How does occupational physical activity influence health? An umbrella review of 23 health outcomes across 158 observational studies

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ABSTRACT

Objective Physical activity (PA) has substantial benefits across a range of health outcomes. There is uncertainty about the PA-specific health effects, and in particular, the occupational domain. In this umbrella review, we synthesised available evidence on the associations between occupational PA (OPA) and health-related outcomes (including cancer, all-cause mortality and cardiovascular disease). This work informed the development of WHO's guidelines on PA and sedentary behaviour (2020).

Design Umbrella review of systematic reviews.

Data source We performed a literature search in PubMed, Web of Science, Embase, CINAHL and Sportdiscuss from database inception to 2 December 2019.

Eligibility criteria for selecting studies We included systematic reviews if they contained a quantitative assessment of OPA and its relationship with at least one health-related outcome.

Results We summarised the evidence of 17 reviews covering 23 unique health-related outcomes. We graded most evidence as low or very low, or moderate quality. We found health benefits for those engaging in high versus low OPA for multiple cancer outcomes (including colon and prostate), ischaemic stroke, coronary heart disease and mental health (ie, mental well-being and life satisfaction). High OPA was associated with unfavourable health outcomes for all-cause mortality in men, mental ill health (ie, depression and anxiety), osteoarthritis, and sleep quality and duration.

Conclusions We found favourable associations for most health-related outcomes with high OPA levels, but we also found some evidence for unfavourable associations due to high OPA levels. At this point, there is a need for better quality evidence to provide a unequivocal statement on the health effects of OPA.

INTRODUCTION

Physical activity (PA) has significant health benefits and contributes to the prevention of a range of lifestyle-related, non-communicable diseases.[1 2] Physical inactivity is one of the global leading risk factors for all-cause mortality.[3] Both national and international PA guidelines for adults, including the 2010 guidelines by WHO, recommend at least 150 min per week of moderate-intensity PA.[1 2] The Global Action Plan on PA highlighted the need to update the 2010 WHO Global recommendations on PA for Health.[4] WHO published the guidelines on PA and sedentary behaviour in 2020, further details of which can be found in the current issue of BJSM.[4]

The 2010 WHO PA guidelines did not differentiate between domains of PA (work, commuting, household and leisure), suggesting comparable health benefits for all these PA domains.[2] Most studies reviewed by the 2010 guidelines were restricted to leisure-time PA (LTPA) domain,[2] and evidence on domain specific health benefits was largely inconclusive. Differential health effects have been reported for LTPA and occupational PA (OPA),[5–7] a phenomenon which is referred to as the PA paradox.[8] For example, a prospective cohort study showed that LTPA was associated with reduced risk of all-cause mortality, while OPA was associated with an increased risk of all-cause mortality.[6] It is not clear whether these differential associations are due to domain-specific PA characteristics (eg, differences in posture, intensity level, frequency, duration and/or recovery time between OPA and LTPA[8]) or down to methodological reasons.[9 10]

As the amount of systematic reviews and meta-analyses accumulates,[11] more advanced evidence synthesis methods such as umbrella reviews can be employed.[12] An umbrella review provides a broader picture of findings for a particular question or phenomenon, and is therefore useful to inform guidelines.[12] PA-related umbrella reviews are mostly restricted to LTPA only,[13–15] with no umbrella review on the health effects of OPA currently.

In this umbrella review, we aimed to provide an overview on the relationships between OPA and a range of health-related outcomes, including cancer, cardiovascular disease (CVD) and all-cause mortality. We also aimed to assess dose–response relationships and whether the relationship between OPA and health differs from that of LTPA.

This review builds on a report on OPA commissioned by WHO to inform the guidelines on PA and sedentary behaviour (2020).

METHODS

Literature search

This protocol was registered in PROSPERO (id: 163090).[16] We searched in PubMed, CINAHL, Web of Science, Embase and Sportdiscuss from database inception up to 2 December 2019 for systematic

reviews assessing the relationship between OPA and health-related outcomes. Searches contained keywords covering OPA, systematic reviews and meta-analyses. See online supplemental material table 1 for a detailed outline of the search strategy. We identified additional reviews by screening the reference list of included reviews and by consulting experts. Two reviewers (BC and ML) independently screened title, abstract and full text of identified references using the online Rayyan application (rayyan.qcri.org).[17] Discrepancies between the two reviewers were resolved in a consensus meeting, or by consulting a third reviewer (PC).

Review inclusion and data extraction

We included full-text systematic reviews of observational (eg, cohort, case–control, cross-sectional) and experimental studies (eg, (randomised) controlled trials) written in English. Reviews had to contain a quantitative assessment of OPA and an association with at least one health-related outcome considered relevant by WHO PA guideline advisory committee. See the full list of outcomes considered in online supplemental material table 2. We excluded articles if the OPA domain was not specifically assessed. We also excluded reviews if they focused on sedentary behaviour only or on biomechanical exposures only (ie, lifting or prolonged postures such as standing or kneeling), without considering energetic components of OPA. We excluded reviews focused on specific (clinical) populations, such as pregnant women or cohorts with an disease.

One reviewer (BC) extracted data from included reviews, which was checked by a second reviewer (ML). Potential conflicts were discussed until consensus was reached. We extracted first author, title, year of publication, outcome, study design, number of included studies, comparison group and effect sizes. If available, effect sizes of LTPA were also extracted.

Methodological quality and certainty of evidence

We rated included systematic reviews using A MeaSurement Tool to Assess systematic Reviews2 (AMSTAR2),[18] a 16-point tool for assessment of the methodological quality of systematic reviews, with good inter-rater agreement, test–retest reliability and content validity.[19] Review quality could be high, moderate, low or critically low, with cut-off values of 100%, ≥75%, ≥50% and <50%, respectively. One reviewer (BC) assessed methodological quality; the second reviewer (ML) checked these assessments. If reviews were rated critically low, they were excluded from further analyses.

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method[20] to rate the quality of evidence for each of the health-related outcomes. The GRADE system rates the quality of evidence as:

- High quality: further research is very unlikely to change our confidence in the estimate of effect.
- Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- Very low quality: any estimate of effect is very uncertain.[20]

The starting point for the quality of the evidence was 'high'.[21 22] We decreased this grading if the reviews showed: risk of bias (ie, selection, performance, detection, attrition and/or reporting bias), inconsistency of results (ie, unexplained heterogeneity or I^2-statistics ≥50%), indirectness of evidence (ie, differences in populations, intervention, outcome measures or indirect comparisons), imprecision (ie, 95% CI includes 1.0) or publication bias (asymmetry in funnel plot). We increased the rating by one level if there was a large magnitude of the effect (eg, RR or OR ≥2.0 or ≤0.5), in case of plausible confounding (which may have reduced an observed effect), or in case of a dose–response gradient.[23]

Data analysis

If more than one review reported on a certain outcome, we only used the most recently published review (typically with the highest number of included studies) for further analyses; unless a less recent review reported higher certainty of evidence (GRADE). Online supplemental material table 3 enumerates the included studies for main and sensitivity analyses. If subgroup analyses (eg, regarding higher quality evidence or different study designs) were provided with different GRADE scores, then evidence from the highest GRADE score was synthesised. We constructed forest plots to display the relationship of high vs low OPA with health-related outcomes. We conducted sensitivity analyses to assess consistency of the synthesised evidence if there was more than one review for the same outcome.

If the original review had estimated the I^2 statistics, we synthesised this information to assess heterogeneity.[24] If reviews did not publish the I^2 statistics, we calculated this where possible.

We synthesised small-study bias or publication bias (when referring to OPA studies). Whenever a review did not provide this information, and included more than ten OPA studies we reanalysed the data and provided funnel plots to assess publication bias on visual inspection. In case no information was provided and less than 10 studies were available, we considered the review at stake to be 'at risk of bias' since a funnel plot would be inaccurate with fewer than 10 studies.[25]

If available, we provided dose–response relationships from reviews that had reported on more than two categories of OPA or on a continuous OPA scale. For the comparison of the relationships of OPA and LTPA with health, we only used already included reviews that reported on both OPA and LTPA. Differences between the effect sizes of OPA and LTPA were statistically tested[26] using a test of interaction. All analyses were conducted using Revman V.3.5.3.

RESULTS

The literature search generated 573 references. After removing duplicates and adding seven reviews from snowball searching, we screened 312 references by title and abstract (figure 1). Full texts of 73 reviews were screened, of which we excluded 37 reviews for various reasons (online supplemental material table 4).

We identified 36 reviews that examined the associations between OPA and 23 unique health-related outcomes.[27–62] The most frequently reported outcome was cancer, with 11 different cancer types (24 reviews). Other reviews evaluated CVD (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) (online supplemental material table 3). We did not detect any reviews on adiposity, cognitive outcomes or health-related quality of life.

Quality assessment

AMSTAR2 scores for methodological quality of the 36 included reviews are shown in online supplemental material table 5. Six reviews scored (17%) critically low which we did not use for further analyses.[30 32 35 49 55 59] Eight reviews (22%) scored

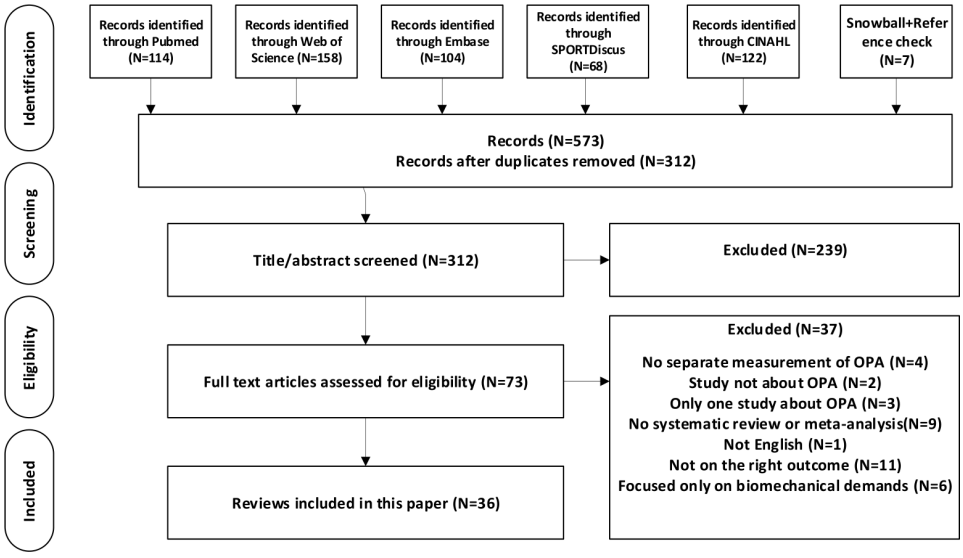


Figure 1 Flow chart depicting the review search and selection procedure. OPA, occupational physical activity.

moderate, and 22 (61%) scored low methodological quality. None of the included reviews scored high on the AMSTAR2 scale, with common methodological issues for example being lack of a priori protocol registration (only done in four reviews), not reporting a comprehensive search strategy (only performed in ten reviews) and not providing a list of excluded studies (only done in five reviews).

Evidence synthesis

Online supplemental material table 6 presents extracted data. Seventeen reviews (on 23 unique outcomes) were synthesised. These reviews reported on 158 studies: 96 (61%) longitudinal cohort studies, 60 (38%) case–control studies and 2 (<1%) cross-sectional studies, while no reviews on experimental studies met the inclusion criteria. Reviews described between three and 27 individual studies, with a median of 7.5 studies per review. We did not synthesise thirteen reviews because there was a more recent published review, or a review with a higher certainty of evidence (online supplemental material table 3).

Grading of Recommendations Assessment, Development and Evaluation

We graded none of the included reviews as high quality; overall the evidence was of moderate quality at best (online supplemental material table 6). Four reviews (17%) on colon cancer, rectal cancer, endometrial cancer and prostate cancer provided moderate quality evidence. Reviews of nine (39%) outcomes provided low quality evidence (all-cause mortality, ischaemic stroke, coronary heart disease (CHD), proximal and distal colon cancer, breast cancer, gastric cancer and renal cancer) and ten other reviews (43%) offered very low-quality evidence.

PA measurement methods varied across reviewed studies, and included self-administered questionnaires, interviews or job titles. Because PA was mostly self-reported, misclassification was reported in almost all included reviews. In some reviews PA was assessed at baseline, but a change in PA over time was not considered. Over half of the reviews reported that there was confounding bias, that the adjustment of variables widely varied between studies, or that important confounding variables were not addressed in reviewed studies. Some review reported language bias; typically only one or two languages were included in the reviews.

Of the 23 health outcomes, 14 (61%) reported an I^2 statistics <50% and seven (30%) reported an I^2 statistics ≥50% (hypertension, mental health, mental ill health, stroke, all-cause mortality, poor sleep duration and/or quality and osteoarthritis). For two outcomes (oesophageal and endometrial cancer) the reviews did not provide I^2 statitics. Re analysis showed a low heterogeneity (I^2=0%) for endometrial cancer and considerable heterogeneity for oesophageal cancer (I^2=89%) (online supplemental material figure 7). Most reviews were precise; the risk estimates of only seven (30%) outcomes had 1.0 included in their 95% CI. Although all 17 reviews used the Eggers asymmetry test to detect publication bias, in most reviews, the association between OPA and a health-related outcome was investigated in a subgroup analysis on OPA only, with the Egger test conducted for 'total PA' (including OPA). Only for four outcomes (17%) (in three reviews) a test for publication bias was conducted, addressing the OPA domain. Only one of these three reviews found a small risk for publication bias. It is likely that reviews did not conduct separate analyses because there were not enough unique OPA studies included: fourteen (61%) outcomes included less than 10 studies on OPA. We reanalysed the data of four outcomes and did not detect publication bias in these reviews (online supplemental material figure 8). One review included more than ten studies, but did not report individual study effect sizes, hence we could not perform an assessment of publication bias.[47]

Evidence

All synthesised reviews are summarised in figure 2, with quality of the evidence ranging from moderate to very low.

