Preventive Medicine 180 (2024) 107879

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Sedentary behavior and the combination of physical activity associated with dementia, functional disability, and mortality: A cohort study of 90,471 older adults in Japan

Zhen Du [a], Koryu Sato [a,*], Taishi Tsuji [b,c], Katsunori Kondo [c,d], Naoki Kondo [a]

[a] Department of Social Epidemiology, Graduate School of Medicine and School of Public Health, Kyoto University, Kyoto, Japan
[b] Institute of Health and Sport Sciences, University of Tsukuba, Tokyo, Japan
[c] Department of Social Preventive Medical Sciences, Center for Preventive Medical Sciences, Chiba University, Chiba, Japan
[d] Department of Gerontological Evaluation, Center for Gerontology and Social Science, Research Institute, National Center for Geriatrics and Gerontology, Obu City, Aichi, Japan

ARTICLE INFO

Keywords:
Sedentary time
Joint association
Cognition
Long-term care
Mortality

ABSTRACT

Objective: To examine the associations of sedentary behavior (SB) and the combination of moderate-to-vigorous intensity physical activity (MVPA) with dementia, functional disability, and mortality in older adults, and the heterogeneity in different subpopulations.
Methods: Nation-wide cohort with 90,471 individuals aged ≥65 years in Japan. SB (<3, 3–<8, and ≥ 8 h per day [h/d]) and MVPA (0, 0 < MVPA<1, and ≥ 1 h/d) were measured in 2016. Long-term care registry-based incidence of outcomes was ascertained through 2021. Cox proportional hazard models were performed.
Results: Compared with SB < 3 h/d group, SB ≥ 8 h/d was associated with higher risks of dementia, functional disability, and mortality with hazard ratios (95% confidence interval) of 1.36 (1.22–1.52), 1.32 (1.19–1.48), and 1.31 (1.18–1.45). The combination of MVPA and SB demonstrated a dose-respond trend of increasing risks of dementia, functional disability, and mortality with increased SB and decreased MVPA, where participants who spent no MVPA with SB ≥ 8 h/d had the highest risks. High MVPA attenuated but didn't eliminate the risks. Participants who spent MVPA≥1 h/d with SB ≥ 8 h/d had comparable risks to those who spent no MVPA with SB < 3 h/d. No heterogeneity was found by MVPA levels, sex, education, comorbidity, and depression conditions.
Conclusions: Prolonged daily SB was associated with higher risks of dementia, functional disability, and mortality in older adults, regardless of MVPA, sex, education, and chronic conditions. Individuals with high MVPA also face considerable risks when engaging in high SB. High MVPA with high SB revealed a comparable risk to no MVPA with low SB.

1. Introduction

Given the rapidly aging population worldwide, numerous older adults suffer from age-related diseases such as dementia (Feigin et al., 2019) and functional disability (Yau et al., 2022), which cause a great burden to individuals, family members, and society (Livingston et al., 2017), and increase the needs and costs for long-term care (LTC) or other health services (Jacobs et al., 2013). Physical activity (PA) is a widely acknowledged contributor to healthy aging. Many studies have demonstrated higher PA to be associated with a lower risk of dementia (del Pozo Cruz et al., 2022a; Yoon et al., 2021), functional disability (Sanchez-Sanchez et al., 2020), cardiovascular disease (del Pozo Cruz et al., 2022b), cancer incidence (del Pozo Cruz et al., 2022a, 2022b), and mortality (del Pozo Cruz et al., 2022a, 2022b; Saint-Maurice et al., 2020; Sanchez-Sanchez et al., 2020). World Health Organization (WHO) recommends at least 150–300 min of moderate-intensity or 75–150 min of vigorous-intensity PA or an equivalent combination of moderate- to-vigorous-intensity PA (MVPA) per week for older adults (WHO, 2020). However, only 27.3% to 44.3% of older adults met the guidelines in the United States (Keadle et al., 2016).

Compared with the increasing prevalence of MVPA, decreasing the time of sedentary behavior (SB) may be more feasible for older adults.

* Corresponding author at: Department of Social Epidemiology, Graduate School of Medicine and School of Public Health, Kyoto University, Floor 2, Science Frontier Laboratory, Yoshida-Konoecho, Sakyo-ku, Kyoto-shi, Kyoto 606-8315, Japan.
E-mail address: sato.koryu.8i@kyoto-u.ac.jp (K. Sato).

https://doi.org/10.1016/j.ypmed.2024.107879
Received 29 September 2023; Received in revised form 19 January 2024; Accepted 22 January 2024
Available online 23 January 2024

Previous studies suggested that greater time spent on SB was associated with a higher risk of developing cardiovascular disease (Bellettiere et al., 2019), dementia (Huang et al., 2022; Raichlen et al., 2022), poor muscle strength (Ramsey et al., 2021), mortality (Chau et al., 2015; Diaz et al., 2017; Ekelund et al., 2019), and functional disability (Chiba et al., 2022; DiPietro et al., 2018). However, we recognize that there are three major research gaps regarding the association between SB and health outcomes among the older population. First, most of the existing literature studied general adults and did not focus on the older population with a few exceptions (Chiba et al., 2022; Diaz et al., 2017; DiPietro et al., 2018; Raichlen et al., 2022; Rojer et al., 2020). Indeed, the WHO's guideline was developed based on evidence in the general population, and the WHO explicitly acknowledges that evidence supporting SB-based recommendations with a focus on older adults is scarce (WHO, 2020). Second, it is still unclear whether reducing SB alone is beneficial or whether a certain amount of MVPA is essential to maintain thehealth of older adults. Thus, exploring the joint association of SB given different levels of MVPA would provide valuable insights into developing recommendations for SB. Third, heterogeneity in the association between SB and health remains understudied. Because there are different patterns in SB and PA by sex (Arnardottir et al., 2013; Huang et al., 2022), socioeconomic status (Huang et al., 2022; Schultz et al., 2018), depression (Schuch et al., 2017), and comorbidity status (He et al., 2021), investigating heterogeneity is essential to develop a meaningful recommendation for these subpopulations. Further research is needed to confirm whether reducing SB can be recommended for everyone.

To fulfill these research gaps, this study examined the independent and joint associations of SB and MVPA with dementia, functional disability, and mortality with a focus on older adults. We also considered potential effect modifications on the association of SB with outcomes, by MVPA, sex, socioeconomic status, comorbidity, and depression status.

2. Methods

2.1. Study population

This study used data from the Japan Gerontological Evaluation Study (JAGES), which is an ongoing nationwide cohort study (Kondo et al., 2018). Participants were older adults aged ≥65 years who had not been certified as needing LTC (i.e., they were physically and cognitively independent) at baseline. Self-report questionnaires were mailed from October to December 2016 in 40 municipalities (Supplementary Method S1). The LTC registry-based incidence of outcomes was ascertained through 2021. After excluding participants who self-reported having dementia or Alzheimer's disease during the 2016 baseline survey as well as those who experienced the outcome events on the day follow-up was initiated (i.e., time zero), 90,471 participants were included in the final analysis (Supplementary Fig. S1). All participants provided informed consent. The research was approved by the ethics review committees of Kyoto University (R3153–2), Chiba University (2493), and the National Center for Geriatrics and Gerontology (992).

2.2. Ascertainment of dementia, functional disability, and mortality

To obtain information on the outcomes, we linked the participants to their data in the public LTC insurance (LTCI) registry. Dementia was determined using the Criteria for Levels of Cognitive Impairment in the Japanese LTCI System when the cognitive impairment was identified as level IIa or higher (Matsunaga et al., 2017; Sato et al., 2021), where an individual exhibits symptoms, behaviors, and communication difficulties that may impede daily activities, yet independence is possible with some assistance (see Supplementary Method S2 for more details). The criteria robustly correlate with the Mini-Mental State Examination, with a Spearman's rank correlation coefficient of −0.73 ($p < 0.001$) (Hisano, 2009). Functional disability was ascertained when participants were newly certified for Care Level 2–5 (Jin et al., 2021; Matsunaga et al., 2017; Noguchi et al., 2019), because individuals identified as Care Level 2 or higher could not perform at least one basic daily activities alone. The information on mortality was also obtained from the registry. It recorded the date when an individual was identified as having dementia, certified as needing LTC, or dead.

