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RESEARCH ARTICLE

Physical Activity Volume, Intensity, and Mortality: Harmonized Meta-Analysis of Prospective Cohort Studies

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Introduction: It is unclear whether moderate-to-vigorous physical activity (MVPA) is associated with a lower mortality risk, over and above its contribution to total physical activity volume.

Methods: 46,682 adults (mean age: 64 years) were included in a meta-analysis of nine prospective cohort studies. Each cohort generated tertiles of accelerometry-measured physical activity volume and volume-adjusted MVPA. Hazard ratios (HR, with 95% confidence intervals) for mortality were estimated separately and in joint models combining volume and MVPA. Data was collected between 2001 and 2019 and analyzed in 2023.

Results: During a mean follow-up of 9 years, 4,666 deaths were recorded. Higher physical activity volume, and a greater contribution from volume-adjusted MVPA, were each associated with lower mortality hazard in multivariable-adjusted models. Compared to the least active tertile, higher physical activity volume was associated with a lower mortality (HRs: 0.62; 0.58, 0.67 and 0.50; 0.42, 0.60 for ascending tertiles). Similarly, a greater contribution from MVPA was associated with a lower mortality (HRs: 0.94; 0.85, 1.04 and 0.88; 0.79, 0.98). In joint analysis, a lower mortality from higher volume-adjusted MVPA was only observed for the middle tertile of physical activity volume.

Conclusions: The total volume of physical activity was associated with a lower risk of mortality to a greater extent than the contribution of MVPA to physical activity volume. Integrating any

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intensity of physical activity into daily life may lower mortality risk in middle-aged and older adults, with a small added benefit if the same amount of activity is performed with a higher intensity.

INTRODUCTION

Moderate-intensity physical activity has been the foundation of health-promoting physical activity guidelines for adults since 1995[1] and continues to be emphasized today.[2] The recommendation for all adults to engage in 150−300 minutes of moderate-to-vigorous physical activity (MVPA) per week is supported by strong evidence demonstrating its benefits to physical function, mental health, quality of life, and a lower risk of many noncommunicable diseases and premature mortality.[2]

Results from recent prospective cohort studies using device-measured physical activity have confirmed the importance of MVPA.[3] These studies have additionally suggested that all movement, including lower intensity (i.e., light) physical activities, are associated with a lower mortality risk.[3,4] A meta-analysis showed that those in the most active quartile of overall physical activity had a 64% lower risk of mortality, compared with those in the least active quartile.[3] In the same study, the most active quartile based on MVPA had a 39% lower risk whereas the most active quartile of light-intensity physical activity had a 56% lower risk. Such findings suggest that public health messages should encourage all types of physical activity, regardless of intensity, in order to maximize longevity.

Higher physical activity volume, measured by the doubly labeled water method as physical activity energy expenditure, is indeed associated with lower mortality in older men.[5] While this method is the gold standard for total physical activity energy expenditure, it does not permit quantification of intensity. Therefore, it cannot determine if certain patterns of energy expenditure are more beneficial compared to others (e.g., same energy expenditure accumulated in shorter duration of higher intensity versus longer duration of lower intensity). Since the total volume of physical activity is calculated as the area under the intensity time series, those with high physical activity volume are likely also those with high levels of MVPA. Therefore, approaches that handle this interdependency are needed to determine their relative contributions. Previous studies have been inconsistent on the added benefit of MVPA, beyond physical activity volume, on mortality risk. In a recent study, accumulating the same volume of physical activity through MVPA was associated with lower mortality risk than accumulating through lower intensity activity.[6] In contrast, a meta-analysis was inconclusive on the added benefits from a higher stepping intensity when the total number of steps was statistically adjusted for.[7] Differences in methodology and analysis across studies may partly explain these inconsistent findings. As such, it remains unclear if there are specific benefits from MVPA on mortality risk, beyond the contribution of MVPA to total physical activity volume.

Here, harmonized device-measured physical activity data from nine prospective cohort studies were used to examine if MVPA is associated with lower mortality over and above its contribution to total physical activity volume.

