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Review

# Should workers be physically active after work? Associations of leisure-time physical activity with cardiovascular and all-cause mortality across occupational physical activity levels—An individual participant data meta-analysis

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### Abstract

*Background*: There is insufficient evidence to provide recommendations for leisure-time physical activity among workers across various occupational physical activity levels. This study aimed to assess the association of leisure-time physical activity with cardiovascular and all-cause mortality across occupational physical activity levels.

*Methods*: This study utilized individual participant data from 21 cohort studies, comprising both published and unpublished data. Eligibility criteria included individual-level data on leisure-time and occupational physical activity (categorized as sedentary, low, moderate, and high) along with data on all-cause and/or cardiovascular mortality. A 2-stage individual participant data meta-analysis was conducted, with separate analysis of each study using Cox proportional hazards models (Stage 1). These results were combined using random-effects models (Stage 2).

*Results*: Higher leisure-time physical activity levels were associated with lower all-cause and cardiovascular mortality risk across most occupational physical activity levels, for both males and females. Among males with sedentary work, high compared to sedentary leisure-time physical activity was associated with lower all-cause (hazard ratios (HR) = 0.77, 95% confidence interval (95%CI): 0.70-0.85) and cardiovascular mortality (HR = 0.76, 95%CI: 0.66-0.87) risk. Among males with high levels of occupational physical activity, high compared to sedentary leisure-time physical activity was associated with lower all-cause (HR = 0.84, 95%CI: 0.74-0.97) and cardiovascular mortality (HR = 0.79, 95%CI: 0.60-1.04) risk, while HRs for low and moderate levels of leisure-time physical activity ranged between 0.87 and 0.97 and were not statistically significant. Among females, most effects were similar but more imprecise, especially in the higher occupational physical activity levels.

*Conclusion*: Higher levels of leisure-time physical activity were generally associated with lower mortality risks. However, results for workers with moderate and high occupational physical activity levels, especially women, were more imprecise. Our findings suggests that workers may benefit from engaging in high levels of leisure-time physical activity, irrespective of their level of occupational physical activity.

Keywords: Mortality; Individual participant data; Physical activity paradox; Job demands

### 1. Introduction

Physical activity is an important factor in the prevention of lifestyle-related diseases.<sup>1</sup> Traditionally, various domains of physical activity, including leisure-time, work, transportation and household activities, have been considered beneficial for health.<sup>2</sup> Consequently, physical activity guidelines recommend engaging in at least 150–300 min of moderate intensity, or 75–150 min of vigorous intensity physical activity per week, irrespective of the domain in which the activity is accrued.<sup>3</sup>

However, in recent years, evidence suggests that occupational physical activity may not have the health-enhancing effects of leisure-time physical activity.<sup>4</sup>

Evidence from systematic reviews indicates that high levels of occupational physical activity are associated with a higher risk of all-cause mortality in men,<sup>5</sup> lung cancer in men,<sup>6</sup> and cardiovascular disease (results not stratified by gender).<sup>7</sup> A review of systematic reviews showed that high level occupational physical activity was associated with an increased risk for some health outcomes (i.e., all-cause mortality and osteoarthritis) and a decreased risk for several other health outcomes (i.e., colon and prostate cancer, stroke and coronary heart disease).<sup>8</sup> However, the quality of the described systematic reviews was rated mostly low or very low, due to the limited numbers of included studies, risk for residual confounding, and heterogeneity of methods.

In the Active Worker consortium we have gathered individual participant data (IPD) to perform a meta-analysis on the health effects of occupational and leisure-time physical activity. In the first outcome paper from the Active Worker IPD (individual participant) meta-analysis,<sup>9</sup> we analyzed data from 22 cohort studies 10-28 and consistently demonstrated that higher levels of leisure-time physical activity were associated with lower risk of all-cause mortality. However, higher levels of occupational physical activity were not found to be associated with a lower all-cause mortality risk. Notably, our findings revealed that men with moderate and high levels of occupational physical activity had significantly higher risks of mortality compared to those working sedentary jobs (hazard ratios (HRs):1.05 and 1.12, respectively). These results suggest that the health-enhancing effects of physical activity may be derived from leisure-time rather than occupational activities, at least in males.

In physically demanding jobs a significant portion of workers' daily physical activity is acquired during working hours.<sup>29</sup> For example, a study including U.S. food service, maintenance, and health care workers found averages of 266 and 55 min per working day of device-measured light and moderate intensity occupational physical activity, respectively.<sup>30</sup> However, while all participants in this study met physical activity guidelines during work, it is unclear what the health effects would be for these workers if they additionally engaged in leisure-time physical activity.

While the benefits of leisure-time physical activity for individuals in sedentary jobs are widely acknowledged, we currently lack robust evidence to provide recommendations concerning (additional) leisure-time physical activity for workers in moderately and/or highly physically demanding jobs.<sup>31</sup> This would help in advising whether workers in these occupations should prioritize physical activity or rest after work.

Examining the health effects of leisure-time physical activity across different occupational physical activity levels can offer valuable insights into the potential benefits that leisure-time physical activity may provide for workers in various occupational contexts. Such evidence can guide the development of targeted physical activity recommendations tailored to workers at these occupational physical activity levels. This study aimed to assess the association of leisure-time physical activity levels, across occupational physical activity levels, with all-cause and cardiovascular mortality.

### 2. Methods

The study protocol for the Active Worker consortium IPD meta-analysis was *a priori* registered in PROSPERO (CRD: 42018085228) and published.<sup>32</sup> The methods described by the

Cochrane Individual Participant Data Meta-analyses Group and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-IPD statement were used to conduct and report our study.<sup>33,34</sup> As acknowledged by the medical ethical committee of Amsterdam University Medical Centre, the Dutch Medical Research Involving Human Subjects Act does not apply to this study (Reference No. 2018.068).

