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Associations of occupational and leisure-time physical activity with all-cause mortality: an individual participant data meta-analysis

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ABSTRACT

Objective Health effects of different physical activity domains (ie, during leisure time, work and transport) are generally considered positive. Using *Active Worker consortium* data, we assessed independent associations of occupational and leisure-time physical activity (OPA and LTPA) with all-cause mortality.

Design Two-stage individual participant data meta-analysis.

Data source Published and unpublished cohort study data.

Eligibility criteria Working participants aged 18–65 years.

Methods After data harmonisation, we assessed associations of OPA and LTPA with all-cause mortality. In stage 1, we analysed data from each study separately using Cox survival regression, and in stage 2, we pooled individual study findings with random-effects modelling.

Results In 22 studies with up to 590 497 participants from 11 countries, during a mean follow-up of 23.1 (SD: 6.8) years, 99 743 (16%) participants died. Adjusted for LTPA, body mass index, age, smoking and education level, summary (ie, stage 2) hazard ration (HRs) and 95% confidence interval (95% CI) for low, moderate and high OPA among men (n=2 96 134) were 1.01 (0.99 to 1.03), 1.05 (1.01 to 1.10) and 1.12 (1.03 to 1.23), respectively. For women (n=2 94 364), HRs (95% CI) were 0.98 (0.92 to 1.04), 0.96 (0.92 to 1.00) and 0.97 (0.86 to 1.10), respectively. In contrast, higher levels of LTPA were inversely associated with mortality for both genders. For example, for women HR for low, moderate and high compared with sedentary LTPA were 0.85 (0.81 to 0.89), 0.78 (0.74 to 0.81) and 0.75 (0.65 to 0.88), respectively. Effects were attenuated when adjusting for income (although data on income were available from only 9 and 6 studies, for men and women, respectively).

WHAT IS ALREADY KNOWN ON THE TOPIC

⇒ Physical activity is important for the prevention of many non-communicable diseases and health effects of different physical activity domains (ie, leisure time, work, household and transport) are generally considered to be positive.

⇒ Some studies indicate that high occupational physical activity is associated with adverse health outcomes, although the quality of the current evidence on this topic is moderate.

⇒ In the Active Worker study, we addressed some of the previous limitations in the literature with an individual participant data meta-analysis.

WHAT THIS STUDY ADDS

⇒ Even after adjusting for the other domain of physical activity, body mass index, age, smoking and education level, we found higher levels of leisure-time physical activity were associated with a lower risk of all-cause mortality, while higher levels of occupational physical activity were associated with a higher risk of mortality in men but not in women.

⇒ Our findings suggest that public health messages, stating that daily physical activity can be accrued as part of any domain, may not be adequate for adults obtaining most of their physical activity at work.

⇒ As the evidence base on this topic develops, more tailored advice for those with physically active occupations, including in work safety regulations and training of occupational health professionals, might be required.

Conclusion Our findings indicate that OPA may not result in the same beneficial health effects as LTPA.

INTRODUCTION

Physical activity is of importance for the prevention of many non-communicable diseases.[1] The health effects of different physical activity domains (ie, leisure time, work, household and transport)[2] are generally considered to be positive. This can be seen in physical activity guidelines that advocate daily engagement in aerobic physical activity of moderate-to-vigorous intensity as part of leisure, transportation, work and/or household activities.[3]

High levels of leisure-time physical activity (LTPA) are associated with lower risk of several non-communicable diseases.[4] Yet, emerging evidence indicates that high levels of occupational physical activity (OPA) are associated with adverse health outcomes. This phenomenon, referred to as the *physical activity paradox*,[5] has been addressed in recent systematic reviews on all-cause mortality,[6] cardiovascular disease[7 8] and cancer.[9] Evidence on the topic is conflicting, as in an umbrella review, high levels of OPA had favourable effects for multiple cancer outcomes, stroke, coronary heart disease and mental health, while unfavourable effects were reported for all-cause mortality in men, mental well-being, osteoarthritis and sleep quality.[10] Workers with lower socioeconomic status are often inactive during leisure time,[11] while accumulating most of their daily physical activity at work.[12] The possible existence of a *physical activity paradox,* therefore, implies that workers with a lower socioeconomic status may be exposed to ambiguous health consequences of OPA, while only benefiting to a limited extent from positive health consequences of LTPA (as engagement in such activities is often limited).

The quality of the current evidence is moderate at best,[10] with residual (unmeasured) confounding a considerable concern and socioeconomic status and smoking believed to be key confounding variables not or insufficiently addressed in many previous studies.[13] Other limitations include uneven geographical coverage of the evidence-base, mainly originating from high income Western-European countries, and biases associated with (self-reported) assessments of physical activity.[13] More high-quality evidence on the possible differential health effects of OPA versus LTPA is needed. An individual participant data (IPD) meta-analysis can reduce some previous limitations, since variable definitions and analytic strategies, including those for confounding, can be harmonised. The value of an IPD meta-analysis is further enhanced if additional unpublished data can be located, harmonised and analysed. Using IPD from the *Active Worker study*, we aimed to assess the association of OPA and LTPA with all-cause mortality.

METHODS

The *Active Worker* study protocol[14] was a-priori registered.[15] We conducted and reported our study using methods described by the Cochrane IPD Meta-analysis Methods Group[16] and the Preferred Reporting Items for Systematic Review and Meta-Analyses of Individual Participant Data (PRISMA-IPD) statement.[17]

Data collection

We identified cohort studies (with published and unpublished data on the topic) using literature searches in electronic databases and scoping searches through personal communication with experts, collaborators and colleagues. The literature search has been described in detail elsewhere.[14] Briefly, we conducted a systematic search for original prospective studies with data on at least OPA and LTPA, socioeconomic status indicators and all-cause and/or cardiovascular mortality among adult part-time or full-time workers (aged 18–65 years at baseline). Data from these cohort studies were eligible regardless of whether associations of physical activity with health outcomes had been previously published from these cohorts or not. Corresponding authors of eligible studies were invited to collaborate, asked to complete our data request form, providing more study details (regarding the design and available data) and sign a policy document. Hereafter, collaborators were asked to transfer their anonymised and encrypted cleaned datasets with complete cases only (ie, with data on at least physical activity and mortality variables) or to conduct the analyses remotely (in cases IPD could not be shared) using the harmonisation and analysis plan described below.