METHODS

Study Sample

This study is based on the *Adult Accelerometer Consortium,* a collaboration of prospective cohort studies that implemented hip- or lower back-mounted accelerometer protocols and had information on mortality outcomes, identified from a systematic review and through personal contacts.[3,8] For this study, two consortium cohorts could not be included due to resource limitations. However, two additional cohorts have been identified and included,[9,10] resulting in a total of nine cohorts contributing to this study. The cohorts were based in Norway (2 cohorts),[9,11] Sweden (2 cohorts),[12,13] the UK (2 cohorts),[14,15] and the U.S. (3 cohorts).[16−18] Physical activity data were collected between 2001 and 2019. The latest available follow-up data from each cohort was used. See Appendix Tables 1 and 2 for a description of the cohorts and their recruitment procedures. Quality assessments are described in our previous work.[3] No institutional review board approval was needed for conducting this study.

Measures

Individual participant accelerometer data were harmonized by each cohort according to a standardized protocol.[3] Data was from the vertical axis in 60-second epochs with nonwear time defined according to the Choi algorithm.[19] Only participants with at least 10 hours of daily wear-time on a minimum of four days (conventional definition of "compliant") were included. The Tromsø Study used a 24-hour wear protocol, so all data between midnight and 6:00 AM was removed to mimic the remove-during-sleep protocols used in the other cohorts.

Physical activity was measured by ActiGraph or Actical accelerometers which provide data on the intensity-time series in a dimensionless unit known as a count.[20] The total number of counts divided by wear-time in minutes (cpm) was used as a measure of the total volume of physical activity, explaining 20%−30% of the variance in physical activity energy expenditure.[21,22] This average acceleration variable was used to reflect physical activity volume because it corrects for variation in total counts due to differences in wear-time. MVPA was defined as minutes with ≥1,952 cpm for ActiGraph monitors[23] (eight studies) and ≥1,535 cpm for Actical monitors[24] (one study). Because physical activity volume is the product of intensity and time, a two-step approach was implemented to statistically remove the dependency between volume and intensity. First, the fraction of total counts attributable to time spent in MVPA was calculated (MVPAfraction, sum of counts during MVPA divided by total counts).[6] Second, the MVPAfraction was regressed on physical activity volume (cpm) in order to calculate a volume-adjusted MVPA variable from the residuals (proportional MVPA, the residuals method[7,25,26]); which was used together with volume in the analytical models. This statistical method ensures volume and intensity are uncorrelated within each study before meta-analysis. Estimates for MVPA in this model are interpreted as the effect of lower or higher MVPA when total volume is held constant.

Statistical Analysis

All cohorts restricted analysis to participants ≥40 years of age. Participants with <2 years of follow-up were excluded to reduce the risk of reverse causality bias from undiagnosed serious disease. Correlations between physical activity volume and the nonadjusted contribution from MVPA (i.e., MVPAfraction) were estimated with the Pearson correlation coefficient, with 95% confidence intervals (CIs) calculated with the Fisher Z transformation. Physical activity volume and volume-adjusted MVPA (i.e., proportional MVPA) were first analyzed separately as tertiles, using the lowest tertile as the reference. For each cohort, Cox proportional hazard regression models were used to estimate hazard ratios (HR) with 95% CIs. An initial model adjusted for age and sex while multivariable-adjusted models also included adjustment for baseline socioeconomic status, smoking status, body mass index, pre-existing cardiovascular disease (CVD), pre-existing cancer, and other cohort-specific putative confounding variables listed in Appendix Table 1. Models including proportional MVPA were additionally adjusted for physical activity volume.[7,27] Participants with missing information on confounding variables were excluded.

Joint associations of physical activity volume and proportional MVPA with mortality hazards were then examined by combining tertiles, yielding nine different volume-intensity combinations. The joint analyses were also repeated stratified by sex and by age and following exclusion of those with pre-existing CVD or cancer as a sensitivity analysis. Cohort-level HR estimates and their precision were meta-analyzed with a DerSimonian and Laird random effects model. The sample weights and the complex survey design of the National Health and Nutrition Examination Study were accounted for prior to analyses.[28] Meta-analyses were performed using MATLAB (R2014a, MathWorks, Natick, MA).

