

The relationship between occupational physical activity and health: an umbrella review

Prepared for the Guideline Development Group for the
WHO Guidelines on physical activity and sedentary behaviour for children and adolescents,
adults and older adults

Authors:

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Background:

The Global Action Plan on Physical Activity 2018-2030 identified the need to update the 2010 guidelines on physical activity (PA) in youth, adults and older adults. At the 142nd meeting of the World Health Organization (WHO) Executive Board (January, 2018), the Member States requested the WHO to prioritize the updating of the 2010 Global Recommendations on PA for Health (1). This request was added to the draft resolution in preparation for the World Health Assembly in May 2019. Over the past decade, there has been a large increase in the amount and quality of evidence on the health impact of different types, amounts and durations of PA. Particular areas of new evidence include the impact of PA on mental wellbeing and cognitive health outcomes, and health outcomes in older adults and in sub-populations, such as those living with chronic conditions or impairments. Updated global guidelines on PA are an essential part of the policy framework and underpin national policy as well as global and national surveillance of physical activity. The guidelines under development will also provide recommendations on PA and sedentary behavior for adults living with chronic conditions, including HIV, pregnant women and adults living with specific impairments. The information provided in this report is intended to inform the WHO Guideline Development Group, thus assisting the update of the WHO Global Recommendations on PA for Health.

The current guidelines for adults (aged 18-64 years) recommend at least 150 minutes per week of moderate-intensity PA of which at least 75 minutes per week of vigorous-intensity PA. The current guidelines do, however, not address the domain of PA (1). This means that no distinction has been made between domains such as leisure time PA (LTPA) or occupational PA (OPA). Work is the most dominant domain for physical activity. However, research on the beneficial health effect of PA is mostly limited to LTPA, while the health effects of other domains of PA (such as OPA) are still poorly understood. However, evidence about the relationship between OPA and health has cumulated substantially over the last decades, leading to several systematic reviews and meta-analyses on this relationship.

The current umbrella review aims to achieve a better understanding about the relationship between OPA and health. More specifically we will assess the dose-response relationship between OPA and health, and how this may be different from that for LTPA.

Aim

To review the evidence on the health effects of OPA on the following outcomes: all-cause mortality, diabetes mellitus type 2, cancer, osteoarthritis, mental health outcomes, adiposity/(prevention of) body weight gain, cognitive outcomes, sleep duration or quality, hypertension, and health-related quality of life.

The main question to be addressed is: what is the relationship between OPA and health-related outcomes? Sub-questions are:

- Is there a dose-response relationship between OPA and health-related outcomes (taking into account dose measures such as frequency, intensity, duration and/or volume)?

- Is there a difference in the relationship between PA and health-related outcomes for OPA, compared to LTPA?

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 behavior 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 (2). 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 assessed using AMSTAR 2 (3) (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 (4). Each item was rated High, Moderate, Low or Critically Low. The cutoff 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.

Data extraction and analysis

First author's name, year of publication, number of studies included (by study design), physical activity domains and summary estimates were extracted from each included systematic review.

For each included review the Grading of Recommendations, Assessment, Development and Evaluation (GRADE)(5) method was used to rate the certainty of evidence for each of the health outcomes of interest. The GRADE system rates the quality of evidence in one of four levels (high, moderate, low and very low). The starting point for the quality of the evidence was 'high' for longitudinal studies that sought to confirm independent relation between the prognostic factor and the outcome (6, 7). This grading may be decreased if the reviews showed: risk of bias (e.g. selection,

performance, detection, attrition, and/or reporting bias), inconsistency of results (e.g. unexplained heterogeneity, if the I^2 statistics was provided a cutoff of >50% was used for an inconsistent result), indirectness of evidence (differences in populations, difference in intervention, difference in outcomes measures, indirect comparisons), imprecision (e.g. 95% Confidence Interval includes Risk Ratio of 1.0) or reporting bias. The rating of evidence could be increased by one level if there was a large magnitude of the effect (RR or OR was >2.0 or <0.5), plausible confounding (which may have reduced an observed effect) or a dose-response gradient (8). If the quality of the evidence was rated high, further research is very unlikely to change the rated confidence regarding the estimate of effect. If the quality was rated very low, any estimate of effect is very uncertain (5).

Evidence was depicted in flow charts (using Review Manager). If more than one review reported on a certain outcome, then only the most recently published review (i.e. with the highest number of included articles) was used (unless a less recent review reported higher quality evidence)

Results

A flowchart of the search and selection process is presented in Figure 1. The literature search generated 451 references. After removing duplicates, 245 references were screened by their title and abstract. Subsequently, 69 articles were screened by full text, of which 33 reviews were excluded because they did not meet the inclusion criteria (Supplementary material 2). A total of 36 reviews (6-41) was identified that examined the relationship between OPA and a health-related outcome. The most reported outcome was cancer, with eleven types of cancer that were reported by 24 different reviews. The other reviews evaluated cardiovascular diseases (n=3), osteoarthritis (n=3), all-cause mortality (n=2), hypertension (n=1), diabetes mellitus type 2 (n=1), insomnia (n=1), and mental health (n=1) (Supplementary material 3). No reviews were identified that evaluated adiposity/(prevention of) body weight gain, cognitive outcomes or health-related quality of life.

