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Joint associations of physical activity and sedentary time with body mass index: A prospective study of mortality risk

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Device-measured physical activity and sedentary time are suggested to be more important determinants of all-cause mortality compared to body mass index (BMI) in mainly older adults. However, the joint associations of physical activity and sedentary time with BMI in relation to mortality risk in relatively healthy middle-aged individuals are unclear. We followed 770 adults (56% women, mean age 55.6 years) from a population-based cohort study for up to 15.3 years. BMI categories were combined with tertiles of total, light, and moderate-to-vigorous physical activity and sedentary time. Cox proportional hazards models estimated hazard ratios (HR) of all-cause mortality with 95% confidence intervals (CI). High total and light intensity physical activity and low sedentary time were associated with a lower risk of mortality in normal weight individuals compared with low active overweight/obese; HR: 0.35 (CI: 0.14, 0.86), HR: 0.33 (CI: 0.12, 0.89), and HR: 0.34 (CI: 0.13, 0.92). Among overweight/obese individuals, those who were medium active in light physical activity had a lower mortality risk, HR: 0.36 (CI: 0.15, 0.83), compared with low active. Medium sedentary individuals had a lower risk, HR: 0.43 (CI: 0.20, 0.94) compared with those who were most sedentary. Associations among the most active or least sedentary tertiles were similar irrespective of BMI category. In conclusion, higher physical activity and lower sedentary time were associated with lower mortality risk irrespective of BMI. Physical activity should be promoted and prescribed to individuals with low physical activity levels irrespective of weight status.

KEYWORDS

accelerometry, BMI, cohort, light intensity, moderate-to-vigorous intensity, obesity, overweight, population-based

1 | INTRODUCTION

Obesity and low physical activity are highly prevalent worldwide.[1] Both are associated with an increased risk of morbidity and premature mortality[2]; thus, understanding ways to alleviate their consequences are major public health priorities. Recent evidence suggests the association between physical activity and excessive weight gain is complex, possibly bidirectional, and that low physical activity may not be the primary agent leading to excessive weight gain.[3] However, there is evidence from prospective observational cohort studies that physical activity may modify the effect of obesity on premature mortality.[4–6] This may be explained by physical activity leading to better control

of cardiometabolic risk factors such as glycaemic control, hypertension, and dyslipidaemia,[7] which are partial mediators of obesity-related diseases.[8]

Determining body mass index (BMI) associated mortality is complex and requires long-term follow-up to limit bias from illness-related weight loss.[9] Illness-related weight loss can artificially increase the number of individuals with poor health in the lower range of body weight, potentially leading to a right-shift of the association between observed BMI and risk of mortality, also known as reverse causation bias. The shape and magnitude of the association between physical activity, sedentary time, and mortality also appear influenced by deaths during the early phase of follow-up, a potential indicator of bias from illness-related low physical activity or fatigue.[10] Previous studies on the combined influence of BMI and physical activity on mortality based on at least 10 years of follow-up have used self-reported measures of physical activity.[5,11] Self-reported physical activity levels are prone to cognitive biases which may also be associated with weight status, thus introducing differential measurement error.[12] Recent work based on device-measured physical activity and sedentary time suggested physical activity, not obesity, was the main determinant of mortality in almost 35 000 individuals from Scandinavia, UK, and the United States.[6] However, in that study, the median follow-up was relatively short at 7.4 years and influenced by some of the larger US cohorts that substantially contributed to the total case count and thus the results. Further, participants were mainly older than 60 years of age at the time of recruitment which may limit generalizability to younger populations as there is some evidence that the slope of the BMI-mortality association is steeper in younger compared with older individuals.[9,13] The potential influence of bias from illness-related weight loss or low physical activity is also lower in a younger, healthier population.

In this study, we used data from the Swedish cohort of an international collaboration based on device-measured physical activity,[6] to revisit the independent and joint associations of physical activity or sedentary time with BMI in relation to risk of all-cause mortality in a population of middle-aged adults with a low prevalent disease burden and long-term follow-up.

2 | MATERIALS AND METHODS

2.1 | Study population

We used data from the Swedish population-based Attitude, Behavior and Change (ABC) cohort study collected 2000–2001. Recruitment and data collection are described in detail elsewhere.[14] In short, from a randomly selected sample of $n = 3300$ persons (52% women) between 18 and 75 years, $n = 2265$ were reached and $n = 1556$ agreed to answer a questionnaire and wear an accelerometer for 1 week. In this study, 834 persons (55% women), 35 years or older at baseline, who provided at least 4 days of valid accelerometer data, defined as ≥10 h of wear time, and self-reported height and weight were included. The study was approved by the ethics committee at the Karolinska Institutet (Dnr 378/02, 2012/707 31/1, 2015 1578/32). All participants provided written informed consent, and all procedures were in accordance with the Declaration of Helsinki.