### 2.1. Identification and inclusion of eligible cohorts

The search to identify published and unpublished cohort studies has been described in detail in our study protocol<sup>32</sup> and first outcome paper.<sup>9</sup> We included original prospective cohort studies in which the associations of occupational physical activity and leisure-time physical activity with all-cause and/or cardiovascular mortality were assessed. Only cohort studies in which cardiovascular and/or all-cause mortality were expressed as a time-to-event variable were included, to allow for execution of survival analysis. We excluded cohorts that had assessed occupational physical activity groups based on task and/or job classification (e.g., blue collar *vs.* white-collar workers).

### 2.2. Data harmonization

Data contributors for each participating study were asked to send data on physical activity, mortality, and other relevant factors (e.g., demographics, pre-existing health conditions, and behavioral factors). In a consensus meeting with the Active Worker consortium core group, data from all cohorts were harmonized by labeling and recoding the variables.<sup>32</sup> The harmonization was verified by the data contributors. A description of the harmonization procedure has been published previously<sup>9</sup> and is shown for the physical activity variables in Supplementary Table 1. No imputation for missing data was performed. In our harmonization procedure the level of detail of variables was limited by the study with the least detailed information.

### 2.2.1. Physical activity

Occupational and leisure-time physical activity variables were harmonized into 1 of 4 categories on the physical activity continuum.<sup>35</sup> For occupational physical activity, the 4 categories were: sedentary (mainly sitting work), low (work that mainly involves standing or walking but without lifting or carrying loads), moderate (work that involves some walking, with occasionally carrying light objects or walking stairs), and high (physically demanding work involving frequent carrying or lifting heavy loads).

For leisure-time physical activity, the 4 categories were: sedentary (almost no regular physical activity), low (occasionally engaging in leisure-time activities such as slow walking or light household activities), moderate (work that involves some walking, with occasionally carrying light objects or walking stairs), and high (regular engagement in activities such as jogging or cycling).

### 2.2.2. All-cause and cardiovascular mortality

Mortality was registry- or hospital record-based and harmonized into dichotomous variables indicating the incidence events (all-cause and cardiovascular mortality (yes/no)) and a continuous variable representing the time to event (in days). More detailed information on the outcome assessment and the International Classification of Diseases (ICD) codes used for cardiovascular mortality in each cohort is shown in Supplementary Table 2.

### 2.2.3. Additional variables

Age was expressed as years and sex as female or male. Body mass index (BMI) was assessed in kg/m<sup>2</sup>, excluding BMI values <14 or >48 (<1% of all BMI values). Current smokers were contrasted with non-smokers (including former smokers). Educational level was categorized into low (preprimary/primary/lower secondary), medium (upper secondary), or high (post-secondary) education. All measurements of physical activity and additional variables were conducted at baseline (Table 1).

### 2.3. Risk of bias assessment

Risk of bias assessment of each of the cohorts was performed by 2 reviewers independently (with authors PC, BC and/or MAH), using a scoring system<sup>36</sup> with criteria related to study participation, attrition, predictor variable measurements (scoring the assessment of occupational and leisure-time physical activity at once, with the score depending on the weakest assessment method) and outcomes (Table 1). Potential conflicts were resolved during a consensus meeting (with authors: PC, BC, MAH, AJvdB, and WvM).

### 2.4. Data analysis

We performed 2-stage meta-analyses to assess the association between leisure-time physical activity and mortality (allcause and cardiovascular) stratified by occupational physical activity levels (sedentary, low, moderate, and high). In the first stage, we analyzed each study separately using multivariable survival Cox regression analyses. This was done either inhouse using the IPD data sent to us or remotely for the data that could for governance reasons not be shared by investigators.

We primarily performed the analysis with sedentary leisuretime physical activity as the reference category but additionally reported findings with low leisure-time physical activity as the reference category because not all cohorts had data on all 4 leisure-time physical activity groups in their dataset (Supplementary Table1). We excluded workers aged under 18 years or above 65 years. HRs with 95% confidence interval (95%CI) were reported. In all analyses, males and females were considered separately, as earlier studies have shown gender differences in the association between occupational physical activity and mortality.<sup>5</sup> As in our first results paper,<sup>9</sup> we removed models with less than 25 data points in any of the exposure variable categories, as well as unstable models that led to improbable effect sizes, defined as a standard error of the  $\beta > 3$  (e.g., for a point estimate of HR = 1.50, this translates to a 95%CI of 0.17–12.88). The latter instances were exceedingly rare and led to removal of <1% of the modeled data.

As reported in our previous study,<sup>9</sup> and guided by directed acyclic graph (DAG) (Supplementary Table 3 and Supplementary Fig. 1), we performed analyses with 2 levels of adjustments. Model 1 included adjustment for BMI, age, and smoking, while Model 2 was additionally adjusted for educational level. Due to substantial heterogeneity in some variables (e.g., diet, medication use, coffee use, and alcohol intake), data harmonization could not be performed. Other variables could not be harmonized due to insufficient information in more than half of the cohort studies, including ethnicity, selfreported health, psychosocial work demands, history of noncommunicable diseases, blood markers, sleep quality, health care utilization, parental socio-economic status, social support, and neighborhood conditions. Blood pressure, income, glucose, diabetes, and marital status were not included as adjustment variables based on our DAG (Supplementary Table 3 and Supplementary Fig. 1). In the second stage of our analysis, results were pooled using the Stata admetan function. Random-effects models were used due to a high statistical heterogeneity  $(I^2 = 70\%)$ .<sup>37</sup>

### 3. Results

### 3.1. Selection of data

Detailed information regarding the inclusion of our selected studies can be found in our protocol paper and our first results paper.<sup>9,32</sup> In brief, after a literature search for relevant studies, the Active Worker core group contacted researchers from a total of 54 studies. Data from 32 of these studies could not be used for various reason. In total, 22 cohorts were included in our Active Worker IPD meta-analysis. The Carla study,<sup>22</sup> which was included in our first results paper, was excluded from the current analyses because all analyses had fewer than 25 data points.