AMSTAR scores for methodological quality of the included reviews are shown in Supplementary material 4. Six reviews were scored critically low and were not used for further analyses. Extracted data, as well as GRADE assessment of the remaining reviews, are shown in Supplementary material 5. An overview of the evidence identified for the relationship between OPA and health outcomes is shown in Figure 2. Evidence from moderate, low or very low quality reviews pointed towards higher levels of OPA being related with a reduced risk of most cancers, CVD, hypertension and diabetes mellitus type 2. From low quality evidence reviews it was concluded that a high level OPA was related with an increased risk of all-cause mortality among males, but not among females. Also from low quality evidence reviews it was concluded that high level OPA was related with an increased risk of poor sleep quality. From very low quality reviews it was concluded that high level OPA was, interestingly, related with both mental health and mental ill-health (findings not depicted in the figure), and with osteoarthritis.

Dose-response associations were only reported for two outcomes. The risk of colon cancer was shown to reduce with increasing OPA levels (RR=0.89, 95% CI: 0.85- 0.93 for 210 MET-hours/week). People who were highly 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.

An overview of the evidence from reviews in which the health effects of both OPA and LTPA were reported is shown in Figure 3. This figure shows that for most cancers, CVD, hypertension and diabetes mellitus type 2, high levels of PA (both OPA and LTPA) were related with decreased risks of these outcomes. For OPA, however, due to the wide confidence intervals, effects appeared to be more imprecise than for LTPA.

Discussion

The presented evidence indicates that high levels of OPA were related with reduced risk of most cancers, CVD, hypertension and diabetes mellitus type 2. These effects seem to be in line with those observed for LTPA, although evidence for OPA is more imprecise. On the other hand, high level OPA was associated with an increased risk of all-cause mortality among males (but not among females), osteoarthritis, adverse sleep quality and adverse mental health outcomes. This suggests that the positive health outcomes that are considered to be associated with PA, may not always be present for OPA. This is an important message, given that for a large part of the working-age population most of the daily PA is spent at work (9) and that high level OPA holds people back in engaging in LTPA (10).

The evidence found was of moderate quality at best, with evidence for some health outcomes (e.g. all-cause mortality, some cancers, stroke, diabetes type II, hypertension, osteoarthritis and sleep quality) and being of low and even very low (i.e. oesophageal and gastric cancer) quality. An important reason for this is that all evidence is currently based on observational studies, which bears the risk of bias, most notably by selection bias and confounding. Confounding is often not properly dealt with, while also effect modification (such as for gender) is most often not considered. Moreover, OPA (but also LTPA) was generally assessed using self-reports, which can be inaccurate. The ways in which OPA was defined (i.e. using energy expenditure or biomechanical-based definitions) varied largely across reviews and studies. Also, effects appeared to be rather inconsistent and imprecise due to the limited amount of evidence (i.e. small number of studies reporting on OPA) used to assess pooled effect sizes. None of the included systematic reviews was rated 'high' on the AMSTAR 2 methodological quality scale. So all included studies had at least one critical weakness (e.g., only 4 out of 36 reviews had a priori registered their study protocol).

We only considered health outcomes that were considered relevant by WHO, thereby excluding evidence for certain health outcomes e.g. musculoskeletal and neurological outcomes. In particular musculoskeletal disorders are considered among the leading causes of disability worldwide (11). For example for musculoskeletal health, it is known that high level OPA activities such as standing, lifting and heavy manual work, are associated with increased risk of outcomes such as (non-specific) low back pain, neck/shoulder pain and lower extremity pain (12-14).

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Figure 1: Flowchart depicting the article search and selection procedure.