2.2 | Outcomes

Participants were followed from the first day of accelerometer measurement until death or censoring on December 31, 2015. Information of all-cause mortality was collected in 2016 from the National Board of Health and Welfare's Cause of Death Register.

Physical activity and sedentary time were assessed with the ActiGraph 7164 accelerometer (ActiGraph Manufacturing Technology Inc., Ft Walton Beach, FL, USA) The accelerometer was initialized as recommended by the manufacturer and recorded counts-per-minute (cpm) on the vertical axis in 1-min epochs. Participants were instructed to wear the accelerometer on a belt around the lower back during waking hours for 7 days, only removing it for water-based activities. Non-wear time was defined as ≥90 consecutive minutes of zero counts, allowing for up to 2 min of non-zero counts if the interruption was preceded or followed by ≥30 min of zero counts.[15] Cutoffs to estimate the time spent sedentary and in different physical activity intensities were as follows: sedentary ≤100 cpm, light physical activity 101–1951 cpm, and moderate-to-vigorous physical activity (MVPA) as ≥1952 cpm.[16] Total physical activity was defined by total cpm/wear time per day in minutes.

Demographic and anthropometric data were self-reported and obtained from the baseline questionnaire delivered by mail together with the accelerometer. BMI was calculated as weight in kg divided by height in m^2 (kg/m^2) and categorized following the World Health Organization's standard criteria: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), obesity (30.0–34.9), and severe obesity class (≥35.0).[17] Covariates were sex, age, education (university, high school, primary school), smoking status (never/former or current), and history of hypertension or diabetes.

2.3 | Data analysis

To reduce the risk of bias from reverse causation, we excluded participants with deaths during the first two years ($n = 1$), BMI <18,5 ($n = 5$), history of cardiovascular disease or cancer at the time of accelerometer assessment ($n = 48$), or missing disease history data ($n = 10$), leaving an analytical sample of 770 participants. We created tertiles (low, medium, high) of total physical activity, light physical activity, MVPA, and sedentary time. Light physical activity, MVPA, and sedentary time were normalized by wear time (percent of wear time) before creating the tertiles. Multivariate cox proportional hazards models were applied to estimate hazard ratios (HR) of all-cause mortality with 95% confidence intervals (CI). All models were checked for the proportional hazard assumption.

First, we performed calculations for the independent associations between three BMI categories (normal weight, overweight, obesity [BMI ≥30.0]), tertiles of physical activity and sedentary time, and mortality. The covariates adjusted for were age, education, smoking status, and history of hypertension and diabetes. The analysis of BMI was additionally adjusted for MVPA, and the analyses of physical activity and sedentary time were additionally adjusted for BMI. Sensitivity analyses were performed without adjustment for hypertension and diabetes. Additional analyses were also performed to test the interaction effect between the three BMI categories and physical activity or sedentary time (continuous), with significant interaction effects found only for total physical activity ($p = 0.04$, remaining p-values ≥0.60).

Second, we performed calculations to examine the combined associations of physical activity and BMI with mortality. Adjusting for age, education, smoking status, and history of hypertension and diabetes. Due to a small number of participants/events (77/7) in the obesity group, we collapsed the BMI categories overweight and obesity into one category. We then combined physical activity and sedentary tertiles with the two BMI categories (normal weight and overweight/obese), yielding six BMI–physical activity combinations. We compared five BMI–physical activity combinations with the least active overweight/obese participants as reference category, that is, lowest tertile for physical activity or highest tertile for sedentary time. We performed sensitivity analyses additionally adjusting for sedentary time (continuous) in MVPA models and adjusting for MVPA (continuous) in the light intensity and sedentary time models.

All analyses were performed using statistical software Stata 16 (StataCorp LP, College Station, TX, USA).

3 | RESULTS

A total of 770 participants, 56% women, age 55.6 years (SD = 10.3) were followed up to 15.3 years, with a mean of 14.3 years (SD = 1.8) and 10 987 person-years at risk. During that time, 67 participants died due to non-accidental causes (26 women), including 20 deaths from cardiovascular disease, 24 deaths from cancer, and 23 from other causes. BMI ranged from 19.0 to 40.8 (median: 25.2). The prevalence of overweight was 41.6%, and the prevalence of obesity was 10.0%, including 15 participants (1.9%) with severe obesity. Mean accelerometer wear time per day was 14 h 47 min (SD = 74 min). Mean time per day spent in MVPA was 33 min (SD = 30 min), time in light physical activity was 5 h 39 min (SD = 92 min), and sedentary time was 8 h 35 min (SD = 98 min). This is equivalent to 3.7%, 38.1%, and 58.2% of the day. Baseline characteristics of the study sample stratified by BMI category are shown in Table 1.