Hence, we used data from 21 studies.<sup>10-28</sup> Most cohorts used population-based samples, but one study used an industry sample, 2 studies<sup>14,15</sup> samples of civil servants and 2 studies<sup>10,21</sup> sampled workers from selected occupational sectors. A description of the sample characteristics and outcome ascertainment of each included cohort is described in Supplementary Table 2. After excluding participants with missing data and participants aged younger than 18 years or older than 65 years, data from 623,257 participants were analyzed. These participants originated from 15 studies<sup>10,12-23</sup> for which individual participant data were provided to the Active Workers core team (n = 124, 221) and 6 additional studies<sup>11,24-28</sup> that were analyzed remotely by the participating researchers of these studies (n = 508,036). In Model 1 (600,574 (95%)) and Model 2 (589,284 (93%)) participants were included. During a mean follow-up of  $23.1 \pm 6.8$  years (mean  $\pm$  SD), 99,725 (16.0%) individuals died; 28,466 (28.5%) of them from cardiovascular disease. An overview of the included cohorts is presented in Table 1 and a description

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

		Sam	ple infor	mation				Exposure										
Reference	Study name	Country	n	Age at baseline (year) (mean ± SD)	Females (%)	Sample	OPA (%) Sed-low Mod-high	LTPA(%) Sed-low Mod-high	Baseline First year <sup>b</sup>	Follow-up period, (year) (mean ± SD)		Incidence CVD-mortality (n (%))	1	2	3	4		
Clays et al. (2014) <sup>10</sup>	BELFIT study	Belgium	2351	$47.2\pm4.4$	0	Industry	64-12-12-12	25-25-25-25	1976	$16.7\pm3.5$	306 (13)	96 (4.1)	Mod	Mod	Mod	Low		
Saidj et al. (2014) <sup>11</sup>	Health 2006 (H2006)	Denmark	2663	$45.9 \pm 11.6$	54	Population	40-39-17-4	20-59-20-1	2006	$10.5\pm1.0$	53 (2)	7 (0.3)	Mod	Mod	Low	Low		
Sjøl et al.(2003) <sup>12</sup>	MONICA Denmark	Denmark	6576	$44.4 \pm 11.1$	50	Population	24-40-15-21	28-52-19-1	1976	$9.5\pm3.5$	395 (6)	No CVD	Mod	Mod	Mod	Low		
Krause et al. $(2017)^{13}$	KIHD study	Finland	1883	$51.8\pm5.0$	0	Population	25-25-25-25	27-27-26-21	1984	$24.6\pm7.9$	923 (49)	407 (21.6)	Low	Low	Low	Low		
Pulsford et al.(2015) <sup>14</sup>	Whitehall II study	UK	3160	$52.2\pm4.2$	29	Civil servants	98-0-2-0	30-28-25-18	1997	$16.9\pm2.0$	221 (7)	52 (1.6)	Mod	Mod	High	Low		
Eaton et al.(1995) <sup>15</sup>	IIHDS study	Israel	9379	$49.0\pm 6.6$	0	Civil servants	48-40-13-0	59-15-18-8	1963	$28.2 \pm 11.3$	7878 (84)	988 (10.5)	Low	Low	Mod	Mod		
Autenrieth et al. $(2011)^{16}$	MONICA/KORA Augsburg	Germany	2628	$42.6\pm10.3$	38	Population	30-26-30-14	28-26-24-22	1989	$18.3\pm2.7$	263 (10)	94 (3.6)	Mod	Low	Mod	Low		
Rosengren et al.(1997) <sup>17</sup>	Primary Prevention Study	Sweden	7317	$51.6\pm2.3$	0	Population	29-40-22-9	25-58-15-1	1970	$27.2\pm10.5$	6366 (87)	3012 (41.2)	Mod	Low	Mod	Low		
Richard et al.(2015) <sup>18</sup>	NHANES study	USA	8984	$40.4\pm13.1$	47	Population	62-10-11-18	47-14-21-18	2005	$5.9 \pm 1.7$	180 (2)	No CVD	Low	Low	Mod	Low		
Moe et al.(2013) <sup>19</sup>	HUNT study	Norway	41,161	$40.9 \pm 11.5$	52	Population	31-31-26-11	15-32-28-26	1995	$20.1 \pm 4.4$	2881 (7)	655 (1.6)	Mod	Low	Mod	Low		
Franzon et al. $(2015)^{20}$	ULSAM study	Sweden	2106	$49.6\pm0.6$	0	Population	36-31-18-15	14-36-45-5	1970	$30.1\pm10.5$	1959 (93)	857 (40.7)	Low	Low	Mod	Low		
Huerta et al. $(2016)^{21}$	EPIC Spain study	Spain	13,752	$46.8\pm 6.3$	66	Population	0-35-0-65	12-17-34-37	1992	$18.7 \pm 2.2$	963 (7)	181 (1.3)	High	Low	Low	Low		
ohnsen et al. $(2016)^{21}$	WOLF study	Sweden	10,333	$42.1\pm10.7$	31	60 companies	26-40-30-4	3-22-38-37	1992	$23.5\pm3.3$	310 (3)	97 (0.9)		Low				
Bahls et al. $(2018)^{22}$	SHIP-START1 study	Germany	1502	$44.3\pm9.5$	53	Population		21-26-28-25	2002	$8.2 \pm 1.4$	30 (2)	6 (0.4)		Mod				
Wanner et al. $(2014)^{23}$	The Swiss MONICA study	Switzerland	8487	$45.2\pm10.0$	50	Population	26-47-15-12	0-35-52-12	1984	$24.5\pm 6.9$	1782 (21)	453 (5.3)	Low	Low	Mod	Low		
Wanner et al. $(2014)^{23}$	NRP 1A study	Switzerland	4602	$39.4 \pm 11.8$	37	Population	34-0-52-14	0-25-64-11	1977	$31.9 \pm 9.9$	1703 (37)	538 (11.7)	Mod	Low	Mod	Low		
Petersen et al. $(2012)^{24}$	Danish National Health Interview Surveys	Denmark	15,466	$40.6\pm13.3$	50	Population	31-26-26-4	14-61-20-5	1987	$11.9 \pm 4.1$	763 (5)	36 (0.3)	Low	Low	Mod	Low		
Dalene et al. $(2021)^{25}$	Norwegian study	Norway	404 239	$41.3 \pm 5.9$	52	Population	34-39-20-7	22-55-19-3	1974	$26.7 \pm 6.6$	57 332 (14)	14,442 (3.5)	Mod	Low	Low	Low		
Holtermann et al. $(2012)^{26}$	Copenhagen City Heart Study	Denmark	,	$52.1 \pm 10.2$		Population		17-56-25-2	1976	$18.4 \pm 7.6$	8615 (79)	3914 (36.4)		Low				
Holtermann et al.(2021) <sup>27</sup>	Copenhagen General Population Study	Denmark	69,652	$52.2\pm10.7$	55	Population	44-32-20-4	7-41-45-7	2003	$10.0\pm3.1$	2001 (3)	411 (0.7)	Mod	Low	Mod	Low		
Holtermann et al.(2009) <sup>28</sup>	Copenhagen male study	Denmark	5082	$48.7\pm5.3$	0	Workers	0-30-52-18	0-18-73-9	1970	$28.9 \pm 1.6$	4801 (92)	2220 (42.6)	Mod	Low	Mod	Low		
	Total		623,257		314,602						99,725 (16)	28,466 (4.6)						

