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) I²21%) **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)