The independent, multivariable-adjusted associations of BMI, physical activity, and sedentary time with mortality risk are presented in Table 2. There were no associations with mortality for either overweight or obesity when compared to being normal weight. For total physical activity and MVPA, the most active individuals had 61% and 49% lower mortality risk compared to the least active individuals: HR: 0.39 (CI: 0.20 to 0.79) and HR: 0.51 (CI: 0.26 to 0.98). For light physical activity, both high and medium active individuals had lower risks, 54% and 49%, than the least active individuals: HR: 0.46 (CI: 0.23 to 0.89) and HR: 0.52 (CI: 0.29 to 0.95). The most sedentary individuals had a higher mortality risk, HR: 2.18 (CI: 1.09 to 4.39), compared to the least sedentary individuals. Sensitivity analysis did not change the results.

The joint multivariable-adjusted associations of BMI–physical activity combinations with mortality are presented in Table 3 (For descriptive data on daily minutes and percentage of time in each of the six BMI–physical activity combinations, see Table S1). High levels of total and light intensity physical activity and low sedentary time were associated with a 65–67% lower risk of mortality in normal weight individuals compared with the low active overweight/obese group, HR: 0.35 (CI: 0.14 to 0.86), HR: 0.33 (CI: 0.12 to 0.89) and HR: 0.34 (CI: 0.13 to 0.92). In the overweight/obese group, those who were medium active in light physical activity had a 64% lower mortality risk, HR: 0.36 (CI: 0.15 to 0.83), compared with the least active individuals, and those who were medium sedentary had a 57% lower risk, HR: 0.43 (CI: 0.20 to 0.94), compared with the most sedentary individuals. HR for MVPA combined with BMI were roughly comparable to estimates for BMI combined with total and light physical activity, yet none of these associations achieved statistical significance.

TABLE 1 Baseline characteristics of the study sample stratified by BMI category.

Variables	Normal weight ($n = 373$)	Overweight ($n = 320$)	Obese ($n = 77$)
Women	232 (62.2)	150 (46.9)	50 (64.9)
Age (years)	51.4 ± 10.6	53.6 ± 10.0	53.4 ± 9.9
Education			
<High school	95 (25.5)	101 (31.6)	33 (42.9)
High school	139 (37.3)	134 (41.9)	24 (31.2)
University	139 (37.3)	85 (26.6)	20 (26.0)
Smoking			
Never/ Former	275 (73.7)	244 (76.2)	61 (79.2)
Current	98 (26.3)	76 (23.8)	16 (20.8)
History of disease			
Diabetes	4 (1.1)	11 (3.4)	3 (3.9)
Hypertension	31 (8.3)	46 (14.3)	22 (28.5)
BMI (kg/m^2)	22.9 ± 1.5	27.0 ± 1.3	32.6 ± 2.6
Physical activity			
CPM	372.6 ± 204.3	342.7 ± 318.2	268.6 ± 118.5
%MVPA/day	4.1 ± 3.2	3.4 ± 3.0	2.2 ± 2.1
%LPA/day	38.8 ± 9.8	37.7 ± 9.0	36.8 ± 10.1
%SED/day	57.0 ± 10.8	58.8 ± 10.0	61.0 ± 11.0
Acc wear time (min/day)	889.6 ± 74.0	885.4 ± 75.5	878.8 ± 68.5
7 valid days	301 (80.7)	275 (85.9)	61 (79.2)

Note: Values presented are mean ± SD or number (%).

Abbreviations: Acc, accelerometer; BMI, body mass index; CI, confidence intervals; CPM, counts-per-minute; HR, hazard ratio; LPA, light intensity physical activity; MVPA, moderate to vigorous physical activity; SED, sedentary time.

The sensitivity analysis with adjustment for other physical activity behaviors attenuated the associations among the normal weight individuals but did not change interpretation of the results.