Notes: 1 =Study participation; 2 =Study attrition; 3 = Predictive variable assessment; 4 =Outcome ascertainment. Risk of bias was assessed according to established criteria.<sup>36</sup> See Appendix C for more details on the risk of bias assessment.

<sup>a</sup> 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 the current metaanalysis. 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 followup measurements were used.Risk of bias for studies where the measurement methods for the 2 domains of physical activity differed substantially (e.g., in the Whitehall study where leisure-time physical activity was determined by measuring time in certain intensity activities while occupational physical activity was assessed in 2 crude categories) and may thus not be fully accurate.

<sup>b</sup> The baseline year in most studies varied; baseline measurements for some participants were conducted in later years.

Abbreviations: BELFIT = Belgian physical fitness study; CVD = cardiovascular disease; EPIC = European Prospective Investigation into Cancer and Nutrition-Spain Study; HUNT = Nord-Trøndelag Health Study; IIHDS = Israel Ischemic Heart Disease Study; KIHD = Kuopio Ischemic Heart Disease Risk Factor Study; KORA = Cooperative Health Research in the Region Augsburg; NHANES = National Health and Nutrition Examination Survey; NRP 1A = National Research Program (NRP) 1A; SHIP = Study of Health in Pomerania; MONICA = The Swiss WHO MONItoring of trends and determinants in CArdiovscular disease; WOLF = Work-Lipids-Fibrinogen; ULSAM = Uppsala Longitudinal Study of Adult Men.

B. Cillekens

### Table 2

Descriptive	characteristics	of the	individual	participant	dataset	comprising				
data from $n = 21$ cohort studies.										

Total		$N^{\mathbf{a}}$	п	%
		21	632,257	
Occupational physical activity <sup>b</sup>	Sedentary	19	217,417	34
	Low	19	227,359	36
	Medium	20	130,418	21
	High	19	55,143	9
Leisure-time physical activity <sup>b</sup>	Sedentary	18	123,227	19
	Low	21	304,794	48
	Medium	21	157,249	25
	High	21	46,973	7
Education level	Low	20	129,727	21
	Medium	20	309,390	50
	High	20	180,781	29
Gender	Male	21	320,286	51
	Female	15	311,565	49
Smoking	No	21	404,151	64
-	Yes	21	224,072	36
Age (year) (mean $\pm$ SD)		21	$43.1 \pm 7.9$	
Body mass index (kg/m <sup>2</sup> ) (mean =	± SD)	21	$25.2\pm3.5$	

Note: N = number of studies from which this variable is available.

<sup>a</sup> Not all studies provide data on all metrics.

<sup>b</sup> Physical activity levels (during work and at leisure-time) reflect the physical activity continuum, i.e., sedentary, low, moderate, and high. For leisure-time physical activity these categories roughly depict: 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 depict: mainly sitting work (sedentary); work that mainly involves standing or walking, with occasionally carrying loads (low); work that involves some walking, with occasionally carrying light objects or walking stairs (moderate); highly physically demanding work involving frequent carrying or lifting heavy loads (high).

# of the characteristics of the individual participant dataset in Table 2.

### 3.2. All-cause and cardiovascular mortality among males

Male workers with sedentary jobs were found to have a significantly decreased all-cause mortality risk with increasing levels of leisure-time physical activity (Table 3). In Model 2, a decreased risk of all-cause mortality was found for low (HR = 0.87, 95%CI: 0.84-0.90), moderate (HR = 0.72,95%CI: 0.64–0.82), and high (HR = 0.77, 95%CI: 0.70–0.85) compared to sedentary leisure-time physical activity. Comparable effects were also found in the other occupational physical activity groups (low, moderate, and high). However, effects attenuated with increasing levels of occupational physical activity. For the group classified as high occupational physical activity, a statistically non-significant decrease was found for low (HR = 0.95, 95%CI: 0.84-1.08) and moderate (HR = 0.87, 95% CI: 0.74 - 1.02) leisure-time physical activity. In this group, a decreased risk of all-cause mortality was found for those with high (HR = 0.84, 95%CI: 0.74-0.97) compared to sedentary leisure-time physical activity.

The results for cardiovascular mortality were mostly in line with those for all-cause mortality. Male workers with increasing levels of leisure-time physical activity were found to have a reduced risk of cardiovascular mortality. For high occupational physical activity, we noted a reduction in cardiovascular mortality risk that did not reach statistical significance, whether it was performed at a low (HR = 0.97, 95%CI: 0.82-1.14), moderate (HR = 0.92, 95%CI: 0.75-1.13), or high (HR = 0.79, 95%CI: 0.60-1.04) compared to sedentary leisure-time physical activity level. Forest plots of the associations of high occupational physical activity levels are shown in Supplementary Fig. 2 and Supplementary Fig. 4. Using low instead of sedentary leisure-time physical activity as the reference category produced similar results (Supplementary Table 4). Statistical heterogeneity assessed as  $(I^{20})$  across the strata was between 0% and 75%.