Moderate quality evidence

A meta-analysis of Mahmood *et al*[33] including five cohort and ten case-control studies showed a statistically significant reduction in risk of colon cancer among those with high compared with low OPA (RR 0.74, 95% CI 0.67 to 0.82). This association was comparable for men (RR 0.74, 95% CI 0.66 to 0.82) and women (RR 0.78, 95% CI 0.65 to 0.93). In the same review, authors presented pooled estimates regarding the association between OPA and rectal cancer from five cohort and seven case–control

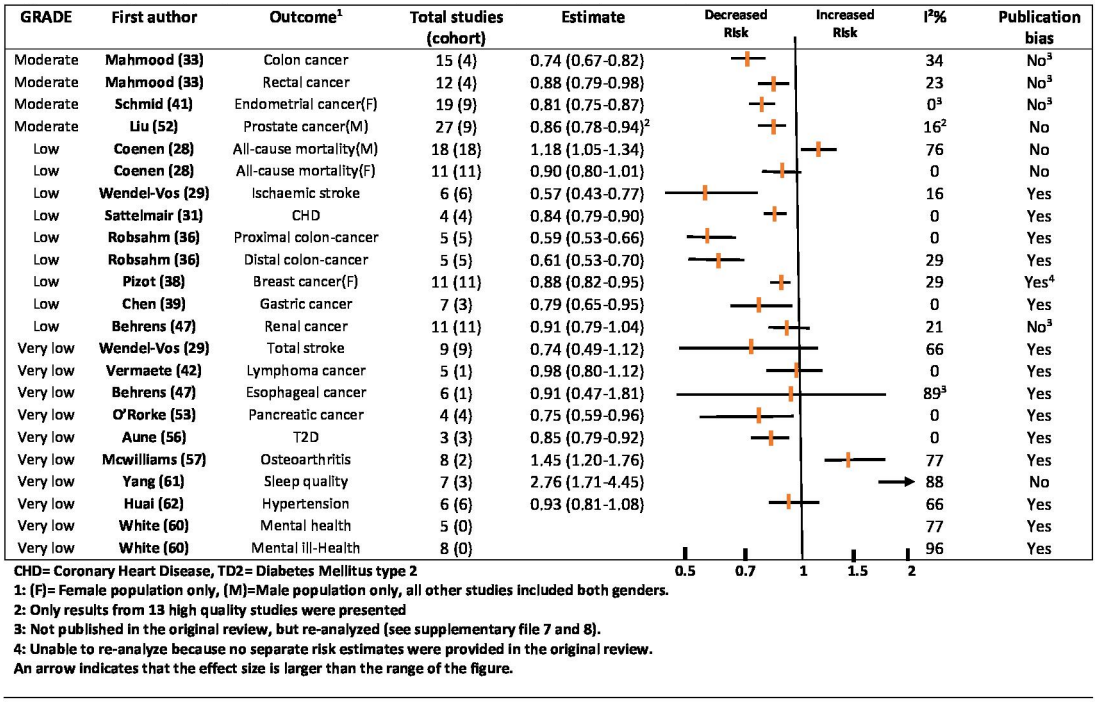


Figure 2 Forest plot depicting the evidence for the association of occupational physical activity and health. (1) (F)= Female population only, (M)=Male population only, all other studies included both genders. (2) Only results from 13 high-quality studies were presented. (3) Not published in the original review, but reanalysed (online supplemental files 7 and 8). (4) Unable to reanalyse because no separate risk estimates were provided in the original review. An arrow indicates that the effect size is larger than the range of the figure. CHD, coronary heart dsease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; TD2, diabetes mellitus type 2.

studies, showing a reduced risk in those with high compared with low OPA (RR 0.88, 95% CI 0.79 to 0.98). Another systematic review that investigated colon cancer subtypes, found comparable effects for proximal (RR 0.72, 95% CI 0.61 to 0.85) and distal colon cancer (RR 0.75, 95% CI 0.63 to 0.88).[36] In our sensitivity analysis, comparable associations were found for both colon cancer (and subtypes) and rectal cancer.[34]

A review on seven cohort and twelve case–control studies found a statistically significant risk reduction of endometrial cancer for women with high compared with low OPA (RR 0.81, 95% CI 0.75 to 0.87).[41] Another review showed comparable results.[40]

A review by Liu *et al*[52] showed that OPA was significantly related with a reduced risk of prostate cancer (RR 0.81, 95% CI 0.73 to 0.91). The reduction in risk was statistically significantly lower for nine cohort studies (RR 0.91, 95% CI 0.87 to 0.95) compared with eighteen case–control studies (RR 0.73, 95% CI 0.62 to 0.87). When stratified for study quality, the higher quality studies showed a lower reduced risk (RR 0.86, 95% CI 0.78 to 0.94) compared with lower quality studies (RR 0.75, 95% CI 0.89 to 1.00). A statistically significant protective effect of OPA only existed in those studies in which the median follow-up duration was >10 years. Comparable results were found in other systematic reviews.[50 51]

Low-quality evidence

In the most recent systematic review,[28] men with high level OPA experienced a statistically significant increased risk of all-cause mortality (HR 1.18, 95% CI 1.05 to 1.34), even after adjusting for possible confounders, such as LTPA. A non-significant reduced risk was observed among women (HR 0.90, 95% CI 0.80 to 1.01). Authors reported considerable heterogeneity in the pooled study findings for men (I^2 statistic=76%), but not for women (I^2 statistic=0%), and some risk of publication bias was discussed by the authors. An earlier review, with a lower number of included studies, showed a reduction in mortality risk for both genders[27] (RR 0.66, 95% CI 0.49 to 0.89 and RR 0.94, 95% CI 0.75 to 1.19, for females and males, respectively). In the this review, high heterogeneity was reported.

A higher level OPA was related to a lower risk of stroke; although, this association was not statistically significant for total stroke (RR 0.74, 95% CI 0.49 to 1.12).[29] In the association between OPA and ischaemic stroke, statistically significant protective effects were found for high vs low OPA (RR 0.57, 95% CI 0.43 to 0.77).

Sattelmair *et al* showed, based on evidence from four studies with low heterogeneity, that high versus low OPA was related to a statistically significant reduced risk of CHD (RR 0.84, 95% CI 0.79 to 0.90).[31] Three out of four studies were based on male samples only (RR 0.87, 95% CI 0.81 to 0.99).

Pizot *et al* observed that high OPA versus low OPA was related to a statistically significantly reduced risk of breast cancer in a female population (RR 0.88, 95% CI 0.82 to 0.95).[38] These results were based on eleven cohort studies with low heterogeneity. Two other reviews showed comparable results.[37 39]

Chen *et al* showed that high versus low OPA had a statistically significantly lower risk of gastric cancer (RR 0.79, 95% CI 0.65 to 0.95).[45] Behrens *et al* observed a statistically non-significant association between OPA and oesophageal cancer (RR 0.91, 95% CI 0.46 to 1.81).[46] Two other reviews found comparable results.[43 44]

Behrens *et al* found that high versus low OPA was related to a statistically non-significant reduction in renal cancer (RR 0.91, 95% CI 0.79 to 1.04). The authors estimated these results

from data of six cohort and five case–control studies[47] with low heterogeneity. Another review showed comparable results.[48]

OPA showed no association with lymphoma (OR 0.98, 95% CI 0.80 to 1.02) from a review with one cohort and four case–control studies.[42]

One review reported on the association between OPA and pancreatic cancer.[54] Three cohort studies showed a statistically significant reduction (RR 0.75, 95% CI 0.58 to 0.96). There was low heterogeneity between the included studies.

Three cohort studies with over 9000 diabetes mellitus type 2 cases showed a lower risk on this outcome (RR 0.85, 95% CI 0.79 to 0.92) for people with high versus low OPA.[56]

Pooled results from two cohort, three cross-sectional and three case–control studies showed that high OPA was related with a statistically significant higher risk of knee osteoarthritis (OR 1.45, 95% CI 1.20 to 1.76).[57] Authors of this review reported high heterogeneity and a high likelihood of publication bias. Cohort studies showed lower risks compared with cross-sectional and case–control studies. Another review showed that cumulative physical workloads were associated with hip osteoarthritis in men; this review showed mixed evidence for physical demands and knee osteoarthritis, hip osteoarthritis and osteoarthritis in multiple other joints.[58]

For high versus low OPA, there was an statistically significant increased risk of insomnia (OR 2.76, 95% CI 1.71 to 4.45),[61] with pooled results from four cross-sectional and three cohort studies, and high heterogeneity.

In comparison with low OPA, high OPA was related with a decreased, but statistically non-significant, risk of hypertension (RR 0.93, 95% CI 0.81 to 1.08).[62] The heterogeneity among six studies was high.

OPA had a weak positive association with mental ill-health (ie, depression and anxiety) (r 0.10, 95% CI 0.04 to 0.16), but also a weak positive association with mental health (ie, mental well-being and life satisfaction) (r 0.02, 95% CI −0.09 to 0.12).[60] Both effects showed high heterogeneity.

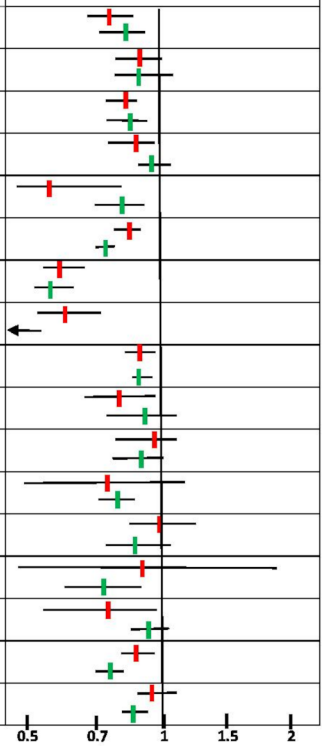
Health effects of occupational versus LTPA

In the included reviews, effect sizes of seventeen outcomes were available for both OPA and LTPA (figure 3). Effect sizes of both OPA and LTPA generally pointed into the same direction, with some differences in estimates provided for OPA and LTPA. The association between OPA and LTPA was statistically significant different for CHD, distal colon cancer and diabetes mellitus type 2. We could not compare OPA and LTPA for all-cause mortality, sleep quality and/or duration, osteoarthritis and mental (ill) health, because LTPA was not included in the reviews for these outcomes.

Dose–response associations

Only five outcomes, presented in three reviews, reported on dose–response associations (figure 4). Three outcomes (stroke, ischaemic stroke and hypertension) showed a gradual risk increase across three groups of OPA (high, moderate, low levels of OPA). For total stroke, the lowest risk reduction was shown for the moderately active vs inactive workers (RR 0.64, 95% CI 0.48 to 0.87). For ischaemic stroke, the most active workers

Outcome	Author (ref)	PA	Number of studies	Estimates
Colon Cancer	Mahmood (33) 2017	OPA	15	0.74 (0.67-0.82)
		LTPA	14	0.80 (0.71-0.90)
Rectal Cancer	Mahmood (33) 2017	OPA	12	0.88 (0.79-0.98)
		LTPA	9	0.87 (0.75-1.01)
Endometrial Cancer	Schmid (41) 2015	OPA	19	0.81 (0.75-0.87)
		LTPA	22	0.84 (0.78-0.91)
Prostate Cancer	Liu (52) 2011	OPA	27	0.86 (0.78-0.94)
		LTPA	34	0.95 (0.90-1.01)
Ischaemic stroke	Wendel-Vos (29) 2004	OPA	6	0.57 (0.43-0.76)
		LTPA	11	0.79 (0.69-0.91)
CHD	Sattelmair (31) 2011	OPA	4	0.84 (0.79-0.90)*
		LTPA	26	0.74 (0.70-0.79)*
Proximal colon	Robsahm (36) 2013	OPA	5	0.59 (0.53-0.66)
		LTPA	13	0.53 (0.44-0.64)
Distal colon	Robsahm (36) 2013	OPA	5	0.61 (0.53-0.70)*
		LTPA	13	0.40 (0.30-0.53)*
Breast cancer	Pizot (38) 2015	OPA	11	0.88 (0.82-0.95)
		LTPA	30	0.87 (0.84-0.91)
Gastric cancer	Chen (39) 2014	OPA	7	0.79 (0.65-0.95)
		LTPA	7	0.89 (0.74-1.06)
Renal cancer	Behrens (47) 2013	OPA	11	0.91 (0.79-1.04)
		LTPA	19	0.88 (0.77-1.00)
Stroke	Wendel-Vos (29) 2004	OPA	9	0.74 (0.49-1.12)
		LTPA	19	0.78 (0.71-0.85)
Lymphoma	Vermaete (42) 2013	OPA	5	0.98 (0.80-1.21)
		LTPA	8	0.86 (0.73-1.02)
Oesophageal	Behrens (47) 2014	OPA	6	0.91 (0.46-1.80)
		LTPA	10	0.72 (0.63-0.83)
Pancreatic cancer	O'Rorke (53) 2010	OPA	3	0.75 (0.59-0.96)
		LTPA	16	0.94 (0.88-1.01)
T2D	Aune (56) 2015	OPA	3	0.85 (0.79-0.92)*
		LTPA	56	0.74 (0.70-0.79)*
Hypertension	Hual (62) 2011	OPA	6	0.93 (0.81-1.07)
		LTPA	12	0.81 (0.77-0.86)



CHD= Coronary Heart Disease, T2D= Diabetes Mellitus type 2
*Effect of LTPA and OPA is statistically significantly different (p=<0.05).
An arrow indicates effect sizes that were out of range of our figure.

