Do highly physically active workers die early? A systematic review with meta-analysis of data from 193 696 participants

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ABSTRACT

Objective Recent evidence suggests the existence of a physical activity paradox, with beneficial health outcomes associated with leisure time physical activity, but detrimental health outcomes for those engaging in high level occupational physical activity. This is the first quantitative systematic review of evidence regarding the association between occupational physical activity and all-cause mortality.

Design Systematic review with meta-analysis.

Data source A literature search was performed in electronic databases PubMed, Embase, CINAHL, PsycINFO and Cochrane.

Eligibility criteria for selecting studies We screened for peer reviewed articles from prospective studies assessing the association of occupational physical activity with all-cause mortality. A meta-analysis assessed the association of high (compared with low) level occupational physical activity with all-cause mortality, estimating pooled hazard ratios (HR) (with 95% CI).

Results 2490 unique articles were screened and 33 (from 26 studies) were included. Data from 17 studies (with 193 696 participants) were used in a meta-analysis, showing that men with high level occupational physical activity had an 18% increased risk of early mortality compared with those engaging in low level occupational physical activity (HR 1.18, 95% CI 1.05 to 1.34). No such association was observed among women, for whom instead a tendency for an inverse association was found (HR 0.90, 95% CI 0.80 to 1.01).

Conclusions The results of this review indicate detrimental health consequences associated with high level occupational physical activity in men, even when adjusting for relevant factors (such as leisure time physical activity). These findings suggest that research and physical activity guidelines may differentiate between occupational and leisure time physical activity.

INTRODUCTION

Physical activity (PA) is considered an important preventive behaviour for non-communicable diseases.[1–4] Physical inactivity has been estimated to account for ~7% of the global health burden,[5] accompanied by considerable economic costs for society.[6] Based on this knowledge, international guidelines encourage people to engage in ≥30 min of at least moderate intensity PA daily.[7] Such guidelines, however, do not distinguish between occupational, leisure time and transportation related domains of PA.

Until recently, the health effects associated with different domains of PA were considered to be alike and beneficial, as exemplified by a meta-analysis of cohort studies published until 2010[8]. Evidence on the beneficial health effects of PA started to develop in the 1950s, with pioneering studies identifying active jobs (among workers of the London public transport system[9] and San Francisco longshore men[10]) as being associated with a lower risk of mortality. Subsequently, traditional PA research has primarily focused on leisure time PA and/or total PA, and less often on occupational PA.

New evidence, however, suggests a contrast between the health effects of leisure time and occupational PA,[11 12] suggesting a PA paradox.[13] Specifically, while beneficial health outcomes have been associated with high level leisure time PA, detrimental health consequences have been documented for high level occupational PA, regarding cardiovascular disorders,[14–17] sickness absence[12] and mortality.[18–21] However, other studies could not confirm this, or even showed opposing findings.[22–24] If confirmed, such a paradox would require revision of current PA public health guidelines,[7] because meeting current guidelines that fail to take the different domains of PA into account might not always be health enhancing.

Until now, the possible existence of a PA paradox has received little attention, and no systematic review has specifically examined the association of occupational PA with mortality. Although there is a trend towards a reduction of occupational PA over the past decades, substantial proportions of the global workforce still operate in physically active jobs.[25] A thorough understanding of the health consequences of occupational PA is therefore highly important. The aim of this study was to summarise evidence from prospective studies regarding the association between occupational PA and all-cause mortality in a meta-analysis.

METHODS

Data sources, literature search and study selection

This systematic review was a priori registered[26] and was executed according to the PRISMA statement[27] guidelines. Systematic searches of the literature were performed in bibliographic databases of PubMed, Embase, CINAHL, PsycINFO and Cochrane, from inception to 20 September 2017, with search terms expressing PA, occupational and mortality (see online supplementary material 1).

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Two reviewers (PC and MAH) independently screened all potentially relevant titles and abstracts and, if necessary, full text articles, for eligibility. In cases of disagreement, consensus was reached, possibly by consulting with a third reviewer (AJvdB). Articles were included if they met the following criteria: published in the English language, description of original research with a prospective assessment of the association of occupational PA with all-cause mortality in adult workers (ie, aged 18–65 years at the time of occupational PA assessment) from a general population sample (eg, excluding clinical patient samples). Occupational PA assessed by self-report or objective measures (eg, using accelerometers or heart rate monitors) was included. To enable evaluation of occupational PA at the level of the individual worker, we excluded studies that did not use self-reports but instead used register based job title or occupational class (eg, blue collar vs white collar, or manual vs non-manual) to estimate occupational PA. Studies with a focus on occupational sedentary behaviour (rather than PA) were included only in cases with relevant reference groups engaging in at least moderate level occupational PA (ie, excluding studies assessing various durations of sedentary behaviour). Moreover, only studies that sufficiently adjusted for relevant factors were included, with sufficiently adjusted being defined as adjustment for age and gender, and at least one other relevant factor, including socioeconomic (eg, education/income), lifestyle (eg, smoking, alcohol use or leisure time PA) or health related factors (eg, adiposity or blood pressure).