2.3. SB and MVPA

Daily SB and MVPA were measured using a questionnaire derived from the Japan Public Health Center-based Prospective Study-PAQ short form (JPHC-PAQ Short). It is a self-report questionnaire asking the total hours they were active and sitting per day, which showed a strong correlation and acceptable agreement with the gold standard, the doubly labeled water (DLW) method (Kikuchi et al., 2020; Sasai et al., 2018). SB is the primary explanatory variable of interest. For SB, participants were asked "How many hours are you sitting a day, including while you're working." The response options were (i) Less than three hours, (ii) Three to less than eight hours, and (iii) Eight hours or more. For MVPA, they were asked "How many hours are you spending performing physical work or intense sports during an average day, including while you're working." The response options were (i) None, (ii) Less than one hour, and (iii) One hour or more. We also generated nine groups by combining MVPA and SB with three categories each to assess the joint association of MVPA and SB with the outcomes.

2.4. Sociodemographic characteristics, lifestyle behaviors, and health conditions

We adjusted potential confounders at baseline, including sex, age (5-year interval), marital status (married, single/divorced/widowed/other), educational attainment (low: ≤9 years, middle: 10–12 years, high: ≥13 years), annual household income (low: <2.0 million Japanese Yen [MJPY], middle: 2.0–<4.0 MJPY, high: ≥4.0 MJPY) (30), employment (employed, retired or never employed), body mass index [BMI] (take height and weight values outside the mean ± 4 times standard deviation as missing values; underweight: <18.5 kg/m2, normal weight: 18.5–24.9 kg/m2, overweight: 25.0–29.9 kg/m2, obesity: ≥30.0 kg/m2), comorbidity (number of chronic diseases: 0, 1, ≥2) (Supplementary Method S3), self-rated health (excellent, good, fair, poor), alcohol (current, past, never), smoking (current, past, never), frequency of eating meat or fish (less than once a day, every day), frequency of eating fruits and vegetables (less than once a day, every day), and social isolation (a partially modified version of the Social Isolation Score (SIS) [0–5 points]: low: 0–1, high: 2–5 [see Supplementary Method S4 for details]) (Koyama et al., 2021; Steptoe et al., 2013).

2.5. Statistical analysis

Cox proportional hazard regressions were used to assess the association between the exposure and time to events. In Model 1, we adjusted for sex and age. In Model 2, we further adjusted for all the covariates including MVPA to examine the independent association between SB and dementia, functional disability, and mortality incidence. Subsequently, we examined the stratified and joint association of SB and MVPA with the three outcomes. Tests for linear trend of the explanatory variable were conducted by including the variable as an ordinal variable in regression models.

To investigate the heterogeneity and the robustness of the findings, we conducted pre-selected subgroup analysis by sex, socioeconomic status (represented by educational attainment (Winkleby et al., 1992)), chronic conditions (represented by comorbidity [number of chronic diseases: <2, ≥2]) and depression (15-item Geriatric Depression Scale (Almeida and Almeida, 1999) [not depressed: ≤4 points, moderately depressed: 5–9 points, severely depressed: ≥ 10 points]).

We applied the chained equations of multiple imputation to deal with the missing data on all variables used in our study (Supplementary

Table S1 shows the percentage of missing data). The proportional hazard assumptions tested by comparing HRs for the first two years and subsequent follow-up years indicated no evidence of violation.

For the sensitivity analysis, first, to reduce potential reverse causation, we excluded those with dementia, functional disability, and mortality events that happened within the first year follow-up time (Chau et al., 2015; Lee et al., 2018; McKeough et al., 2018; Sattar and Preiss, 2017), respectively. Second, to confirm that the missing data did not affect our findings, we conducted analyses using the complete data set (i.e., the sample who had valid cases in all the covariates, MVPA, SB, and outcomes). Third, we further adjusted for depression. All the analyses were performed using STATA software, version 17.0 (Stata Corp, College Station, Texas, USA).

3. Results

3.1. Baseline characteristics and incidence of the outcomes of the participants

Of the 90,471 participants, 41,643 (46.0%) were male, and the median age was 73 (interquartile range, 69–78; maximum value: 101) years (Table 1). During a median follow-up of 3.4 years (maximum follow-up: 1646 days), dementia, functional disability, and mortality occurred in 4135 (4.6%), 4201 (4.6%), and 4599 (5.1%) participants, with an overall incidence of 47.4, 47.3 and 42.1 per 1000 person-years, respectively. Supplementary Table S2 presents a comprehensive overview of the sample sizes and event counts, categorized by SB and MVPA.

3.2. Independent association between SB and dementia, functional disability, and mortality

In the model that adjusted for sex and age, both 3–<8 and > 8 h/d of SB were associated with increased risks in three outcomes compared to SB < 3 h/d. Adjusting for all covariates including MVPA attenuated the associations, still, SB ≥ 8 h/d was associated with higher hazard ratios [HRs] (95% confidence interval [CI]) of 1.36 (1.22–1.52) for dementia, 1.32 (1.19–1.48) for functional disability, and 1.31 (1.18–1.45) for mortality, and the associations indicated a dose-response trend (*P* for trend <0.001; Table 2).

3.3. Joint association of MVPA and SB with dementia, functional disability, and mortality

The joint association indicated a dose-response trend (*P* for trend <0.001) of higher risks of dementia (Fig. 1A), functional disability (Fig. 1C), and mortality (Fig. 1E) with the increase in SB and decrease in MVPA. The highest risks observed in those with the highest SB and lowest MVPA. As MVPA levels decreased from ≥1 h/d to 0, individuals who spent the highest SB experienced higher HRs (95% CI) for dementia from 1.53 (1.10–2.12) to 2.03 (1.74–2.38), for functional disability from 1.35 (0.97–1.89) to 2.01 (1.73–2.35), and for mortality from 1.59 (1.20–2.11) to 1.75 (1.50–2.03), compared with the most active group (the lowest SB with highest MVPA). High levels of MVPA attenuated the risks associated with SB but did not eliminate them. Notably, the point estimate of hazard ratio for individuals with the highest SB and highest MVPA appeared to be comparable with that of those with the lowest SB and lowest MVPA. See joint association in Supplementary Table S4 for details.

3.4. Stratified association of MVPA and SB with dementia, functional disability, and mortality

Compared with those with SB < 3 h/d, participants with SB ≥ 8 h/d had higher risks of dementia (Fig. 1B) and mortality (Fig. 1F) in all MVPA stratums. Functional disability (Fig. 1D) showed a similar trend to dementia and mortality though it had wider confidence intervals. When

Table 1
Descriptive statistics among older adults in Japan, 2016.

