Associations of total, domain-specific, and intensity-specific physical activity with all-cause and cause-specific mortality in China: A population-based cohort study

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Abstract

Background: Evidence of an association between physical activity (PA) and mortality has mainly focused on leisure-time physical activity (LTPA) and moderate-to-vigorous-intensity physical activity (MVPA). We aimed to assess the associations of total, domain-specific, and intensity-specific PA with all-cause and cause-specific mortality.

Methods: We used baseline PA data from the China Kadoorie Biobank, including 482,067 participants aged 30–79 years from 10 areas in China. PA via self-report was quantified as a metabolic equivalent of task hours per day. Total PA was calculated by summing occupational, commuting, household, and leisure-time PA, and domain- and intensity-specific PAs were also calculated. Cox regression was used to estimate the associations of quintiles of different types of PA with all-cause and cause-specific mortality and adjust for potential confounders. Cause-specific mortalities were also examined in a competing risk analysis.

Results: During a median follow-up of 12.1 years, 47,281 deaths occurred. Total PA was inversely associated with the risk of all-cause mortality, with a hazard ratio (HR) (95% confidence interval [95% CI]) of 0.69 (0.67–0.71) in the highest quintile as compared with the lowest quintile. Similar associations were observed for disease-specific mortality risks from cardiovascular disease, cancer, respiratory disease, diabetes, and nervous system disease, with HR (95% CI) for top *vs*. bottom quintile of PA of 0.68 (0.64–0.71), 0.80 (0.76–0.83), 0.39 (0.35–0.44), 0.44 (0.35–0.55), and 0.52 (0.38–0.73), respectively. In addition, the risk of all-cause mortality was lowered by 34%, 13%, 17%, and 30% for occupational PA, non-occupational PA, low-intensity PA, and MVPA, respectively, when comparing the highest quintile with the lowest quintile.

Conclusions: PA was inversely associated with the risk of all-cause and cause-specific mortality, regardless of domain and intensity. Any PA can bring long-term beneficial health effects.

Keywords: Physical activity; Mortality; Cardiovascular diseases; Metabolic equivalent; Leisure activities; Diabetes mellitus; Neoplasms; Nervous system diseases

Introduction

Physical inactivity is associated with various chronic diseases and premature death, which was identified globally as the fourth most important risk factor for non-communicable diseases.[1] It brings a substantial economic burden, leads to morbidity as well as mortality, and is a global public health problem.[2]

Increasing evidence suggests that physical activity (PA) is inversely associated with mortality.[3–7] However, this evidence is mainly based on leisure-time physical activity (LTPA)[6,7] and moderate-to-vigorous-intensity physical activity (MVPA).[4,8] In low- and lower-middle-income countries such as China, PA in other domains (e.g., occupation) and other intensities (i.e., low intensity) accounts for a substantial proportion of daily PA. Still,

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associations with mortality remain relatively understudied.[9] Furthermore, previous studies have only considered a narrow range of diseases, such as all-cause mortality and cause-specific mortality for major diseases (e.g., cardiovascular mortality), due to limited sample size. Uncertainty remains about mortality from other diseases, such as respiratory diseases, diabetes, and nervous system diseases.

Therefore, this study aimed to assess the associations of total, domain-specific, and intensity-specific PA with all-cause and cause-specific mortality based on data from the China Kadoorie Biobank (CKB) study to address this gap in the evidence.

Method

Ethics approval

The project was approved by the Ethical Committee and Research Council of the Chinese Center for Disease Control and Prevention (Beijing, China, 005/2004) and the Oxford Tropical Research Ethics Committee at the University of Oxford (UK, 025-04), and written informed consent was obtained from each participant.

Study population

The CKB study recruited 512,724 participants aged 30–79 years from 10 areas (5 urban and 5 rural) across China from 2004 to 2008 at baseline. Details of the study design and methods have been reported previously.[10,11] In addition, about 5% of the surviving participants were randomly selected for resurveys every 4–5 years after completing the baseline survey. The members of the steering committee and collaborative group are listed in the online-only Supplementary Material 1, http://links.lww.com/CM9/C314.

In this study, we excluded participants with previous self-reported physician-diagnosed coronary heart disease (n = 15,472), stroke (n = 8884), cancer (n = 2578) at baseline, with implausibly small (total PA equals 0), large (reported spending more than 20 h daily on all waking activities), or conflicting levels of PA (e.g., reported not working but had non-zero commuting-related PA) (n = 6185), with missing data for covariates (body mass index [BMI], n = 2) or lost to follow-up shortly after baseline (n = 1), leaving 482,067 participants for the primary analysis.

Assessment of PA

At baseline survey and subsequent resurveys, participants were asked about PA type, frequency, and duration in four domains (occupation, commuting, household, and leisure-time activity) and leisure hours spent on sitting activities per week during the past 12 months [Supplementary Material 2, http://links.lww.com/CM9/C314] using interviewer-administered electronic questionnaires. The PA and sedentary leisure time-related questions were adapted from validated questionnaires from previous studies.[12,13] For occupational and commuting PA, we stratified the participants based on occupation (e.g., farmer *vs*. non-farmer). We assessed the intensity level of PA by the metabolic equivalent of tasks (METs) based on the updated 2011 Compendium of Physical Activity,[14] multiplied by the hours spent on that activity per day to calculate each PA level as the metabolic equivalent of task hours per day (MET-h/d). Domain-specific PA levels were calculated by summing all the MET-h/d spent on occupational physical activity (OPA) and non-occupational physical activity (NOPA; commuting, household, and leisure-time activity). Similarly, intensity-specific PA levels, including low-intensity physical activity (LPA) (<3.0 METs) and MVPA (≥3.0 METs), were calculated by summing the MET-h/d for all corresponding intensity PA, regardless of domain. The total PA level was the sum of all PA levels.