Figure 3 Forest plot depicting the evidence for the association of physical activity and health. Association for occupational and leisure-time physical activity are depicted. *Effect of LTPA and OPA is statistically significantly different (p≤0.05). An arrow indicates effect sizes that were out of range of our figure. CHD, coronary heart disease; LTPA, leisure-time physical activity; OPA, occupational physical activity; T2D, diabetes mellitus type 2.

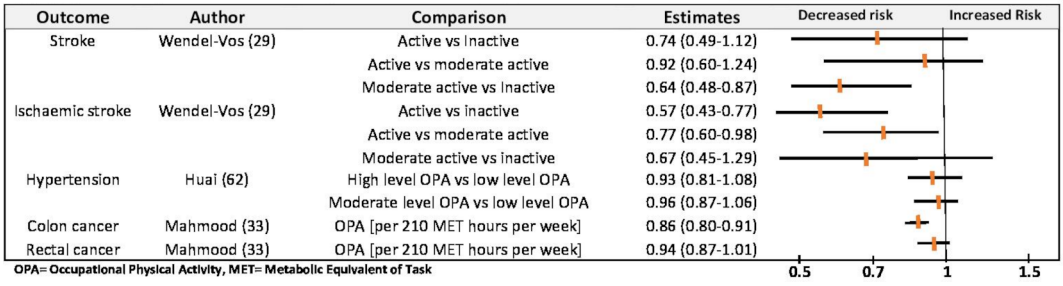


Figure 4 Dose–response associations for occupational physical activity and health. MET, metabolic equivalent of task; OPA, occupational physical activity.

category was found to have the highest reduced risk.[29] The results also showed that there was no evidence for an association between high-level or moderate-level OPA and hypertension.[62] Mahmood reported the pooled RR for colon cancer with an OPA level per 210 metabolic equivalent of task (MET) hour/week (RR 0.86, 95% CI 0.80 to 0.91). This effect was stronger for men (RR 0.82, 95% CI 0.76 to 0.88) than for women (RR 0.96, 95% CI 0.86 to 1.08). In the same review, the pooled RR with OPA level per 210 MET our/week for rectal cancer was (RR 0.94, 95% CI 0.87 to 1.01).[33]

DISCUSSION

Main findings

In this umbrella review, we summarised the evidence on the associations between OPA and 23 health-related outcomes based on 17 systematic reviews that included 158 individual studies. Engaging in high versus low OPA showed beneficial health effects for multiple cancer outcomes, stroke, CHD and mental health. In contrast, high versus low OPA showed unfavourable health outcomes regarding all-cause mortality in men, mental ill health, osteoarthritis and sleep duration and/or quality. For some outcomes, our results are inconclusive (ie, for several cancer outcomes, hypertension, all-cause mortality in females). We identified no reviews on adiposity, cognitive outcomes or health-related quality of life. The associations between OPA and health-related outcomes, for most outcomes, were not differential from that of LTPA in direction and/or magnitude. Although for three health outcomes we found a significant difference in magnitude (figure 3), LTPA showed a higher protective effect in distal colon cancer, CHD and diabetes type 2 than OPA. Reviews that reported unfavourable health outcomes for OPA (ie, all-cause mortality in men, osteoarthritis and sleep duration and/or sleep quality) did not report on LTPA, as a result of which we could not make a comparison between OPA and LTPA.

Only three reviews, addressing five outcomes, reported dose–response associations of OPA and health. We can, therefore, only make limited inferences on the health effects of the full OPA continuum. Higher OPA-specific energy expenditure was associated with a gradually reduced risk of colon cancer and to a lesser extent a reduced risk for rectal cancer. For hypertension and ischaemic stroke, the highest OPA groups were associated with the lowest risk (although non-significant for hypertension).

Interpretation of the results

In this umbrella review, we applied the GRADE method. Other criteria to evaluate the quality of evidence have been proposed in other reviews[13–15] and by other organisations.[63] Using such criteria could have possibly led to other results in the interpretation of the reviews identified in our umbrella review. None of the relationships we identified were supported by strong evidence (with moderate GRADE scores at best) and therefore results should be interpreted with caution. We only detected evidence from systematic reviews of observational studies, which bears a higher risk of selection bias and confounding.[64] All identified evidence suffers from risk of bias (eg, misclassification, publication bias and confounding bias) and reviews showed high heterogeneity and/or inconsistent results. Studies varied widely regarding the confounding variables that were considered and relevant variables such as socioeconomic status, body mass index and lifestyle factors (eg, smoking, alcohol and diet) were not addressed in every study. All reviews reported issues with the measurements of PA, specifically with the use of self-reported methods to assess OPA in all reviews and studies. Measuring OPA can be challenging as the occupational dose and intensity can fluctuate over time (eg, between days, weeks or seasons) and a general shift in OPA from physically demanding jobs to more sedentary occupations has been seen over the last decades.[65] As most studies of the current evidence base assessed OPA only at a single instance, changes over time were not considered, which could have led to misclassification. On the other hand, OPA could be less subjected to recall bias than LTPA because of the routine nature of OPA and relatively long (ie, sometimes livelong) exposure to OPA.[66] Self-reported PA may suffer from several biases[67 68] induced by socially desirable or culturally influenced answers; for example, variation across socioeconomic and demographic groups,[69] participants' inability to assess PA at different intensities and recall bias.[70] Arbitrary cut-off points (with heterogeneous definitions) to operationalise OPA categories were used and precision was reduced by using dichotomous OPA categories.

Most reviews were able to include a substantial number of studies on LTPA since reviews often had their main focus on either LTPA or total PA (ie, OPA and LTPA combined). Only limited evidence was available for OPA, sometimes from subgroup analyses only. In addition, reviews could or did not detect heterogeneity/publication bias for OPA. Some reviews did not draw any conclusions on OPA or stated that more evidence was needed on this topic. In contrast, reviews with a relatively high number of included studies on OPA showed the importance of subgroup analyses to provide more profound insight. The review about prostate cancer showed, for example, that higher quality studies had a lower reduced risk in comparison with lower quality studies; cohort studies showed a lower reduced risk in comparison with case–control studies.[52] In this review, a statistically significant beneficial health effect of OPA was only evident in studies with a long follow-up (median >10 years).[52] Coenen *et al* showed that high OPA was related to an increased risk of all-cause mortality for men, but a non-significant decreased risk for women.[28]

Sensitivity analyses were used to assess the consistency of the evidence when multiple reviews were available per health outcome. These analyses showed that almost all reviews provided comparable direction and magnitude of effect sizes. The two reviews on all-cause mortality, however, showed opposite effects. Coenen *et al* reported that the risk of all-cause mortality was higher for male workers,[28] while Samitz *et al* reported in an earlier review with fewer studies that men with higher OPA had a reduced risk of all-cause mortality.[27] While both reviews had a low GRADE-score, we synthesised the findings from the most recent review, which also included more studies.[28] The evidence was therefore considered to be more up to date. Nevertheless, while in the male population high level OPA was associated with all-cause mortality, other included reviews on the leading causes of death,[71] such as CVD and cancer outcomes, showed favourable health outcomes for high versus low OPA. The aforementioned and other methodological issues could partly explain these contradictory findings.[9 10] There are also several plausible physiological explanations as to why OPA might not confer the cardiovascular health benefits of LTPA.[8] For example, LTPA entails dynamic movements which is mostly performed voluntarily over short time periods with sufficient recovery time, while OPA is most often of too low intensity or of too long duration to be health beneficial.

Methodological strengths and limitations

We followed a systematic methodology including search strategy in electronic databases and independent study selection and extraction by two researchers. We also used standard approaches to assess the quality of methods (AMSTAR2) and to rate the quality of the evidence (GRADE). GRADE has increasingly been adopted by organisations worldwide for grading evidence and for guideline development.[20] Moreover, if a review did not report on heterogeneity (in terms of I^2 statistics) or publication bias (eg, using funnel plots), we reanalysed the available data, leading to more accurate GRADE scores.

A limitation of our umbrella review is that with the rapidly evolving body of evidence on the health effects of OPA, evidence may have only recently been published and as a consequence has not been summarised in reviews yet. For example, since the review by Coenen *et al* (with literature search until September 2017) at least six new studies reporting on all-cause mortality and OPA would have met the inclusion criteria for systematic reviews included in our umbrella review.[10] None of the systematic reviews included experimental studies, although some individual experimental studies addressed the relationship between OPA and health-related outcomes.[72 73] Experimental studies provide more insight into causality and deal with issues such as selection bias and confounding.

We included reviews that addressed OPA with at least an aerobic component and excluded reviews with only biomechanical (eg, lifting, kneeling) OPA components. We only included health-related outcomes prioritised by WHO (online supplemental material table 2); thereby excluding evidence on outcomes such as musculoskeletal and neurological disorders. The limitation of the exclusion of neurological outcomes seems to have hardly any influence on our findings. For example, Morgan *et al* could not provide any convincing evidence on the associations between OPA and dementia in later life.[74] Stephen *et al* showed that there was inconclusive evidence regarding the associations between OPA and Alzheimer's disease.[75] However, it is known that high biomechanical demands at work, such as lifting and heavy manual work, are associated with increased risk of musculoskeletal disorders such as low back, neck/shoulder and lower extremity pain.[76–78] We also reported on outcomes that are closely related (eg, colon cancer and rectal cancer) because they were addressed in separate systematic reviews.[33 34 36]

Implications for future research

WHO guidelines on PA and sedentary behaviour (2020) state that more evidence is needed on the health effects of occupational OPA.[79] We recommend that further research addressing OPA should be based on more sophisticated OPA assessments (eg, using a combination of device measured PA and a diary to distinguish domains of PA). This will help to address biases due to self-reports and can additionally measure PA metrics, such as intensity, duration and frequency.[10] Second, we recommend that reviews and prospective cohort studies examine health effects by PA domains, so that possible differential health effects of LTPA and OPA can further be explored. Third, to get a better understanding of the health-related outcomes of OPA, it is important to consider biomechanical demands at work and musculoskeletal disorders. Particularly since musculoskeletal disorders, such as (low) back and neck pain, result in considerable healthcare spending,[80] as well as substantial indirect cost due to presenteeism and absenteeism,[81] and are among the leading causes of disability worldwide.[82 83] To increase the quality of evidence, more experimental studies comparing OPA with health-related outcomes should be conducted and included in systematic reviews. Lastly, we urge researchers to conduct subgroup analyses, if possible (such as for gender), since these seem to provide a more thorough understanding of the health effects of OPA.

Implications for practice

High-quality evidence on the relationship between LTPA and the prevention of non-communicable diseases is available and has been incorporated in national and global guidelines.[3] WHO guidelines advise that some PA is better than none and recommend working age adults to engage in at least 150–300 min of moderate-intensity PA per week. The recommended amounts of PA can be done as part of leisure, transportation, work and household activities.[79]

There is inconclusive evidence of very low to moderate quality for OPA to provide comparable beneficial health effects to LTPA. At this point, there is a need for better quality evidence to provide a unequivocal statement on the health effects of OPA.

As the evidence base develops, a more nuanced message concerning the health effects of OPA may be possible. Such a nuanced message will be relevant to large parts of the working population, in particular, those from low socioeconomic groups and people in low-income and middle-income countries who do most of their daily PA at work.[84 85] Although more high-quality evidence is still needed on health effects of OPA, OPA holds many workers back from engaging in sufficient LTPA due to fatigue and exertion from work, and therefore, it may limit the beneficial health effects of engaging in LTPA for a large fraction of the adult population.[86]

CONCLUSION

We found that high OPA has favourable health associations with most health-related outcomes (multiple cancer outcomes, stroke, CHD and mental health). Other reviews showed unfavourable health associations with high OPA levels (all-cause mortality in men, mental ill health, osteoarthritis and poor sleep duration and/or quality).

Included reviews were of very low to moderate quality. To increase the quality, future research should focus on sophisticated PA measurements, include relevant confounders such as socioeconomic status, lifestyle factors and other types of PA and regular updating of existing systematic reviews. Improved research will lead to a better understanding of the associations between OPA and health-related outcomes.

What is already known

- Adequate physical activity (PA) prevents a range of lifestyle-related, non-communicable diseases.
- It is uncertain if all domains of PA have comparable health effects, with some evidence suggesting that leisure time PA (LTPA) and occupational PA (OPA) may have differential health effects.
- Methodological issues or differences posture, intensity level, frequency, duration and/or recovery time between OPA and LTPA could explain these differential health effects of different PA domains.

What are the new findings

- This umbrella review, which is the first of its kind, suggests that high occupational physical activity (OPA) was beneficial for most health outcomes including coronary heart disease and several cancers.
- High OPA showed unfavourable associations with all-cause mortality in men, mental ill health, osteoarthritis and sleep duration and/or quality.
- This review synthesised a heterogeneous evidence base of very low to moderate quality, highlighting the need for better quality research in this area.

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Competing interests For the avoidance of doubt, WvM wishes to declare that he is a non-executive board member of Arbo Unie B.V. WvM and AJvdB are director and advisor, respectively, of Evalua Nederland B.V. Both Arbo Unie and Evalua Nederland operate in the Dutch occupational healthcare market.