### 3.3. All-cause and cardiovascular mortality among females

Female workers with sedentary jobs were found to have a significant reduction in all-cause mortality risk with increasing levels of leisure-time physical activity (Table 4). In Model 2, decreased risks were found for low (HR = 0.82, 95%CI: 0.78-0.85), moderate (HR = 0.71, 95%CI: 0.67-0.76), and high (HR = 0.58, 95%CI: 0.40-0.83) compared to sedentary leisure-time physical activity. Other occupational physical activity levels showed comparable results, but some effects were more imprecise for females in moderate and high occupational physical activity group, a significantly decreased risk was found for low (HR = 0.88, 95%CI: 0.68-0.94) but not moderate (HR = 0.88, 95%CI: 0.68-1.13) and high (HR = 0.92, 95%CI: 0.76-1.13) as compared to sedentary leisure-time physical activity.

Also for females, the results for cardiovascular mortality were mostly in line with those for all-cause mortality: substantially smaller and more imprecise beneficial associations were found for females with low and moderate occupational physical activity who were more physically active during leisuretime. For those in the high occupational physical activity group, a small non-statistically significant reduction in risk was found for low (HR = 0.96, 95%CI: 0.67-1.37) or high (HR = 0.93, 95% CI: 0.55 - 1.58) compared to sedentary leisure-time physical activity, while a non-statistically significant increased risk was observed for moderate (HR = 1.15, 95%CI: 0.76–1.72) leisure-time physical activity. Forest plots of the associations of high occupational physical activity levels are shown in Supplementary Fig. 3 and Supplementary Fig. 5. Using low instead of sedentary leisure-time physical activity as the reference category produced comparable results (Supplementary Table 5). Statistical heterogeneity assessed as  $(I^2\%)$  across the strata was between 0% and 100%.

### 4. Discussion

This is the first IPD meta-analysis on the association between leisure-time physical activity and all-cause and cardiovascular mortality across different occupational physical Table 3 The association between LTPA across OPA groups with all-cause and cardiovascular mortality among males (sedentary LTPA reference category).

	All-cause mortality									Cardiovascular mortality							
		Ν	Aodel 1		Model 2					Model 1	Model 2						
Sedentary OPA	п	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	п	N	HR (95%CI)	$I^2$	п	N	HR (95%CI)	$I^2$	
Sedentary LTPA	27,557	15	1.00 (reference)	_	27,043	14	1.00 (reference)	_	26,309	12	1.00 (reference)	_	25,390	11	1.00 (reference)	_	
Low LTPA	48,013	15	0.85 (0.82-0.88)	0	46,797	14	0.87 (0.84-0.90)	0	47,175	12	0.87 (0.82-0.93)	0	45,649	11	0.90 (0.84-0.96)	0	
Moderate LTPA	31,964	15	0.72 (0.64-0.80)	72	31,619	14	0.72 (0.64-0.82)	75	31,179	12	0.65 (0.54-0.78)	72	30,549	11	0.65 (0.52-0.82)	75	
High LTPA	9539	12	0.71 (0.63-0.80)	37	9562	12	0.77 (0.70-0.85)	0	8975	10	0.72 (0.64-0.82)	0	8612	10	0.76 (0.66-0.87)	0	
Low OPA	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	
Sedentary LTPA	14,877	17	1.00 (reference)	_	14,378	16	1.00 (reference)	_	13,955	11	1.00 (reference)	_	13,194	10	1.00 (reference)	_	
Low LTPA	38,300	16	0.86 (0.80-0.92)	29	36,498	16	0.86 (0.79-0.94)	31	34,114	11	0.86 (0.77-0.97)	29	31,904	10	0.88 (0.78-1.00)	18	
Moderate LTPA	23,101	16	0.78 (0.70-0.86)	54	22,675	16	0.81 (0.73-0.91)	51	18,428	11	0.74 (0.64-0.85)	45	17,759	10	0.78 (0.66-0.93)	40	
High LTPA	7355	14	0.80 (0.70-0.91)	30	7230	14	0.81 (0.71-0.93)	32	5692	9	0.76 (0.57-1.01)	53	5328	9	0.78 (0.59-1.04)	50	
Moderate OPA	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	п	N	HR (95%CI)	$I^2$	
Sedentary LTPA	12,251	16	1.00 (reference)	_	11,802	15	1.00 (reference)	_	11,809	12	1.00 (reference)	_	11,272	11	1.00 (reference)	_	
Low LTPA	27,592	16	0.88 (0.80-0.97)	40	26,679	15	0.87 (0.77-0.98)	49	27,015	12	0.95 (0.88-1.03)	0	25,944	11	0.94 (0.86-1.03)	0	
Moderate LTPA	17,881	16	0.79 (0.71-0.88)	44	17,647	15	0.79 (0.70-0.88)	35	17,068	12	0.88 (0.79-0.97)	4	16,712	11	0.85 (0.75-0.97)	8	
High LTPA	5094	11	0.76 (0.62-0.92)	55	5091	11	0.76 (0.62-0.92)	58	4802	9	0.66 (0.56-0.78)	0	4576	9	0.67 (0.57-0.80)	0	
High OPA	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	п	N	HR (95%CI)	$I^2$	п	N	HR (95%CI)	$I^2$	
Sedentary LTPA	8526	13	1.00 (reference)	_	8282	12	1.00 (reference)	_	7774	10	1.00 (reference)	_	7435	9	1.00 (reference)	-	
Low LTPA	13,987	13	0.99 (0.89-1.10)	32	13,689	12	0.95 (0.84-1.08)	34	13,462	10	0.99 (0.86-1.14)	20	13,088	9	0.97 (0.82-1.14)	21	
Moderate LTPA	11,893	13	0.87 (0.75-1.00)	50	11,786	12	0.87 (0.74-1.02)	52	11,509	10	0.95 (0.78-1.15)	26	11,261	9	0.92 (0.75-1.13)	34	
High LTPA	4729	9	0.84 (0.73-0.97)	12	4729	9	0.85 (0.74-0.97)	12	4455	8	0.79 (0.60-1.04)	28	4333	8	0.79 (0.60-1.04)	28	