To test the reproducibility of the total PA, we included 1300 participants who completed the same questionnaire twice within 1.5 years after the baseline survey. Their intraclass correlation coefficient was 0.59.[15]

Assessment of covariates

Information on sociodemographic characteristics (age, sex, education, occupation, annual household income, and marital status), lifestyle factors (smoking status, alcohol consumption, and fresh fruit consumption), personal medical history (hypertension, diabetes, chronic obstructive pulmonary disease [COPD], chronic hepatitis or cirrhosis, and chronic kidney diseases), and family history (heart attack, stroke, cancer, and diabetes) at baseline were collected from an interviewer-administered laptop-based questionnaire. Physical measurements were measured by trained staff using calibrated instruments at baseline, including height, body weight, and blood pressure. All participants provided a 10 mL blood sample for an immediate on-site test of random plasma glucose. BMI was calculated by dividing weight (kg) by the square of height (m). Prevalent hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mm Hg, self-reported doctor-diagnosed hypertension, or self-reported use of antihypertensive drugs at baseline. Prevalent diabetes was defined as fasting blood glucose ≥7.0 mmol/L, random blood glucose ≥11.1 mmol/L, or self-reported doctor-diagnosed diabetes.

Assessment of deaths

The vital status of participants was obtained via linkage to the local death registries and the national health insurance system, supplemented by annual active visits to local communities or direct contact with participants. The cause of death was coded by trained staff blinded to baseline information of participants, using the International Classification of Disease, 10th Revision (ICD-10). In this study, the outcomes comprised death from overall causes, as well as the specific causes, including cardiovascular disease (CVD) (I00–I99; ischemic heart disease [IHD], I20–I25; ischemic stroke [IS], I63; intracerebral hemorrhage [ICH], I61), cancer (C00–C97; lung cancer, C33–C34),

respiratory diseases (J00–J99; COPD, J41–J44), diabetes mellitus (E10–E14), and nervous system diseases (G00–G99). These particular outcomes were selected as they are representative of the leading causes of years of life lost in China in 2017.[16] Participants were followed up from the date of completing baseline questionnaires to the date of death, loss to follow-up, or December 31, 2018, whichever came first.

Statistical analysis

Each type of PA (total, domain-specific, and intensity-specific) was categorized into five groups based on quintiles of their distribution. Baseline characteristics were presented as means or percentages across total PA categories adjusted for age at baseline (in 5-year intervals), sex, and study areas when appropriate. Quantitative data was described by mean ± standard deviation (SD) if conforming to normal distribution; otherwise, it will be described by the median (interquartile range [IQR]). Qualitative data was represented by rate or constituent ratio (%).

Cox proportional hazard models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for associations of PA with all-cause and cause-specific mortality, with age as the underlying time scale, stratified by age (in 5-year intervals), and 10 study areas. The assumption of proportional hazards was verified using the Schoenfeld residuals. Multivariate models were adjusted for sex, education (no formal school, primary school, middle school, high school, technical school/college, university), household income (<2500, 2500–4999, 5000–9999, 10,000–19,999, 20,000–34,999, ≥35,000 Chinese Yuan/year), and marital status (married, widowed, separated/divorced, never married) in model 1, additionally adjusted for smoking status (never or occasional, ex-regular, and among current daily smokers: <15, 15–24, ≥25 cigarettes/day), alcohol consumption (never or occasional, ex-regular, weekly, and among daily drinkers: <15, 15–29, 30–59, ≥60 g/day), consumption frequency of fresh fruits (0, 0.5, 2.0, 5.0, 7.0 days/week), and sedentary leisure time (self-reported hours spent on leisure-time sedentary activities every day, such as watching television or reading) in model 2, and additionally adjusted for BMI (<18.5, 18.5–23.9, 24.0–27.9, ≥28.0 kg/m^2), prevalent hypertension and diabetes (presence or absence), family history of heart attack, stroke, cancer, and diabetes (presence or absence) in model 3. The domains or intensities were further mutually adjusted for domain-specific and intensity-specific analyses. For exposure variables with more than two categories, all HRs were computed using the floating absolute risk method to facilitate comparisons between groups.[17] If a linear association was detected, PA was also modeled as a continuous variable to estimate the risk associated with a 4 MET-h/d higher level of PA (approximately equivalent to 1 h/day cycling or brisk walking).

A single measurement of PA may underestimate the actual association between the usual PA level and mortality risk because of within-person variation or change over time.[18] About 20,000 participants who attended the second resurvey of CKB were included to estimate the regression dilution ratios (RDRs) using the McMahon-Peto method [Supplementary Table 1, http://links.lww.com/CM9/C314].[19] Log HRs per 4 MET-h/d higher in baseline PA were divided by RDRs to calculate HRs and 95% CIs for usual PA levels. Results were reported as HRs per 4 MET-h/d increment in usual PA with mortality.

Subgroup analyses were conducted by age (<60 years, ≥60 years), sex (male, female), region (rural, urban), smoking status (current or non-current), alcohol consumption (current or non-current), healthy diet (healthy: daily fresh vegetable consumption, daily fresh fruits consumption and not daily meat consumption; if not, unhealthy), and sedentary leisure time (<3h, ≥3 h), BMI (<24.0 kg/m^2, ≥24.0 kg/m^2) at baseline to examine potential effect modification. All the interaction *P* values were adjusted using the Benjamini–Hochberg false discovery rate (FDR) method.[20]

Several sensitivity analyses were conducted to examine the robustness of the main findings: (1) excluding participants who died in the first five years of follow-up to avoid reverse causation bias; (2) excluding participants with COPD, chronic hepatitis, cirrhosis, chronic kidney diseases, diabetes, bronchitis, asthma, or poor self-rated general health at baseline; and (3) fitting a Fine–Gray subdistribution hazards regression model to account for the competing risks when estimating cause-specific mortality risks (other causes of death are treated as competing events when analyzing specific causes of death).[21]

Unless otherwise stated, all analyses were performed with Stata 15.0 (StataCorp, College Station, Texas, USA). The competing risk analysis was performed using SAS (version 9.4, SAS Institute Inc, Cary, North Carolina, USA). Statistical tests were two-sided, and *P* <0.05 indicated statistical significance.