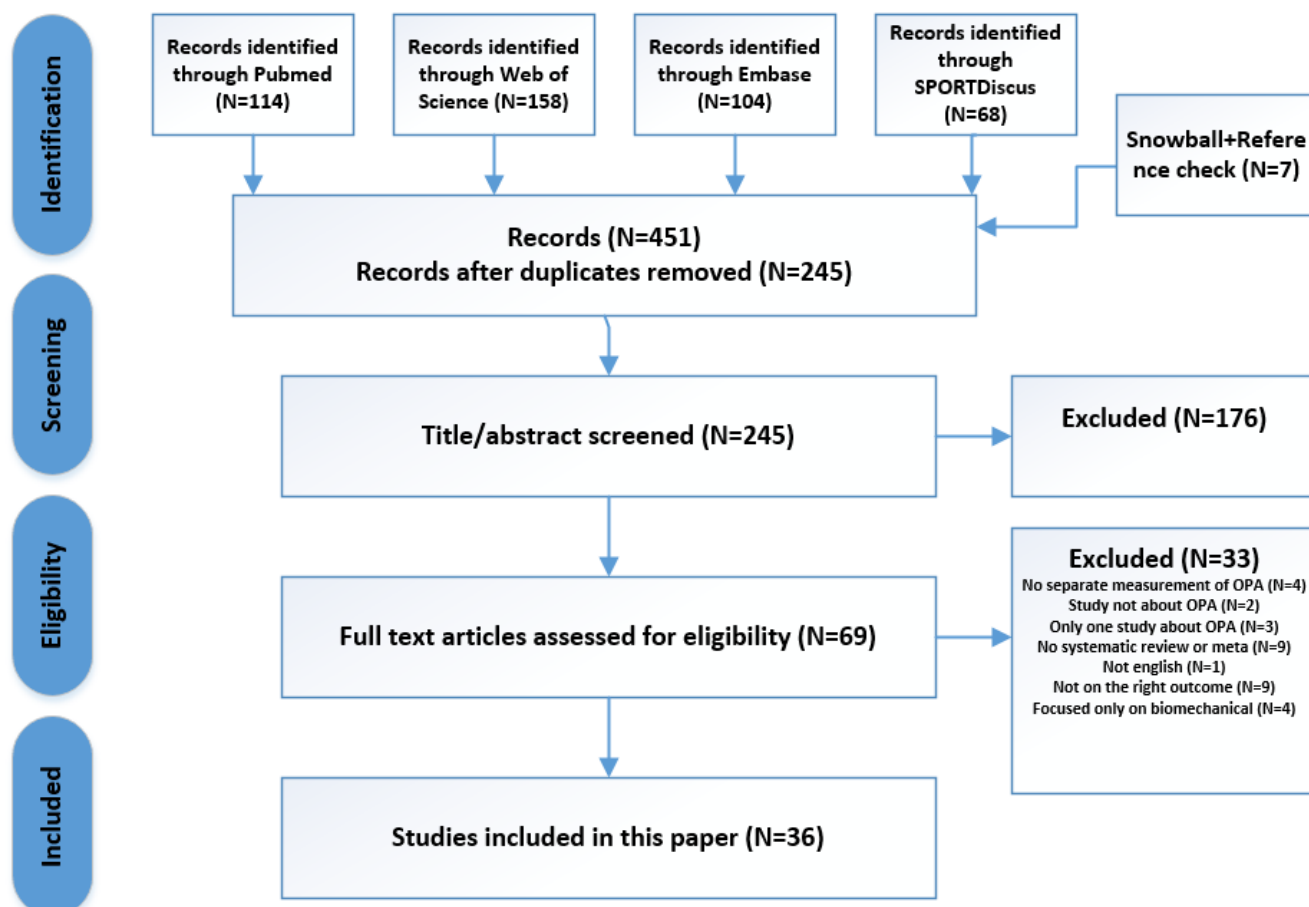


Figure 2. Forrest plot depicting the evidence for the association of occupational physical activity and health.