4 | DISCUSSION

This prospective study comprising middle-aged adults with low disease burden showed that higher physical activity levels and lower levels of sedentary time were associated with lower rate of all-cause mortality in both normal-weight and overweight/obese individuals. These results support findings from previous studies, suggesting that low physical activity is a more pronounced risk factor for all-cause mortality than weight status,[6,11,18] although the associations are complex. Engaging in light physical activity corresponding to at least 5 h 35 min/day or no more than 8 h 35 min of sedentary time/day provided a risk reduction of approximately 60% for overweight/obese individuals in this study (Table S1). There was no survival benefit of being normal weight if physical activity levels were low.

While the association between MVPA and risk of mortality did not reach statistical significance, the point estimates clearly indicated that high amounts of MVPA in the overweight/obese group and both medium and high MVPA in the normal-weight group reduced the risk of mortality. Whether levels of MVPA corresponding to the middle tertile (27 min/day) are sufficient to lower mortality rates in individuals with obesity, or if higher levels are needed, should be further investigated. Interestingly, we observed a greater magnitude of associations for light intensity physical activity than for MVPA, similar to the results from previous research using accelerometry.[19] The point estimates in the BMI–physical activity combinations, as well as the independent associations suggest a dose–response relationship for risk reductions from light intensity physical activity, which also is in line with previous observations.[19]

It is an important finding that light intensity physical activity was inversely associated with mortality in both overweight/obese and normal weight individuals. The positive health effects of everyday activities are especially interesting from a public health perspective, and our results are in agreement with the World Health

TABLE 2 Multivariable adjusted independent associations between physical activity, sedentary time, and BMI with all-cause mortality.

Categories / tertiles	*n* / deaths	HR (95% CI)
BMI		
Normal weight	373 / 28	Reference
Overweight	320 / 32	1.03 (0.61, 1.74)
Obesity	77 / 7	1.05 (0.43, 2.52)
Total PA		
Low	257 / 39	Reference
Medium	257 / 17	0.73 (0.40, 1.32)
High	256 / 11	**0.39 (0.20, 0.79)**
MVPA		
Low	257 / 37	Reference
Medium	257 / 16	0.75 (0.41, 1.39)
High	256 / 14	**0.51 (0.26, 0.98)**
Light PA		
Low	257 / 39	Reference
Medium	257 / 16	**0.52 (0.29, 0.95)**
High	256 / 12	**0.46 (0.23, 0.89)**
Sedentary time		
Low	257 / 11	Reference
Medium	257 / 20	1.25 (0.59, 2.65)
High	256 / 36	**2.18 (1.09, 4.39)**

Note: Analyses are restricted to individuals with >2 years of follow-up and excluding individuals with cardiovascular disease or cancer at baseline. Models are adjusted for sex, age, education, smoking, hypertension, and diabetes. Statistically significant results shown in bold.

Abbreviations: BMI, body mass index; CI, confidence intervals; HR, hazard ratio; MVPA, moderate to vigorous physical activity; PA, physical activity.

Organization's (WHO) recommendations for physical activity and sedentary behavior, that is, that all adults benefit from regular physical activity of any intensity and that "Every move counts."[20] This is also important from a clinical perspective. Healthcare professionals should promote and prescribe physical activity to individuals with low physical activity levels irrespective of weight status.[21] In addition, practitioners and other health professionals should emphasize the multiple health benefits of regular physical activity,[20,22] even in the absence of weight loss in obesity management.

We were not able to analyze individuals with obesity separately due to the relatively small sample and low prevalence of obesity. Even though the impact of sedentary time and higher physical activity levels on all-cause mortality in obese individuals has been studied using accelerometry,[6] more studies including younger persons are still needed. There is also lack of studies investigating the role of physical activity for reducing the risk of premature death in severely obese individuals. Severe obesity is associated with substantially elevated rates of death,[23] and given the effect of physical activity may have on obesity-related diseases these associations need to be further investigated.

The main strengths of our study include the population-based design with long follow-up time, the highly reliable registry data on mortality, as well as the use of device-based physical activity and sedentary time, which is less prone to biases usually associated with self-report. The compliance to accelerometer wearing per day must be considered high with 83% of the sample providing data from seven valid days, covering a high proportion of awake time. Our participants are also noticeable younger than in larger contemporary cohorts with device-measured activity,[24,25] with a corresponding lower burden of disease as indicated by the low prevalence of hypertension and diabetes in the ABC cohort. Our results may therefore be less susceptible to bias from, for example, illness-related weight loss or low physical activity at study baseline.