Results

Baseline characteristics of the study participants

Of the 482,067 participants, the mean ± SD age was 51.50 ± 10.51 years, 59.46% were women, and 43.13% lived in urban areas at baseline. The average total PA was 21.68 ± 13.73 MET-h/d. Participants with a higher level of total PA were more likely to be young and to live in rural areas. They also tended to have less sedentary leisure time and to report a lower prevalence of diabetes [Table 1].

Association of total PA with mortality

During a median follow-up of 12.12 years (IQR: 11.16 ± 13.11 years; 5,684,280 person-years), 47,281 deaths were documented, including 18,178 deaths from CVD, 15,469 deaths from cancer, 4582 deaths from respiratory diseases, 1336 deaths from diabetes, and 422 deaths from nervous system diseases. Total PA was inversely associated with the risk of all-cause mortality, with HRs (95% CIs) of 0.84 (0.82–0.86), 0.77 (0.75–0.78), 0.74 (0.73–0.76), and 0.69 (0.67–0.71) in the higher quintile (Q2–Q5) of total PA, compared with the lowest quintile

Table 1: Characteristics of 482,067 adult participants from 10 areas in China by baseline total PA (MET-h/d).

Characteristic	≤9.40	9.41–14.94	14.95–22.60	22.61–33.79	≥33.80
N of participants	97,257	95,619	96,473	96,331	96,387
Demographic factors					
Age (years)	57.78 ± 10.86	53.73 ± 10.52	50.31 ± 9.88	48.38 ± 9.13	47.10 ± 8.21
Female	55,382 (56.94)	65,438 (68.44)	60,884 (63.11)	55,368 (57.48)	49,571 (51.43)
Urban	53,310 (54.81)	44,393 (46.43)	43,572 (45.16)	35,670 (37.03)	30,984 (32.15)
Socioeconomic and lifestyle factors					
Middle school and above	48,463 (49.83)	48,010 (50.21)	49,741 (51.56)	46,961 (48.75)	44,425 (46.09)
Household income ≥RMB 20,000 Yuan/year	38,154 (39.23)	42,751 (44.71)	44,599 (46.23)	41,403 (42.98)	40,136 (41.64)
Married	87,677 (90.15)	87,147 (91.14)	88,147 (91.37)	87,719 (91.06)	88,078 (91.38)
Manual workers	26,182 (26.92)	43,067 (45.04)	60,460 (62.67)	71,333 (74.05)	73,177 (75.92)
Current smokers	27,893 (28.68)	27,519 (28.78)	27,707 (28.72)	28,292 (29.37)	28,714 (29.79)
Current drinkers	13,149 (13.52)	14,534 (15.20)	15,002 (15.55)	14,960 (15.53)	14,950 (15.51)
Fresh fruits consumption (>4 days/week)	18,187 (18.70)	18,713 (19.57)	19,478 (20.19)	16,184 (16.80)	14,979 (15.54)
Total PA, MET-h/d	6.57 ± 4.49	12.31 ± 4.32	18.44 ± 4.22	27.93 ± 4.33	43.20 ± 4.49
Sedentary leisure time, hours/day	3.53 ± 1.47	3.30 ± 1.42	2.94 ± 1.39	2.64 ± 1.42	2.56 ± 1.47
BMI, kg/m^2	23.82 ± 3.46	23.86 ± 3.33	23.55 ± 3.25	23.40 ± 3.34	23.37 ± 3.46
Disease history					
Hypertension	34,020 (34.98)	33,859 (35.41)	31,826 (32.99)	30,990 (32.17)	31,008 (32.17)
Diabetes	6448 (6.63)	5699 (5.96)	4708 (4.88)	4113 (4.27)	3653 (3.79)
Family history					
Diabetes	6545 (6.73)	6952 (7.27)	7071 (7.33)	6348 (6.59)	6159 (6.39)
Heart attack	2889 (2.97)	3203 (3.35)	3135 (3.25)	2909 (3.02)	3113 (3.23)
Stroke	16,281 (16.74)	17,269 (18.06)	17,240 (17.87)	17,108 (17.76)	17,224 (17.87)
Cancer	15,522 (15.96)	15,787 (16.51)	16,391 (16.99)	16,001 (16.61)	16,280 (16.89)

Values are shown as mean ± standard deviation or *n* (%) of participants adjusted for age, sex, and study areas when appropriate. All *P* for trend <0.001, except for household income ≥ RMB 20,000 yuan/year ($P = 0.206$) and family history of heart attack ($P = 0.494$). BMI: Body mass index; MET-h/d: Metabolic equivalents of task per hour per day; PA: Physical activity.

(Q1) [Supplementary Table 2, http://links.lww.com/CM9/C314]. The risk of all-cause mortality was lowered by 10% (HR = 0.90; 95% CI: 0.89–0.91) with a 4 MET-h/d higher level of total PA [Figure 1].

In the analysis for cause-specific mortality, a dose–response association was observed for total PA (all *P* for trend <0.05, Figure 1 and Supplementary Table 2, http://links.lww.com/CM9/C314). CVD mortality risk was lowered by 32% (HR = 0.68; 95% CI: 0.64–0.71) among participants in Q5. Cancer mortality risk was reduced by 20% (HR = 0.80; 95% CI: 0.76–0.83). Among these cause-specific mortalities, mortality from respiratory diseases had the most substantial effect (HR = 0.39; 95% CI: 0.35–0.44), followed by diabetes (HR = 0.44; 95% CI: 0.35–0.55) and nervous system diseases (HR = 0.52; 95% CI: 0.38–0.73), and their mortality risks per 4 MET-h/d were lowered by 27% (HR = 0.73; 95% CI: 0.70–0.76), 25% (HR = 0.75; 95% CI: 0.70–0.81), and 17% (HR = 0.83; 95% CI: 0.73–0.93), respectively [Figure 1]. The subtypes of the above cause-specific mortality had similar results [Figure 2 and Supplementary Table 3, http://links.lww.com/CM9/C314].