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REFERENCES

1 U.S. Department of Health and Human Services. *Physical activity guidelines for Americans. in: services DoHaH, editor. physical activity guidelines for Americans 2018*. Washington,DC, 2018.
2 Organization WH. *Global recommendations on physical activity for health*. Geneva: World Health Organization, 2010.
3 World Health Organiszation. *Global action plan for the prevention and control of noncommunicable diseases 2013-2020*. WHO, editor. Geneva, 2013.
4 Bull F A-AS, Biddle S, Borodulin K, *et al*. Guidelines on physical activity and sedentary behaviour. *Br J Sports Med*. In Press 2020.
5 Clays E, Lidegaard M, De Bacquer D, *et al*. The combined relationship of occupational and leisure-time physical activity with all-cause mortality among men, accounting for physical fitness. *Am J Epidemiol* 2014;179:559–66.
6 Harari G, Green MS, Zelber-Sagi S. Combined association of occupational and leisure-time physical activity with all-cause and coronary heart disease mortality among a cohort of men followed-up for 22 years. *Occup Environ Med* 2015;72:617–24.
7 Richard A, Martin B, Wanner M, *et al*. Effects of leisure-time and occupational physical activity on total mortality risk in NHANES III according to sex, ethnicity, central obesity, and age. *J Phys Act Health* 2015;12:184–92.
8 Holtermann A, Krause N, van der Beek AJ, *et al*. The physical activity paradox: six reasons why occupational physical activity (opa) does not confer the cardiovascular health benefits that leisure time physical activity does. *Br J Sports Med* 2018;52:149–50.
9 Shephard RJ. Is there a 'recent occupational paradox' where highly active physically active workers die early? Or are there failures in some study methods? *Br J Sports Med* 2019;53:1557–9.
10 Coenen P, Huysmans MA, Holtermann A, *et al*. Towards a better understanding of the 'physical activity paradox': the need for a research agenda. *Br J Sports Med* 2020;54:1055–7.
11 Bastian H, Glasziou P, Chalmers I. Seventy-Five trials and eleven systematic reviews a day: how will we ever keep up? *PLoS Med* 2010;7:e1000326.
12 Aromataris E, Fernandez R, Godfrey CM, *et al*. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. *Int J Evid Based Healthc* 2015;13:132–40.
13 Rezende LFMde, Sá THde, Markozannes G, *et al*. Physical activity and cancer: an umbrella review of the literature including 22 major anatomical sites and 770 000 cancer cases. *Br J Sports Med* 2018;52:826–33.
14 Erickson KI, Hillman C, Stillman CM, *et al*. Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines. *Med Sci Sports Exerc* 2019;51:1242–51.
15 Dipietro L, Evenson KR, Bloodgood B, *et al*. Benefits of physical activity during pregnancy and postpartum: an umbrella review. *Med Sci Sports Exerc* 2019;51:1292–302.
16 PROSPERO. PROSPERO registration; the evidence on the associaton between occupational physical activity and healh; an umbrella review, 2020. Available: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=163090
17 Ouzzani M, Hammady H, Fedorowicz Z, Mourad Ouzzani H, *et al*. Rayyan—a web and mobile APP for systematic reviews. *Syst Rev* 2016;5.
18 Shea BJ, Reeves BC, Wells G, *et al*. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;358:j4008.
19 Shea BJ, Hamel C, Wells GA, *et al*. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. *J Clin Epidemiol* 2009;62:1013–20.
20 Guyatt GH, Oxman AD, Vist GE, *et al*. Grade: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
21 Huguet A, Hayden JA, Stinson J, *et al*. Judging the quality of evidence in reviews of prognostic factor research: adapting the grade framework. *Syst Rev* 2013;2:71.
22 van der Molen HF, Foresti C, Daams JG, *et al*. Work-Related risk factors for specific shoulder disorders: a systematic review and meta-analysis. *Occup Environ Med* 2017;74:745–55.
23 Guyatt GH, Oxman AD, Kunz R, *et al*. What is "quality of evidence" and why is it important to clinicians? *BMJ* 2008;336:995–8.
24 Higgins JPT, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
25 Sterne JAC, Sutton AJ, Ioannidis JPA, *et al*. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:d4002.
26 Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ* 2003;326:219.
27 Samitz G, Egger M, Zwahlen M. Domains of physical activity and all-cause mortality. systematic review and dose-response meta-analysis of cohort studies. *Gynakologische Praxis* 2012;36:137–43.

28 Coenen P, Huysmans MA, Holtermann A, *et al*. Do highly physically active workers die early? A systematic review with meta-analysis of data from 193 696 participants. *Br J Sports Med* 2018;52:1320–6.
29 Wendel-Vos GCW, Schuit AJ, Feskens EJM, *et al*. Physical activity and stroke. A meta-analysis of observational data. *Int J Epidemiol* 2004;33:787–98.
30 Li J, Loerbroks A, Angerer P. Physical activity and risk of cardiovascular disease: what does the new epidemiological evidence show? *Curr Opin Cardiol* 2013;28:575–83.
31 Sattelmair J, Pertman J, Ding EL, *et al*. Dose response between physical activity and risk of coronary heart disease: a meta-analysis. *Circulation* 2011;124:789–95.
32 Wolin KY, Yan Y, Colditz GA, *et al*. Physical activity and colon cancer prevention: a meta-analysis. *Br J Cancer* 2009;100:611–6.
33 Mahmood S, MacInnis RJ, English DR, *et al*. Domain-Specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: a systematic review and meta-analysis. *Int J Epidemiol* 2017;46:1797–813.
34 Boyle T, Keegel T, Bull F, *et al*. Physical activity and risks of proximal and distal colon cancers: a systematic review and meta-analysis. *J Natl Cancer Inst* 2012;104:S332–3.
35 Samad AKA, Taylor RS, Marshall T, *et al*. A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. *Colorectal Dis* 2005;7:204–13.
36 Robsahm TE, Aagnes B, Hjartåker A, *et al*. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. *Eur J Cancer Prev* 2013;22:492–505.
37 Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. *Breast Cancer Res Treat* 2013;137:869–82.
38 Pizot C, Boniol M, Mullie P, *et al*. Physical activity, hormone replacement therapy and breast cancer risk: a meta-analysis of prospective studies. *Eur J Cancer* 2016;52:138–54.
39 Chen X, Wang Q, Zhang Y, *et al*. Physical activity and risk of breast cancer: a meta-analysis of 38 cohort studies in 45 study reports. *Value Health* 2019;22:104–28.
40 Voskuil DW, Monninkhof EM, Elias SG, *et al*. Physical activity and endometrial cancer risk, a systematic review of current evidence. *Cancer Epidemiol Biomarkers Prev* 2007;16:639–48.
41 Schmid D, Behrens G, Keimling M, *et al*. A systematic review and meta-analysis of physical activity and endometrial cancer risk. *Eur J Epidemiol* 2015;30:397–412.
42 Vermaete NVH, Wolter P, Verhoef GEG, *et al*. Physical activity and risk of lymphoma: a meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2013;22:1173–84.
43 Singh S, Devanna S, Edakkanambeth Varayil J, *et al*. Physical activity is associated with reduced risk of esophageal cancer, particularly esophageal adenocarcinoma: a systematic review and meta-analysis. *BMC Gastroenterol* 2014;14:101.
44 Psaltopoulou T, Ntanasis-Stathopoulos I, Tzanninis I-G, *et al*. Physical activity and gastric cancer risk: a systematic review and meta-analysis. *Clin J Sport Med* 2016;26:445–64.
45 Chen Y, Yu C, Li Y. Physical activity and risks of esophageal and gastric cancers: a meta-analysis. *PLoS One* 2014;9:e88082.
46 Behrens G, Jochem C, Keimling M, *et al*. The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis. *Eur J Epidemiol* 2014;29:151–70.
47 Behrens G, Leitzmann MF. The association between physical activity and renal cancer: systematic review and meta-analysis. *Br J Cancer* 2013;108:798–811.
48 Shephard RJ. Can habitual physical activity contribute to reducing the health burden of renal cancer? *IJASS* 2016;28:148–63.
49 Krstev S, Knutsson A. Occupational risk factors for prostate cancer: a meta-analysis. *J Cancer Prev* 2019;24:91–111.
50 Benke IN, Leitzmann MF, Behrens G, *et al*. Physical activity in relation to risk of prostate cancer: a systematic review and meta-analysis. *Ann Oncol* 2018;29:1154–79.
51 Shephard RJ. Physical activity and prostate cancer: an updated review. *Sports Med* 2017;47:1055–73.
52 Liu Y, Hu F, Li D, *et al*. Does physical activity reduce the risk of prostate cancer? A systematic review and meta-analysis. *Eur Urol* 2011;60:1029–44.
53 O'Rorke MA, Cantwell MM, Cardwell CR, *et al*. Can physical activity modulate pancreatic cancer risk? A systematic review and meta-analysis. *Int J Cancer* 2010;126:NA–68.
54 Bao Y, Michaud DS. Physical activity and pancreatic cancer risk: a systematic review. *Cancer Epidemiol Biomarkers Prev* 2008;17:2671–82.
55 Keimling M, Behrens G, Schmid D, *et al*. The association between physical activity and bladder cancer: systematic review and meta-analysis. *Br J Cancer* 2014;110:1862–70.
56 Aune D, Norat T, Leitzmann M, *et al*. Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. *Eur J Epidemiol* 2015;30:529–42.
57 McWilliams DF, Leeb BF, Muthuri SG, *et al*. Occupational risk factors for osteoarthritis of the knee: a meta-analysis. *Osteoarthritis Cartilage* 2011;19:829–39.
58 Gignac MAM, Irvin E, Cullen K, *et al*. 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. *Arthritis Care Res* 2020;72:378–96.
59 Palmer KT. Occupational activities and osteoarthritis of the knee. *Br Med Bull* 2012;102:147–70.
60 White RL, Babic MJ, Parker PD, *et al*. Domain-Specific physical activity and mental health: a meta-analysis. *Am J Prev Med* 2017;52:653–66.
61 Yang B, Wang Y, Cui F, *et al*. Association between insomnia and job stress: a meta-analysis. *Sleep Breath* 2018;22:1221–31.
62 Huai P, Xun H, Reilly KH, *et al*. Physical activity and risk of hypertension: a meta-analysis of prospective cohort studies. *Hypertension* 2013;62:1021–6.
63 WCRFAIfC R. *Food, nutrition, physical activity, and the prevention of cancer:a global perspective*. Washington, DC: American Institute for Cancer Research, 2007.
64 Renjith V. Blinding in randomized controlled trials: what researchers need to know? *Manipal J Nurs Health Sci* 2017;3:45–50.
65 Church TS, Thomas DM, Tudor-Locke C, *et al*. Trends over 5 decades in U.S. occupation-related physical activity and their associations with obesity. *PLoS One* 2011;6:e19657.
66 Mantel N. Avoidance of bias in cohort studies. *Natl Cancer Inst Monogr* 1985;67:169–72.
67 Prince SA, Adamo KB, Hamel ME, *et al*. A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *Int J Behav Nutr Phys Act* 2008;5:56.
68 Shephard RJ. Limits to the measurement of habitual physical activity by questionnaires. *Br J Sports Med* 2003;37:197–206.
69 Kapteyn A, Banks J, Hamer M, *et al*. What they say and what they do: comparing physical activity across the USA, England and the Netherlands. *J Epidemiol Community Health* 2018;72:471–6.
70 Skender S, Ose J, Chang-Claude J, *et al*. Accelerometry and physical activity questionnaires - a systematic review. *BMC Public Health* 2016;16:515.
71 Hannah Ritchie MR. Causes of death, 2020. Available: https://ourworldindataorg/causes-of-death
72 Korshøj M, Krause N, Clays E, *et al*. Does aerobic exercise increase 24-hour ambulatory blood pressure among workers with high occupational physical activity?—a RCT. *Am J Hypertens* 2017;30:444–50.
73 Korshøj M, Ravn MH, Holtermann A, *et al*. Aerobic exercise reduces biomarkers related to cardiovascular risk among cleaners: effects of a worksite intervention RCT. *Int Arch Occup Environ Health* 2016;89:239–49.
74 Morgan GS, Gallacher J, Bayer A, *et al*. 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. *J Alzheimers Dis* 2012;31:569–80.
75 Stephen R, Hongisto K, Solomon A, *et al*. Physical activity and Alzheimer's disease: a systematic review. *J Gerontol A Biol Sci Med Sci* 2017;72:733–9.
76 Coenen P, Gouttebarge V, van der Burght ASAM, *et al*. The effect of lifting during work on low back pain: a health impact assessment based on a meta-analysis. *Occup Environ Med* 2014;71:871–7.
77 Lötters F, Burdorf A, Kuiper J, *et al*. Model for the work-relatedness of low-back pain. *Scand J Work Environ Health* 2003;29:431–40.
78 Coenen P, Willenberg L, Parry S, *et al*. Associations of occupational standing with musculoskeletal symptoms: a systematic review with meta-analysis. *Br J Sports Med* 2018;52:176–83.
79 World Health Organization. Public consultation on the draft WHO guidelines on physical activity and sedentary behaviour for children and adolescents adults and older adults, 2020. Available: https://www.who.int/news-room/articles-detail/public-consultation-on-the-draft-who-guidelines-on-physical-activity-and-sedentary-behaviour-for-children-and-adolescents-adults-and-older-adults-20202020
80 Dieleman JL, Cao J, Chapin A, *et al*. Us health care spending by payer and health condition, 1996-2016. *JAMA* 2020;323:863–84.
81 Lambeek LC, van Tulder MW, Swinkels ICS, *et al*. The trend in total cost of back pain in the Netherlands in the period 2002 to 2007. *Spine* 2011;36:1050–8.
82 Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the global burden of disease study 2013. *Lancet* 2015;386:743–800.
83 Clark S, Horton R. Low back pain: a major global challenge. *Lancet* 2018;391:2302.
84 Beenackers MA, Kamphuis CBM, Giskes K, *et al*. Socioeconomic inequalities in occupational, leisure-time, and transport related physical activity among European adults: a systematic review. *Int J Behav Nutr Phys Act* 2012;9:116.
85 Guthold R, Stevens GA, Riley LM, *et al*. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1·9 million participants. *Lancet Glob Health* 2018;6:e1077–86.
86 Rasmussen CL, Palarea-Albaladejo J, Bauman A, *et al*. Does physically Demanding work hinder a physically active lifestyle in low socioeconomic workers? A compositional data analysis based on Accelerometer data. *Int J Environ Res Public Health* 2018;15:1306.

