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Non-vigorous physical activity and all-cause mortality: systematic review and meta-analysis of cohort studies

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Background Although previous studies have found physical activity to be associated with lower mortality, the dose–response relationship remains unclear. In this systematic review and meta-analysis we quantify the dose–response relationship of non-vigorous physical activity and all-cause mortality.

Methods We aimed to include all cohort studies in adult populations with a sample size of more than 10 000 participants that estimated the effect of different levels of light or moderate physical activity on all-cause mortality. We searched Medline, Embase, Cochrane (DARE), Web of Science and Global Health (June 2009). We used dose–response meta-regression models to estimate the relation between non-vigorous physical activity and mortality.

Results We identified 22 studies that met our inclusion criteria, containing 977 925 (334 738 men and 643 187 women) people. There was considerable variation between the studies in their categorization of physical activity and adjustment for potential confounders. We found that 2.5 h/week (equivalent to 30 min daily of moderate intensity activity on 5 days a week) compared with no activity was associated with a reduction in mortality risk of 19% [95% confidence interval (CI) 15–24], while 7 h/week of moderate activity compared with no activity reduced the mortality risk by 24% (95% CI 19–29). We found a smaller effect in studies that looked at walking alone.

Conclusion Being physically active reduces the risk of all-cause mortality. The largest benefit was found from moving from no activity to low levels of activity, but even at high levels of activity benefits accrue from additional activity.

Keywords Physical activity, exercise, walking, mortality, systematic review, meta-analysis, cohort study, dose–response

Introduction

Non-vigorous physical activity is a central focus of health promotion.[1,2] Nevertheless, the expected benefit of different amounts of physical activity on all-cause mortality remains unclear. Many cohort studies have estimated a dose response but these have varied in their size, precision and findings, while some suggest a linear relationship with increasing activity, other suggest no additional benefit from higher doses.[3–6] We aimed to quantify and characterize the nature of the association between non-vigorous physical activity and all-cause mortality.[7]

Active travel is frequently recommended as a way to increase physical activity; and walking is the most popular form of physical activity.[1] Therefore, in addition to studies looking at multiple aspects of non-vigorous activity, we looked for studies that estimated the exclusive effects of walking or cycling on all-cause mortality. Furthermore, we investigated if there was a difference in effect according to different gender, age, the quality of the study and the extent of adjustment for potentially intermediary variables.

Methods

Selection criteria

Inclusion criteria were: (i) prospective cohort study in a healthy/general population with more than 10 000 people at baseline; (ii) measure of light or moderate physical activity (either in terms of duration, frequency, distance or a combination); and (iii) association with all-cause mortality. We excluded studies that only measured work-related activity. We only included studies of physical activity and not physical fitness. We included only those studies that compared more than two exposure levels.

Search strategy

We searched Medline, Embase, Cochrane (DARE), Web of Science and Global Health (in July 2008 and then an update in June 2009) for cohort studies. No time-period restrictions were included. Key words used in Medline included, 'physical activity', 'bicycling', 'walking', 'exercise', 'active travel', 'active commuting', 'active transport', in combination with 'mortality', 'life expectancy' and 'death' (see 'Online Appendix: Search strategy' available as Supplementary data at *IJE* online). MeSH headings included, 'Exercise', 'Exercise Therapy', 'Physical Fitness' and 'Exertion'. We searched the reference lists of included studies and other systematic reviews. We also contacted authors of all studies with over 10 000 participants identified as on February 2009 for unpublished studies. All remaining references were assessed by two independent reviewers (J.W. and O.H.F.) and any disagreements were resolved by discussion and mutual agreement. No language restrictions were employed.

Data extraction

We used a data collection form designed before the search for studies took place. We collected information on participants and study characteristics (including age, sex, setting and follow-up); measurement of exposure (including domain, restrictions on intensity or duration of activity, physical activity instrument tool and whether this used a questionnaire or interview); ascertainment of outcome; study exclusion criteria and adjustment for potential confounders (e.g. smoking, education); and estimate of treatment effect (the estimate most adjusted for potential confounders).