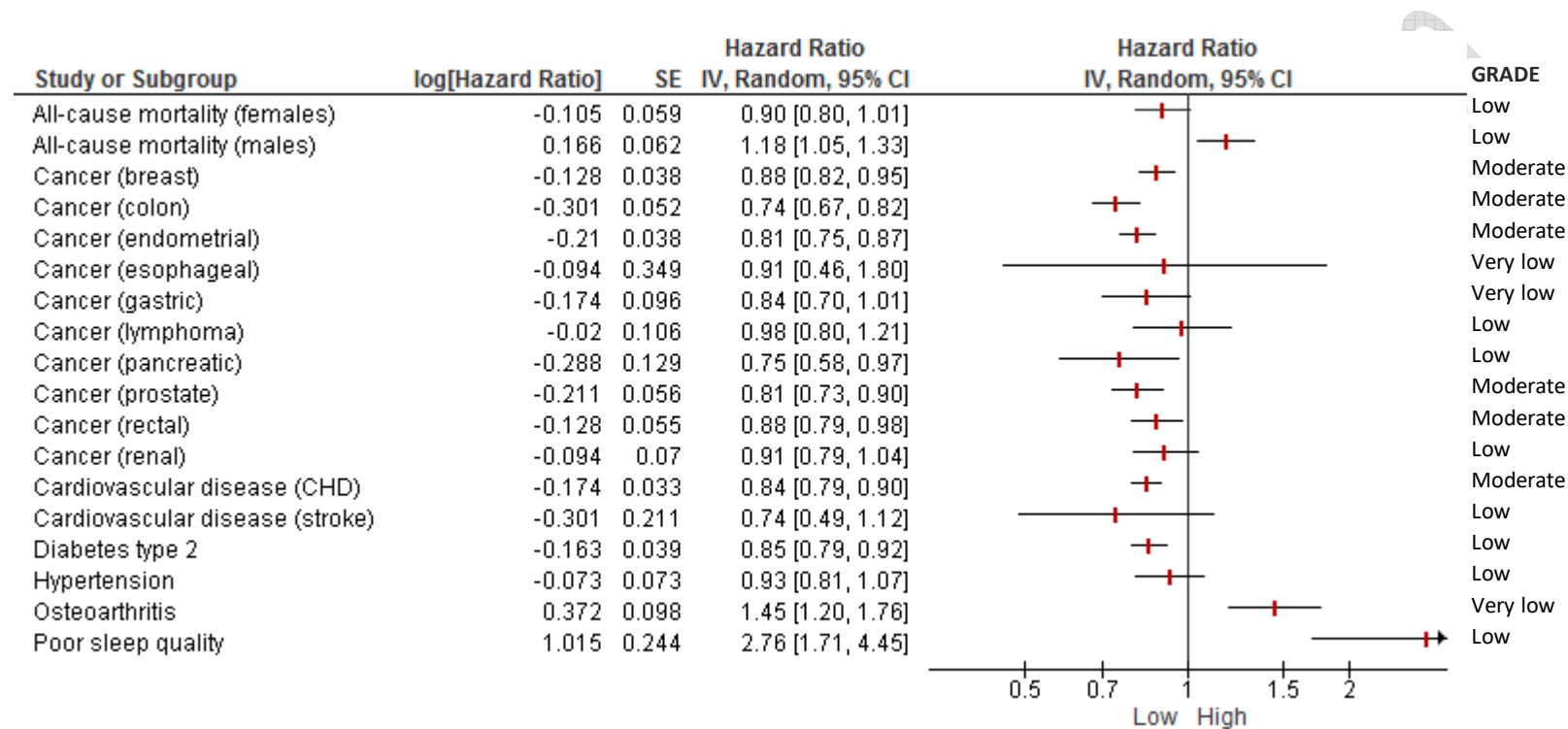
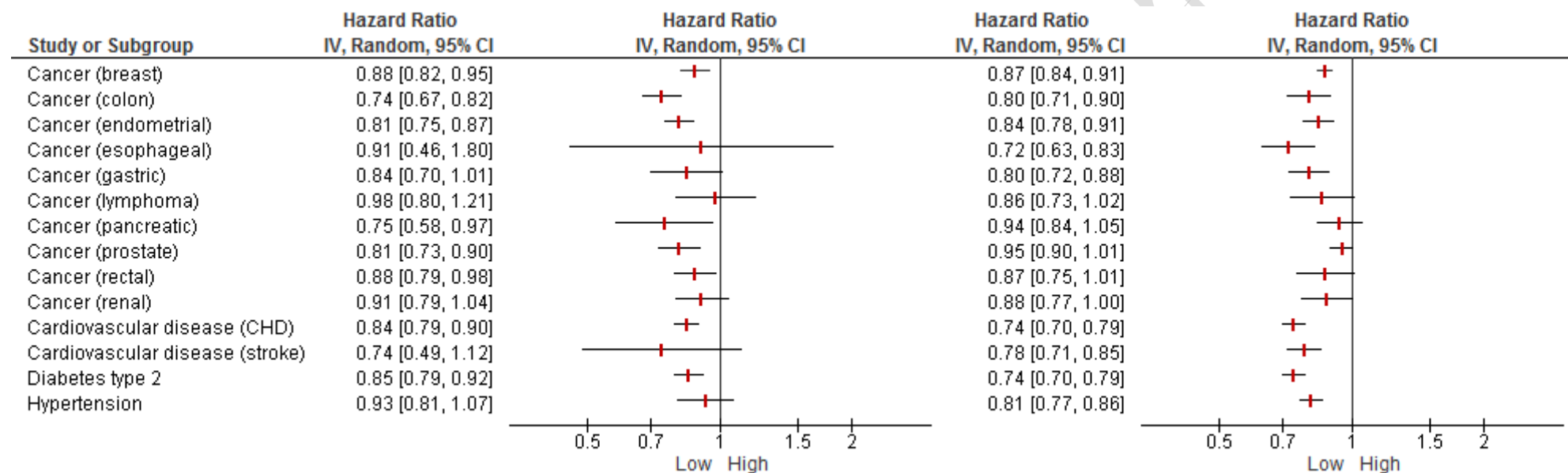


Figure 3. Forrest plot depicting the evidence for the association of physical activity and health. Associations for occupational (left panel) and leisure-time physical activity are depicted.



Supplementary material 1. Search strategies.

Search strategy in PubMed (read from bottom-up).