Data harmonisation

Data on OPA and LTPA and relevant additional variables (all measured at baseline) and all-cause mortality were retrieved from all participating studies (see the list of requested variables in online supplemental appendix 1). Data of all studies were harmonised according to definitions that were published in our study protocol,[14] which were further developed in an iterative process of Active Worker core group consensus meetings, seeking verification by data contributors. Our final definitions are described in more detail in a codebook (available on request). Definitions were also shared with collaborators that analysed their data remotely, so that they could follow similar harmonisation procedures. The most detailed level of data available (eg, continuous rather than categorical) was used for harmonisation. However, the level of detail after the harmonisation procedure depended on the study with the least detailed data. If a study consisted of multiple data collection waves, the wave with the longest follow-up period was chosen for harmonisation, to obtain more events.[18] Data were checked for consistency, which included identifying outliers and missing data. Queries were discussed and resolved with the study collaborator. No imputation on missing data was performed.

Physical activity

Physical activity (during work and leisure time—the latter sometimes also incorporating transportation) from categorical and continuous variables was harmonised into four categories along the physical activity continuum.[19] OPA categories roughly reflect: mainly sitting work (sedentary), work that mainly involves standing or walking, without lifting or carrying (low level), work that involves carrying light objects or walking stairs (moderate level) and physically demanding work involving frequent carrying or lifting heavy loads (high level). LTPA categories roughly reflect: almost no regular physical activity, spending most leisure-time sitting (sedentary), occasionally engaging in leisure-time activities such as slow walking or household activities (low level), engaging in activities such as brisk walking or dancing (moderate level) and regular engagement in activities such as jogging or cycling (high level). Although we requested device-based and self-reported data on physical activity, only the latter were provided to us and used for harmonisation. OPA assessment methods included self-reported OPA (eg, in terms of tasks conducted, physical activity intensity or self-perceived load). One study assessed relative aerobic workload taking objectively measured cardiorespiratory fitness into account[20] and one

study used self-reported occupational classification codes, which were further categorised into OPA exposures[21] (online supplemental appendix 2).

If possible, we recoded existing categorical variables into the four aforementioned categories. Continuous data were categorised using tertiles or quartiles, with arbitrary cut-off points, since established cut-off points were not available or could not be feasibly used for all measurement tools. This was done on a study level, but not on a gender level. The above was determined in an iterative process in which we sought consensus among the Active Worker core group members, using input from the data contributors.

All-cause mortality

Outcome ascertainment was registry-based or hospital record-based (online supplemental appendix 3). All-cause mortality was harmonised as dichotomous variable depicting incidence (yes/no) and time-to-event (in days).

Additional variables

We differentiated low (preprimary/primary/lower secondary), moderate (upper secondary) and high (postsecondary) education, using the ISCED-97 classification. Income (in most studies: household income) was harmonised using predefined income categories or tertiles of continuous variables to categorise low/moderate/high income. Age and gender were harmonised as a continuous (in years) and dichotomous (man/woman) variable, respectively. We used body mass index (BMI; in kg/m^2) as a measure of adiposity, with other measures of adiposity (eg, waist circumference and skinfold thickness) being insufficiently available across studies. Data were restricted to BMI values >14 or <48[22] (<1% of the total sample). Smoking was dichotomised into current smokers and non-smokers (including those who smoked in the past).

Risk of bias assessment

Risk of bias (RoB) was assessed by two reviewers independently (PC/MH/BC) based on the original articles (see table 1 for references), using a scoring system[23] with criteria regarding: (1) participation, (2) attrition, (3) exposure assessment (scoring OPA and LTPA together, with the score depending on the weakest assessment method) and (4) outcomes. Conflicts were resolved during a consensus meeting (with authors PC/BC/MH/AJvdB/WvM).

Data analysis

We performed a two-stage meta-analysis where in the first stage, each study was analysed separately. In the second stage, the results per study were statistically pooled using Stata's *admetan* function. Due to high statistical heterogeneity in some of the models (I^2>70%), random-effect models were used.

We used Cox proportional hazards models, estimating HRs with 95% CI, to assess associations of OPA and LTPA with all-cause mortality. Per our study protocol,[14] we a-priori decided to consider man and woman separately, as gender differences in health outcomes of OPA have previously been reported.[6] Clustering was assessed using random intercepts. Correlations between variables were assessed on the data available to the core team. As all correlation coefficients were below our prespecified threshold of <0.70 (ie, <0.35; online supplemental appendix 4) multicollinearity was rendered unlikely. Models were not used if (1) <25 data points were available in any of the exposure variable categories (with ≥5 participants per covariate)[24] or (2) models had imprecise effect sizes (with a beta SE >3); for example, for a point estimate of HR=1.50, this translates to a (0.17 to 12.88) 95% CI.

Based on directed acyclic graphs (DAG) drawn using Daggity software (dagitty.net; online supplemental appendix 5), analyses were done with several levels of adjustment. First, we estimated unadjusted associations. Second, we adjusted for BMI, age, smoking and the other domain of physical activity. In a third set of models, we additionally adjusted for education level. The role of education was additionally considered by stratifying on education level. Data on income were not available from more than half of the cohorts, yet since it is unclear whether it is a confounder or mediator or both (online supplemental appendix 5), we chose to adjust for income in a sensitivity analysis. Analyses were performed on the subset of participants for which relevant data were available.