The associations of total PA with mortality remained stable after excluding participants dying in the first five years of follow-up or excluding participants with histories of COPD, chronic hepatitis, cirrhosis, chronic kidney diseases, diabetes, bronchitis, asthma, or poor self-rated general health at baseline. The results remained robust when the competing risks of death from other causes for cause-specific mortality were considered [Supplementary Table 4, http://links.lww.com/CM9/C314].

Most results were similar across strata in the subgroup analysis of 4 MET-h/d higher total PA with mortality [Table 2]. However, a stronger association with all-cause mortality was observed in females (FDR corrected *P* for interaction = 0.032) and non-current drinkers (FDR corrected *P* for interaction <0.001). The decrease in CVD mortality was also greater in non-current drinkers (FDR corrected *P* for interaction <0.001). Urban residents had a larger reduction of respiratory disease mortality (FDR corrected *P* for interaction = 0.048).

Association of domain-specific PA with mortality

Both OPA and NOPA were inversely associated with the risk of all-cause mortality, with HRs (95% CIs) of 0.66 (0.64–0.69) and 0.87 (0.85–0.89), respectively [Figure 3 and Supplementary Table 5, http://links.lww.com/CM9/C314]. Inverse associations were also observed with CVD, respiratory disease, diabetes, and nervous system disease mortality. The risk of cancer mortality was lower in Q5

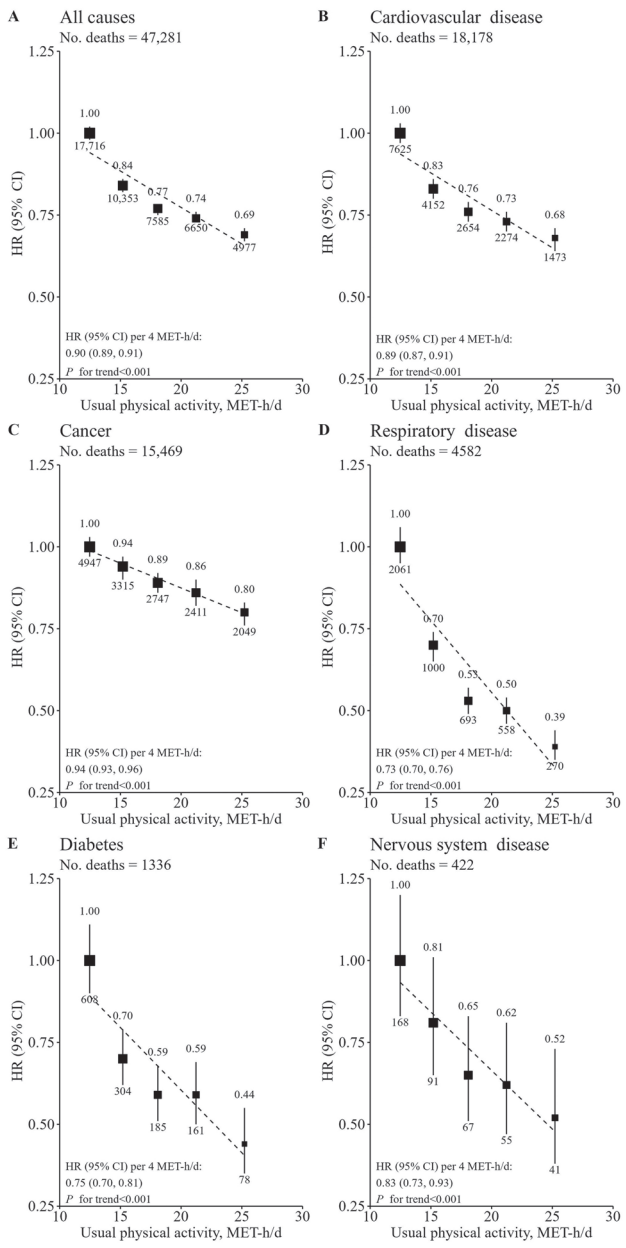

Figure 1: Associations of total PA with mortality in 482,067 adult participants from 10 areas in China. (A) Associations of total PA with mortality from all causes; (B) Associations of total PA with mortality from cardiovascular disease; (C) Associations of total PA with mortality from cancer; (D) Associations of total PA with mortality from respiratory disease; (E) Associations of total PA with mortality from diabetes; (F) Associations of total PA with mortality from nervous system disease. Cox proportional hazard models were stratified by age (in 5-year intervals) and study areas; adjusted for sex, education, household income, marital status, smoking status, alcohol consumption, sedentary leisure time, consumption frequency of fresh fruits, BMI, prevalent hypertension, and diabetes at baseline; and family history of heart attack, stroke, cancer, or diabetes (only adjusted for in the corresponding analysis of cause-specific mortality). HRs are plotted against the mean level in each category of total PA. The squares represent HR and the size is proportional to the inverse variance of each effect size. The numbers above and below the squares are HR and the number of deaths of the group, respectively. The vertical lines represent 95% CI. The dashed lines represent the slope from a linear regression. BMI: Body mass index; CI: Confidence interval; HRs: Hazard ratios; MET-h/d: Metabolic equivalents of task per hour per day; PA: Physical activity.

of OPA (HR = 0.80; 95% CI: 0.76–0.85), but no protective effect was observed in NOPA. For all-cause and cause-specific mortality, OPA exhibited a stronger protective effect, while the effects in commuting PA, household PA, and LTPA were similar [Supplementary Tables 5 and 6, http://links.lww.com/CM9/C314].

Association of intensity-specific PA with mortality

MVPA showed inverse associations with risks of all-cause, CVD, cancer, respiratory disease, diabetes, and nervous system disease mortality [Figure 4 and Supplementary Table 7, http://links.lww.com/CM9/C314], with HR (95% CI) of 0.70 (0.67–0.72) for all-cause mortality. LPA had similar results, with HR (95% CI) of 0.83 (0.81–0.86) for all-cause mortality, but had no significant association with cancer mortality.