Notes: N = number of studies. n = number of participants. The number of studies differs across comparisons, as not all occupational physical activity categories were available from all studies (see Supplementary Table 1 for an overview). Occupational physical activity levels reflect the physical activity continuum, i.e. sedentary, low, moderate, and high. Categories roughly depict: mainly sitting work (sedentary), work that mainly involves standing or walking but without lifting or carrying loads (low), work that involves some walking, with occasionally carrying light objects or walking stairs (moderate), physically demanding work involving frequent carrying or lifting heavy loads (high).

Model 1: Adjusted for, age, body mass index, and smoking. Model 2: Adjusted for age, body mass index, smoking, and educational level.

Abbreviations: 95% CI = 95% confidence interval; HR = hazard ratio; LTPA = leisure-time physical activity; OPA = occupational physical activity.

Table 4
The association between LTPA across OPA groups with all-cause and cardiovascular mortality among females (sedentary LTPA reference category).

	All-cause mortality																	
		N	Model 1		Model 2				Model 1				Model 2					
Sedentary OPA	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	<i>n N</i> HR (95%CI)		$I^2$	n	N	HR (95%CI)	$I^2$			
Sedentary LTPA	20,590	10	1.00 (reference)	_	20,467	10	1.00 (reference)	_	18,125	5	1.00 (reference)	_	16,780	3	1.00 (reference)	_		
Low LTPA	48,297	10	0.82 (0.76-0.88)	100	48,024	10	0.82 (0.78-0.85)	0	44,799	5	0.83 (0.74-0.93)	0	37,897	3	0.85 (0.75-0.96)	0		
Moderate LTPA	18,663	10	0.77 (0.61-0.97)	83	18,365	10	0.71 (0.67-0.76)	0	17,196	4	0.68 (0.57-0.80)	0	10,081	3	0.73 (0.61-0.87)	0		
High LTPA	3853	6	0.60 (0.39-0.92)	100	3480	6	0.58 (0.40-0.83)	44	3535	4	0.71 (0.40-1.27)	23	2479	3	0.67 (0.42-1.06)	0		
Low OPA	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$		
Sedentary LTPA	24,429	12	1.00 (reference)	_	24,298	10	1.00 (reference)	_	23,554	6	1.00 (reference)	_	23,463	6	1.00 (reference)	_		
Low LTPA	83,179	11	0.85 (0.75-0.96)	40	82,824	10	0.86 (0.76-0.97)	48	80,623	6	0.88 (0.68-1.14)	66	80,342	6	0.90 (0.70-1.16)	0		
Moderate LTPA	22,853	12	0.73 (0.68-0.77)	0	22,474	10	0.76 (0.73-0.80)	0	22,060	5	0.75 (0.57-0.98)	62	21,746	5	0.79 (0.60-1.03)	8		
High LTPA	5225	6	0.72 (0.53-0.97)	33	4913	4	0.74 (0.57-0.97)	50	5176	4	0.87 (0.37-2.03)	65	3347	4	0.92 (0.43-1.96)	65		
Moderate OPA	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$		
Sedentary LTPA	10,659	9	1.00 (reference)	_	10,623	8	1.00 (reference)	_	9858	4	1.00 (reference)	_	9796	4	1.00 (reference)	_		
Low LTPA	32,000	8	0.88 (0.83-0.94)	0	30,849	8	0.88 (0.83-0.94)	0	26,709	4	0.74 (0.54-1.01)	66	26,475	4	0.75 (0.55-1.01)	62		
Moderate LTPA	13,181	7	0.79 (0.72-0.86)	0	12,982	7	0.88 (0.68-1.13)	70	8994	4	0.73 (0.63-0.85)	0	8681	4	0.75 (0.65-0.88)	0		
High LTPA	3060	4	0.89 (0.73-1.09)	9	2692	4	0.92 (0.76-1.13)	7	2657	3	0.73 (0.41-1.29)	57	2289	3	0.75 (0.43-1.31)	52		
High OPA	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$	n	N	HR (95%CI)	$I^2$		
Sedentary LTPA	2320	5	1.00 (reference)	_	2296	5	1.00 (reference)	_	1854	4	1.00 (reference)	_	1838	4	1.00 (reference)	_		
Low LTPA	3779	5	0.87 (0.70-1.07)	27	3677	5	0.89 (0.75-1.04)	6	2988	2	0.97 (0.67-1.39)	0	2983	2	0.96 (0.67-1.37)	0		
Moderate LTPA	3210	5	0.85 (0.60-1.2)	51	3197	5	0.86 (0.61-1.20)	48	3087	4	1.13 (0.76-1.69)	0	3074	4	1.15 (0.76-1.72)	0		
High LTPA	2617	3	0.74 (0.58-0.95)	0	2616	3	0.64 (0.43-0.97)	57	2617	3	0.85 (0.51-1.41)	0	2585	3	0.93 (0.55-1.58)	0		

Notes: N = number of studies. *n* = number of participants. The number of studies differs across comparisons, as not all occupational physical activity categories were available from all studies (see Supplementary Table 1 for an overview). Occupational physical activity levels reflect the physical activity continuum, i.e. sedentary, low, moderate, and high. Categories roughly depict: 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). Model 1: Adjusted for, age, body mass index, and smoking. Model 2: Adjusted for age, body mass index, smoking, and educational level. Abbreviations: 95%CI = 95% confidence interval; HR = hazard ratio; LTPA = leisure-time physical activity; OPA = occupational physical activity.

activity levels. Results suggest that higher levels of leisuretime physical activity were generally associated with lower risks of all-cause and cardiovascular mortality in nearly all occupational physical activity levels, for both males and females. However, protective effects of leisure-time physical activity were smaller and less certain for both men and women with high occupational physical activity as well as for women in the moderate occupational physical activity level.