If a study produced multiple estimates based on different kinds of physical activity, we selected the estimate most relevant to non-vigorous activities of daily living, rather than activity done as exercise. If the study also presented results for a group undertaking vigorous activity we ignored this group but included other results from the study, even if this reduced the sample size to fewer than 10 000 people. For secondary analyses we selected estimates exclusive of walking or cycling. If multiple publications were available on the same cohort, then we chose the most recent publication that met all other inclusion criteria. Some analyses exclude deaths that occur soon after measurement of baseline data to reduce the risk of reverse causation. If available, we took the results for the full-time period but in the sensitivity analysis we considered studies excluding a time period.

We extracted available data on the duration and intensity of physical activity per week. The intensity of activities can be categorized according to subjective exertion or with a fixed measure for each activity, usually measured as metabolic equivalent tasks (METs). MET is a unit of energy expenditure adjusted for body mass, with the reference category of 1 MET being the typical energy expenditure of an individual at rest (4.18 kJ/kg/h).[8] Activities <6 METs are generally defined as moderate and those <3 METs as light for adults <65 years.[2] The intensity of selected activities were based on the compendium of physical activities by Ainsworth *et al*.[8] We did not include study results based on activities of intensity >6 METs. Time spent in activities of different intensities over a week can be combined to give an estimate of total MET-hours/week. The measure of MET-hours/week incorporates both the intensity and the total time spent per week on physical activity.

Quality assessment

We assessed the quality of the studies using the Newcastle Ottawa Scale.[9] In this scale studies are assessed in three areas: the selection of exposed and unexposed participants; the comparability of the groups; and the assessment of the outcome. A star is awarded for high quality in each area. The Newcastle Ottawa Scale requires selection of a confounder considered to be the most important and in this case, because of its strong association with mortality,[10] we selected smoking.

Analysis

We pooled the studies using two-stage random effects dose–response meta-regression models developed by Greenland and Longnecker as implemented by Orsini and colleagues.[11,12] This method allows estimation of the dose–response gradient of mortality risk across studies taking into account non-independent relative risks (RRs) presented within a single study. For each study we assigned the mid-point of each exposure interval as the median dose corresponding to the RR. If the highest exposure interval was defined as greater than a given value we imputed the median exposure for that interval by assuming a linear decline in the population density function (the number of people in each exposure interval divided by the width of the exposure interval) with increasing exposure. The population density function at the start of the highest exposure interval was estimated based on the population density function for the lower exposure interval.

We converted exposure measures from each study into MET-hours of activity per week using the data available in the report and by selecting the estimate from the compendium of activities,[8] which appeared most applicable. If an exposure interval could either represent a given duration of moderate intensity physical activity or a shorter duration of more intensive physical activity we assumed the exposure was based on the longer duration of moderate intensity physical activity. If activity was represented as number of sessions, then an average duration of 0.5 h per session was assumed. For estimates that included MET-hours spent in sedentary activities, we assumed a minimum level of activity in the lowest group based on the available data and calibrated all other estimates to this. If the reference category was high activity, we used the method suggested by Hamling[13] to convert the reference category to the lowest exposure category. If information on person-years of follow-up and deaths per group was not provided, we decided to impute these based on the study size, length of follow up and differing mortality rates. Statistical heterogeneity among studies included in the meta-analysis was assessed using the Q statistic and I-squared.[14] Small study effects were assessed by the Egger's regression asymmetry test[15] and by visual inspection of a funnel plot.