Discussion

In this large-scale prospective cohort study of Chinese adults, we found that total PA was inversely associated with all-cause and major cause-specific mortality, including CVD, cancer, respiratory diseases, diabetes, and nervous system diseases. In addition, different domains and intensities were also associated with lower mortality risks. This study provides a comprehensive insight into the association between PA and mortality risk, suggesting potential benefits of increasing PA.

Association of total PA with mortality

Our findings confirmed previous evidence of the inverse association between total PA and all-cause mortality.[3–5,22,23] A meta-analysis of 80 studies with 1,338,143 participants showed that total PA was associated with a 35% (risk ratio [RR] = 0.65; 95% CI: 0.60–0.71) lower risk of all-cause mortality, and this lower mortality was more pronounced in women.[5] Previous studies reported an L-shaped dose–response association. However, we observed a log-linear association between total PA and mortality.[24]

This study examined the association between total PA and cause-specific mortality risk. We confirmed previous studies' findings that total PA was associated with lowered mortality from CVD, such as IHD, IS, and ICH.[23,25,26] However, we observed a weaker inverse association with cancer mortality. This dilution of effect is mostly likely due to several cancer sites with different etiologies and pathophysiologies being considered as a single entity.[27]

Few studies have investigated the association with mortality from respiratory diseases, diabetes, and nervous system diseases in a population-based setting. A study based on the National Health Interview Survey reported that cause-specific mortality risks were lower in participants who met PA guidelines compared with those who did not, with HRs (95% CIs) of 0.42 (0.37–0.47) for chronic lower respiratory tract diseases, 0.63 (0.53–0.74) for diabetes mellitus, and 0.74 (0.62–0.87) for Alzheimer's disease, respectively.[28] A study conducted among COPD patients found that total PA was inversely associated with respiratory disease-related mortality.[29] Existing evidence has suggested potential beneficial effects of total PA on

Table 2: Subgroup analysis of total PA (per 4 MET-h/d increment) with all-cause and cause-specific mortality from 482,067 adult participants from 10 areas in China.

	All causes			CVDs			Cancer			Respiratory disease			Diabetes			Nervous system diseases		
Subgroups	**HR (95% CI)**	***Z* value**	***P*-value***	**HR (95% CI)**	***Z* value**	***P*-value***	**HR (95% CI)**	***Z* value**	***P*-value***	**HR (95% CI)**	***Z* value**	***P*-value***	**HR (95% CI)**	***Z* value**	***P*-value***	**HR (95% CI)**	***Z* value**	***P*-value***
Sex		−3.02	0.032		−2.23	0.150		1.92	0.264		−1.41	0.399		−1.49	0.397		0.84	0.661
Male	0.92 (0.90, 0.93)			0.91 (0.89, 0.93)			0.95 (0.93, 0.97)			0.75 (0.72, 0.79)			0.81 (0.73, 0.90)			0.81 (0.69, 0.94)		
Female	0.86 (0.84, 0.88)			0.84 (0.81, 0.87)			0.93 (0.90, 0.96)			0.65 (0.60, 0.70)			0.69 (0.61, 0.77)			0.84 (0.70, 1.00)		
Age		−2.13	0.176		0.29	0.906		1.57	0.374		0.69	0.710		−0.41	0.841		−0.06	0.971
<60 years	0.93 (0.91, 0.94)			0.91 (0.88, 0.93)			0.95 (0.93, 0.97)			0.73 (0.68, 0.79)			0.84 (0.77, 0.93)			0.89 (0.75, 1.06)		
≥60 years	0.89 (0.87, 0.90)			0.90 (0.87, 0.92)			0.95 (0.93, 0.98)			0.73 (0.69, 0.76)			0.72 (0.64, 0.81)			0.83 (0.71, 0.97)		
Region		−0.14	0.971		−2.25	0.150		0.10	0.971		−2.80	0.048		1.32	0.437		0.58	0.796
Rural	0.89 (0.88, 0.90)			0.86 (0.85, 0.88)			0.94 (0.92, 0.96)			0.78 (0.75, 0.81)			0.74 (0.68, 0.80)			0.85 (0.73, 0.97)		
Urban	0.87 (0.86, 0.89)			0.79 (0.76, 0.82)			0.95 (0.93, 0.98)			0.72 (0.66, 0.79)			0.78 (0.68, 0.89)			1.01 (0.84, 1.21)		
Smoking status		1.46	0.397		1.15	0.524		−1.64	0.374		0.43	0.841		−0.23	0.930		−0.85	0.661
Non-current	0.88 (0.87, 0.90)			0.87 (0.85, 0.90)			0.94 (0.91, 0.96)			0.68 (0.63, 0.72)			0.75 (0.68, 0.83)			0.83 (0.72, 0.97)		
Current	0.92 (0.90, 0.93)			0.90 (0.88, 0.93)			0.95 (0.93, 0.97)			0.77 (0.73, 0.81)			0.75 (0.67, 0.85)			0.81 (0.67, 0.97)		
Alcohol consumption		6.12	<0.001		5.20	<0.001		0.37	0.850		−0.82	0.661		1.03	0.597		0.84	0.661
Non-current	0.89 (0.88, 0.90)			0.87 (0.85, 0.89)			0.94 (0.92, 0.96)			0.71 (0.68, 0.75)			0.74 (0.68, 0.81)			0.81 (0.71, 0.93)		
Current	0.94 (0.92, 0.97)			0.94 (0.90, 0.98)			0.95 (0.92, 0.99)			0.77 (0.70, 0.84)			0.86 (0.70, 1.07)			0.88 (0.68, 1.12)		
Healthy diet		0.70	0.710		−1.42	0.397		0.52	0.828		0.02	0.983		0.10	0.971		−0.46	0.841
Not healthy	0.90 (0.89, 0.91)			0.89 (0.87, 0.91)			0.95 (0.93, 0.96)			0.72 (0.69, 0.75)			0.74 (0.68, 0.80)			0.82 (0.73, 0.92)		
Healthy	0.92 (0.87, 0.97)			0.88 (0.79, 0.97)			0.94 (0.87, 1.02)			0.79 (0.63, 0.99)			0.96 (0.61, 1.50)			0.81 (0.42, 1.56)		
Sedentary leisure time		−1.04	0.597		−0.42	0.841		−1.58	0.374		−1.37	0.413		1.77	0.336		0.86	0.661
<3 h	0.91 (0.89, 0.92)			0.90 (0.87, 0.92)			0.95 (0.93, 0.98)			0.74 (0.69, 0.78)			0.71 (0.63, 0.80)			0.80 (0.69, 0.94)		
≥3 h	0.90 (0.88, 0.91)			0.88 (0.86, 0.90)			0.94 (0.91, 0.96)			0.71 (0.67, 0.75)			0.79 (0.71, 0.87)			0.85 (0.71, 1.01)		
BMI		2.29	0.150		1.60	0.374		1.21	0.497		0.06	0.971		−2.33	0.150		0.74	0.710
<24 kg/m^2	0.89 (0.88, 0.90)			0.88 (0.86, 0.90)			0.94 (0.92, 0.96)			0.71 (0.67, 0.74)			0.78 (0.71, 0.86)			0.83 (0.72, 0.96)		
≥24 kg/m^2	0.92 (0.91, 0.94)			0.90 (0.87, 0.93)			0.95 (0.93, 0.98)			0.77 (0.70, 0.84)			0.72 (0.63, 0.82)			0.84 (0.68, 1.02)		