To date, there is only a single systematic review that has examined the contrasting effect of leisure-time sedentary behavior and physical activity across different occupational intensity levels.<sup>31</sup> The findings of that review were generally consistent with those of our study, indicating that higher levels of leisure-time physical activity were consistently beneficial for individuals with low occupational physical activity levels for a broad range of health outcomes, but also that benefits from leisure-time physical activity were less certain and with inconsistent trends for cardiovascular disease in those with moderate and high occupational physical activity levels.<sup>31</sup> The range of health outcomes was, however, broader than in the current study and consisted of all-cause mortality, cardiovascular incidence and mortality, musculoskeletal pain, diabetes, metabolic syndrome, arrhythmias, and depression. The most robust evidence reported in that review was observed for cardiovascular mortality, indicating a protective effect of leisure-time physical activity across all occupational physical activity levels.<sup>31</sup> However, the aforementioned systematic review differs from the current study, because the authors could not perform a meta-analysis,<sup>31</sup> let alone an IPD metaanalysis, in which various levels of occupational and leisuretime physical activity could be harmonized and assessed. Results were also based on fewer studies and individual participants.<sup>31</sup>

### 4.1. Interpretation of the findings

While there is substantial evidence that leisure-time physical activity is beneficial for sedentary workers,<sup>31</sup> our results indicate that higher levels of leisure-time physical activity may also benefit workers performing higher levels of occupational physical activity. However, these effects are found to be smaller and less certain at higher occupational physical activity levels, especially among women.

The differential health effects of leisure-time physical activity and occupational physical activity, respectively, on mortality can be attributed to the distinct characteristics of the 2 domains of physical activity. Leisure-time physical activity often involves higher intensity activities, shorter duration, and more dynamic postures.<sup>4</sup> These features of leisure-time physical activity might contribute to health benefits, by promoting cardiorespiratory fitness and endurance, and by facilitating muscular adaptation, recovery, and stress relief—things that may not be observed with occupational physical activity, which is often sustained for several hours per day, multiple days per week.<sup>4,38</sup>

Regarding the benefits of increased leisure-time physical activity, the smaller effects observed in workers with the

highest levels of occupational physical activity may be attributed to the fact that adding more physical activity after work might not afford the body sufficient time to recover and restore energy levels.<sup>38,39</sup> Some evidence suggests a curvilinear association between physical activity and health outcomes, implying that there may exist an upper limit to the health benefits of physical activity,<sup>40,41</sup> although some other studies suggest upper limits may not exist.<sup>42</sup> Exceeding a certain threshold could potentially lead to detrimental effects on health, such as overexertion and fatigue. Furthermore, these observations may be influenced by unmeasured residual confounding factors, such as exposure to chemicals and air pollution, which often coincide with higher levels of occupational physical activity.<sup>43</sup>

In our first article based on this IPD study,<sup>9</sup> we observed gender differences in the association between occupational physical activity and mortality. High levels of occupational physical activity were associated with higher all-cause mortality risks in males and we found null effects in females. In the current study, we showed mostly consistent results for both genders, albeit with some variations. For example, while males with high levels of occupational physical activity and moderate leisure time physical activity showed a non-significant decrease in risk, females in the same category exhibited a non-significant increase in risk for cardiovascular mortality. This larger variation among females could be attributed to the smaller number of cohorts providing data on this subgroup (9 cohorts for males *vs.* 4 for females).

Our findings reveal clinical and statistical heterogeneity (the latter depicted in high  $I^2$  scores), likely influenced by various factors including the operationalization of occupational and leisure-time physical activity, and differences in study characteristics. However, some strata displayed minimal heterogeneity ( $I^2$ %), which may be influenced by the limited number of studies included in the meta-analysis for that particular stratum.<sup>44</sup>

### 4.2. Recommendations for practice

Encouraging and promoting leisure-time physical activity among workers with high levels of occupational physical activity could contribute to improved overall health and fitness of these workers. This is an important public health message for workers in physically demanding jobs, who may think that they already meet physical activity guidelines by their physical activity at work.<sup>45</sup> Our findings suggest that integrating leisure-time physical activity, even within physically demanding occupations, could offer notable additional health benefits for these workers.

At the same time, we must recognize that workers in physically demanding jobs can find it challenging to incorporate regular leisure-time physical activity into their daily routines without any reduction in physical demands at work. Factors such as long working hours, inadequate recovery time, and the physical demands of their work can result in feelings of fatigue and exhaustion,<sup>46–50</sup> making it challenging for individuals to engage regularly in leisure-time physical activity.

Moreover, it is crucial to consider that workers with high levels of occupational physical activity often belong to lower socioeconomic classes, in which a higher prevalence of lifestyle-related chronic health issues appears. Therefore, providing high-quality and tailored advice to this group is particularly important for addressing their unique health challenges effectively. This underscores the importance of implementing workplace safety regulations or similar measures within workplaces to ensure safer working conditions and promote employee well-being.

### 4.3. Recommendations for research

Future research should prioritize exploring strategies to enable workers in physically demanding occupations to incorporate beneficial physical activity in their daily leisure-time routines. One potential approach is to focus on reducing fatigue and alleviating pain by replacing some high occupational physical activity with more sedentary or low occupational physical activity. A recent implementation study among industrial workers demonstrated that incorporating more sedentary tasks resulted in reduced fatigue, decreased pain, and increased energy levels after their workdays.<sup>51</sup> Investigating whether such interventions lead to increased physical activity during leisure-time and subsequent health improvements would be a valuable avenue for future studies.