Data extraction and risk of bias assessment

We extracted the following: first author and year of publication, study name and design (and follow-up period), sample description (number of participants, inclusion/exclusion criteria, per cent female, age, country, type of work), adjustment, description of occupational PA (method and calendar year of assessment, and exposure categories), description of mortality (method of assessment and incidence) and effect measures (eg, hazard ratio (HR)). Two reviewers (PC and MAH) independently extracted the relevant data and assessed the risk of bias of the included articles. In cases of disagreement, consensus was reached during a meeting, and possibly by consulting with a third reviewer (AJvdB). In instances where the above mentioned study information could not be retrieved from the published articles, respective authors were asked for additional information.

For risk of bias assessment, we used a previously published and often used scoring system[28] with 12 criteria related to reporting of study methods and results (see online supplementary material 2). This scoring system has shown inter-rater agreement in individual items, ranging from 60% to 100%. Summary scores were calculated (ranging from 0% to 100%) according to the published system, with studies scoring >75% considered to be of high methodological quality, and hence low risk of bias.

Data analysis

Included studies were described according to their extracted data and risk of bias. If multiple articles reported on the same study data, only those data from articles with the longest follow-up period were used for further quantitative analyses (with longer exposure periods expected to be more likely to influence mortality than short term exposures).

Quantitative analyses of homogenous studies with sufficient overlap in exposure, outcome and sample were performed in a meta-analysis, using effect measures from time to event analyses, such as Cox models (typically expressed in HRs).[29] Due to differences in the definition of occupational PA, during a consensus meeting (with authors PC, MAH and AJvdB) categorical occupational PA exposure variables from each study were harmonised, classifying them into one of the four PA categories from the PA continuum (see online supplementary material 3).[30 31] These four PA categories are: occupational sedentary behaviour, low level occupational PA, moderate level occupational PA and high level occupational PA, to which (based on postures and energy expenditure) all occupational PA levels provided by the original articles were assigned exclusively. For example, Etemadi *et al*'s[22] four categories of 'sedentary work', 'standing or occasional walking', 'mild increase in heart rate' and 'significant elevation in heart rate' were categorised as sedentary, low, moderate and high occupational PA, respectively. The exposures of 'not active–light' and 'moderate–hard' by Harari *et al*[19] were, on the other hand, categorised as low and high level occupational PA, respectively. Since we aimed to assess the risk of all-cause mortality in highly physically active workers, only the high category of occupational PA was compared with the low category of occupational PA (as shown in online supplementary material 3). Authors were asked to re-analyse their data in cases where information on such a comparison was not available from the published articles (eg, when the association with all-cause mortality was only presented for the high level occupational PA compared with occupational sedentary behaviour, but not compared with low level occupational PA). Also, authors from articles in which effect sizes were not stratified by gender were asked to provide these additional stratified analyses. Authors of three studies provided such extra data (as indicated in online supplementary material 6).

Analyses were performed with inverse variance random effects models using Review Manager (RevMan, the Cochrane Collaboration, Copenhagen) V.5.3. HRs with 95% CI were reported, depicting individual study and pooled associations of high (compared with low) level occupational PA with all-cause mortality in forest plots. Due to apparent gender differences in occupational PA levels[32] and physiological responses to PA,[33] analyses were stratified by gender (as stipulated in our a priori registered protocol[26]). Funnel plots were generated to assess publication bias.[34] Heterogeneity of the findings was assessed using I^2 statistics and by visual inspection of the forest plots. We performed a sensitivity analysis for the association of individual study findings on the pooled results, in which we assessed whether any particular study influenced the pooled effect size by systematically excluding each single study effect sizes, one at a time.