*FDR adjusted *P* for interaction. HRs were stratified by age (in 5-year intervals) and study areas; adjusted for sex, education, household income, marital status, alcohol consumption, smoking status, sedentary leisure time, consumption frequency of fresh fruits, BMI, prevalent hypertension, and diabetes at baseline; and family history of heart attack, stroke, cancer, or diabetes (only adjusted for in the corresponding analysis of cause-specific mortality) in the model when appropriate. BMI: Body mass index; CI: Confidence interval; CVDs: Cardiovascular diseases; FDR: False discovery rate; HRs: Hazard ratios; MET-h/d: Metabolic equivalents of task per hour per day; PA: Physical activity.

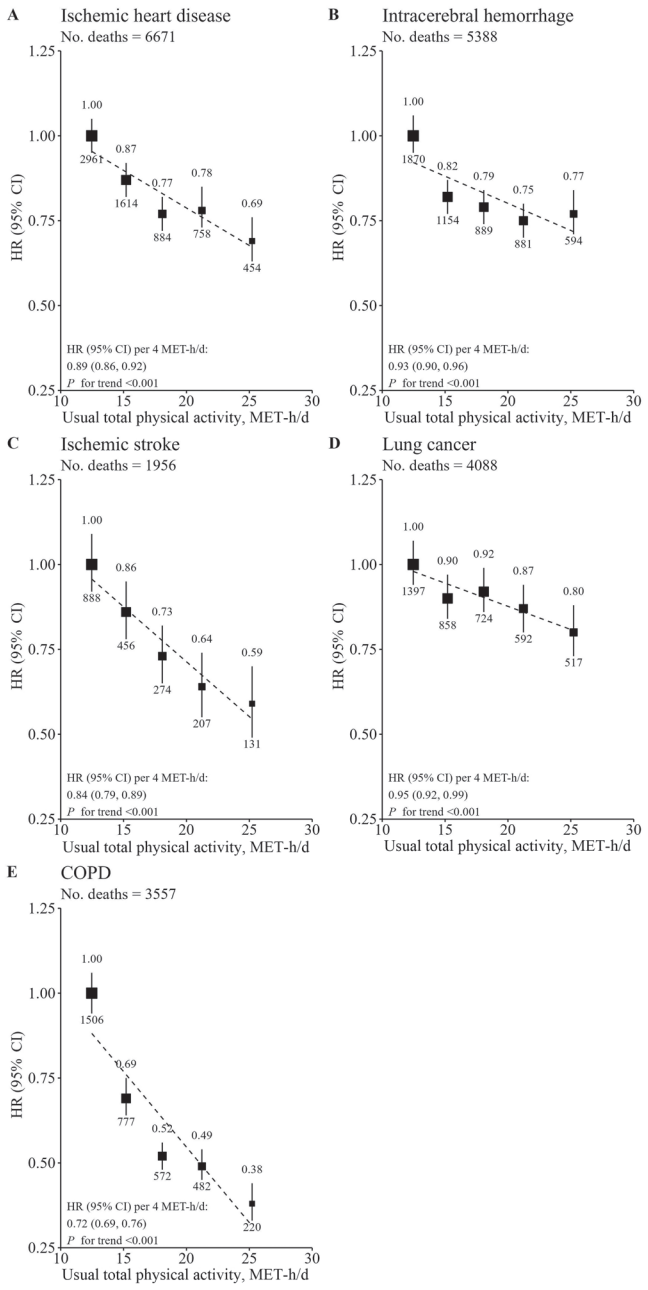

Figure 2: Associations of total PA with cause-specific mortality in 482,067 adult participants from 10 areas in China. (A) Associations of total PA with mortality from ischemic heart disease; (B) Associations of total PA with mortality from intracerebral hemorrhage; (C) Associations of total PA with mortality from ischemic stroke; (D) Associations of total PA with mortality from lung cancer; (E) Associations of total PA with mortality from COPD. Cox proportional hazard models were stratified by age (in 5-year intervals) and study areas; adjusted for sex, education, household income, marital status, smoking status, alcohol consumption, sedentary leisure time, consumption frequency of fresh fruits, BMI, prevalent hypertension, and diabetes at baseline; and family history of heart attack, stroke, cancer, or diabetes (only adjusted for in the corresponding analysis of cause-specific mortality). HRs are plotted against the mean level in each category of total PA. The squares represent HR and the size is proportional to the inverse variance of each effect size. The numbers above and below the squares are HR and the number of deaths of the group, respectively. The vertical lines represent 95% CI. The dashed lines represent the slope from a linear regression. COPD: Chronic obstructive pulmonary disease. BMI: Body mass index. CI: Confidence interval; HRs: Hazard ratios; MET-h/d: Metabolic equivalents of task per hour per day; PA: Physical activity.