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 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")	5.728

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	4756

	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'	

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 “po OR "pooled data")oled analyses”)	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

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

No.	Query	Items found
#3	#1 AND #2	122
#2	(cochrane review OR ''systematic review'' OR meta analysis) Published Date: -20191231	175.427
#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') AND TI (cochrane review OR ''systematic review'' OR meta analysis) Published Date: -20191231	4859

Supplementary material 2: Health-related outcomes addressed by WHO

The WHO Guideline Development Group decided on the scope of their guidelines to use PICO (Population-Intervention-Control-Outcome) questions.

Population: Adults (18-64years), Working population
Exposure: Greater volume, duration, frequency or intensity of Occupational Physical Activity.
Comparison: No Occupational Physical Activity or a lesser volume, duration, frequency or intensity.

Outcomes	Importance
All cause of mortality	**Critical**
Cardio Vascular Disease	**Critical**
Cancer	**Critical**
Diabetes type 2	**Critical**
Osteoarthritis	**Critical**
Adiposity/Prevention of weight gain	**Critical**
Cognitive outcomes (dementia, cognition)	**Critical**
Mental Health problems	**Critical**
Health Related quality of life	**Important**
Hypertension	**Important**
Sleep duration and quality	**Important**

Supplementary material 3: Included studies for main and sensitivity analyses.

			Number of studies					Random effect model performed in the original meta-analysis*	
Author	**Year**	**Outcome**	**Cohort**	**Case-Control**	**Total**	**Selection discussion**	**Reason for exclusion**	**RR/OR/HR (High vs low)**	**95%CI**
All-cause mortality									
Coenen et al. (1)	2018	All-cause mortality	17	0	17	Included		Males= **HR=1.18** Females= **HR=0.90**	Males= **(1.05-1.34)** Females= **(0.80-1.01)**
Samitz G et al. (2)	2012	All-cause mortality	6	0	6	Included sensitivity analyses **Excluded (Funnel plot)**	Fewer studies than Coenen et al.	Both **OR=0.83** Males= **OR=0.94** Females= **OR=0.66**	Both **(0.71-0.97)** Males= **(0.75-1.19)** Females= **(0.49-0.89)**
Cardio-vascular diseases									
Wendel-Vos et al. (3)	2004	Stroke	11	0	11	Included		Stroke= *Physical active vs inactive* **RR=0.74** *Physical active vs moderate* **RR= 0.92** Ischemic stroke= *Physical active vs inactive* **RR= 0.57** *Physical active vs moderate* **RR= 0.84**	**(0.49-1.12)** **(0.68-1.24)** **(0.43-0.77)** **(0.60-0.98)**

Sattelmair et al. (4)	2011	Coronary Heart Disease	4	0	4	Included		CHD **RR=0.84**	**0.79-0.90**
Li J et al. (5)	2013	CVD/CHD/Unclassified CVD	-	-	-	Excluded	Critically low AMSTAR	**-**	
Colon cancer									
Mahmood et al. (6)	2017	Colon cancer	10	5	15	Included		**RR=0.74**	**(0.67-0.82)**
Robsahm et al. (7)	2013	Proximal Distal	5	0	5	Included		Proximal colon cancer **RR=0.59** Distal Colon cancer **RR=0.61**	**(0.53-0.66)** **(0.53-0.70)**
Boyle et al. (8)	2012	Proximal Distal	6	4	10	Included sensitivity analyses **Excluded (Funnel plot)**	Lower AMSTAR score than Boyle	Proximal colon **RR=0.72** Distal colon **RR=0.75**	**(0.61-0.85)** **(0.66-0.83)**
Wolin et al. (9)	2009	Colon cancer	-	-	-	Excluded	Critically low AMSTAR score		
Samad et al. (10)	2005	Colon cancer	-	-	-	Excluded	Critically low AMSTAR score		
Rectal cancer									
Mahmood et al . (6)	2017	Rectal cancer	5	7	12	Included		**RR=0.88**	**(0.79-0.98)**
Robsahm et al. (7)	2013	Rectal cancer	3	0	3	Included sensitivity analyses **Excluded (Funnel plot)**	Fewer studies included than Mahmood.	**RR=0.80**	**(0.72-0.89)**
Breast cancer									
Pizot et al. (11)	2015	Breast cancer	11	0	11	Included		**RR=0.88**	**(0.82-0.95)**
Chen et al (12)	2019	Breast cancer	6	0	6	Included sensitivity analyses **Excluded (Funnel plot)**	Fewer studies included than Pizot.	**RR=0.91**	**(0.84-0.99)**
Wu Y et al (13)	2013	Breast cancer	7	0	7	Included sensitivity analyses	Fewer studies included than Pizot	**RR=0.90**	**0.83-0.97)**

						Excluded (Funnel plot)			
Endometrial cancer									
Schmid et al. (14)	2015	Endometrial cancer	12	7	19	Included		**RR-0.81**	**0.75-0.87**
Voskuil et al. (15)	2007	Endometrial cancer	4	10	14	Included sensitivity analyses **Excluded (Funnel plot)**	Fewer studies included than Pizot, and lower GRADE score	Case Control studies **0.80** Cohort studies **Not estimated**	**0.66-0.96**
Lymphoma									
Vermaete et al. (16)	2013	Lymphoma	1	4	5	Included		**OR=0.98**	**(0.80-1.21)**
Gastric cancer									
Chen et al. (17)	2014	Gastric	3	3	6	Included		**RR=0.79**	**(0.65-0.95)**
Behrens et al. (18)	2014	Gastric	4	3	7	Included sensitivity analyses **Excluded (Funnel plot)**	Lower GRADE score than Chen	**RR=0.84**	**(0.70-1.02)**
Singh et al. (19)	2014	Gastric	2	4	6	Included sensitivity analyses **Excluded (Funnel plot)**	Lower GRADE score than Chen	**OR=0.90**	**(0.69-1.18)**
Psaltopoulou et al. (20)	2016	Gastric	2	3	5	Included sensitivity analyses **Excluded (Funnel plot)**	Lower GRADE score than Chen	**RR=0.89**	**(0.62-1.27)**
Oesophageal cancer									
Behrens et al. (18)	2014	Oesophageal	4	2	6	Included		**RR=0.91**	**(0.46-1.81)**
Chen et al. (17)	2014	Oesophageal	-	-	-	Excluded	Not enough studies about oesophageal		
Renal									

Behrens et al. (21)	2013	Renal	6	5	11	Included		**RR=0.91**	**(0.79-1.04)**
Shephard et al. (22)	2016	Renal	7	7	14	Included sensitivity analyses **Excluded (Funnel plot)**	Did not provide meta-analyses	No meta-analyses only narrative	
Prostate									
Liu et al. (23)	2011	Prostate	9	18	27	Included		Combined **RR=0.81** Cohort **RR= 0.91** Case control **RR= 0.71** High quality studies (13) **RR = 0.86** Low quality studies **RR 0.75**	**(0.73-0.91)** **(0.87-0.95)** **(0.62-0.87)** **(0.78-0.94)** **(0.61-0.94)**
Benke et al. (24).	2018	Prostate	28	-	-	Included sensitivity analyses **Excluded (Funnel plot)**	Lower GRADE score than Liu	Overall **RR=0.91** Long term (10 years) **RR=0.83**	**(0.82-1.01)** **(0.71-0.98)**
Shephard et al. (25)	2017	Prostate	19	16	35	Included sensitivity analyses **Excluded (Funnel plot)**	Lower GRADE score than Liu	No meta analyis	
Krstev et al. (26)	2019	Prostate	-	-	-	Excluded	Excluded because of critically low AMSTAR	-	
Pancreatic cancer									
O Rorke et al. (27)	2010	Pancreatic	4	-	4	Included		**RR=0.75**	**(0.59-0.96)**
Bao et al (28)	2008	Pancreatic	3	-	3	Included sensitivity analyses	Lower included studies	**RR=0.75**	**(0.58-0.96)**

						Excluded (funnel plots)			
Bladder cancer									
Keimling et al. (29)	2014	Bladder cancer	-	-	-	Excluded	Excluded because of critically low AMSTAR	-	-
Diabetes Mellitus type 2									
Aune et al. (30)	2015	Diabetes type 2	3	0	3	Included		**RR=0.85**	**(0.79-0.92)**
Osteoarthritis									
McWilliams (31)	2011	Knee osteoarthritis	2	6	8	Included		Knee osteoarthritis **OR=1.45**	**(1.20-1.76)**
Gignac et al. (32)	2019	Osteoarthritis	6	2	3	Included sensitivity analyses **Excluded (Funnel plot)**	No-meta analysis	-	
Palmer et al (33)	2012	Osteoarthritis	-	-	-	Excluded	Excluded because of critically low AMSTAR		
Mental Health									
White et al. (34)	2017	Mental-Health Mental-Ill Health	1	12	13	Included		Mental ill-health ***R=0.10*** Mental health **R=0.13**	**(0.04-0.16)** **(0.08-0.18)**
Insomnia									
Yang (35)	2018	Insomnia	3	4	7	Included		**OR=2.76**	**(1.71-4.45)**
Hypertension									
Haui (36)	2013	Hypertension	6	0	6	Included		High level OPA **RR=0.93** Moderate level OPA **RR=0.96**	**(0.81-1.08)** **(0.87-1.06)**

References

1. Coenen P, Huysmans MA, Holtermann A, Krause N, van Mechelen W, Straker LM, et al. Do highly physically active workers die early? A systematic review with meta-analysis of data from 193 696 participants. British journal of sports medicine. 2018;52(20):1320-6.
2. Samitz G, Egger M, Zwahlen M. Domains of physical activity and all-cause mortality. Systematic review and dose-response meta-analysis of cohort studies. Gynakologische Praxis. 2012;36(1):137-43.
3. Wendel-Vos GC, Schuit AJ, Feskens EJ, Boshuizen HC, Verschuren WM, Saris WH, et al. Physical activity and stroke. A meta-analysis of observational data. International journal of epidemiology. 2004;33(4):787-98.
4. Sattelmair J, Pertman J, Ding EL, Kohl HW, 3rd, Haskell W, Lee IM. Dose response between physical activity and risk of coronary heart disease: a meta-analysis. Circulation. 2011;124(7):789-95.
5. Li J, Loerbroks A, Angerer P. Physical activity and risk of cardiovascular disease: What does the new epidemiological evidence show? Current opinion in cardiology. 2013;28(5):575-83.
6. Mahmood S, MacInnis RJ, English DR, Karahalios A, Lynch BM. Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: A systematic review and meta-analysis. International journal of epidemiology. 2017;46(6):1797-813.
7. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP). 2013;22(6):492-505.
8. Boyle T, Keegel T, Bull F, Heyworth J, Fritschi L. Physical activity and the risk of proximal colon and distal colon cancers: A systematic review and meta-analysis. Journal of science and medicine in sport. 2012;15:S332-S3.
9. Wolin KY, Yan Y, Colditz GA, Lee IM. Physical activity and colon cancer prevention: a meta-analysis. British journal of cancer. 2009;100(4):611-6.
10. Samad AK, Taylor RS, Marshall T, Chapman MA. A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland. 2005;7(3):204-13.
11. Pizot C, Boniol M, Mullie P, Koechlin A, Boniol M, Boyle P, et al. Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of prospective studies. European Journal of Cancer. 2016;52:138-54.
12. Chen X, Wang Q, Zhang Y, Xie Q, Tan X. Physical Activity and Risk of Breast Cancer: A Meta-Analysis of 38 Cohort Studies in 45 Study Reports. Value in Health. 2019;22(1):104-28.
13. Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. Breast cancer research and treatment. 2013;137(3):869-82.
14. Schmid D, Behrens G, Keimling M, Jochem C, Ricci C, Leitzmann M. A systematic review and meta-analysis of physical activity and endometrial cancer risk. European journal of epidemiology. 2015;30(5):397-412.
15. Voskuil DW, Monninkhof EM, Elias SG, Vlems FA, Van Leeuwen FE. Physical activity and endometrial cancer risk, a systematic review of current evidence. Cancer Epidemiology Biomarkers and Prevention. 2007;16(4):639-48.
16. Vermaete NV, Wolter P, Verhoef GE, Kollen BJ, Kwakkel G, Schepers L, et al. Physical activity and risk of lymphoma: a meta-analysis. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2013;22(7):1173-84.
17. Chen Y, Yu C, Li Y. Physical activity and risks of esophageal and gastric cancers: a meta-analysis. PloS one. 2014;9(2):e88082.
18. Behrens G, Jochem C, Keimling M, Ricci C, Schmid D, Leitzmann MF. The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis. European journal of epidemiology. 2014;29(3):151-70.