RESULTS

A total of 46,682 participants (69% women) with a mean age across cohorts of 64 years (range: 53−72 years) were included. The mean follow-up ranged from 4.5 to 14.2 years (mean of means: 9.0), during which 4,666 participants died (10%). Table 1 presents characteristics of the participants. The cohort-mean contribution from MVPA to physical activity volume varied from 14% in U.S. women to 40% in Swedish men (Table 1) with correlations ranging from 0.47 to 0.77 (Appendix Table 3). Within cohorts, the contribution from MVPA to physical activity volume was consistently greater in men than in women. Physical activity metrics in the nine volume-intensity combinations are shown in Appendix Tables 4−6.

Higher physical activity volume and a higher proportion of volume from MVPA were each associated with lower mortality risk in separate multivariable-adjusted models, with 50% (HR: 0.50, 95% CI: 0.42, 0.60) and 38% (0.62, 95% CI: 0.58, 0.67) lower mortality hazard in the highest and middle volume tertiles, respectively, compared to the lowest volume tertile (Table 2). For the association with proportional MVPA, mortality was 12% lower (0.88, 95% CI: 0.79, 0.98) in the highest MVPA tertile compared to the lowest but the CI for the 6% difference in the middle tertile was inconclusive of a benefit (0.94, 95% CI: 0.85, 1.04). The volume- and proportional MVPA-mortality association across the contributing cohorts are shown in Figure 1. The proportional MVPA associations were largely consistent across subgroups of sex and age (Table 2).

In the joint volume-intensity analysis, using the lowest physical activity volume and lowest proportional MVPA tertile as the reference, there was no difference in

