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. <u>Blood Pressure (Systolic BP, Diastolic BP, Mean Arterial BP):</u> ***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.