With these models, we deviated from our original meta-analysis protocol[14] for various reasons. Data on diet, medication use, coffee use and alcohol intake could not be harmonised due to the large heterogeneity in definitions and measurement methods across studies. The following variables could also not be used due to insufficient information (with data from <50% of studies) being available: ethnicity (available in 41% of studies), self-reported health (47%), psychosocial work demands (47%), history of non-communicable diseases (<35%), blood markers (eg, cholesterol, triglycerides, haemoglobin, insulin or thyroglobulin <35%), sleep quality (41%), healthcare utilisation (35%), parental socioeconomic status (24%), social support (29%) and neighbourhood conditions (12%). Finally, we did not adjust for blood pressure, glucose, diabetes or marital status as these variables were not deemed confounders according to our DAGs (online supplemental appendix 5).

In sensitivity analyses assessing the role of RoB on the association of OPA with all-cause mortality, we compared findings from studies with low versus moderate/high RoB. Only RoB considering participation, attrition and exposure measurements were assessed. The item on outcome measurements provided insufficient variation between studies (all, except one,[25] were appraised low RoB). Since the level of OPA changed during the last decades,[26] we assessed the role of baseline assessment moment on our findings, by comparing studies with baseline assessment before and after 1990. We assessed the role of individual study findings by subsequently leaving individual study findings out of the analyses. Funnel plots were generated to assess publication bias (using visual inspection). We also performed a sensitivity analysis, in which we excluded participants who died within the first 3 years of follow-up. Because the health effects of LTPA are well established,[4] abovementioned sensitivity analyses were only conducted on OPA models. All sensitivity analyses were performed on model 3.

Equity, diversity and inclusion statement

In this study, we compared people with various levels of LTPA and OPA, who are by definition from a variety of socioeconomic positions. We performed gender-specific analyses. Also, we intended to collect published and unpublished data, and thereby include authors, from across the globe. Despite our efforts, most included cohorts (and authors) were from Western European countries. Our author team, however, shows diversity in gender and age groups.

Patient and public involvement

An advisory group of public and occupational health professionals provided, in multiple meetings, their input on the

Table 1 Overview of included studies, their main characteristics and risk of bias

			Sample information							Risk of bias			
Reference	Study name	Country	n	Age at baseline	Females	Sample	Baseline	FU	Incidence	1	2	3	4
Clays *et al*[27]	BELFIT study	Belgium	2351	47.2 (4.4)	0%	Industry	1976	16.7 (3.5)	306 (13%)	Mod	Mod	Mod	Low
Saidj *et al*[64]	Health 2006 (H2006)*	Denmark	2663	45.9 (11.6)	54%	Gen pop	2006	10.5 (1.0)	53 (2%)	Mod	Mod	Low	Low
Sjøl *et al*[65]	MONICA Denmark	Denmark	6576	44.4 (11.1)	50%	Gen Pop	1976	9.5 (3.5)	395 (6%)	Mod	Mod	Mod	Low
Krause *et al*[20]	KIHD study	Finland	1883	51.8 (5.0)	0%	Gen Pop	1984	24.6 (7.9)	923 (49%)	Low	Low	Low	Low
Pulsford *et al*[31]	Whitehall II study	UK	3160	52.2 (4.2)	29%	Civil servants	1997	16.9 (2.0)	221 (7%)	Mod	Mod	High	Low
Eaton *et al*[25]	IIHDS study	Israel	9379	49.0 (6.6)	0%	Civil servants	1963	28.2 (11.3)	7878 (84%)	Low	Low	Mod	Mod
Autenrieth *et al*[66]	MONICA/KORA Augsburg	Germany	2628	42.6 (10.3)	38%	Gen Pop	1989	18.3 (2.7)	263 (10%)	Mod	Low	Mod	Low
Rosengren and Wilhelmsen[29]	Primary Prevention Study	Sweden	7317	51.6 (2.3)	0%	Gen Pop	1970	27.2 (10.5)	6366 (87%)	Mod	Low	Mod	Low
Richard *et al*[21]†	NHANES study	USA	8984	40.4 (13.1)	47%	Gen Pop	2005	5.9 (1.7)	180 (2%)	Low	Low	Mod	Low
Moe *et al*[67]	HUNT study	Norway	41 161	40.9 (11.5)	52%	Gen Pop	1995	20.1 (4.4)	2881 (7%)	Mod	Low	Mod	Low
Franzon *et al*[68]	ULSAM study	Sweden	2106	49.6 (0.6)	0%	Gen Pop	1970	30.1 (10.5)	1959 (93%)	Low	Low	Mod	Low
Huerta *et al*[69]	EPIC Spain study	Spain	13 752	46.8 (6.3)	66%	Gen Pop	1992	18.7 (2.2)	963 (7%)	High	Low	Low	Low
Johnsen *et al*[32]	WOLF study	Sweden	10 333	42.1 (10.7)	31%	60 companies	1992	23.5 (3.3)	310 (3%)	Low	Low	Mod	Low
Bahls *et al*[70]	SHIP-START1 study	Germany	1502	44.3 (9.5)	53%	Gen Pop	2002	8.2 (1.4)	30 (2%)	Mod	Mod	Low	Low
Bahls *et al*[70]	CARLA study	Germany	386	53.7 (4.3)	39%	Gen Pop	2002	11.7 (1.3)	19 (5%)	Mod	Mod	Low	Low
Wanner *et al*[71]	The Swiss MONICA study	Switzerland	8487	45.2 (10.0)	50%	Gen Pop	1984	24.5 (6.9)	1782 (21%)	Low	Low	Mod	Low
Wanner *et al*[71]	NRP 1A study	Switzerland	4602	39.4 (11.8)	37%	Gen Pop	1977	31.9 (9.9)	1703 (37%)	Mod	Low	Mod	Low
Petersen *et al*[72]	Danish National Health Interview Surveys*	Denmark	15 466	40.6 (13.3)	50%	Gen Pop	1987	11.9 (4.1)	763 (5%)	Low	Low	Mod	Low
Dalene *et al*[38]	Norwegian study*	Norway	404 239	41.3 (5.9)	52%	Gen Pop	1974	26.7 (6.6)	57 332 (14%)	Mod	Low	Low	Low
Holtermann *et al*[73]	Copenhagen City Heart Study*	Denmark	10 934	52.1 (10.2)	58%	Gen Pop	1976	18.4 (7.6)	8615 (79%)	Mod	Low	Mod	Low
Holtermann *et al*[37]	Copenhagen General Population Study*	Denmark	69 652	52.2 (10.7)	55%	Gen Pop	2003	10 (3.1)	2001 (3%)	Mod	Low	Mod	Low
Holtermann *et al*[30]	Copenhagen male study*	Denmark	5082	48.7 (5.3)	0%	Working pop	1970	28.9 (1.6)	4801 (92%)	Mod	Low	Mod	Low
	Total		632 643	43.1 (7.9)	49%			23.1 (6.8)	99 743 (16%)				