Table 1. Descriptive Characteristics of Cohorts

Characteristics	ABC, Sweden	EPIC-Norfolk, UK	HAI, Sweden	NHANES, U.S.	NNPAS, Norway	REGARDS, U.S.[a]	The Tromsø Study, Norway	WAT2D, UK	WHS, U.S.
Follow-up, years	14.2	9.9	4.5	13.3	8.9	9.2	7.0	5.7	8.0
Women									
Participants/deaths	457/31	4,126/253	1,749/35	1,882/486	1,148/37	4,070/651	2,381/64	242/4	16,185/1,052
Age, years	52.6 (10.1)	69.7 (7.5)	70.4 (0.2)	57.2 (11.7)	55.8 (11.0)	68.2 (8.7)	62.0 (10.1)	62.3 (8.8)	71.9 (5.6)
Physical activity volume, cpm	341 (213)	237 (107)	273 (121)	268 (120)	318 (129)	84 (64)	246 (105)	263 (118)	222 (103)
MVPA, minutes/day	30.5 (30.7)	27.3 (21.6)	30.5 (23.8)	16.2 (16.8)	33.2 (22.7)	6.7 (11.6)	29.1 (22.1)	19.5 (18.1)	14.9 (14.8)
MVPAfraction, (range: 0−1)	0.29 (0.16)	0.24 (0.16)	0.36 (0.21)	0.17 (0.13)	0.36 (0.18)	0.14 (0.19)	0.32 (0.18)	0.21 (0.15)	0.17 (0.10)
BMI, kg/m^2	25.4 (3.8)	26.8 (4.6)	26.4 (4.6)	28.9 (6.6)	25.2 (4.2)	29.0 (6.2)	26.7 (4.5)	34.0 (5.8)	26.4 (4.8)
BMI ≥30, *n* (%)	56 (12.2)	827 (20.0)	330 (18.9)	658 (35.0)	136 (12)	1,504 (37.0)	481 (20.2)	179 (74)	3,221 (19.9)
Smoking, *n* (%)									
Never	185 (40.8)	2,449 (59.4)	862 (49.3)	1,072 (57.0)	527 (46)	2,326 (57.4)	931 (39.1)	-	8,169 (50.5)
Former	139 (30.7)	1,420 (34.4)	750 (42.9)	504 (26.8)	390 (34)	1,311 (32.3)	1,162 (48.8)	-	7,465 (46.1)
Current	129 (28.5)	257 (6.2)	137 (7.8)	306 (16.3)	231 (20)	418 (10.3)	288 (12.1)	15 (6.2)	551 (3.4)
Pre-existing CVD, *n* (%)	6 (1.3)	1,133 (33.8)	104 (6.0)	189 (10.0)	54 (5)	340 (8.5)	152 (6.4)	20 (8.3)	380 (2.4)
Pre-existing cancer, *n* (%)	13 (2.9)	449 (13.4)	613 (35.1)	250 (13.3)	74 (6)	-	235 (9.9)	6 (2.5)	1,887 (11.7)
Men									
Participants/deaths	371/47	3,356/352	1,761/65	1,848/575	1,033/77	3,356/808	2,308/110	409/19	-
Age, years	53.1 (10.5)	70.9 (7.5)	70.4 (0.2)	55.9 (11.6)	57.1 (10.7)	69.9 (8.4)	63.0 (10.0)	64.4 (7.0)	-
Physical activity volume, cpm	358 (289)	249 (127)	298 (142)	322 (157)	325 (147)	105 (79)	257 (123)	318 (142)	-
MVPA, minutes/day	35.5 (30.0)	34.1 (26.9)	34.6 (26.7)	27.0 (24.6)	37.3 (26.8)	10 (15.2)	31.5 (25.3)	33.0 (26.5)	-
MVPAfraction, (range: 0−1)	0.33 (0.17)	0.30 (0.19)	0.40 (0.21)	0.25 (0.16)	0.39 (0.19)	0.19 (0.21)	0.34 (0.19)	0.32 (0.17)	-
BMI, kg/m^2	25.9 (2.9)	27.2 (3.7)	26.8 (3.7)	28.7 (4.9)	26.4 (3.3)	28.3 (4.6)	27.8 (3.8)	30.9 (4.7)	-
BMI ≥30, *n* (%)	32 (8.6)	635 (18.9)	306 (17.4)	614 (33.2)	136 (13)	988 (29.4)	556 (24.1)	211 (51.6)	-
Smoking, *n* (%)									
Never	160 (43.1)	1,399 (41.7)	795 (45.1)	717 (38.8)	447 (43)	1,354 (40.5)	874 (37.9)	-	-
Former	136 (36.7)	1,772 (52.8)	861 (48.9)	715 (38.7)	424 (41)	1,647 (49.2)	1,194 (51.7)	-	-
Current	75 (20.2)	185 (5.5)	105 (6.0)	416 (22.5)	162 (16)	344 (10.3)	240 (10.4)	36 (8.8)	-
Pre-existing CVD, *n* (%)	22 (6.0)	964 (23.4)	291 (16.5)	237 (12.8)	117 (11)	558 (16.9)	337 (14.6)	76 (18.6)	-
Pre-existing cancer, *n* (%)	8 (2.2)	727 (17.6)	360 (20.4)	185 (10.0)	66 (6)	-	243 (10.5)	4 (1.0)	-

Note: Mean with standard deviations unless otherwise specified.
[a]Physical activity measured by Actical device, otherwise by ActiGraph.
ABC, Sweden Attitude, Behaviour and Change study; BMI, body mass index; Cpm, counts per minute; CVD, cardiovascular disease; EPIC-Norfolk, The European Prospective Investigation into Cancer and Nutrition−Norfolk; HAI, Healthy Aging Initiative; MVPA, moderate-to-vigorous physical activity; NHANES, National Health and Nutrition Examination Study; NNPAS, Norwegian National Physical Activity Survey; REGARDS, REasons for Geographical and Racial Differences in Stroke; WAT2D, walking away from type 2 diabetes; WHS, Women's Health Study.