Sensitivity analyses were conducted, comparing subgroups using χ^2 statistics, in which we addressed the following issues. First, we tested whether our results were affected by studies that did assess relatively healthy study samples (in which the original authors excluded participants with certain diseases or those who deceased early in the follow-up period) compared with studies that did not. Second, we tested whether the choice of the reference group (ie, sedentary behaviour rather than low level occupational PA) affected the results in those studies reporting on both the comparison of sedentary versus high occupational PA and low versus high occupational PA. Sedentary behaviour (defined as low intensity activities or sitting[30]) is known to be conceptually different from physical inactivity, and has been shown to be an (at least partially) independent risk factor for ill health.[35] Thirdly, we tested whether effect sizes differed in studies that did adjust for leisure time PA compared with studies that did not. According to the a priori registered protocol,[26] we aimed to assess whether adjustments of relevant other variables (eg, smoking or alcohol use) and risk of bias impacted on the overall

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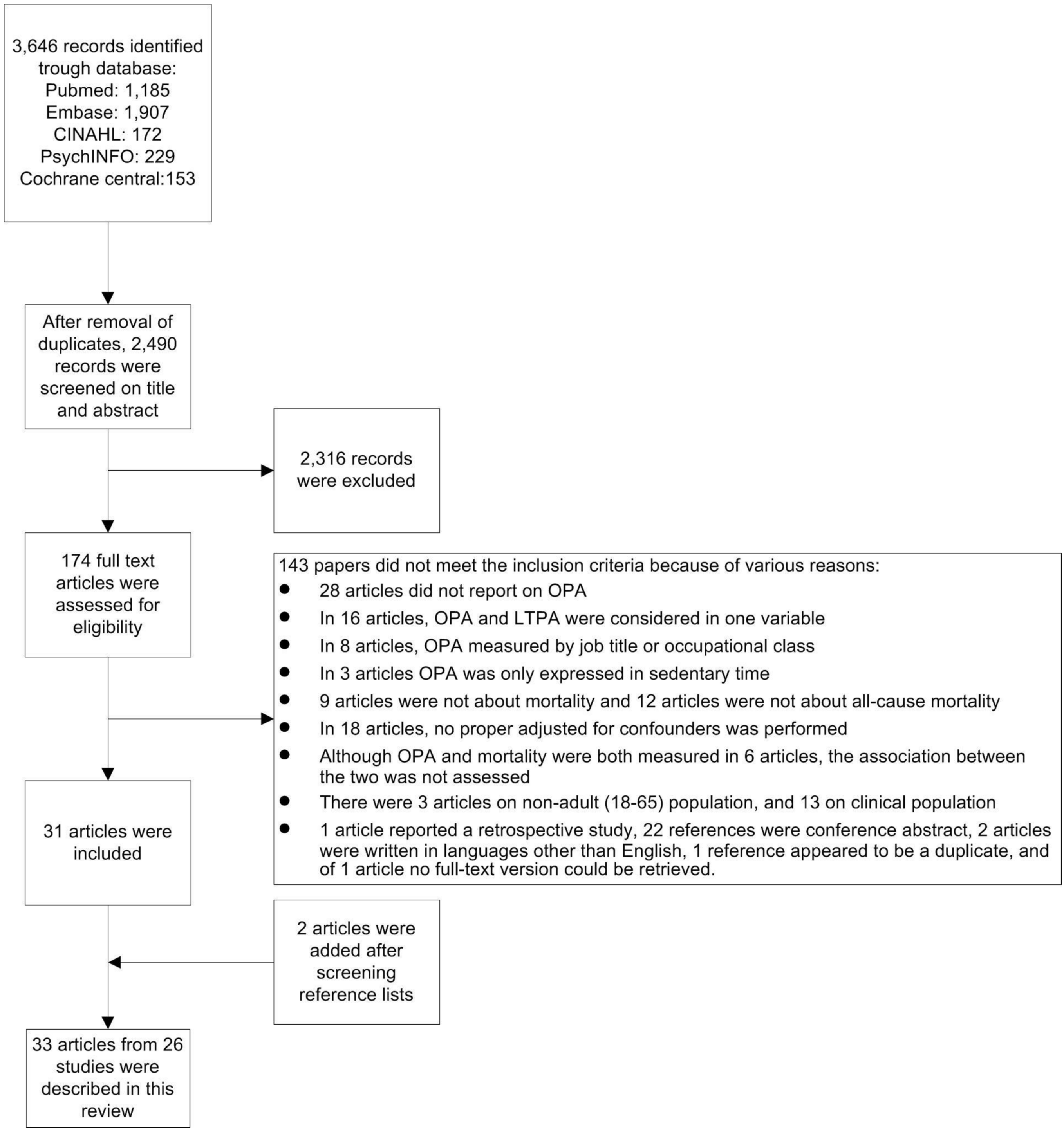

Figure 1 Flowchart depicting the article search and selection procedure. LTPA, leisure time physical activity; OPA, occupational physical activity.

effect sizes. However, these planned sensitivity analyses could not be performed due to insufficient data.