Variables, n (%)	Sedentary time			
	<3 h/d	3- < 8 h/d	≥8 h/d	Total
Sample size (no.)	33,038 (36.5)	51,501 (56.9)	5932 (6.7)	90,471 (100.0)
Sex				
Male	15,091 (45.7)	23,424 (45.5)	3127 (52.7)	41,641 (46.0)
Female	17,947 (54.3)	28,078 (54.5)	2805 (47.3)	48,830 (54.0)
Age (years)				
Minimum–maximum	65–101	65–101	65–101	65–101
65–69	9703 (29.4)	15,226 (29.6)	1731 (29.2)	26,660 (29.5)
70–74	9138 (27.7)	13,995 (27.2)	1322 (22.3)	24,455 (27.0)
75–79	8031 (24.3)	11,551 (22.4)	1179 (19.9)	20,761 (22.9)
80–84	4373 (13.2)	7108 (13.8)	962 (16.2)	12,443 (13.8)
≥85	1793 (5.4)	3621 (7.0)	739 (12.5)	6152 (6.8)
Marital status				
Married	24,729 (74.9)	37,268 (72.4)	3849 (64.9)	65,846 (72.8)
Single/divorced/ widowed/other	8309 (25.1)	14,234 (27.6)	2083 (35.1)	24,625 (27.2)
Educational attainment (years)				
Low: ≤9	12,900 (39.0)	16,668 (32.4)	2029 (34.2)	31,596 (34.9)
Middle: 10–12	12,935 (39.2)	21,949 (42.6)	2380 (40.1)	37,264 (41.2)
High: ≥13	7203 (21.8)	12,885 (25.0)	1523 (25.7)	21,611 (23.9)
Annual household income[a]				
Low	17,977 (54.4)	25,717 (49.9)	3121 (52.6)	46,815 (51.7)
Middle	11,796 (35.7)	20,362 (39.5)	2148 (36.2)	34,306 (37.9)
High	3266 (9.9)	5423 (10.5)	663 (11.2)	9351 (10.3)
Employment status				
Retired/never employed	21,790 (66.0)	38,945 (75.6)	4722 (79.6)	65,457 (72.4)
Employed	11,248 (34.0)	12,557 (24.4)	1210 (20.4)	25,015 (27.6)
BMI (kg/m$^{2)}$				
Underweight: <18.5	2397 (7.3)	3579 (6.9)	470 (7.9)	6446 (7.1)
Normal weight: 18.5–24.9	23,635 (71.5)	35,835 (69.6)	3846 (64.8)	63,316 (70.0)
Overweight: 25–29.9	6355 (19.2)	10,826 (21.0)	1389 (23.4)	18,570 (20.5)
Obesity: ≥30	650 (2.0)	1262 (2.5)	227 (3.8)	2139 (2.4)
Comorbidity				
No disease	7104 (21.5)	9351 (18.2)	893 (15.1)	17,348 (19.2)
One disease	12,610 (38.2)	18,083 (35.1)	1815 (30.6)	32,508 (35.9)
Two or more disease	13,324 (40.3)	24,069 (46.7)	3223 (54.3)	40,615 (44.9)
Self-rated health				
Excellent	5677 (17.2)	6275 (12.2)	535 (9.0)	12,487 (13.8)
Good	23,384 (70.8)	37,482 (72.8)	3771 (63.6)	64,637 (71.4)
Fair	3427 (10.4)	6831 (13.3)	1341 (22.6)	11,599 (12.8)
Poor	549 (1.7)	915 (1.8)	286 (4.8)	1749 (1.9)
Alcohol				
Never	17,094 (51.7)	26,364 (51.2)	2902 (48.9)	46,360 (51.2)
Past	3390 (10.3)	5599 (10.9)	857 (14.4)	9845 (10.9)

(*continued on next page*)

Table 1 (*continued*)

Variables, n (%)	Sedentary time			
	<3 h/d	3- < 8 h/d	≥8 h/d	Total
Current	12,553 (38.0)	19,539 (37.9)	2173 (36.6)	34,265 (37.9)
Smoking				
Never	20,833 (63.1)	31,216 (60.6)	3189 (53.8)	55,238 (61.1)
Past	8712 (26.4)	14,979 (29.1)	1938 (32.7)	25,629 (28.3)
Current	3492 (10.6)	5307 (10.3)	805 (13.6)	9603 (10.6)
Eating meat or fish				
Less than once a day	16,866 (51.1)	25,113 (48.8)	2953 (49.8)	44,931 (49.7)
Everyday	16,172 (48.9)	26,389 (51.2)	2979 (50.2)	45,540 (50.3)
Eating fruits and vegetables				
Less than once a day	6905 (20.9)	10,065 (19.5)	1422 (24.0)	18,391 (20.3)
Everyday	26,133 (79.1)	41,437 (80.5)	4510 (76.0)	72,080 (79.7)
Social isolation[b]				
Low	18,007 (54.5)	26,458 (51.4)	2087 (35.2)	46,552 (51.5)
High	15,031 (45.5)	25,044 (48.6)	3845 (64.8)	43,919 (48.5)
MVPA (h/d)				
0	12,308 (37.3)	25,064 (48.7)	4130 (69.6)	41,501 (45.9)
<1	6424 (19.4)	11,314 (22.0)	946 (15.9)	18,684 (20.7)
≥1	14,305 (43.3)	15,124 (29.4)	856 (14.4)	30,285 (33.5)

Abbreviations: BMI, body mass index; MVPA, moderate-to-vigorous physical activity.

[a] Classified by million Japanese yen (MJPY): Low: < 2.0, middle: 2.0- < 4.0, high: ≥ 4.0.

[b] Defined by an index based on a partially modified version of the social isolation score (0–5 points): Low: 0–1, high: 2–5.

MVPA≥1, SB > 8 h/d associated with higher HRs (95% CI) of 1.47 (1.05–2.05), 1.31 (0.93–1.85), and 1.57 (1.17–2.10) for dementia, functional disability, and mortality, respectively. No evidence of heterogeneity by MVPA levels was found (*P* for interaction = 0.40, 0.80, 0.23 for dementia, functional disability, and mortality, respectively). See stratified association in Supplementary Table S4 for details.

3.5. Subgroup analysis by sex, educational level, comorbidity, and depression status

No evidence of heterogeneity between SB and the outcomes across sex, education, comorbidity, and depression stratums was found (*p* for interaction >0.05); thus, the association between SB and outcomes remained consistent regardless of sex, education, comorbidity, and depression conditions (Fig. 2).

3.6. Sensitivity analysis

When excluding the outcome events occurring within one year of follow-up (Supplementary Tables S5-S6), using the complete dataset (Supplementary Tables S7-S8), or further adjusting for depression (Supplementary Tables S9), the results demonstrated no materiality differences from the main analysis, although the statistical power may have been reduced owing to the limited number of participants and events.

4. Discussion

In this large and nationwide cohort study conducted on older adults aged ≥65 years, we found that total SB >8 h/d was associated with 36%, 33%, and 31% increased risks of dementia, functional disability, and mortality. Our findings are consistent with previous studies showing the association between 6 and 8 h/d of total SB and increased mortality (Cao et al., 2022; Li et al., 2022; Patterson et al., 2018). Moreover, expanding outcomes of interest to dementia and functional disability, our study provides a comprehensive understanding for the detrimental associations of SB. In addition, we showed that the associations were constant across different levels of MVPA, sex, education, comorbidity, and depression status. Thus, our findings suggest that reducing SB is a recommendation applicable to the entire population.

The clear dose-response association in the joint association highlighted the importance and potential benefits of reducing SB as well as increasing MVPA for achieving optimal health benefits, which is consistent with the results of some previous studies (Cao et al., 2022; Li et al., 2022). While, considering that nearly half of the participants reported no engagement in MVPA, it is worth emphasizing that reducing SB was associated with lower risks of dementia, functional disability, and mortality, even if they don't engage in any MVPA. Moreover, individuals with the lowest SB and lowest MVPA may face the similar risks with those with the highest SB and highest MVPA. This is encouraging news for individuals who are unable to engage in MVPA owing to busy work or other difficulties. Nevertheless, it should never be considered as a justification for not engaging in MVPA or other PAs. However, even for individuals who engage in a considerable amount of MVPA each day, SB ≥ 8 h/d can substantially diminish the health benefits derived from the high MVPA; these individuals are also exposing themselves to an increased risk of adverse health outcomes. This finding differs from that of a meta-analysis (Ekelund et al., 2016), since Ekelund and colleagues found no association between SB and mortality among the most active population. Indeed, our study targeted a different population, as we specifically investigated individuals aged ≥65 years, while the previous research was conducted in general adults. Regardless, further research is

Table 2
Associations between sedentary behavior and outcomes among older adults in Japan, 2016–2021[a].