No.	Query	Items found
#3	#1 AND #2	114
#2	(systematic[sb] OR meta-analysis[pt] OR "systematic review"[tiab] OR "systematic literature review"[tiab] OR metaanalysis[tiab] OR "meta analysis"[tiab] OR metanalyses[tiab] OR "meta analyses"[tiab] OR "meta-analyses"[tiab] OR "pooled analysis"[tiab] OR "pooled analyses"[tiab] OR "pooled data"[tiab])	276539
#1	("occupational physical activity"[tiab] OR "Occupational physical activity"[tiab] OR "work-related physical activity"[tiab] OR "Work-related physical activity"[tiab] OR "occupation-related physical activity"[tiab] OR "Occupation-related physical activity"[tiab] OR "work-time physical activity"[tiab] OR "Work-time physical activity"[tiab] OR "work physical activity"[tiab] OR "Work physical activity"[tiab] OR "Occupational energy expenditure"[tiab] OR "occupational energy expenditure"[tiab] OR "work-related energy expenditure"[tiab] OR "Work-related energy expenditure"[tiab] OR "domain-specific physical activity"[tiab] OR "domains of physical activity"[tiab] OR "physical activity domains"[tiab] OR "domain-related physical activity"[tiab] OR "work-related physical activity domain"[tiab] OR "occupational activity" [tiab] OR "physical workload" [tiab] OR "occupational load" [tiab] OR "heavy workload" [tiab] OR "heavy work" [tiab] OR "heavy labor" [tiab] OR "heavy labour" [tiab] OR "physical labor" [tiab] OR "physical labour" [tiab] OR "occupational activities" [tiab] OR "physical demanding occupations" [tiab] OR "occupational load" [tiab])	4146

Search strategy in Web of Science (Databases= WOS, KJD, MEDLINE, RSCI, SCIELO Timespan=All years)

No.	Query	Item found
#3	#1 AND #2	158
#2	TS=(systematic review OR meta-analysis OR "systematic review" OR "systematic literature review" OR "meta-analysis" OR "meta analysis" OR "meta-analyses" OR "meta analyses" OR "pooled analysis" OR "pooled analyses" OR "pooled data")	435971
#1	TS=("physical workload" OR "occupational activity" OR "occupational activities" OR "physical labor" OR "physical labour" OR "physical demanding occupation" OR "occupational physical activity" OR "Occupational physical activity" OR "work-related physical activity" OR "Work-related physical activity" OR "occupation-related physical activity" OR "Occupation-related physical activity" OR "work-time physical activity" OR "Work-time physical activity" OR "work physical activity" OR "Work physical activity" OR "Occupational energy expenditure" OR "occupational energy expenditure" OR "work-related energy expenditure" OR "Work-related	5.728

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	energy expenditure" OR "domain-specific physical activity" OR "domains of physical activity" OR "physical activity domains" OR "domain-related physical activity" OR "work-related physical activity domain" OR "heavy work" OR "occupational load")	
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Search strategy in Embase (read from bottom-up).

No.	Query	Items found
#2	('physical workload' OR 'occupational activity' OR 'occupational activities' OR 'physical labor' OR 'physical labour' OR 'physical demanding occupation' OR 'occupational physical activity' OR 'work-related physical activity' OR 'occupation-related physical activity' OR 'work-time physical activity' OR 'work physical activity' OR 'occupational energy expenditure' OR 'work-related energy expenditure' OR 'domain-specific physical activity' OR 'domains of physical activity' OR 'physical activity domains' OR 'domain-related physical activity' OR 'work-related physical activity domain' OR 'heavy work' OR 'occupational load') AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim)	104
#1	'physical workload' OR 'occupational activity' OR 'occupational activities' OR 'physical labor' OR 'physical labour' OR 'physical demanding occupation' OR 'occupational physical activity' OR 'work-related physical activity' OR 'occupation-related physical activity' OR 'work-time physical activity' OR 'work physical activity' OR 'occupational energy expenditure' OR 'work-related energy expenditure' OR 'domain-specific physical activity' OR 'domains of physical activity' OR 'physical activity domains' OR 'domain-related physical activity' OR 'work-related physical activity domain' OR 'heavy work' OR 'occupational load'	4756