RESULTS

A flowchart of the search and selection process is presented in figure 1. The literature search generated a total of 3646 references. After removing duplicates, 2490 unique references were screened by their title and abstract, and 174 articles by full text. Of the latter, 143 were excluded for various reasons (see online supplementary material 4), yielding 31 eligible articles. Two additional articles were retrieved from screening reference lists, resulting in 33 articles included in this review.[14–16 18–20 22 23 36–55]

Risk of bias and extracted data of the included articles are shown in online supplementary material 5 and 6. Included articles showed an average (SD) methodological quality of 87 (13)% (range 38–100%), with 28 articles classified as low risk of bias.

Included articles reported data from 26 different studies; only those articles reporting the longest follow-up period were used for further analyses.[15 16 18–20 22 23 36–44 46 48–54] Of 3 13 317 participants in these studies, 29 639 (19%) died during follow-up

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(ranging from 4 to 50 years, mean 19.9). In all studies, mortality was ascertained using official national or regional registers, and occupational PA exposure was obtained by individual self-report. Calendar year of exposure assessment ranged from 1960 to 2010. Fifteen studies examined both genders, 10 were limited to men and 1 to women. Fifteen studies used a relatively healthy sample and 11 a sample representative of health in the general population. Only two studies reported on specific working populations (ie, industry[18] and manufacturing workers[56]); other studies used either a random working population sample or a sample holding a range of jobs.

Quantitative analysis

We statistically pooled data from 17 studies (193 696 participants).[15 16 18–20 22 23 36 40 43 44 50 52 54] Data from three of these studies were retrieved after the original authors re-analysed their study data on request.[36 40 43]

Pooled results showed that male workers with high level occupational PA had a statistically significant higher mortality risk than those engaging in low level occupational PA (HR 1.18, 95% CI 1.05 to 1.34, I^2=76%) (figure 2). A non-significant tendency for an inverse association was found among women (HR 0.90, 95% CI 0.80 to 1.01, I^2=0%). Individual study data did not substantially influence the pooled effect size and/or the heterogeneity of our findings. Visual inspection of funnel plots (online supplementary material 7) suggested some degree of asymmetry, with larger samples showing lower HRs than smaller samples (in particular among men).

Sensitivity analyses showed higher HRs in relatively healthy compared with relatively unhealthy populations (online supplementary material 8), with statistically significant subgroup differences among men (χ^2=4.64, P=0.03, I^2=78.5) but not women (χ^2=3.38, P=0.07; I^2=70.4). Associations tended to be stronger among studies that adjusted for leisure time PA,

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
1.1.2 Males				
Menotti 2016	-0.274	0.087	7.7%	0.76 [0.64, 0.90]
Turi 2017 (males)	-0.245	1.269	0.2%	0.78 [0.07, 9.41]
Etemadi 2014 (males)	-0.174	0.107	7.2%	0.84 [0.68, 1.04]
Huerta 2016 (males)	-0.01	0.128	6.6%	0.99 [0.77, 1.27]
Wanner 2014 (males)	0.01	0.073	8.1%	1.01 [0.88, 1.17]
Andersen 2010 (males)	0.02	0.106	7.2%	1.02 [0.83, 1.26]
Petersen 2012 (males)	0.02	0.157	5.8%	1.02 [0.75, 1.39]
Clays 2014	0.191	0.25	3.7%	1.21 [0.74, 1.98]
Holtermann 2012A (males)	0.199	0.075	8.0%	1.22 [1.05, 1.41]
Krause 2017 (IHD)	0.223	0.287	3.1%	1.25 [0.71, 2.19]
Krause 2017 (no IHD)	0.262	0.098	7.4%	1.30 [1.07, 1.57]
Richard 2015 (males)	0.27	0.193	4.9%	1.31 [0.90, 1.91]
Holtermann 2010A	0.285	0.063	8.3%	1.33 [1.18, 1.50]
Chau 2015 (males)	0.293	0.233	4.0%	1.34 [0.85, 2.12]
Harari 2015	0.351	0.103	7.3%	1.42 [1.16, 1.74]
Holtermann 2012B (males)	0.464	0.19	4.9%	1.59 [1.10, 2.31]
Stender 1993	0.647	0.341	2.5%	1.91 [0.98, 3.73]
Hu 2014 (males)	1.224	0.286	3.1%	3.40 [1.94, 5.96]
Subtotal (95% CI)			**100.0%**	**1.18 [1.05, 1.34]**
Heterogeneity: Tau² = 0.04; Chi² = 69.70, df = 17 (P < 0.00001); I² = 76%				
Test for overall effect: Z = 2.70 (P = 0.007)				
1.1.3 Females				
Turi 2017 (females)	-0.629	0.435	1.8%	0.53 [0.23, 1.25]
Etemadi 2014 (females)	-0.565	0.214	7.6%	0.57 [0.37, 0.86]
Huerta 2016 (females)	-0.248	0.239	6.1%	0.78 [0.49, 1.25]
Wanner 2014 (females)	-0.211	0.215	7.5%	0.81 [0.53, 1.23]
Andersen 2010 (females)	-0.094	0.163	13.1%	0.91 [0.66, 1.25]
Petersen 2012 (females)	-0.062	0.234	6.3%	0.94 [0.59, 1.49]
Holtermann 2012A (females)	-0.051	0.091	42.0%	0.95 [0.80, 1.14]
Chau 2015 (females)	-0.051	0.661	0.8%	0.95 [0.26, 3.47]
Richard 2015 (females)	-0.01	0.404	2.1%	0.99 [0.45, 2.19]
Hu 2014 (females)	0.049	0.228	6.7%	1.05 [0.67, 1.64]
Holtermann 2012B (females)	0.223	0.241	6.0%	1.25 [0.78, 2.00]
Subtotal (95% CI)			**100.0%**	**0.90 [0.80, 1.01]**
Heterogeneity: Tau² = 0.00; Chi² = 9.43, df = 10 (P = 0.49); I² = 0%				
Test for overall effect: Z = 1.82 (P = 0.07)				