Despite the potential benefits, designing and implementing interventions for workers with physically demanding jobs poses challenges. Workplace health promotion programs, in general, have shown limited effectiveness and are less likely to be adopted by workers in lower socioeconomic positions, which are more prevalent in high occupational physical activity groups.<sup>52</sup> Therefore, it is important to develop tailored interventions that consider the unique needs and demands of workers in physically demanding jobs.

In future research, it will be crucial to explore the associations between various constructs and components of occupational physical activity and their impact on health outcomes. For example, in our study individuals engaging in static standing work (e.g., manufacturing) and those with walkingintensive jobs (e.g., postmen) have been categorized into the same group (moderate). However, while standing for long periods may have detrimental effects on health,<sup>53–55</sup> walking might lead to beneficial health effects.<sup>56</sup> Therefore, understanding specific health implications of various components of occupational physical activity is crucial.

To minimize exposure misclassification bias, and thus the accuracy of findings, future studies should adopt a combined approach using device-based measurements of leisure-time physical activity as well as occupational physical activity, alongside self-reported information. At present, employing device-based measurements using accelerometers or inclinometers can offer more precise assessments of both occupational and leisure-time physical activity levels. However, it is essential to acknowledge that these devices have limitations, particularly in measuring certain crucial aspects of occupational physical activity, such as lifting heavy loads or assessing the biomechanical load.<sup>57</sup> Additionally, the use of wearable sensors in large prospective general population-based cohort studies might not be feasible and will not remove the need to repeatedly or retroactively assess cumulative life-time exposures using validated questionnaires, administrative records, and information about exposures in previously held jobs, which can be assessed objectively by applying job exposure matrix methodologies.<sup>36</sup>

### 4.4. Methodological strengths and limitations

The current study has multiple methodological strengths. By utilizing IPD we harmonized analytical methods and conducted meta-analyses beyond what could be done in the original studies. This approach allowed us to assess the association between leisure-time physical activity and all-cause and cardiovascular mortality, respectively, across occupational physical activity levels. Furthermore, our study adhered to a pre-registered protocol and involved a large collaboration of nearly 50 researchers,<sup>32</sup> making it perhaps the most extensive study on the combined effect of leisure-time and occupational physical activity.<sup>31</sup>

Although IPD studies are often considered the golden standard of systematic reviews,<sup>58</sup> our IPD study does have some limitations. Firstly, most studies included in the current IPD relied on self-reported and rather crude measures for both occupational and leisure-time physical activity, as well as most confounders. The substantial differences in the definitions used across studies contribute to variations in exposures and increase the risk of exposure misclassification bias.<sup>9</sup> As suggested in earlier research, this misclassification bias could potentially lead to an underestimation of reported effect sizes.<sup>43</sup>

Moreover, it is important to note that all measurements were taken at baseline (with the year of baseline measurements indicated in Table 1). However, given that some baseline data span several decades, it is plausible that the levels of both occupational physical activity and leisure-time physical activity may differ from contemporary levels.<sup>59</sup> However, still large segments of the working population engage in physically demanding jobs, and this proportion is particularly high in developing countries.<sup>29,60</sup> Consequently, our approach overlooks changes in physical activity levels and confounders over time, thus failing to capture current activity patterns and their potential impact on health outcomes.

Secondly, validity and accuracy of harmonized variables was limited by the study with the least detailed information. For example, some studies only included a dichotomous smoking status variable, forcing us to harmonize data from cohorts with more detailed information on smoking into these two categories. Moreover, the adjusted analyses were limited to the confounders that were available for all cohorts, increasing the possibility of residual confounding.

In contrast to our published protocol, we encountered challenges in conducting a one-stage meta-analysis, as the models did not converge due to their complexity. Consequently, we adopted a two-stage meta-analysis, which offered the advantage of incorporating aggregated data from studies where collaborators could not provide IPD due to legal restrictions.

It is important to note that cohorts from our analyses come from different (e.g., general or specific working) populations for which various inclusion and exclusion criteria are used (e.g., excluding participants with pre-existing conditions). These different approaches could have masked health risks and benefits, and may limit the generalizability of our results.

Although we aimed to gather data from across the globe, most studies included in our Active Worker consortium IPD were from high-income Western countries. As a result, the generalizability of the current findings to low- and middle-income countries is limited. In such countries, occupational physical activity may constitute a higher proportion of the total daily physical activity.<sup>29</sup> Finally, the observed associations might be subject to healthy worker selection bias.<sup>61</sup> It is possible that the healthiest workers remained in the highest occupational physical activity category, while individuals with (chronic) diseases or impaired health may have reduced leisure-time physical activity, shifted to less strenuous jobs, or left the workforce entirely, potentially inflating benefits and masking risks of leisure-time physical activity among higher occupational physical activity levels.

### 5. Conclusion

In this IPD meta-analysis we showed that higher levels of leisure-time physical activity were generally associated with a reduced risk of all-cause and cardiovascular mortality across most occupational physical activity levels, in both males and females. Engaging in physical activity during leisure-time seems to confer health benefits across the examined levels of occupational physical activity, although the relative benefit may be higher in those with sedentary and low levels of occupational physical activity. Effect estimates for leisure-time physical activity in the moderate and high occupational physical activity levels were more imprecise. These findings are important to consider, especially for those working in physically demanding jobs, in which workers may already meet physical activity guidelines at work.

### Authors' contributions

The "Active Worker core team" (authors PC, MAH, AH, RPT, PJM, SK, EC, WvM, and AJvdB) developed the project's protocol, including the analysis plan. Author BC conducted the analyses, while consulting author NK and JT. All other authors (DdB, MA, LLK, AS, LBA, JK, AV, RMP, ES, UG, AP, BT, AR, LB, KS, KF, MRB, LLB, AK, LA, MB, TI, MW, MB, JLM, PS, BGN, KED, UE, JC, MTJ, CBP) contributed by either providing their individual participant data or analyzing their data remotely using our analysis plan. All authors reviewed the manuscript for important intellectual content. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

### **Competing interests**

The authors declare that they have no competing interests.

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### Supplementary materials

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