diabetes and nervous system diseases, consistent with our results.[30,31]

Association of domain-specific PA with mortality

Previous epidemiological evidence has been focused on the association between LTPA and mortality.[5,6] The Rotterdam Study demonstrated a protective effect of NOPA against the risk of all-cause, CVD, and chronic lung disease mortality.[32] Our findings contribute new evidence for the role of PA in cancer, diabetes, and nervous system disease mortality. Our results also suggest that in addition to LTPA, other non-occupational activities, such as commuting and household PA, could also provide beneficial health effects.

Among most working Chinese adults, OPA constitutes the majority of their overall daily PA.[9] Consistent with our results, a meta-analysis of 80 studies with 1,338,143 participants (HR = 0.83; 95% CI: 0.71–0.97 in men) also observed the inverse association between OPA and all-cause mortality.[5] Some studies found no evidence of an association,[33,34] probably due to the differences in the PA assessment and confounder adjustments. In addition, we saw no evidence of the "physical activity paradox" in the previous literature, which suggests that LTPA is beneficial while OPA may be detrimental.[33] Therefore, the risk of mortality may be lowered by undertaking physical activities across the various domains, including unstructured OPA.

Association of intensity-specific PA with mortality

In line with this study, previous studies demonstrated that MVPA was associated with a lower mortality risk.[4,5,8,34] A meta-analysis including nine studies of 122,417 participants aged 60 years older showed that even a low dose of MVPA (1–499 MET-min per week) led to a 22% (RR = 0.78; 95% CI: 0.71–0.87) lower risk of all-cause mortality compared with no activity.[8] Previous studies have emphasized the protective effect of MVPA, but this may dampen the motivation of those with difficulty in engaging in MVPA. Our results indicated that LPA had a similar protective effect. Consistently, a meta-analysis including eight studies of more than 36,000 middle-aged and older participants suggested that mortality risk reduction ranged from 35% to 45% when comparing the second quarter for LPA and MVPA with the first quarter.[4] The findings of this study suggested that different intensities of PA can be combined in numerous ways to lower the risk of death, especially for those less able or willing to do MVPA.

Public health implications

According to the results of this study, an increase of 1 h/day of moderate-intensity PA, such as cycling or brisk walking, was associated with a 10% lower all-cause mortality risk. In addition, the risk of death from CVDs, cancer, respiratory diseases, diabetes, and nervous system diseases was reduced by approximately 11%, 6%, 27%, 25%, and 17%, respectively. Current PA guidelines primarily advocate moderate-to-vigorous-intensity LTPA. By contrast, we advocate that any domain and intensity of PA is better than doing nothing at all. This provides more options for people who are not feasible or unwilling to engage

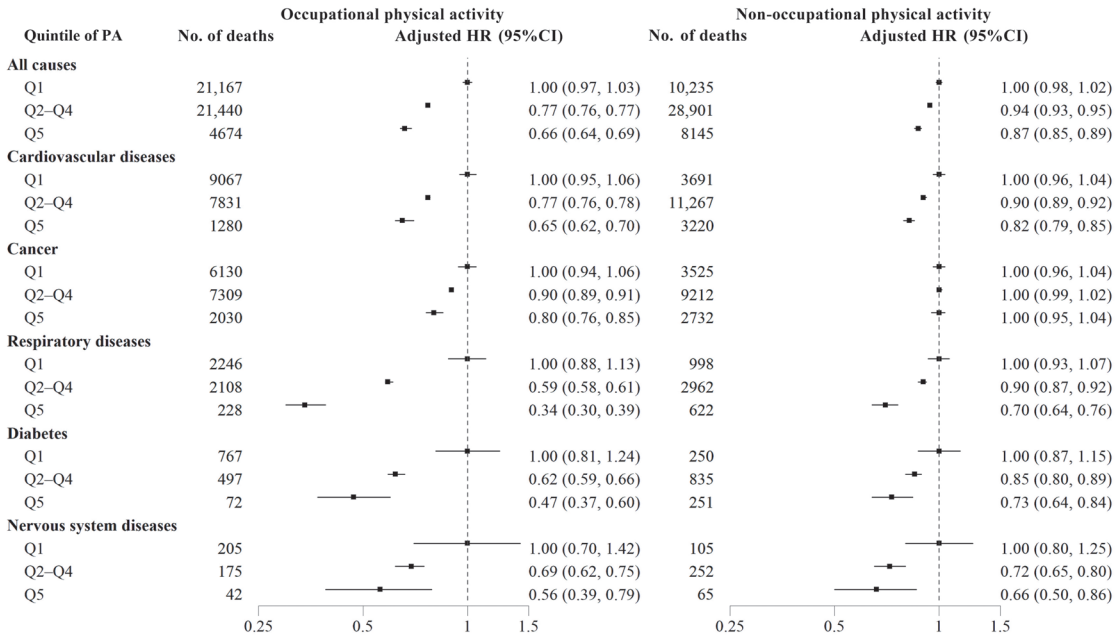

Figure 3: Associations of domain-specific PA with mortality in 482,067 adult participants from 10 areas in China. Q2–Q4 were combined due to the skewed distribution of domain-specific PA. Q1, Q2–Q4, and Q5 of OPA were ≤0.19, 0.20–25.71, and ≥25.72 MET-h/d, respectively. Q1, Q2–Q4, and Q5 of NOPA were ≤3.98, 3.99–11.61, and ≥11.62 MET-h/d, respectively. HRs were stratified by age (in 5-year intervals) and study areas; adjusted for sex, education, household income, marital status, smoking status, alcohol consumption, sedentary leisure time, PA of other domains, consumption frequency of fresh fruits, BMI, prevalent hypertension, and diabetes at baseline; and family history of heart attack, stroke, cancer or diabetes (only adjusted for in the corresponding analysis of cause-specific mortality) in the model. The amount of domain-specific PA was categorized by splitting at quintiles and HRs were estimated by comparing the highest quintile, the middle three quintiles, and the lowest quintile of PA. BMI: Body mass index; CI: Confidence interval; HRs: Hazard ratios; MET-h/d: Metabolic equivalents of task per hour per day; NOPA: Non-occupational physical activity; OPA: Occupational physical activity; PA: Physical activity.