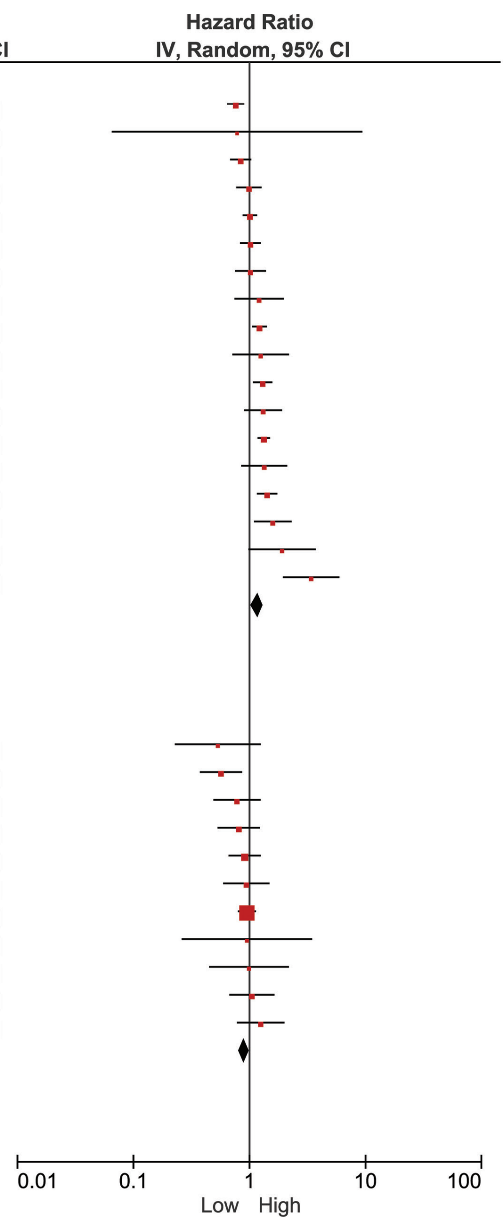

Figure 2 Forest plot of the effect of high compared with low levels of occupational physical activity on all-cause mortality, based on 17 studies with 193 696 participants. Individual study as well as pooled effects are presented. Data from men (upper panel) and women (lower panel) are shown. IV, inverse variance.

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especially among men (HR 1.25, 95% CI 1.07 to 1.47, I^2=75%) compared with studies that did not (HR 1.12, 95% CI 0.93 to 1.34) (online supplementary material 9). Moreover, we showed an attenuated (but non-significant subgroup difference) risk of mortality in men engaging in high level occupational PA when compared with sedentary behaviour instead of low level occupational PA (HR 1.04, 95% CI 0.69 to 1.55, I^2=70% and HR 1.11, 95% CI 0.85 to 1.45, I^2=85%, respectively) (online supplementary material 10).

