Brien, 2004: Downgraded to LOW because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used. This low GRADE was then upgraded to HIGH due to the evident dose-response relationship in the findings.
4. O'Brien, 2008: Downgraded to LOW because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the Hawthorn effect. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants. This was then upgraded to HIGH because of evidence of a dose-response relationship.
5. Nixon, 2005: Downgraded to LOW due to (a) RoB due to attrition bias as a result of high withdrawal rates ranging from 4-76% (b) indirectness which may have been caused by the heterogeneity of outcome measures. This was later upgraded to HIGH due to the evident dose-response relationship in the findings.
6. O'Brien, 2017:

   - VO_{2max}: Graded MODERATE because the authors of the review were moderately confident in the effect estimate demonstrating a significant increase of 3.71 ml/kg/min for VO2max comparing PRE exercise (or combined PRE and aerobic exercise). The authors downgraded the outcome from HIGH to MODERATE GRADE quality of evidence because the lower level of the confidence interval did not cross the estimated clinically important change in VO2max (despite the estimate surpassing their hypothesized clinically important change in VO2max of 2 ml/kg/min).
   - HRmax: Downgraded to LOW because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention. Furthermore, Heterogeneity was present in both meta-analyses ($p < 0.1$) used for this outcome.

- Exercise time: Downgraded to VERY LOW because a high risk of performance bias existed across the included studies as 85% of them had a high risk of performance bias due to lack of participant blinding to the exercise intervention. Furthermore, Heterogeneity was present in both meta-analyses ($p < 0.1$) used for this outcome. This was then upgraded to HIGH due to the presence of a dose-response relationship.
- Strength: The authors of the review graded the outcome as LOW because their confidence was limited in the effect estimate of a significant increase of 11.86 kg for 1-repetition maximum for chest press comparing PRE exercise (or combined PRE and aerobic exercise) with non-exercising control. The outcome was downgraded from HIGH to LOW on the GRADE quality of evidence due to incomplete outcome data (withdrawals of included studies were >15%), publication bias suspected, and moderate heterogeneity (I^2=46%).

7. Pedro, 2017: Downgrade to MODERATE due to indirectness which might have been caused by different type of individuals in different studies, different types of exercise interventions and different types of assessment methods.
8. Chaparro, 2018: Graded LOW because there was publication bias on the systematic review and indirectness which could have been caused by the various differences among the included studies. This was then upgraded to HIGH due to the presence of a dose-response relationship.
9. Gomes Neto, 2015: Moderate due to RoB because the risk to selective reporting was uncertain and none of the studies described blinding of therapists. This was then upgraded to HIGH due to the presence of a dose-response relationship.
10. Zech, 2019: Downgraded to MODERATE because 9 of the 27 included studies showed a high risk of bias and potential publication bias.
11. Poton 2017: Downgraded to MODERATE due to RoB, inconsistency and imprecision as there is insufficient information in the review.
12. Voigt, 2018: downgraded to MODERATE due to heterogeneity as a result of the different exercise intervention and small sample size. This was then upgraded to HIGH due to the presence of a dose-response relationship.
13. Ibeneme, 2019a: Downgraded to MODERATE due to RoB, inconsistency in the outcome measure and variability in the types of intervention used in the study. This was then upgraded to HIGH due to the presence of a dose-response relationship.

Table E.1.4.d.5: Effects of physical activity on cardio metabolic markers among people living with HIV

Questions: What is the association between physical activity and markers of cardiometabolic risk? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People living with HIV
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Markers of cardiometabolic risk (blood lipids, glucose and insulin, blood pressure)

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsis-tency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	No systematic reviews identified									
Resistance Exercise	No systematic reviews identified									
	Pedro, 2017 *(72)*	5 RCTs, N=253	high	No serious risk of bias	Serious Inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	This review focused on PLWHA and HIV-associated lipodystrophy syndrome (HALS) an important subset of PLWHA. Participants had HIV, HALS and had been on ARTs for longer than 3-months. The age of participants ranged between 18 -60 years. This review included studies of males only (Lindegaard ,2008), females only (Dolan, 2006) and mixed sex groups (Medes, 2013., Mutimura 2008, and Terry 2006). Aerobic training resulted in a reduction of total cholesterol in two studies (Lindegaard ,2008 and Mutimura 2008) and a reduction in LDL specifically in Lindegaards study, yet Terry 2006 demonstrating no decrease in total cholesterol under controlled dietary (mixed diet) conditions after aerobic intervention. With concurrent training total cholesterol dropped in Dolan 2006. Triglyceride levels were found by Lindegaard to improve after resistance training and that free fatty acids dropped, and HDL increased after either aerobic or resistance training. There was no effect demonstrated on HOMA or insulin concentrations by any exercise modality. Glucose levels reduced after aerobic training in only one study conclusively. Body fat percentage was reduced in response to all forms of training	LOW (+ve effect)

									(aerobic, resistance and concurrent) in all but one study. This is inconclusive however due to the poor methods of assessment used in all the studies barring Dolan 2006 and Lindegaard 2008. Only one study assessed inflammatory markers (which are important in the development of HALs) This study demonstrated that hs-CRP, TNF-α, IL-6 and IL-18 decreased after aerobic training and only IL-18 decreased after resistance training. There was no demonstrable effect on CD4 count in this population group indicating that training is safe in HALS patients. Aerobic and concurrent training improve VO2max while resistance training reduces fat mass and improves muscle strength. All of the above should improve the inflammatory and lipid profile but there is no true consensus/not enough evidence to support this.	
	Fillipas, 2006 *(80)*	9 RCTs, N=469	low	Serious Risk of Bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	Of the 469 adult participants in this systematic review, 41% were female within RCTs where the interventions were either aerobic, progressive resistance exercises or a combination of the two. . The studies had to have a minimum intervention period of 4 weeks with a frequency of 2 sessions per week. The participants were at various stages of HIV with CD4 counts <100 to>1000 cells/mm^3. With 5 out of the 9 studies including participants who were on HAART (Fillipas 2006, Dolan 2006, Smith 2001, Lindegaard 2008 and Mutimura 2008), one study did not describe antiretroviral use (Terry 1999) and the others used non-HAART participants. No adverse events were attributable to training interventions although the dosage, intensity, frequency and type varied, all were safe. Aerobic exercise and resistance training are effective in improving BMI, fat mass(%) and WHR while resistance training increased body weight and muscle strength and was slightly better at reducing fat mass. Concurrent exercise studies included in this review were inconclusive. Where aerobic training (in one study of moderate effect size) had a small advantage over resistance training at reducing total cholesterol and LDL. Few studies examined blood lipids, glucose, and bone density which are important factors in participants with chronic HIV and HAART.	LOW (inconclusive)

	Quiles, 2019 *(82)*	9 RCTs, N=638	low	Serious Risk of Bias	Serious Inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	This review aimed to investigate the effects of exercise on lipid profiles and blood glucose levels in adults >18 years living with HIV. The studies had to have a min intervention period of 4 weeks with a frequency of 2 sessions per week as with Fillipas, 2010. All studies included participants actively taking ART and 58.6% of the 638 participants were female. Aerobic activity alone caused an increase in HDL and a lack of activity to decrease blood glucose in one study given a homebased physical activity program (Roos 2014). Resistance training alone was also shown by only one study (Zanetti 2016) to decrease triglycerides, total cholesterol and LDL with a concomitant increase in HDL compared to baseline. Concurrent or combined aerobic and resistance training studies were inconsistent with some markers changing and others remaining as is. Those who indicated that glucose levels improve (from a 12-24week intervention) reported no changes in blood lipids (Ogalha 2011, Tiozzo 2013). While in a population with some body fat redistribution (Mutimura 2008) a drop in blood glucose saw slight improvements in total cholesterol and triglycerides but no improvements in LDL and HDL. Only one study indicated HDL improvements with concurrent training without any other lipid or glucose markers improving (Grinspoon 200) . Overall studies reported positive results for reductions in glucose levels and triglycerides with increases in HDL overall. Total cholesterol only slightly improved with the combined training. This suggests that inclusion of exercise can only help the metabolic profile of PLWH.	MODERATE (+ve effect)

Abbreviations: PICO = population, intervention, comparator, outcome; RoB = risk of bias; RCTs = randomised controlled trials

1. Pedro, 2017: downgraded to LOW due to indirectness which might have been caused by different type of individual indifference studies, and different type of intervention and different type of assessment methods. There were also inconsistencies in the findings of the study (Lindegaard 2008; Mutimura 2008 established reductions in total cholesterol after aerobic training. Whereas Terry 2006 did not showed reductions in total cholesterol).
2. Fillipas 2006: Rated LOW because there is possible RoB, first due to the few studies that focused on the effects of exercise on cardiometabolic markers and because some trials were of short duration (4 wks). Heterogeneity and indirectness may have been due to differences in exercise interventions, outcome measures, and participants. Furthermore, dose-response is not evident and the results of the effects of exercise on cardiometabolic markers in these few studies are inconclusive
3. Quiles 2019: There is a possibility of RoB due to a limited number of studies investigating the effects of exercise on metabolic profile. Attrition rates were also relatively high in among some studies, with rates as high as 39% in one study (Roos et al., 2014). Also, the quality of the included RCTs as assessed by the PEDro scale was a median 5 out of a possible score of 10. Failure to do blinding of the participants and personnel to the exercise intervention, led to an overall high risk of the Hawthorne effect across all the included studies. Inconsistency

might have been caused by heterogeneity due to differences in exercise interventions, assessment protocols, outcomes and populations. There, we downgraded it to LOW. There is evidence of a dose-response relationship in most studies., and as result, we upgraded it to MODERATE.

Table E.1.4.d.6: Effects of physical activity on viral load and CD4+ cell count among people living with HIV

Questions: What is the association between physical activity and disease progression? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People living with HIV
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Markers of disease progression (CD4 count, CD4 percentage, viral load)

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsis-tency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	Nixon, 2005 *(70)*	10 RCTs, N=276	High	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No publication bias	All ten included studies reported immunological/virological outcomes with a total of 276 participants aged between 18 and 58 years. The $CD4^{+}$ cell count of the participants ranged from <100 to greater than 1000 cells/mm^3, and women comprised less than 15% of the total number of participants. Meta-analysis showed no difference in $CD4^{+}$ cell count for participants in the exercise intervention groups compared to the non-exercising control groups (Weighted Mean Difference: 14.3 cells/mm^3, 95% CI: -25.8, 54.5, n=209, p=0.48) (Baigis 2002; LaPerriere 1990; Lox 1995; Perna 1999; Smith 2001; Stringer 1998). Meta-analysis also showed no difference in $CD4^{+}$ percentage for participants in the exercise interventions groups compared to the non-exercising control groups (Weighted Mean Difference: -0.2%, 95% CI: -3.1, 2.7, n=118, p=0.90) (Baigis 2002; Smith 2001). Meta-analysis demonstrated no difference in viral load for participants in the exercise intervention groups compared to the non-exercising control groups (Weighted Mean Difference: 0.40 log10 copies, 95% CI: -0.3, 1.1, n=63, p=0.25) (Smith 2001; Stringer 1998).	LOW (no effect)
	O'Brien, 2004 *(73)*	10 RCTs, N=458 HIV+ only participants	high	Serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	Serious publication bias	All ten studies included used $CD4^{+}$ cell count as an outcome. Participants were aged between 18 and 58 years and their $CD4^{+}$ cell count ranged from <100 to greater than 1000 cells/mm^3, with women comprising less than 15% of the total number of participants. Five meta-analyses showed no difference in $CD4^{+}$ cell count for participants in any type of aerobic exercise intervention group compared with the non-exercising control group (weighted mean difference: 14 cells·mm^{-3}, 95% CI: -26, 54, N= 209), no difference in $CD4^{+}$ cell count of participants in the constant aerobic exercise group compared with non-exercising control group (weighted mean difference: -4 cells·mm^{-3}, 95% CI: -50, 42, N	LOW (no effect)

									164) and non-significant improvement in CD4$^+$ cell count of 70 cells·mm^{-3} (95% CI: -11, 151, N 45) for participants in the interval aerobic exercise group compared with the non-exercising control group. Although not statistically significant, the point estimate was above 50 cells·mm^{-3}, which represents a possible clinically important increase in CD4$^+$ cell count. There was no difference in CD4$^+$ cell count in the moderate intensity aerobic exercise group compared with the heavy-intensity exercise group (weighted mean difference: -34, 95% CI: -156, 89, N 39) and no difference in CD4$^+$ cell count for participants in the combined aerobic and progressive resistive exercise group compared with non-exercising control group (weighted mean difference: 6 cells·mm-3, 95% CI: -71, 83, N 46). Meta-analysis of three studies showed no difference in viral load for participants in the exercise intervention groups compared with the non-exercising control groups (weighted mean difference: 0.40 log10 copies, 95% CI: -0.28, 1.07, N 63).	
	O'Brien, 2016 *(67)*	24 RCTs, N=1242	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	Serious publication bias	Twenty-four studies with 936 participants (at study completion), who were mostly male, taking ART (19 studies) were included in the review. Seven meta-analyses showed non-statistically significant changes in CD4+ cell count between comparison groups. Results showed a trend towards an increase in CD4+ cell count for participants in the aerobic or combined aerobic and PRE intervention group compared with the non-exercising control group; constant or PRE compared with no exercise; and a significant increase in CD4+ cell count for interval aerobic exercise compared with no exercise. The point estimate in the latter two meta-analyses was above 50 cells/mm3, which suggests a trend towards a potentially clinically important improvement in CD4+ cell count among exercisers compared with non-exercisers. Meta-analyses showed no difference in CD4+ cell count for constant or interval aerobic exercise compared with no exercise; constant aerobic exercise compared with no exercise; as well as combined aerobic exercise and diet and/or nutrition counselling group compared with diet and/or nutrition counselling. No difference in CD4+ cell count was found for participants exercising at moderate compared to heavy intensity exercise. Four meta-analyses showed no difference in viral load	MODERATE (no effect)

									for participants in the aerobic exercise intervention group compared with the non-exercising control group, as well as the constant aerobic exercise group compared with the non-exercising control group; no difference in the combined aerobic and PRE group compared with the non-exercising control group; and no difference for participants in the aerobic or combined aerobic and PRE intervention group compared with the non-exercising control group.	
	O'Brien, 2010 *(69)*	14 RCTs, N=454	high	**$CD4^+$ cell count**					Five meta-analyses showed no significant change in $CD4^+$ cell count between exercise and no exercise groups.	MODERATE (no effect)
				Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				CD4 Percentage					Two meta-analyses demonstrated no difference in $CD4^+$ percentage for participants in the exercise intervention group compared with the non-exercising control group, as well as the constant aerobic exercise group compared with the non-exercising control group (WMD: -0.33%, 95% CI: -1.98, 1.32, n=118, *P*=0.69) (Smith, 2001, Baigis, 2002).	High (no effect)
				No serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias		
				Viral Load					Three meta-analyses demonstrated no difference in viral load for participants in the exercise intervention group compared with the non-exercising control group, as well as the constant aerobic exercise group compared with the non-exercising control group (WMD: 0.40 log10copies, 95% CI: -0.28, 1.07, n=63, *P*=0.25) (Smith, 2001; Stringer, 1998), and no difference in the combined aerobic and PRE	HIGH (no effect)

<table>
<tr><td></td><td></td><td></td><td></td><td>No serious risk of bias</td><td>No serious inconsistency</td><td>No serious imprecision</td><td>No serious indirectness</td><td>No serious publication bias</td><td>group compared with the non-exercising control group (WMD: 0.31 log10copies, 95% CI: -0.13, 0.74, n=60, P=0.17) (Grinspoon, 2000, Dolan, 2006).</td><td></td></tr>
<tr><td rowspan="5">Resistance Exercise</td><td>Poton, 2016 (78)</td><td>13 RCTs, N=291</td><td>moderate</td><td>No serious risk of bias</td><td>No serious inconsistency</td><td>No serious imprecision</td><td>No serious indirectness</td><td>No serious publication bias</td><td>The review included a total of 291 participants and 43.1% were female. A slight increase in CD4⁺ cell count occurred with an overall effect size of 0.37 (0.13–0.61; P = 0.003; ~26.1%).</td><td>MODERATE (+ve effect)</td></tr>
<tr><td rowspan="4">O'Brien, 2017 (72)</td><td rowspan="4">20 RCTs, N=764</td><td rowspan="4">high</td><td colspan="5">CD4 count</td><td rowspan="2">Two meta-analyses demonstrated no statistically significant changes in CD4⁺ cell count between comparison groups, one demonstrated a significant increase in CD4⁺ cell count favouring exercise, and the other demonstrated a significant decrease in CD4⁺ cell count favouring testosterone alone. Point estimates were >50 cells/mm³ for two meta-analyses comparing exercise to control, which suggested a positive trend towards a potentially clinically important improvement in CD4⁺ cell count with exercise compared to no exercise.</td><td rowspan="2">VERY LOW (+ve effect)</td></tr>
<tr><td>Serious risk of bias</td><td>No serious inconsistency</td><td>No serious imprecision</td><td>Serious indirectness</td><td>No serious publication bias</td></tr>
<tr><td colspan="5">Viral load</td><td rowspan="2">Three meta-analyses demonstrated no difference in viral load for participants in the combined PRE and aerobic exercise intervention group compared with the non-exercising control group, as well as the combined PRE and aerobic exercise group with diet and/or nutrition compared with the non-exercising diet and/or nutrition only group. None of the meta-analyses were significant for heterogeneity.</td><td rowspan="2">MODERATE (no effect)</td></tr>
<tr><td>Serious risk of bias</td><td>No serious inconsistency</td><td>No serious imprecision</td><td>Serious indirectness</td><td>No serious publication bias</td></tr>
<tr><td>O'Brien, 2008 (74)</td><td>10 RCTs, N=332</td><td>high</td><td>Serious risk of bias</td><td>No serious inconsistency</td><td>No serious imprecision</td><td>Serious indirectness</td><td>No serious publication bias</td><td>The review included a total of 332 participants, whose age ranged from 18 - 66 years. Their CD4 counts ranged from under 100 to greater than 1000 cells/ mm³. Less than 30% of the participants were women (87/332 participants). Three meta-analyses showed no difference in CD4⁺ cell count for participants in the combined aerobic and PRE group compared to the non-exercising control group (WMD: 24.83 cells/mm3; 95% CI: -23.70, 73.36; p = 0.32; n = 84) and for participants in the PRE or combined PRE and aerobic exercise group compared to the non-exercising control group (WMD: 38.51 cells/mm3; 95% CI: -7.54, 84.56; p = 0.10; n = 106). A significant decrease in CD4+ cell</td><td>LOW (no effect)</td></tr>
</table>

									count was found in the combined PRE plus testosterone or combined PRE and aerobic exercise plus testosterone group compared with the testosterone only group (WMD: -32.13 cells/mm3 ; 95% CI: -56.96, -7.30; p = 0.01; n = 51). These results did not reach the authors' pre-specified threshold for clinical importance (50 cells/mm3). One meta-analysis demonstrated no difference in viral load among participants in the combined PRE and aerobic exercise group compared with the non-exercising control group (WMD: 0.31 log10 copies; 95% CI: -0.13; 0.74; p = 0.17; n = 60). Individual studies also showed no difference in viral load among exercisers compared with non-exercisers.	
Multimodal Exercise	Ibeneme, 2019b *(65)*	19 RCTs, N=661 participants included for QoL.	high	Serious risk of bias	No serious inconsistency	No serious imprecision	No serious indirectness	No serious publication bias	Farinatti (2010) reported no significant change in the $CD4^+$ cell count in either the exercise group or the control group. The exercise group (n = 19) were involved in aerobic training (cycle ergometer) for 30 min of moderate intensity, strengthening exercise (2 sets of 12 repetitions of 5 exercises at 60–80% 12 Repetition Maximum) for 50 min and flexibility exercise (2 sets of 30s at maximum range of motion of 8 exercises) while the control group (n = 8) received no treatment. The study reported no significant change in the CD4 T-cell count in either the exercise group or the control group (p = 0.19 for CD4 T-cells and p = 0.22 for CD4 %).	MODERATE (no effect)
	Pedro, 2017 *(72)*	5 RCTs, N=253	high	No serious risk of bias	No serious inconsistency	No serious imprecision	Serious indirectness	No serious publication bias	CD4 cell count was not influenced by physical training.	MODERATE (no effect)

Abbreviations:; PICO = population, intervention, comparator, outcome;; RoB = risk of bias; RCTs = randomised controlled trials

1. O'Brien 2016: The authors reported a MODERATE grade for CD4+ cell count and did not report for viral load. CD4+ cell count was assigned a MODERATE GRADE due to incomplete outcome data (withdrawals of included studies were >15 %). We also assigned a MODERATE GRADE for viral load due to attrition bias and performance bias in the review.

2. O'Brien, 2010

   - CD4 cell count: Downgraded to MODERATE due to heterogeneity in the included studies.
   - CD4 Percentage: HIGH, no reason to downgrade even if RoB is unclear.
   - Viral Load: HIGH, no reason to downgrade even if RoB is unclear.

3. O'Brien, 2004: Downgraded to LOW because the authors report a possibility of publication bias, there was also attrition bias (20% drop out in 6 studies and more than 50% dropout in 2 studies), the review is also based on a small number of trials and participants. Heterogeneity may have occurred due to a variety of exercise interventions being used.

4. O'Brien, 2008: Downgraded to LOW because of a lot of variation among individual studies in the types of interventions, participants and outcomes, which may have led to heterogeneity and Indirectness. Also, there is RoB due to attrition bias because of high withdrawal rates (>15%). There was also lack of blinding to the PRE intervention which may have resulted in the Hawthorn effect. The authors also report a possibility of performance bias due to increased levels of interaction between the investigators and participants in the exercise group resulting in more

favourable outcomes for exercisers compared to non-exercisers. The review also used a small number of studies (n = 10) and there was total outcome data not available for 69 (17%) participants.

5. Nixon, 2005: Downgraded to LOW due to (a) RoB due to attrition bias as a result of high withdrawal rates ranging from 4-76% (b) indirectness which may have been caused by the heterogeneity of outcome measures.

6. O'Brien, 2017

   - CD4 count: First downgraded to LOW because RoB due to a high risk of performance bias existing across the included studies since 85% of them lacked participant blinding to the exercise intervention. There was also a high risk of attrition bias as 555 of the included studies reported rates of withdrawal greater than 15%. Indirectness could have been caused by heterogeneity as it was reported to be present in 47% of the meta-analyses due to participant variability in ART use, body composition, comorbidity, gender, type and location of intervention and method of outcome measurement. For CD4 count the LOW grade was further downgraded to VERY LOW because for CD4 count, 3 of the 4 meta-analyses that were done were statistically significant for heterogeneity.
   - Viral load: The authors of the review graded the result as MODERATE because they were moderately confident in the non-significant effect estimate of 0.12 log10copies demonstrating no difference in change in viral load comparing PRE exercise (or combined PRE and aerobic exercise). This outcome was downgraded from HIGH to MODERATE GRADE quality of evidence due to incomplete outcome data (withdrawals of included studies were >15%).

7. Poton, 2017: Downgraded to MODERATE because we are uncertain about the status of RoB, inconsistency and imprecision as there insufficient information about these in the review.

8. Pedro, 2017: Downgraded to MODERATE due to indirectness which might have been caused by different type of individuals in different studies, different types of exercise interventions and different types of assessment methods.

Table E.1.4.d.6: Effects of physical activity on cognition among people living with HIV

Questions: What is the association between physical activity and cognition? Is there a dose response association (volume, duration, frequency, intensity)? Does the association vary by type or domain of PA?
Population: People living with HIV
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Cognition, measures of cognitive function

Exercise modality	Study	No. of Studies No. of participants	AMSTAR 2 Score	GRADE CRITERIA					Summary of findings	CERTAINTY
				Risk of Bias	Inconsis-tency	Imprecision	Indirectness	Publication Bias		
Aerobic Exercise	No systematic reviews identified									
Resistance Exercise	No systematic reviews identified									
Multimodal Exercise	No systematic reviews identified									

Abbreviations: PICO = population, intervention, comparator, outcome; RoB = risk of bias;

Appendix A. Data Extractions of Included Reviews

Cancer

<table>
<tr><td colspan="2">SR/MA
Citation: Friedenreich CMS, C.R.; Cheung, W.Y.; Hayes, S.C. Physical activity and mortality in cancer survivors: A systematic review and meta-analysis. JNCI Cancer Spectrum 2019. https://doi.org/10.1093/jncics/pkz080</td></tr>
<tr><td>Purpose: To evaluate the association between pre-diagnosis and postdiagnosis PA and survival for all cancer and by specific cancer sites</td><td rowspan="5">Abstract:
Background: Recommendations for improved survival after cancer through physical activity (PA) exist, although the evidence is still emerging. Our primary objective was to conduct a systematic review and meta-analysis of the association between pre- and post-diagnosis PA and survival (cancer-specific, all-cause and cardiovascular disease mortality) for all-cancers and by tumour site. Secondary objectives were to examine the associations within population subgroups, by PA domain, and to determine the optimal dose of PA related to survival.
Methods: PubMed, EMBASE and SportsDiscus databases were searched to November 1, 2018. DerSimonian-Laird random-effects models were used to estimate the summary hazards ratios (HRs) and 95% confidence intervals for primary and secondary analyses, and to conduct dose-response analyses.
Results: Evidence from 136 studies showed improved survival outcomes with highest versus lowest levels of pre- or post-diagnosis total/recreational PA for all-cancers combined (cancer-specific mortality: HR = 0.82, 95% CI = 0.79-0.86; and HR = 0.63, 95% CI = 0.53-0.75 respectively) as well as for 11 specific cancer sites. For breast and colorectal cancers, greater reductions were observed for post-diagnosis PA (HRs=0.58-0.63) compared with pre-diagnosis PA (HRs=0.80-0.86), for cancer-specific and all-cause mortality. Survival benefits through PA were observed in most subgroups (within sex, body mass index, menopausal status, colorectal subtypes and PA domain) examined. Inverse dose-response relationships between PA and breast cancer-specific and all-cause mortality were observed, with steep reductions in hazards to 10-15 MET-hours/week.
Conclusion: Higher pre- and post-diagnosis levels of PA were associated with improved survival outcomes for at least 11 cancer types, providing support for global promotion of PA guidelines following cancer.</td></tr>
<tr><td>Timeframe: Nov 1, 2018</td></tr>
<tr><td>Total # studies included: 136</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Data from available observational epidemiologic studies and RCTs</td></tr>
<tr><td>Outcomes addressed: Cancer- and all-cause mortality</td></tr>
</table>

Hypertension

<table>
<tr><td colspan="2">SR/MA
Citation: Cao L, Li X, Yan P, Wang X, Li M, Li R, Shi X, Liu X, Yang K. The effectiveness of aerobic exercise for hypertensive population: A systematic review and meta-analysis. The Journal of Clinical Hypertension. 2019 Jun 6.</td></tr>
<tr><td>Purpose: duration of aerobic exercise on blood pressure and heart rate</td><td rowspan="5">Abstract:
The study aims to evaluate the effectiveness of different durations of aerobic exercise on hypertensive patients. Four electronic databases (PubMed, Embase,
Cochrane Library, and Web of Science) were searched from their inception until July 2018. English publications and randomized controlled trials involving aerobic exercise treatment for hypertensive population were included. Two reviewers independently extracted the data. The Cochrane's Risk of Bias tool was used to assess the quality of included studies. In this systematic review, a total of 14 articles were included, involving 860 participants. The quality of the included studies ranged from moderate to high. The results of the meta-analysis showed that compared with the control group,significant effects of aerobic exercise were observed on reducing systolic blood
pressure (SBP) (mean difference [MD] = −12.26 mm Hg, 95% confidence interval [CI] = −15.17 to −9.34, P < 0.05), diastolic blood pressure (DBP; MD = −6.12 mm Hg, 95% CI = −7.76 to −4.48, P < 0.05), and heart rate (MD = −4.96 bpm, 95% CI = −6.46 to −3.43, P < 0.05). In addition, significant reductions were observed in ambulatory DBP (MD = −4.90 mm Hg, 95% CI = −8.55 to −1.25, P < 0.05) and ambulatory SBP (MD = −8.77mm Hg, 95% CI = −13.97 to −3.57, P < 0.05). Therefore, aerobic exercise might be an effective treatment for blood pressure improvement in hypertensive patients. However, the effectiveness between the duration of different treatment needs to be well-designed and rigorous studies will be required to verify the dataset.</td></tr>
<tr><td>Timeframe: inception to July 2018</td></tr>
<tr><td>Total # studies included: 14</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Diastolic BP
Systolic BP
Heart Rate
Amubulator DBP
Abulatory SBP</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Costa EC, Hay JL, Kehler DS, Boreskie KF, Arora RC, Umpierre D, Szwajcer A, Duhamel TA. Effects of high-intensity interval training versus moderate-intensity continuous training on blood pressure in adults with pre-to established hypertension: a systematic review and meta-analysis of randomized trials. Sports Medicine. 2018 Sep 1;48(9):2127-42.</td></tr>
<tr><td>Purpose: high intensity vs. moderate intensity for reducing BP in adults with pre or established hypertension</td><td rowspan="5">Abstract:

Background Aerobic exercise reduces blood pressure (BP), but it is unknown whether a high-intensity training approach can elicit a greater BP reduction in populations with elevated BP. This systematic review compared the efficacy of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) for reducing BP in adults with pre- to established hypertension.
Methods Five electronic databases (MEDLINE, EMBASE, CENTRAL, PEDro, and SPORTDiscus) were searched for randomized trials comparing the chronic effects of HIIT versus MICT on BP in individuals with resting systolic BP C 130 mmHg and/or diastolic BP C 85 mmHg and/or under antihypertensive medication. Random-effects modelling was used to compare changes from pre- to post-intervention in resting and ambulatory BP between HIIT and MICT. Changes from pre- to post-intervention
in maximal oxygen uptake (_V O2max) between HIIT and MICT were also meta-analyzed. Data were reported as weighted mean difference (MD) and 95%
confidence interval (CI).
Results Ambulatory BP was excluded from the meta-analysis due to the limited number of studies (two studies). Comparing changes from pre- to post-intervention, no differences in resting systolic BP (MD - 0.22 mmHg [CI 95%, - 5.36 to 4.92], p = 0.93, I2 = 53%) and diastolic BP (MD - 0.38 mmHg [CI 95%, - 3.31 to 2.54], p = 0.74,
I2 = 0%) were found between HIIT and MICT (seven studies; 164 participants). HIIT improved _V O2max to a greater magnitude than MICT (MD 2.13 ml/kg/min [CI
95%, 1.00 to 3.27], p\0.01, I2 = 41%) with similar completion rates of the intervention and attendance at the exercise training sessions (nine studies; 245 participants).
Limited data were available to compare the incidence of adverse events between HIIT and MICT.
Conclusion HIIT and MICT provided comparable reductions in resting BP in adults with pre- to established hypertension. HIIT was associated with greater improvements in VO2max when compared to MICT. Future randomized trials should investigate the efficacy of HIIT versus MICT for reducing ambulatory BP in adults with
pre- to established hypertension.
Registration PROSPERO registration</td></tr>
<tr><td>Timeframe: June 1996 to June 2016</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Systolic BP
Diastolic BP
VO2 max</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: De Sousa EC, Abrahin O, Ferreira AL, Rodrigues RP, Alves EA, Vieira RP. Resistance training alone reduces systolic and diastolic blood pressure in prehypertensive and hypertensive individuals: meta-analysis. Hypertension Research. 2017 Nov;40(11):927.</td></tr>
<tr><td>Purpose: Resistance training along on blood pressure</td><td rowspan="5">Abstract: The purpose of this study was to evaluate the effects of resistance training alone on the systolic and diastolic blood pressure in prehypertensive and hypertensive individuals. Our meta-analysis, followed the guidelines of PRISMA. The search for articles was realized by November 2016 using the following electronic databases: BIREME, PubMed, Cochrane Library, LILACS and SciELO and a search strategy that included the combination of titles of medical affairs and terms of free text to the key concepts: ‘hypertension’ ‘hypertensive’, ‘prehypertensive’, ‘resistance training’, ‘strength training’, and ‘weight-lifting’. These terms were combined with a search strategy to identify randomized controlled trials (RCTs) and identified a total of 1608 articles: 644 articles BIREME, 53 SciELO, 722 PubMed, 122 Cochrane Library and 67 LILACS. Of these, five RCTs met the inclusion criteria and provided data on 201 individuals. The results showed significant reductions for systolic blood pressure (−8.2 mm Hg CI − 10.9 to − 5.5; I2: 22.5% P valour for heterogeneity=0.271 and effect size=− 0.97) and diastolic blood pressure (−4.1 mm Hg CI − 6.3 to − 1.9; I2: 46.5% P valour for heterogeneity=0.113 and effect size=− 0.60) when compared to group
control. In conclusion, resistance training alone reduces systolic and diastolic blood pressure in prehypertensive and hypertensive subjects. The RCTs studies that investigated the effects of resistance training alone in prehypertensive and hypertensive patients support the recommendation of resistance training as a tool for management of systemic hypertension.</td></tr>
<tr><td>Timeframe: inception to Nov 2016</td></tr>
<tr><td>Total # studies included: 5</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Diastolic BP
Systolic BP</td></tr>
</table>