Data from 16 studies were combined in one dataset and data from an additional 6 studies (denoted with a * sign) were analysed remotely and combined in the second stage of the two-stage meta-analysis.
Age in years (mean (SD)).1=study participation; 2=study attrition; 3=predictive variable assessment; 4=outcome ascertainment. Risk of bias was assessed according to established criteria.[23] See online supplemental appendix 7 for more details on the risk of bias assessment.
*Studies that were analysed remotely.
†Although a reference is made to the paper by Richard and colleagues (which is the only paper we identified on the topic using NHANES data), different measurement waves were included for our meta-analysis. Measurements of the following waves were used in which all dependent and confounding variables were assessed: 2005–2006, 2007–2008, 2009–2010 and 2011–2012. For outcomes the 2015 follow-up measurements were used.
FU, follow-up period in years (mean (SD)); Gen pop, general population; Working pop, working population.

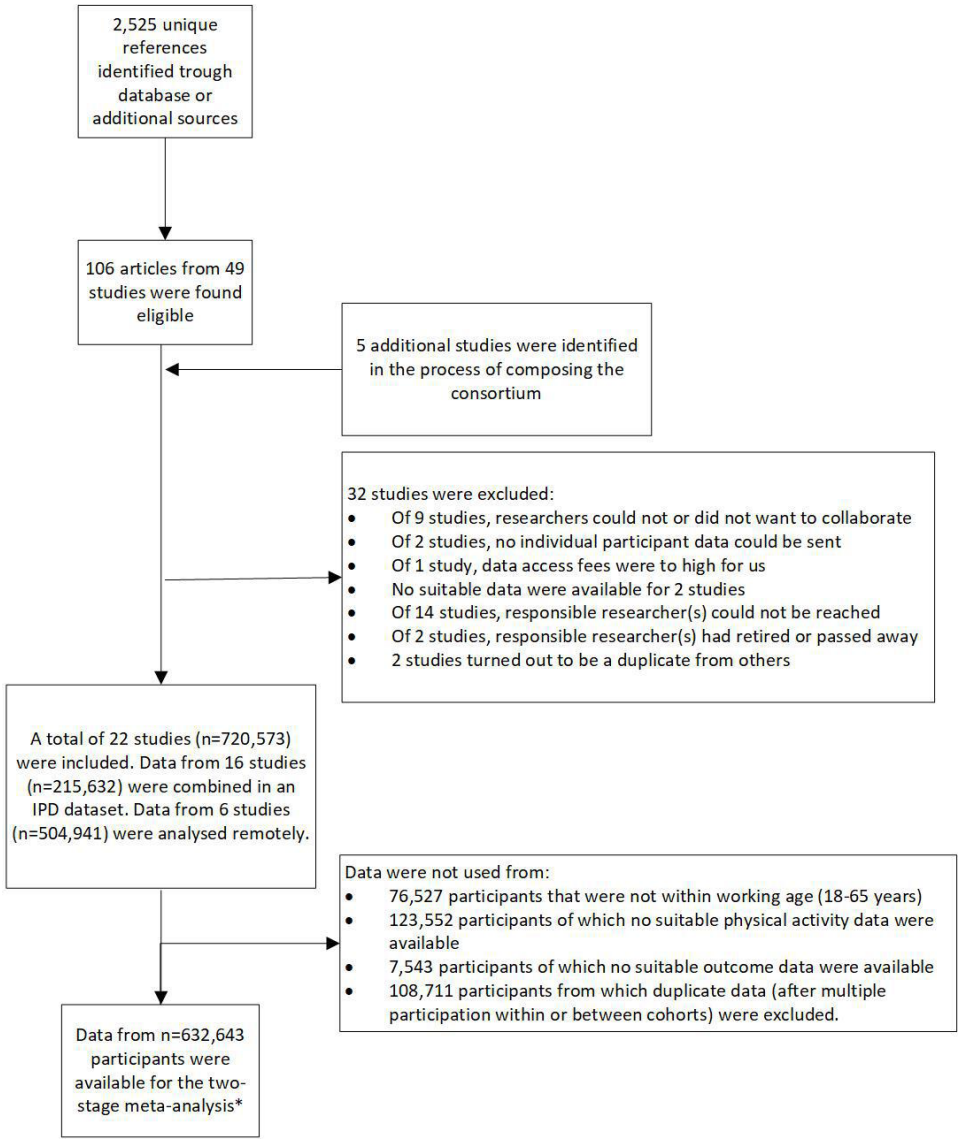

Figure 1 Flowchart showing the process of the composition of our individual participant data (IPD) two-stage meta-analysis. *Although the full dataset has data on 632 643 participants, note that the number of participants varies between the various models. Please refer to tables 3 and 4 for the number of participants per model.

design and results of this study to secure practical relevance. In particular, the advisory group helped developing our models, which were based on the DAGs (online supplemental appendix 5), using their expertise. Also they helped to interpret our findings and its implications for practice. Patients nor members of the general public were involved in this research project.