Search strategy in SportDiscus

No.	Query	Items found
#2	('physical workload' OR 'occupational activity' OR 'occupational activities' OR 'physical labor' OR 'physical labour' OR 'physical demanding occupation' OR 'occupational physical activity' OR 'work-related physical activity' OR 'occupation-related physical activity' OR 'work-time physical activity' OR 'work physical activity' OR 'occupational energy expenditure' OR 'work-related energy expenditure' OR 'domain-specific physical activity' OR 'domains of physical activity' OR 'physical activity domains' OR 'domain-related physical activity' OR 'work-related physical activity domain' OR 'heavy work' OR 'occupational load') AND (=(systematic review OR meta-analysis OR "systematic review" OR "systematic literature review" OR "meta-analysis" OR "meta analysis" OR "meta-analyses" OR "meta analyses" OR "pooled analysis" OR "pooled analyses") OR "pooled data")	68
#1	('physical workload' OR 'occupational activity' OR 'occupational activities' OR 'physical labor' OR 'physical labour' OR 'physical demanding occupation' OR 'occupational physical activity' OR 'work-related physical activity' OR 'occupation-related physical activity' OR 'work-time physical activity' OR 'work physical activity' OR 'occupational energy expenditure' OR 'work-related energy expenditure' OR 'domain-specific physical activity' OR 'domains of physical activity' OR 'physical activity domains' OR 'domain-related physical activity' OR 'work-related physical activity domain' OR 'heavy work' OR 'occupational load')	1.911

	activity' OR 'occupation-related physical activity' OR 'work-time physical activity' OR 'work physical activity' OR 'occupational energy expenditure' OR 'work-related energy expenditure' OR 'domain-specific physical activity' OR 'domains of physical activity' OR 'physical activity domains' OR 'domain-related physical activity' OR 'work-related physical activity domain' OR 'heavy work' OR 'occupational load')	
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Supplementary material 2: Reason for exclusion after full text screening.

		Reference (first author, year and title)	Reason
1	1	Kyu. H.H. et al. 2016. Physical activity and the risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: Systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013	No separate measurement of OPA.
2	2	Wahid et al. 2015. Quantifying the association between physical activity and cardiovascular disease: A meta-analysis	No separate measurement of OPA
3	3	Morgan et al. 2012. Physical activity in middle-age and dementia in later life: findings from a prospective cohort of men in Caerphilly, South Wales and a meta-analysis	No separate measurement of OPA
4	4	Dieker et al 2019. The contribution of work and lifestyle factors to socioeconomic inequalities in self-rated health – a systematic review	No separate measurement of OPA.
5	1	Ma Peng et al. 2017. Daily sedentary time and its association with risk for colorectal cancer in adults A dose-response meta-analysis of prospective cohort studies	Study is not about OPA
6	2	Stamatakis et al. 2013 Are sitting occupations associated with increased all-cause, cancer, and cardiovascular disease mortality risk? A pooled analysis of seven British population cohorts	Study is not about OPA
7	1	Theorell et al. 2016. A systematic review of studies in the contributions of the work environment to ischaemic heart disease development	It is not possible to determine if there is any association between exposure and outcome.
8	1	Abioye et al. 2015. Physical activity and risk of gastric cancer: a meta-analysis of observational studies	Included only one study about OPA.
9	2	Teychenne et al. 2013. Physical Activity, Sedentary Behavior, and Postnatal Depressive Symptoms A Review	Included only one study about OPA.
10	3	Anzuini 2011, Physical activity and cancer prevention: A review of current evidence and biological mechanisms	Included only one study about OPA.
11	1	Kitahara et al. 2012 : Physical activity, diabetes, and thyroid cancer risk: a pooled analysis of five prospective studies	No systematic review or meta analyses.

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12	2	Cochero. 2008. The effect of income and occupation on body mass index among women in the Cebu Longitudinal Health and Nutrition Surveys (1983-2002)	No systematic review or meta analyses
13	3	Oczkowski, 2005: Complexity of the relation between physical activity and stroke: a meta-analysis	No systematic review or meta analyses.
14	4	Nordander et al. 2016: Exposure-response relationships for work-related neck and shoulder musculoskeletal disorders - Analyses of pooled uniform data sets	No systematic review or meta analyses.
15	5	Engel, 2018. Work and Female Breast Cancer: The State of the Evidence, 2002-2017	No systematic review or meta analyses
16	6	Barengo 2007 Physical activity and hypertension: Evidence of cross-sectional studies, cohort studies and meta-analysis	No systematic review or meta analyses
17	7	Cooper, 1995. Occupational activity and the risk of osteoarthritis	No systematic review or meta analyses
18	8	Bierma-Zeilstra 2007 Risk factors and prognostic factors of hip and knee osteoarthritis	No systematic review or meta analyses.
19	9	Moore 2010; Physical activity, sedentary behaviours, and the prevention of endometrial cancer	No systematic review or meta analyses.
20	1	Porru et al 2003 [Bladder cancer and occupational activity]	Non-English
21	1	De Zwart et al 1995: Physical workload and the ageing worker: A review of the literature	Not on the right outcome ¹
22	2	Boggild et al 1997: Occupational environment and strain induced gout. A review of epidemiological studies of the connection between occupational environment and coxarthrosis	Not on the right outcome ¹
23	3	Hamidou, 2013. Amyotrophic lateral sclerosis, physical activity and sport: A literature review	Not on the right outcome ¹
24	4	Lacorte et al. 2014: Physical activity, and physical activity related to sports, leisure and occupational activity as risk factors for ALS: A systematic review	Not on the right outcome ¹
25	5	Lam et al. 2017: Does physical activity protect against the development of gastroesophageal reflux disease, Barrett's	Not on the right outcome ¹