Diabetes

Citation: Chao M, Wang C, Dong X, et al. The Effects of Tai Chi on Type 2 Diabetes Mellitus: A Meta-Analysis. J Diabetes Res. 2018;2018:7350567. PMID: 30116744. 10.1155/2018/7350567	
Purpose: **Last Search Date:** Jun-16 **Total # studies included:** 14 RCTs **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** Glycemic control	**Abstract:** Objective: To investigate the effects of Tai chi in type 2 diabetes mellitus (type-2 DM) patients using systematic review and meta-analysis. Methods: Seven electronic resource databases were searched, and randomized controlled trials on the role of Tai chi in type-2 DM patients were retrieved. The meta-analysis was performed with RevMan 5.3, and research quality evaluation was conducted with the modified Jadad scale. Results: Fourteen studies, with 798 individuals related to the intervention of Tai chi on diabetes, were included. The results showed that, compared with non-exercise, Tai chi had the effect of lowering fasting blood glucose [MD = -1.39, 95% CI (-1.95, -0.84), P < 0.0001] and the subgroup effect size decreased with the increase of total exercise amount, there is no significant difference between Tai chi and other aerobic exercises [MD = -0.50, 95% CI (-1.02, 0.02), P = 0.06]; compared with non-exercise, Tai chi could reduce HbA1c [MD = -0.21, 95% CI (-0.61, 0.19), P = 0.31], and the group effect size decreased with the increase of total exercise amount. The reducing HbA1c effect of Tai chi was better than that of other aerobic exercises, but the difference was at the margin of statistical significance [MD = -0.19, 95% CI (-0.37, 0.00), P = 0.05]; compared with non-exercise, Tai chi had the effect of reducing 2 h postprandial blood glucose [MD = -2.07, 95% CI (-2.89, -1.26), P = 0.0002], there is no significant difference between Tai chi and other aerobic exercises in reducing 2 h postprandial blood glucose [MD = -0.44, 95% CI (-1.42, 0.54), P = 0.38]. Conclusion: Tai chi can effectively affect the management of blood glucose and HbA1c in type-2 DM patients. Long-term adherence to Tai chi has a better role in reducing blood glucose and HbA1c levels in type 2 DM patients.
Populations Analyzed: Type-2 DM (no restrictions on age or gender) without serious DM-related complications	**Author-Stated Funding Source:**

Citation: De Nardi AT, Tolves T, Lenzi TL, et al. High-intensity interval training versus continuous training on physiological and metabolic variables in prediabetes and type 2 diabetes: A meta-analysis. Diabetes Res Clin Pract. 2018;137:149-59. PMID: 29329778. 10.1016/j.diabres.2017.12.017	
Purpose:	**Abstract:** AIMS: To compare the effects of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) on functional capacity and cardiometabolic markers in individuals prediabetes and type 2 diabetes (T2D). METHODS: The search was performed in PubMed (MEDLINE), EMBASE, PEDro, CENTRAL, Scopus, LILACS database, and Clinical Trials from the inception to July 2017, included randomized clinical trials that compared the use of HIIT and MICT in prediabetes and T2D adults. The risk of bias was defined by Cochrane Handbook and quality of evidence by GRADE. RESULTS: From 818 relevant records, seven studies were included in systematic review (64 prediabetes and 120 T2D patients) and five with T2D were meta-analyzed. HIIT promoted significantly increased of 3.02mL/kg/min (CI95% 1.42-4.61) of VO2max, measured for functional capacity, compared to MICT. No differences were found between two modalities of exercises considering the outcomes HbA1c, systolic and diastolic blood pressure, total cholesterol, HDL and LDL cholesterol, triglycerides, BMI, and waist-to-hip ratio. Most of the studies presented unclear risk of bias, and low and very low quality of evidence. CONCLUSION: HIIT induces cardiometabolic adaptations similar to those of MICT in prediabetes and T2D, and provides greater benefits to functional capacity in patients with T2D. PROSPERO: CRD42016047151.
Last Search Date: Jul-17	
Total # studies included: 7 RCTs	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Glycemic control, cardiorespiratory fitness, body composition, blood pressure, or lipid profiles	
Populations Analyzed: T2D adults aged 18+	**Author-Stated Funding Source:**

<table>
<tr><td colspan="2">Citation:
Jang JE, Cho Y, Lee BW, et al. Effectiveness of Exercise Intervention in Reducing Body Weight and Glycosylated Hemoglobin Levels in Patients with Type 2 Diabetes Mellitus in Korea: A Systematic Review and Meta-Analysis. Diabetes Metab J. 2019;43(3):302-18. PMID: 30604592. 10.4093/dmj.2018.0062</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
BACKGROUND: This study aimed to assess the effectiveness of exercise intervention in reducing body weight and glycosylated hemoglobin (HbA1c) level in patients with type 2 diabetes mellitus (T2DM) in Korea. METHODS: Cochrane, PubMed, Embase, KoreaMed, KMbase, NDSL, KCI, RISS, and DBpia databases were used to search randomized controlled trials and controlled clinical trials that compared exercise with non-exercise intervention among patients with non-insulin-treated T2DM in Korea. The effectiveness of exercise intervention was estimated by the mean difference in body weight changes and HbA1c level. Weighted mean difference (WMD) with its corresponding 95% confidence interval (CI) was used as the effect size. The pooled mean differences of outcomes were calculated using a random-effects model. RESULTS: We identified 7,692 studies through literature search and selected 23 articles (723 participants). Compared with the control group, exercise intervention (17 studies) was associated with a significant decline in HbA1c level (WMD, -0.58%; 95% CI, -0.89 to -0.27; I(2)=73%). Although no significant effectiveness on body weight was observed, eight aerobic training studies showed a significant reduction in body weight (WMD, -2.25 kg; 95% CI, -4.36 to -0.13; I(2)=17%) in the subgroup analysis. CONCLUSION: Exercise significantly improves glycemic control; however, it does not significantly reduce body weight. Aerobic training can be beneficial for patients with non-insulin-treated T2DM in Korea.</td></tr>
<tr><td>Last Search Date:
Aug-17</td></tr>
<tr><td>Total # studies included:
23 RCTs</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
HbA1c levels and weight</td></tr>
<tr><td>Populations Analyzed:
Patients with T2DM who are not on insulin therapy</td><td>Author-Stated Funding Source:</td></tr>
</table>

<table>
<tr><td colspan="2">Citation:
Lauche R, Peng W, Ferguson C, et al. Efficacy of Tai Chi and qigong for the prevention of stroke and stroke risk factors: A systematic review with meta-analysis. Medicine (Baltimore). 2017;96(45):e8517. PMID: 29137055. 10.1097/md.0000000000008517</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
BACKGROUND: This review aims to summarize the evidence of Tai Chi and qigong interventions for the primary prevention of stroke, including the effects on populations with major stroke risk factors. METHODS: A systematic literature search was conducted on January 16, 2017 using the PubMed, Scopus, Cochrane Library, and CINAHL databases. Randomized controlled trials examining the efficacy of Tai Chi or qigong for stroke prevention and stroke risk factors were included. Risk of bias was assessed using the Cochrane Risk of Bias tool. RESULTS: Twenty-one trials with n = 1604 patients with hypertension, hyperlipidaemia, diabetes, overweight or obesity, or metabolic syndrome were included. No trials were found that examined the effects of Tai Chi/qigong on stroke incidence. Meta-analyses revealed significant, but not robust, benefits of Tai Chi/qigong over no interventions for hypertension (systolic blood pressure: -15.55 mm Hg (95% CI: -21.16; -9.95); diastolic blood pressure: -10.66 mm Hg (95% CI: -14.90, -6.43); the homeostatic model assessment (HOMA) index (-2.86%; 95% CI: -5.35, -0.38) and fasting blood glucose (-9.6 mg/dL; 95% CI: -17.28, -1.91), and for the body mass index compared with exercise controls (-1.65 kg/m; 95% CI: -3.11, -0.20). Risk of bias was unclear or high for the majority of trials and domains, and heterogeneity between trials was high. Only 6 trials adequately reported safety. No recommendation for the use of Tai Chi/qigong for the prevention of stroke can be given. CONCLUSION: Although Tai Chi and qigong show some potential more robust studies are required to provide conclusive evidence on the efficacy and safety of Tai Chi and qigong for reducing major stroke risk factors.</td></tr>
<tr><td>Last Search Date:
1-Jan-17</td></tr>
<tr><td>Total # studies included:
6 RCTs</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Stroke incidence, gylcemic control, behavioral outcomes, safety</td></tr>
<tr><td>Populations Analyzed:
Diagnosed with type 2 diabetes mellitus</td><td>Author-Stated Funding Source:</td></tr>
</table>

Citation: Lee J, Kim D, Kim C. Resistance Training for Glycemic Control, Muscular Strength, and Lean Body Mass in Old Type 2 Diabetic Patients: A Meta-Analysis. Diabetes Ther. 2017;8(3):459-73. PMID: 28382531. 10.1007/s13300-017-0258-3	
Purpose:	**Abstract:** INTRODUCTION: Type 2 diabetes (T2D) in elderly patients is associated with accelerated loss of skeletal muscle mass and strength. However, there are few meta-analysis reviews which investigate the effects of resistance training (RT) on glycemic control and skeletal muscle in the patients. METHODS: Three electronic databases were searched (from the earliest date available to November 2016). Studies were included according to the inclusion criteria: T2D patients at least 60 years old, fasting plasma glucose of at least 7.0, and at least 8 weeks of RT. RESULTS: Fifteen cohorts of eight studies (360 patients, average age 66 years) met the inclusion criteria. RT groups lowered glycosylated hemoglobin (HbA1c) (mean ES = -0.37, 95% CI = -0.55 to -0.20, P < 0.01) but did not result in a significant effect on lean body mass (LBM) (mean ES = 0.08, 95% CI = -0.15 to 0.30, P = 0.50). Homogeneity was shown between studies regarding HbA1c and LBM (Q = 15.70, df = 9, P = 0.07 and Q = 0.12, df = 4, P = 0.998, respectively). High-intensity subgroups showed a slight tendency to improve (rather than duration, frequency, and weekly volume) and to decrease HbA1c levels more than low-intensity subgroups (P = 0.37). RT increased muscular strength (mean ES = 1.05, 95% CI = 0.26-1.84, P = 0.01). No training components explained the heterogeneity between studies with changes in muscle strength. CONCLUSION: RT improves glycemic control and muscle strength in elderly patients with T2D. RT with high intensity can be a strategy to treat patients with T2D and sarcopenia associated with aging.
Last Search Date: Nov-16	
Total # studies included: 10 RCTs	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Glycemic control, muscular strength	
Populations Analyzed: Participants were at least 60 years old and had T2D	**Author-Stated Funding Source:**

Citation: Liao F, An R, Pu F, et al. Effect of Exercise on Risk Factors of Diabetic Foot Ulcers: A Systematic Review and Meta-Analysis. *Am J Phys Med Rehabil*. 2019;98(2):103-16. PMID: 30020090. 10.1097/phm.0000000000001002	
Purpose:	**Abstract:** The objectives of this study were to examine the effectiveness of different types of exercise on risk factors of diabetic foot ulcers, including glycated hemoglobin, peripheral arterial disease, and diabetic peripheral neuropathy, in people with type 2 diabetes mellitus. PubMed, Web of Science, Cochrane Library, Scopus, and CINAHL were searched from inception to January 2018 for relevant articles. Eligible studies were randomized controlled trials that examined effects of exercise on the selected risk factors. Twenty randomized controlled trials with 1357 participants were included in the meta-analyses. The differences in postintervention values of glycated hemoglobin and ankle brachial index between exercise and control groups were synthesized, yielding mean differences of -0.45% (P < 0.00001) and 0.03 (P = 0.002), respectively; the differences in within-group changes in glycated hemoglobin were synthesized, yielding mean differences of -0.19% (P = 0.1), -0.25% (P = 0.0006), and -0.64% (P = 0.006) for aerobic versus resistance, combined versus aerobic, and combined versus resistance exercise, respectively. Exercise has a significant effect on reducing glycated hemoglobin, whereas combined exercise is more effective compared with aerobic or resistance exercise alone. Exercise also improves ankle brachial index. However, evidence regarding the association between exercise and peripheral neuropathy and risks of diabetic foot ulcers in people with type 2 diabetes mellitus remains insufficient.
Last Search Date: Jan-18	
Total # studies included: 20 RCTs	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: HbA1c, peripheral neuropathy, and vascular structure or function or cutaneous microvascular function of the lower limbs	
Populations Analyzed: T2DM 18 yrs and older	**Author-Stated Funding Source:**

<table>
<tr><td colspan="2">Citation:
Liu JX, Zhu L, Li PJ, et al. Effectiveness of high-intensity interval training on glycemic control and cardiorespiratory fitness in patients with type 2 diabetes: a systematic review and meta-analysis. Aging Clin Exp Res. 2019;31(5):575-93. PMID: 30097811. 10.1007/s40520-018-1012-z</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
We investigated the influence of resistance exercise (RE) with different intensities on HbA1c, insulin and blood glucose levels in patients with type 2 diabetes (T2D). Diabetes trials that compared RE group with a control were included in meta-analysis. Exercise intensities were categorized into low-to-moderate-intensity and high-intensity subgroups. Intensity effect on glycemic control was determined by meta-regression analysis, and risk-of-bias was assessed using Cochrane Collaboration tool. 24 trials met the inclusion criteria, comprised of 962 patients of exercise (n = 491) and control (n = 471). Meta-regression analysis showed decreased HbA1c (p = 0.006) and insulin (p = 0.015) after RE was correlated with intensity. Subgroup analysis revealed decreased HbA1c was greater with high intensity (-0.61; 95% CI -0.90, -0.33) than low-to-moderate intensity (-0.23; 95% CI -0.41, -0.05). Insulin levels were significantly decreased only with high intensity (-4.60; 95% CI -7.53, -1.67), not with low-to-moderate intensity (0.07; 95% CI -3.28, 3.42). Notably, values between the subgroups were statistically significant for both HbA1c (p = 0.03) and insulin (p = 0.04), indicative of profound benefits of high-intensity RE. Pooled outcomes of 15 trials showed only a decreased trend in blood glucose with RE (p = 0.09), and this tendency was not associated with intensity. Our meta-analysis provides additional evidence that high-intensity RE has greater beneficial effects than low-to-moderate-intensity in attenuation of HbA1c and insulin in T2D patients.</td></tr>
<tr><td>Last Search Date:
Sep-18</td></tr>
<tr><td>Total # studies included:
24 RCTs</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Glycemic control</td></tr>
<tr><td>Populations Analyzed:
Patients with definite T2D</td><td>Author-Stated Funding Source:</td></tr>
</table>

Citation: Liu Y, Ye W, Chen Q, et al. Resistance Exercise Intensity is Correlated with Attenuation of HbA1c and Insulin in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2019;16(1). PMID: 30621076. 10.3390/ijerph16010140	
Purpose:	**Abstract:** AIMS: The aim of this systematic review and meta-analysis was to quantify the effect of high-intensity interval training (HIIT) on glycemic control and cardiorespiratory fitness compared with moderate-intensity training (MICT) and no training at all in patients with type 2 diabetes (T2D). METHODS: Relevant articles were sourced from PubMed, Embase, the Web of Science, EBSCO, and the Cochrane Library. Randomized-controlled trials were included based upon the following criteria: participants were clinically diagnosed with T2D, outcomes that included glycemic control (e.g., hemoglobin A1c); body composition (e.g., body weight); cardiorespiratory fitness (e.g., VO2peak) are measured at baseline and post-intervention and compared with either a MICT or control group. RESULTS: Thirteen trials involving 345 patients were finally identified. HIIT elicited a significant reduction in BMI, body fat, HbA1c, fasting insulin, and VO2peak in patients with type 2 diabetes. Regarding changes in the body composition of patients, HIIT showed a great improvement in body weight (mean difference: - 1.22 kg, 95% confidence interval [CI] - 2.23 to - 0.18, P = 0.02) and body mass index (mean difference: - 0.40 kg/m(2), 95% CI - 0.78 to - 0.02, P = 0.04) than MICT did. Similar results were also found with respect to HbA1c (mean difference: - 0.37, 95% CI - 0.55 to - 0.19, P < 0.0001); relative VO2peak (mean difference: 3.37 ml/kg/min, 95% CI 1.88 to 4.87, P < 0.0001); absolute VO2peak (mean difference: 0.37 L/min, 95% CI 0.28 to 0.45, P < 0.00001). CONCLUSIONS: HIIT may induce more positive effects in cardiopulmonary fitness than MICT in T2D patients.
Last Search Date: Apr-18	
Total # studies included: 13 RCTs	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Glycemic control, body composition, cardiorespiratory fitness	
Populations Analyzed: Clinically diagnosed with type 2 diabetes	**Author-Stated Funding Source:**

Citation: Meng D, Chunyan W, Xiaosheng D, et al. The Effects of Qigong on Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Evid Based Complement Alternat Med. 2018;2018:8182938. PMID: 29507593. 10.1155/2018/8182938	
Purpose:	**Abstract:** Objective. The purpose of this study was to investigate the effects of Qigong on type 2 diabetes mellitus (DM) using the systematic review and meta-analysis. Methods. All prospective, randomized, controlled clinical trials published in English or Chinese and involving the use of Qigong by patients with DM were searched in 7 electronic databases from their respective inception to June 2016. The meta-analysis was conducted using the Revman 5.2. The quality of the included trials was assessed using the Jadad rating scale. Two researchers independently completed the inclusion, data extraction, and quality assessment. Results. Twenty-one trials with 1326 patients met the inclusion criteria and were reviewed. The meta-analysis demonstrated that, compared with no exercise, the Qigong had significant effects on fasting blood glucose (MD = −0.99, 95% CI (−1.23, 0.75), P<0.0001), HbA1c (MD = −0.84, 95% CI (−1.02, −0.65), P<0.0001), and postprandial blood glucose (MD = −1.55, 95% CI (−2.19, −0.91), P<0.00001). Conclusion. The Qigong training can improve the blood glucose status of the type 2 DM patients and has positive effects on the management of type 2 DM. However, future research with better quality still needs to be conducted to address the effects of Qigong on type 2 DM.
Last Search Date: Jun-16	
Total # studies included: 21 RCTs	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Glycemic control	
Populations Analyzed: Diabetic patients (assume T2DM) without serious DM related complications.	**Author-Stated Funding Source:**

<table>
<tr><td colspan="2">Citation:
Pan B, Ge L, Xun YQ, et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. Int J Behav Nutr Phys Act. 2018;15(1):72. PMID: 30045740. 10.1186/s12966-018-0703-3</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
INTRODUCTION: Current international guidelines recommend aerobic, resistance, and combined exercises for the management of type 2 diabetes mellitus (T2DM). In our study, we conducted a network meta-analysis to assess the comparative impact of different exercise training modalities on glycemic control, cardiovascular risk factors, and weight loss in patients with T2DM. METHODS: We searched five electronic databases to identify randomized controlled trials (RCTs) that compared the differences between different exercise training modalities for patients with T2DM. The risk of bias in the included RCTs was evaluated according to the Cochrane tool. Network meta-analysis was performed to calculate mean difference the ratio of the mean and absolute risk differences. Data were analyzed using R-3.4.0. RESULTS: A total of 37 studies with 2208 patients with T2DM were included in our study. Both supervised aerobic and supervised resistance exercises showed a significant reduction in HbA1c compared to no exercise (0.30% lower, 0.30% lower, respectively), however, there was a less reduction when compared to combined exercise (0.17% higher, 0.23% higher). Supervised aerobic also presented more significant improvement than no exercise in fasting plasma glucose (9.38 mg/dl lower), total cholesterol (20.24 mg/dl lower), triacylglycerol (19.34 mg/dl lower), and low-density lipoprotein cholesterol (11.88 mg/dl lower). Supervised resistance showed more benefit than no exercise in improving systolic blood pressure (3.90 mmHg lower]) and total cholesterol (22.08 mg/dl lower]. In addition, supervised aerobic exercise was more powerful in improving HbA1c and weight loss than unsupervised aerobic (HbA1c: 0.60% lower; weight loss: 5.02 kg lower) and unsupervised resistance (HbA1c: 0.53% lower) exercises. CONCLUSION: Compared with either supervised aerobic or supervised resistance exercise alone, combined exercise showed more pronounced improvement in HbA1c levels; however, there was a less marked improvement in some cardiovascular risk factors. In terms of weight loss, there were no significant differences among the combined, supervised aerobic, and supervised resistance exercises. TRIAL REGISTRATION: Our study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO); registration number: CRD42017067518 .</td></tr>
<tr><td>Last Search Date:
Apr-17</td></tr>
<tr><td>Total # studies included:
37 RCTs</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Glycemic control, body composition, blood pressure, or lipid profiles</td></tr>
<tr><td>Populations Analyzed:
T2DM aged ≥18 years</td><td>Author-Stated Funding Source:</td></tr>
</table>

<table>
<tr><td colspan="2">Citation:
Qiu S, Cai X, Sun Z, et al. Aerobic Interval Training and Cardiometabolic Health in Patients with Type 2 Diabetes: A Meta-Analysis. Front Physiol. 2017;8:957. PMID: 29218018. 10.3389/fphys.2017.00957</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
Vigorous to maximal aerobic interval training (INT) has received remarkable interest in improving cardiometabolic outcomes for type 2 diabetes patients recently, yet with inconsistent findings. This meta-analysis was aimed to quantify its effectiveness in type 2 diabetes. Randomized controlled trials (RCTs) were identified by searches of 3 databases to October 2017, which evaluated the effects of INT with a minimal training duration of 8 weeks vs. moderate-intensity continuous training (MICT) or non-exercise training (NET) among type 2 diabetes patients on outcomes including cardiorespiratory fitness, glycemic control, body composition, blood pressure, and lipid profiles. Weighted mean differences with 95% confidence intervals (CIs) were calculated with the random-effects model. Nine datasets from 7 RCTs with 189 patients were included. Compared with MICT, INT improved maximal oxygen consumption (VO2max) by 2.60 ml/kg/min (95% CI: 1.32 to 3.88 ml/kg/min, P <0.001) and decreased hemoglobin A1c (HbA1c) by 0.26% (95% CI: -0.46% to -0.07%, P = 0.008). These outcomes for INT were also significant vs. energy expenditure-matched MICT, with VO2max increased by 2.18 ml/kg/min (P = 0.04) and HbA1c decreased by 0.28% (P = 0.01). Yet their magnitudes of changes were larger compared with NET, with VO2max increased by 6.38 ml/kg/min (P <0.001) and HbA1c reduced by 0.83% (P = 0.004). Systolic blood pressure could be lowered by INT compared with energy expenditure-matched MICT or NET (both P <0.05), but other cardiometabolic markers and body composition were not significantly altered in general. In conclusion, despite a limited number of studies, INT improves cardiometabolic health especially for VO2max and HbA1c among patients with type 2 diabetes, and might be considered an alternative to MICT. Yet the optimal training protocols still require to be established.</td></tr>
<tr><td>Last Search Date:
Oct-17</td></tr>
<tr><td>Total # studies included:
9 RCTs</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Cardiorespiratory fitness, glycemic control, body composition, blood pressure, or lipid profiles</td></tr>
<tr><td>Populations Analyzed:
Patients with T2DM</td><td>Author-Stated Funding Source:</td></tr>
</table>

<table>
<tr><td colspan="2">Citation:
Rees JL, Johnson ST, Boule NG. Aquatic exercise for adults with type 2 diabetes: a meta-analysis. Acta Diabetol. 2017;54(10):895-904. PMID: 28691156. 10.1007/s00592-017-1023-9</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
AIMS: The purpose of this systematic review and meta-analysis was to examine the effects of aquatic exercise (AquaEx) on indicators of glycemic control (i.e., glycated hemoglobin [A1c] and fasting plasma glucose) in adults with type 2 diabetes mellitus (T2DM). It was hypothesized that AquaEx would improve glycemic control to a similar extent as land-based exercise (LandEx), but to a greater extent than non-exercise control (Ctrl). METHODS: A literature search was completed in February 2017 for studies examining AquaEx training in adults with T2DM. Assessment of glycemic control was necessary for inclusion, while secondary outcomes such as quality of life and cardiometabolic risk factors (i.e., blood pressure, triglycerides and total cholesterol) were considered, but not required for inclusion. Outcomes were measured before and after at least 8 weeks of AquaEx, and data were analyzed using weighted mean differences (WMDs) and fixed effect models, when appropriate. RESULTS: Nine trials including 222 participants were identified. Three trials compared AquaEx to LandEx, two compared AquaEx to Crtl, and four had a pre-/post-design without a comparison group. Results indicate no difference in A1c between LandEx and AquaEx (WMD = -0.02%, 95% confidence interval = [-0.71, 0.66]). Post-intervention A1c was lower in AquaEx when compared to Crtl (WMD = -0.96%, [-1.87, -0.05]). Post-AquaEx A1c was lower compared to baseline (WMD = -0.48%, [-0.66, -0.30]). CONCLUSIONS: A1c can be reduced after eight-twelve weeks of AquaEx. However, at this time few studies have examined whether changes in A1c are different from LandEx or Crtl.</td></tr>
<tr><td>Last Search Date:
Feb-17</td></tr>
<tr><td>Total # studies included:
9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
HBA1c</td></tr>
<tr><td>Populations Analyzed:
Adults with T2DM</td><td>Author-Stated Funding Source:</td></tr>
</table>

<table>
<tr><td colspan="2">Citation:
Sampath Kumar A, Maiya AG, Shastry BA, et al. Exercise and insulin resistance in type 2 diabetes mellitus: A systematic review and meta-analysis. Ann Phys Rehabil Med. 2019;62(2):98-103. PMID: 30553010. 10.1016/j.rehab.2018.11.001</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
BACKGROUND: Insulin resistance is a determining factor in the pathophysiology of type 2 diabetes mellitus (T2DM). Exercise is known to improve insulin resistance, but a systematic review of the literature is lacking. OBJECTIVE: This systematic review and meta-analysis focused on identifying evidence for the effectiveness of a structured exercise intervention program for insulin resistance in T2DM. METHODS: We searched MEDLINE via PubMed, CINHAL, Scopus and Web of Science, and the Cochrane Central Register of Controlled Trials for reports of studies on fasting insulin, homeostatic model assessment for insulin resistance (Homa-IR), fasting blood sugar, glycated hemoglobin and body mass index in patients with T2DM and healthy controls that were published between 1990 and 2017. Data are reported as the standardized mean difference or mean difference with 95% confidence intervals (CIs). RESULTS: Among 2242 records retrieved, only 11 full-text articles were available for meta-analysis. Data for 846 participants were analyzed, 440 in the intervention group, and 406 in the control group. The mean difference for fasting insulin level was-1.64 (95% CI; -3.38 to 0.10), Homa-Ir 0.14 (-1.48 to 1.76), fasting blood sugar-5.12 (-7.78 to-2.45), hemoglobin A1c 0.63 (-0.82 to 2.08) and body mass index-0.36 (-1.51 to 0.79). CONCLUSION: The evidence highlights the effectiveness of a structured exercise intervention program for insulin resistance in T2DM with a moderate level 2 of evidence.</td></tr>
<tr><td>Last Search Date:
Jun-17</td></tr>
<tr><td>Total # studies included:
11 RCT or CCT</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Glycemic control, BMI</td></tr>
<tr><td>Populations Analyzed:
T2DM in people 18 years or older</td><td>Author-Stated Funding Source:</td></tr>
</table>

<table>
<tr><td colspan="2">Citation:
Song G, Chen C, Zhang J, et al. Association of traditional Chinese exercises with glycemic responses in people with type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. J Sport Health Sci. 2018;7(4):442-52. PMID: 30450253. 10.1016/j.jshs.2018.08.004</td></tr>
<tr><td>Purpose:

Last Search Date:
Sep-17

Total # studies included:
39 RCTs

Other details (e.g. definitions used, exclusions etc)

Outcomes addressed:
Glycemic control, body composition, blood pressure, or lipid profiles</td><td>Abstract:
Background: There is increasing evidence showing the health benefits of various forms of traditional Chinese exercises (TCEs) on the glycemic profile in people with type 2 diabetes. However, relatively little is known about the combined clinical effectiveness of these traditional exercises. This study was designed to perform a systematic review and meta-analysis of the overall effect of 3 common TCEs (Tai Ji Quan, Qigong, Ba Duan Jin) on glycemic control in adults with type 2 diabetes. Methods: We conducted an extensive database search in Cochrane Library, EMBASE, PubMed, Web of Science, EBSCO, and China National Knowledge Infrastructure on randomized controlled trials published between April 1967 and September 2017 that compared any of the 3 TCEs with a control or comparison group on glycemic control. Data extraction was performed by 2 independent reviewers. Study quality was evaluated using the Cochrane Handbook for Systematic Reviews of Interventions, which assessed the risk of bias, including sequence generation, allocation concealment, blinding, completeness of outcome data, and selective outcome reporting. The resulting quality of the reviewed studies was characterized in 3 grades representing the level of bias: low, unclear, and high. All analyses were performed using random effects models and heterogeneity was quantified. We a priori specified changes in biomarkers of hemoglobin A1c (in percentage) and fasting blood glucose (mmol/L) as the main outcomes and triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein-cholesterol, 2-h plasma glucose, and fasting plasma glucose as secondary outcomes. Results: A total of 39 randomized, controlled trials (Tai Ji Quan=11; Qigong=6; Ba Duan Jin=22) with 2917 type 2 diabetic patients (aged 41-80 years) were identified. Compared with a control or comparison group, pooled meta-analyses of TCEs showed a significant decrease in hemoglobin A1c (mean difference (MD)=-0.67%; 95% confidence interval (CI): -0.86% to -0.48%; p < 0.00001) and fasting blood glucose (MD=-0.66 mmol/L; 95%CI: -0.95 to -0.37 mmol/L; p < 0.0001). The observed effect was more pronounced for interventions that were medium range in duration (i.e., >3-<12 months). TCE interventions also showed improvements in the secondary outcome measures. A high risk of bias was observed in the areas of blinding (i.e., study participants and personnel, and outcome assessment). Conclusion: Among patients with type 2 diabetes, TCEs were associated with significantly lower hemoglobin A1c and fasting blood glucose. Further studies to better understand the dose and duration of exposure to TCEs are warranted.</td></tr>
<tr><td>Populations Analyzed:
Adults with type 2 diabetes</td><td>Author-Stated Funding Source:</td></tr>
</table>

<table>
<tr><td colspan="2">Citation:
Thind H, Lantini R, Balletto BL, et al. The effects of yoga among adults with type 2 diabetes: A systematic review and meta-analysis. Prev Med. 2017;105:116-26. PMID: 28882745. 10.1016/j.ypmed.2017.08.017</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
The purpose of this meta-analysis was to examine the effects of yoga for glycemic control among adults with type 2 diabetes (T2DM). Comprehensive electronic databases searches located 2559 unique studies with relevant key terms. Studies were included if they (1) evaluated a yoga intervention to promote T2DM management, (2) used a comparison group, (3) reported an objective measure of glycemic control at post-intervention, and (4) had follow-up length or post-test of at least 8weeks from baseline. Independent raters coded participant, design and methodological characteristics and intervention content. Summary effect sizes and 95% confidence intervals (CI) were calculated. Twenty-three studies with 2473 participants (mean age=53years; 43% women) met eligibility criteria. Compared with controls, yoga participants were successful in improving their HbA1c (d+=0.36, 95% CI=0.16, 0.56; k=16), FBG (d+=0.58, 95% CI=0.40, 0.76; k=20), and PPBG (d+=0.40, 95% CI=0.23, 0.56; k=14). Yoga was also associated with significant improvements in lipid profile, blood pressure, body mass index, waist/hip ratio and cortisol levels. Overall, studies satisfied an average of 41% of the methodological quality (MQ) criteria; MQ score was not associated with any outcome (Ps >0.05). Yoga improved glycemic outcomes and other risk factors for complications in adults with T2DM relative to a control condition. Additional studies with longer follow-ups are needed to determine the long-term efficacy of yoga for adults with T2DM.</td></tr>
<tr><td>Last Search Date:
Feb-16</td></tr>
<tr><td>Total # studies included:
23</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Glycemic control, body composition, blood pressure, or lipid profiles</td></tr>
<tr><td>Populations Analyzed:
T2DM adults≥18 years of age</td><td>Author-Stated Funding Source:</td></tr>
</table>