Assessment of non-linear dose–response relationships

We investigated potential departure from linearity between physical activity and mortality by using first-degree fractional polynomials with different power transformations (0.25, 0.375, 0.50, 0.75) and a log transformation of the exposure (MET-hours/week).[16] We used the Akaike's Information Criterion (AIC, a summary measure that combines fit and complexity) to choose the model that best (lowest AIC value) fitted the data.[17]

Sensitivity and stratified analyses

We pre-specified five subgroup/sensitivity analyses: (i) studies that provided an estimate based on walking alone; and (ii) studies that provided an estimate on cycling alone. We looked (iii) at the extent to which the study controlled for cardio-metabolic variables (blood pressure, blood glucose, lipid levels and cholesterol) with the hypothesis that greater adjustment may be associated with a lower effect estimate of physical activity on all-cause mortality. To investigate (iv) the robustness, we investigated if effects were sensitive to the exclusion of deaths that occurred soon after collection of baseline data, the exclusion of non-brisk walking and the quality of the studies. Finally, (v) we investigated if the effect varied by age, sex or year of study by stratifying our analyses by these variables. For each stratified variable, if individual studies reporting stratified results by that variable were identified then we meta-analysed only that subset of studies. All analyses were conducted using Stata, release 10 (StataCorp, College Station, TX, USA). All statistical tests were two-sided.

Results

Search results

We retrieved 6210 records. Initial screening of title and abstract excluded 5725 records (Figure 1). No additional reports were retrieved by searching reference lists. We identified one additional report from personal communication.[18] We retrieved 44 reports for further inspection. We excluded 13 reports on examination of full text, including 5 for not assessing the exposure and outcome in at least 10 000 participants,[19–23] 5 for not providing an estimate for non-vigorous activity,[24–28] 3 for not reporting on all-cause mortality,[29–31] and 1 for only comparing two exposure levels.[32] Contact with one author produced additional data on hazard ratios for physical activity categories.[6]

Table 1 presents the characteristics of the 22 independent studies[3–6,33–51] reported in 30 reports.[18,52–58] The studies included nearly 1 million participants (977 925), with more women participants (643 187) than men (334 738). The cohort studies were conducted in Europe (eight studies), North America (eight studies), East Asia (five studies) and Australasia (one study), with the most recent report for each study being published between 1996 and 2009. The studies covered a broad range of populations of middle and older age, but younger adults were under represented (Table 1). Mean age at