RESULTS

Our data collection procedure is shown in figure 1. Through contacting researchers from 49 eligible studies, we identified five additional studies. Data from 32 studies could not be used for various reasons (online supplemental appendix 6). Data from 22 studies were included in our study (table 1). Data from 16 studies (n=1 24 607) were combined in one dataset and data from an additional six studies (n=5 09 524) were analysed remotely and combined in the second stage of the two-stage meta-analysis. Excluding participants who were outside predefined age ranges had missing data for physical activity and/or all-cause mortality, or were duplicates, a final dataset of 632 643 participants was composed. Hereof, 590 497 (97%) and 597 002 (97%) were included in the final adjusted models for OPA and LTPA, respectively.

Table 2 and online supplemental appendix 3 describe the characteristics of the study sample and protocol, respectively. All but one study from Israel[25] were from Western Europe and the USA. Seventeen studies included men and women, five included men only.[25 27–30] Most studies used population-based samples; one study—an industry sample,[27] two studies—samples of civil servants[25 31] and two studies—sampled workers from selected occupational sectors.[30–32] Mean age at baseline was 43.1 (SD: 7.9) years, and 99 743 (16%) participants died during an average 23.1 years (SD: 6.8) follow-up period.

RoB regarding participation (ie, participation rates being low) and attrition was noted for 14 studies (table 1; online supplemental appendix 7). Six studies had a low risk of exposure assessment bias, they all used questionnaires with established validity and/or reliability (see online supplemental

Table 2 Descriptive characteristics of the individual participant dataset comprising data from n=22 cohort studies

		N	n	%	Mean	SD
Total		22	632 643			
Occupational physical activity*	Sedentary	22	217 504	34		
	Low	22	227 453	36		
	Medium	22	130 524	21		
	High	22	55 242	9		
Leisure-time physical activity*	Sedentary	22	123 311	19		
	Low	22	304 905	48		
	Medium	22	157 357	25		
	High	22	47 056	7		
Education level	Low	21†	129 736	21		
	Medium	21†	309 613	50		
	High	21†	181 528	29		
Gender	Men	22	320 523	51		
	Women	22	311 714	49		
Smoking	No	22	404 430	64		
	Yes	22	224 179	36		
Age (years)		22			43.1	7.9
BMI (kg/m^2)		22			25.2	3.8

*Physical activity levels (during work and at leisure time) reflect the physical activity continuum, ie, sedentary, low, moderate and high. For leisure-time physical activity, these categories roughly indicate: spending most leisure time sitting (sedentary), occasionally engaging in light intensity physical activities during leisure time such as slow walking or household activities (low), engaging in physical activities of moderate intensity such as intense household activities or brisk walking (moderate), regular engagement in high intensity physical activities such as jogging or cycling, thereby meeting physical activity guidelines (high). For occupational physical activity, categories roughly indicate: mainly sitting work (sedentary), work that mainly involves standing or walking, but without lifting or carrying loads (low), work that involves carrying light objects or walking stairs (moderate), highly physically demanding works involving frequent carrying or lifting heavy loads (high).
†No data on this metric provided by Primary Prevention Study.[29]
BMI, body mass index; N, number of studies from which this variable is available; n, number of participants.

appendix 2). Except for one study,[25] all studies used register data to ascertain mortality (low RoB).

Association of occupational and LTPA with all-cause mortality

The associations of OPA and LTPA with all-cause mortality are shown for men and women in tables 3 and 4.

Occupational physical activity

For men, higher levels of OPA were associated with higher risks of all-cause mortality in all models. Adjustment for confounders, especially adding education in model 3, attenuated risks to adjusted HRs of 1.01 (95% CI 0.99 to 1.03), 1.05 (95% CI 1.01 to 1.10) and 1.12 (95% CI 1.03 to 1.23) for low, moderate and high OPA, respectively, when compared with sedentary. Associations using low level OPA as reference category showed a similar trend, although with a slightly stronger attenuation (online supplemental appendix 8). These analyses were based on a slightly different set of studies as not all studies had data on all four physical activity categories. Forest plots are shown in online supplemental appendix 9. In sensitivity analyses, additionally adjusting for income, estimates were further attenuated yielding null findings (online supplemental appendix 10). When stratifying by educational level, estimates in the moderate and high education strata were similar to estimates from model 3, but no association was observed in the low education stratum (online supplemental appendix 11).

Funnel plots (online supplemental appendix 12) showed some degree of publication bias. Moreover, we found stronger associations among studies with low compared with moderate/high RoB regarding attrition, and the opposite for RoB regarding participation. Studies with different levels of RoB regarding exposure assessment were comparable (online supplemental appendix 13). Associations did vary somewhat when testing for the impact of individual studies (online supplemental appendix 14). We showed comparable HRs for studies with baseline assessment before/after 1990 (online supplemental appendix 15), and when only analysing participants that survived the first 3 years after baseline (online supplemental appendix 16).

For women, unadjusted estimates suggested higher levels of OPA were associated with higher risks of all-cause mortality. Estimates were substantially attenuated in models 2–3. Model 3 yielded HRs of 0.98 (95% CI 0.92 to 1.04), 0.96 (95% CI 0.92 to 1.00) and 0.97 (95% CI 0.86 to 1.10) for low, moderate and high OPA, respectively. Associations were not substantially impacted by individual studies. Associations remained relatively unchanged when stratifying for educational level, when additionally adjusting for income, for studies with baseline assessment before/after 1990, when assessing the role of RoB and when only analysing participants who survived the first 3 years after baseline.

Leisure-time physical activity

Unadjusted and adjusted analyses consistently showed lower risks of all-cause mortality with higher LTPA levels across all models. For men, model 3 indicated an inverse association for low (HR: 0.87, 95% CI 0.83 to 0.92), moderate (HR: 0.79, 95% CI 0.73 to 0.86) and high (HR: 0.79, 95% CI 0.72 to 0.86), compared with sedentary LTPA. For women, comparable associations were found for low (HR: 0.85, 95% CI 0.81 to 0.89), moderate (HR: 0.78, 95% CI 0.74 to 0.81) and high (HR: 0.75, 95% CI 0.65 to 0.88), compared with sedentary LTPA. Associations were not substantially impacted by stratification on education level (online supplemental appendix 11) nor by individual studies (online supplemental appendix 14).