<table>
<tr><td colspan="2">Citation:
Xia TW, Yang Y, Li WH, et al. Different training durations and styles of tai chi for glucose control in patients with type 2 diabetes: a systematic review and meta-analysis of controlled trials. BMC Complement Altern Med. 2019;19(1):63. PMID: 30871517. 10.1186/s12906-019-2475-y</td></tr>
<tr><td>Purpose:</td><td rowspan="5">Abstract:
BACKGROUND: Physical activity is an important part of the diabetes management plan. However, the effects caused by different training durations and styles of Tai Chi have not been evaluated. We conducted an updated systematic review of the effects of Tai Chi on patients with type 2 diabetes based on different training durations and styles. METHODS: We performed a search for Chinese and English studies in 8 databases. Two reviewers independently selected the eligible trials and conducted a critical appraisal of the methodological quality. RESULTS: Seventeen trials were included. Tai Chi was found to have reduced fasting blood glucose (FBG) [SMD = - 0.54, 95% CI (- 0.91, - 0.16), P = 0.005] and HbA1c [SMD = - 0.68, 95% CI (- 1.17, - 0.19), P = 0.006] overall, compared with a control group. Considering the subgroup analysis, the pooled results showed that 24 movements or Yang-style Tai Chi did not significantly reduce FBG after a duration of </=3 months [SMD = - 0.46, 95% CI (- 1.42, 0.50), P = 0.35] or > 3 months [SMD = - 0.50, 95% CI (- 1.49, 0.49), P = 0.32], nor did it reduce HbA1c [SMD = - 1.22, 95% CI (- 2.90, 0.47), P = 0.16] after a duration > 3 months in all studies. However, other styles of Tai Chi significantly reduced FBG [SMD = - 0.90, 95% CI (- 1.28, - 0.52), P < 0.00001] and HbA1c [SMD = - 0.90, 95% CI (- 1.28, - 0.52), P < 0.00001] after a duration > 3 months, while no significant reduction in FBG [SMD = - 0.34, 95% CI (- 0.76, 0.08), P = 0.12] or HbA1c [SMD = - 0.34, 95% CI (- 0.76, 0.08), P = 0.12] was found after a duration </=3 months. CONCLUSIONS: Tai Chi seems to be effective in treating type 2 diabetes. Different training durations and styles result in variable effectiveness. The evidence was insufficient to support whether long-term Tai Chi training was more effective.</td></tr>
<tr><td>Last Search Date:
Apr-18</td></tr>
<tr><td>Total # studies included:
17 RCTs</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Glycemic control, body composition, blood pressure, or lipid profiles</td></tr>
<tr><td>Populations Analyzed:
Clear diagnosis of T2D</td><td>Author-Stated Funding Source:</td></tr>
</table>

Citation: Yu X, Chau JPC, Huo L. The effectiveness of traditional Chinese medicine-based lifestyle interventions on biomedical, psychosocial, and behavioral outcomes in individuals with type 2 diabetes: A systematic review with meta-analysis. Int J Nurs Stud. 2018;80:165-80. PMID: 29471267. 10.1016/j.ijnurstu.2018.01.009	
Purpose: **Last Search Date:** Dec-16 **Total # studies included:** 20 RCTs or CCTs **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** Glycemic control, body composition, blood pressure, or lipid profiles; QOL and depression measures; behavioral outcomes	**Abstract:** BACKGROUND: Integrative diabetes care, which combines conventional diabetes therapy with traditional Chinese medicine (TCM)-based interventions, has gained popularity worldwide. Numerous TCM-based lifestyle modification approaches have been proposed for individuals with type 2 diabetes (T2DM). OBJECTIVES: To synthesize and present the best available evidence on the effectiveness of TCM-based lifestyle interventions in individuals with T2DM. DESIGN: We undertook a systematic review of randomized controlled trials or controlled clinical trials. DATA SOURCES: Six English and four Chinese electronic databases were searched from their inceptions to December 2016. REVIEW METHODS: Trials investigating the effectiveness of various TCM-based lifestyle interventions among adults with T2DM were reviewed. Studies were excluded if TCM-based lifestyle interventions were only part of the intervention regimen. Two reviewers independently selected studies according to pre-specified inclusion and exclusion criteria and appraised the risk of bias of the included studies. One reviewer extracted details of the included studies and the second reviewer checked the extracted data critically. When feasible, data were statistically pooled for meta-analysis. Otherwise, narrative summaries were used. RESULTS: Twenty-four studies were included. The pooled analysis of the eight studies on tai chi showed tai chi practice for at least 150min per week was beneficial in lowering glycosylated hemoglobin (mean difference, -1.48%; 95%CI, -2.58% to -0.39%; p<0.001). Tai chi was effective in reducing fasting blood glucose (mean difference, -1.14mmol/L; 95%CI, -1.78 to -0.50mmol/L; p<0.001) and body mass index (mean difference, -0.62; 95%CI, -1.14 to -0.11; p=0.02), and improving quality of life. The effects of tai chi on blood pressure and waist circumference were inconclusive due to the limited number of studies. The meta-analysis of the 12 studies on ba duan jin demonstrated beneficial effects on glycosylated hemoglobin (mean difference, -0.77%; 95%CI, -0.97% to -0.56%; p<0.001), fasting blood glucose (mean difference, -0.82mmol/L; 95%CI, -1.05 to -0.59mmol/L; p<0.001), body mass index (mean difference, -2.77; 95%CI, -4.11 to -1.43; p<0.001), and depression (mean difference, -4.53; 95%CI, -7.12 to -1.94; p<0.001). Conclusions on the effects of ba duan jin on quality of life cannot be drawn because only two studies measured the outcome. Evidence regarding the effectiveness of other TCM-based lifestyle interventions is limited. CONCLUSIONS: Tai chi and ba duan jin are potentially effective options for individuals with T2DM to improve biomedical and psychosocial well-being. Further well-designed studies are needed to explore the optimal intervention dose and to investigate the effectiveness of other TCM-based lifestyle interventions.
Populations Analyzed: Adults (≥18 years old) with a clinical diagnosis of T2DM	**Author-Stated Funding Source:**

Citation: Zhou Z, Zhou R, Li K, et al. Effects of tai chi on physiology, balance and quality of life in patients with type 2 diabetes: A systematic review and meta-analysis. J Rehabil Med. 2019;51(6):405-17. PMID: 30968941. 10.2340/16501977-2555	
Purpose:	**Abstract:**
Last Search Date: Mar-18	OBJECTIVE: To systematically synthesize and critically evaluate evidence on the effects of tai chi for patients with type 2 diabetes mellitus. DATA SOURCES: Seven electronic databases (Wan Fang, SinoMed, China National Knowledge Infrastructure, VIP, PubMed, Embase, and Cochrane Library) were systematically searched from their inception to March 2018. STUDY SELECTION: Randomized controlled trials investigating the effects of tai chi on individuals with type 2 diabetes mellitus were eligible. DATA EXTRACTION: Biomedical outcomes (fasting plasma glucose, glycosylated haemoglobin (HbA1c), fasting insulin, insulin resistance, body mass index, total cholesterol, blood pressure) as well as balance and quality of life-related outcomes were extracted independently by 2 reviewers. Stata 12.0 software was used to synthesize data if there was no or moderate heterogeneity across studies. Otherwise, narrative summaries were performed. DATA SYNTHESIS: A total of 23 studies (25 articles) involving 1,235 patients were included in this meta-analysis. Significant changes in tai chi-related effects were observed in lowering fasting plasma glucose (standardized mean difference; SMD -0.67; 95% confidence interval (95% CI) -0.87 to -0.47; p <0.001), HbA1c (mean difference; MD-0.88%; 95% CI -1.45% to -0.31%; p =0.002) and insulin resistance (MD -0.41; 95% CI -0.78 to -0.04; p = 0.029). Beneficial effects of tai chi were also found in decreasing body mass index (MD -0.82 kg/m2; 95% CI -1.28 to -0.37 kg/m2; p < 0.001) and total cholesterol (SMD -0.59; 95% CI -0.90 to -0.27; p < 0.001). In addition, tai chi reduced blood pressure (systolic blood pressure (MD -10.03 mmHg; 95% CI -15.78 to -4.29 mmHg; p = 0.001), diastolic blood pressure (MD -4.85 mmHg; 95% CI -8.23 to -1.47 mmHg; p = 0.005)) and improved quality of life-related outcomes (physical function (MD 7.07; 95% CI 0.79-13.35; p = 0.027), bodily pain (MD 4.30; 95% CI 0.83-7.77; p = 0.015) and social function (MD 13.84; 95% CI 6.22-21.47; p < 0.001)). However, no impact was exerted on fasting insulin (SMD -0.32; 95% CI -0.71 to 0.07; p = 0.110) or balance (MD 2.71 s; 95% CI -3.29 to 8.71 s; p = 0.376). CONCLUSION: Tai chi is effective in controlling biomedical outcomes and improving quality of life-related outcomes in individuals with type 2 diabetes mellitus, although no effects were observed on balance and fasting insulin. Further high-quality research is needed to elucidate the effects of different types of tai chi, the long-term effects of tai chi, the impact on respiratory function, and the association between tai chi and the risk of developing type 2 diabetes mellitus in healthy individuals.
Total # studies included: 23 RCTs	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Glycemic control, body composition, blood pressure, or lipid profiles, QOL	
Populations Analyzed: Patients diagnosed with T2DM age > 18 years	**Author-Stated Funding Source:**

Human Immunodeficiency Virus (HIV)

<table>
<tr><td colspan="2">SR/MA
Citation: Ibeneme SC, Omeje C, Myezwa H, Ezeofor SN, Anieto EM, Irem F, Nnamani AO, Ezenwankwo FE, Ibeneme GC. Effects of physical exercises on inflammatory biomarkers and cardiopulmonary function in patients living with HIV: a systematic review with meta-analysis. BMC Infectious Diseases. 2019 Dec; 19(1):359.</td></tr>
<tr><td>Purpose: To evaluate the effects of physical exercises on 1) inflammatory biomarkers and 2) cardiopulmonary function (VO_2 Max) in PLWH.
Timeframe: Variable start dates to January 2018
Total # studies included: 23
Other details (e.g. definitions used, exclusions etc)
Only randomized control trials investigating the effects of either aerobic or resistance or a combination of both exercise types with a control/other intervention(s) for a period of at least 4 weeks among adults living with HIV, were included.
Outcomes addressed:
Cardio risk metabolic markers</td>
<td>Abstract:
Background: Pro-inflammatory cytokines expressed in human immune deficiency virus (HIV) infection, may induce oxidative stress that is likely to compromise the patency of the airways or damage the lung tissues/cardiac function. However, physical (aerobic and/or resistance) exercise-induced release of heat shock protein, immune function alteration or reduced tissue hypoxia, have been highlighted as possible mechanisms by which increasing physical activity may reduce plasma pro-inflammatory cytokines in uninfected individuals and should be appraised in the literature for evidence of similar benefits in people living with HIV (PLWH). Therefore, we evaluated the effects of physical exercises on 1) inflammatory biomarkers and 2) cardiopulmonary function (VO_2 Max) in PLWH.
Method: A systematic review was conducted using the Cochrane Collaboration protocol. Searching databases, up to January 2018. Only randomized control trials investigating the effects of either aerobic or resistance or a combination of both exercise types with a control/other intervention(s) for a period of at least 4 weeks among adults living with HIV, were included. Two independent reviewers determined the eligibility of the studies. Data were extracted and risk of bias (ROB) was assessed with the Cochrane Collaboration ROB tool. Meta-analyses were conducted with random effect models using the Review Manager (RevMan) computer software.
Result: Twenty-three studies met inclusion criteria (n = 1073 participants at study completion) comprising male and female with age range 18–65 years. Three meta-analyses across three sub-groups comparisons were performed. The result showed no significant change in biomarkers of inflammation (IL-6 and IL-1β) unlike a significant ($Z = 3.80$, $p < 0.0001$) improvement in VO_2 Max. Overall, the GRADE evidence for this review was of moderate quality.
Conclusion: There was evidence that engaging in either aerobic or resistance exercise, or a combination of both exercises, two to five times per week can lead to a significant improvement in cardiopulmonary function but not biomarkers of inflammation (IL-6 and IL-1β). However, this should not be interpreted as “No evidence of effect” because the individual trial studies did not attain sufficient power to detect treatment effects. The moderate grade evidence for this review suggests that further research may likely have an important impact on our confidence in the estimate of effects and may change the estimate.</td></tr>
</table>

SR/MA	
Citation: Ibeneme SC, Irem FO, Iloanusi NI, Ezuma AD, Ezenwankwo FE, Okere PC, Nnamani AO, Ezeofor SN, Dim NR, Fortwengel G. Impact of physical exercises on immune function, bone mineral density, and quality of life in people living with HIV/AIDS: a systematic review with meta-analysis. BMC Infectious Diseases. 2019 Dec;19(1):340.	
Purpose: The main study objective was to evaluate the impact of physical (aerobic and resistance) exercises on CD_{4+} count, BMD and QoL in PLWHA. **Timeframe:** Variable start dates to June 2017 **Total # studies included:** 19 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** HRQOL, Viral load/$CD4^+$ count	**Abstract:** **Background**: Compromised immune function, associated with human immune deficiency virus (HIV) infection, is improved by antiretroviral therapy (ART) which also decreases bone mineral density (BMD), and possibly the quality of life (QoL). However, physical (aerobic/resistance) exercises, were reported to induce reverse effects in uninfected individuals and were appraised in the literature for evidence of similar benefits in people living with HIV/AIDS (PLWHA). The main study objective was to evaluate the impact of physical (aerobic and resistance) exercises on CD_{4+} count, BMD and QoL in PLWHA. **Methods**: A systematic review was conducted using the Cochrane Collaboration protocol. Searching databases, up to June 2017, only randomized control trials investigating the effects of either aerobic, resistance or a combination of both exercise types with a control/other intervention(s) for a period of at least 4 weeks among adults living with HIV, were included. Two independent reviewers determined the eligibility of the studies. Data were extracted and risk of bias (ROB) was assessed with the Cochrane Collaboration ROB tool. Meta-analyses were conducted using random effect models using the Review Manager (RevMan) computer software. **Results**: Nineteen studies met inclusion criteria (n = 491 participants at study completion) comprising male and female with age range 22–66 years. Two meta-analyses across 13 sub-group comparisons were performed. However, there were no RCTs on the impact of physical exercises on BMD in PLWHA. The result showed no significant change in CD_{4+} count unlike a significant effect of 5.04 point (95%CI:-8.49,-3.74, p = 0.00001) for role activity limitation due to physical health (QoL sub-domain). Overall, the GRADE evidence for this review was of moderate quality. **Conclusion**: There was evidence that engaging in moderate intensity aerobic exercises (55–85% Maximum heart rate-MHR), for 30–60 min, two to five times/week for 6–24 weeks significantly improves role activity limitation due to physical health problems, otherwise physical(aerobic or/and resistance) exercises have no significant effects on $CD4_{+}$ count and other domains of QoL. Also, there is lack of evidence on the impact of exercises on BMD in PLWHA due to the paucity of RCTs. The moderate grade evidence for this review suggests that further research may likely have an important impact on our confidence in the estimate of effects and may change the estimate.

<table>
<tr><td colspan="2">SR/MA
Citation: O'Brien KK, Tynan AM, Nixon SA, Glazier RH. Effectiveness of Progressive Resistive Exercise (PRE) in the context of HIV: systematic review and meta-analysis using the Cochrane Collaboration protocol. BMC Infectious Diseases. 2017 Dec;17(1):268.</td></tr>
<tr><td>Purpose: The study examined the safety and effectiveness of progressive resistive exercise (PRE) interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.</td><td rowspan="5">Abstract:
Background: HIV is increasingly considered a chronic illness. More individuals are living longer and aging with the health-related consequences associated with HIV and multi-morbidity. Exercise is a self-management approach that can promote health for people aging with HIV. We examined the safety and effectiveness of progressive resistive exercise (PRE) interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.
Methods: We conducted a systematic review using the Cochrane Collaboration protocol. Searching databases up to April 2013, we included randomized controlled trials that compared PRE with no exercise or another intervention performed at least three times per week for at least four weeks with adults living with HIV. Two reviewers independently determined study eligibility. We extracted data from included studies and assessed risk of bias using the Cochrane Collaboration risk of bias tool. Meta-analyses were conducted using random effects models with Review Manager (RevMan) computer software.
Results: Twenty studies met inclusion criteria (n = 764 participants at study completion); the majority of participants were men (77%) taking antiretroviral therapy (14/20 included studies). Exercise interventions included PRE alone (8 studies) or a combination of resistive and aerobic exercise (12 studies) ranging from 6 to 52 weeks in duration. Thirty-four meta-analyses were performed. Results demonstrated statistically significant improvements in cardiorespiratory status (maximum oxygen consumption, exercise time), strength (chest press, knee flexion), weight, and body composition (arm and thigh girth, leg muscle area) among exercisers versus non-exercisers. We found no significant differences in change in CD4 count and viral load. We were unable to perform meta-analyses for psychological outcomes however results from individual studies demonstrated improvements in health-related quality of life with exercisers compared with non-exercisers.
Conclusion: Performing progressive resistive exercise (PRE) or a combination of resistive and aerobic exercise at least three times per week for at least six weeks is safe and can lead to improvements in cardiorespiratory fitness, strength, weight, and body composition for adults with HIV. Exercise may be considered a safe and beneficial for enhancing the health of medically stable adults aging with HIV.</td></tr>
<tr><td>Timeframe: Variable start dates to April 2013.</td></tr>
<tr><td>Total # studies included: 20</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, Body composition, Fitness and functional capacity, Cardio metabolic markers, Viral load/$CD4^+$ count.</td></tr>
</table>

SR/MA

Citation: O'Brien KK, Tynan AM, Nixon SA, Glazier RH. Effectiveness of aerobic exercise for adults living with HIV: systematic review and meta-analysis using the Cochrane Collaboration protocol. BMC Infectious Diseases. 2016 Dec;16(1):182.

<table>
<tr>
<td>Purpose: Our aim was to examine the safety and effectiveness of aerobic exercise interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.</td>
<td rowspan="5">Abstract:
Background: People with HIV are living longer with the health-related consequences of HIV, multi-morbidity, and aging. Exercise is a key strategy that may improve or sustain health for people living with HIV. Our aim was to examine the safety and effectiveness of aerobic exercise interventions on immunological, virological, cardiorespiratory, strength, weight, body composition, and psychological outcomes in adults living with HIV.
Methods: We conducted a systematic review using the Cochrane Collaboration protocol. We searched databases up to April 2013. We included randomized controlled trials comparing aerobic exercise with no exercise or another intervention performed at least three times per week for at least four weeks among adults living with HIV. Two reviewers independently determined study eligibility. Data were extracted from studies that met inclusion criteria using standardized forms. We assessed risk of bias using the Cochrane Collaboration's tool for assessing risk of bias. Outcomes were analyzed as continuous and meta-analyses conducted using random effects models with Review Manager (RevMan) computer software.
Results: Twenty-four studies met inclusion criteria (n = 936 participants at study completion); the majority of participants were men (73 %) and the majority were taking antiretroviral therapy (19/24 included studies). The exercise intervention included aerobic exercise alone (11 studies) or a combination of aerobic and resistive exercise (13 studies) ranging from 5 to 52 weeks. Fifty-eight meta-analyses were performed. Main results indicated statistically significant improvements in selected outcomes of cardiorespiratory status (maximum oxygen consumption, exercise time), strength (chest press, knee flexion), body composition (lean body mass, percent body fat, leg muscle area), depression symptoms, and quality of life (SF-36 questionnaire) among exercisers compared with non-exercisers. No significant differences in change in CD4 count and viral load were found.
Conclusions: Performing aerobic exercise or a combination of aerobic and resistive exercise at least three times per week for at least five weeks is safe and can lead to improvements in cardiorespiratory fitness, strength, body composition and quality of life for adults with HIV. Aerobic exercise is safe and beneficial for adults living with HIV who are medically stable.</td>
</tr>
<tr><td>Timeframe: Variable start dates to April 2013.</td></tr>
<tr><td>Total # studies included: 24</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, body composition, anxiety/depression, fitness and functional capacity, viral load/CD4+ count</td></tr>
</table>

SR/MA **Citation:** Gomes-Neto MG, Conceição CS, Carvalho VO, Brites C. Effects of combined aerobic and resistance exercise on exercise capacity, muscle strength and quality of life in HIV-infected patients: a systematic review and meta-analysis. PloS One. 2015 Sep 17;10(9):e0138066.	
Purpose: The aim of this systematic review with meta-analysis was to analyse the published RCTs that investigated the effects of combined aerobic and resistance exercise (CARE) on peak oxygen consumption, muscle performance, and quality of life in HIV infected patients.	**Abstract:** **Background:** Many HIV-infected patients demonstrate disability and lower aerobic capacity. The inclusion of resistance training combined with aerobic exercise in a single program is known as combined aerobic and resistance exercise (CARE) and seems to be an effective strategy to improve muscle weakness, as well as aerobic capacity in HIV-infected patients. We performed a meta-analysis to investigate the effects of CARE in HIV-infected patients. **Method:** We searched MEDLINE, Cochrane Controlled Trials Register, EMBASE, CINAHL (from the earliest date available to august 2014) for controlled trials that evaluated the effects of CARE in HIV-infected patients. Weighted mean differences (WMD) and 95% confidence intervals (CIs) were calculated, and heterogeneity was assessed using the I^2 test. **Result:** Seven studies met the study criteria. CARE resulted in improvement in Peak VO2 WMD (4.48 mL kg^{-1} min^{-1} 95% CI: 2.95 to 6.0), muscle strength of the knee extensors WMD (25.06 Kg 95% CI: 10.46 to 39.66) and elbow flexors WMD (4.44 Kg 95% CI: 1.22 to 7.67) compared with no exercise group. The meta-analyses also showed significant improvement in Health status, Energy/Vitality and physical function domains of quality of life for participants in the CARE group compared with no exercise group. A non-significant improvement in social function domain of quality of life was found for participants in the CARE group compared with no exercise group. **Conclusion:** Combined aerobic and resistance exercise may improve peak VO2, muscle strength and health status, energy and physical function domains of quality of life and should be considered as a component of care of HIV-infected individuals.
Timeframe: Up to august 2014	
Total # studies included: 7	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Peak oxygen consumption (peak VO2, mL/Kg/min), Muscle performance, and quality of life.	

SR/MA **Citation:** O'Brien K, Nixon S, Tynan AM, Glazier R. Aerobic exercise interventions for adults living with HIV/AIDS. Cochrane Database of Systematic Reviews. 2010(8).	
Purpose: To examine the safety and effectiveness of aerobic exercise interventions on immunologic and virologic, cardiopulmonary, psychologic outcomes and strength, weight, and body composition in adults living with HIV.	**Abstract:** **Background:** Access to combination antiretroviral therapy has turned HIV into a chronic and manageable disease for many. This increased chronicity has been mirrored by increased prevalence of health-related challenges experienced by people living with HIV (Rusch 2004). Exercise is a key strategy for people living with HIV and by rehabilitation professionals to address these disablements; however, knowledge about the effects of exercise among adults living with HIV still is emerging. **Objectives:** To examine the safety and effectiveness of aerobic exercise interventions on immunologic and virologic, cardiopulmonary, psychologic outcomes and strength, weight, and body composition in adults living with HIV. **Search methods:** Searches of MEDLINE, EMBASE, SCIENCE CITATION INDEX, CINAHL, HEALTHSTAR, PsycINFO, SPORTDISCUS and Cochrane Review Group Databases were conducted between 1980 and June 2009. Searches of published and unpublished abstracts and proceedings from major international and national HIV/AIDS conferences were conducted, as well as a hand search of reference lists and tables of contents of relevant journals and books. **Selection criteria:** We included studies of randomised controlled trials (RCTs) comparing aerobic exercise interventions with no aerobic exercise interventions or another exercise or treatment modality, performed at least three times per week for at least four weeks among adults (18 years of age or older) living with HIV. **Data collection and analysis:** Data on study design, participants, interventions, outcomes, and methodological quality were abstracted from included studies by two reviewers. Meta-analyses, using RevMan 5 computer software, were performed on outcomes when possible. **Results:** A total of 14 studies met inclusion criteria for this review and 30 meta-analyses over several updates were performed. Main results indicated that performing constant or interval aerobic exercise, or a combination of constant aerobic exercise and progressive resistive exercise for at least 20 minutes at least three times per week for at least five weeks appears to be safe and may lead to significant improvements in selected outcomes of cardiopulmonary fitness (maximum oxygen consumption), body composition (leg muscle area, percent body fat), and psychological status (depression-dejection symptoms). These findings are limited to participants who continued to exercise and for whom there were adequate follow-up data. **Conclusion:** Aerobic exercise appears to be safe and may be beneficial for adults living with HIV. These findings are limited by the small sample sizes and large withdrawal rates described in the studies. Future research would benefit from participant follow-up and intention-to-treat analysis. Further research is required to determine the optimal parameters in which aerobic exercise may be most beneficial for adults living with HIV.
Timeframe: Searches of papers from 1980 to June 2009.	
Total # studies included: 14	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Viral load, Body composition, HRQOL, Fitness and functional capacity, Cardio metabolic markers, Anxiety/Depression	

<table>
<tr><td colspan="2">SR/MA
Citation: Nixon S, O'Brien K, Glazier R, Tynan AM. Aerobic exercise interventions for adults living with HIV/AIDS. Cochrane Database of Systematic Reviews. 2005(2).</td></tr>
<tr><td>Purpose: To examine the safety and electiveness of aerobic exercise interventions on immunological/virological, cardiopulmonary and psychological parameters in adults living with HIV/AIDS.</td><td rowspan="5">Abstract:
Background: The profile of HIV infection is constantly changing. Although once viewed as an illness progressing to death, among those with access to antiretroviral therapy, HIV can now present as a disease with an uncertain natural history, perhaps a chronic manageable disease for some. This increased chronicity of HIV infection has been mirrored by increased prevalence of disablement in the HIV-infected population (Rusch 2004). Thus, the needs of these individuals have increasingly included the management of impairments (problems with body function or structure as a significant deviation or loss, such as pain or weakness), activity limitations (diliculties an individual may have in executing activities, such as inability to walk) and participation restrictions (problems an individual may experiences in involvement in life situations, such as inability to work) (WHO2001). Exercise is a key strategy employed by people living with HIV/AIDS and by rehabilitation professionals to address these issues. Exercise has been shown to improve strength, cardiovascular function and psychological status in seronegative populations (Bouchard 1993), but what are the elects of exercise for adults living with HIV? If the risks and benefits of exercise for people living with HIV are better understood, appropriate exercise may be undertaken by those living with HIV/AIDS and appropriate exercise prescription may be practiced by healthcare providers. If effective and safe, exercise may enhance the effectiveness of HIV management, thus improving the overall outcome for adults living with HIV.
Objectives: To examine the safety and effectiveness of aerobic exercise interventions on immunological/virological, cardiopulmonary and psychological parameters in adults living with HIV/AIDS. Search methods: To identify the appropriate studies, we conducted a search using MEDLINE, EMBASE, SCIENCE CITATION INDEX, AIDSLINE, CINAHL, HEALTHSTAR, PSYCHLIT, SOCIOFILE, SCI, SSCI, ERIC and DAI. We also reviewed both published and unpublished abstracts and proceedings from major international and national HIV/AIDS conferences such as the Intersciences Conference on Antimicrobial Agents and Chemotherapy (ICAAC), the Conference on Retroviruses and Opportunistic Infections (CROI), the Infectious Diseases Society of America Conference (IDSA) and the International AIDS Conference (IAC). Reference lists from pertinent articles and books were reviewed and personal contacts with authors were used, as well as Collaborative Review Group databases. Targeted journals were hand searched for relevant articles. There were no language restrictions. Searches for the original review covered the period from 1980 to July 1999. The first update of this review included an additional search of the literature, followed by identification of included studies that met the inclusion criteria from August 1999 to January 2001. For the second update, we conducted a search to identify additional studies published from February 2001 to August 2003. Selection criteria: Studies were included if they were randomized controlled trials (RCTs) comparing aerobic exercise interventions with no aerobic exercise interventions or another exercise or treatment modality, performed at least three times per week for at least four weeks among adults (18 years of age or older) living with HIV/AIDS.</td></tr>
<tr><td>Timeframe: From February 2001 to August 2003</td></tr>
<tr><td>Total # studies included: 10</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, Anxiety/Depression, Fitness and Functional capacity, Viral load/CD4+ count</td></tr>
</table>

	Data collection and analysis: Data on study design, participants, interventions, outcomes and methodological quality were abstracted from studies that met the inclusion criteria onto specifically designed data collection forms by at least two reviewers. Meta-analysis was conducted using RevMan 4.2 computer soLware on outcomes whenever possible. **Main results:** A total of 10 studies (six from the original search, two from the first updated search and two from this second updated search) met the inclusion criteria for this review. Main results indicated that performing constant or interval aerobic exercise, or a combination of constant aerobic exercise and progressive resistive exercise for at least 20 minutes, at least three times per week for four weeks appears to be safe and may lead to significant reductions in depressive symptoms and potentially clinically important improvements in cardiopulmonary fitness. These findings are limited to those participants who continued to exercise and for whom there was adequate follow-up data. **Authors' conclusions**: Aerobic exercise appears to be safe and may be beneficial for adults living with HIV/AIDS. These findings are limited by the small sample sizes and large withdrawal rates of the included studies. Future research would benefit from an increased attention to participant follow-up and intention-to-treat analysis. Further research is required to determine the optimal parameters of aerobic exercise and stage of disease in which aerobic exercise may be most beneficial for adults living with HIV.