	<3 h/d	3–<8 h/d	p	≥8 h/d	p	P_{trend}
Dementia						
Model 1	1 (ref)	**1.07 (1.00–1.15)**	**0.045**	**1.71 (1.54–1.91)**	**<0.001**	**<0.001**
Model 2	1 (ref)	1.02 (0.95–1.10)	0.56	**1.36 (1.21–1.52)**	**<0.001**	**<0.001**
Functional disability						
Model 1	1 (ref)	**1.12 (1.04–1.20)**	**0.002**	**1.83(1.65–2.03)**	**<0.001**	**<0.001**
Model 2	1 (ref)	1.03 (0.96–1.11)	0.43	**1.33 (1.19–1.48)**	**<0.001**	**<0.001**
Mortality						
Model 1	1 (ref)	**1.13 (1.06–1.21)**	**<0.001**	**1.78 (1.61–1.97)**	**<0.001**	**<0.001**
Model 2	1 (ref)	1.06 (1.00–1.14)	0.07	**1.31 (1.18–1.46)**	**<0.001**	**<0.001**

Abbreviations: SB, sedentary behavior. [a] Values are hazard ratios (95% confidence intervals). Model 1 adjusted for sex and age. Model 2 adjusted for sex, age, marital status, educational attainment, family equivalent income, employment, BMI, comorbidity, self-rated health, alcohol, smoking, frequency of eating meat or fish, frequency of eating fruits and vegetables, social isolation and moderate-to-vigorous intensity physical activity.
Note: Researchers concerned about multiple comparisons can apply a Bonferroni correction when interpreting *p*-values. (α = 0.05/3 outcomes = 0.017).

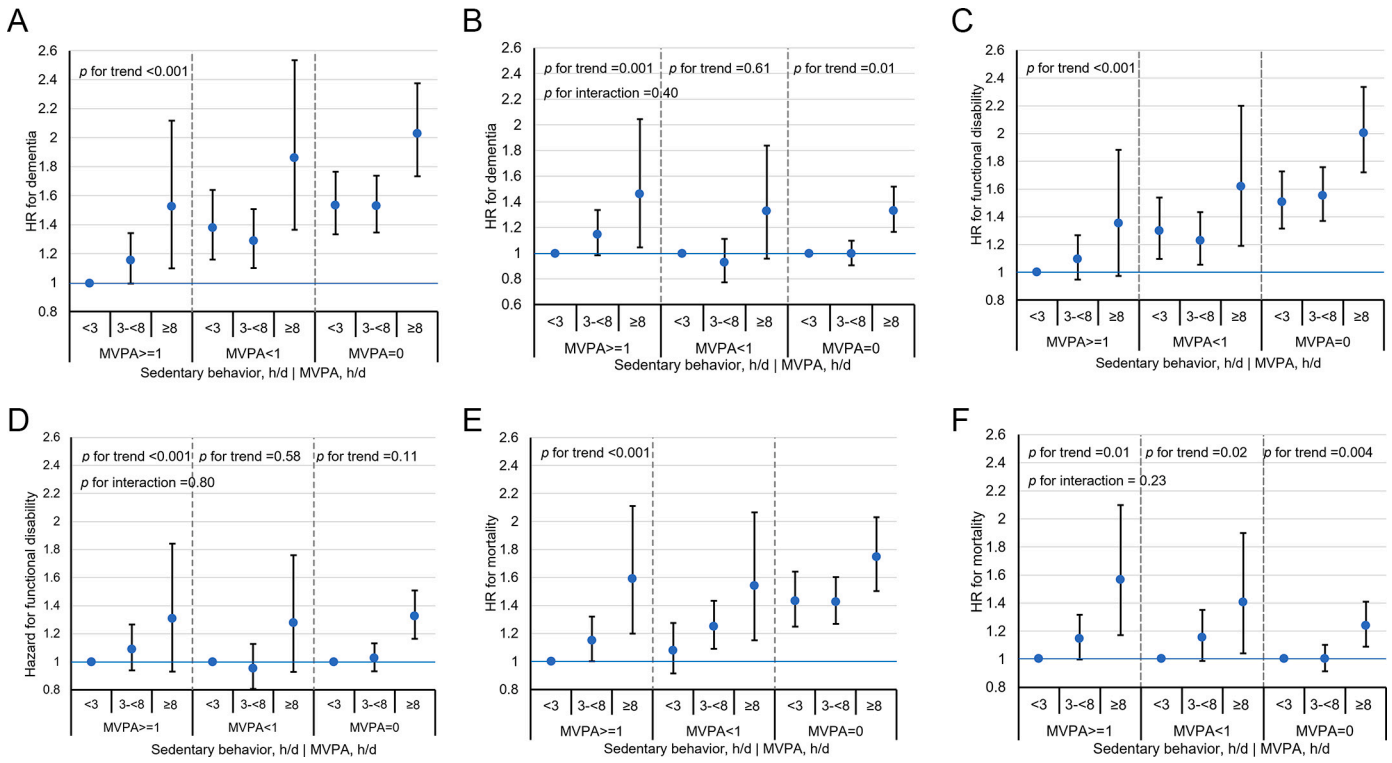

Fig. 1. Joint and stratified associations of sedentary behavior and physical activity with outcomes among older adults in Japan, 2016–2021.
The categorization of MVPA corresponds to =0, <1, and ≥ 1 h per day of moderate-to-vigorous intensity physical activity. A and B, Joint and stratified association for dementia, respectively; C and D, Joint and stratified association for functional disability, respectively; and E and F, Joint and stratified association for mortality, respectively. Adjusted for sex, age, marital status, educational attainment, family equivalent income, employment, BMI, comorbidity, self-rated health, alcohol, smoking, frequency of eating meat or fish, frequency of eating fruits and vegetables, and social isolation. HR, hazard ratio.
See Supplementary Table S3 for the Joint and stratified associations in the sex- and age-adjusted analysis. Data are listed in Supplementary Table S4.

needed to support the association of SB combined with MVPA with the health risks in older adults.

Our study demonstrates consistent findings regarding the associations between SB and outcomes across MVPA, sex, education, comorbidity, and depression status. This is consistent with the study by Bellettiere et al. (Bellettiere et al., 2019), but not Pavey et al. (Pavey et al., 2015); Pavey et al. found a heterogeneity by PA that the detrimental association of SB and mortality only among those who didn't meet PA guideline. However, among those who met PA guidelines, there was small outcome events of 43 and 11 in the 8 ≤ SB < 11 and SB ≥ 11 groups, which may affect the reliability of their findings (Pavey et al., 2015). However, while recognizing the limitations of our definition and cut-off values for those variables, we anticipate that future larger-scale, well-designed studies will examine associations between those subgroups.

4.1. Strengths

To our knowledge, this is the first study conducted on older adults to analyze the independent associations of SB, the stratified and joint associations of SB and MVPA, as well as the heterogeneous associations by chronic conditions with dementia, functional disability, and mortality, simultaneously. Moreover, this study included a large sample of 90,471 older adults and >4000 outcome events. Importantly, our study indicated the detrimental association between prolonged daily SB and health outcomes, regardless of the MVPA levels, sex, education, comorbidity, and depression conditions, which provide valuable insights for formulating public health recommendations. We highlight the significance of decreasing SB, because over a finite and constant 24-h day, reducing SB could also indicate replacing SB with PA of any intensity. As isotemporal substitution analyses demonstrate that replacing SB with PA of any intensity was associated with lower health risks (Li et al., 2022). Furthermore, SB-based recommendations have the advantage of easier implementation and adherence for older adults, compared to that for MVPA declared by the WHO (WHO, 2020). Whereas, the dose-response trend indicated that if prolonged daily SB is unavoidable, increasing MVPA may be a good strategy to reduce the risks. Still, the risks can be only attenuated, not eliminated. In fact, even individuals who engage in high levels of MVPA are facing higher risks during prolonged daily SB.