Table 2. Physical Activity Volume, Proportional MVPA, and Risk of Mortality

Tertile	Lowest tertile	Middle tertile	Highest tertile
Physical activity volume			
Participants/deaths	15,845/2,811	15,430/1,145	15,407/710
Physical activity volume (cpm)[a]	100	178	364
Age-sex adjusted, HR (95% CI)	1.00 (reference)	0.56 (0.52, 0.60)	0.42 (0.36, 0.51)
Multivariable-adjusted, HR (95% CI)	1.00 (reference)	0.62 (0.58, 0.67)	0.50 (0.42, 0.60)
Proportional MVPA			
Participants/deaths	15,634/1,458	15,593/1,956	15,455/1,252
MVPAfraction[a]	0.12	0.17	0.39
Age-sex adjusted, HR (95% CI)	1.00 (reference)	1.02 (0.86, 1.20)	0.82 (0.74, 0.92)
Multivariable-adjusted, HR (95% CI)	1.00 (reference)	0.94 (0.85, 1.04)	0.88 (0.79, 0.98)
Proportional MVPA by sex			
Women/deaths	11,211/839	10,924/1,142	10,105/632
HR (95% CI)	1.00 (reference)	0.95 (0.84, 1.09)	0.91 (0.82, 1.01)
Men/deaths	4,423/619	4,669/814	5,350/620
HR (95% CI)	1.00 (reference)	0.95 (0.84, 1.07)	0.84 (0.71, 0.99)
Proportional MVPA by age, years			
<65/deaths	4,066/229	3,752/212	4,296/179
HR (95% CI)	1.00 (reference)	0.97 (0.66, 1.42)	0.88 (0.69, 1.12)
≥65/deaths	9,961/1,168	10,436/1,713	9,702/1,041
HR (95% CI)	1.00 (reference)	0.97 (0.89, 1.06)	0.89 (0.78, 1.00)

Note: Multivariable adjustment includes age, sex (when applicable), socioeconomic status, smoking, body mass index, pre-existing CVD, pre-existing cancer, and the study-specific covariates listed in Appendix Table 1. Proportional MVPA additionally adjusted for physical activity volume. Proportional MVPA is volume-adjusted using the residual method.
[a]Weighted cohort-means based on weights used in the meta-analysis.
cpm, counts per minute; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity.

mortality for higher contributions from MVPA at low volume but there was a graded association from 24% (0.76, 95% CI: 0.66, 0.87) to 43% (0.57, 95% CI: 0.47, 0.71) lower mortality from the lowest to the highest MVPA tertile within the middle tertile of overall volume. In the highest volume tertile, the trend across MVPA tertiles was less clear, with all three estimates hovering around 50% lower mortality (Figure 2). Results were consistent in across subgroups of age and sex (Appendix Figure 1) and in sensitivity analysis excluding those with pre-existing CVD or cancer (Appendix Figure 2).

DISCUSSION

In this meta-analysis of nine prospective cohort studies with harmonized device-measured physical activity in middle-aged and older adults from four countries, both physical activity volume and a greater contribution from MVPA to total volume (above and beyond the contribution to total volume) were associated with a lower risk of mortality when examined separately. The total volume of physical activity was associated with a lower risk of mortality to a greater extent than the contribution of MVPA to physical activity volume. When modeled together, the importance of intensity appeared to only be apparent in the middle volume tertile where the association suggested an additional inverse dose-response relationship for proportional MVPA. This was not the case in the lowest volume tertile and was less evident in the highest volume tertile. Irrespective of the underlying intensity accumulation pattern, those in the highest tertile of physical activity volume had a 50% lower mortality than those in the lowest tertile. These findings support the message that integrating any intensity of physical activity into daily life may lower mortality risk in middle-aged and older adults, with a small added benefit if the same amount of activity is performed with a higher intensity.

Based on UK Biobank data, accumulating the same volume of physical activity through a higher contribution from MVPA was associated with a markedly lower risk of all-cause mortality, most pronounced for individuals with a lower physical activity volume.[6] For example, mortality was 30% lower when 20% versus 10% of physical activity volume was from MVPA and volume was held constant at 15 kJ/kg/day (roughly equivalent to half the median activity volume in the least active quartile). As such, these results agree with the findings from this study in that both volume and intensity are important for mortality risk but disagree on the importance of intensity when modeled together with physical activity volume.