Of nine studies not eligible for pooling, two studies did not report high level occupational PA at all[37 49] and showed a reduced mortality risk for moderate compared with low occupational PA (HR 0.69, 95% CI 0.48 to 1.00[37]) and no effect for occupational standing/walking compared with sitting (HR 0.97, 95% CI 0.78 to 1.19 for men only[49]). Four studies neither reported on the association of high (compared with low) level occupational PA with mortality nor were the authors able to provide us with a re-analysis of their data.[38 39 42 51] Two studies did not use any time to event analyses,[41 48] and one study did not sufficiently adjust for potential confounders.[46] Some of these studies showed (univariate) associations of higher longevity for those engaging in high occupational PA compared with low occupational PA (HR 0.77, 95% CI 0.71 0.84[38]). Other studies showed high intensity occupational PA being associated with an increased risk of early mortality (HR 1.10, 95% CI 0.73 1.64[51]), while there were also studies showing no clear associations of occupational PA with all-cause mortality.[48 41]

DISCUSSION

Our meta-analysis of 193 696 participants showed that men engaging in high (compared with low) level occupational PA have an 18% increased risk of all-cause mortality, even after adjustment for relevant confounders, such as leisure time PA. These findings suggest that a PA paradox may exist in male workers, with high levels of occupational PA being associated with detrimental health consequences, in contrast with the existing evidence of beneficial health consequences with moderate and/or high level leisure time PA.[1–4] This study is the first to systematically synthesise the respective epidemiological evidence for all-cause mortality. If the observed association is causal, then PA guidelines need to differentiate between occupational and leisure time PA because meeting current PA guidelines via occupational PA may not provide the intended health benefits or even confer a health risk. PA guidelines recommend increasing moderate intensity PA up to 300 min per week.[7] Workers who engage in high level occupational PA are likely to exceed this duration. This is particularly important as (despite a general trend of a reduction in energy expenditure at work over the past decades) a large fraction of the working population worldwide is still engaging in high level occupational PA,[25] with even higher effective workloads for those working in outdoor or in insufficiently controlled indoor climate environments.[57] Workers who are active at work are furthermore known to be fairly inactive during their leisure time.[58] When the empirical evidence for the PA paradox is confirmed in more high quality studies, specific guidance on the appropriate type of PA and on safe levels of occupational PA are needed, especially for physically active workers.

Our results are consistent with those from studies that have classified occupational PA based on job or occupational sector (eg, blue collar vs white collar, or manual vs non-manual),[59 60] including studies that were excluded from this review.[61–63] These studies, in general, showed increased mortality risks for workers in physically active (ie, blue collar or manual) jobs and/or from low socioeconomic classes compared with workers in inactive jobs and/or high socioeconomic classes. This is however in contrast with early research on workers of the London public transport system[9] and San Francisco longshore men.[10] Moreover, our findings are in contrast with the evidence from studies on the association of total PA that show an inverse association of PA with all-cause mortality[64 65] despite the fact that occupational PA contributes a large share to PA in these studies for many workers.

An explanation for the PA paradox may be differences in the nature of occupational and leisure time PA.[32] High levels of occupational PA, commonly reached by tasks involving manual handling, repetitive work and prolonged static postures, elevate heart rate and blood pressure and are performed over long periods of time (often ≥40 hours/week), with insufficient time for recovery. Leisure time PA, on the other hand, typically takes place in short moderate or high intensity bouts of predominantly aerobic activities, accompanied by much longer recovery periods. Because of these differences, occupational and leisure time PA are likely to differ in acute and chronic physiological responses. For example, it has been shown in a sample of cleaners that, even though highly active at work, occupational PA levels did not reach intensity levels required to achieve cardiorespiratory fitness improvements.[66] High level occupational PA can, on the other hand, lead to chronic exhaustion and elevated resting blood pressure[67] and heart rate,[68] established risk factors for cardiovascular diseases[69 70] and haemodynamic phenomena that are typically related to suboptimal arterial wall stress, endothelial injury and inflammatory processes, that may ultimately result in atherosclerosis and related cardiovascular diseases.[56 71]

Although these hypothesised mechanisms hold for blue collar occupations, involving manual handling, lifting, prolonged postures and/or prolonged activity, they may not apply to all high level occupational PA jobs. A distinct occupational group is, for example, that of the elite athlete, for which the evidence suggests they may have a superior longevity, at least when compared with the general population.[72] Also, the aforementioned mechanisms apply mainly to cardiovascular disease and findings are in line with studies on cardiovascular health outcomes,[11] although they differ from those on other health outcomes (eg, type 2 diabetes,[73] and colon and breast cancer[74 75]). Our findings regarding all-cause mortality indicate that the potential detrimental effects on cardiovascular health may outweigh the potential beneficial effects on these other health outcomes. Moreover, neither our hypotheses nor the studies described in this review addressed other health risks associated with jobs of high occupational PA, such as fatal work related injuries or illnesses, that are relatively prevalent in some occupational sectors (eg, construction and agriculture).[76] Future work should therefore assess the role of occupational PA on specific cause of death outcomes.