4.2. Limitations

This study has several limitations. First, the population included older adults living in Japan within the same race and ethnicity; thus, generalizability of the results was limited since other study have demonstrated race and ethnicity differences (Kornblith et al., 2022). Second, the self-reported data could be subject to recall bias, which could compromise the accuracy of the research findings. It is worth noting that participants may underestimate the time spent on SB, potentially resulting in an underestimation of the association between SB and health risks. Third, SB and MVPA were assessed during one point of time, which could increase the possibility of reverse causation. If people in the early stage of physical and cognitive decline presented greater SB and lower MVPA at the baseline, the observed associations could be overstated. However, our sensitivity analysis showed that there was no substantial change after excluding outcome events within one year of follow-up. Further studies considering lifetime changes in SB and MVPA are needed. Fourth, this study solely employed total SB, with a coarse categorization, but did not distinguish the type or context of SB, as evidence suggested that mentally positive and negative SB could play different roles on outcomes (Raichlen et al., 2022). Fifth, residual confounding may exist. Unmeasured variables, such as frailty, type of

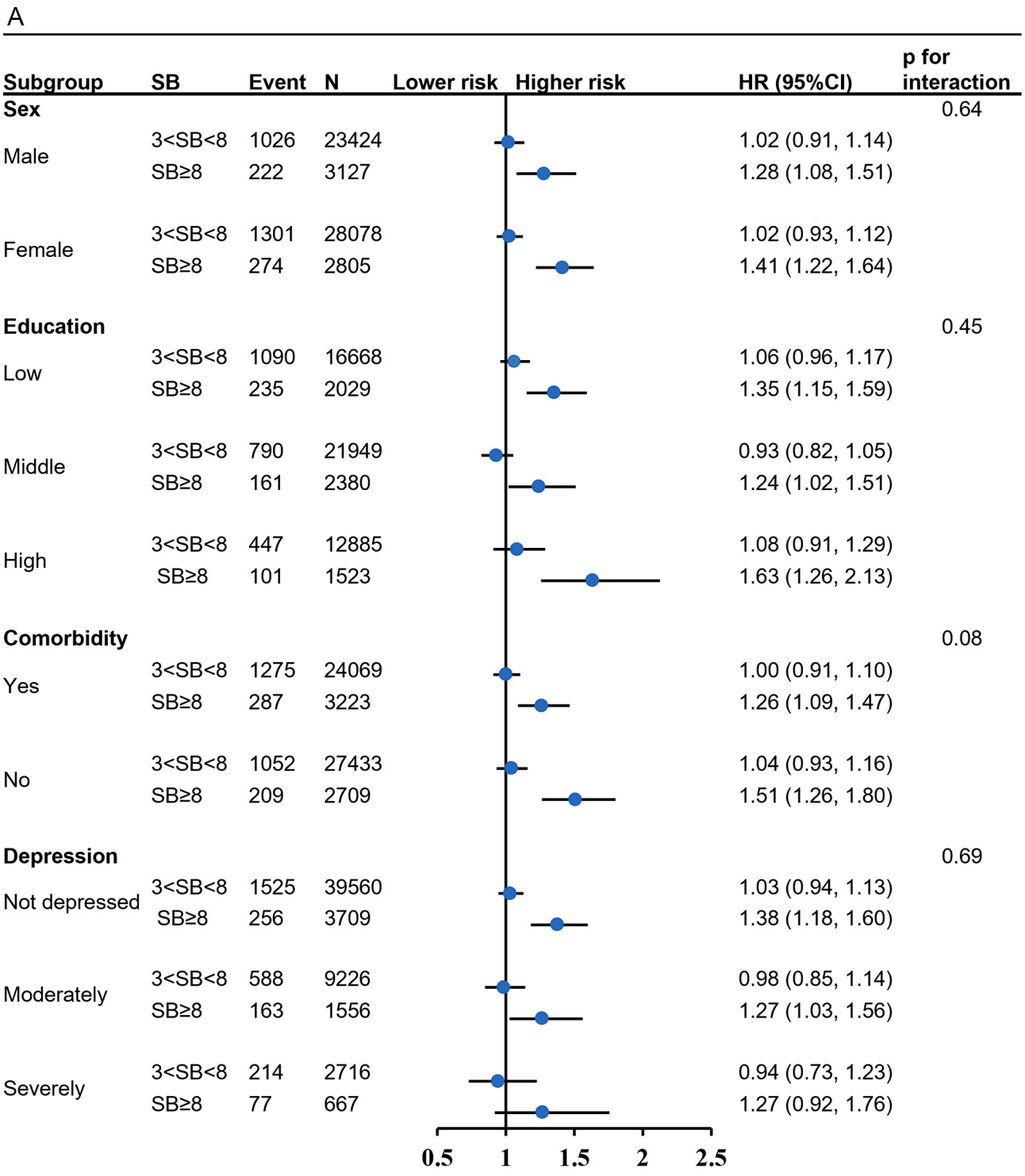

Fig. 2. Associations between sedentary behavior and outcomes by subgroups among older adults in Japan, 2016–2021.
The categorization of education corresponds to ≤9, 10–12, and ≥ 13 years of education; comorbidity corresponds to the number of chronic diseases <2, ≥ 2. A, Stratified association for dementia; B, Stratified association for functional disability; and C, Stratified association for mortality. Adjusted for sex, age, marital status, educational attainment, family equivalent income, employment, BMI, comorbidity, self-rated health, alcohol, smoking, frequency of eating meat or fish, frequency of eating fruits and vegetables, and social isolation. HR, hazard ratio. N, sample size.

employment, medication use, *APOE* genotype, sleeping, and environmental factors could distort our results, even after adjusting for many available confounders. Sixth, the outcome events were identified by the Japan public LTCI registry and could result in a less accurate diagnosis than a comprehensive clinical dementia examination. Seventh, the small sample size in SB ≥ 8 and MVPA≥1 h/d subgroups limited the interpretation of the results with reduced accuracy and stability. Therefore, the results for these groups should be interpreted with caution. Eighth, the follow-up period for this study was breif. Consequently, the study may provide valuable insights into the short-term associations; however,