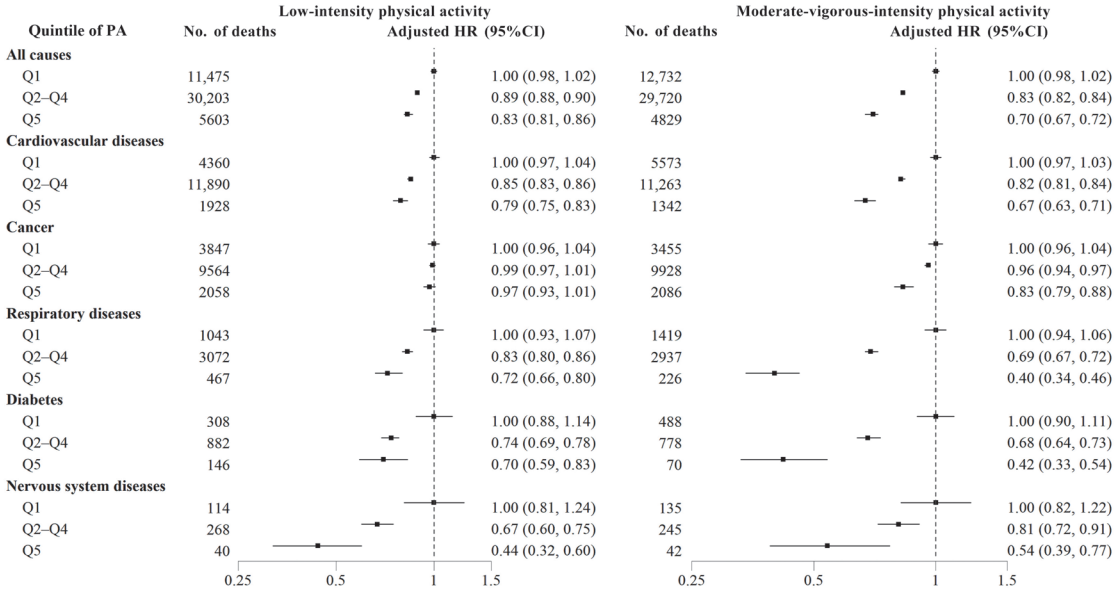

Figure 4: Associations of intensity-specific PA with mortality in 482,067 adult participants from 10 areas in China. Q2–Q4 were combined due to the skewed distribution of intensity-specific PA. Q1, Q2–Q4, and Q5 of LPA were ≤3.22, 3.23–14.00, and ≥14.01 MET-h/d, respectively. Q1, Q2–Q4, and Q5 of MVPA were ≤0.05, 0.06–26.39, and ≥26.40 MET-h/d, respectively. HRs were stratified by age (in 5-year intervals) and study areas; adjusted for sex, education, household income, marital status, smoking status, alcohol consumption, sedentary leisure time, PA of other intensity, consumption frequency of fresh fruit, BMI, prevalent hypertension, and diabetes at baseline; and family history of heart attack, stroke, cancer, or diabetes (only adjusted for in the corresponding analysis of cause-specific mortality) in the model. The amount of intensity-specific PA was categorized by splitting at quintiles and HRs were estimated by comparing the highest quintile, the middle three quintiles, and the lowest quintile of PA. BMI: Body mass index; CI: Confidence interval; HRs: Hazard ratios; LPA: Low-intensity physical activity; MET-h/d: Metabolic equivalents of task per hour per day; MVPA: Moderate-to-vigorous-intensity physical activity; PA: Physical activity.

in structured exercise, adding non-leisure-time PA such as OPA, commuting and household PA, and LPA such as walking or gardening to their daily lives can also bring long-term beneficial health effects. Public health efforts may emphasize increasing PA levels with flexibility across all domains and intensities, helping people realize that

even if they do not exercise regularly with high intensity, they may still benefit from any PA.

This study was a prospective cohort study with a large sample size of nearly 0.5 million and an average follow-up period of 12 years, enabling us to assess the association between PA and both all-cause and cause-specific mortality. Besides, our study collected detailed information on PA in different domains and intensities as well as various confounders and covariates for adjustment. In addition, we utilized data from a resurvey to correct for within-person variation and ascertain the associations of usual PA with all-cause and cause-specific mortality.

However, this study has several limitations. First, PA was self-reported, so the potential for recall or social desirability bias cannot be ruled out. Second, we used covariates measured at baseline and did not consider their changes over time during follow-up. Third, on the one hand, participants in poor health, such as CVD, cancer, respiratory diseases, and other underlying diseases, may be less active, leading to the possibility of reverse causality. However, the association in this study remained stable in a series of sensitivity analyses: excluding participants who died in the first five years of follow-up or participants who had other chronic diseases at baseline. On the other hand, we excluded participants with major chronic diseases at baseline, so the results may not be extrapolated to populations with these chronic conditions. Finally, although established and potential risk factors for mortality have been adjusted, residual confounding might still be possible due to unmeasured or unknown factors.

This study found that PA was inversely associated with the risk of mortality from all causes, CVD, cancer, respiratory diseases, diabetes, and nervous system diseases in a dose–response manner, regardless of domain and intensity.

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Data sharing

Details of how to access China Kadoorie Biobank data and details of the data release schedule are available from https://www.ckbiobank.org/data-access.

Conflicts of interest

None.

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