SR/MA **Citation:** Bhatta DN, Liabsuetrakul T, McNeil EB. Social and behavioral interventions for improving quality of life of HIV infected people receiving antiretroviral therapy: a systematic review and meta-analysis. Health and Quality of Life Outcomes. 2017 Jan;15(1):80.	
Purpose: This review appraises the evidence for available interventions that focused on quality of life of HIV infected people receiving antiretroviral therapy (ART).	**Abstract:** **Background:** Improvement in quality of life is crucial for HIV infected people. Social and behavioural interventions have been implemented in different contexts to improve the quality of life among HIV infected people. This review appraises the evidence for available interventions that focused on quality of life of HIV infected people receiving antiretroviral therapy (ART). **Methods**: We searched electronic databases for randomized controlled trials of interventions to improve the quality of life of HIV infected people receiving ART. We searched PUBMED and the Cochrane Centre Register of Controlled Trials (CENTRAL) with the terms "social", "behavioural", "educational", "quality of life", "HIV", and "RCT". Searches were conducted for articles published from 1980 to December 16, 2015. Standardized data abstraction methods and searching steps were applied. **Results**: Twenty-eight studies reported the impact of social or behavioural interventions in quality of life among HIV infected people, of which 15 were conducted in United States of America. A total of 4136 participants were enrolled. Of the 28 studies, four studies included females, two studies included males and remaining studies excluded both males and females. The overall reported methodological quality of the studies was subject to a high risk of bias and the study criteria were unclear in most studies. Twenty-one studies reported a significant intervention effect on at least one quality of life domain. Meta-analyses showed significant improvement in general health, mental health, physical function and environment domains of quality of life among intervention groups. However, the expected impact of the intervention was low to moderate because the rigorousness of the studies was low, information was limited, the sample sizes were small and other the quality of the study designs were poor. **Conclusions:** Although the available evidence suggests that existing social and behavioural interventions can improve some quality of life domains, the quality of evidence was insufficient to support the notion that these interventions can improve the overall quality of life of HIV infected people receiving ART. Well-designed and rigorous randomized controlled trials with high methodological quality are required.
Timeframe: From 1980 to December 16, 2015.	
Total # studies included: 28	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: HRQOL	

SR **Citation:** Pedro RE, Guariglia DA, Peres SB, Moraes SM. Effects of physical training for people with HIV-associated lipodystrophy syndrome: a systematic review. The Journal of Sports Medicine and Physical Fitness. 2017 May;57(5):685-94.	
Purpose: The aim was systematically review the literature for physiological, metabolic, immunologic, and morphologic adaptations to aerobic, resistance, and concurrent training in people living with HALS.	**Abstract:** **INTRODUCTION**: Human immunodeficiency virus-associated lipodystrophy syndrome (HALS) is a major problem among people living with HIV/aids. The exercise training has been used for its treatment; however, the knowledge about benefits and safety still is emerging. The aim was systematically review the literature for physiological, metabolic, immunologic, and morphologic adaptations to aerobic, resistance, and concurrent training in people living with HALS. **EVIDENCE ACQUISITION**: A search of the Medline, Embase, Cinahl, Lilacs, Scielo, Web of Science, the Cochrane Controlled Trials Register Library and PEDro was performed. The study selection was performed by two blinded researchers follow screening of titles, abstracts, and full-text articles. Therefore, only randomised clinical trials, which investigated the effects of physical training in people with HALS, were included in the present review. The risk of bias was assessed using a Jadad's scale. **EVIDENCE SYNTHESIS**: From the electronic and manual searches, 332 studies were selected by title, 139 abstracts were read and 95 were excluded, leaving 44 studies, which were read in full. After full text examination only five studies were included in the qualitative analyses. The limitations were: heterogeneity in training prescription, nutritional recommendations, and diagnosis of lipodystrophy, small sample size, utilization of methods with questionable validity for assessments. **CONCLUSIONS**: There is no effect of physical training on CD4 cell count. In addition, aerobic and concurrent training improve VO2max, likewise resistance and concurrent training improve muscular strength.
Timeframe: July 2013 and updated in July 2016	
Total # studies included: 5	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: HRQOL, Body composition, Fitness and Functional capacity, Cardiometabolic markers, Viral load/CD4+ count	

<table>
<tr><td colspan="2">SR/MA
Citation: O Brien KE, Nixon S, Tynan AM, Glazier RH. Effectiveness of aerobic exercise in adults living with HIV/AIDS: systematic review. Medicine and science in sports and exercise. 2004 Oct 1;36:1659-66.</td></tr>
<tr><td>Purpose: The objective of this systematic review was to examine the effectiveness and safety of aerobic exercise interventions on immunological/virological, cardiopulmonary and psychological outcomes in adults living with HIV/AIDS.</td><td rowspan="5">Abstract:
Purpose: The objective of this systematic review was to examine the effectiveness and safety of aerobic exercise interventions on immunological/virological, cardiopulmonary and psychological outcomes in adults living with HIV/AIDS.
Methods: Ten randomized trials of HIV-positive adults performing aerobic exercise three times per week for at least 4 wk were identified by searching 13 electronic databases, abstracts from conferences, reference lists, and personal contact with authors from 1980 to November 2002. At least two independent reviewers assessed articles for inclusion, extracted data, and assessed methodological quality. Random effects models were used for meta-analysis.
Results: Main results indicated that aerobic exercise was associated with small non-significant changes in CD4 count (weighted mean difference: 14 cells-mm- 3, 95% CI: -26, 54), viral load (weighted mean difference: 0.40 log IO copies, 95% CI: -0.28, 1.07), and VO2. (weighted mean difference: 1.84 mL-kg-1, min-1, 95% CI: -0.53, 4.20). Individual studies suggested that aerobic exercise may improve psychological well-being for adults living with HIV/AIDS. These findings are limited to those participants who continued to exercise and for whom there was adequate follow-up.
Conclusion: In conclusion, performing constant or interval aerobic exercise, or a combination of constant aerobic exercise and progressive resistive exercise for at least 20 min, at least three times per week for 4 wk may be beneficial and appears to be safe for adults living with HIV/AIDS. However, these findings should be interpreted cautiously due to small sample sizes and large dropout rates within the included studies. Future research would benefit from increased attention to participant follow-up and intention-to-treat analysis.</td></tr>
<tr><td>Timeframe: From 1980 to November 2002.</td></tr>
<tr><td>Total # studies included: 10</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, Anxiety/Depression, Fitness and functional capacity, Viral load/CD4+ count</td></tr>
</table>

SR/MA **Citation:** O'Brien K, Tynan AM, Nixon S, Glazier RH. Effects of progressive resistive exercise in adults living with HIV/AIDS: systematic review and meta-analysis of randomized trials. AIDS Care. 2008 Jul 1; 20(6):631-53.	
Purpose: This systematic review examined the effectiveness and safety of progressive resistive exercise (PRE) interventions on immunological/virological, cardiopulmonary, weight, and body composition, strength and psychological outcomes in adults living with HIV.	**Abstract:** **Aim:** This systematic review examined the effectiveness and safety of progressive resistive exercise (PRE) interventions on immunological/virological, cardiopulmonary, weight, and body composition, strength and psychological outcomes in adults living with HIV. **Methods:** Using Cochrane Collaboration protocol, we included randomized controlled trials from 1980 to 2006 comparing PRE interventions with no PRE or another intervention. Ten studies met inclusion criteria. Seventeen meta-analyses were performed. **Results**: Results indicated that PRE or a combination of PRE and aerobic exercise may lead to statistically significant increases in weight (WMD: 2.68 kg; 95%CI: 0.40, 4.97) and arm and thigh girth (WMD: 7.91 cm; 95%CI: 2.18, 13.65) among exercisers versus non-exercisers. Trends toward improvement in submaximal heart rate and exercise time also were found. **Conclusions**: Individual studies suggested that PRE contributed to improved strength and psychological status. Findings are limited to participants who continued to exercise. Progressive resistive exercise appears to be safe and may be beneficial for medically stable adults living with HIV.
Timeframe: From 1980 to 2006	
Total # studies included: 9	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: HRQOL, Body composition, Fitness and functional capacity, Viral load/CD4+ count	

SR/MA **Citation:** Zech P, Pérez-Chaparro C, Schuch F, Wolfarth B, Rapp M, Heissel A. Effects of Aerobic and Resistance Exercise on Cardiovascular Parameters for People Living With HIV: A Meta-analysis. Journal of the Association of Nurses in AIDS Care. 2019 Mar 1; 30(2):186-205.	
Purpose: The aim was to examine the effect of aerobic and resistance exercise alone and in combination on cardiovascular parameters.	**Abstract:** **Background**: People living with HIV (PLWH) have limited exercise capacity because of anaemia, neuromuscular disorders, and pulmonary limitations. **Methods**: We used a meta-analysis to examine the effect of aerobic and resistance exercise alone and in combination on cardiovascular parameters. Subgroup meta-analyses were conducted and long-term effects of exercise were investigated. A systematic literature search was conducted up to July/August 2017. The Physiotherapy Evidence Database-scale was used to rate quality and assess the risk of bias on the papers. Standardized mean differences (SMDs) were calculated to assess the effect of exercise. **Results**: Post treatment comparison between the exercise and control groups revealed moderate and large effect sizes in favour of the intervention group for VO2max (SMD50.66, p,.0001) and the 6-minute walk test (SMD51.11, p5.0001). Exercise had a positive effect on cardiovascular parameters in PLWH. **Conclusion**: Exercise can be a prevention factor for PLWH dealing with multiple comorbidities.
Timeframe: Up to August 2017	
Total # studies included: 27	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Fitness and functional capacity	

<table>
<tr><td colspan="2">SR
Citation: Voigt N, Cho H, Schnall R. Supervised physical activity and improved functional capacity among adults living with HIV: A systematic review. Journal of the Association of Nurses in AIDS Care. 2018 Sep 1;29(5):667-80.</td></tr>
<tr><td>Purpose: The purpose of this review was to investigate whether supervised PA interventions improved functional capacity among adults living with HIV.</td><td rowspan="5">Abstract:
Background: Physical activity (PA) is an important strategy for healthy aging. Regular PA has been shown to be safe and combat the effects of inflammation, multi-morbidity, and long-term effects of antiretroviral therapy among people living with HIV. However, people living with HIV often fail to meet recommended guidelines for PA. It is recommended that people living with HIV engage in 20-40 minutes of combined aerobic and resistance training at least three times per week. Supervised PA interventions in the uninfected population have produced greater increases in muscular strength, cardiovascular fitness, and body composition compared to control study participants. The purpose of this review was to investigate whether supervised PA interventions improved functional capacity among adults living with HIV.
Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed for this review. Five databases were searched for randomized controlled trials in English, with adults aged 18 and over, where supervised PA was the intervention. Supervised PA was defined as a physical activity intervention that was supervised by a health care or allied health professional.
Results: The database literature search yielded 8,267 articles. After the title/abstract and full-text screening phases, 15 articles were included in the review. Using the Cochrane Collaboration's tool for assessing risk of bias, most studies fell in the 'low risk of bias' category within and across studies. Combined aerobic and progressive resistance training (PRT) improved strength, cardiovascular, and flexibility outcomes; three of four studies showed no significant improvements with aerobic interventions; PRT improved strength outcomes in all studies; yoga or combined yoga/meditation showed no difference between intervention and control groups; and, t'ai chi showed improvements in cardiovascular and flexibility outcomes.
Conclusions: Supervised PA interventions increase functional capacity among adults living with HIV. Combined aerobics and PRT showed improvements in strength, cardiovascular, and flexibility outcomes. Self-reported measures showed inconsistent results of functional capacity across studies.</td></tr>
<tr><td>Timeframe: Not available</td></tr>
<tr><td>Total # studies included: 15</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Fitness and Functional capacity</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Poton R, Polito M, Farinatti P. Effects of resistance training in HIV-infected patients: A meta-analysis of randomised controlled trials. Journal of sports sciences. 2017 Dec 17;35(24):2380-9.</td></tr>
<tr><td>Purpose: The purpose of this study was to perform a meta-analysis to determine the effects of RT upon muscle strength, muscle mass and CD4 cells count and to identify potential moderators of those outcomes in HIV-infected patients.</td><td rowspan="5">Abstract:
Background: The relative effects of resistance training (RT) upon muscle fitness and immune function among HIV infected patients are uncertain. The purpose of this study was to perform a meta-analysis to determine the effects of RT upon muscle strength, muscle mass and CD4 cells count and to identify potential moderators of those outcomes in HIV-infected patients.
Methods: Meta-analyses use random or fixed-effects model depending on the heterogeneity of effect sizes, complemented with Hedge’s g correction factor. Thirteen trials were meta-analysed.
Results: Overall, RT increased muscle strength (35.5%, P < 0.01) and CD4 cell count (26.1%, P = 0.003) versus controls (P < 0.03), but not muscle mass (P = 0.051). Meta-regression followed by subgroup moderator analysis showed that gains in muscle strength followed a dose– response pattern with largest increase detected among trials with longer (24 weeks; 49.3%) than shorter intervention (< 0.01).
Conclusions: RT appears to be efficacious to improve muscular strength (~35.5%) and CD4 cell count (~26.1%), but not muscle mass of HIV infected patients. Effects upon strength were greater in studies with higher quality and among trials with longer RT and HAART.</td></tr>
<tr><td>Timeframe: Up to June 2016</td></tr>
<tr><td>Total # studies included: 13</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Body composition, Fitness and functional capacity, Viral load/CD4 + count</td></tr>
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<table>
<tr><td colspan="2">SR
Citation: Gomes Neto M, Ogalha C, Andrade AM, Brites C. A systematic review of effects of concurrent strength and endurance training on the health-related quality of life and cardiopulmonary status in patients with HIV/AIDS. BioMed Research International. 2013b;2013.</td></tr>
<tr><td>Purpose: To determine the effects of concurrent strength and endurance training (concurrent training) on the Health-Related Quality of Life (HRQOL) and cardiopulmonary status among HIV-infected patients, using a systematic search strategy of randomized, controlled trials (RCTs).</td><td rowspan="5">Abstract:
Purpose: To determine the effects of concurrent strength and endurance training (concurrent training) on the Health-Related Quality of Life (HRQOL) and cardiopulmonary status among HIV-infected patients, using a systematic search strategy of randomized, controlled trials (RCTs).
Methods: A systematic review was performed by two independent reviewers using Cochrane Collaboration protocol. The sources used in this review were Cochrane Library, EMBASE, LILACS, MEDLINE, PEDro and Web of Science from1950 to August 2012.ThePEDro score was used to evaluate methodological quality.
Result: Individual studies suggested that concurrent training contributed to improved HRQOL and cardiovascular status. Concurrent training appears to be safe and may be beneficial for medically stable adults living with HIV. The rates of non-adherence were of 16%.
Conclusion: Concurrent training improves the HRQOL and cardiopulmonary status. It may be an important intervention in the care and treatment of adults living with HIV. Further research is needed to determine the minimal and optimal duration, frequency, and intensity of exercise needed to produce beneficial changes in the HIV-infected population subgroups.</td></tr>
<tr><td>Timeframe: From1950 to August 2012.</td></tr>
<tr><td>Total # studies included: 8</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, Fitness and functional capacity</td></tr>
</table>

<table>
<tr><td colspan="2">SR
Citation: Fillipas S, Cherry CL, Cicuttini F, Smirneos L, Holland AE. The effects of exercise training on metabolic and morphological outcomes for people living with HIV: a systematic review of randomised controlled trials. HIV Clinical Trials. 2010 Oct 1;11(5):270-82.</td></tr>
<tr><td>Purpose: To determine the effects of exercise on metabolic and morphological outcomes among people with HIV using a systematic search strategy of randomized, controlled trials (RCTs).</td><td rowspan="5">Abstract:
Purpose: To determine the effects of exercise on metabolic and morphological outcomes among people with HIV using a systematic search strategy of randomized, controlled trials (RCTs).
Methods: Two independent reviewers assessed studies using a predetermined protocol.
Results: Nine RCTs (469 participants, 41% females) of moderate quality were included. Compared to non-exercising controls, aerobic exercise (AE) resulted in decreased body mass index (weighted mean difference [WMD] −1.31; 95% CI, −2.59, −0.03; n=186), triceps skinfold thickness of subcutaneous fat (WMD −1.83 mm; 95% CI,−2.36, −1.30; n=144), total body fat (%) (standardised mean difference [SMD],−0.37; 95% CI, −0.74, −0.01; n=118), waist circumference (SMD −0.74 mm, 95% CI, −1.08, −0.39; n=142), and waist:hip ratio (SMD −0.94; 95% CI, −1.30, −0.58; n=142). Progressive resistive exercise (PRE) resulted in increased body weight (5.09 kg; 95% CI, 2.13, 8.05; n=46) and arm and thigh girth (SMD 1.08 cm; 95% CI, 0.35, 1.82; n=46). Few studies examined blood lipids, glucose, and bone density.
Conclusions: Few RCTs exist and their quality varies. AE decreases adiposity and may improve certain lipid subsets. PRE increases body weight and limb girth. No additional effects of combining AE and PRE are evident. Larger, higher quality trials are needed to understand the effects of exercise on metabolic outcomes (eg, lipids, glucose, bone density) relevant to persons with chronic, treated HIV.</td></tr>
<tr><td>Timeframe: From 1980 to November 2009</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Body composition, Cardiometabolic markers</td></tr>
</table>

<table>
<tr><td colspan="2">SR/MA
Citation: Heissel A, Zech P, Rapp MA, Schuch FB, Lawrence JB, Kangas M, Heinze S. Effects of exercise on depression and anxiety in persons living with HIV: A meta-analysis. Journal of Psychosomatic Research. 2019 Sep 2:109823.</td></tr>
<tr><td>Purpose: The purpose of this systematic review and meta-analysis was to examine the effects of exercise on depression and anxiety in people living with HIV (PLWH), and to evaluate, through subgroup analysis, the effects of exercise type, frequency, supervision by exercise professionals, study quality, and control group conditions on these outcomes.

Timeframe: Up to February 2019

Total # studies included: 10

Other details (e.g. definitions used, exclusions etc)

Outcomes addressed:
Anxiety/Depression</td><td>Abstract:
Objective: The purpose of this systematic review and meta-analysis was to examine the effects of exercise on depression and anxiety in people living with HIV (PLWH), and to evaluate, through subgroup analysis, the effects of exercise type, frequency, supervision by exercise professionals, study quality, and control group conditions on these outcomes.
Method: A literature search was conducted through four electronic databases from inception to February 2019. Considered for inclusion were randomized controlled trials (RCTs) investigating exercise interventions and depression or anxiety as outcomes in people living with HIV (≥ 18 years of age). Ten studies were included (n = 479 participants, 49.67% females at baseline), and the standardized mean difference (SMD) and heterogeneity were calculated using random-effect models. An additional pre-post meta-analysis was also conducted.
Results: A large effect in favour of exercise when compared to controls was found for depression (SMD = −0.84, 95%CI = [−1.57, −0.11], p = 0.02) and anxiety (SMD = −1.23, 95%CI = [−2.42, −0.04], p = 0.04). Subgroup analyses for depression revealed large effects on depression for aerobic exercise only (SMD = −0.96, 95%CI = [−1.63, −0.30], p = 0.004), a frequency of ≥3 exercise sessions per week (SMD = −1.39, 95%CI = [−2.24, −0.54], p < 0.001), professionally supervised exercise (SMD = −1.40, 95%CI = [−2.46, −0.17], p = 0.03]), and high-quality studies (SMD = −1.31, 95%CI = [−2.46, −0.17], p = 0.02).
Conclusion: Exercise seems to decrease depressive symptoms and anxiety in PLWH, but other larger and high quality studies are needed to verify these effects.</td></tr>
</table>

SR **Citation:** Quiles NN, Piao L, Ortiz A. The effects of exercise on lipid profile and blood glucose levels in people living with HIV: A systematic review of randomized controlled trials. AIDS Care. 2019 Sep 14:1-8.	
Purpose: This systematic review was performed in order to examine the effects of exercise interventions on lipid profile and glucose levels on PLWH	**Abstract:** **Background:** Exercise is commonly prescribed to improve lipid profile and glucose levels in people living with HIV (PLWH). This systematic review was performed in order to examine the effects of exercise interventions on lipid profile and glucose levels on PLWH. **Methods**: Randomized controlled trials (RCTs) investigating the effects of exercise on blood glucose, triglycerides (TG), total cholesterol (TC), HDL and LDL published up to November 2017 were reviewed. Two reviewers assessed inclusion and exclusion criteria, methodological quality and extracted the data. The PEDro scale was used to assess the quality of the included studies. **Results**: Nine RCTs involving 638 PLWH met inclusion criteria. The median PEDro scale score was 5 out of 10. Three combined aerobic exercise + resistance exercise studies (AE+RE) showed improvements in blood glucose levels, one study showed improvements in HDL, one showed improvements in TG, and one showed improvements in TC. The AE only study reported improvements in HDL, while the RE only study reported improvements in TG, TC, HDL and LDL. **Conclusions:** Exercise can be effective for the improvement of some metabolic parameters, especially blood glucose and HDL. However, due to methodological issues, small number of studies and differences in exercise protocols, these findings should be interpreted with caution.
Timeframe: From January 1980 to November 2017	
Total # studies included: 9	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Cardiometabolic markers	

<table>
<tr><td colspan="2">SR/MA
Citation: Chaparro CG, Zech P, Schuch F, Wolfarth B, Rapp M, Heiβel A. Effects of aerobic and resistance exercise alone or combined on strength and hormone outcomes for people living with HIV. A meta-analysis. PloS One. 2018 Sep 4;13(9):e0203384.</td></tr>
<tr><td>Purpose: To examine the effect of RT alone or combined with AE on strength parameters and hormones amongst PLWHA</td><td rowspan="5">Abstract:
Background: Infection with human immunodeficiency virus (HIV) affects muscle mass, altering independent activities of people living with HIV (PLWH). Resistance training alone (RT) or combined with aerobic exercise (AE) is linked to improved muscle mass and strength maintenance in PLWH. These exercise benefits have been the focus of different meta-analyses, although only a limited number of studies have been identified up to the year 2013/4. An up-to-date systematic review and meta-analysis concerning the effect of RT alone or combined with AE on strength parameters and hormones is of high value, since more and recent studies dealing with these types of exercise in PLWH have been published.
Methods: Randomized controlled trials evaluating the effects of RT alone, AE alone or the combination of both (AERT) on PLWH was performed through five web-databases up to December 2017. Risk of bias and study quality was attained using the PEDro scale. Weighted mean difference (WMD) from baseline to post-intervention changes was calculated. The I^2 statistics for heterogeneity was calculated.
Results: Thirteen studies reported strength outcomes. Eight studies presented a low risk of bias. The overall change in upper body strength was 19.3 Kg (95% CI: 9.8–28.8, p< 0.001) after AERT and 17.5 Kg (95% CI: 16–19.1, p< 0.001) for RT. Lower body change was 29.4 Kg (95% CI: 18.1–40.8, p< 0.001) after RT and 10.2 Kg (95% CI: 6.7–13.8, p< 0.001) for AERT. Changes were higher after controlling for the risk of bias in upper and lower body strength and for supervised exercise in lower body strength. A significant change towards lower levels of IL-6 was found (-2.4 ng/dl (95% CI: -2.6, -2.1, p< 0.001).
Conclusion: Both resistance training alone and combined with aerobic exercise showed a positive change when studies with low risk of bias and professional supervision were analyzed, improving upper and, more critically, lower body muscle strength. Also, this study found that exercise had a lowering effect on IL-6 levels in PLWH.</td></tr>
<tr><td>Timeframe: Up to December 2017</td></tr>
<tr><td>Total # studies included: 13</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Fitness and Functional capacity</td></tr>
</table>

<table>
<tr><td colspan="2">SR
Citation: Nosrat S, Whitworth JW, Ciccolo JT. Exercise and mental health of people living with HIV: A systematic review. Chronic illness. 2017 Dec;13(4):299-319.</td></tr>
<tr><td>Purpose: This study aimed to conduct a systematic literature review of the effects of exercise on mental health in people living with HIV.</td><td rowspan="5">Abstract:
Objective: Mental illness is highly prevalent among people living with HIV. Poor mental health is linked to HIV disease progression, making the treatment of mental illness alongside HIV essential. While the benefits of exercise on the physical health of people living with HIV are well established, the effect of exercise on mental health in this population is less examined. Therefore, this study aimed to conduct a systematic literature review of the effects of exercise on mental health in people living with HIV.
Methods: A search of electronic databases (PubMed, Web of Science, PsycINFO) through 30 November 2016 was completed. The methodological framework for scoping studies was used to conduct the review process. RISMA guidelines were used to report the results.
Results: The search resulted in 2273 articles and 52 were determined to be relevant. After review of the full text of potentially relevant studies, 24 studies were included for the analysis.
Discussion: Both aerobic and resistance exercise have independent and combined positive effects on various indicators of mental health in people living with HIV. Major limitations include high attrition rate, small sample size, and poor study designs. Higher quality studies with more diverse populations such as women, older adults, and transgender individuals are required.</td></tr>
<tr><td>Timeframe: Variable start dates to November 2016.</td></tr>
<tr><td>Total # studies included: 24</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, anxiety/depression</td></tr>
</table>

<table>
<tr><td colspan="2">SR
Citation: Gomes-Neto M, Conceicao CS, Carvalho VO, Brites C. A systematic review of the effects of different types of therapeutic exercise on physiologic and functional measurements in patients with HIV/AIDS. Clinics. 2013a;68(8):1157-67.</td></tr>
<tr><td>Purpose: The aim of this study was to determine the effects of different types of exercise on physiologic and functional measurements in patients with HIV using a systematic strategy for searching randomized controlled trials.</td><td rowspan="5">Abstract:
Background: Several studies have reported the benefits of exercise training for adults with HIV, although there is no consensus regarding the most efficient modalities. The aim of this study was to determine the effects of different types of exercise on physiologic and functional measurements in patients with HIV using a systematic strategy for searching randomized controlled trials.
Methods: The sources used in this review were the Cochrane Library, EMBASE, MEDLINE, and PEDro from 1950 to August 2012. We selected randomized controlled trials examining the effects of exercise on body composition, muscle strength, aerobic capacity, and/or quality of life in adults with HIV. Two independent reviewers screened the abstracts using the Cochrane Collaboration's protocol. The PEDro score was used to evaluate methodological quality. In total, 29 studies fulfilled the inclusion criteria.
Results: Individual studies suggested that exercise training contributed to improvement of physiologic and functional parameters, but that the gains were specific to the type of exercise performed. Resistance exercise training improved outcomes related to body composition and muscle strength, with little impact on quality of life. Aerobic exercise training improved body composition and aerobic capacity. Concurrent training produced significant gains in all outcomes evaluated, although moderate intensity and a long duration were necessary.
Conclusion: We concluded that exercise training was shown to be a safe and beneficial intervention in the treatment of patients with HIV.</td></tr>
<tr><td>Timeframe: Variable start dates to August 2012.</td></tr>
<tr><td>Total # studies included: 29</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Body composition, HRQOL, Fitness and functional capacity</td></tr>
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<table>
<tr><td colspan="2">SR
Citation: Lopez J, Richardson E, Tiozzo E, Lantigua L, Martinez C, Abreut G, Prendergast T, Atlas SE, Pangilinan AR, Ferris SM, Martinez AH. The effect of exercise training on disease progression, fitness, quality of life, and mental health in people living with HIV on antiretroviral therapy: a systematic review. Journal of Clinical and Translational Research. 2015 Dec 30;1(3):129.</td></tr>
<tr><td>Purpose: To summarizes the findings on the effects of aerobic or resistance training alone or combined aerobic and resistance exercise training (CARET) on disease progression, fitness, physical functioning, mental health, and quality of life (QOL) in PLWH receiving ART.</td><td rowspan="5">Abstract:
Background: Exercise has been associated with improvements in adverse physiological and psychological effects of long-term antiretroviral therapy (ART) in people living with HIV (PLWH).
Aim: To summarizes the findings on the effects of aerobic or resistance training alone or combined aerobic and resistance exercise training (CARET) on disease progression, fitness, physical functioning, mental health, and quality of life (QOL) in PLWH receiving ART. A systematic search of articles was performed in several databases, and 20 articles that met inclusion criteria were summarized.
Relevance for patients: Aerobic exercise was associated with improvements in aerobic capacity, QOL, and depressive symptoms, while resistance training improved strength. CARET was related to improved aerobic fitness, strength, physical functioning, QOL, and self-efficacy. At least one of the exercise interventions resulted in improvements in CD4+ cell count and HIV RNA viral load. Moreover, another study showed that HIV-specific biomarkers remained unchanged in the exercise intervention group, while they significantly worsened in the non-exercise group. In general, in spite of their well-known benefits, exercise programs have not been extensively utilized or widely recognized as viable therapeutic treatment options for this patient population. Knowing the possible health benefits of increasing physical activity level is important to better recommend exercise programs. However, the prescription must be done carefully and on an individual basis. Additional studies investigating the efficiency and effectiveness of different exercise training regimens for PLWH are needed.</td></tr>
<tr><td>Timeframe: From 1996 to 2015.</td></tr>
<tr><td>Total # studies included: 18</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: HRQOL, Anxiety/Depression, Fitness and functional capacity, Viral load/CD4+ count</td></tr>
</table>

SR **Citation:** Lofgren SM, Nakasujja N, Boulware DR. Systematic review of interventions for depression for people living with HIV in Africa. AIDS and Behavior. 2018 Jan 1;22(1):1-8.	
Purpose: To identify depression interventions for HIV-infected adults in Africa. **Timeframe:** Up to February 2017 **Total # studies included:** 18 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** Anxiety/Depression	**Abstract:** **Background**: Depression interventions for individuals with HIV/AIDS in Africa are being increasingly evaluated. **Methods**: MEDLINE was searched using key terms: depression, Africa, and HIV, to identify depression interventions for HIV-infected adults in Africa. Perinatal women were excluded. Results were extracted and relative change in depression scores for interventions and net effect calculated. **Results:** The MEDLINE search yielded 18 articles. Six of seven studies evaluating feasibility were positive, and seven of seven studies evaluating acceptability were also positive. Three studies investigated the effect of psychotherapy (% relative decrease of depressive symptoms for intervention: %net decrease compared to controls) (73%:39% decrease). Four studies investigated task-shifting of psychotherapy (47%:34% decrease). Three studies evaluated antidepressants (79%:39% decrease). Three studies investigated task-shifting of antidepressant treatment (82%:65% decrease). An exercise intervention was evaluated (66%:49% decrease). One trial investigated minocycline with non-statistically significant results. Finally, three studies investigated other psychosocial interventions (44%:21% decrease). **Conclusions**: Overall, the results highlight the need for large, randomized trials to establish efficacy as well as implementation studies.

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<tr><td colspan="2">SR
Citation: Leyes P, Martínez E, Forga MD. Use of diet, nutritional supplements and exercise in HIV-infected patients receiving combination antiretroviral therapies: a systematic review. Antiviral Therapy. 2008 Jan 1;13(2):149.</td></tr>
<tr><td>Purpose: To examine the the effects of diet, nutrition support and exercise on body composition and metabolic complications in patients receiving cART</td><td rowspan="5">Abstract:
Background: The use of combination of antiretroviral therapy (cART) has improved the prognosis of HIV infections, but it has also been linked to a spectrum of body composition changes and metabolic alterations known as lipodystrophy syndrome. Nutrition status could influence body composition changes.
Method: we performed a systematic search of published peer-reviewed data on the effect on the effects of diet, nutrition support and exercise on body composition and metabolic complications in patients receiving cART
Result: Few controlled studies, most of them with small sample size were found. Oral nutritional support increases protein and energy intake, and a results in body weight and fat mass gains. Resistance exercise, with or without aerobic component, increases lean mass and can improve insulin resistance. Low-fat diet or exercise can result in loss of fat mass, and they should be used with caution in subjects with lipoatrophy.
Conclusion: Nutritional support and exercise results in small but significant body composition changes and can be used as complementary intervention. There is a need for further research on nutritional intervention in HIV-infected patients receiving cART.</td></tr>
<tr><td>Timeframe: From 1996 onwards</td></tr>
<tr><td>Total # studies included: 9</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Body composition, Fitness and functional capacity, Viral load/CD4+ count</td></tr>
</table>

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F1: EVIDENCE ON PHYSICAL ACTIVITY FOR CHILDREN, ADOLESCENTS AND ADULTS LIVING WITH DISABILITY

Guiding Questions

F1. What is the association between **physical activity** and health-related outcomes?

Inclusion Criteria

Inclusion Criteria

Population: People living with impairments as a result of any of the following health conditions:

F1.a. Multiple sclerosis (MS)

F1.b Spinal cord injury (SCI)

F1.c Intellectual Disability (ID)

F1.d Parkinson's disease (PD)

F1.d Stroke (Str)

F1.e Major clinical depression (MCD)

F1.g Schizophrenia (Sch)

F1.h ADHD

Exposure: Greater volume, duration, frequency or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity

		Outcomes		
Population	1.1 Comorbidity	1.2 Physical functioning	1.3 Cognition	1.4 Quality of Life
F1.a Multiple sclerosis	X	X	X	X
F1.b Spinal cord injury	X	X		X
F1.c Intellectual disability	X	X		X
F1.d Parkinson's disease		X	X	
F1.e Stroke		X	X	
F1.f Major clinical depression				X
F1.g Schizophrenia			X	X
F1.h ADHD			X	

Evidence identified

Twenty-seven reviews were identified (published from 2016 to 2019) that examined the association between physical activity and health-related outcomes among people with impairments (**Table F1.1**) *(1-38).* Each of the reviews focused on different subpopulations with impairments including four reviews that included people with multiple sclerosis, no reviews among people with a spinal cord injury, two reviews among children and adolescents with intellectual disabilities including Down syndrome, three reviews among older adults with Parkinson's disease, 12 reviews included people with a history of stroke, two reviews including people with major clinical depression, 3 reviews among adults with schizophrenia, and one among children with attention deficit hyperactivity disorder (**Table F1.1**).

The primary outcomes for each review varied according to the population of interest. For instance, measures of physical function were most commonly reported for reviews of exercise interventions among adults with a history of stroke whereas measures of cognition were most commonly reported for the reviews among children with ADHD. None of the reviews included evidence published in 2019; most reviews included evidence published through 2017. The included bodies of evidence for each review was relatively small ranging from 3 to 39 included studies. Three reviews were reviews-of-reviews and synthesized the evidence from existing systematic reviews and meta-analyses. Extracted data for each review is included in **Appendix A.** A summary of the U.S. Physical Activity Guidelines evidence for people with common chronic conditions is provided within each Evidence Profile.