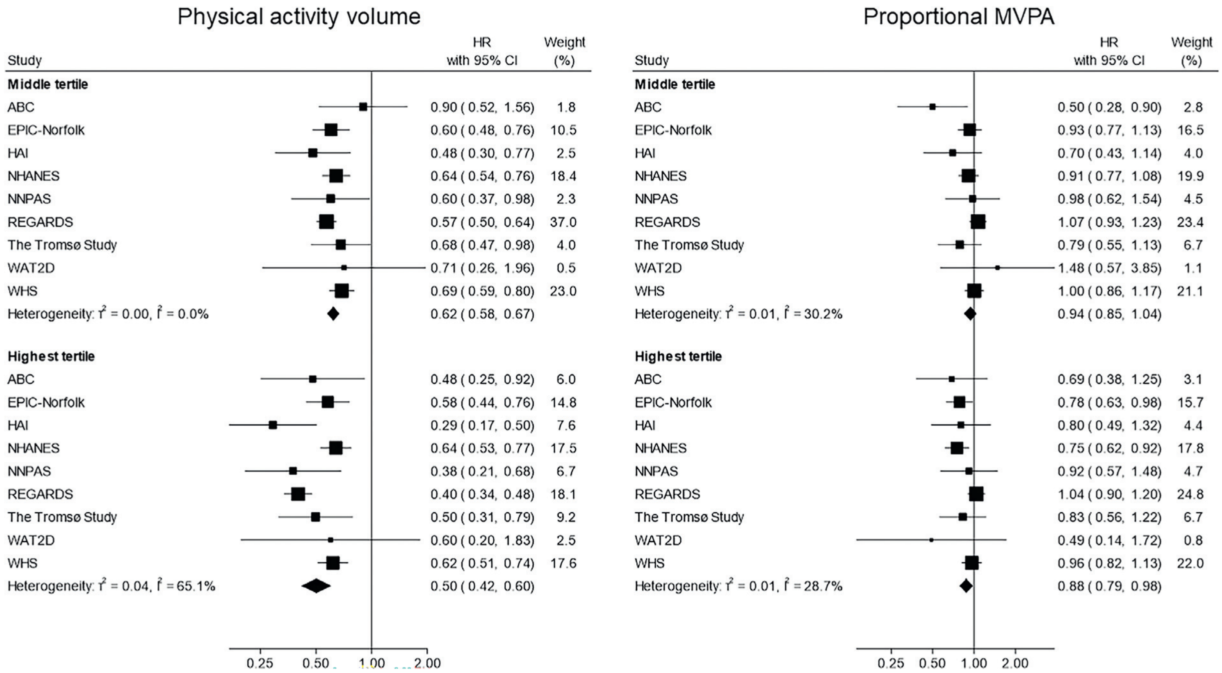

Figure 1. Physical activity volume, proportional MVPA, and risk of mortality by cohort. Multivariable adjustment includes age, sex (when applicable), socioeconomic status, smoking, body mass index, pre-existing CVD, pre-existing cancer, and the study-specific covariates listed in Appendix Table 1. Proportional MVPA additionally adjusted for physical activity volume. Proportional MVPA is volume-adjusted using the residual method. The reference is the tertile with lowest physical activity volume/proportional MVPA. ABC, Sweden Attitude, Behaviour and Change study; EPIC-Norfolk, The European Prospective Investigation into Cancer and Nutrition−Norfolk; HAI, Healthy Aging Initiative; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; NHANES, National Health and Nutrition Examination Study; NNPAS, Norwegian National Physical Activity Survey; REGARDS, REasons for Geographical and Racial Differences in Stroke; WAT2D, walking away from type 2 diabetes; WHS, Women's Health Study.

In another study, nonexercise incidental vigorous activities performed for only a few minutes per day, and thus making only a negligible contribution to total physical activity volume, were associated with lower risk of morbidity and mortality.[29,30] However, while these initial observations were controlled for time spent in other intensity categories, they were not controlled for the overall volume of activity and thus not immediately comparable to our results. In support of primacy of volume, a meta-analysis from The Steps for Health Collaborative (including three of the cohorts analyzed in this study) demonstrated that associations between different measures of stepping intensity and all-cause mortality were attenuated or eliminated following statistical adjustment for the total number of daily steps taken.[7] Again, methodological and analytical differences mean their results are not directly comparable to results from this study.