Our study also has several limitations that should be mentioned. The ABC study sample was nationally representative, but as in any research study the participants may be healthier and more physically active than the general population. This might have affected the number of events and limited our statistical power, as indicated by the wide confidence intervals associated with some of the point estimates. Prevalent disease, height and weight were self-reported and may therefore be subject to cognitive biases. However, the prevalence of obesity was consistent with other data sources.[26,27] There were no independent associations between mortality and BMI in our sample. In addition, BMI is not a direct measure of body fat, and we cannot rule out misclassification due to high lean mass in individuals with overweight/obesity.

Despite the advantages of device-based assessment of physical activity and sedentary time using accelerometry, there are some limitations with this method.[28,29] The analyses rely on the chosen cutoff points for classification of intensities which may introduce classification bias.

Hip-worn devices do not capture all activities important for health, such as bicycling, strength training, and water-based activities. Sedentary time was estimated from movement based cutoff points and not body position, which means that time standing still might be included.[30]

Physical activity and BMI were only assessed at baseline, and we do not have information about possible changes in the participants' physical activity habits, sedentary behavior, or BMI status that may have influenced the observed associations. However, the results from a sub-study showed that physical activity levels and BMI status in the ABC cohort were unchanged from 2001 to

TABLE 3 Joint multivariable-adjusted associations of BMI–physical activity combinations with mortality.

	Total PA		MVPA		Light PA		Sedentary	
Tertiles	***n* / events**	**HR (95% CI)**	***n* / events**	**HR (95% CI)**	***n* / events**	**HR (95% CI)**	***n* / events**	**HR (95% CI)**
OW + Obese								
Low	163 / 27	Ref	166 / 24	Ref	141 / 25	Ref	111 / 6	0.47 (0.19, 1.16)
Medium	125 / 7	0.56 (0.24, 1.32)	123 / 10	1.02 (0.47, 2.19)	138 / 7	**0.36 (0.15, 0.83)**	142 / 9	**0.43 (0.20, 0.94)**
High	109 / 5	0.40 (0.15, 1.06)	108 / 5	0.41 (0.16, 1.11)	118 / 7	0.44 (0.19, 1.04)	144 / 24	Ref
Normal weight								
Low	94 / 12	0.89 (0.44, 1.78)	91 / 13	1.14 (0.56, 2.30)	116 / 14	0.72 (0.37, 1.40)	146 / 5	**0.34 (0.13, 0.92)**
Medium	132 / 10	0.81 (0.38, 1.71)	134 / 6	0.55 (0.22, 1.37)	119 / 9	0.57 (0.26, 1.23)	115 / 11	0.60 (0.29, 1.23)
High	147 / 6	**0.35 (0.14, 0.86)**	148 / 9	0.58 (0.26, 1.28)	138 / 5	**0.33 (0.12, 0.89)**	112 / 12	0.79 (0.39, 1.60)

Note: Analyses are restricted to individuals with >2 years of follow-up and excluding individuals with cardiovascular disease or cancer at baseline. Models are adjusted for sex, age, education, smoking, hypertension, and diabetes. Statistically significant results shown in bold.

Abbreviations: BMI, body mass index; CI, confidence intervals; HR, hazard ratio; MVPA, moderate to vigorous physical activity; PA, physical activity; OW, overweight.

2008, suggesting that potential changes in physical activity are small and may not impact on our results.[31]

From a public health point of view, understanding the associated health benefits of, for example, reallocating time spent sedentary into time in light intensity physical activity, is important. An increasing number of observational studies have addressed these associations using isotemporal substitution or compositional data analysis.[32,33] The findings suggest that reallocating time into MVPA from light physical activity or sedentary time and reallocating sedentary time into light physical activity or MVPA may reduce the risk of obesity and all-cause mortality.[32,33] It is still unclear if these associations differ by BMI categories, and this should be further investigated.

As in any observational study, we cannot infer causality. Even so, randomization within a trial appears unfeasible when examining the effect of lifestyle behaviors on mortality. We excluded events that occurred the first two years to limit the influence of reverse causation and we adjusted for several relevant factors, but as in any observational study, our results may be subject to residual confounding, selection and other biases.

5 | PERSPECTIVE

In this cohort consisting of relatively young and healthy participants followed for up to 15.3 years, we observed that higher physical activity and lower sedentary time were associated with lower mortality risk irrespective of BMI. We found no survival benefit of being normal weight if physical activity was low or if sedentary time was high. Our results are in line with findings from cohorts including mainly older adults.[6] Light intensity physical activity was inversely associated with mortality in both overweight/obese and normal weight individuals. The positive health effects of everyday activities are especially interesting from a public health perspective and support the message "Every move counts."[20] Healthcare professionals should promote and prescribe physical activity to individuals with low physical levels irrespective of weight status.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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