DISCUSSION

In line with harmonised analyses on large datasets, using self-reported[33] or device-based physical activity,[34] we consistently found higher levels of LTPA to be associated with lower risks of all-cause mortality. OPA did not show such associations, as higher levels of OPA were associated with higher all-cause mortality in men and with null effects in women. Results for both OPA and LTPA remained mostly unchanged in sensitivity analyses. Our findings indicate that LTPA is associated with lower risk of mortality while OPA is not and, to the contrary, is associated with higher mortality risk among men in some of our models. These findings could be highly relevant for large parts of the working population, in particular, those who accrue most of their daily physical activity at work.[12] OPA is still prevalent in our working societies, in both affluent Western and low and middle-income countries. For example, in the USA, in 2010, approximately 20% of the jobs consisted of a combination of tasks with a metabolic equivalent, indicating at least moderate intensity-level physical activity.[26] However, in several low to middle-income countries, OPA makes up most of daily physical activity.[35] For example, a study across 22 African countries revealed that only 5% of physical activity was accrued during leisure time,[36] despite the vast

Table 3 Association of occupational (left panels) and leisure-time physical activity (right panels) with all-cause mortality in men

	Occupational physical activity			Leisure-time physical activity		
Model 1*	n	N	HR (95% CI)	n	N	HR (95% CI)
Sedentary	122 419	20	1.00 (reference)	64 306	19	1.00 (reference)
Low	84 029	18	1.12 (1.07 to 1.17)	131 670	19	0.81 (0.77 to 0.85)
Moderate	65 449	20	1.21 (1.13 to 1.30)	86 317	19	0.66 (0.55 to 0.79)
High	38 514	18	1.36 (1.22 to 1.51)	27 938	17	0.53 (0.36 to 0.79)
Model 2†						
Sedentary	119 487	19	1.00 (reference)	63 534	19	1.00 (reference)
Low	83 441	18	1.08 (1.05 to 1.10)	128 470	19	0.87 (0.83 to 0.91)
Moderate	64 841	19	1.17 (1.15 to 1.20)	85 677	19	0.77 (0.71 to 0.84)
High	38 317	18	1.23 (1.15 to 1.31)	27 546	17	0.77 (0.70 to 0.85)
Model 3‡						
Sedentary	116 316	18	1.00 (reference)	61 375	18	1.00 (reference)
Low	79 957	17	1.01 (0.99 to 1.03)	126 414	18	0.87 (0.83 to 0.92)
Moderate	62 564	18	1.05 (1.01 to 1.10)	83 892	18	0.79 (0.73 to 0.86)
High	37 297	17	1.12 (1.03 to 1.23)	26 538	16	0.79 (0.72 to 0.86)

Physical activity levels (during work and at leisure time) reflect the physical activity continuum, ie, sedentary, low, moderate and high. For occupational physical activity, categories roughly indicate: mainly sitting work (sedentary), work that mainly involves standing or walking, but without lifting or carrying loads (low), work that involves carrying light objects or walking stairs (moderate), physically demanding work involving frequent carrying or lifting heavy loads (high). For leisure-time physical activity, these categories roughly indicate: almost no regular physical activity, spending most leisure time sitting (sedentary), occasionally engaging in leisure time activities such as slow walking or household activities (low), engaging in activities such as intense household activities or brisk walking (moderate), regular engagement in activities such as jogging or cycling (high).
Note that the number of studies (N) differs across comparisons, as not all occupational and leisure-time physical activity categories were available from all studies (see online supplemental appendix 2 for an overview).
*Model 1: Unadjusted model.
†Model 2: Adjusted for the other domain of physical activity, body mass index, age and smoking.
‡Model 3: Additionally adjusted for education level.
N, number of studies; n, number of participants.

Table 4 Association of occupational (left panels) and leisure-time physical activity (right panels) with all-cause mortality in women

	Occupational physical activity			Leisure-time physical activity		
Model 1*	n	N	HR (95% CI)	n	N	HR (95% CI)
Sedentary	94 114	14	1.00 (reference)	58 946	13	1.00 (reference)
Low	137 007	13	1.11 (1.03 to 1.20)	169 993	13	0.73 (0.61–0.88)
Moderate	62 129	12	1.06 (0.98 to 1.14)	59 877	13	0.56 (0.39–0.81)
High	6744	11	1.35 (1.07 to 1.70)	16 910	11	0.49 (0.31–0.78)
Model 2†						
Sedentary	93 254	14	1.00 (reference)	58 110	13	1.00 (reference)
Low	136 244	13	1.01 (0.94 to 1.08)	168 007	13	0.83 (0.78–0.88)
Moderate	61 536	12	1.02 (0.98 to 1.06)	59 265	13	0.74 (0.71–0.77)
High	6623	11	1.06 (0.98 to 1.14)	16 624	11	0.74 (0.62–0.88)
Model 3‡						
Sedentary	92 215	14	1.00 (reference)	57 812	13	1.00 (reference)
Low	135 154	13	0.98 (0.92 to 1.04)	167 175	13	0.85 (0.81–0.89)
Moderate	60 482	12	0.96 (0.92 to 1.00)	58 332	13	0.78 (0.74–0.81)
High	6512	11	0.97 (0.86 to 1.10)	15 464	11	0.75 (0.65–0.88)

Physical activity levels (during work and at leisure time) reflect the physical activity continuum, ie, sedentary, low, moderate and high. For occupational physical activity, categories roughly indicate: mainly sitting work (sedentary), work that mainly involves standing or walking, but without lifting or carrying loads (low), work that involves carrying light objects or walking stairs (moderate), physically demanding work involving frequent carrying or lifting heavy loads (high). For leisure-time physical activity, these categories roughly indicate: almost no regular physical activity, spending most leisure time sitting (sedentary), occasionally engaging in leisure time activities such as slow walking or household activities (low), engaging in activities such as intense household activities or brisk walking (moderate), regular engagement in activities such as jogging or cycling (high).
Note that the number of studies (N) differs across comparisons, as not all occupational and leisure-time physical activity categories were available from all studies (see online supplemental appendix 2 for an overview).
*Model 1: Unadjusted model.
†Model 2: Adjusted for the other domain of physical activity, body mass index, age and smoking.
‡Model 3: Additionally adjusted for education level.
N, number of studies; n, number of participants.

majority of individuals in these countries (ie, 84% among men) meeting physical activity guidelines.