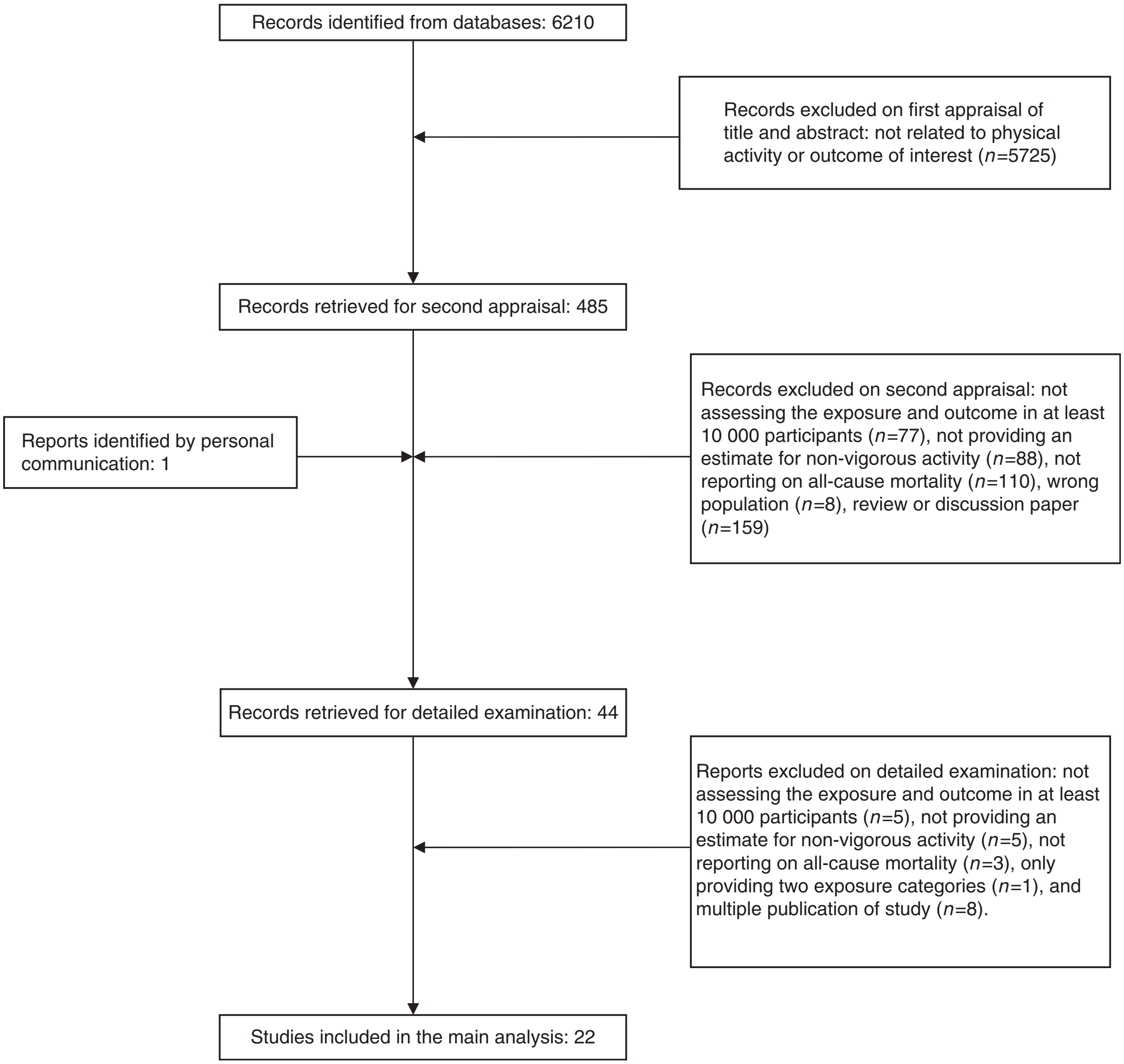

Figure 1 Flow chart for selection of studies

baseline ranged from 38[48] to 72.[41] Estimated exposure in the studies and the associated RRs and confidence intervals (CIs) are presented in Supplementary Tables 1 and 2 (available as Supplementary data at *IJE* online).

Quality

Out of a maximum of nine stars, we found that the median and mean number of stars awarded to a study was six. The highest score was eight stars (two studies[3,37]) and the lowest score was four stars (three studies[40,50,51]) (Table 2).

The majority of the included studies was of the general population of men or women from a geographically defined area[3–6,33–39,59,60] and all selected controls from the same population. Most studies excluded people or adjusted the analysis on the basis of self-reported health status, rather than clinical assessment. All studies controlled for smoking, using variables ranging from a simple yes or no question on current smoking status (seven studies[3,33,38,40,41,50,51]) to current smoking status plus pack years.[4,6,48] Three studies presented equivalent data suitable for inclusion both with and without exclusion of deaths in the first few years.[33,43,50] Four studies only provided suitable data after excluding deaths that occurred soon after measurement of baseline data,[6,40,46,48] four studies said excluding such deaths did not substantially alter the effect estimate but did not provide the numbers.[4,36,38,39] Six studies adjusted for physical activity in other domains.[34,35,38,39,44,47]