This study was based on harmonized and pooled data from nine studies across four countries which increases the range of movement profiles and the underlying behaviors of participants. To remove the high within-cohort correlation between volume and intensity, this study used an approach based on calculating the fraction of total movement counts that were attributable to MVPA and then predicting residuals adjusted for physical activity volume. Expressing intensity proportional to overall movement facilitates integrated analysis of overall movement volume and its underlying intensity distribution, and thus addresses the research question. This approach is complimentary to compositional or iso-temporal analyses of time-based exposure metrics[31]—e.g., replacing light-intensity physical activity with sedentary, moderate, or vigorous activity—because these contrasts do not clarify whether associations are explained by the higher intensity per se as overall activity volume is not held constant by the units of time constraint. On the other hand, the residuals method may have the disadvantage of representing the most conservative joint estimate of the contribution from MVPA within overall volume. Modeling volume and intensity in their natural continuous form[6] could have provided further insights into the joint distribution of intensity within volume which was only approximated with categorical models. Broadly speaking, however, the two approaches point to the same conclusion that building up activity volume is

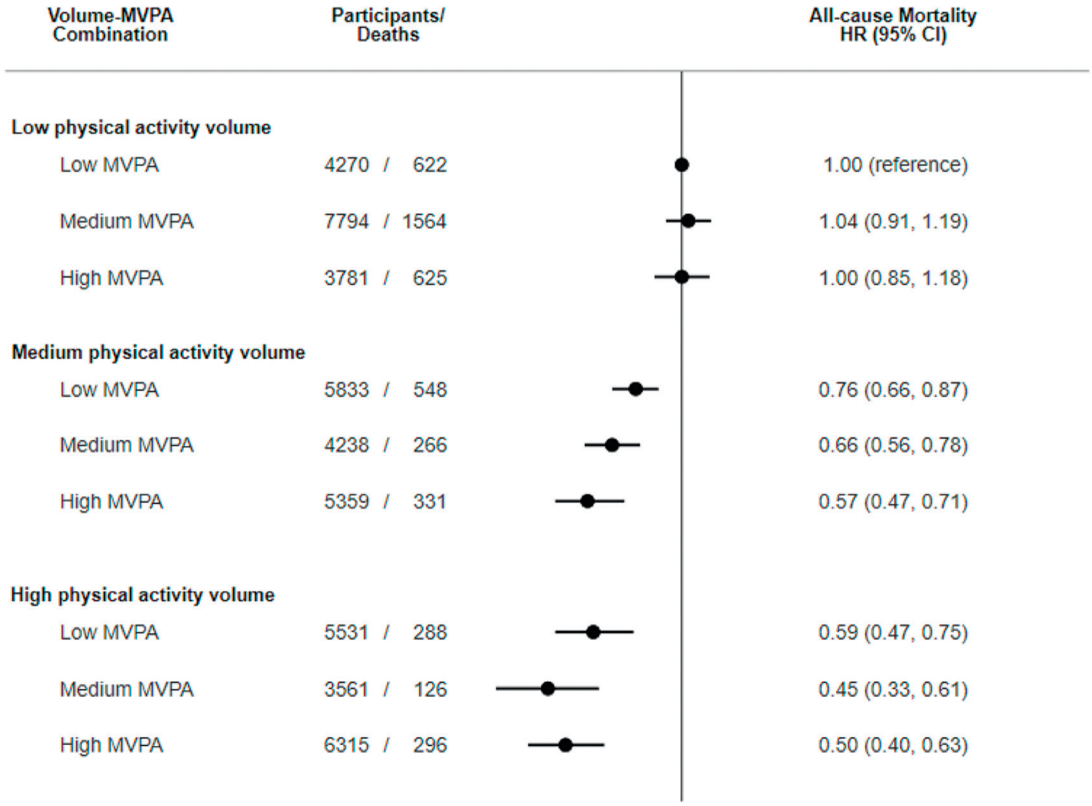

Figure 2. Risk of mortality for joint associations of physical activity volume and proportional MVPA. Multivariable adjustment includes age, sex (when applicable), socioeconomic status, smoking, body mass index, pre-existing CVD, pre-existing cancer, and the study-specific covariates listed in Appendix Table 1. Proportional MVPA is volume-adjusted using the residual method. HR, hazard ratio; MVPA, moderate-to-vigorous physical activity.

beneficial for health, with potential additional benefits of doing this through the incorporation of activities of at least moderate intensity.