Interpretation of findings

Our findings on differential health effects of LTPA and OPA are in line with an earlier systematic review[6] and with some individual studies published after that review (including studies incorporated in this meta-analysis).[37] Findings are, however, in contrast with a Norwegian study, also incorporated in our meta-analyses, that showed beneficial health effects of OPA.[38] Other studies, such as those based on the NIH-AARP Diet and Health Study[39] and the UK Biobank,[40] which were not part of this meta-analysis, showed null findings in the association of OPA and mortality.

Both methodological[13] and physiological[41] explanations have been raised for these conflicting findings. Methodological limitations of the evidence include study selection bias (with most evidence originating from Western European countries), misclassification of physical activity in original assessment and during analysis, insufficient control of confounding,[13] healthy worker selection bias and heterogeneity of methods. While in this IPD meta-analysis, we addressed some of these issues (most notably dealing with heterogeneity in methods), for others, our results still do not provide an unequivocal resolution. Despite our efforts to include studies from across the globe and incorporating unpublished data to address study selection bias, our database still originates mainly from affluent Western countries. Thirty-two eligible studies, including several from low-to-middle income countries (eg, Iran[42] and China)[43] or from non-Western countries (eg, Japan),[44] could unfortunately not be incorporated (online supplemental appendix 6), and some degree of publication bias was seen in our funnel plots. As associations of physical activity and health may differ between countries,[45] with OPA making up most of daily physical activity in low-to-middle income countries,[35] our results may not be generalisable to those countries. Providing evidence from such countries should be a research priority. Moreover, this research field has shown to be rapidly emerging and since the start of this study, several studies that could be relevant to include in a future IPD meta-analysis have been published.[46 47]

All studies included in our meta-analysis relied on self-reports of physical activity, possibly resulting in exposure misclassification bias.[48] Emerging evidence from studies with accelerometer assessed (total) physical activity indicate stronger associations with health than earlier studies that assessed (leisure time) physical activity with self-reports.[34] The harmonisation procedure, in which we categorised physical activity measures (even those on a continuous scale) in four crude categories, has also introduced misclassification bias. Nevertheless, we were able to provide some insights into the association of OPA and LTPA with all-cause mortality across four levels of physical activity. This is an advantage of our study over earlier systematic reviews in which only the health effects of low and high level OPA were compared.[6] Nonetheless, in harmonising OPA, information was inevitably lost due to categorising different modalities (eg, tasks, physical activity intensity or self-perceived load) and using tertiles or quartiles to categorise continuous data. Our harmonised categories did not allow for inferring intensity, frequency and duration of physical activity. Moreover, the arbitrary cut-off points that stem from our methodology of using tertiles or quartiles for continuous data may have resulted in unbalanced categories. Future studies should ideally combine device-measured physical activity data with self-reports, not accruing it in crude categories, to obtain detailed and accurate assessments of OPA and LTPA (eg, regarding life-time exposures and the duration, frequency and intensity of physical activity). Measurements on, for example, muscle activity, heart rate or postures of specific body regions can provide additional insights into modalities of OPA, of which the health effects should be explored in future research.

We asked for an array of (sub-)constructs (online supplemental appendix 1) from contributing researchers to enable adjustment for as much relevant confounding as possible. Unfortunately, due to the limited data provided and the harmonising process, only few variables were available from all studies (ie, gender, age, BMI, smoking and education level). Additional variables were available from few studies and used in sensitivity analyses. While IPD meta-analyses have the potential to deal with limitations in the literature, for example, by unlocking evidence on previously unmeasured confounding variables, unfortunately our study does not add evidence beyond what is already available in the literature on this aspect. This asks for more carefully designed cohort studies with standardised measurements, or even other research designs, in the future. Nonetheless, in our study, associations between OPA and mortality remained mostly unchanged across these and other sensitivity analyses but were substantially attenuated when additionally adjusting for income (online supplemental appendix 11). This might indicate residual socioeconomic confounding. However, income may also be on the pathway from OPA to all-cause mortality (online supplemental appendix 5). There is insufficient evidence to determine which of these two pathways is most likely, which has been further complicated by the fact that the variable income in our dataset consists of a combination of household and individual income. Nonetheless, income cannot only be viewed as confounder that one needs to adjust for but also a mediator that one should not adjust for. Other potential confounders such as alcohol use, psychosocial work demands and other work characteristics could unfortunately not be incorporated in the analyses, while available variables were crudely categorised during the harmonisation procedure. Additional adjustment for confounding has not shown to substantially affect the association of OPA and health in some studies.[37] However, it has resulted in substantially different[39 40] (and even opposite[38] association in others). As we cannot rule out residual confounding, future studies on the topic should strive for better ways to consider confounding. Evidence from experimental studies and alternative research designs (eg, analyses on natural experiments)[49] may help to address this issue, providing better insights in the causality of the association.

When stratifying by education level, associations between LTPA and all-cause mortality remained consistent across strata, but associations for OPA changed in both directions, for example, among men, estimates for the moderate and high education strata were similar to estimates in non-stratified analyses, but no association was observed in the low education strata. Among women in the high education stratum, high OPA levels were associated with up to 18% higher mortality risks in contrast to zero risks in non-stratified analyses. These effect moderation patterns may be due to the reference category of 'sitting work' being rather physically demanding among people with low education level (performing demanding upper extremity work while sitting). In our analyses where low OPA was used as reference category, we see a slight attenuation of the associations, potentially since the 'low' category 'mainly standing with some walking' might be associated with a higher risk of adverse health outcomes in itself.[50] On the other hand, evidence from LTPA has shown that, compared with none, already low-intensity physical activity can

bring benefits to health.[4] For OPA, such associations should be explored further in future research.