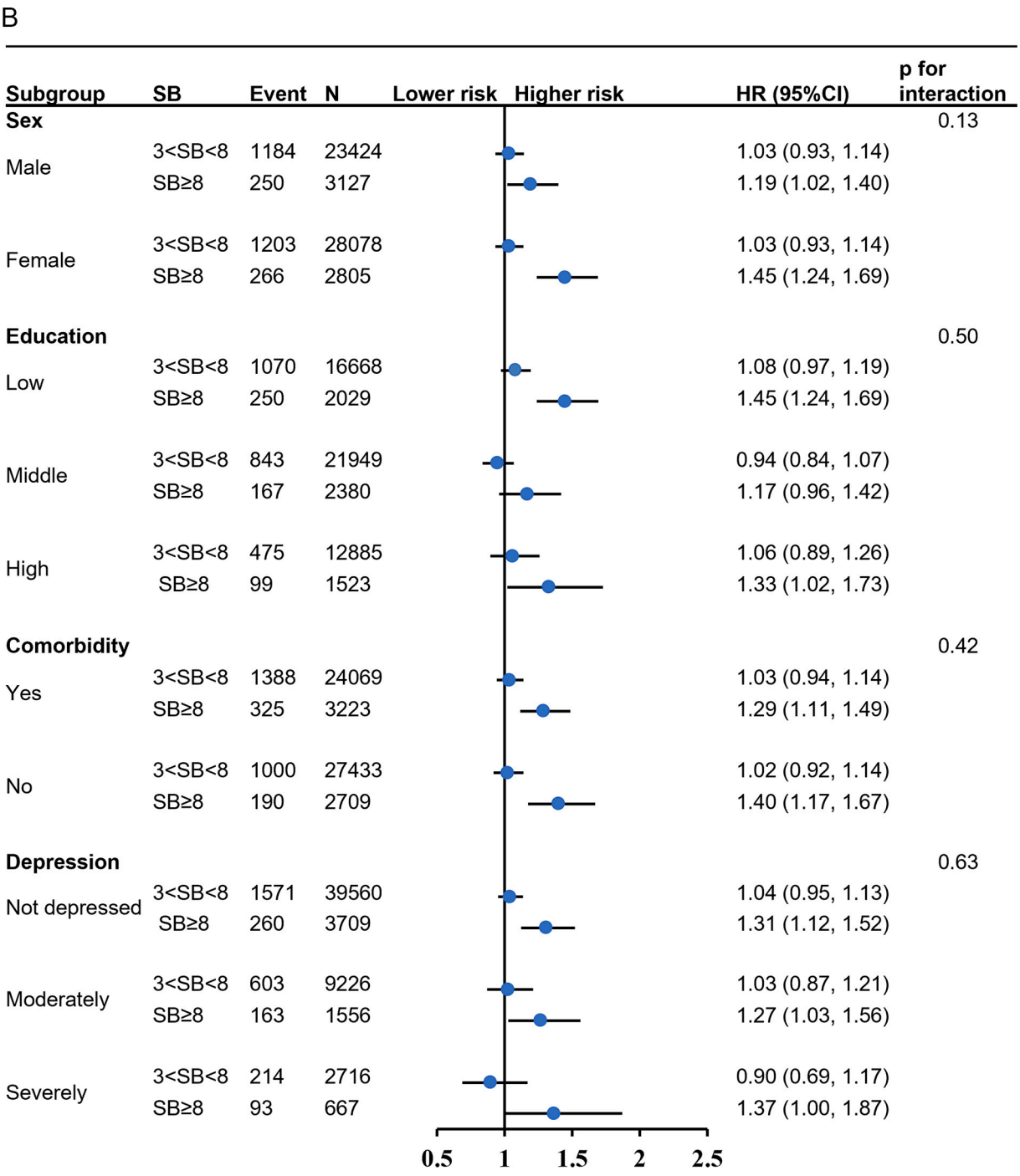

Fig. 2. (*continued*).

it may not capture the long-term progression and the potential late-onset consequences of SB and PA. Future large-scale, long-term follow-up, prospective studies, and randomized controlled trials are still required.

5. Conclusions

For older adults, prolonged daily SB was associated with higher risks of dementia, functional disability, and mortality, regardless of MVPA levels, sex, education, comorbidity, and depression conditions. Individuals with high MVPA also face considerable risks when engaging in high SB. Additionally, those with high MVPA and high SB had comparable risks to those with no MVPA and low SB. High SB with no MVPA is associated with the highest risks. Accordingly, older adults should be encouraged to sit less, especially for those who face challenges in engaging in MVPA.

Declaration of Sources of Funding

This work was supported by Japan Society for the Promotion of Sciences [15H01972, 23H03164]; Japanese Ministry of Health, Labor and Welfare [H28-Choju-Ippan-002]; Japan Agency for Medical Research and Development [JP17dk0110017, JP18dk0110027, JP18ls0110002, JP18le0110009]; National Center for Geriatrics and Gerontology [29–42]; and Japan Science and Technology Agency [JPMJOP1831].

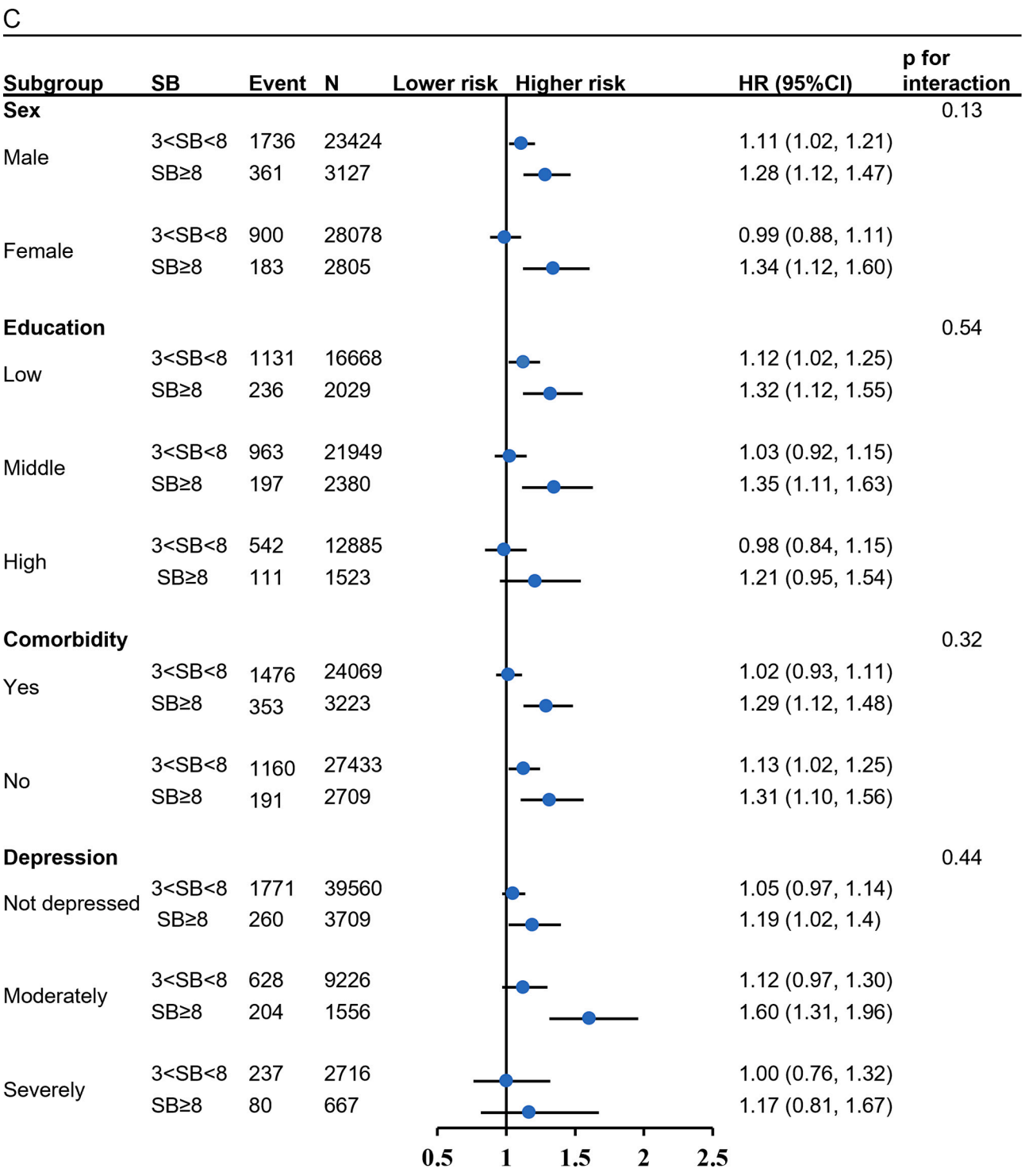

Fig. 2. (*continued*).