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		esophagus, and esophageal adenocarcinoma? A review of the literature with a meta-analysis	
26	6	Stephen 2017. Physical Activity and Alzheimer's Disease: A Systematic Review	Not on the right outcome ¹
27	7	Svendson, 2013: Risk and prognosis of inguinal hernia in relation to occupational mechanical exposures - a systematic review of the epidemiologic evidence	Not on the right outcome ¹
28	8	Togo et al. 2009. Heart Rate Variability in Occupational Health --A Systematic Review	Not on the right outcome ¹
29	9	Yang F. 2015. Physical activity and risk of Parkinson's disease in the Swedish National March Cohort	Not on the right outcome ¹
30	1	Sun, Y. 2019 Hip Osteoarthritis and Physical Workload: Influence of Study Quality on Risk EstimationsA Meta-Analysis of Epidemiological Findings	focused only on biomechanical (i.e. ergonomic) physical work exposures, rather than (occupational) physical activity;
31	2	Richmond, 2013 Are joint injury, sport activity, physical activity, obesity, or occupational activities predictors for osteoarthritis? A systematic review	focused only on biomechanical (i.e. ergonomic) physical work exposures, rather than (occupational) physical activity;
32	3	Ezzat, 2012. Occupational activity and the risk of osteoarthritis	focused only on biomechanical (i.e. ergonomic) physical work exposures, rather than (occupational) physical activity;
33	4	Lievensen 2001 Influence of work on the development of osteoarthritis of the hip: a systematic review	focused only on biomechanical (i.e. ergonomic) physical work exposures, rather than (occupational) physical activity;

1. The Global Action Plan on Physical Activity 2018-2030 identified the following outcomes: Mortality, CVD, Cancer, Diabetes type 2, Osteoarthritis, Adiposity/prevention of weight gain, mental health, cognitive outcomes, adverse effects, sleep duration/quality, incidence hypertension

Supplementary material 3: Outcome-specific Amstar 2 summary rating of the included systematic reviews.

	Author, Year	AMSTAR 2: Overall rating	All-Cause Mortality	Cardio-vascular diseases	Cancer											Diabetes type 2	Osteoarthritis	Mental Health	Sleep duration and quality	Hypertension
					Colon	Rectal	Breast	Endometrial	Lymphoma	Gastric	Esophageal	Renal	Prostate	Pancreatic	Bladder					
1	Samitz 2011 (15)	Low	X																	
2	Coenen 2018 (16)	Moderate	X																	
3	Wendel-vos 2004 (17)	Low		X																
4	Li J 2013 (18)	Critical		X																
5	Sattelmair 2011 (19)	Low		X																
6	Wolin 2009 (20)	Critical			X															
7	Mahmood 2017 (21)	Low			X	X														
8	Boyle 2012 (22)	Moderate			X															
9	Samad 2005 (23)	Critical			X															
10	Robsahm 2013 (24)	Low			X	X														
11	Wu Y 2013 (25)	Low					X													
12	Pizot 2016 (26)	Low					X													
13	Chen X 2019 (27)	Moderate					X													
14	Voskuil 2007 (28)	Low						X												
15	Schmid 2015 (29)	Low						X												
16	Vermaete 2013 (30)	Low							X											
17	Singh 2014 (31)	Moderate								X										
18	Psaltopoulou 2016 (32)	Moderate								X										
19	Chen Y 2014 (33)	Low								X	X									
20	Behrens 2014 (34)	Low								X	X									
21	Behrens 2013(35)	Low										X								
22	Shephard 2016(36)	Low										X								
23	Krstev 2019 (37)	Critical											X							
24	Benke 2018 (38)	Low											X							

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25	Shephard 2017 (39)	Low												X						
26	Liu 2011 (40)	Moderate												X						
27	O'Rorke 2010 (41)	Critical													X					
28	Bao 2008 (42)	Low													X					
29	Keimling 2014 (43)	Critical														X				
30	Aune 2015 (44)	Moderate															X			
31	McWilliams 2011 (45)	Low																X		
32	Gignac 2019(46)	Low																X		
33	Palmer 2012 (47)	Critical																X		
34	White 2017 (48)	Moderate																	X	
35	Yang B 2018 (49)	Low																	X	
36	Huai 2013 (50)	Low																		X

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Supplementary material 4. 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 Assessment 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

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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?

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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 (3).