Despite methodological issues, it is possible that the different nature and characteristics of OPA and LTPA explain differential health effects.[41] High levels of OPA commonly involve lifting, manual handling, repetitive work and prolonged static postures performed over long time periods (ie, multiple hours/day, multiple days/week). LTPA is voluntary and typically carried out in short bouts with moderate or high intensity, accompanied by long recovery periods. Because of these differences, OPA and LTPA could differ in their acute and chronic physiological responses. For example, in a sample of cleaners who were highly active at work in terms of the number of steps taken at work, OPA did not reach intensity levels that may be required to achieve substantial cardiorespiratory fitness improvements.[51] In a prospective study, LTPA was associated with a reduced age-related decline in cardiorespiratory fitness, while OPA was not.[52] Also, whereas high levels of OPA have been suggested to cause chronic exhaustion and elevated resting blood pressure[53] and heart rate,[54] which are established risk factors for cardiovascular diseases,[55 56] aerobic exercise (eg, brisk walking, jogging, cycling) and strength training have shown to improve these cardiometabolic risk factors.[3] Another explanation for the differential health effects of OPA and LTPA is that physical activities at work are known to be associated with higher levels and longer duration of exhaustion[57] and additional mental (and thus physical) stress[58] than similar but usually much shorter self-determined activities during leisure time. This may be reinforced by the phenomenon of status inconsistency, which is the mismatch of education level and work status. For example, for those with a moderate or high education level and a physically demanding job, the mismatch may cause them to experience high levels of occupational stress and lack of social support impacting their health.[59 60] Future studies should further build the evidence base on these mechanisms to better understand potential differential health effects of OPA and LTPA. Such studies should also explore why we found adverse health effects for men and null effects for women regarding the association of OPA and all-cause mortality. One explanation for these gender differences is that physically demanding jobs are typically men dominated,[61] while we combined men and women with different relative levels of OPA into the same crude categories. Other potential explanations are differential reporting bias across genders, or that women who engage in high levels of OPA are more healthy and/or fit than men doing the same OPA. As women are more likely to work in part-time jobs than men,[62] shorter working hours and longer recovery periods could also explain gender differences. However, no data on working hours were available in our study.

Implications for practice

Current physical activity guidelines state that adults should engage in ≥150–300 min of moderate intensity, or ≥75–150 of vigorous intensity, aerobic physical activity per week.[3] As evidence has been insufficient to determine whether specific health benefits vary by physical activity domain, guidelines state that this physical activity can be accrued as part of leisure, household, transportation and work activities.[3] As the evidence on the topic develops with emerging studies such as ours, this message may not be adequate for men in physically demanding jobs, as many types of OPA (eg, standing, walking, carrying and lifting or other manual handling activities) may not be health enhancing. High levels of OPA might discourage these workers from engaging in sufficient amounts of LTPA due to fatigue and physical exertion at work,[63] or because they believe they get sufficient physical activity through work.[40] As the evidence-base on this topic develops, more tailored and gender-specific advice for those with physically active occupations, including in work safety regulations and training of occupational health professionals, might be required.

Methodological strengths and limitations

Our study has several methodological strengths, including the preregistered protocol (to address reporting bias), combining and harmonising a range of variables, uncovering unpublished data to address publication bias and assessing various sources of bias (eg, the role of single studies, RoB, and pre-existing conditions).

The use of IPD allows harmonisation of variables and statistical analysis and increases statistical power. However, the harmonisation procedure also reduced the level of detail of variables for some constructs. The costs of increased misclassification bias due to harmonisation may outweigh the benefits of IPD analyses as long as there are few studies with high-quality fine-grained data. This loss of detailed information is an inherent implication when harmonising data from various studies and can only be addressed if future studies make use of generic variables and construct operationalisations. Additionally, not all variables were available in all studies, with only nine and six studies (men and women, respectively) providing data on income that we used in our sensitivity analysis (online supplemental appendix 10). The main models reported in tables 3 and 4, however, are for a fair share based on similar samples with only 3% missing data in model 3 compared with model 1.

The associations of OPA with all-cause mortality had larger HRs for studies with low compared with moderate/high RoB regarding attrition, but reversely for participation and exposure variable measurement. A limitation of the RoB assessment for exposure measurement is that we assessed RoB based on the exposure (either LTPA or OPA) with the highest RoB. RoB for studies where the measurement methods for the two domains of physical activity differed, for example, in the Whitehall study where LTPA was by measuring time in certain intensity activities while OPA was assessed in two crude categories,[31] which may thus not be accurate.

In contrast to our a-priori registered[15] and published protocol,[14] we did not conduct a one-stage meta-analysis, since a single analysis on the full IPD dataset did not converge due to the complexity of the model. This was mainly due to the multilevel structure of the data, with clustering at the level of studies, and sometimes clustering within studies (ie, one study used clustered sampling).[21] Moreover, a two-stage approach allowed us to incorporate aggregated data from studies of which collaborators were unable to send us IPD (but used the same analysis plan). One study consisted of multiple waves of data, for which the wave with the longest follow-up period was chosen, to obtain more endpoints.[18] This procedure could, however, lead to misclassification, and future studies should strive to incorporate repeated measurements to get a better insight into the health effects of OPA and LTPA.

CONCLUSION

This IPD meta-analysis showed higher risks of all-cause mortality to be associated with higher levels of LTPA, but not

for OPA. Higher levels of occupational were associated with higher mortality risks in men in some models and showed no such association among women. These findings indicate that OPA may not have the health-enhancing effects of LTPA in men but not women. These findings could be relevant to large parts of the working population, in particular, those who accrue most of their daily physical activity at work.

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Author note The authors confirm that that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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