Another explanation for the association of occupational PA with mortality (in men) may be the possibility of residual confounding, as high intensity occupational PA is typically prevalent among blue collar workers from lower socioeconomic positions[77] and low socioeconomic status is associated with higher mortality.[60] However, instead of being a confounder, occupational PA may actually be one pathway for the known mortality risks associated with low socioeconomic status, and adjustment for socioeconomic position would thus constitute an over-adjustment, introducing a conservative bias. Socioeconomic position may also exert its effects through other pathways. Compared with high socioeconomic position groups, those with a lower socioeconomic position are known to live for shorter times and in poorer health.[60] This may be related to lifestyle (eg,

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smoking, diet and leisure time PA) and other factors. Certain lifestyle factors may or may not have been sufficiently adjusted for in the currently presented data, despite the fact that we only included studies that adjusted for a minimum number of relevant factors. Moreover, some of these factors might actually be effect modifiers or pathway variables, for which interaction or mediation analyses would be more appropriate. These types of analyses have recently been performed with regard to leisure time PA[71] and should be one focus of future occupational PA research.

The positive association of occupational PA with all-cause mortality appears to be present in men but not in women (with even a tendency for an inverse association). Men are more likely to be involved in physically demanding work than women,[32] causing dissimilar stress on the cardiovascular system according to the aforementioned mechanisms. This notion may be reinforced by the fact that occupational PA was assessed by self-reports in all studies and the intensity of occupational PA may be perceived differently by women than by men. Moreover, the differences in jobs performed by men and women may bring along a different set of (socioeconomic and associated lifestyle) factors, possibly explaining the gender differences found in our study. Finally, as it has been shown that men and women respond differently to cardiovascular risk factors,[78] including PA,[33] a different response to occupational PA by gender is possible.

Apart from gender differences, the adverse health effect appears to be stronger in workers with low compared with high cardiorespiratory fitness,[17 54] however, due to insufficient data we could not statistically test this in a sensitivity analysis. Only one study used relative aerobic workload as an occupational PA exposure measure that inherently accounts for individual fitness level, and this measure was more predictive of mortality than exposure assessment by energy expenditure based on metabolic equivalents of occupational PA alone in the same study.[21] These findings suggest that future research on occupational PA needs to take individual fitness into account. It also implies that jobs need to be designed to meet individual worker capacities and that good fitness for those being active at work (possibly by being physically active during leisure time) is also important. Adverse health effects were also stronger in studies of relatively healthy compared with relatively unhealthy study subjects[55] (online supplementary material 8). This finding should not be interpreted that those with a relatively good health are more vulnerable to the risks of high level occupational PA. Instead, this finding is probably due to so-called healthy worker effect, a form of selection bias were more healthy subjects select into and remain in the most physically strenuous occupations. The presence of this effect was demonstrated in one of the reviewed studies[21] and in a previous study on occupational PA and cardiovascular disease incidence.[17]

When using sedentary behaviour as the reference category instead of low occupational PA, we found a weaker association of high level occupational PA with all-cause mortality. Sedentary behaviour is suggested to be a risk factor for all-cause mortality, which is (at least partially) independent from being physically inactive.[35] It is therefore likely that in the continuum of occupational activities, both sedentary and high level occupational PA may pose increased health risks for workers. Non-linear associations of PA with health outcomes such as U-shaped or J-shaped dose–response relationships have previously been reported for leisure time[79] and occupational PA.[43] It is, however, also known that a longer sitting time (in particular during work related computer tasks) is more frequent in higher socioeconomic groups,[80] while high occupational PA occurs more often among lower socioeconomic groups.

Strengths and limitations

The results presented in this review were obtained from low risk of bias studies using prospective data from 193 696 participants in the meta-analysis. On request, study data were re-analysed by the original authors in a harmonised manner to be able to include as much study data as possible. Sensitivity analyses showed the robustness of our findings, notably our findings remained relatively stable when adjusting for leisure time PA (if anything, HRs were higher).