19. Singh S, Devanna S, Edakkanambeth Varayil J, Murad MH, Iyer PG. Physical activity is associated with reduced risk of esophageal cancer, particularly esophageal adenocarcinoma: A systematic review and meta-analysis. BMC gastroenterology. 2014;14(1).
20. Psaltopoulou T, Ntanasis-Stathopoulos I, Tzanninis I-G, Kantzanou M, Georgiadou D, Sergentanis TN. Physical Activity and Gastric Cancer Risk: A Systematic Review and Meta-Analysis. Clinical Journal of Sport Medicine. 2016;26(6):445-64.
21. Behrens G, Leitzmann MF. The association between physical activity and renal cancer: systematic review and meta-analysis. British journal of cancer. 2013;108(4):798-811.
22. Shephard RJ. Can habitual physical activity contribute to reducing the health burden of renal cancer? IJASS(International Journal of Applied Sports Sciences). 2016;28(2):148-63.
23. Liu Y, Hu F, Li D, Wang F, Zhu L, Chen W, et al. Does physical activity reduce the risk of prostate cancer? A systematic review and meta-analysis. European urology. 2011;60(5):1029-44.
24. Benke IN, Leitzmann MF, Behrens G, Schmid D. Physical activity in relation to risk of prostate cancer: A systematic review and meta-analysis. Annals of Oncology. 2018;29(5):1154-79.
25. Shephard R. Physical Activity and Prostate Cancer: An Updated Review. Sports Medicine. 2017;47(6):1055-73.
26. Krstev S, Knutsson A. Occupational Risk Factors for Prostate Cancer: A Meta-analysis. Journal of cancer prevention. 2019;24(2):91-111.
27. O'Rorke MA, Cantwell MM, Cardwell CR, Mulholland HG, Murray LJ. Can physical activity modulate pancreatic cancer risk? A systematic review and meta-analysis. International journal of cancer. 2010;126(12):2957-68.
28. Bao Y, Michaud DS. Physical activity and pancreatic cancer risk: A systematic review. Cancer Epidemiology Biomarkers and Prevention. 2008;17(10):2671-82.
29. Keimling M, Behrens G, Schmid D, Jochem C, Leitzmann MF. The association between physical activity and bladder cancer: Systematic review and meta-analysis. British journal of cancer. 2014;110(7):1862-70.
30. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis. European journal of epidemiology. 2015;30(7):529-42.
31. McWilliams DF, Leeb BF, Muthuri SG, Doherty M, Zhang W. Occupational risk factors for osteoarthritis of the knee: A meta-analysis. Osteoarthritis and cartilage. 2011;19(7):829-39.
32. Gignac MAM, Irvin E, Cullen K, Van Eerd D, Beaton DE, Mahood Q, et al. 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. Arthritis care & research. 2019.
33. Palmer KT. Occupational activities and osteoarthritis of the knee. British Medical Bulletin. 2012;102(1):147-70.
34. White RL, Babic MJ, Parker PD, Lubans DR, Astell-Burt T, Lonsdale C. Domain-Specific Physical Activity and Mental Health: A Meta-analysis. American journal of preventive medicine. 2017;52(5):653-66.
35. Yang B, Wang Y, Cui F, Huang T, Sheng P, Shi T, et al. Association between insomnia and job stress: a meta-analysis. Sleep & breathing = Schlaf & Atmung. 2018;22(4):1221-31.
36. Huai P, Xun H, Reilly KH, Wang Y, Ma W, Xi B. Physical Activity and Risk of Hypertension A Meta-Analysis of Prospective Cohort Studies. Hypertension. 2013;62(6):1021-6.

Supplementary material 4: 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.
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 esophagus, and esophageal adenocarcinoma? A review of the literature with a meta-analysis	Not on the right outcome[1]
26	6	Stephen 2017. Physical Activity and Alzheimer's Disease: A Systematic Review	Not on the right outcome[1]
27	7	Svendsen, 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	Lievense 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:] Health-related outcomes addressed by WHO (Supplementary file 2)

Supplementary material 5: Criterion-specific AMSTAR 2 credibility rating, over-all rating score, overall rating, for each included review.

Author, Year	PECO[1]	A-priori Methods[2]	Study Design Selection[3]	Search Strategy[4]	Study Selection[5]	Data Extraction[6]	Excluded Studies[7]	Included Studies[8]	RoB Assess-ment[9]	Funding Sources[10]	Statistical Methods[11]	Impact of RoB[12]	RoB Results[13]	Heterogeneity[14]	Publication Bias[15]	COI[16]	Rating score[17]	Overall Rating[18]
Samitz 2011	Yes	No	Yes	Yes	PY	PY	Yes	Yes	No	Yes	Yes	Yes	No	PY	Yes	Yes	**0.71**	**Low**
Coenen 2018	Yes	Yes	Yes	Yes	PY	PY	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	**0.78**	**Moderate**
Wendel Vos 2004	Yes	No	PY	No	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	**0.59**	**Low**
Jian Li 2013	Yes	No	Yes	PY	No	No	No	Yes	No	No	PY	No	No	No	PY	Yes	**0.34**	**Critically low**
Sattelmair 2011	Yes	No	Yes	PY	PY	PY	PY	Yes	No	Yes	Yes	No	No	no	Yes	Yes	**0.56**	**Low**
Wolin 2009	Yes	No	Yes	PY	No	No	No	No	No	No	PY	PY	No	PY	Yes	No	**0.31**	**Critically low**
Mahmood, 2017	Yes	Yes	Yes	PY	PY	PY	PY	Yes	No	No	Yes	No	No	PY	Yes	Yes	**0.59**	**Low**
Boyle 2012	Yes	No	Yes	PY	PY	PY	PY	Yes	Yes	Yes	Yes	Yes	Yes	PY	Yes	Yes	**0.78**	**Moderate**
Samad 2005	Yes	No	Yes	PY	No	No	No	Yes	No	No	Yes	No	No	No	No	No	**0.28**	**Critically low**
Robsahm 2013	Yes	No	Yes	PY	No	No	No	Yes	PY	No	Yes	Yes	Yes	Yes	No	Yes	**0.56**	**Low**
Wu Y, 2013	Yes	No	Yes	PY	PY	PY	No	Yes	No	No	Yes	No	No	Yes	Yes	PY	**0.5**	**Low**
Pizot 2016	Yes	No	Yes	PY	PY	No	No	Yes	No	Yes	No	no	No	Yes	Yes	Yes	**0.5**	**Low**
Chen X 2019	Yes	No	Yes	PY	PY	PY	No	Yes	Yes	Yes	Yes	N/A	N/A	Yes	Yes	Yes	**0.75**	**Moderate**
Voskuil 2007	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	No	No	PY	Yes	No	**0.53**	**Low**
Schmid 2015	Yes	No	Yes	PY	No	PY	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	**0.69**	**Low**
Vermaete 2013	Yes	No	Yes	PY	No	Yes	PY	Yes	Yes	Yes	Yes	No	No	PY	No	Yes	**0.56**	**Low**
Singh 2014	Yes	Yes	Yes	PY	Yes	PY	No	Yes	Yes	Yes	Yes	Yes	PY	PY	Yes	Yes	**0.75**	**Moderate**

Psaltopoulou 2015	Yes	No	Yes	PY	PY	PY	PY	Yes	Yes	No	Yes	No	No	PY	Yes	Yes	**0.81**	**Moderate**
Chen Y 2014	Yes	No	Yes	PY	PY	PY	PY	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	**0.69**	**Low**
Behrens 2014	Yes	No	Yes	Yes	No	No	No	Yes	Yes	No	Yes	Yes	PY	PY	No	No	**0.5**	**Low**
Behrens, 2013	Yes	no	Yes	Yes	No	No	PY	Yes	Yes	No	Yes	Yes	No	Yes	Yes	no	**0.59**	**Low**
Shephard 2016	Yes	No	Yes	PY	No	No	No	Yes	No	Yes	N/A	N/A	N/A	N/A	N/A	Yes	**0.5**	**Low**
Krstev 2019	Yes	No	Yes	No	No	no	PY	Yes	no	Yes	NO	No	No	PY	no	Yes	**0.38**	**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	Yes	Yes	Yes	Yes	No	No	PY	Yes	No	**0.59**	**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	N/A	N/A	No	no	**0.38**	**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**
Total amount of Yes	36	4	34	10	3	5	3	35	21	23	26	11	7	11	24	23		

Abbreviations: COI = conflict of interest; PECO = population, exposure, 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/PECO?

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

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

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

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

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

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

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

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

Supplementary material 6: GRADE tables

Cillekens B, *et al. Br J Sports Med* 2020;0:1–9. doi: 10.1136/bjsports-2020-102587

1.0. All-cause mortality

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Domains of physical activity and all-cause mortality: systematic review and dose–response meta-analysis of cohort studies (Samitz, G. 2012)(1) 82412/17069 (no of participants/deaths)									
6[a]	Prospective studies	Serious[c]	Serious[d]	Not serious	Not serious	None	This review compared highest with lowest PA levels in the association with mortality. **OPA** Associations were found for OPA (RR=0.83; 95% CI 0.71–0.97) OPA: 4 studies in men; (RR=0.94; 95% CI 0.75-1.19) 90,8% I^2 OPA: 3 studies in women: (RR=0.66; 95% CI 0.49-0.89) 89% I^2 **LTPA:** The strongest associations between PA and mortality were observed for LTPA (RR 0.74; 95% CI 0.70–0.77),	Low[i]	Critically
Do highly physically active workers die early? A systematic review with meta-analysis of data from 193 696 participants. (Coenen, 2018)(2)									
17[b]	Prospective cohort studies	Serious[e]	Serious[f]	Not serious	Not serious	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 MEN:** 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%) **LTPA:** LTPA not assessed in this review	Low[j]	Critically
11	Prospective cohort studies	Serious[e]	Not serious	Not serious	Serious[g]	Some risk of publication bias[h]	**OPA WOMEN:** A non-significant tendency for an inverse association was found among women (HR=0.90; 95% CI 0.80 to 1.01), I2 =0%).	Low[k]	Critically

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

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

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

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

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

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

g: Serious imprecision for women because 1.00 was in Confidence interval.

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

k: rated down from high to low because of serious risk of bias and serious imprecision.

2.0 Cardio-vascular disease

2.1 Stroke

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity and stroke. A meta-analysis of observational data. (Wendel-Vos 2004) (3)									
11[a]	Cohort studies	Serious [c]	Serious[d]	Not serious	Serious[e]	Serious[j]	This review compared three groups (active, moderately active and inactive) **OPA:** People who were physically active at work were at lower risk of stroke compared with both physically inactive (RR = 0.74, 95% CI: 0.49- 1.12) and moderately physically active (RR = 0.92, 95% CI: 0.6, 1.24) people at the workplace. **LTPA:** People who were active in their leisure time were at lower risk of total stroke compared with both physically active were (RR=0.78, 95% 0.71-0.85) and moderately physically active (RR=0.95, 95% 0.68- 1.32)	*Total stroke:* Very low[g]	Critically
5	Cohort studies	Serious	Not serious	Not serious	Not serious	Serious[j]	**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. **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).	*Ischaemic stroke:* Low[h]	Critically

Physical activity and risk of cardiovascular disease: What does the new epidemiological evidence show? (Li J. 2013) (4) **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) (5) Coronary Heart Disease.

4[b]	Cohort studies	Serious[f]	Not Serious	Not serious	Not serious	Serious[j]	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.	Low[i]	Critically

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

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

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

d: Serious; High heterogeneity

e: Serious imprecision for total stroke, but not for ischaemic stroke.

f: 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.

g: certainty downgraded from high to very low because of serious risk of bias and serious inconsistency and serious imprecision and publication bias

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

i: certainty downgraded form high to low because of serious risk of bias and publication bias

J: Rated down for publication bias because it was not calculated and could not be re-analysed

3.0 Cancer

3.1 Colon cancer

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity and colon cancer prevention: a meta-analysis (Wolin, 2009) (6)									
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) (7)									
15[a]	5 Cohort studies 10 case control	Serious[d]	Not serious	Not serious	Not serious	Not serious	This review compared the highest vs the lowest category of PA. **OPA**: OPA was inversely associated with risk of colon cancer (RR=0.74, 95% CI: 0.67-0.82). The OPA association was stronger for men than for women, but sex also explained little of the heterogeneity. **Dose response:** From the dose-response analyses, the pooled RR per 210 MET h/week was RR=0.89, 95% CI: 0.85- 0.93) **LTPA:** LTPA was inversely associated with risk of colon cancer(RR=0.80 ,95% CI: 0.71-0.89) The LTPA association was stronger for men than for women, but sex also explained little of the heterogeneity.	Moderate[h]	Critically
Physical Activity and Risks of Proximal and Distal Colon Cancers: A Systematic Review and Meta-analysis (Boyle, 2012) (8)									
10[b]	6 cohort studies 4 case control	Serious[e]	Serious[f]	Not serious	Not serious	Publication bias	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)	Very low[i]	Critically

A **meta-analysis of the association of physical activity with reduced risk of colorectal cancer (Samad, 2005)** (9)

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 sub sites: a systematic review and meta-analysis of cohort studies (Robsahm. 2013) (10)

5[c]	Cohort studies	Serious[g]	Not serious	Not serious	Not serious	Publication bias	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)	low[j]	Critically

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

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

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

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

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

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

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

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

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

j: certainty downgraded from high to low because of serious risk of bias and publication bias.

3.2 Rectal cancer

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: A systematic review and meta-analysis (Mahmood, 2017) (7)									
12[a]	5 cohort 7 case control	Serious[c]	Not serious	Not serious	Not serious	none	This review compared the highest versus the lowest category of PA. **OPA:** OPA was inversely associated with rectal cancer risk (RR= 0.88, 95% CI: 0.79, 0.98). Low heterogeneity for rectal cancer. **LTPA:** A weak association was observed with rectal cancer: (RR= 0.87, 95% CI: 0.75, 1.01)	Moderate[e]	Critically
Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies (Robsahm. 2013) (10)									
3[b]	Cohort studies	Very serious[d]	Not serious	Not serious	Not serious	Publication bias	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)	Very low[f]	Critically

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

b: Friedenreich 2006; Larsson 2006; Moradi 2008.