In general, these reviews had many limitations in their design, execution, and reporting. None of the systematic reviews were rated as having high credibility based on the AMSTAR 2 instrument. Ten were rated as having moderate credibility, 14 were rated as having low credibility, and the remaining 12 were rated as having critically low credibility. Given concerns regarding the comprehensiveness and the validity of the results presented in reviews rated as having critically low credibility, they were not incorporated into the final Evidence Profiles. **Table F1.2** presents the ratings for each review according to all the AMSTAR 2 main domains. Two additional reviews were excluded given the scope or focus of the reviews *(7, 17)*. The paper by Christiansen 2019 *(7)* is not a systematic review and the review by Hendrey (2018) *(17)* was excluded given the research question (do resistance training interventions that have been studied among patients with a history of stroke adhere to American College of Sports Medicine guidelines?).

Table F1.1. Systematic Reviews Assessed, by condition

	Conditions								Outcomes						
Author, Year	**MS**	**SCI**	**ID**	**Park**	**Stroke**	**MCD**	**Schizo-phrenia**	**ADHD**	**Risk of co-morbid conditions**	**Physical function**	**Cognitive function**	**QOL**	**Last search date**	**# of included studies**	**AMSTAR 2**
People with multiple sclerosis															
Alphonsus, 2019 *(1)*	X											X	NR 2017	18	Low
Campbell, 2018 *(5)*	X									X			Sep 2017	7	Low
Charron, 2018 *(6)*	X									X			Nov 2016	12	Critically Low
Manca, 2018 *(24)*	X									X			May 2017	11	Moderate
Morrison, 2017 *(27)*	X										X		May 2016	19	Critically Low
Patterson, 2018 *(28)*	X	X			X					X			Aug 2017	9	Moderate
Veneri, 2018 *(34)*	X				X					X	X	X	May 2016	32	Critically Low
People with spinal cord injury															
Eitivipart, 2019[a] *(12)*		X								X			Aug 2018	16	Critically Low
Gaspar, 2019 *(14)*		X								X		X	Feb 2017	25	Critically Low
Melo, 2019 *(25)*		X								X			Nov 2015	7	Critically Low
Patterson, 2018 *(28)*	X	X			X					X			Aug 2017	9	Critically Low
People with intellectual disabilities															
Maïano, 2018 *(23)*			X							X			Mar 2018	15	Low
Maïano, 2019 *(22)*			X							X			Jun 2017	11	Moderate
People with Parkinson's disease															
Cugusi, 2017a *(8)*				X						X		X	Feb 2017	6	Low
Ćwiękała-Lewis, 2017 *(10)*				X						X		X	Apr 2015	11	Critically Low
Dos Santos Delabary, 2017 *(11)*				X						X		X	Aug 2017	5	Low
Kalyani, 2019 *(19)*				X						X	X		Sep 2017	12	Critically Low

	Conditions								Outcomes						
Author, Year	MS	SCI	ID	Park	Stroke	MCD	Schizo-phrenia	ADHD	Risk of co-morbid conditions	Physical function	Cognitive function	QOL	Last search date	# of included studies	AMSTAR 2
Stuckenschneider, 2019 *(32)*				X							X		Mar 2018	11	Moderate
People with a history of stroke															
Bonini-Rocha, 2018 *(3)*					X					X			Mar 2017	11	Moderate
Boyne, 2017 *(4)*					X					X			Nov 2015	20	Low
Cugusi, 2017b *(9)*					X					X			Oct 2016	15	Moderate
Ge, 2017 *(15)*					X					X			Feb 2017	32	Moderate
Hendrey, 2018[b] *(17)*					X					X			Oct 2016	39	N/A
Ilunga Tshiswaka, 2018 *(18)*					X					X			Oct 2016	29	Critically Low
Li, 2018 *(21)*					X					X			NR	5	Low
Miranda, 2018 *(26)*					X					X			Nov 2017	12	Low
Patterson, 2018 *(28)*	X	X			X					X			Aug 2017	9	Moderate
Pogrebnoy, 2019 *(29)*					X					X			Aug 2018	10	Low
Schröder, 2019 *(30)*					X					X			Apr 2018	7	Low
Veneri, 2018 *(34)*	X				X					X	X	X	NR	32	Critically Low
Wiener, 2019 *(35)*					X					X			Jan 2018	6	Low
Wu, 2018 *(36)*					X					X			May 2017	6	Critically Low
Zou, 2018a *(37)*					X					X			NR	20	Low
Zou, 2018b *(38)*					X				X	X			NR	16	Low
People with major clinical depression															
Ashdown-Franks, 2019[a] *(2)*						X	X	X	X		X		Jan 2018	27	Moderate
Krogh, 2017 *(20)*						X			X			X	Jun 2017	35	Moderate
Stubbs, 2018[a] *(31)*						X	X		X	X	X	X	Jan 2018	20	Moderate
People with schizophrenia															
Ashdown-Franks, 2019[a] *(2)*						X	X	X	X		X		Jan 2018	27	Moderate
Firth, 2016 *(13)*							X				X		Apr 2016	10	Low

	Conditions								Outcomes						
Author, Year	**MS**	**SCI**	**ID**	**Park**	**Stroke**	**MCD**	**Schizo-phrenia**	**ADHD**	**Risk of co-morbid conditions**	**Physical function**	**Cognitive function**	**QOL**	**Last search date**	**# of included studies**	**AMSTAR 2**
Stubbs, 2018[a] *(31)*						X	X		X	X	X	X	Jan 2018	20	Critically Low
People with attention deficit hyperactivity disorder															
Ashdown-Franks, 2019[a] *(2)*						X	X	X	X		X		Jan 2018	27	Moderate
Christiansen, 2019[c] *(7)*								X			X		NR	18	N/A
Grassmann, 2017 *(16)*								X			X		NR 2013	3	Critically Low
Suarez-Manzano, 2018 *(33)*								X			X		Jan 2017	16	Critically Low

Abbreviations: ADHD = attention deficit hyperactivity disorder; ID = intellectual disorder; MCD = major clinical depression; MS = multiple sclerosis; NR = month and/or year not reported; QOL = quality of life; SCI = spinal cord injury

[a] Review-of-reviews
[b] Review excluded given scope
[c] Not a systematic review

Table F1.2. Credibility Ratings (AMSTAR 2)

Author, Year	PICO[1]	Apriori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Hetero-geneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Alphonsus, 2019	Y	N	N	PY	Y	N	PY	N	PY	N	Y	Y	Y	Y	Y	N	**Low**
Ashdown-Franks, 2019	Y	N	N	PY	Y	Y	PY	Y	Y	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Bonini-Rocha, 2018	Y	N	N	PY	Y	N	PY	PY	Y	N	Y	N	Y	Y	Y	Y	**Moderate**
Boyne, 2017	Y	N	N	PY	N	N	PY	PY	PY	N	Y	N	N	Y	Y	N	**Low**
Campbell, 2018	Y	N	N	PY	N	N	PY	PY	PY	N	N/A	N/A	N	Y	N/A	Y	**Low**
Charron, 2018	Y	N	N	PY	N	N	PY	PY	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Cugusi, 2017a	Y	N	N	PY	Y	Y	Y	PY	PY	N	N/A	N/A	N	Y	N/A	Y	**Low**
Cugusi, 2017b	N	N	N	PY	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	**Moderate**
Ćwiękała-Lewis, 2017	N	N	N	PY	N	N	PY	PY	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Dos Santos Delabary, 2017	Y	N	N	PY	Y	Y	PY	PY	Y	N	Y	N	N	Y	Y	Y	**Low**
Eitivipart, 2019[18]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	**Critically Low**
Firth, 2016	Y	N	N	PY	Y	N	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	**Low**
Gaspar, 2019	N	N	N	PY	Y	Y	N	N	N	N	N/A	N/A	N	Y	N/A	N	**Critically Low**
Ge, 2017	Y	N	N	PY	Y	Y	PY	PY	Y	N	Y	N	Y	Y	Y	N	**Moderate**
Grassmann, 2017	Y	N	N	PY	N	N	N	PY	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Ilunga Tshiswaka, 2018	N	N	N	PY	Y	N	N	N	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Kalyani, 2019	Y	PY	N	PY	Y	Y	PY	PY	Y	N	N	N	Y	N	N	N	**Critically Low**
Krogh, 2017	Y	PY	N	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Moderate**
Li, 2018	Y	N	N	PY	Y	Y	PY	PY	Y	N	Y	N	Y	Y	N	Y	**Low**
Maïano, 2018	Y	N	N	PY	Y	Y	N	Y	PY	N	Y	Y	Y	Y	Y	Y	**Low**
Maïano, 2019	Y	N	N	PY	Y	Y	PY	Y	Y	N	N/A	N/A	Y	N	N/A	Y	**Moderate**
Manca, 2018	Y	N	N	PY	Y	Y	Y	PY	Y	N	Y	N	Y	Y	Y	Y	**Moderate**

Author, Year	PICO[1]	Apriori Methods[2]	Study Design Selection[3]	Lit Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assessment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Hetero-geneity[14]	Publication Bias[15]	COI[16]	Overall Rating[17]
Melo, 2019	Y	N	N	PY	Y	Y	PY	PY	N	N	N/A	N/A	N	N	N/A	N	**Critically Low**
Miranda, 2018	N	N	N	PY	N	Y	Y	Y	PY	N	N/A	N/A	Y	Y	N/A	Y	**Low**
Morrison, 2017	N	N	N	PY	N	N	N	Y	PY	N	N/A	N/A	Y	N	N/A	Y	**Critically Low**
Patterson, 2018	Y	N	N	PY	Y	Y	PY	PY	Y	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Pogrebnoy, 2019	Y	N	Y	PY	Y	N	PY	PY	PY	N	Y	N	N	Y	N	N	**Low**
Schröder, 2018	Y	N	N	PY	Y	Y	N	PY	Y	N	N/A	N/A	Y	Y	N/A	Y	**Low**
Stubbs, 2018	Y	N	Y	PY	Y	Y	PY	PY	Y	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Stuckenschneider, 2019	Y	N	N	PY	N	Y	PY	Y	PY	N	N/A	N/A	Y	Y	N/A	Y	**Moderate**
Suarez-Manzano, 2018	N	N	N	PY	Y	N	N	PY	N	N	N/A	N/A	N	N	N/A	Y	**Critically Low**
Veneri, 2018	N	N	N	PY	Y	N	N	PY	N	N	N	N	N	N	N	Y	**Critically Low**
Wiener, 2019	Y	N	N	PY	Y	N	N	PY	PY	N	N/A	N/A	N	Y	N/A	Y	**Low**
Wu, 2018	Y	N	N	PY	Y	Y	N	PY	N	N	N	N	Y	Y	N	N	**Critically Low**
Zou, 2018a	Y	N	N	PY	Y	Y	PY	PY	PY	N	Y	Y	Y	Y	Y	N	**Low**
Zou, 2018b	Y	N	N	PY	Y	Y	PY	PY	PY	N	N	N	Y	Y	N	Y	**Low**

Abbreviations: COI = conflict of interest; N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

[1] Did the research questions and inclusion criteria for the review include the components of PICO?
[2] Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
[3] Did the review authors explain their selection of the study designs for inclusion in the review?
[4] Did the review authors use a comprehensive literature search strategy?
[5] Did the review authors perform study selection in duplicate?
[6] Did the review authors perform data extraction in duplicate?
[7] Did the review authors provide a list of excluded studies and justify the exclusions?
[8] Did the review authors describe the included studies in adequate detail?
[9] Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

[10] Did the review authors report on the sources of funding for the studies included in the review?
[11] If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
[12] If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
[13] Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
[14] Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
[15] If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
[16] Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
[17] Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.
[18] Eitivipart, 2019 is a review-of-reviews. All included reviews were rated as critically low by review authors and was therefore rated as critically low overall.

F.1. Physical Activity in children, adolescents and adults living with disability

Table F.1.a. People with multiple sclerosis, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with multiple sclerosis
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Risk of co-morbid conditions (including disease progression and symptoms of disease), physical function, cognitive function, health-related QOL

Outcome	**Systematic review evidence** **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment** **Risk of bias**	**Inconsis-tency**	**Indirectness†**	**Imprecision**	**Other**	**Description of evidence** **Summary of findings**	**Certainty**	**US PAGAC evidence** *(39)*
Risk of co-morbid condition s	No systematic review identified									No review evidence Insufficient evidence is available to determine the relationship between physical activity and risk of comorbid conditions in adults with multiple sclerosis. **PAGAC Grade: Not Assignable**.
Physical function[a]	Campbell 2018 *(5)* Low	5 RCTs 2 before-after N = 249	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Five studies included participants that were predominantly mildly disabled (EDSS < 4.0), one study recruited moderately disabled persons (EDSS 4.0-6.0), and one recruited those who were more severely disabled (EDSS 6.0-8.0). All studies conducted HIIT, in a supervised setting, on a cycle ergometer or upper limb ergometer. Four studies compared HIIT to a form of continuous training, one compared HIIT and in-patient rehabilitation to just in-patient rehabilitation, and two studies had no comparator. 6/7 studies found improvements in measures of cardiorespiratory fitness (VO_2peak or VO_2max, HRMax, peak power) or muscle strength following 3-12 weeks of HIIT using cycle ergometry; however, minimal information on between-group differences for HIIT vs. control results.	HIGH[b]	12 ESRs Strong evidence demonstrates that physical activity—particularly aerobic and muscle-strengthening activities—improves physical function, including walking speed and endurance, in adults with multiple sclerosis. **PAGAC Grade: Strong.** **.**
	Manca 2019 *(24)* Moderate	11 RCTs N = 426	No serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	Possible publica-tion bias	Median EDSS score was 3.9. Mean age ranged from 33.1 to 53.0 years. Strength training programs training whole lower limb (8 studies), knee extensor muscles (2 studies), or ankle plantar flexors (1 study). No study focused on upper limb strength.	LOW[c]	

								Average training duration was 13.2 weeks. All control groups received no intervention. Pooled analyses found increased strength by 23.1% (95% CI, 11.8 to 34.4) among those in strength training group compared with control groups (ES = 0.37 [95% CI, 0.16 to 0.57] (11 RCTs, n=366) as measured by isokinetic dynamometer and 1RM testing. No statistically significant differences in strength outcomes when limited dynamometer and 1RM measures separately.		
	Patterson 2018 *(28)* Moderate	1 case reports 1 before-after N = 9	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	One case study reported improved functional mobility following a dance intervention and the other reported improved balance after the intervention.	VERY LOW[d]	
Cognitive function	No systematic review included[e]									1 ESR Moderate evidence indicates that moderate-to-vigorous physical activity can have beneficial effects on cognition in individuals with diseases or disorders that impair cognitive function, including attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson's disease, and stroke. **PAGAC Grade: Moderate.** Results regarding the efficacy of interventions to improve cognitive function in individuals with MS are conflicting. However, interventions show the largest effects on executive function, learning, memory, and processing speed *(39)*.
Health-related QOL	Alphonsus 2019 *(1)* Low	12 RCTs 6 obs N = 725	No serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Participant characteristics (age, disability status) NR. Seven studies tested aerobic exercise interventions, 4 tested anaerobic exercise studies, 3 tested a yoga intervention, 3 used physiotherapy, and 5 studies tested combinations of exercises. Aerobic exercise had small statistically significant effect on physical (ES = 0.35 [95% CI, 0.08 to 0.62], *p*=0.01), mental (ES = 0.42 [95% CI, 0.11 to 0.72], *p*=0.007), and social (ES = 0.42 [95% CI, 0.15 to	VERY LOW[f]	11 ESRs Limited evidence suggests that physical activity improves quality of life, including symptoms of fatigue and depressive symptoms, in adults with

								0.69], *p*=0.002) domains of QOL. Anaerobic exercise, combinations of exercise, and yoga did not have a significant effect on measures of QOL. Medium to large effects associated with physical and social domains of QOL were seen for physiotherapy, though few studies (3) measured this relationship.		multiple sclerosis. **PAGAC grade: Limited.**

Abbreviations: 1RM = 1 repetition maximum; CI = confidence interval; EDSS = Expanded Disability Status Scale; ERS = existing systematic review; ES = effect size; HIIT = high-intensity interval training; NR = not reported; obs = observational study design; PAGAC = Physical Activity Guidelines Advisory Committee; QOL = quality-of-life; RCT = randomized clinical trial

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] One review *(6)* was identified by rated as very low credibility and was not included.
[b] Certainty of evidence not downgraded due to indirectness in outcome measures; the SOE indicates the certainty in measures of cardiorespiratory fitness or muscle strength
[c] Certainty of evidence downgraded due to substantial degree of heterogeneity (I^2=62%) in pooled analyses, serious imprecision given wide confidence intervals around estimates of effects, and possible publication bias serious inconsistency, indirectness, imprecision, and possible publication bias
[d] Certainty of evidence not upgraded
[e] Two reviews *(27, 34)* were identified but were rated as very low credibility and were not included.
[f] Certainty of evidence downgraded for serious unexplained inconsistency (moderate heterogeneity (I2>50%) in most pooled analyses; individual study effects include benefit and no benefit), serious indirectness (lack of detail regarding populations and interventions), and imprecision (wide confidence intervals around measures of effect)

Table F.1.b. People with spinal cord injury, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with spinal cord injury
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Risk of co-morbid conditions (including disease progression and symptoms of disease), physical function, health-related QOL

Outcome	Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment Risk of bias	Inconsistency	Indirectness †	Imprecision	Other	Summary of findings	Certainty	US PAGAC evidence *(39)*
Risk of co-morbid conditions	No systematic reviews identified									3 ESRs Limited evidence suggests that physical activity reduces shoulder pain and improves vascular function in paralyzed limbs in individuals with spinal cord injury. **PAGAC Grade: Limited.**
Physical function[a]	No systematic review included									8 ESRs Moderate evidence indicates that physical activity improves walking function, muscular strength, and upper extremity function for persons with spinal cord injury. **PAGAC Grade: Moderate.**
Health-related QOL	No systematic review included[b]									2 ESRs Limited evidence suggests physical activity improves health-related quality of life in individuals with spinal cord injury. **PAGAC Grade: Limited.**

Abbreviations: ESR = existing systematic review; PAGAC = Physical Activity Guidelines Advisory Committee; QOL = quality-of-life
† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Three additional reviews were identified *(12, 14, 25)* but were rated as very low credibility and are not included. One additional review *(28)* included data from the abstracts of two studies among persons with spinal cord injury. Results are not presented here given no full-text article available.
[b] One systematic review was identified *(14)* but was rated as very low credibility and was not included.

Table F.1.c. People with intellectual disabilities, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with intellectual disabilities
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Risk of co-morbid conditions (including disease progression and symptoms of disease), physical function, health-related QOL

Outcome	Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Summary of findings	Certainty	US PAGAC evidence *(39)*
			Risk of bias	Inconsistency	Indirectness †	Imprecision	Other			
Risk of co-morbid conditions	No systematic review identified									1 ESR Insufficient evidence is available to determine the relationship of physical activity with risk of comorbid conditions in individuals with intellectual disabilities. **PAGAC Grade: Not assignable.**

Outcome	Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Summary of findings	Certainty	US PAGAC evidence *(39)*
			Risk of bias	Inconsistency	Indirectness †	Imprecision	Other			
Physical function	Maïano 2018 *(23)* Low	9 RCTs 6 before-after N=403	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	Possible publication bias Effects higher for before-after studies than RCTs	Mean age was 13 years with most participants recruited from schools. Half had mild intellectual disabilities (53%) and most were males (71%). Seven studies used balance and/or strength exercises and remaining used computerized balance exercises, creative dance activities, hippotherapy exercises, rope-skipping exercise, swiss ball exercises, tai chi exercise, and trampoline with interventions lasting 6 to 16 weeks. Pooled analysis showed large and statistically significant improvement in static balance (ES = 0.98 [95% CI, 0.65 to 1.32], *p*<0.001, 11 studies) and dynamic balance (ES = 1.43 [95% CI, 0.71 to 1.97], *p*<0.001, 7 studies) among those in exercise groups vs. control groups.	VERY LOW[a]	3 ESRs Limited evidence suggests that physical activity improves physical function in children and adults with intellectual disabilities. **PAGAC Grade: Limited.**
	Maïano 2019 *(22)* Moderate	7 RCTs 4 NRSIs N=281	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	8/11 studies focused on children(mean age 12 years) with Down syndrome and 3/11 focused on adolescents (mean age 15 years) with Down syndrome. Interventions focused on balance and included walking backwards, hopscotch, computerized balance training using visual feedback, strengthening, vibration platforms, or combined exercise with interventions lasting 6 to 24 weeks. Among children, all studies showed that the exercise intervention groups had significant higher posttest static, dynamic, and static-dynamic balance than the control groups. None of the trials among adolescents found differences in any measures of balance between groups.	VERY LOW[b]	
Outcome	Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment					Summary of findings	Certainty	US PAGAC evidence *(39)*
			Risk of bias	Inconsistency	Indirectness †	Imprecision	Other			

Health-related QOL	No systematic review identified	1 ESR Insufficient evidence is available to determine the relationship of physical activity with health-related quality of life in individuals with intellectual disabilities. **PAGAC Grade: Not assignable.**

Abbreviations: CI = confidence interval; ERS = existing systematic review; ES = effect size (Hedge's *g*); NR = not reported; NRSI = non-randomized study of an intervention; PAGAC = Physical Activity Guidelines Advisory Committee; QOL = quality-of-life; RCT = randomized clinical trial

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious risk of bias (12/15 studies were rated as having low quality), serious inconsistency (substantial statistical heterogeneity [I^2>70%] in all pooled analyses), serious indirectness (measures of static, dynamic , and static-dynamic balance of unclear clinical relevance), serious imprecision (wide CIs), and possible publication bias
[b] Certainty of evidence downgraded given serious risk of bias, inconsistency, serious indirectness (measures of static, dynamic , and static-dynamic balance of unclear clinical relevance), and serious imprecision (wide CIs)

Table F.1.d. People with Parkinson's disease, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with Parkinson's disease
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Physical function, cognitive function

			Quality Assessment							
Outcome	**Systematic review evidence** **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Risk of bias**	**Inconsistency**	**Indirectness †**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence *(39)***
Physical function[a]	Dos Santos Delabary 2018 *(11)* Low	5 RCTs N=159	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Mean age of participants ranged from 61 to 72 years; most participants were men. Studies represented older adults at all stage of Parkinson's disease (H&Y stage 0-4). Interventions consisted of any type of dance for at least 3 weeks of practice, with most consisting of Tango classes. Participants in dance groups were found to have more favourable outcomes related to motor symptoms (UPSDRS III scale), functional mobility (TUG test), endurance (6MWT), freezing of gait (FOG_Q), and velocity of forward and backward walking compared with no intervention or another form of exercise; although most differences between groups were not statistically significant.	MODERATE[b]	20 ESRs Strong evidence demonstrates that physical activity improves a number of physical function outcomes, including walking, balance, strength, and disease-specific motor scores in older adults with Parkinson's disease. **PAGAC Grade: Strong.**
	Cugusi 2017 *(8)* Low	6 RCTS N=221	No serious risk of bias	Serious inconsistency	Serious indirectness	No serious imprecision	None	Mean age of participants ranged from 40 to 80 years. Duration of Parkinson's ranged from 1.5 to 7 years since diagnosis at all stages (H&Y stage 1-4). Trials tested the differences between Nordic walking and other exercise protocols (5 studies) or no exercise (1 study) for 4-24 weeks. Mixed findings. 3/5 trials found greater improvements in motor symptoms (e.g., UPSDRS III scale) and functional performance (e.g., 6MWT, TUG) in Nordic walking groups compared with other exercise groups and the remaining 2/5 found superior outcomes in the other exercise groups compared with the Nordic walking group.	MODERATE[c]	

Outcome	Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment Risk of bias	Inconsistency	Indirectness †	Imprecision	Other	Summary of findings	Certainty	US PAGAC evidence *(39)*
Cognitive function[d]	Stucken-schneider 2019 *(32)* Moderate	11 RCTs N=508	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean age was 68 years and Parkinson's disease severity ranged from 1-4 on the H&Y. Five studies evaluated aerobic exercise, 1 studied resistance exercise, and 5 studied coordination exercise; intervention duration ranged from 4 and 26 weeks. Mixed evidence within and between studies on various measures of cognition. 1/7 studies found a statistically significant effect of an exercise intervention on global cognitive function vs. no exercise; 3/10 studies found an effect on executive function; 1/0 studies found an effect on memory. No studies found favourable effects of exercise vs. control on measures of attention or speed of processing.	HIGH[e]	1 ESR Moderate evidence indicates that moderate-to-vigorous physical activity can have beneficial effects on cognition in individuals with diseases or disorders that impair cognitive function, including attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson's disease, and stroke. **PAGAC Grade: Moderate.**

Abbreviations: 6MWT = 6 min walk test; ESR = existing systematic review; FOG_Q = Freezing of Gait Questionnaire; H&Y = Hoehn and Yahr scale; PAGAC = Physical Activity Guidelines Advisory Committee; PDQ-39 = Quality of Life Parkinson's Disease Questionnare-39 items; QOL = quality of life; RCT = randomized clinical trial; TUG = timed up and go test; UPDRS III = Unified Parkinson's Diseases rating scale

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Two additional review *(10, 19)* identified, but were rated as critically low credibility and are not included
[b] Certainty of evidence downgraded due to serious indirectness (outcome measures), serious imprecision (small n's produced wide confidence intervals)
[c] Certainty of evidence downgraded due to serious inconsistency (mixed direction of effects), serious indirectness in outcome measures
[d] One additional review *(19)* identified, but was rated as critically low credibility and was not included
[e] Certainty of evidence not downgraded
[f] One additional review *(10)* identified, but was rated as critically low credibility and was not included

Table F.1.e. People with history of stroke, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with history of stroke
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Physical function, cognitive function

Outcome	Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment Risk of bias	Inconsistency	Indirectness †	Imprecision	Other	Description of evidence Summary of findings	Certainty	US PAGAC evidence *(39)*
Physical function[b]	Bonini-Rocha 2018 (23) Moderate	11 RCTs N = 750	Serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Mean age was between 38 and 91 years old. Time of stroke diagnosis ranged from 1 to 157 months. Interventions included circuit-based exercises lasting from 4 to 19 weeks, with the frequency of exercise from 2 to 7 times per week for 30-90 minutes each session. Circuit-based training was associated with improvements in **gait speed** compared with other interventions (MD = 0.11 m/s [95% CI, 0.02 to 0.18; *p*=0.03; 7 trials; n=516). There was no effect of the intervention on **balance** or **functional mobility**.	LOW[c]	2 ESRs Moderate evidence indicates that that mobility-oriented physical activity improves walking function for individuals after a stroke. **PAGAC Grade: Moderate.**
	Boyne 2017 (24) Low	16 RCTs 4 NRSIs N=882	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	None	Participants ranged from 0.4 to 70 months post—stroke. Few other details provided regarding participants. Aerobic exercise was associated with greater change in **cardiorespiratory fitness** (VO_2Peak) than control groups (pooled MD = 2.2 mL/kg/min [95% CI 1.3 to 3.1], 16 trials, 598) and **walking speed** (MD = 0.06 m/s [95% CI, 0.01 to 0.11); 13 studies; n=415), but there was substantial heterogeneity present.	VERY LOW[d]	
Physical function[b]	Cugusi 2017b *(9)* Moderate	2 RCTs N = 50	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean age was 53 and 57 of two trial; stroke onset was >6 months in both studies. Both trials compared Nordic treadmill walking vs. standard treadmill training. Both studies found improvement in measures of **walking distance** and **walking endurance** in both groups, with only one trial reporting these improvements to be statistically significantly greater among the Nordic walking group.	MODERATE[e]	
	Ge 2017 (26) Moderate	31 RCTs N=2,349	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	No evidence of a dose-response	Traditional Chinese exercise included Tai Chi (20 studies), Yijinjing (2 studies, Daoyin (3 studies), and Baduanjin (6 studies) ranging from 2 to 52 weeks duration.	MODERATE[f]	

							relation- ship	Traditional Chinese exercises compared with control groups were associated with **limb motor function** (SMD = 1.21 [95% CI, 0.66 to 1.77] *p*< 0.01), **balance function** (SMD = 2.07 [95% CI, 1.52 to 2.62, *p*< 0.01), **timed-up-and-go test** (MD = -1.77 [95%CI, -2.87 to -0.67], *p*< 0.01), and **ADLs** (MD = 15.60 [95% CI, 7.57 to 23.63, *p*< 0.01).		
	Li 2018 (29) Low	5 RCTs N = 346	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean age ranged from 55 to 73 years old. All studies evaluated the effects of 6 to 12 weeks of tai chi on standing balance and gait ability. A significant association was found for participants of tai chi vs. control groups for **gait ability** (e.g., TUG) (SMD = -0.26 [95% CI, -0.50 to -0.03]; *p*=0.027; 5 trials), but not **standing balance** (SMD = 0.15 [95% CI, -0.26 TO==to -0.59]; *p*=0.475; 3 trials).	LOW[f]	
	Miranda 2018 (30) Low	2 RCTs N = 39	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Mean age was 63 and 68 years. One study reported greater improvement in **functional status** (TUG) and **cardiorespiratory fitness** (VO_2max) among those in a Pilates intervention group vs. control. The other study reported greater improvement in **balance** among those in the Pilates vs. control.	MODERATE[g]	
	Patterson 2018 *(28)* Moderate	2 case reports 1 before-after N = 11	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	All 3 studies reported improvements in balance (BBS) 1 to 8 weeks following a dance intervention.	VERY LOW[h]	
Physical function[b]	Pogrebnoy 2019 (31) Low	8 RCTs N = 499	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Participants were mostly male with a mean age of 69 years. Range of 2.5 to 71 months post-stroke with most not reporting severity of stroke score. All trials evaluated outpatient exercise programs, including aerobic and resistance training from 12 weeks to 6 months in duration. Meta-analysis found that combined aerobic and resistance training was associated with improved **habitual walking speed** (MD 0.07 m/s [95% IC -0.01 to 0.16], 5 trials, n=248) and **walking enduran**ce (MD = 39.2 [95% CI 17.2 to 61.2], 6 trials, n=320) compared with usual care. There was no difference between groups for the TUG test and stair climb.	LOW[i]	
	Schröder 2018 *(30)* Low	4 RCTs 2 case studies 1 case-control N = 120	Serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	None	Included stroke patients in the late sub-acute (3-6 months post-stroke) and chronic (>6 months post-stroke) phase. Most studies included persons at mild-to-moderate disability (BBS score>31). Interventions included tele-rehabilitation or virtual reality exercise interventions (e.g., Wii, PlayStation 2 EyeToy, Microsoft Kinect). All four RCTs found improvements in measures of **balance** (BBS), but there were no statistically significant differences between groups.	LOW[f]	