Role of the funder/sponsor

The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

CRediT authorship contribution statement

Zhen Du: Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Koryu Sato:** Writing – review & editing, Validation, Supervision. **Taishi Tsuji:** Writing – review & editing. **Katsunori Kondo:** Writing – review & editing, Project administration, Funding acquisition, Data curation. **Naoki Kondo:** Writing – review & editing, Supervision, Data curation.

Declaration of competing interest

None declared.

Data availability

Data will be made available on request.

Acknowledgments

We would like to thank Editage (www.editage.com) for English language editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2024.107879.

References

Almeida, O.P., Almeida, S.A., 1999. Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. Int. J. Geriatr. Psychiatr. 14 (10), 858–865. https://doi.org/10.1002/(sici)1099-1166(199910)14:10<858::aid-gps35>3.0.co;2-8.

Arnardottir, N.Y., Koster, A., Van Domelen, D.R., Brychta, R.J., Caserotti, P., Eiriksdottir, G., Sveinsson, T., 2013. Objective measurements of daily physical activity patterns and sedentary behaviour in older adults: age, Gene/Environment Susceptibility-Reykjavik Study. Age Ageing 42 (2), 222–229. https://doi.org/10.1093/ageing/afs160.

Bellettiere, J., LaMonte, M.J., Evenson, K.R., Rillamas-Sun, E., Kerr, J., Lee, I.M., LaCroix, A.Z., 2019. Sedentary behavior and cardiovascular disease in older women: the OPACH study. Circulation 139 (8), 1036–1046. https://doi.org/10.1161/CIRCULATIONAHA.118.035312.

Cao, C., Friedenreich, C.M., Yang, L., 2022. Association of daily sitting time and leisure-time physical activity with survival among US cancer survivors. JAMA Oncol. 8 (3), 395–403. https://doi.org/10.1001/jamaoncol.2021.6590.

Chau, J.Y., Grunseit, A., Midthjell, K., Holmen, J., Holmen, T.L., Bauman, A.E., Van der Ploeg, H.P., 2015. Sedentary behaviour and risk of mortality from all-causes and cardiometabolic diseases in adults: evidence from the HUNT3 population cohort. Br. J. Sports Med. 49 (11), 737–742. https://doi.org/10.1136/bjsports-2012-091974.

Chiba, I., Lee, S., Bae, S., Makino, K., Shinkai, Y., Katayama, O., Shimada, H., 2022. Isotemporal substitution of sedentary behavior with moderate to vigorous physical activity is associated with lower risk of disability: a prospective longitudinal cohort study. Phys. Ther. 102 (5) https://doi.org/10.1093/ptj/pzac002 pzac002.

del Pozo Cruz, B., Ahmadi, M.N., Lee, I.M., Stamatakis, E., 2022a. Prospective associations of daily step counts and intensity with cancer and cardiovascular disease incidence and mortality and all-cause mortality. JAMA Intern. Med. 182 (11), 1139–1148. https://doi.org/10.1001/jamainternmed.2022.4000.

del Pozo Cruz, B., Ahmadi, M., Naismith, S.L., Stamatakis, E., 2022b. Association of daily step count and intensity with incident dementia in 78 430 adults living in the UK. JAMA Neurol. 79 (10), 1059–1063. https://doi.org/10.1001/jamaneurol.2022.2672.

Diaz, K.M., Howard, V.J., Hutto, B., Colabianchi, N., Vena, J.E., Safford, M.M., Hooker, S. P., 2017. Patterns of sedentary behavior and mortality in U.S. middle-aged and older adults: a national cohort study. Ann. Intern. Med. 167 (7), 465–475. https://doi.org/10.7326/M17-0212.

DiPietro, L., Jin, Y., Talegawkar, S., Matthews, C.E., 2018. The joint associations of sedentary time and physical activity with mobility disability in older people: the NIH-AARP diet and health study. J. Gerontol. Series A, Biol. Sci. Med. Sci. A. Newman (Ed.) 73 (4), 532–538. https://doi.org/10.1093/gerona/glx122.

Ekelund, U., Steene-Johannessen, J., Brown, W.J., Fagerland, M.W., Owen, N., Powell, K. E., Lancet Sedentary Behaviour Working Group, 2016. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet 388 (10051), 1302–1310. https://doi.org/10.1016/S0140-6736(16)30370-1.

Ekelund, U., Tarp, J., Steene-Johannessen, J., Hansen, B.H., Jefferis, B., Fagerland, M.W., Lee, I.M., 2019. Dose–response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. BMJ 366, l4570. https://doi.org/10.1136/bmj.l4570.

Feigin, V.L., Nichols, E., Alam, T., 2019. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the global burden of disease study 2016. Lancet Neurol. 18 (5), 459–480. https://doi.org/10.1016/S1474-4422(18)30499-X.

He, L., Biddle, S.J.H., Lee, J.T., Duolikun, N., Zhang, L., Wang, Z., Zhao, Y., 2021. The prevalence of multimorbidity and its association with physical activity and sleep duration in middle aged and elderly adults: a longitudinal analysis from China. Int. J. Behav. Nutr. Phys. Act. 18 (1), 77. https://doi.org/10.1186/s12966-021-01150-7.

Hisano, S., 2009. The relationship between revised Hasegawa dementia scale (HDS-R), Mini-mental state examination (MMSE), bed-fast scale, and dementia scale. Jpn J. Geriatr. Psychiatr. 20, 883.

Huang, S.Y., Li, Y.Z., Zhang, Y.R., Huang, Y.Y., Wu, B.S., Zhang, W., Yu, J.T., 2022. Sleep, physical activity, sedentary behavior, and risk of incident dementia: a prospective cohort study of 431,924 UK biobank participants. Mol. Psychiatry 27 (10), 4343–4354. https://doi.org/10.1038/s41380-022-01655-y.

Jacobs, J.M., Rottenberg, Y., Cohen, A., Stessman, J., 2013. Physical activity and health service utilization among older people. J. Am. Med. Dir. Assoc. 14 (2), 125–129. https://doi.org/10.1016/j.jamda.2012.10.023.

Jin, X., Tamiya, N., Uda, K., Yasunaga, H., 2021. The impact of additional payments on functional decline among long-term care health facility residents in Japan. Age Ageing 50 (6), 2055–2062. https://doi.org/10.1093/ageing/afab121.

Keadle, S.K., McKinnon, R., Graubard, B.I., Troiano, R.P., 2016. Prevalence and trends in physical activity among older adults in the United States: a comparison across three national surveys. Prev. Med. 89, 37–43. https://doi.org/10.1016/j.ypmed.2016.05.009. PubMed: 27196146, PubMed Central: PMC4969157.

Kikuchi, H., Inoue, S., Odagiri, Y., Ihira, H., Inoue, M., Sawada, N., Tsugane, S., 2020. Intensity-specific validity and reliability of the Japan public health center-based prospective study-physical activity questionnaire. Prev. Med. Rep. 20, 101169 https://doi.org/10.1016/j.pmedr.2020.101169.

Kondo, K., Rosenberg, M., World Health Organization. Advancing Universal Health Coverage through Knowledge Translation for Healthy Ageing: Lessons Learnt from the Japan Gerontological Evaluation Study [Internet]. Retrieved from. https://apps.who.int/iris/handle/10665/279010.

Kornblith, E., Bahorik, A., Boscardin, W.J., Xia, F., Barnes, D.E., Yaffe, K., 2022. Association of race and ethnicity with incidence of dementia among older adults. JAMA 327 (15), 1488–1495. https://doi.org/10.1001/jama.2022.3550.