The benefits of physical activity on longevity are multifactorial involving pathways related to inflammation, metabolism, and healthy aging.[32,33] Several of the putative protective mechanisms involving the cardiorespiratory and cardiometabolic systems[32]—including increased cardiorespiratory fitness[34] and possibly lower ectopic fat deposition[35]—are intensity-dependent. In the joint model, particularly pronounced effects of intensity among those with the lowest physical activity volume were therefore anticipated, but this was not the case. Experimental and observational evidence showing that very low levels of light-intensity physical activity can improve cardiometabolic risk markers[36,37] provides mechanistic support for lower mortality with higher volume of any intensity of physical activity. Total physical activity volume may also be superior to intensity in the association with body fatness.[38]

Results from this study extend previous evidence by investigating whether mortality is lower in more active individuals because of physical activity volume or because of more time spent in MVPA. According to the findings, the 38% lower mortality in the middle tertile of physical activity volume can be achieved using different strategies for being active which would not necessarily need to include "huff and puff" activities. The joint model did suggest some additional benefits of MVPA in the middle volume tertile, but this was not seen at low or high volumes, suggesting emphasis should first and foremost be placed on promoting any intensity of physical activity. For example, to increase physical activity volume from the lowest to the second tertile (70,200 acceleration counts, assuming a wear-time of 15 hours/day), one could either take up walking at a slower pace of 3.2 km/hour (2 miles/hour) for an additional ≈70 minutes/day or do brisk walking at 4.8 km/hour (3 miles/hour) for ≈30 minutes/day.[39] Importantly, this can be tailored based on individual capacity, preference and feasibility. Consequently, this has significant implications for population-wide and individual-level health promotion by expanding the range of health-promoting physical activities compared with an MVPA-centric approach.

Further nuances can be inferred from the joint model. An equivalent approximately 40% risk reduction can be achieved by having a total activity volume corresponding to the middle tertile and a high contribution from MVPA (e.g., having a sedentary occupation combined with regular leisure-time exercise), or by having a high total volume and a low contribution from MVPA (e.g., a standing/walking occupation such as a shop assistant). Importantly, the lack of dose-response relationship for proportional MVPA in the high volume tertile also suggests that prolonged engagement in MVPA is not needed to maximize health benefits from physical activity. Finally, it is important to acknowledge that the relative importance of volume versus intensity remains an ongoing field of research and their separate contributions may differ for different health conditions.

Limitations

Although each cohort followed the same data-cleaning and analytical protocol, the analysis was based on study-specific tertiles which makes translation of the findings into quantitative targets difficult due to variation in the underlying intensity distributions. Study-specific volume and intensity metrics are provided in the Appendix material which illustrates significant cohort differences in activity volume and intensity composition. For example, the mean contribution from MVPA in the low volume-low MVPA combination ranges from 0% to 9% across cohorts. An absolute cut-point was used to define MVPA which is not equally appropriate across age, health, and fitness status.[40] It is thus likely that the biological meaning of MVPA has varied across cohorts, particularly for those representing elderly and inactive individuals. The expected direction of this misclassification bias would be to attenuate effect sizes for the intensity component, potentially partly explaining the lack of benefit from intensity in those with the lowest physical activity. Examining morbidity and mortality risk based on volume-intensity combinations derived from individualized or relative MVPA thresholds is an important area for further research. Only a modest number of deaths were recorded in some cohorts which makes their contribution to the pooled estimates small. Finally, as an observational study, the possibility of unmeasured or residual confounding and other biases, that may have affected our results cannot be refuted.

CONCLUSIONS

In summary, both physical activity volume and a greater contribution from MVPA to total volume were associated with a lower risk of mortality in middle-aged and older adults. The added benefit of intensity, beyond physical activity volume, was less clear when volume and MVPA were analyzed together in joint models. These findings emphasize the importance of physical activity of any intensity, while also suggesting there may be some added benefit if the same amount of activity is performed with a higher intensity.

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SUPPLEMENTAL MATERIAL

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