								Observational studies reported feasibility of interventions.		
	Wiener 2019 (33) Low	3 RCTs 3 before-after N = 140	No serious risk of bias	No serious inconsistency	Serious indirectness	Serious impression	None	HIIT protocols (treadmill or bicycle training) ranged 20 to 30 minutes per session, 2 to 5 times a week, for 2 to 8 weeks total. Significant improvements in **cardiorespiratory fitness** were seen among HIIT participants but were not statistically significantly different than those in moderate-intensity exercise groups. There was no consistent effect of HIIT on measures of **balance** or **functional mobility.**	LOW[j]	
	Zou 2018a *(37)* Low	20 RCTs N = 1,286	Serious risk of bias	No serious inconsistency	Serious indirectness	Serious imprecision	None	Mean age ranged from 43 to 78 years old; course of disease varied from 14.5 days to 82 months; stroke type was often not reported. Interventions included qigong (4 study), yoga (2 studies), and tai chi (14 studies) for a duration of 4 to 12 weeks. Only 1 study included longer term follow-up at 12 months. Mind-body exercises were associated with greater **sensorimotor function of the lower limb** (SMD = 0.79 [95% CI, 0.43 to 1.15]; *p*<0.01; 8 trials; n=371), **upper limb function** (SMD = 0.7 [95% CI, 0.39 to 1.01]; *p*<0.001; 6 trials; n=276), and **gait speed** (SMD = 0.24 [95% CI, 0.01 to 0.48]; *p*=0.04; 5 trials; n=288). Mind-body exercises were not statistically significantly associated with **overall motor function** (SMD = 0.26 [95% CI, -0.06 to 0.57]; *p*=0.011; 3 trials; n=198).	LOW[k]	
Physical function[b]	Zou 2018b (36) Low	16 RCTs N = 1,136	Serious risk of bias	Serious inconsistency	No serious indirectness	Serious imprecision	None	Course of stroke disease ranged from 2 weeks to 82 months. Interventions included qigong (1 study), toga (1 study), and tai chi (14 studies) for a duration of 4 to 12 weeks. Only 2 studies included longer term follow-up at 6 and 12 months. Mind-body exercises were associated with significantly improved **ADLs** (Hedge's g = 1.31 [95% CI, 0.85 to 1.77], *p*<0.001, 6 trials) and **mobility** (Hedge's g = 0.67 [95% CI, 0.25 to 1.09], *p*<0.001, 5 trials).	VERY LOW[l]	
Cognitive function	No systematic review identified[m]									1 ESR Moderate evidence indicates that moderate-to-vigorous physical activity can have beneficial effects on cognition in individuals with diseases or disorders that impair cognitive function, including attention deficit hyperactivity disorder, schizophrenia,

		multiple sclerosis, Parkinson's disease, and stroke. **PAGAC Grade: Moderate.**

Abbreviations: ADL = activities of daily living; BBS = Berg Balance Scale CI = confidence interval; ESR = existing systematic review; HIIT = high-intensity interval training; MD = mean difference; m/s = meters per second; NR = not reported; NRSI = non-randomized study of an intervention; PAGAC = Physical Activity Guidelines Advisory Committee; QOL = quality of life; RCT = randomized clinical trial; SMD = standardized mean difference; TUG = Timed Up and Go test

[†] Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Certainty of evidence downgraded given serious risk of bias (lack of blinding of outcome assessors, missing data), serious inconsistency (substantial statistical heterogeneity), and serious imprecision (very wide CIs)
[b] Three additional reviews were identified *(18, 34, 36)* but were rated as critically low credibility and are not included
[c] Certainty of evidence downgraded given serious risk of bias, serious indirectness (variable and distally measured outcomes), and serious imprecision (wide CIs, small n's)
[d] Certainty of evidence downgraded given serious risk of bias, serious inconsistency (substantial statistical heterogeneity, I^2>70%), and serious imprecision (wide CIs, small n's)
[e] Certainty of evidence downgraded given considerable indirectness in interventions and outcome measures
[f] Certainty of evidence downgraded given serious risk of bias and serious indirectness of measures
[g] Certainty of evidence downgraded given considerable indirectness in interventions and outcome measures
[h] Certainty of evidence not upgraded
[i] Certainty of evidence assigned by review authors as High for habitual walking speed and Low for walking endurance given serious imprecision. Further downgraded here given serious indirectness of outcome measures and comparators
[j] Certainty of evidence downgraded given serious indirectness (intervention protocols and outcome measures) and serious imprecision
[k] Certainty of evidence downgraded given serious risk of bias (lack of blinding of outcome assessors, missing data), serious indirectness (variable distal outcome measures), and serious imprecision (very wide CIs)
[l] Certainty of evidence downgraded given serious risk of bias (lack of blinding of outcome assessors, missing data), serious inconsistency (substantial statistical heterogeneity), and serious imprecision (very wide CIs)
[m] One additional review was identified *(18, 34, 36)* but was rated as critically low credibility and was not included

Table F.1.f. People with major clinical depression, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with major clinical depression
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Health-related QOL

Outcome	Systematic review evidence Review credibility	No. of studies/ Study design No. of participants	Quality Assessment Risk of bias	Inconsistency	Indirectness †	Imprecision	Other	Summary of findings	Certainty	US PAGAC evidence *(39)*
Health-related QOL	Stubbs 2018[a] *(31)* Moderate	1 ESR (6 RCTs, N=198)	NA[c]					One high credibility review found exercise was associated with improved overall QOL (SMD = 0.39 [95% CI, 0.27 to 0.74], *p*=0.002, 5 trials) and physical and psychological QOL domains. There was no effect seen for social or environmental QOL domains.	MODERATE[g, h]	3 ESRs Limited evidence suggests that physical activity improves quality of life for adults with major clinical depression. **PAGAC Grade: Limited**
	Krogh 2017 *(20)* Moderate	9 RCTs N=827	Serious risk of bias	Serious inconsistency	Serious indirectness	Serious imprecision	NR	Mean age ranged from 21 to 75 years and 5 trials included participants with a mean age >60 years. Ten trials included inpatients. Comparisons were variable including exercise intervention vs. control group, comparison of various intensities of exercise, and comparison of one type of exercise vs. another. Pooled analysis found no statistically significant difference in QOL scores among exercise vs. control groups (SMD = 0.40 [95% CI, -0.03 to 0.83], 9 trials).	VERY LOW[ii]	

Abbreviations: CI = confidence interval; CRF = cardiorespiratory fitness; ESR = existing systematic review; NA = not applicable; NR = not reported; NRSI = non-randomized study of an intervention; PAGAC = Physical Activity Guidelines Advisory Committee; QOL = quality of life; RCT = randomized clinical trial; RR = risk ratio; SMD = standardized mean difference
† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Both Stubbs et al. 2018 and Ashdown-Franks et al. 2019 were review-of-reviews and included the same existing systematic reviews for evidence related to adults with major depression
[b] Total N calculated by adding n's of each review; total number may be lower if reviews included overlapping studies
[c] Not able to assign given review-of-review methodology
[d] Certainty of evidence not downgraded
[e] Stubbs 2018 *(31)* rated as 1+ evidence (Well-conducted meta-analyses, systematic reviews or RCTs with a low risk of bias)
[f] As reported by review authors. Certainty of evidence downgraded due to serious risk of bias of included studies, serious inconsistency (I2>70%), serious indirectness (heterogeneity and applicability of populations and comparisons), and possible publication bias

[g] Certainty of evidence downgraded given limited number of RCTs with no long-term data
[h] Stubbs 2018 *(31)* rated as -1 evidence (Meta-analyses, systematic reviews or RCTs with a high risk of bias)
[I] As reported by review authors. Certainty of evidence downgraded given serious risk of bias, inconsistency, and imprecision

Table F.1.g. People with schizophrenia, relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with schizophrenia
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Cognitive function, health-related QOL

Outcome	Systematic review evidence Review credibility	Quality Assessment No. of studies/ Study design No. of participants	Risk of bias	Inconsistency	Indirectness †	Imprecision	Other	Summary of findings	Certainty	US PAGAC evidence *(39)*
Cognitive function	Firth 2017[f] *(13)* Low	10 RCTs N=455	No serious risk of bias	No serious inconsistency	Serious indirectness	No serious imprecision	Evidence of a dose-response relation-ship	Mean age of participants was 37.3 years (range 23-55 years). Ninety-two percent had schizophrenia/schizoaffective disorder and 7.9% had other nonaffective psychotic disorders and mean duration of illness was 13.4 years. About half (56%) of the total sample was male. Exercise programs were, on average, 12.2 weeks long and primarily focused on aerobic exercise. Exercise was statistically significant associated with improved global cognition (Hedge's g = 0.33 [95% CI, 0.13 to 0.53], *p*=0.001), working memory, social cognition, and attention/vigilance but there was no effect on processing speed, verbal memory, visual memory, reasoning, and problem solving.	HIGH[g]	1 ESR Moderate evidence indicates that moderate-to-vigorous physical activity can have beneficial effects on cognition in individuals with diseases or disorders that impair cognitive function, including attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson's disease, and stroke. **PAGAC Grade: Moderate.**
Health-related QOL	Stubbs 2018[a] *(31)* Moderate	1 ESR (3 RCTs, N=NR)	NA[b]					Two RCTs, which both used 120 min of MVPA per week, reported significant improvements in QOL and disability, whilst 1 RCT of lower intensity did not lead to any significant results.	LOW[d, e]	3 ESRs Moderate evidence indicates that physical activity improves quality of life in individuals with schizophrenia. **PAGAC Grade: Moderate.**

Abbreviations: ESR = existing systematic review; MVPA = moderate-to-vigorous physical activity; NA = not applicable; NR = not reported; PAGAC = Physical Activity Guidelines Advisory Committee; SMD = standardized mean difference; QOL = quality of life; RCT = randomized clinical trial

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Both Stubbs et al. 2018 and Ashdown-Franks et al. 2019 were review-of-reviews and included the same existing systematic review
[b] Not able to assign given review-of-review methodology
[c] Certainty of evidence downgraded given small number of RCTs and low credibility of review
[d] Stubbs 2018 *(31)* rated as -1 evidence (Meta-analyses, systematic reviews or RCTs with a high risk of bias)
[e] Certainty of evidence downgraded given small number of studies and sample size
[f] Review also included in review-of-reviews by Stubbs et al. 2018 *(31)* and Ashdown-Franks et al. 2019 *(2)*
[g] Certainty of evidence not downgraded

Table F.1.h. People with attention deficit hyperactivity disorder (ADHD), relationship between physical activity and health-related outcomes

Questions: What is the association between **physical activity** and health-related outcomes?
Population: People with attention deficit hyperactivity disorder (ADHD)
Exposure: Greater volume, duration, frequency, or intensity of physical activity
Comparison: No physical activity or lesser volume, duration, frequency, or intensity of physical activity
Outcome: Cognitive function

Outcome	**Systematic review evidence** **Review credibility**	**No. of studies/ Study design** **No. of participants**	**Quality Assessment** **Risk of bias**	**Inconsistency**	**Indirectness †**	**Imprecision**	**Other**	**Summary of findings**	**Certainty**	**US PAGAC evidence** *(39)*
Cognitive function	Ashdown-Franks 2019[a, d] *(2)* Moderate	1 ESR (5 RCTs, N=NR)	NA[b]					One low credibility review of 5 RCTs found evidence to suggest that exercise is more effective than usual are or education in children (mean age 11 years) on measures of attention (SMD = 0.84 [95% CI, 0.48 to 1.20], trials NR) and executive function (SMD = 0.58 [95% CI, 0.15 to 1.00], 3 trials, n=102), and social disorders (SMD =0.59 [95% CI 0.03 to 1.16], 2 RCTs, n=53).	LOW[c]	2 ESRs Moderate evidence indicates that moderate-to-vigorous physical activity can have beneficial effects on cognition in individuals with diseases or disorders that impair cognitive function, including attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson's disease, and stroke. **PAGAC Grade: Moderate.**

Abbreviations: ESR = existing systematic review; NR = not reported; PAGAC = Physical Activity Guidelines Advisory Committee; RCT = randomized clinical trial; QOL = quality of life

† Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

[a] Review-of-reviews
[b] Not able to assign given review-of-review methodology
[c] Certainty of evidence downgraded given small number of trials and unknown risk of bias, consistency, and precision
[d] Two additional reviews *(7 Suarez-Manzano, 2018 #113)* were identified but were rated as critically low credibility and are not included

Appendix A. Data Extractions

<table>
<tr><td colspan="2">SCI 1. SYSTEMATIC REVIEW
Citation: A. C. Eitivipart; C. Q. Oliveira; M. Arora; J. Middleton; G. M. Davis (2019) Overview of Systematic Reviews of Aerobic Fitness and Muscle Strength Training after Spinal Cord Injury</td></tr>
<tr><td>Purpose: This overview was undertaken to assimilate evidence about the effectiveness of different types of physical activities, exercises, and therapeutic interventions for improving aerobic fitness and muscle strength in people with SCI.</td><td rowspan="5">Abstract:
The number of systematic reviews on the effects of exercise on aerobic fitness and muscle strength in people with spinal cord injury (SCI) has recently increased. However, the results of some of these reviews are inconclusive or inconsistent. To strengthen recommendations, this overview was undertaken to assimilate evidence about the effectiveness of different types of physical activities, exercises, and therapeutic interventions for improving aerobic fitness and muscle strength in people with SCI. Cochrane Overview of reviews methods were adopted to undertake this overview. An online search was conducted in August 2018 on eight databases based on predefined search criteria. Potential systematic reviews were screened, selected, and assessed on methodological quality by two independent authors, and discussed and resolved with a third author, when necessary. Only systematic reviews published in the English language were included. The protocol was registered on PROSPERO. Overall, 16 systematic reviews were included (aerobic fitness, n = 10; muscle strength, n = 15). For all 16 reviews, the quality of evidence was rated as critically low." Despite low evidence, this overview strengthens the existing guidelines for people with SCI, providing specific advice on exercise domains (types, intensities, frequency, and duration) for improving aerobic fitness and muscle strength. The evidence from this overview suggests that ergometry training with/without additional therapeutic interventions (20 min, moderate to vigorous intensity, twice weekly for 6 weeks) may improve aerobic fitness; similarly, resistance training with/without additional therapeutic interventions (three sets of 8-10 repetitions, moderate to vigorous intensity, twice weekly for 6 weeks) may improve muscle strength."</td></tr>
<tr><td>Timeframe: Variable start dates to 2018</td></tr>
<tr><td>Total # studies included: 16</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Adults over the age of 16</td></tr>
<tr><td>Outcomes addressed:
Aerobic fitness and muscle strength</td></tr>
</table>

<table>
<tr><td colspan="2">SCI 2 SYSTEMATIC REVIEW
Citation: R. Gaspar; N. Padula; T. B. Freitas; J. P. J. de Oliveira; C. Torriani-Pasin (2019) Physical Exercise for Individuals With Spinal Cord Injury: Systematic Review Based on the International Classification of Functioning, Disability, and Health</td></tr>
<tr><td>Purpose: To review and evaluate the literature on physical exercise interventions for individuals with SCI, based on the International Classification of Functioning, Disability and Health, as well as physiological parameters for exercise prescription</td><td rowspan="5">Abstract:
Introduction: Considering the reduction of physical activity performed daily in people with spinal cord injury, it is necessary to analyze the interventions based on physical exercises in order to provide recommendations based on evidence. Objectives: To review and evaluate the literature on physical exercise interventions for individuals with SCI, based on the International Classification of Functioning, Disability and Health, as well as physiological parameters for exercise prescription. Method: A systematic review of the literature produced from August 2016 to February 2017 within the PubMed, Embase, Cochrane Library, and MEDLINE databases. Results: Two independent examiners conducted a search in which 223 articles were initially found. A third evaluator verified possible divergences and generated a final list of 25 articles that strictly met the inclusion criteria, 5 of which investigated the effects of aerobic exercise, 2 of resistance training, 2 of balance training, 12 of gait training, and 4 evaluating the combined effect of 2 or more forms of training. Conclusion: Considering studies classified as of high and moderate quality of evidence, positive effects were observed in the domains of structures and functions, in aerobic, resistance training and combined exercises, and in some studies with gait training. In the domain of activities and participation, positive effects were observed in the studies with gait training, balance training, and combined interventions.</td></tr>
<tr><td>Timeframe:
August 2016 – February 2017</td></tr>
<tr><td>Total # studies included: 25</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Gait performance
Quality of life
Depression</td></tr>
</table>

<table>
<tr><td colspan="2">SCI 3 SYSTEMATIC REVIEW
Citation: F. C. M. Melo; K. K. F. de Lima; A. Silveira; K. P. M. de Azevedo; I. K. Dos Santos; H. J. de Medeiros; J. C. Leitao; M. I. Knackfuss (2019) Physical Training and Upper-Limb Strength of People With Paraplegia: A Systematic Review</td></tr>
<tr><td>Purpose: To investigate the scientific implications of the impact of physical training on the strength of the upper limbs of people with paraplegias</td><td rowspan="5">Abstract:
CONTEXT: Physical training improves the strength of upper limbs, contributing directly to the performance of activities of daily life, confirming one more time that the strengthened muscle is imperative for a rapid rehabilitation. OBJECTIVE: To investigate the scientific implications of the impact of physical training on the strength of the upper limbs of people with paraplegias. EVIDENCE ACQUISITION: The search strategy with truncations and Boolean operator was defined as: (spinal cord inju* OR traumatic myelopat* OR paraplegi*) AND (physical exercise OR strength training OR resisted training) AND (upper limb* OR arm OR armrest), for all of the databases. There were included experimental and quasi-experimental studies, published in the English language and with the complete text available, with at least 1 physical exercise that worked with the strength of the upper limbs. Two independent evaluators extracted from each article data on study characteristics (publishing year, country of origin, and study design), of the subjects (gender and age), and of the disability (level of lesion and cause). EVIDENCE SYNTHESIS: Seven articles were included in the systematic revision. The procedure used the most for measuring the maximum strength was the 1-repetition maximum test, followed by the isokinetic dynamometer and Quantitative Muscle Testing System. Furthermore, the most commonly associated variables in the included studies were pain in the shoulder, cardiorespiratory capacity, and functionality, respectively. The results showed that all of the variables improved because of the training. CONCLUSIONS: The training improved the strength, the functionality, and reduced the pain in the shoulder of the people with paraplegia.</td></tr>
<tr><td>Timeframe:
Inception – November 2015</td></tr>
<tr><td>Total # studies included: 7</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Upper limb strength</td></tr>
</table>

<table>
<tr><td colspan="2">ID 1: Systematic Review & Meta-Analysis
Citation: C. Maiano; O. Hue; G. Lepage; A. J. S. Morin; D. Tracey; G. Moullec 2019 Do Exercise Interventions Improve Balance for Children and Adolescents With Down Syndrome? A Systematic Review 10.1093/ptj/pzz012</td></tr>
<tr><td>Purpose:
To investigate the effects of exercise interventions designed to improve balance in young people with intellectual disabilities.</td><td rowspan="5">Abstract: AIM To conduct a systematic review and meta-analysis of the effects of exercise interventions designed to improve balance in young people with intellectual disabilities. METHOD A systematic literature search was performed on 10 databases. Studies in press or published in English in a peer-reviewed journal were included if: (1) participants were young people with intellectual disabilities; (2) exercise interventions were designed to improve balance; and (3) they used quasi-experimental or experimental designs. Studies focusing only on a specific subpopulation of young people with intellectual disabilities or having a specific physical characteristic were excluded. Risk of bias was assessed for randomization, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting, and other biases. RESULTS The search strategy identified 937 articles and 15 studies, published between 1991 and 2017, that met the inclusion criteria. Exercise intervention groups showed a significant and larger improvement in static (pooled effect size, Hedges' g=0.98) and dynamic (g=1.34) balance compared with the control groups. However, although the pooled improvement of static–dynamic balance was large (g=2.80), the result was non-significant. None of the subgroup analyses were significant, except for the improvement in: (1) static balance (higher in quasi-experimental than in experimental studies); and (2) dynamic balance (higher in young people with a mild vs a mild–moderate intellectual disability). INTERPRETATION The reviewed exercise interventions seem to represent an effective means for improving the static and dynamic balance of young people with intellectual disabilities. However, the present findings should be considered as preliminary given the small number of studies and their limitations.</td></tr>
<tr><td>Timeframe: 1991-2017 search conducted March 17th, 2018</td></tr>
<tr><td>Total # studies included: 15</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) In English/ school-aged (from 5–22y) with intellectual disabilities or mixed samples.
Subpopulation excluded.
Exercise intervention to improve balance.
Quasi-experimental or experimental design.</td></tr>
<tr><td>Outcomes addressed:
Static and dynamic Balance</td></tr>
</table>

ID2: Systematic Review and Meta-Analysis **Citation:** C. Maiano; O. Hue; A. J. S. Morin; G. Lepage; D. Tracey; G. Moullec 2019 Exercise interventions to improve balance for young people with intellectual disabilities: a systematic review and meta-analysis 10.1111/dmcn.14023	
Purpose: to summarize the findings from studies examining the effects of exercise interventions designed to improve balance in youths with Down syndrome.	**Abstract: Background.** Youths with Down syndrome are characterized by deficits in balance/postural stability. One way to palliate balance deficits among this population is through exercise interventions. However, to the authors' knowledge, the effects of exercise interventions designed to improve the balance of youths with Down syndrome have never been systematically reviewed. **Purpose.** The purpose of this review was to summarize the findings from studies examining the effects of exercise interventions designed to improve balance in youths with Down syndrome. **Data Sources.** A systematic literature search was performed in 10 databases (Academic Search Complete, CINAHL Plus With Full-Text, Education Source, ERIC, Medline With FullText, PsycARTICLES, Psychology and Behavioral Sciences Collection, Scopus, SocINDEX, and SPORTDiscus With Full-Text) on June 12, 2017. Study Selection. Randomized controlled trials and controlled trials examining the effects of exercise interventions designed to improve balance in youths with Down syndrome were included. **Data Extraction.** Two authors selected the studies and extracted their characteristics and results. Three authors assessed the risk of bias in the studies using the Cochrane Collaboration tool. Data Synthesis. Eleven studies, published between 2010 and 2017, met the inclusion criteria. The findings showed that exercise interventions were more effective than control conditions for improving the static balance of children with Down syndrome and the static-dynamic balance (ie, global balance score obtained with a scale measuring both static and dynamic balance) of children and adolescents with Down syndrome. Nevertheless, the findings on dynamic balance in children and static balance in adolescents were inconclusive. **Limitations.** With a small number of studies and their high risk of bias, the present findings must be interpreted with caution. **Conclusions.** The reviewed exercise interventions were successful in improving the static balance of children with Down syndrome and the static-dynamic balance of children and adolescents with Down syndrome.
Timeframe: 2010-2017	
Total # studies included: 11	
Other details (e.g. definitions used, exclusions etc) Exclusion criteria: Case study. Mean age < 18. Not Balance intervention. Not intervenion study. No control. Sample of infants.	
Outcomes addressed: static and dynamic balance/ postural stability	

MS 1. Systematic review with Meta-analysis **Citation:** K. B. Alphonsus; Y. Su; C. D'Arcy 2019. The effect of exercise, yoga and physiotherapy on the quality of life of people with multiple sclerosis: Systematic review and meta-analysis 10.1016/j.ctim.2019.02.010	
Purpose: examine the effect of exercise, yoga and physiotherapy on the physical, mental and social QOL among individuals living with MS	**Abstract: Introduction:** Multiple sclerosis (MS) is a chronic autoimmune disease affecting the myelinated axons of the central nervous system causing neurological deterioration. People living with MS have a poor quality of life (QOL) because of the symptoms caused by the disease and there are various types of treatments to manage the symptoms aside from medication. **Objective:** This meta-analysis examines the effect of exercise, yoga and physiotherapy on the physical, mental and social QOL among individuals living with MS. **Setting:** A systematic review with meta-analysis was conducted using PubMed, Medline, and Scopus from 1990 to 2017. The standard mean difference scores were computed in each study for the domains of physical, mental and social functioning. **Results:** Eighteen studies met the inclusion criteria for this meta-analysis. Aerobic exercise was effective in improving satisfaction with physical functioning, d = 0.35 (95% CI = 0.08 to 0.62), mental functioning d = 0.42 (95% CI = 0.11 to 0.72), and social functioning d = 0.42 (95% CI = 0.15 to 0.69). Physiotherapy was also found to be effective for physical functioning d = 0.50 (95% CI 0.19 to 0.80), mental functioning d = 0.44 (95% CI 0.14 to 0.75) and social functioning d = 0.60 (95% CI 0.21 to 0.90). However yoga and combination of exercises did not have a significant effect on any of the QOL domains. **Conclusion:** These findings suggest that aerobic exercise and physiotherapy improves the satisfaction of MS patients with their physical, mental and social functioning and may be included as normal practice in the treatment of MS.
Timeframe: 1990-2017	
Total # studies included: 18	
Other details (e.g. definitions used, exclusions etc) Quality of life (QOL) was categorized into three domains: a) physical, b) mental and c) social health.	
Outcomes addressed: QoL	

<table>
<tr><td colspan="2">MS 2. Systematic Review
Citation: E. Campbell; E. H. Coulter; L. Paul 2018 High intensity interval training for people with multiple sclerosis: A systematic review 10.1016/j.msard.2018.06.005</td></tr>
<tr><td>Purpose: investigate the efficacy and safety of HIIT in people with MS</td><td rowspan="5">Abstract: Background: Aerobic high intensity interval training (HIIT) is safe in the general population and more efficient in improving fitness than continuous moderate intensity training. The body of literature examining HIIT in multiple sclerosis (MS) is expanding but to date a systematic review has not been conducted. The aim of this review was to investigate the efficacy and safety of HIIT in people with MS. Methods: A systematic search was carried out in September 2017 in EMBASE, MEDline, PEDro, CENTRAL and Web of Science Core collections using appropriate keywords and MeSH descriptors. Reference lists of relevant articles were also searched. Articles were eligible for inclusion if they were published in English, used HIIT, and included participants with MS. Quality was assessed using the PEDro scale. The following data were extracted using a standardised form: study design and characteristics, outcome measures, significant results, drop-outs, and adverse events. Results: Seven studies (described by 11 articles) were identified: four randomised controlled trials, one randomised cross-over trial and two cohort studies. PEDro scores ranged from 3 to 8. Included participants (n = 249) were predominantly mildly disabled; one study included only people with progressive MS. Six studies used cycle ergometry and one used arm ergometry to deliver HIIT. One study reported six adverse events, four which could be attributed to the intervention. The other six reported that there were no adverse events. Six studies reported improvements in at least one outcome measure, however there were 60 different outcome measures in the seven studies. The most commonly measured domain was fitness, which improved in five of the six studies measuring aspects of fitness. The only trial not to report positive results included people with progressive and a more severe level of disability (Extended Disability Status Scale 6.0–8.0). Conclusion: HIIT appears to be safe and effective in increasing fitness in people with MS and low levels of disability. Further research is required to explore the effectiveness of HIIT in people with progressive MS and in those with higher levels of disability.</td></tr>
<tr><td>Timeframe: inception - 2017</td></tr>
<tr><td>Total # studies included: 7</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) included if Human subjects, English, used HIIT, and included participants with MS or mixed with separate reporting for MS. Included clinical trials using HIIT or combination.</td></tr>
<tr><td>Outcomes addressed: cardiovascular fitness and muscle strength</td></tr>
</table>

<table>
<tr><td colspan="2">MS 3: Systematic Review
Citation: S. Charron; K. A. McKay; H. Tremlett 2018 Physical activity and disability outcomes in multiple sclerosis: A systematic review (2011-2016) 10.1016/j.msard.2018.01.021</td></tr>
<tr><td>Purpose: examining the relationship between physical activity and physical ability outcomes in persons with MS</td><td rowspan="5">Abstract: Background: Physical activity may be neuroprotective in multiple sclerosis (MS). One review (2011) of exercise and MS disability was inconclusive, but highlighted the need for more studies. Objective: To perform an updated systematic literature review examining the relationship between physical activity and physical ability outcomes in persons with MS. Methods: EMBASE and MEDLINE were searched for original interventional studies (2011–2016) evaluating exercise on quantitative outcomes of physical disability in MS. We also assessed any reported adverse outcomes. Results: Of the 153 articles identified, 12 were included; 3 examined endurance training; 6 resistance training; and 3 explored less conventional exercises, specifically, tai chi, kickboxing, and vestibular rehabilitation, each lasting 5–24 weeks. In total, 568 unique individuals were included, and > 10 different scales used to assess outcomes. Endurance training provided benefits in walking ability, while mindfulness exercises (tai chi and vestibular rehabilitation), and dynamic workouts (kickboxing) led to improvements in balance and coordination. Resistance training alone did not improve walking ability, but improved lower limb muscular strength and endurance. When resistance and endurance training were combined, improvements were seen in mobility, balance and coordination. Four studies assessed discontinuation; most reported a return to pre-intervention function. Adverse outcomes were reported in 6 studies, and appeared generally mild, ranging from mild muscle soreness to exacerbation of MS symptoms. Conclusions: Physical activity was associated with measurable benefits on ability outcomes, but continuation is likely required to maintain benefits. While adverse events were generally mild, approximately half of studies actually reported safety outcomes.</td></tr>
<tr><td>Timeframe: 2011-2016</td></tr>
<tr><td>Total # studies included: 12</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) Studies were in English. Populations with MS. Impact of a physical activity-intervention /quantitative measure of ability/ disability as an outcome</td></tr>
<tr><td>Outcomes addressed: physical ability outcomes</td></tr>
</table>

<table>
<tr><td colspan="2">MS 4 Meta-Analysis and Scoping Study
Citation: A. Manca; Z. Dvir; F. Deriu 2019 Meta-analytic and Scoping Study on Strength Training in People With Multiple Sclerosis 10.1519/jsc.0000000000002381</td></tr>
<tr><td>Purpose: determine a pooled estimate of effect on muscle strength and functional capacity induced by strength training in people with multiple sclerosis</td><td rowspan="5">Abstract: Aim of the study was to determine a pooled estimate of effect on muscle strength and functional capacity induced by strength training in people with multiple sclerosis (PwMS). Five databases and 2 public registries were searched from inception to May 2017. Indexing terms used were: “multiple sclerosis,” “resistance training,” and “strength training.” After title/abstract screening, 2 independent reviewers evaluated the studies’ eligibility, which were retained if PwMS were randomly assigned to strength training or to a no intervention group. Of the 1,467 items retrieved, 30 randomized controlled trials formed the initial database with 11 trials (426 subjects) entering the final meta-analysis. The quality of the included studies was assessed by the PEDro scale and the risk of bias using the Cochrane Risk-of-Bias tool. All meta-analyses were conducted using a random effects model. After interventions, PwMS increased strength by 23.1% (confidence interval [CI] 11.8–34.4; +12.1 N; CI 4.5–19.8; p = 0.002; n = 366 subjects) at a small-to moderate effect size (0.37; CI 0.2–0.6). Walking speed increased by 16.3 6 10.7% (p = 0.0002; effect size 0.54; n = 275 subjects), distance covered in the 2-minute walking test by 6.7 6 6.4% (p = 0.04; effect size 0.50; n = 111 subjects). People with MS respond to resistance training with consistent strength gains. Methodological inconsistencies among studies and inadequate reporting of the findings limited a comprehensive determination of the impact of strength improvements on patient functioning, except for walking performance which seemed significantly improved. Methodological steps and scoping lines are provided to establish a common platform for future trials.</td></tr>
<tr><td>Timeframe: inception to May 2017</td></tr>
<tr><td>Total # studies included: 11</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Exclusions - absence of control, healthy controls, combined training, unconventional protocols/ same dataset as other study</td></tr>
<tr><td>Outcomes addressed: muscle strength and functional capacity</td></tr>
</table>

<table>
<tr><td colspan="2">MS 5 Integrative Review (SysRev)
Citation: J. D. Morrison; L. Mayer 2017 Physical activity and cognitive function in adults with multiple sclerosis: an integrative review
10.1080/09638288.2016.1213900</td></tr>
<tr><td>Purpose: To identify and synthesize the research evidence concerning (1) the relationship between physical activity and cognitive performance in persons with multiple sclerosis (MS) and (2) to review the reported effects of physical activity interventions on neurocognitive performance conducted in this population</td><td rowspan="5">Abstract: Purpose: To identify and synthesize the research evidence concerning (1) the relationship between physical activity and cognitive performance in persons with multiple sclerosis (MS) and (2) to review the reported effects of physical activity interventions on neurocognitive performance conducted in this population. Methods: Relevant peer-reviewed journal articles were identified by searching PubMed, PsychINFO, and SPORTDiscus through May 2016. Full-text articles meeting the inclusion criteria were evaluated for quality using tools developed by the National Institutes of Health. Studies deemed to be of poor quality were excluded from the review. Results: Nineteen studies meeting the inclusion/exclusion criteria were analyzed. Nine studies reported significant relationships between higher levels of physical activity or cardiorespiratory fitness and measures of cognitive function. Data extracted from 10 physical activity intervention studies reported mixed results on the effectiveness of physical activity to improve selected domains of cognitive function in persons with MS. Conclusion: Although correlational studies provide evidence to support a linkage between physical activity and cognitive function in persons with MS, this linkage is confounded by factors that may have influenced the studies' results. Evidence derived from intervention studies that could support a positive effect of physical activity on cognition in persons with MS is equivocal.</td></tr>
<tr><td>Timeframe: inception to May 2016</td></tr>
<tr><td>Total # studies included: 19</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) MS age 18 or older and that addressed both physical activity and cognitive function. In English. Self-report of cognitive impairment excluded.</td></tr>
<tr><td>Outcomes addressed: cognition</td></tr>
</table>