GRADE: Grading the body of evidence (see supplementary file 6 for all extracted data)

1.0.	All-cause mortality	27
2.0.	Cardio-vascular disease	29
2.1.	Stroke	29
2.2.	Coronary Heart Disease	30
3.0.	Cancer	31
3.1.	Colon cancer	31
3.2.	Rectal cancer	34
3.3.	Breast cancer	36
3.4.	Endometrial cancer	38
3.5.	Lymphoma (Hodgkin and non-Hodgkin)	40
3.6.	Gastric cancer	41
3.7.	Esophageal cancer	44
3.8.	Renal cancer	45
3.9.	Prostate cancer	47
3.10.	Pancreatic cancer	51
3.11.	Bladder cancer	52
4.0.	Diabetes Mellitus type 2	53
5.0.	Osteoarthritis	54
6.0.	Mental Health	56
7.0.	Sleep quality and/or duration	57
8.0.	Hypertension	58
9.0.	Abbreviation list	59

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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
No 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)(15)
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% I² OPA: 3 studies in women: (RR=0.66; 95% CI 0.49-0.89) 89% I² LTPA: The strongest associations between PA and mortality were observed for LTPA (RR 0.74; 95% CI 0.70–0.77),	Low ⁱ	Critically
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Do highly physically active workers die early? A systematic review with meta-analysis of data from 193 696 participants. (Coenen, 2018)(16)

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 ⁱ	Critically
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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.

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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
No 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) (17)

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
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Physical activity and risk of cardiovascular disease: What does the new epidemiological evidence show? (Li J. 2013) (18) 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) (19) 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
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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 from 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
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

Physical activity and colon cancer prevention: a meta-analysis (Wolin, 2009) (20)

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 behavior in relation to colon and rectal cancer risk: A systematic review and meta analyses (Mahmood, 2017) (21)

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
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Physical Activity and Risks of Proximal and Distal Colon Cancers: A Systematic Review and Meta-analysis (Boyle, 2012) (22)

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
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A meta-analysis of the association of physical activity with reduced risk of colorectal cancer (Samad, 2005) (23)

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) (24)

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
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a: Cohort studies 5; Morati, 2008; Larsson 2006; Colbert 2001; Thune 1996; Boyle 2011; Case control 10: Parent 2011; Isomura 2006; Kato 1990; Arbmman 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

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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

DRAFT - for consultation

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
Ne 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) (21)

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
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Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies (Robsahm. 2013) (24)

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
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a: Cohort studies 5; Morati, 2008; Larsson 2006; Colbert 2001; Thune 1996; Boyle 2011. Case control 7 studies; Parent 2011; Isomura 2006; Kato 1990; Arbmman 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

DRAFT - for consultation

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
No 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) (25)

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
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Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of prospective studies (Pizot, 2015) (26)

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
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Physical Activity and Risk of Breast Cancer: A Meta-Analysis of 38 Cohort Studies in 45 Study Reports (Chen, 2019) (27)

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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
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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
No 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) (28)

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

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A systematic review and meta-analysis of physical activity and endometrial cancer risk (Schmid. 2015) (29).

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
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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; Freidenreich 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 received 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
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

Physical Activity and Risk of Lymphoma: A Meta-Analysis (Vermaete, 2013) (30)

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
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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
No 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). (31)

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
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Physical Activity and Gastric Cancer Risk: A Systematic Review and Meta-Analysis (Psaltopoulou 2016) (32)

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
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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 ^f	Critically
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Physical Activity and Risks of Esophageal and Gastric Cancers: A Meta-Analysis (Chen, 2014) (33)

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
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The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis (Behrens, 2014) (34)

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
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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; Suwanrungruang 2008 ; Vigen 2006

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

e: Huerta 2010; Severson 1989; Brownson 1991; Dosemeci 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

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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: Esophageal cancer

Certainty assessment							Summary of findings	Certainty	Importance
No 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) (33)

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) (34)

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 ⁱ	Critically
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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
No 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) (35)

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
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Can habitual physical activity contribute to reducing the health burden of renal cancer? (Shephard, 2016) (36)

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 control; 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

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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 '5 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
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

Occupational Risk factors for prostate cancer; A meta-analyses (Krstev, 2019) (37)

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) (38)

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
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Physical activity and prostate cancer: An updated review (Shephard, 2017) (39)

19^b	Cross sectional and prospective cohort	Serious ^h	Serious ⁱ	Not serious	Serious ⁱ	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 ⁱ	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) (40)

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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), Laggiou (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; Laggiou 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), Laggiou (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.

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I: 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
No 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) (41)

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) (42)

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
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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

3.11. 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
No 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) (43)

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
No 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) (44)

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
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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
No 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) (45)

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
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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) (46)

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 ⁱ	Critically
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Occupational activities and osteoarthritis of the knee (Palmer, 2012) (47)

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 observed (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
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

Domain-Specific Physical Activity and Mental Health: A Meta-analysis (White, 2017) (48)

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
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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
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

Association between insomnia and job stress: a meta-analysis (Yang, 2018) (49)

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
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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
No 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) (50)

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
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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 Activity
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