A previously reported scoring tool with documented good inter-rater agreement was used for risk of bias assessment.[28] However, the sum scores of methodological quality obtained with this tool (in accordance with the authors' score scale and with our pre-registered study protocol) were not able to clearly differentiate studies of high from low risk of bias, due to inclusion of criteria reflecting complete reporting rather than bias risk and thus identifying very few studies that did not meet the 'high' quality criterion of a sum score ≥75%. Other risk assessment tools may be better able to do so and should be explored in future research. However, in order to be able to assess the role of risk of bias on the current study findings, some of the methodological components that were also included in the scale (ie, sample selection, adjustment for confounders and exposure assessment) were separately addressed by the sensitivity analyses (ie, in online supplementary material 8–10, respectively).

There was considerable heterogeneity in our pooled study findings, with up to 77% heterogeneity in the main findings. Visual inspection of funnel plots (online supplementary material 7) indicated some risk of publication bias with under-publication of negative and underpowered results. Such a bias may have been reinforced by studies in which occupational PA did not end up in the final multivariate model,[46 53] and because we were not able to pool data from several studies with null findings.[38 39 42 48] Alternatively, the counterintuitive nature of the PA paradox may have caused a bias towards under-publication of positive findings.

When multiple articles were published on the same cohort, only data from articles with the longest follow-up period were included in our quantitative analysis. As such, short term effects among the most vulnerable workers may have been missed. Furthermore, it has previously been shown that exposure outcome associations may attenuate over time in prospective studies,[81] as a result of which even stronger associations may have been found if we had reported on shorter follow-up periods. In fact, data from the only study that allowed for a direct comparison of effect sizes between short (8 years; HR 1.82, 95% CI 1.48 to 2.81)[45] and long follow-up periods (22 years; HR 1.42, 95% CI 1.15 to 1.74),[19] confirm this notion. Insufficient information on cumulative dose–response associations (in terms of years of occupational PA) is currently available. Due to a lack of repeated measurements of occupational PA in the identified studies, the effect of changes in occupational PA over time (eg, on retirement) could not be accounted for.

Studies included in this review were based only on self-reports of occupational PA and all but one[21] used crude categories (with heterogeneous definitions) to operationalise occupational PA exposure. The reduction of continuous data or multiple occupational PA categories into a dichotomous variable as performed either by the original study authors or by us for the purpose of our meta-analysis may have resulted in a conservative misclassification bias, leading to an underestimation of the magnitude of the association of occupational PA with mortality. A better understanding of this phenomenon requires future studies

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using objectively and continuously measured occupational PA, re-analyses of existing data and full utilisation of rank ordered occupational PA categories when available. Moreover, future research should clearly distinguish PA domains (ie, work and leisure time, as well as transportation) when studying the association of PA with health outcomes. This can, for example, be done by combining accelerometer based measurements with logs or self-reported diaries regarding time use (eg, the time spent at work).[82] Consistent reporting of PA outcomes, across different domains of PA, can facilitate future harmonisation of data.

In future studies, more detailed information on various causes of death, and studies on physiological outcomes (eg, heart rate, blood pressure) and more proximal (early non-symptomatic) disease outcomes (eg, arterial intima media thickness, heart rate variability, pulse wave velocity) should be examined. Studies of non-symptomatic outcomes are less vulnerable to healthy worker selection bias, and may be advantageous to further elucidate the underlying mechanisms of the association of occupational PA with adverse health outcomes.

CONCLUSION

This systematic review shows that men with high levels of occupational PA experience higher mortality risks from all causes compared with those engaging in low levels of occupational PA, even after controlling for relevant factors (including leisure time PA). These findings suggest that a PA paradox may exist in male workers. The mechanisms behind this should be explored further. If the observed associations are causal, then PA guidelines should differentiate between occupational and leisure time PA. Meeting current general PA guidelines through occupational PA instead of leisure time PA may not provide the intended health benefits or may even confer health risks.

What is already known?

- The importance of physical activity for the prevention of non-communicable diseases has been well described.
- Health effects associated with different (ie, occupational, leisure time and transportation) domains of physical activity are considered to be beneficial and alike.
- New evidence, however, suggests a physical activity paradox with a contrast between the health effects associated with leisure time and occupational physical activity.
- This evidence, surprisingly, suggests beneficial health outcomes associated with high level leisure time physical activity, but detrimental health consequences associated with those exposed to high level occupational physical activity.

What are the new findings?

- We are the first to find evidence consistent with the physical activity paradox in a systematic review with meta-analysis, summarising evidence from 17 longitudinal studies with 1 93 696 participants.
- We showed that men engaging in high (compared with low) level occupational physical activity have a 18% increased risk of all-cause mortality, even after adjustment for relevant factors, such as leisure time physical activity.
- This evidence indicates that physical activity guidelines should differentiate between occupational and leisure time physical activity.

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