MS 6 Meta-Analysis **Citation:** D. Veneri; M. Gannotti; M. Bertucco; S. E. Fournier Hillman 2018 Using the International Classification of Functioning, Disability, and Health Model to Gain Perspective of the Benefits of Yoga in Stroke, Multiple Sclerosis, and Children to Inform Practice for Children with Cerebral Palsy: A Meta-Analysis 10.1089/acm.2017.0030	
Purpose: to determine the domains of the International Classification of Functioning, Disability, and Health (ICF) model and levels of evidence for yoga and adults with stroke and multiple sclerosis (MS), and children	**Abstract: Objective**: Research pertaining to yoga and children with cerebral palsy (CP) is negligible. The primary purpose of this study was to determine the domains of the International Classification of Functioning, Disability, and Health (ICF) model and levels of evidence for yoga and adults with stroke and multiple sclerosis (MS), and children. A secondary purpose was to decide whether any inferences could be made for children with CP. **Design:** This study included a meta-analysis. Interventions: A systematic review was performed of yoga and said populations. Outcome measures were categorized according to the ICF model domains of body structures and function, activity, and quality of life. Effect sizes (ESs) were calculated by using Cohen's d. Since there were few commonalities among outcome measures and reporting of outcomes within and among diagnostic groups, direct comparisons of ESs were difficult. Hence, we chose to evaluate the impact of yoga as compared with the control group or other physical exercise by using a General Linear Mixed Model. **Results:** There were 5 yoga studies with stroke, 15 with MS, and 12 with children. Studies with children used outcomes related to body structure and function, whereas those with stroke and MS used outcomes across all three domains of the ICF. ESs varied from negligible to medium for stroke, from negligible to large for MS and children. **Conclusions:** The findings of this meta-analysis indicate that yoga is no better or worse than other exercise modalities as a treatment intervention for adults with stroke and MS, and children. Group yoga classes are typically social environments that can contribute to increased physical progress and feelings that contribute to quality of life, which may benefit individuals with CP. More research on yoga and particularly in children and adults with CP would yield valuable information for creating effective and safe yoga programs with a rich array of benefits.
Timeframe: to May 2016	
Total # studies included: 32	
Other details (e.g. definitions used, exclusions etc) yoga as an intervention and OM examining body structures and function, physical capacity or performance, and/or quality of life. Exclusion criteria included SRs.	
Outcomes addressed: body structures and function, activity, quality of life	

PFn 1 SYSTEMATIC REVIEW Citation: L. Cugusi; A. Manca; D. Dragone; F. Deriu; P. Solla; C. Secci; M. Monticone; G. Mercuro. Nordic Walking for the Management of People With Parkinson Disease: A Systematic Review. PM R 9 (2017) 1157-1166	
Purpose: to bring together current knowledge on the effects of NW compared with other exercise interventions on motor and nonmotor symptoms, functional performance, and QOL in people with PD. Second, we sought to appraise the clinical relevance of the findings arising from the studies and, finally, to propose a sharable design for upcoming research that might allow the uniformity and usefulness of future trials on this field	Abstract: BACKGROUND: It is well known that physical exercise is the main therapeutic element of rehabilitation programs for people with Parkinson disease (PD). As traditional forms of exercise can guarantee significant health benefits, the emergence of nonconventional physical activities, such as Nordic walking (NW), may add positive effects. OBJECTIVE: To appraise the available evidence on the main effects of NW in the rehabilitation programs for people with PD and to propose a design for upcoming research that might improve the uniformity of future trials. STUDY DESIGN: Systematic review. LITERATURE SURVEY: A literature search of 5 established databases (PubMed, MEDLINE, Scopus, Web of Science, and Cochrane) was conducted. METHODOLOGY: Any relevant randomized controlled trials pertinent to NW in PD published in English from inception to February 2017 were included. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed, and the methodologic quality of each study was assessed by the Physiotherapy Evidence Database scale. DATA SYNTHESIS: Sixty-six studies were retrieved, and 6 randomized controlled trials (221 subjects) were entered into the qualitative synthesis. Overall, these studies portrayed NW as feasible and likely to be effective in improving the functional and clinical outcomes of people with PD. When we compared NW with other exercise-based interventions, such as treadmill training, free walking, a program of standardized whole-body movements with maximal amplitude (Lee Silverman Voice Treatment BIG training), or a home-based exercise program, the findings proved controversial. CONCLUSIONS: High heterogeneity and methodologic discrepancies among the studies prevent us from drawing firm conclusions on the effectiveness of NW in comparison with other exercise-based interventions currently used by people with PD. Further investigations with a common design are necessary to verify whether NW may be included within conventional rehabilitation programs commonly recommended to people with PD. LEVEL OF EVIDENCE: II.
Timeframe: from inception to February 2017	
Total # studies included: 6	
Other details (e.g. definitions used, exclusions etc) Inclusion criteria: (1) people with PD; (2) an analysis of the main outcomes arising from a mid- to long-term (defined as ≥2 weeks) NW program; (3) only RCTs were included	
Outcomes addressed: Motor and nonmotor symptoms Functional performance Quality of life	

PFn 2. SYSTEMATIC REVIEW Citation: K. J. Ćwiękała-Lewis; M. Gallek; R. E. Taylor-Piliae. The effects of Tai Chi on physical function and well-being among persons with Parkinson's Disease: A systematic review. Journal of Bodywork & Movement Therapies (2017) 21, 414e421	
Purpose: to evaluate the effects of Tai Chi on physical function and well-being among persons with Parkinson's disease	Abstract: Current medical treatments for Parkinson's disease (PD) are mainly palliative, though research indicates Tai Chi exercise improves physical function and well-being. An electronic database search of PubMed, CINAHL, Web of Science, Cochrane Library, PsycINFO and Embase was conducted, to examine current scientific literature for potential benefits of Tai Chi on physical function and well-being among persons with PD. A total of 11 studies met the inclusion criteria: 7 randomized clinical trials and 4 quasi-experimental studies. PD participants (n = 548) were on average age 68 years old and 50% women. Overall, participants enrolled in Tai Chi had better balance and one or more aspect of well-being, though mixed results were reported. Further research is needed with more rigorous study designs, larger sample sizes, adequate Tai Chi exercise doses, and carefully chosen outcome measures that assess the mechanisms as well as the effects of Tai Chi, before widespread recommendations can be made.
Timeframe: January 2000 through April 2015	
Total # studies included: 12	
Other details (e.g. definitions used, exclusions etc) PD participants were assigned to a Tai Chi exercise intervention and if physical function or well-being outcomes were assessed	
Outcomes addressed: Physical function outcomes Well-being outcomes	

PFn 3. SYSTEMATIC REVIEW Citation: M. Dos Santos Delabary; I. G. Komeroski; E. P. Monteiro; R. R. Costa; A. N. Haas. Effects of dance practice on functional mobility, motor symptoms and quality of life in people with Parkinson's disease: a systematic review with meta-analysis. Aging Clin Exp Res (2018) 30:727–735.	
Purpose: to conduct a systematic review with meta-analysis in the aim to analyze the effects of dance classes when compared to other interventions or to the absence of intervention, in randomized clinical trials on functional mobility, motor symptoms and Quality of life of patients with Parkinson's disease	Abstract: BACKGROUND: Patients with Parkinson's Disease (PD) undergo motor injuries, which decrease their quality of life (QL). Dance, added to drug therapy, can help treating these patients AIMS: To conduct a systematic review with meta-analysis with the aim to analyze the effects of dance classes in comparison to other interventions or to the absence of intervention, in randomized clinical trials (RCTs), on functional mobility, motor symptoms and QL of PD patients METHODS: The search was conducted in MEDLINE, LILACS, SciELO, Cochrane and PsycINFO (last searched in August 2017). RCTs analyzing dance effects in comparison to other physical training types or to no intervention, on functional mobility, motor symptoms and QL of PD patients were selected. The outcomes assessed were motor symptoms with Unified PD Rating Scale III (UPDRSIII), functional mobility with Timed Up and Go Test (TUG), endurance with 6 min walking test (6MWT), freezing of gait with Freezing of Gait Questionnaire (FOG_Q), walking velocity with GAITRite and QL with PD Questionnaire (PDQ39). Two reviewers independently extracted methodological quality and studies data. Results are presented as weighted mean differences. RESULTS: Five RCTs were included, totalling 159 patients. Dance promoted significant improvements on UPDRSIII, and a decrease in TUG time when compared to other types of exercise. In comparison to the absence of intervention, dance practice also showed significant improvements in motor scores. CONCLUSION: Dance can improve motor parameters of the disease and patients' functional mobility.
Timeframe: up to August 2017	
Total # studies included: 5	
Other details (e.g. definitions used, exclusions etc) RCTs that compared an intervention group undergoing any type of dance for at least 3 weeks of practice, with Parkinson's disease patients at any stage of the disease, of both sexes and at any age, which analyzed functional and biomechanical parameters of the gait and/or quality of life of the participants were included	
Outcomes addressed: Functional and biomechanical parameters of the gait Quality of life	

<table>
<tr><td colspan="2">PFn 4. SYSTEMATIC REVIEW
Citation: H. H. N. Kalyani; K. Sullivan; G. Moyle; S. Brauer; E. R. Jeffrey; L. Roeder; S. Berndt; G. Kerr. Effects of Dance on Gait, Cognition, and Dual-Tasking in Parkinson's Disease: A Systematic Review and Meta-Analysis. Journal of Parkinson's Disease 2019.</td></tr>
<tr><td>Purpose: to 1) appraise the literature evaluating dance as an intervention to improve gait, cognition and dual-tasking in people with Parkinson's disease; and 2) identify strengths and limitations of this evidence through a formal risk of bias analysis, in order to inform future researchers and practitioners.</td><td rowspan="5">Abstract:
Dance-based interventions have been proposed for the management of Parkinson's disease (PD) symptoms. This review critically appraises and synthesises the research on the effects of dance interventions on gait, cognition and dual-tasking in PD, through a meta-analysis of peer-reviewed literature from seven databases. Eligible studies included people with PD, used a parallel-group or cohort design with a dance-based intervention, reported outcome measures of gait, cognition or dual-tasking, and were published in English up until September 2017. Of the initial 1079 articles, 677 articles were reviewed for eligibility, and 25 articles were retained. Only 12 articles had sufficient common assessment items for meta-analysis. Two independent reviewers extracted the data and assessed the risk of bias of each study using the Cochrane risk-of-bias tool. Based on pre-post change scores, gait speed, Timed Up and Go (TUG) test performance, freezing of gait questionnaire, and six-minute walk test times significantly improved after a dance intervention compared to controls. Global cognition assessed with Montreal Cognitive Assessment, and cognitive dual-tasking measured using dual-task TUG, also exhibited greater improvement in dance groups. There was limited evidence to determine the most effective intensity, frequency, duration of dance interventions or the most beneficial music. Findings must be interpreted cautiously because of the lack of randomised control trials, and the moderate to high risk of bias of studies. However, the results of papers with level-I and level-II.1 evidence suggest that dance may have the potential to ameliorate PD symptoms, particularly gait, global cognition and cognitive dual-tasking.</td></tr>
<tr><td>Timeframe: up to 28th September 2017</td></tr>
<tr><td>Total # studies included: 12</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Inclusion criteria: 1) study participants had PD (any stage of the disease, any age, and gender); 2) at least one study group underwent a type of dance intervention lasting for at least two weeks (changed from 3 weeks in PROSPERO registration to 2 weeks which allowed inclusion of two more studies); 3) the study reported on at least one outcome measure for gait or cognition or dual-tasking; 4) randomised and quasi-randomised (studies where participants were not strictly randomised to intervention arms) controlled trials and observational studies (case-control, cohort and crossover studies). Only fully peer-reviewed articles with full text available in English were included without a date limitation.</td></tr>
<tr><td>Outcomes addressed:
Gait
Cognition
Dual-tasking</td></tr>
</table>

<table>
<tr><td colspan="2">PCog 1. SYSTEMATIC REVIEW
Citation: T. Stuckenschneider; C. D. Askew; A. L. Meneses; R. Baake; J. Weber; S. Schneider. The Effect of Different Exercise Modes on Domain-Specific Cognitive Function in Patients Suffering from Parkinson's Disease: A Systematic Review of Randomized Controlled Trials. Journal of Parkinson's Disease 9 (2019) 73–95.</td></tr>
<tr><td>Purpose: to compare the effects of different exercise modes on various measures of cognitive function in individuals with Parkinson's disease by systematically reviewing previous randomized controlled trials</td><td rowspan="5">Abstract:
BACKGROUND: Supervised exercise training alleviates motor symptoms in people with Parkinson's disease (PD). However, the efficacy of exercise to improve nonmotor symptoms such as cognitive function is less well known. OBJECTIVE: To systematically review evidence on the efficacy of different exercise modes (coordination exercise, resistance exercise, aerobic exercise) on domain-specific cognitive function in patients with PD. METHODS: Parallel-group randomized controlled trials published before March 2018 were included. Primary outcome measures included global cognitive function and its subdomains, and the Unified Parkinson's Disease Rating Scale was included as a secondary outcome. Methodological quality was assessed using the Physiotherapy Evidence Database scale. RESULTS: The literature search yielded 2,000 articles, of which 11 met inclusion criteria. 508 patients (mean age 68+/-4 years) were included with a disease severity from 1 to 4 on the Hoehn & Yahr stage scale. Overall study quality was modest (mean 6+/-2, range 3-8/10). In 5 trials a significant between-group effect size (ES) was identified for tests of specific cognitive domains, including a positive effect of aerobic exercise on memory (ES = 2.42) and executive function (ES = 1.54), and of combined resistance and coordination exercise on global cognitive function (ES = 1.54). Two trials found a significant ES for coordination exercise (ES = 0.84-1.88), which led to improved executive function compared with that of non-exercising control subjects. CONCLUSION: All modes of exercise are associated with improved cognitive function in individuals with PD. Aerobic exercise tended to best improve memory; however, a clear effect of exercise mode was not identified.</td></tr>
<tr><td>Timeframe: not specified</td></tr>
<tr><td>Total # studies included: 11</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Only randomized controlled trials were included. Study populations consisted of individuals with idiopathic PD without any restriction placed on the stage of the disease or its severity. Trials targeting secondary or acquired PD were excluded. Exercise programs lasting at least 4 weeks with at least one supervised exercise session per week were considered eligible. Exercise interventions included aerobic training, resistance training, coordination training or a combination of any of these exercise modes. Studies that evaluated the combination of an exercise intervention with other treatments (e.g., drug therapy, education programs) were excluded.</td></tr>
<tr><td>Outcomes addressed:
Cognitive function</td></tr>
</table>

<table>
<tr><td colspan="2">PCog 2. SYSTEMATIC REVIEW
Citation: H. H. N. Kalyani; K. Sullivan; G. Moyle; S. Brauer; E. R. Jeffrey; L. Roeder; S. Berndt; G. Kerr. Effects of Dance on Gait, Cognition, and Dual-Tasking in Parkinson's Disease: A Systematic Review and Meta-Analysis. Journal of Parkinson’s Disease 2019.</td></tr>
<tr><td>Purpose: to 1) appraise the literature evaluating dance as an intervention to improve gait, cognition and dual-tasking in people with Parkinson’s disease; and 2) identify strengths and limitations of this evidence through a formal risk of bias analysis, in order to inform future researchers and practitioners.</td><td rowspan="5">Abstract:
Dance-based interventions have been proposed for the management of Parkinson's disease (PD) symptoms. This review critically appraises and synthesises the research on the effects of dance interventions on gait, cognition and dual-tasking in PD, through a meta-analysis of peer-reviewed literature from seven databases. Eligible studies included people with PD, used a parallel-group or cohort design with a dance-based intervention, reported outcome measures of gait, cognition or dual-tasking, and were published in English up until September 2017. Of the initial 1079 articles, 677 articles were reviewed for eligibility, and 25 articles were retained. Only 12 articles had sufficient common assessment items for meta-analysis. Two independent reviewers extracted the data and assessed the risk of bias of each study using the Cochrane risk-of-bias tool. Based on pre-post change scores, gait speed, Timed Up and Go (TUG) test performance, freezing of gait questionnaire, and six-minute walk test times significantly improved after a dance intervention compared to controls. Global cognition assessed with Montreal Cognitive Assessment, and cognitive dual-tasking measured using dual-task TUG, also exhibited greater improvement in dance groups. There was limited evidence to determine the most effective intensity, frequency, duration of dance interventions or the most beneficial music. Findings must be interpreted cautiously because of the lack of randomised control trials, and the moderate to high risk of bias of studies. However, the results of papers with level-I and level-II.1 evidence suggest that dance may have the potential to ameliorate PD symptoms, particularly gait, global cognition and cognitive dual-tasking.</td></tr>
<tr><td>Timeframe: up to 28th September 2017</td></tr>
<tr><td>Total # studies included: 12</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Inclusion criteria: 1) study participants had PD (any stage of the disease, any age, and gender); 2) at least one study group underwent a type of dance intervention lasting for at least two weeks (changed from 3 weeks in PROSPERO registration to 2 weeks which allowed inclusion of two more studies); 3) the study reported on at least one outcome measure for gait or cognition or dual-tasking; 4) randomised and quasi-randomised (studies where participants were not strictly randomised to intervention arms) controlled trials and observational studies (case-control, cohort and crossover studies). Only fully peer-reviewed articles with full text available in English were included without a date limitation.</td></tr>
<tr><td>Outcomes addressed:
Gait
Cognition
Dual-tasking</td></tr>
</table>

SFn 1 META-ANALYSIS **Citation:** A. C. Bonini-Rocha; A. L. S. de Andrade; A. M. Moraes; L. B. Gomide Matheus; L. R. Diniz; W. R. Martins. (2018) Effectiveness of Circuit-Based Exercises on Gait Speed, Balance, and Functional Mobility in People Affected by Stroke: A Meta-Analysis	
Purpose: To examine the effectiveness of circuit-based exercise in the treatment of people affected by stroke.	**Abstract:** BACKGROUND: Several interventions have been proposed to rehabilitate patients with neurologic dysfunctions due to stroke. However, the effectiveness of circuit-based exercises according to its actual definition, ie, an overall program to improve strength, stamina, balance or functioning, was not provided. OBJECTIVE: To examine the effectiveness of circuit-based exercise in the treatment of people affected by stroke. METHODS: A search through PubMed, Embase, Cochrane Library, and Physiotherapy Evidence Database databases was performed to identify controlled clinical trials without language or date restriction. The overall mean difference with 95% confidence interval was calculated for all outcomes. Two independent reviewers assessed the risk of bias. RESULTS: Eleven studies met the inclusion criteria, and 8 presented suitable data to perform a meta-analysis. Quantitative analysis showed that circuit-based exercise was more effective than conventional intervention on gait speed (mean difference of 0.11 m/s) and circuit-based exercise was not significantly more effective than conventional intervention on balance and functional mobility. CONCLUSION: Our results demonstrated that circuit-based exercise presents better effects on gait when compared with conventional intervention and that its effects on balance and functional mobility were not better than conventional interventions. LEVEL OF EVIDENCE: I.
Timeframe: November 2016 - March 2017	
Total # studies included: 11	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Gait speed, balance, functional mobility	

SFn 2 META-ANALYSIS **Citation:** P. Boyne; J. Welge; B. Kissela; K. Dunning. (2017) Factors Influencing the Efficacy of Aerobic Exercise for Improving Fitness and Walking Capacity After Stroke: A Meta-Analysis With Meta-Regression	
Purpose: To assess the influence of dosing parameters and patient characteristics on the efficacy of aerobic exercise (AEX) poststroke **Timeframe:** No publication date restrictions were imposed **Total # studies included:** 20 **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** VO2peak from graded exercise testing Comfortable or fastest walking speed over a short distance (eg, 10-m walk test) Timed walking distance test (eg, 6-min walk test)	**Abstract:** OBJECTIVE: To assess the influence of dosing parameters and patient characteristics on the efficacy of aerobic exercise (AEX) poststroke. DATA SOURCES: A systematic review was conducted using PubMed, MEDLINE, Cumulative Index of Nursing and Allied Health Literature, Physiotherapy Evidence Database, and Academic Search Complete. STUDY SELECTION: Studies were selected that compared an AEX group with a nonaerobic control group among ambulatory persons with stroke. DATA EXTRACTION: Extracted outcome data included peak oxygen consumption (V o2peak) during exercise testing, walking speed, and walking endurance (6-min walk test). Independent variables of interest were AEX mode (seated or walking), AEX intensity (moderate or vigorous), AEX volume (total hours), stroke chronicity, and baseline outcome scores. DATA SYNTHESIS: Significant between-study heterogeneity was confirmed for all outcomes. Pooled AEX effect size estimates (AEX group change minus control group change) from random effects models were V o2peak, 2.2mLkg(-1)min(-1) (95% confidence interval [CI], 1.3-3.1mLkg(-1)min(-1)); walking speed, .06m/s (95% CI, .01-.11m/s); and 6-minute walk test distance, 29m (95% CI, 15-42m). In meta-regression, larger V o2peak effect sizes were significantly associated with higher AEX intensity and higher baseline V o2peak. Larger effect sizes for walking speed and the 6-minute walk test were significantly associated with a walking AEX mode. In contrast, seated AEX did not have a significant effect on walking outcomes. CONCLUSIONS: AEX significantly improves aerobic capacity poststroke, but may need to be task specific to affect walking speed and endurance. Higher AEX intensity is associated with better outcomes. Future randomized studies are needed to confirm these results.

SFn 3 META-ANALYSIS **Citation:** L. Cugusi; A. Manca; T. J. Yeo; P. P. Bassareo; G. Mercuro; J. C. Kaski (2017) Nordic walking for individuals with cardiovascular disease: A systematic review and meta-analysis of randomized controlled trials	
Purpose: to appraise research evidence on the effects of Nordic walking for individuals with cardiovascular disease **Timeframe:** from inception to November 2016 **Total # studies included:** 15 IN TOTAL, ONLY 2 WITH STROKE **Other details (e.g. definitions used, exclusions etc)** **Outcomes addressed:** functional mobility	**Abstract:** Background Exercise is the cornerstone of rehabilitation programmes for individuals with cardiovascular disease (IwCVD). Although conventional cardiovascular rehabilitation (CCVR) programmes have significant advantages, non-conventional activities such as Nordic walking (NW) may offer additional health benefits. Our aim was to appraise research evidence on the effects of Nordic walking for individuals with cardiovascular disease. Design Systematic review and meta-analysis. Methods A literature search of clinical databases (PubMed, MEDLINE, Scopus, Web of Science, Cochrane) was conducted to identify any randomized controlled trials, including: (i) individuals with cardiovascular disease, (ii) analyses of the main outcomes arising from Nordic walking (NW) programmes. Data from the common outcomes were extracted and pooled in the meta-analysis. Standardized mean differences (SMDs) were calculated and pooled by random effects models. Results Fifteen randomized controlled trials were included and eight trials entered this meta-analysis. Studies focused on coronary artery disease, peripheral arterial disease, heart failure and stroke. In coronary artery disease, significant differences between NW+CCVR and CCVR were found in exercise capacity (SMD: 0.49; $p = 0.03$) and dynamic balance (SMD: 0.55; $p = 0.01$) favouring NW+CCVR. In peripheral artery disease, larger changes in exercise duration (SMD: 0.93; $p < 0.0001$) and oxygen uptake (SMD: 0.64; $p = 0.002$) were observed following NW compared with controls. In heart failure, no significant differences were found between NW and CCVR or usual care for peak VO2 and functional mobility. In post-stroke survivors, functional mobility was significantly higher following treadmill programmes with poles rather than without (SMD: 0.80; $p = 0.03$). Conclusions These data portray NW as a feasible and promising activity for individuals with cardiovascular disease. Further studies are necessary to verify whether NW may be incorporated within CCVR for individuals with cardiovascular disease.

<table>
<tr><td colspan="2">SFn 4 META-ANALYSIS
Citation: L. Ge; Q. X. Zheng; Y. T. Liao; J. Y. Tan; Q. L. Xie; M. Rask (2017) Effects of traditional Chinese exercises on the rehabilitation of limb function among stroke patients: A systematic review and meta-analysis</td></tr>
<tr><td>Purpose: To determine the rehabilitative effects of traditional Chinese exercises on limb function among patients with stroke</td><td rowspan="5">Abstract:
OBJECTIVE: To systematically review literature about the rehabilitative effects of traditional Chinese exercises (TCEs) on limb function among patients with stroke. METHODS: Systematic review and meta-analysis of randomized controlled trials (RCTs). Twelve electronic databases were searched from their inceptions to February 2017, including PudMed, The Cochrane Library, Web of Science, EMBase, Science Direct, PsycINFO, Cumulative Index to Nursing and Allied Health Literature, Allied and Complementary Medicine, Chinese Scientific Journal Database, China National Knowledge Infrastructure, Chinese Biomedical Literature Database and WanFang Data. RCTs were located to examine the rehabilitative effects of TCEs on limb function among stroke patients. Two authors independently screened the literature, extracted data and assessed the risk bias of the included studies. Methodological quality evaluation and meta-analysis of included studies was performed by using Cochrane Collaboration's tool (RevMan 5.3). RESULTS: A total of 31 RCTs with 2349 participants were included. Results of meta-analysis showed that TCEs produced positive effects on limb motor function (random effects model, standardized mean difference [SMD] = 1.21, 95% confidence interval [CI] = 0.66 to 1.77, P < 0.01), balance function (Berg balance scale: (random effects model, SMD = 2.07, 95%CI = 1.52 to 2.62, P < 0.01), timed-up-and-go test: (fixed effects model, mean difference [MD] = -1.77, 95%CI = -2.87 to -0.67, P < 0.01)) activities of daily living (ADL) ability {Barthel Index scale: (random effects model, MD = 15.60, 95%CI = 7.57 to 23.63, P < 0.01), Modified Barthel Index scale: (random effects model, MD = 12.30, 95%CI = 7.48 to 17.12, P < 0.01), and neurological impairment (fixed effects model, MD = -2.57, 95%CI = -3.14 to -2.00, P < 0.01). After subgroup analysis and sensitivity analysis, the positive effects did not be affected by different types of TCEs and different lengths of intervention time. However, TCEs were no benefit to physical function on Short Physical Performance Battery and 2-min Step Test among stroke patients. CONCLUSION: Current evidence showed that TCEs produced positive effects on limb motor function, balance function, ADL ability and neurological impairment among stroke patients. More large-scale, high-quality, multiple center RCTs are required to further verify above conclusions in the future.</td></tr>
<tr><td>Timeframe:
Inception – Feb 2017</td></tr>
<tr><td>Total # studies included: 31</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Limb motor function
Balance</td></tr>
</table>

<table>
<tr><td colspan="2">SFn 5 SYSTEMATIC REVIEW
Citation: G. Hendrey; A. E. Holland; B. F. Mentiplay; R. A. Clark; G. Williams (2018) Do Trials of Resistance Training to Improve Mobility After Stroke Adhere to the American College of Sports Medicine Guidelines? A Systematic Review</td></tr>
<tr><td>Purpose: To determine whether adherence to the American College of Sports Medicine (ACSM) guidelines on resistance training is associated with better mobility outcomes after stroke</td><td rowspan="5">Abstract:
OBJECTIVE: To determine whether resistance training to improve mobility outcomes after stroke adheres to the American College of Sports Medicine (ACSM) guidelines, and whether adherence was associated with better outcomes. DATA SOURCES: Online databases searched from 1975 to October 30, 2016. STUDY SELECTION: Randomized controlled trials examining the effectiveness of lower limb strength training on mobility outcomes in adult participants with stroke. DATA EXTRACTION: Two independent reviewers completed data extraction. Quality of trials was determined using the Cochrane Risk of Bias Tool. Trials were scored based on their protocol's adherence to 8 ACSM recommendations. To determine if a relation existed between total adherence score and effect size, Spearman rho was calculated, and between individual recommendations and effect size, Mann-Whitney U or Kruskal-Wallis tests were used. DATA SYNTHESIS: Thirty-nine trials met the inclusion criteria, and 34 were scored on their adherence to the guidelines. Adherence was high for frequency of training (100% of studies), but few trials adhered to the guidelines for intensity (32%), specificity (24%), and training pattern (3%). Based on the small number of studies that could be included in pooled analysis (n=12), there was no relation between overall adherence and effect size (Spearman rho=-.39, P=.21). CONCLUSIONS: Adherence to the ACSM guidelines for resistance training after stroke varied widely. Future trials should ensure strength training protocols adhere more closely to the guidelines, to ensure their effectiveness in stroke can be accurately determined.</td></tr>
<tr><td>Timeframe: trials published
after 1975 – 30 October 2016</td></tr>
<tr><td>Total # studies included:</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: walking outcome (e.g., gait velocity, 6-minute walk test, or timed up and go test)</td></tr>
</table>

SFn 6 SYSTEMATIC REVIEW	
Citation: D. Ilunga Tshiswaka; C. Bennett; C. Franklin (2018) Effects of walking trainings on walking function among stroke survivors: a systematic review	
Purpose: to assess the impact of walking training on enhancing walking for stroke survivors	**Abstract:** Physical function is often compromised as a result of stroke event. Although interventions propose different strategies that seek to improve stroke survivors' physical function, a need remains to evaluate walking training studies aimed at improving such physical function. The aim of this review was to assess the available literature that highlights the impact of walking training on enhancing walking for stroke survivors. We performed a systematic literature review of online databases - Google Scholar, PubMed, CINHAL, Cochrane Library, Scopus, and EBSCO - with the following inclusion criteria: manuscript published from 2005 to 2016, written in English, with treatment and control groups, for walking training studies aimed at improving physical function among stroke survivors. Findings indicated that walking speed, walking distance, and gait speed were the most used outcome variables for measuring improved physical function among stroke survivors. Importantly, proposed interventions involved either overground or treadmill walking trainings, if not both. Preserved locomotor improvements were not noted in all interventions at follow-up. Some interventions that used walking treadmill training augmented by auditory stimulations reported significant improvements in physical function compared with over ground walking training augmented by auditory stimulations. The imperative to improve physical function among stroke survivors with physical impairment is paramount, as it allows survivors to be socially, emotionally, and physically more independent. In general, we note an insufficiency of research on the interaction between physical function and socialization among stroke survivors.
Timeframe: from 2005 to 2016	
Total # studies included: 29	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Walking function	

<table>
<tr><td colspan="2">SFn 7 META-ANALYSIS
Citation: G. Y. Li; W. Wang; G. L. Liu; Y. Zhang (2018) Effects of Tai Chi on balance and gait in stroke survivors: A systematic meta-analysis of randomized controlled trials</td></tr>
<tr><td>Purpose: To investigate the effects of tai chi on balance and gait in stroke survivors</td><td rowspan="5">Abstract:
OBJECTIVE: To investigate the effects of tai chi on balance and gait in stroke survivors. METHODS: A systematic meta-analysis of randomized controlled trials on the effects of tai chi on balance and gait in stroke survivors. RESULTS: Five randomized controlled trials, with a total of 346 patients, were included in the meta-analysis. All of these studies had a high bias based on the Cochrane Collaboration recommendation, and a relatively small sample size. In the pooled analysis, the tai chi group exhibited a significantly better gait ability than the control group, as evaluated with the Timed Up and Go (TUG) test and Short Physical Performance Battery (SPPB) (-0.26 [-0.50 to -0.03], p = 0.027; I2=0%, p = 0.682), but no significant difference in dynamic standing balance scores was found between tai chi and control groups (0.154 [-0.269 to 0.578], p = 0.475; I2=26.6%, p = 0.256). CONCLUSION: Tai chi may be beneficial for stroke survivors with respect to gait ability in the short term, but further large, long-term randomized controlled trials with standard evaluation indicators are needed to confirm this conclusion.</td></tr>
<tr><td>Timeframe: No limitation on publication year</td></tr>
<tr><td>Total # studies included: 5</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc.)</td></tr>
<tr><td>Outcomes addressed:
Balance
Gait</td></tr>
</table>