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

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

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

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

3.3 Breast cancer

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity and risk of breast cancer: a meta-analysis of prospective studies (Wu Y, 2013) (11)									
7[a]	Cohort studies	Serious[d]	Not serious[e]	Not serious	Not serious	Serious	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)	Very low[h]	Critically
Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of prospective studies (Pizot, 2015) (12)									
11[b]	Cohort studies	Serious[f]	Not serious	Not serious	Not serious	Serious	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)	low[i]	Critically
Physical Activity and Risk of Breast Cancer: A Meta-Analysis of 38 Cohort Studies in 45 Study Reports (Chen, 2019) (13)									
6[c]	Cohort studies	Serious[g]	Not serious	Not serious	Not serious	Serious	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)	low[i]	Critically

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

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

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

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

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

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

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

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

i: Certainty was downgraded from high to low because of serious risk of bias and publication bias

j: Certainty was downgraded from high to low because of serious risk of bias publication bias

3.4 Endometrial cancer.

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical Activity and Endometrial Cancer Risk, a Systematic Review of Current Evidence (Voskuil, 2007) (14)									
4 [a]	Cohort studies	Serious[d]	Serious[e]	Not serious	Serious	Publication bias[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	Publication bias [f]	Effect estimates of eight case-control studies that reported on OPA and that included 95% CIs (summary OR, 0.80; 95% CI, 0.66-0.96). Six of 10 studies reporting on OPA found a decreased risk of endometrial cancer. Two of these studies also showed some evidence for a dose-response effect; however, no P values were reported	Very low[i]	Critically
A systematic review and meta-analysis of physical activity and endometrial cancer risk (Schmid. 2015) (15).									
19[c]	7 Cohort 12 Case control	Serious[g]	Not serious	Not serious	Not serious	none	This review compared high versus low levels of PA. **OPA:** OPA resulted in summary (RR= 0.81; 95 % CI 0.75–0.87) in risk reduction for endometrial cancer. **LTPA:** LTPA resulted in summary risk reduction for endometrial cancer (RR= 0.84; 95% CI 0.78-0.91).	Moderate[J]	Critically

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

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

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

d: Serious; the number of high-quality prospective cohort studies is still limited. Most studies on occupational activity used crude methods for exposure assessment (i.e., job title) and a large number of women were not, or only shortly, engaged in paid employment. This may have resulted in errors in the measurement of physical activity and consequently risk estimation for risk of endometrial cancer. Several issues have not receiver sufficient attention in the epidemiologic studies thus

far. Some studies have used very rough assessments of physical activity, without specifically taking into account the frequency, duration, and intensity of physical activities, and the different periods in life during which activity patterns may have changed. In addition, the association of physical activity and premenopausal endometrial cancer risk has been insufficiently studied. Future epidemiologic studies will need to address these issues to specify the association between physical activity and endometrial cancer risk.

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

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

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

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

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

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

3.5 Lymphoma (Hodgkin and non-Hodgkin)

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical Activity and Risk of Lymphoma: A Meta-Analysis (Vermaete, 2013) (16)									
5[a]	4 case control 1 cohort	Serious [b]	Not serious	Not serious	Serious imprecision[c]	Publication bias.	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)	Very low[d]	Critically

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

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

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

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

3.6 Gastric cancer

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity is associated with reduced risk of gastric cancer: A systematic review and meta-analysis (Singh 2014). (17)									
6[a]	2 cohort 4 Case-control	Serious[f]	Serious[g]	Not serious	Serious[n]	publication bias	This review compared the most physically active people vs. the least physically active people **OPA:** An not significant inverse relationship between OPA and gastric cancer risk was found (OR =0.90; 95% CI; 0.69–1.18) **LTPA:** A significant inverse relationship between LTPA and gastric cancer risk was found (OR=0.82; 95% CI; 0.72-0.94)	Very Low[p]	Critically
Physical Activity and Gastric Cancer Risk: A Systematic Review and Meta-Analysis (Psaltopoulou 2016) (18)									
2[b]	Cohort studies	Very serious[h]	Serious[i]	Not serious	Serious[n]	Publication bias	This review compared the highest level of PA vs. those at the lowest level **OPA:** A not significant inverse relationship between OPA and gastric cancer was found. Combined cohort and case control effect estimates were (RR=0.89, 95% CI; 0.62-1.27). OPA and gastric cancer; (RR=1.25, 95% CI; 0.67-2.33) (2 cohort studies) **LTPA:** LTPA showed a total not significant effect of (RR=0.88, 95% CI; 0.76-1.02) (Cohort and case control combined LTPA and gastric cancer: (RR=0.92, 95% CI; 0.74-1.15) (7 cohort studies)	Very Low[q]	Critically
3[c]	Case control	Very serious[h]	Serious[i]	Not serious	Not serious	Publication bias	**OPA:** OPA and gastric cancer; (RR=0.72, 95% CI; 0.55-0.93) **LTPA:** LTPA and gastric cancer: (RR=0.86; 95% CI; 0.69-1.07) 9 case control)	Very low[r]	Critically

Physical Activity and Risks of Esophageal and Gastric Cancers: A Meta-Analysis (Chen, 2014) (19)

6[d]	3 cohort studies 3 case-control	Serious[j]	Not serious	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).	Low[s]	Critically

The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis (Behrens, 2014) (20)

7[e]	4 cohort 3 case control	Serious[l]	Serious[m]	Not serious	Serious[n]	Publication bias	This review compared the highest versus lowest PA **OPA:** High levels **of** OPA statistically non-significant inverse relations to gastric cancer (RR=0.84, 95% CI; 0.70-1.02) **LTPA:** High levels of LTPA showed statistically significant inverse relationship with gastric cancer (RR=0.80, 95% CI; 0.73-0.89)	Very low[t]	Critically

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

b: Huerta 2010; Severson 1989.

c: Parent 2011; Suwanrunguang 2008 ; Vigen 2006

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

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

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

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

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

i: Serious because of a High heterogeneity

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

k: Serious; High heterogeneity

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

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

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

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

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

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

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

s: Rated from high to low because of serious risk of bias and possible serious publication bias.

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

3.7 Oesophageal 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: Oesophageal cancer

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical Activity and Risks of Esophageal and Gastric Cancers: A Meta-Analysis (Chen, 2014) (19)									
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) (20)									
6[a]	4 cohort 2 Case control	Serious[b]	Serious[c]	Not serious	Serious[d]	Publication bias	This review was comparing highest versus lowest PA level. **OPA** No statistically significant relationship was observed between OPA and oesophageal cancer (RR=0.91, 95% CI; 0.46, 1.81) **LTPA:** LTPA was associated with statistically significant reduction of the risk for oesophageal cancer (RR=0.72, 95% CI; 0.63-0.83)	Very low[e]	Critically

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

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

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

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

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

3.8 Renal cancer

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
The association between physical activity and renal cancer: systematic review and meta-analysis (Behrens, 2013) (21)									
11[a]	6 cohort studies 5 case control	Serious[d]	Not serious	Not serious	Serious[f]	None	This review compared the high vs low levels of PA. **OPA:** The effects of OPA showed a not significant reduction in renal cancer risk (RR=0.91, 95% CI; 0.79, 1.04) I²21%) **LTPA:** The effects of LTPA showed a not significant reduction in renal cancer risk **(RR=**0.88, 95% CI; 0.77, 1.00).	Low[g]	Critically
Can habitual physical activity contribute to reducing the health burden of renal cancer? (Shephard, 2016) (22)									
7[b]	Cohort	Serious[e]	Not serious	Not serious	Serious[f]	Publication bias	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	Very low[h]	Critically
7[c]	Case control	Serious[e]	Not serious	Not serious	Serious[f]	publication bias	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.	Very low[i]	Critically

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

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

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

d: One limitation of this meta-analysis is the large variation in the underlying studies regarding their definitions of exposure to physical activity – ranging from 'physically very active' to '5 h of vigorous physical activity per week or more'. Similarly, the definitions of physical activity referent groups ranged from 'not physically active' to <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: Certainty downgraded from high to low because of serious risk of bias and serious imprecision

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

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

3.9 Prostate cancer

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Occupational Risk factors for prostate cancer; A meta-analyses (Krstev, 2019) (23)									
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) (24)									
28[a]	Prospective studies	Serious[f]	Serious[g]	Not serious	Not serious	none	This study is comparing the highest versus the lowest level of overall PA **OPA:** A not significant inverse relationship between OPA and total PCa (prostate cancer) risk was observed (RR=0.91, 95% CI 0.82-1.01) (28 studies) A statistically significant inverse relationship between long-term (>10 years, 13 studies) OPA and total PCa was observed (RR=0.83, 95% CI 0.71–0.98) Evaluated by cancer subtype, an inverse association with long term OPA was noted for nonadvanced/non-aggressive PCa (RR=0.51, 95% CI; 0.37–0.71) (2 studies) **LTPA:** The relationship between Recreational physical activity and total PCA was (RR=1.03, 95% CI; 1.00-1.06)	Low[m]	Critically
Physical activity and prostate cancer: An updated review (Shephard, 2017) (25)									
19[b]	Cross sectional and prospective cohort	Serious[h]	Serious[i]	Not serious	Serious[j]	publication bias	A total of seven analyses found no effect of OPA. Six analyses identified a possible trend favoring the more active workers Six analyses demonstrated a significantly lower risk of prostate cancer in the most active and/or the least well-educated individuals.	Very low[n]	Critically
16[c]	Case control studies	Serious[h]	Serious[i]	Not serious	Serious[j]	publication bias	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) (26)									

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 0.78-0.94) than the lower quality OPA studies (RR: 0.75, 95% CI: 0.61-0.94). **LTPA:** LTPA was related with a non-significant reduced risk of PCa: (RR: 0.95; 95%CI 0.89-1.00) In cohort studies LTPA was related with a significantly reduced risk (RR=0.95, 95% CI: 0.89-1.00)	Moderate[p]	Critically
18[e]	Case control	Serious[k]	Serious [l]	Not serious	Not serious	none	**OPA**: OPA case-control studies showed a significantly reduced PCa risk (OR: 0.73; 95% CI, 0.62–0.87) **LTPA:** LTPA case control studies showed a reduced not significant PCA risk: (OR= 0.98, 95% CI: 0.85-1.14)	Low[q]	Critically

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

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

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

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

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

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

g: Serious inconsistency due to a high inconsistency

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

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

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

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

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

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

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

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

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

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

3.10 Pancreatic cancer

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Can physical activity modulate pancreatic cancer risk? a systematic review and meta-analysis (O'Rorke, 2010) (27)									
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) (28)									
3[a]	Cohort	Very serious[b]	Not serious	Not serious	Not serious	Publication bias	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)	Very low[c]	Critically

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

b: In addition, the observed association could be due to unmeasured confounding. However, the confounding may exist in both directions: on one hand, individuals who have medical conditions such as diabetes are ordinarily excluded from employment as manual labourers', 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
№ 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) (29)									
This article was excluded from further analyses as it was judged to not provide an accurate summary of the available evidence. (AMSTAR2 rating)									

4.0 Diabetes Mellitus type 2

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis (Aune, 2015) (30)									
3[a]	Cohort studies	Very serious[a]	Not serious	Not serious	Not serious	publication bias	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)	Very low[c]	Critically

a: Hu G 2003; Chien 2009; Steinbrecher 2012

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

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

5.0 Osteoarthritis

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Occupational risk factors for osteoarthritis of the knee: a meta-analysis (McWilliams 2011) (31)									
8[a]	2 cohort 3 cross sectional 3 case control	Serious[c]	Serious[d]	Not serious	Not serious	Publication bias[e]	Heavy or manual work (546.853 subjects) was associated with knee osteoarthritis (OR=1.45, 95% CI; 1.20-1.76) **Cohort studies;** 1 study non-significant increase 1 study non-significant decrease **Case-control;** 3 study significant increase **Cross sectional;** 1 study non-significant decrease 1 study non-significant increase 1 study significant increase	Very low[i]	Critically
Men and women's occupational activities and the risk of developing osteoarthritis of the knee, hip or hands: A systematic review and recommendations for future research (Gignac, 2019) (32)									
11[b]	6 cohort 2 case control 3 cross sectional	Serious[f]	Serious[g]	Not serious	Serious[h]	publication bias	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

Occupational activities and osteoarthritis of the knee (Palmer, 2012) (33)

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

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

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

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

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

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

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 reported

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

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

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

j: Certainty downgraded 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: Mental Health

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Domain-Specific Physical Activity and Mental Health: A Meta-analysis (White, 2017) (34)									
8[a]	7 cross sectional 1 cohort[b]	Serious[c]	Serious[d]	Not serious	Serious[e]	Publication bias	**OPA:** work-related PA had a weak positive relationship with mental ill-health among adults (r=0.10, 95% CI: 0.04-0.16) **LTPA:** LTPA had a negative relationship with mental ill-health (r=-0.11, 95% CI; -0.16- -0.06)	Very low[f]	Critically
5[a]	5 cross sectional	Serious	Serious	Not serious	Serious[e]	Publication bias	**OPA:** 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 positive relationship with mental health (r=0.13, 95% CI; 0.08-0.18)	Very low	Critically

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

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

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

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

e: Serious imprecision since r crosses 0.0.

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

7.0 Sleep quality and/or duration

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Association between insomnia and job stress: a meta-analysis (Yang, 2018) (35)									
7[a]	4 cross sectional 3 prospective	Serious [b]	Serious[c]	Not serious	Serious[d]	Strong association Publication bias	**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.	Very low[e]	Important

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

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

c: High heterogeneity

d: Serious imprecision due to the broad confidence intervals.

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

8.0 Hypertension

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

Certainty assessment							Summary of findings	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical Activity and Risk of Hypertension A Meta-Analysis of Prospective Cohort Studies (Huai, 2013) (36)									
6[a]	Cohort studies	Serious[b]	Serious[c]	Not serious	Serious[d]	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).	Very low[e]	Important

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

b: In addition, the association between RPA and decreased risk of hypertension in this meta-analysis might be confounded by various factors. Second, because of the inability to obtain raw data, we could perform only a study-level but not a patient-level meta-analysis, which would have enabled us to adjust for multiple factors

c: heterogeneity was I^2: 66,3%.

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 and imprecision.