Koyama, S., Saito, M., Cable, N., Ikeda, T., Tsuji, T., Noguchi, T., Aida, J., 2021. Examining the associations between oral health and social isolation: a cross-national comparative study between Japan and England. Soc. Sci. Med. 277, 113895 https://doi.org/10.1016/j.socscimed.2021.113895.

Lee, I.M., Shiroma, E.J., Evenson, K.R., Kamada, M., LaCroix, A.Z., Buring, J.E., 2018. Accelerometer-measured physical activity and sedentary behavior in relation to all-cause mortality: the women's health study. Circulation 137 (2), 203–205. https://doi.org/10.1161/CIRCULATIONAHA.117.031300.

Li, S., Lear, S.A., Rangarajan, S., Hu, B., Yin, L., Bangdiwala, S.I., Yusuf, S., 2022. Association of sitting time with mortality and cardiovascular events in high-income, middle-income, and low-income countries. JAMA Cardiol. 7 (8), 796–807. https://doi.org/10.1001/jamacardio.2022.1581.

Livingston, G., Sommerlad, A., Orgeta, V., Costafreda, S.G., Huntley, J., Ames, D., Mukadam, N., 2017. Dementia prevention, intervention, and care. Lancet 390 (10113), 2673–2734. https://doi.org/10.1016/S0140-6736(17)31363-6.

Matsunaga, T., Naito, M., Wakai, K., Ukawa, S., Zhao, W., Okabayashi, S., Tamakoshi, A., 2017. Leisure-time physical activity and risk of disability incidence: a 12-year prospective cohort study among young elderly of the same age at baseline. J. Epidemiol. 27 (11), 538–545. https://doi.org/10.1016/j.je.2016.11.004.

McKeough, Z., Cheng, S.W.M., Alison, J., Jenkins, C., Hamer, M., Stamatakis, E., 2018. Low leisure-based sitting time and being physically active were associated with reduced odds of death and diabetes in people with chronic obstructive pulmonary disease: a cohort study. Aust. J. Phys. 64 (2), 114–120. https://doi.org/10.1016/j.jphys.2018.02.007.

Noguchi, T., Kondo, K., Saito, M., Nakagawa-Senda, H., Suzuki, S., 2019. Community social capital and the onset of functional disability among older adults in Japan: a multilevel longitudinal study using Japan Gerontological evaluation study (JAGES) data. BMJ Open 9 (10), e029279. https://doi.org/10.1136/bmjopen-2019-029279.

Patterson, R., McNamara, E., Tainio, M., de Sá, T.H., Smith, A.D., Sharp, S.J., Wijndaele, K., 2018. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur. J. Epidemiol. 33 (9), 811–829. https://doi.org/10.1007/s10654-018-0380-1.

Pavey, T.G., Peeters, G.G., Brown, W.J., 2015. Sitting-time and 9-year all-cause mortality in older women. Br. J. Sports Med. 49 (2), 95–99. https://doi.org/10.1136/bjsports-2012-091676.

Raichlen, D.A., Klimentidis, Y.C., Sayre, M.K., Bharadwaj, P.K., Lai, M.H.C., Wilcox, R.R., Alexander, G.E., 2022. Leisure-time sedentary behaviors are differentially associated with all-cause dementia regardless of engagement in physical activity. Proc. Natl. Acad. Sci. USA 119 (35), e2206931119. https://doi.org/10.1073/pnas.2206931119.

Ramsey, K.A., Rojer, A.G.M., D'Andrea, L., Otten, R.H.J., Heymans, M.W., Trappenburg, M.C., Maier, A.B., 2021. The association of objectively measured physical activity and sedentary behavior with skeletal muscle strength and muscle power in older adults: a systematic review and meta-analysis. Ageing Res. Rev. 67, 101266 https://doi.org/10.1016/j.arr.2021.101266.

Rojer, A.G.M., Ramsey, K.A., Trappenburg, M.C., van Rijssen, N.M., Otten, R.H.J., Heymans, M.W., Maier, A.B., 2020. Instrumented measures of sedentary behaviour and physical activity are associated with mortality in community-dwelling older adults: a systematic review, meta-analysis and meta-regression analysis. Ageing Res. Rev. 61, 101061 https://doi.org/10.1016/j.arr.2020.101061.

Saint-Maurice, P.F., Troiano, R.P., Bassett, D.R., Graubard, B.I., Carlson, S.A., Matthews, C.E., 2020. Association of daily step count and step intensity with mortality among US adults. JAMA 323 (12), 1151–1160. https://doi.org/10.1001/jama.2020.1382.

Sanchez-Sanchez, J.L., Izquierdo, M., Carnicero-Carreño, J.A., García-García, F.J., Rodríguez-Mañas, L., 2020. Physical activity trajectories, mortality, hospitalization, and disability in the Toledo study of healthy aging. J. Cachexia. Sarcopenia Muscle 11 (4), 1007–1017. https://doi.org/10.1002/jcsm.12566.

Sasai, H., Nakata, Y., Murakami, H., Kawakami, R., Nakae, S., Tanaka, S., Miyachi, M., 2018. Simultaneous validation of seven physical activity questionnaires used in Japanese cohorts for estimating energy expenditure: a doubly labeled water study. J. Epidemiol. 28 (10), 437–442. https://doi.org/10.2188/jea.JE20170129.

Sato, K., Kondo, N., Hanazato, M., Tsuji, T., Kondo, K., 2021. Potential causal effect of physical activity on reducing the risk of dementia: a 6-year cohort study from the

Japan Gerontological evaluation study. Int. J. Behav. Nutr. Phys. Act. 18 (1), 140. https://doi.org/10.1186/s12966-021-01212-w.

Sattar, N., Preiss, D., 2017. Reverse causality in cardiovascular epidemiological research: more common than imagined? Circulation 135 (24), 2369–2372. https://doi.org/10.1161/CIRCULATIONAHA.117.028307.

Schuch, F., Vancampfort, D., Firth, J., Rosenbaum, S., Ward, P., Reichert, T., Stubbs, B., 2017. Physical activity and sedentary behavior in people with major depressive disorder: a systematic review and meta-analysis. J. Affect. Disord. 210, 139–150. https://doi.org/10.1016/j.jad.2016.10.050.

Schultz, W.M., Kelli, H.M., Lisko, J.C., Varghese, T., Shen, J., Sandesara, P., Sperling, L. S., 2018. Socioeconomic status and cardiovascular outcomes: challenges and interventions. Circulation 137 (20), 2166–2178. https://doi.org/10.1161/CIRCULATIONAHA.117.029652.

Steptoe, A., Shankar, A., Demakakos, P., Wardle, J., 2013. Social isolation, loneliness, and all-cause mortality in older men and women. Proc. Natl. Acad. Sci. USA 110 (15), 5797–5801. https://doi.org/10.1073/pnas.1219686110.

WHO, 2020. WHO Guidelines on Physical Activity and Sedentary Behaviour. Who. int. World Health Organization. Available at: https://www.who.int/publications/i/item/9789240015128 (Accessed: December 26, 2023).

Winkleby, M.A., Jatulis, D.E., Frank, E., Fortmann, S.P., 1992. Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. Am. J. Public Health 82 (6), 816–820. https://doi.org/10.2105/ajph.82.6.816.

Yau, P.N., Foo, C.J.E., Cheah, N.L.J., Tang, K.F., Lee, S.W.H., 2022. The prevalence of functional disability and its impact on older adults in ASEAN region: a systematic review and meta-analysis. Epidemiol. Health 44, e2022058. https://doi.org/10.4178/epih.e2022058.

Yoon, M., Yang, P.S., Jin, M.N., Yu, H.T., Kim, T.H., Jang, E., Joung, B., 2021. Association of physical activity level with risk of dementia in a nationwide cohort in Korea. JAMA Netw. Open 4 (12), e2138526. https://doi.org/10.1001/jamanetworkopen.2021.38526.