<table>
<tr><td colspan="2">SFn 8 SYSTEMATIC REVIEW
Citation: S. Miranda; A. Marques (2018) Pilates in noncommunicable diseases: A systematic review of its effects</td></tr>
<tr><td>Purpose: To investigate the effects of Pilates in the four major groups of NCD</td><td rowspan="5">Abstract:
OBJECTIVES: Chronic cardiovascular diseases, cancer, chronic respiratory diseases and diabetes are the four major groups of non-communicable diseases (NCDs) and the main cause of mortality worldwide. Pilates has been described as an effective intervention to promote healthy behaviours and physical activity in people with chronic diseases. However, the evidence of its effects in NCDs have not been systematized. We investigated the effects of Pilates in the four major groups of NCDs. DESIGN: A systematic review was performed. Searches were conducted on Cochrane Library, EBSCO, PubMed, Science Direct, Scopus and Web of Science databases. Studies were rated with the quality assessment tool for quantitative studies. As a meta-analysis was not possible to conduct, a best-evidence synthesis was used. RESULTS: Twelve studies, mostly of moderate quality, were included with 491 participants (78.6% females; age range 13-70 years old) with breast cancer (n=3), diabetes (n=3), chronic stroke (2 years post stroke) (n=2), chronic obstructive pulmonary disease (n=1), cystic fibrosis (n=1), heart failure (n=1) and arterial hypertension (n=1). The best-evidence synthesis revealed strong evidence for improving exercise tolerance; moderate evidence for improving symptoms, muscle strength and health-related quality of life and limited or conflicting evidence on vital signs, metabolic parameters, body composition, respiratory function, functional status, balance, flexibility and social support. CONCLUSIONS: Pilates should be considered for patients with NCDs, as it improves exercise tolerance. Future studies with robust methodologies are still needed to clarify its effectiveness on outcomes with moderate, limited or conflicting evidence and to establish the most suitable intervention protocol.</td></tr>
<tr><td>Timeframe:
Variable start dates up to 2017</td></tr>
<tr><td>Total # studies included: 12 IN TOTAL, ONLY 2 IN STROKE</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc.)</td></tr>
<tr><td>Outcomes addressed:
Functional status
Peak VO2 consumption</td></tr>
</table>

<table>
<tr><td colspan="2">SFn 9 SYSTEMATIC REVIEW
Citation: K. K. Patterson; J. S. Wong; E. C. Prout; D. Brooks (2018) Dance for the rehabilitation of balance and gait in adults with neurological conditions other than Parkinson's disease: A systematic review</td></tr>
<tr><td>Purpose: To examine the effect of dance interventions on balance, gait and functional mobility outcomes in adults with neurological conditions other than Parkinson's disease</td><td rowspan="5">Abstract:
Purpose: To conduct a systematic review that examined the effect of dance interventions on balance, gait and functional mobility outcomes in adults with neurological conditions other than Parkinson's disease. Methods: A systematic search of relevant databases was conducted. Data extraction and methodological appraisal were performed by two independent authors. Results: Nine studies were included (4 pre-post studies with no control group, 3 case reports, and 2 controlled studies) and results of the methodological quality assessment ranged from poor to good. Study groups included stroke, multiple sclerosis, spinal cord injury, and Huntington's disease. Dance interventions varied in frequency, type and duration, and only 1 study reported intensity. Study dropout rates ranged from 20-44%, and 88-100% of dance classes were attended. Only 3 studies mentioned adverse events, of which there were none. A summary of results revealed significant changes in spatiotemporal gait parameters, Berg Balance Scale scores, Timed Up and Go test and six-minute walk test that were similar to or greater than those previously reported in a review of dance for individuals with Parkinson's disease. Conclusions: There is emerging evidence to support the use of dance as a feasible intervention for adults with neurological conditions. Further investigation of the effects of dance with randomized controlled trials using larger sample sizes and better reporting of the intervention, participant tolerance, and adverse events is warranted.</td></tr>
<tr><td>Timeframe: 1946 - 21 December 2016</td></tr>
<tr><td>Total # studies included: 9 IN TOTAL, 3 WITH STROKE</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Balance
Gait
Functional mobility</td></tr>
</table>

<table>
<tr><td colspan="2">SFn 10 META-ANALYSIS
Citation: D. Pogrebnoy; A. Dennett (2019) Exercise programs delivered according to guidelines improve mobility in people with stroke: A Systematic Review and meta-analysis</td></tr>
<tr><td>Purpose: To determine if prescribing a combined aerobic and resistance training exercise program in accordance with American Stroke Association physical activity guidelines improves mobility and physical activity levels of people after stroke.</td><td rowspan="5">Abstract:
OBJECTIVE: To determine if prescribing a combined aerobic and resistance training exercise program in accordance with American Stroke Association physical activity guidelines improves mobility and physical activity levels of people after stroke. DATA SOURCES: Online database search from earliest available date to August 27, 2018. STUDY SELECTION: Randomized controlled trials evaluating the effectiveness of exercise programs prescribed in accordance with guidelines for improving mobility and physical activity levels in adults with sub-acute or chronic stroke. DATA EXTRACTION: Two independent reviewers completed data extraction. Risk of bias was assessed using the Physiotherapy Evidence Database Scale and overall quality of evidence was assessed using the Grades of Research, Assessment, Development and Evaluation approach. DATA SYNTHESIS: Data was pulled from a total of 499 participants for meta-analysis. There was high-level evidence that exercise programs adhering to guidelines improve habitual walking speed (Mean Difference 0.07m/s, 95% CI - 0.01 to 0.16) and walking endurance (Mean Difference 39.2 meters, 95% CI 17.2 to 61.2). A sensitivity analysis demonstrated high level evidence of improvements in walking endurance (Mean Difference 51.1 meters, 95% CI 19.96 to 82.24) and moderate-level evidence of improvements on the timed up and go test (Standardized Mean Difference 0.57, 95% CI 0.16 to 0.99). No differences were detected for other mobility outcome measures or physical activity levels. Adherence was high and few adverse events were reported. CONCLUSION: A combined exercise program comprising aerobic and resistance training that adheres to the American Stroke Association guidelines, is safe, and should be prescribed in addition to usual care to improve mobility. Further research is needed to understand the relationship between exercise programs and behaviour change requirements to improve long term physical activity levels.</td></tr>
<tr><td>Timeframe: Online database search from earliest available date to 27 August 2018.</td></tr>
<tr><td>Total # studies included: 10 Papers from 8 trials</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed: Function e.g. sit to stand, walking speed Physical activity</td></tr>
</table>

<table>
<tr><td colspan="2">SFn 11 SYSTEMATIC REVIEW
Citation: J. Schroder; T. van Criekinge; E. Embrechts; X. Celis; J. Van Schuppen; S. Truijen; W. Saeys (2019) Combining the benefits of tele-rehabilitation and virtual reality-based balance training: a systematic review on feasibility and effectiveness</td></tr>
<tr><td>Purpose: To investigate whether it is feasible to combine virtual reality (VR) which allows exercising in game-like environments with tele-rehabilitation in a community-dwelling stroke population.</td><td rowspan="5">Abstract:
PURPOSE: A motivational surrounding is desirable in stroke rehabilitation considering the need to train repetitively to improve balance, even after discharge from rehabilitation facilities. This review aims to investigate whether it is feasible to combine virtual reality (VR) which allows exercising in game-like environments with tele-rehabilitation in a community-dwelling stroke population. METHODS: Literature searches were conducted in five databases, for example, PubMed and the Cochrane Library. Randomized controlled trial (RCT) and non-RCT investigating feasibility and effectiveness of VR-based tele-rehabilitation were included. Based on the risk of bias and study design, methodological quality is ranked according to the GRADE guidelines. RESULTS: Seven studies (n = 120) were included, of which four are RCTs. Evidence regarding therapy adherence and perceived enjoyment of VR, as well as a cost-benefit of tele-rehabilitation emphasizes feasibility. Equal effects are reported comparing this approach to a therapist-supervised intervention in the clinical setting on balance and functional mobility. CONCLUSIONS: Tele-rehabilitation could be a promising tool to overcome burdens that restrict accessibility to rehabilitation in the future. VR can increase motivation allowing longer and more training sessions in community-dwelling stroke survivors. Therefore, combining the benefits of both approaches seems convenient. Although evidence is still sparse, functional improvements seem to be equal compared to a similar intervention with therapist-supervision in the clinic, suggesting that for cost-efficient rehabilitation parts of therapy can be transferred to the homes. Implications for rehabilitation The use of tele-rehabilitation could be a promising tool to overcome burdens that restrict the access of stroke survivors to long-term rehabilitative care. VR-based interventions are game-like and therefore seem to provide a motivational environment which allows longer exercise sessions and greater adherence to therapy.</td></tr>
<tr><td>Timeframe: up to 04/01/2018</td></tr>
<tr><td>Total # studies included: 7</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Balance
Functional mobility</td></tr>
</table>

SFn 12 SYSTEMATIC REVIEW **Citation:** J. Wiener; A. McIntyre; S. Janssen; J. T. Chow; C. Batey; R. Teasell (2019) Effectiveness of High-Intensity Interval Training for Fitness and Mobility Post Stroke: A Systematic Review	
Purpose: To evaluate the evidence on the effectiveness of high-intensity interval training (HIIT) in improving fitness and mobility post stroke.	**Abstract:** OBJECTIVE: To evaluate the evidence on the effectiveness of high-intensity interval training (HIIT) in improving fitness and mobility post stroke. TYPE: Systematic review. LITERATURE SURVEY: Medline, Embase, CINAHL, PsycINFO, and Scopus were searched for articles published in English up to January 2018. METHODOLOGY: Studies were included if the sample was adult human participants with stroke, the sample size was >/=3, and participants received >1 session of HIIT. Study and participant characteristics, treatment protocols, and results were extracted. SYNTHESIS: Six studies with a total of 140 participants met inclusion criteria: three randomized controlled trials and three pre-post studies. HIIT protocols ranged 20 to 30 minutes per session, 2 to 5 times per week, and 2 to 8 weeks in total. HIIT was delivered on a treadmill in five studies and a stationary bicycle in one study. Regarding fitness measures, HIIT produced significant improvements in peak oxygen consumption compared to baseline, but the effect was not significant compared to moderate intensity continuous exercise (MICE). Regarding mobility measures, HIIT produced significant improvements on the 10-Meter Walk Test (10MWT), 6-Minute Walk Test (6MWT), Berg Balance Scale (BBS), Functional Ambulation Categories (FAC), Timed Up and Go Test, and Rivermead Motor Assessment compared to baseline. The effect of HIIT was significant compared to MICE on the 10MWT and FAC but not on the 6MWT or BBS. CONCLUSIONS: There is preliminary evidence that HIIT may be an effective rehabilitation intervention for improving some aspects of cardiorespiratory fitness and mobility post stroke. LEVEL OF EVIDENCE: I.
Timeframe: up to January 2018.	
Total # studies included: 6	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Fitness Mobility	

SFn 13 META-ANALYSIS **Citation:** S. Wu; J. Chen; S. Wang; M. Jiang; X. Wang; Y. Wen (2018) Effect of Tai Chi Exercise on Balance Function of Stroke Patients: A Meta-Analysis	
Purpose: To evaluate the effect of Tai Chi exercise on balance function in stroke patients	**Abstract:** BACKGROUND Tai Chi is an ancient form of physical activity that has been shown to improve cardiovascular function, but to date there had been no comprehensive systematic review on the effect of Tai Chi exercise on balance function of patients with stroke. This study evaluated the effect of Tai Chi exercise on balance function in stroke patients. MATERIAL AND METHODS PubMed, Cochrane library, and China National Knowledge Information databases and the Wan Fang medical network were searched to collect the articles. The random-effects model was used to assess the effect of Tai Chi exercise on balance function of stroke patients. RESULTS Six studies were chosen to perform the meta-analysis according to the inclusion and exclusion criteria. There were significant improvements of balance on Berg Balance Scale score (MD=4.823, 95% CI: 2.138-7.508), the standing balance with fall rates (RR=0.300, 95%CI: 0.120-0.770), functional reach test and dynamic gait index in Tai Chi intervention group compared to the control intervention group. However, the short physical performance battery for balance (SPBB) showed Tai Chi did not significantly improve the ability of balance for stroke patients (MD=0.293, 95%CI: -0.099~0.685). CONCLUSIONS Tai Chi exercise might have a significant impact in improving balance efficiency by increasing BBS score and reducing fall rate.
Timeframe: up to May 2017	
Total # studies included: 6	
Other details (e.g. definitions used, exclusions etc)	
Outcomes addressed: Balance	

<table>
<tr><td colspan="2">SFn 14 META-ANALYSIS
Citation: L. Zou; J. E. Sasaki; N. Zeng; C. Wang; L. Sun (2018) A Systematic Review With Meta-Analysis of Mindful Exercises on Rehabilitative Outcomes Among Poststroke Patients</td></tr>
<tr><td>Purpose: To critically evaluate the rehabilitative effects of mindful exercises for poststroke patients.</td><td rowspan="5">Abstract:
OBJECTIVE: To critically evaluate the rehabilitative effects of mindful exercises for poststroke patients. DATA SOURCES: Six databases (PubMed, Physiotherapy Evidence Database, Cochrane Library, Web of Science, Wanfang, Chinese National Knowledge Infrastructure) and reference lists of relevant articles were searched. STUDY SELECTION: Randomized controlled trials on the effects of mindful exercises on rehabilitative outcomes such as sensorimotor function, gait speed, leg strength, aerobic endurance, cognitive function, and overall motor function. DATA EXTRACTION: Two investigators independently screened eligible studies according to the eligible criteria, extracted data, and assessed risk of bias. DATA SYNTHESIS: A total of 20 studies that satisfied the eligibility criteria were finally included. The sum scores of 5-9 points in the adapted Physiotherapy Evidence Database scale indicates low-to-medium risk of bias. The study results of meta-analysis indicate that mindful exercise intervention was significantly associated with improved sensorimotor function on both lower limb (standardized mean difference=0.79; 95% confidence interval, 0.43-1.15; P<.001; I(2)=62.67%) and upper limb (standardized mean difference=0.7; 95% confidence interval, 0.39-1.01; P<.001; I(2)=32.36%). CONCLUSIONS: This review suggests that mindful exercises are effective in improving sensorimotor function of lower and upper limbs in poststroke patients. The effects on gait speed, leg strength, aerobic endurance, overall motor function, and other outcomes (eg, cognitive function, gait parameters) require further investigation for allowing evidence-based conclusions.</td></tr>
<tr><td>Timeframe:
publication date was not limited</td></tr>
<tr><td>Total # studies included: 20</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Sensorimotor function
Gait speed
Leg strength
Aerobic endurance
Cognitive function
Overall motor function</td></tr>
</table>

<table>
<tr><td colspan="2">SFn 15 META-ANALYSIS
Citation: L. Zou; A. Yeung; N. Zeng; C. Wang; L. Sun; G. A. Thomas; H. Wang (2018) Effects of Mind-Body Exercises for Mood and Functional Capabilities in Patients with Stroke: An Analytical Review of Randomized Controlled Trials</td></tr>
<tr><td>Purpose: to critically evaluate and statistically synthesize the existing literature regarding the effects of mind-body exercises on mood and functional capabilities in patients with stroke.</td><td rowspan="5">Abstract:
Objective: The effects of stroke are both physical and mental in nature and may have serious implications on the overall well-being of stroke survivors. This analytical review aims to critically evaluate and statistically synthesize the existing literature regarding the effects of mind-body (MB) exercises on mood and functional capabilities in patients with stroke. Methods: A structured literature review was performed in both English (PubMed, PEDro, and Cochrane Library) and Chinese (Wanfang and CNKI (Chinese National Knowledge Information Database)) databases. Sixteen randomized controlled trials were considered eligible for meta-analysis. Based on the random effects model, we used the pooled effect size to determine the magnitude of rehabilitative effect of MB exercise intervention on depression, anxiety, activities of daily living, and functional mobility among stroke survivors. The sum PEDro score ranged from five to nine points (fair-to-good methodological quality), but the absence of concealed allocation and blinded assessors were reported in most studies. Results: The aggregated results showed that MB exercise intervention is associated with significantly improved ADL (Hedges' g = 1.31, 95% CI 0.85 to 1.77, p < 0.001, I(2) = 79.82%) and mobility (Hedges' g = 0.67, 95% CI 0.25 to 1.09, p < 0.001, I(2) = 69.65%), and reduced depression (Hedges' g = -0.76, 95% CI -1.16 to -0.35, p < 0.001, I(2) = 74.84%). Conclusions: as add-on treatments, the MB exercises may potentially improve depression, activities of daily living, and mobility of these post-stroke patients. Future studies with more robust methodology will be needed to provide a more definitive conclusion.</td></tr>
<tr><td>Timeframe: no restriction on publication date</td></tr>
<tr><td>Total # studies included: 16</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)</td></tr>
<tr><td>Outcomes addressed:
Depression
Anxiety
Activities of daily living
Functional mobility</td></tr>
</table>

ADHD 1 SYSTEMATIC REVIEW OF REVIEWS **Citation:** G. Ashdown-Franks; J. Firth; R. Carney; A. F. Carvalho; M. Hallgren; A. Koyanagi; S. Rosenbaum; F. B. Schuch; L. Smith; M. Solmi; D. Vancampfort; B. Stubbs (2019) Exercise as Medicine for Mental and Substance Use Disorders: A Meta-review of the Benefits for Neuropsychiatric and Cognitive Outcomes	
Purpose: To review the evidence on the impact of exercise on neuropsychiatric and cognitive symptoms in people with mental disorders	**Abstract:** BACKGROUND: Exercise may improve neuropsychiatric and cognitive symptoms in people with mental disorders, but the totality of the evidence is unclear. We conducted a meta-review of exercise in (1) serious mental illness (schizophrenia spectrum, bipolar disorder and major depression (MDD)); (2) anxiety and stress disorders; (3) alcohol and substance use disorders; (4) eating disorders (anorexia nervosa bulimia nervosa, binge eating disorders, and (5) other mental disorders (including ADHD, pre/post-natal depression). METHODS: Systematic searches of major databases from inception until 1/10/2018 were undertaken to identify meta-analyses of randomised controlled trials (RCTs) of exercise in people with clinically diagnosed mental disorders. In the absence of available meta-analyses for a mental disorder, we identified systematic reviews of exercise interventions in people with elevated mental health symptoms that included non-RCTs. Meta-analysis quality was assessed with the AMSTAR/+. RESULTS: Overall, we identified 27 systematic reviews (including 16 meta-analyses representing 152 RCTs). Among those with MDD, we found consistent evidence (meta-analyses = 8) that exercise reduced depression in children, adults and older adults. Evidence also indicates that exercise was more effective than control conditions in reducing anxiety symptoms (meta-analyses = 3), and as an adjunctive treatment for reducing positive and negative symptoms of schizophrenia (meta-analyses = 2). Regarding neurocognitive effects, exercise improved global cognition in schizophrenia (meta-analyses = 1), children with ADHD (meta-analyses = 1), but not in MDD (meta-analyses = 1). Among those with elevated symptoms, positive mental health benefits were observed for exercise in people with pre/post-natal depression, anorexia nervosa/bulimia nervosa, binge eating disorder, post-traumatic stress disorder and alcohol use disorders/substance use disorders. Adverse events were sparsely reported. CONCLUSION: Our panoramic meta-overview suggests that exercise can be an effective adjunctive treatment for improving symptoms across a broad range of mental disorders.
Timeframe: from inception until 1/10/2018	
Total # studies included: 27 systematic reviews (including 16 meta-analyses representing 152 RCTs)	
Other details (e.g. definitions used, exclusions etc) Did not include adults Review of reviews	
Outcomes addressed: Attention Hyperactivity Impulsivity Anxiety symptoms Executive function Social disorders	

<table>
<tr><td colspan="2">ADHD 2. (SYSTEMATIC) REVIEW OF REVIEWS AND META-ANALYSES
Citation: L. Christiansen; M. M. Beck; N. Bilenberg; J. Wienecke; A. Astrup; J. Lundbye-Jensen (2019) Effects of Exercise on Cognitive Performance in Children and Adolescents with ADHD: Potential Mechanisms and Evidence-based Recommendations</td></tr>
<tr><td>Purpose: To review existing evidence that exercise affects cognitive functions in children with and without ADHD and present likely neurophysiological mechanisms of action</td><td rowspan="5">Abstract:
Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder with a complex symptomatology, and core symptoms as well as functional impairment often persist into adulthood. Recent investigations estimate the worldwide prevalence of ADHD in children and adolescents to be ~7%, which is a substantial increase compared to a decade ago. Conventional treatment most often includes pharmacotherapy with central nervous stimulants, but the number of non-responders and adverse effects call for treatment alternatives. Exercise has been suggested as a safe and low-cost adjunctive therapy for ADHD and is reported to be accompanied by positive effects on several aspects of cognitive functions in the general child population. Here we review existing evidence that exercise affects cognitive functions in children with and without ADHD and present likely neurophysiological mechanisms of action. We find well-described associations between physical activity and ADHD, as well as causal evidence in the form of small to moderate beneficial effects following acute aerobic exercise on executive functions in children with ADHD. Despite large heterogeneity, meta-analyses find small positive effects of exercise in population-based control (PBC) children, and our extracted effect sizes from long-term interventions suggest consistent positive effects in children and adolescents with ADHD. Paucity of studies probing the effect of different exercise parameters impedes finite conclusions in this regard. Large-scale clinical trials with appropriately timed exercise are needed. In summary, the existing preliminary evidence suggests that exercise can improve cognitive performance intimately linked to ADHD presentations in children with and without an ADHD diagnosis. Based on the findings from both PBC and ADHD children, we cautiously provide recommendations for parameters of exercise.</td></tr>
<tr><td>Timeframe: not specified – study is very narrative, with no methods section</td></tr>
<tr><td>Total # studies included: unclear</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Review of reviews
Unclear if it was ‘systematic’
Did not include adults</td></tr>
<tr><td>Outcomes addressed:
Cognitive function</td></tr>
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<tr><td colspan="2">ADHD 3. SYSTEMATIC REVIEW
Citation: V. Grassmann; M. V. Alves; R. F. Santos-Galduroz; J. C. Galduroz (2017) Possible Cognitive Benefits of Acute Physical Exercise in Children With ADHD</td></tr>
<tr><td>Purpose: To review the acute effects of exercise in executive function in children with ADHD</td><td rowspan="5">Abstract:
OBJECTIVE: Studies have suggested that even a single session of physical exercise enhances executive functions. ADHD is among the most common developmental disorders in childhood, but little is known about alternative treatments for this disorder. Therefore, we performed a systematic review of the literature to analyze articles that evaluated the executive functions of children with ADHD after an acute exercise session. METHOD: We reviewed articles indexed in the PubMed, American Psychiatric Association (APA) psychNET, Scopus, and Web of Knowledge databases between 1980 and 2013. RESULTS: Of 231 articles selected, only three met the inclusion criteria. CONCLUSION: Based on these 3 articles, we concluded that 30 min of physical exercise reportedly improved the executive functions of children with ADHD. Due to the small number of articles selected, further studies are needed to confirm these benefits.</td></tr>
<tr><td>Timeframe: 1980 - 2013</td></tr>
<tr><td>Total # studies included: 3</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc)
Did not include adults</td></tr>
<tr><td>Outcomes addressed:
Executive function</td></tr>
</table>

ADHD 4. SYSTEMATIC REVIEW **Citation:** S. Suarez-Manzano; A. Ruiz-Ariza; M. De La Torre-Cruz; E. J. Martinez-Lopez (2018) Acute and chronic effect of physical activity on cognition and behaviour in young people with ADHD: A systematic review of intervention studies	
Purpose: To analyse the acute and chronic effect of physical activity on the cognition and behaviour of children and adolescents with ADHD	**Abstract:** BACKGROUND: Young people with attention deficit hyperactivity disorder (ADHD) often have learning and behavioural control difficulties. AIM: The aim of this review is analyse the acute and chronic effect of physical activity (PA) on the cognition and behaviour of children and adolescents with ADHD. METHODS: Studies were identified in five databases (PubMed, SPORTDiscus, ProQuest, Web of Science, and SCOPUS), from January 2000 through to January 2017. A total of 16 interventional studies met the inclusion criteria. RESULTS/CONCLUSIONS: PA practice of 20-30min (intensity 40-75%) produces a positive acute effect on processing speed, working memory, planning and problem solving in young people with ADHD. However, these effects on behaviour are contradictory and vary depending on age. Chronic PA practice (>/=30min per day, >/=40% intensity, >/=three days per week, >/=five weeks) further improves attention, inhibition, emotional control, behaviour and motor control. The results must be treated with caution, because only 25% of the studies used confounders. IMPLICATION: More research is needed to justify the causes of these effects. It is necessary to establish programs with regard to the duration, intensity, kind of exercise, and time of PA to improve cognition and behaviour in young people with ADHD taking into account potential confounders.
Timeframe: from January 2000 through to January 2017	
Total # studies included: 16	
Other details (e.g. definitions used, exclusions etc) Did not include adults	
Outcomes addressed: Cognitive function	

Systematic Review and Meta-Analysis **Citation:** J. Firth; B. Stubbs; S. Rosenbaum; D. Vancampfort; B. Malchow; F. Schuch; R. Elliott; K. H. Nuechterlein; A. R. Yung 2017 Aerobic Exercise Improves Cognitive Functioning in People With Schizophrenia: A Systematic Review and Meta-Analysis 10.1093/schbul/sbw115	
Purpose: investigating the cognitive outcomes of exercise interventions in schizophrenia	**Abstract:** Cognitive deficits are pervasive among people with schizophrenia and treatment options are limited. There has been an increased interest in the neurocognitive benefits of exercise, but a comprehensive evaluation of studies to date is lacking. We therefore conducted a meta-analysis of all controlled trials investigating the cognitive outcomes of exercise interventions in schizophrenia. Studies were identified from a systematic search across major electronic databases from inception to April 2016. Meta-analyses were used to calculate pooled effect sizes (Hedges g) and 95% CIs. We identified 10 eligible trials with cognitive outcome data for 385 patients with schizophrenia. Exercise significantly improved global cognition ($g = 0.33$, 95% CI = 0.13–0.53, $P = .001$) with no statistical heterogeneity ($I2 = 0\%$). The effect size in the 7 studies which were randomized controlled trials was $g = 0.43$ ($P < .001$). Meta-regression analyses indicated that greater amounts of exercise are associated with larger improvements in global cognition ($\beta = .005$, $P = .065$). Interventions which were supervised by physical activity professionals were also more effective ($g = 0.47$, $P < .001$). Exercise significantly improved the cognitive domains of working memory ($g = 0.39$, $P = .024$, $N = 7$, $n = 282$), social cognition ($g = 0.71$, $P = .002$, $N = 3$, $n = 81$), and attention/vigilance ($g = 0.66$, $P = .005$, $N = 3$, $n = 104$). Effects on processing speed, verbal memory, visual memory and reasoning and problem solving were not significant. This meta-analysis provides evidence that exercise can improve cognitive functioning among people with schizophrenia, particularly from interventions using higher dosages of exercise. Given the challenges in improving cognition, and the wider health benefits of exercise, a greater focus on providing supervised exercise to people with schizophrenia is needed.
Timeframe: inception to April 2016	
Total # studies included: 10	
Other details (e.g. definitions used, exclusions etc) Exclusion: review or abstract, ineligible population, study protocol only, no neurocognitive outcomes, no exercise interventions, no control conditions. Interventions using only yoga or tai-chi were excluded as these theoretically confer benefits for cognition which are distinct from the physical activity itself.	
Outcomes addressed: Global Cognition/ Cognitive Functioning: (significant) working memory, social cognition, attention/ vigilance (Not significant) processing speed, verbal memory, visual memory and reasoning and problem solving.	

MCL 1 Systematic Review **Citation:** J. Krogh; C. Hjorthoj; H. Speyer; C. Gluud; M. Nordentoft 2017 Exercise for patients with major depression: a systematic review with meta-analysis and trial sequential analysis 10.1136/bmjopen-2016-014820	
Purpose: assess the effect of exercise in participants diagnosed with depression **Timeframe**: inception to July 2017 **Total # studies included:** 35 Other details (e.g. definitions used, exclusions etc.) **Outcomes addressed:** depression severity, lack of remission and serious adverse events (eg, suicide). Secondary outcomes QoL and adverse events such as injuries, as well as assessment of depression severity and lack of remission during follow-up after the intervention.	**Abstract: Objectives** To assess the benefits and harms of exercise in patients with depression. **Design:** Systematic review **Data sources:** Bibliographical databases were searched until 20 June 2017. **Eligibility criteria and outcomes:** Eligible trials were randomised clinical trials assessing the effect of exercise in participants diagnosed with depression. Primary outcomes were depression severity, lack of remission and serious adverse events (eg, suicide) assessed at the end of the intervention. Secondary outcomes were quality of life and adverse events such as injuries, as well as assessment of depression severity and lack of remission during follow-up after the intervention. **Results** Thirty-five trials enrolling 2498 participants were included. The effect of exercise versus control on depression severity was −0.66 standardised mean difference (SMD) (95% CI −0.86 to −0.46; p<0.001; grading of recommendations assessment, development and evaluation (GRADE): very low quality). Restricting this analysis to the four trials that seemed less affected of bias, the effect vanished into −0.11 SMD (−0.41 to 0.18; p=0.45; GRADE: low quality). Exercise decreased the relative risk of no remission to 0.78 (0.68 to 0.90; p<0.001; GRADE: very low quality). Restricting this analysis to the two trials that seemed less affected of bias, the effect vanished into 0.95 (0.74 to 1.23; p=0.78). Trial sequential analysis excluded random error when all trials were analysed, but not if focusing on trials less affected of bias. Subgroup analyses found that trial size and intervention duration were inversely associated with effect size for both depression severity and lack of remission. There was no significant effect of exercise on secondary outcomes. **Conclusions** Trials with less risk of bias suggested no antidepressant effects of exercise and there were no significant effects of exercise on quality of life, depression severity or lack of remission during follow-up. Data for serious adverse events and adverse events were scarce not allowing conclusions for these outcomes.

<table>
<tr><td colspan="2">MCD 2 Meta Review of Systematic Reviews with or without Meta-Analysis.
Citation: B. Stubbs; D. Vancampfort; M. Hallgren; J. Firth; N. Veronese; M. Solmi; S. Brand; J. Cordes; B. Malchow; M. Gerber; A. Schmitt; C. U. Correll; M. De Hert; F. Gaughran; F. Schneider; F. Kinnafick; P. Falkai; H. J. Moller; K. G. Kahl 2018 EPA guidance on physical activity as a treatment for severe mental illness: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH) 10.1016/j.eurpsy.2018.07.004</td></tr>
<tr><td>Purpose: 1. establish the benefits of physical activity / exercise across all categories of severe mental illness (SMI), 2. examine how the benefits of physical activity may differ across specific SMIs, including schizophrenia- pectrum disorders, BD and MDD. 3. Use findings to provide guidance for clinical practice, policy and future research.</td><td rowspan="5">Abstract: Physical activity (PA) may be therapeutic for people with severe mental illness (SMI) who generally have low PA and experience numerous lifestyle-related medical complications. We conducted a metareview of PA interventions and their impact on health outcomes for people with SMI, including schizophrenia-spectrum disorders, major depressive disorder (MDD) and bipolar disorder. We searched major electronic databases until January 2018 for systematic reviews with/without meta-analysis that investigated PA for any SMI. We rated the quality of studies with the AMSTAR tool, grading the quality of evidence, and identifying gaps, future research needs and clinical practice recommendations. For MDD, consistent evidence indicated that PA can improve depressive symptoms versus control conditions, with effects comparable to those of antidepressants and psychotherapy. PA can also improve cardiorespiratory fitness and quality of life in people with MDD, although the impact on physical health outcomes was limited. There were no differences in adverse events versus control conditions. For MDD, larger effect sizes were seen when PA was delivered at moderate-vigorous intensity and supervised by an exercise specialist. For schizophrenia-spectrum disorders, evidence indicates that aerobic PA can reduce psychiatric symptoms, improves cognition and various subdomains, cardiorespiratory fitness, whilst evidence for the impact on anthropometric measures was inconsistent. There was a paucity of studies investigating PA in bipolar disorder, precluding any definitive recommendations. No cost effectiveness analyses in any SMI condition were identified. We make multiple recommendations to fill existing research gaps and increase the use of PA in routine clinical care aimed at improving psychiatric and medical outcomes.</td></tr>
<tr><td>Timeframe: inception to Jan 2018</td></tr>
<tr><td>Total # studies included: 20</td></tr>
<tr><td>Other details (e.g. definitions used, exclusions etc) :Included 1) SRs 2) physical activity/ exercise interventions, including aerobic, high intensity and resistance exercise as monotherapy or in conjunction with other treatment options, 3) systematic reviews of PA, which included people with pooled SMI or schizophrenia-spectrum disorders, BD or MDD, confirmed through validated assessment measures 4) systematic reviews, which included a non-active/ non-exercise control group (e.g., does not include physical activity). We excluded mind-body physical activity interventions, such as yoga and tai-chi.</td></tr>
<tr><td>Outcomes addressed: incl. Cognitive functioning, e.g. performance in neuropsychological tests</td></tr>
</table>

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