Abbreviations

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

References

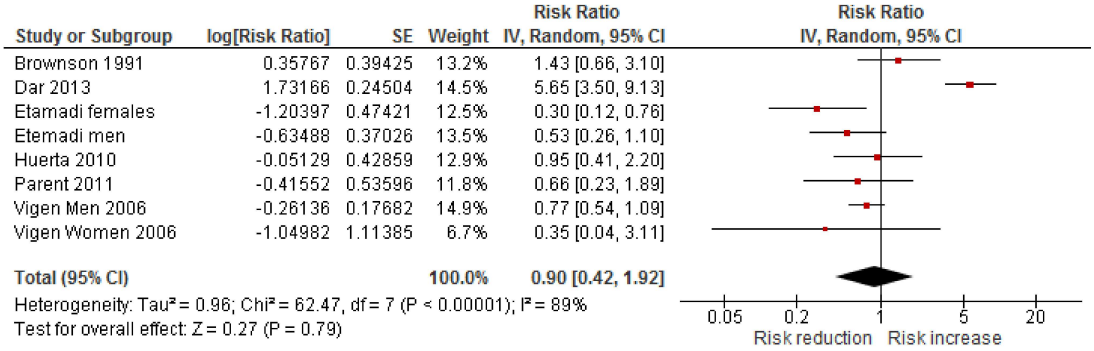
1. Samitz G, Egger M, Zwahlen M. Domains of physical activity and all-cause mortality: systematic review and dose-response meta-analysis of cohort studies. *International journal of epidemiology*. 2011;40(5):1382-400.
2. Coenen P, Huysmans MA, Holtermann A, Krause N, van Mechelen W, Straker LM, et al. Do highly physically active workers die early? A systematic review with meta-analysis of data from 193 696 participants. *British journal of sports medicine*. 2018;52(20):1320-6.
3. Wendel-Vos GC, Schuit AJ, Feskens EJ, Boshuizen HC, Verschuren WM, Saris WH, et al. Physical activity and stroke. A meta-analysis of observational data. *International journal of epidemiology*. 2004;33(4):787-98.
4. Li J, Loerbroks A, Angerer P. Physical activity and risk of cardiovascular disease: what does the new epidemiological evidence show? *Current opinion in cardiology*. 2013;28(5):575-83.
5. Sattelmair J, Pertman J, Ding EL, Kohl HW, 3rd, Haskell W, Lee IM. Dose response between physical activity and risk of coronary heart disease: a meta-analysis. *Circulation*. 2011;124(7):789-95.
6. Wolin KY, Yan Y, Colditz GA, Lee IM. Physical activity and colon cancer prevention: a meta-analysis. *British journal of cancer*. 2009;100(4):611-6.
7. Mahmood S, MacInnis RJ, English DR, Karahalios A, Lynch BM. Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: a systematic review and meta-analysis. *International journal of epidemiology*. 2017;46(6):1797-813.
8. Boyle T, Keegel T, Bull F, Heyworth J, Fritschi L. Physical activity and the risk of proximal colon and distal colon cancers: A systematic review and meta-analysis. 2012;15:S332-S3.
9. Samad AK, Taylor RS, Marshall T, Chapman MA. A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2005;7(3):204-13.
10. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. 2013;22(6):492-505.
11. Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. *Breast cancer research and treatment*. 2013;137(3):869-82.
12. Pizot C, Boniol M, Mullie P, Koechlin A, Boniol M, Boyle P, et al. Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of prospective studies. 2016;52:138-54.
13. Chen X, Wang Q, Zhang Y, Xie Q, Tan X. Physical Activity and Risk of Breast Cancer: A Meta-Analysis of 38 Cohort Studies in 45 Study Reports. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2019;22(1):104-28.
14. Voskuil DW, Monninkhof EM, Elias SG, Vlems FA, van Leeuwen FE. Physical activity and endometrial cancer risk, a systematic review of current evidence. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2007;16(4):639-48.
15. Schmid D, Behrens G, Keimling M, Jochem C, Ricci C, Leitzmann M. A systematic review and meta-analysis of physical activity and endometrial cancer risk. *European journal of epidemiology*. 2015;30(5):397-412.
16. Vermaete NV, Wolter P, Verhoef GE, Kollen BJ, Kwakkel G, Schepers L, et al. Physical activity and risk of lymphoma: a meta-analysis. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2013;22(7):1173-84.
17. Singh S, Edakkanambeth Varayil J, Devanna S, Murad MH, Iyer PG. Physical activity is associated with reduced risk of gastric cancer: a systematic review and meta-analysis. *Cancer prevention research (Philadelphia, Pa)*. 2014;7(1):12-22.
18. Psaltopoulou T, Ntanasis-Stathopoulos I, Tzanninis I-G, Kantzanou M, Georgiadou D, Sergentanis TN. Physical Activity and Gastric Cancer Risk: A Systematic Review and Meta-Analysis. 2016;26(6):445-64.

19. Chen Y, Yu C, Li Y. Physical activity and risks of esophageal and gastric cancers: a meta-analysis. 2014;9(2):e88082.
20. Behrens G, Jochem C, Keimling M, Ricci C, Schmid D, Leitzmann MF. The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis. 2014;29(3):151-70.
21. Behrens G, Leitzmann MF. The association between physical activity and renal cancer: systematic review and meta-analysis. *British journal of cancer*. 2013;108(4):798-811.
22. Shephard RJ. Can habitual physical activity contribute to reducing the health burden of renal cancer? 2016;28(2):148-63.
23. Krstev S, Knutsson A. Occupational Risk Factors for Prostate Cancer: A Meta-analysis. *Journal of cancer prevention*. 2019;24(2):91-111.
24. Benke IN, Leitzmann MF, Behrens G, Schmid D. Physical activity in relation to risk of prostate cancer: a systematic review and meta-analysis. *Annals of oncology : official journal of the European Society for Medical Oncology*. 2018;29(5):1154-79.
25. Shephard R. Physical Activity and Prostate Cancer: An Updated Review. 2017;47(6):1055-73.
26. Liu Y, Hu F, Li D, Wang F, Zhu L, Chen W, et al. Does physical activity reduce the risk of prostate cancer? A systematic review and meta-analysis. *European urology*. 2011;60(5):1029-44.
27. O'Rorke MA, Cantwell MM, Cardwell CR, Mulholland HG, Murray LJ. Can physical activity modulate pancreatic cancer risk? a systematic review and meta-analysis. *International journal of cancer*. 2010;126(12):2957-68.
28. Bao Y, Michaud DS. Physical activity and pancreatic cancer risk: a systematic review. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2008;17(10):2671-82.
29. Keimling M, Behrens G, Schmid D, Jochem C, Leitzmann MF. The association between physical activity and bladder cancer: systematic review and meta-analysis. *British journal of cancer*. 2014;110(7):1862-70.
30. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. *European journal of epidemiology*. 2015;30(7):529-42.
31. McWilliams DF, Leeb BF, Muthuri SG, Doherty M, Zhang W. Occupational risk factors for osteoarthritis of the knee: a meta-analysis. *Osteoarthritis and cartilage*. 2011;19(7):829-39.
32. Gignac MAM, Irvin E, Cullen K, Van Eerd D, Beaton DE, Mahood Q, et al. 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. *Arthritis care & research*. 2019.
33. Palmer KT. Occupational activities and osteoarthritis of the knee. 2012;102(1):147-70.
34. White RL, Babic MJ, Parker PD, Lubans DR, Astell-Burt T, Lonsdale C. Domain-Specific Physical Activity and Mental Health: A Meta-analysis. *American journal of preventive medicine*. 2017;52(5):653-66.
35. Yang B, Wang Y, Cui F, Huang T, Sheng P, Shi T, et al. Association between insomnia and job stress: a meta-analysis. *Sleep & breathing = Schlaf & Atmung*. 2018;22(4):1221-31.
36. Huai P, Xun H, Reilly KH, Wang Y, Ma W, Xi B. Physical Activity and Risk of Hypertension A Meta-Analysis of Prospective Cohort Studies. 2013;62(6):1021-6.

Supplementary material 7: Assessing heterogeneity

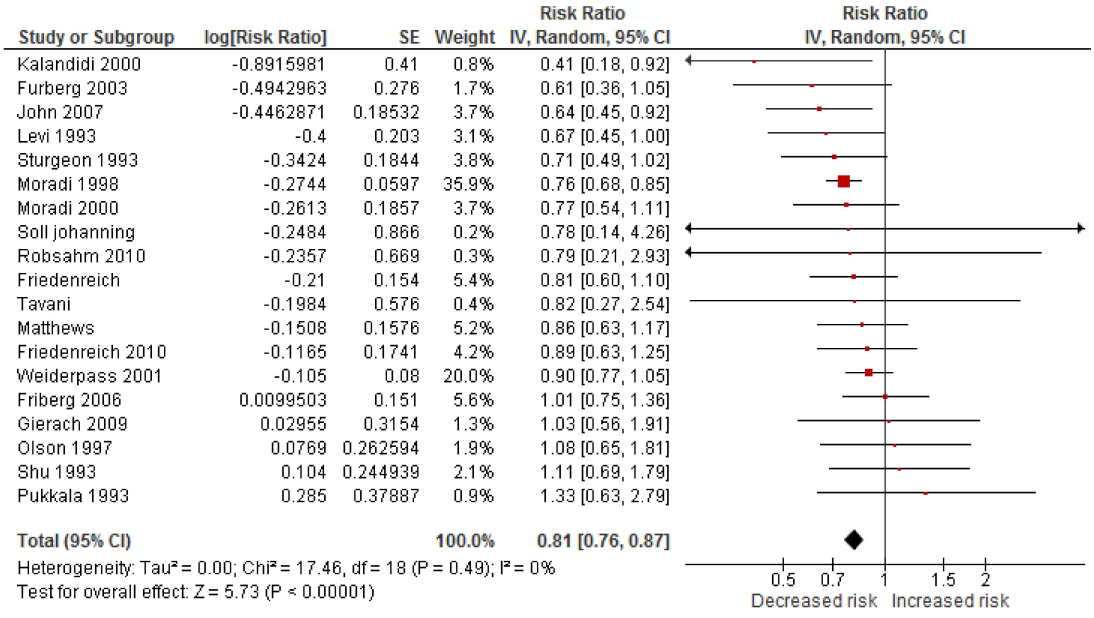
Forest plot oesophageal cancer:

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



Forest plot Endometrial cancer.

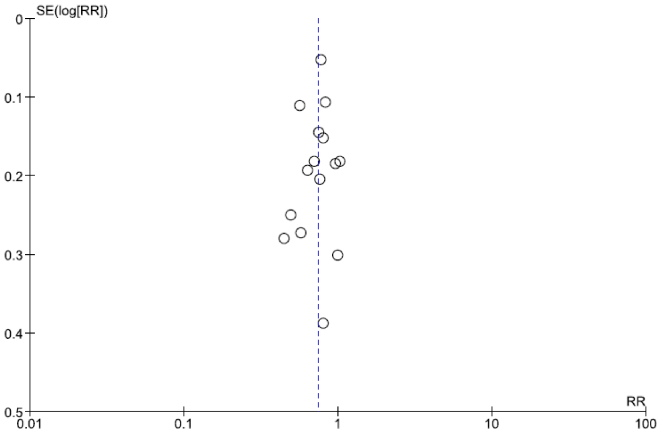
Schmid 2015: A systematic review and meta-analysis of physical activity and endometrial cancer risk



Supplementary material 8: Test for publication bias.

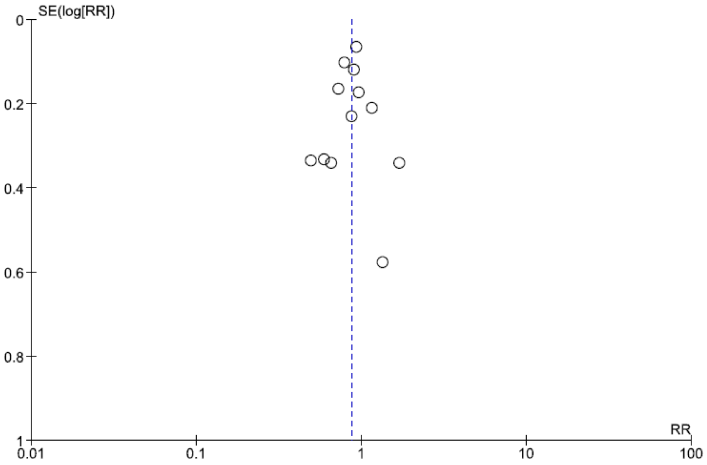
Colon cancer:

Mahmood 2017: Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: A systematic review and meta-analysis



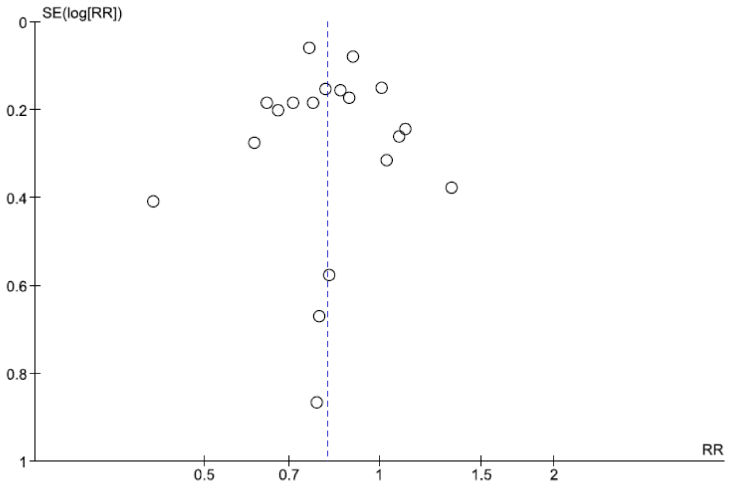
Rectal:

Mahmood 2017: Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: A systematic review and meta-analysis



Endometrial cancer:

Schmid 2015: A systematic review and meta-analysis of physical activity and endometrial cancer risk



Renal cancer:

Behrens 2013: The association between physical activity and renal cancer: systematic review and meta-analysis