Table 1 Summary of studies

Author	Study name	Follow-up length (years)	Number in cohort	Sex	Age at baseline (years)	Adjustments
Hayasaka *et al.*[3]	Jichi Medical School Cohort Study, Japan	12	10 831	F/M	Mean 55	Age, area, BMI, systolic blood pressure, and total cholesterol. Smoking: yes/no
Arrieta and Russell[33]	NHANES I, USA	20	10 474	F/M	35–74	Age (years), female, black race, smoking, BMI, systolic blood pressure, total cholesterol, education and chronic conditions. Smoking: yes/no
Besson *et al.*[34]	European Prospective Investigation into Cancer in Norfolk, UK	7	14 903	F/M	49–83	Age, sex, social class, alcohol consumption, diabetes, cancer, cardiovascular disease, and stroke. Smoking: never, former, current
Ford *et al.*[37]	Australian Longitudinal Study on Women's Health	9	12 422	F	70–75	Self rated health, comorbidity score, BMI, marital status. Smoking: current, never, quit <5 years, quit 5–10 years, quit 11–20 years, quit >20 years.
Inoue *et al.*[35]	Japan Public Health Center-based Prospective Study, Japan	Mean 8.7	83 034	F/M	45–74	Age (5-year age categories), area, occupation, diabetes, alcohol intake status, BMI (3 groups), and total energy intake. Smoking: never, former, current
Orsini *et al.*[6]	Cohort of Swedish Men, Sweden	9.7	37 633	M	45–79	Age, alcohol consumption, educational level, parental history of coronary heart disease and cancer. Excluded current and former smokers.
Pedersen *et al.*[36]	Copenhagen City Heart study, Denmark	⩾11	11 914	F/M	⩾20	Age, BMI, education, marital status, known diabetes, and alcohol intake. Smoking: never, former, 1–14 g/day, >14 g/day
Leitzmann *et al.*[39]	National Institutes of Health-American Association of Retired Persons Diet and Health Study, USA	~5	252 925	F/M	50–71	Sex, BMI, ethnicity, education, marital status, family history of cancer, menopausal hormone therapy, aspirin use, multivitamin use, vegetable intake, fruit, red meat and alcohol, vigorous activity Smoking: never, past 1–19/day, past ⩾20/day, current 1–19/day, current ⩾20/day
Matthews *et al.*[38]	Shanghai Women's Health Study, China	Mean 5.7	67 143	F	40–70	Age, marital status, education, household income, alcohol drinking, number of pregnancies, oral contraceptive use, menopausal status, other types of physical activity, pre-existing medical conditions (including diabetes and hypertension). Smoking: never, ever
Carlsson *et al.*[40]	Swedish Mammography Cohort, Sweden	5	27 734	F	51–83	Age, education, number of children, hormone replacement therapy, intake of fruit and vegetables, BMI, hypertension, thrombosis, angina pectoris, myocardial infarction, stroke, diabetes, asthma, cataract, fractures, arthritis, bile stones, renal calculus, high cholesterol, benign node in breast, disablement pension and cancer. Smoking: yes, no

(continued)

Table 1 Continued

Author	Study name	Follow-up length (years)	Number in cohort	Sex	Age at baseline (years)	Adjustments
Schooling *et al.*[41]	Hong Kong, China	Average 4.1	54 088	F/M	⩾65	Age, sex, socio-economic status, ever use of alcohol. Smoking: ever, never
Trolle-Lagerros *et al.*[4]	Women's Lifestyle and Health cohort, Norway and Sweden	Average 11.4	99 099	F	30–49	Age, years of education, BMI, alcohol intake and country of origin and physical activity at earlier ages. Smoking: current, former, never/mean number of cigarettes, years smoking
Fujita *et al.*[43]	Miyagi, Japan	11	41 163	F/M	40–64	Age, education, marital status, past history of diseases, drinking, BMI (grouped), and dietary variables. Smoking: never, former, current 1–19/day, >20/day
Barengo *et al.*[44]	North Karelia project & FINMONICA/Finrisk studies, Finland	20	32 677	F/M	30–59	Age, study year, BMI, systolic blood pressure, cholesterol, and education. Work and leisure physical activity. Smoking: never, former, current
Batty *et al.*[45]	Whitehall Study, UK	25	12 552	M	40–64	Age, employment grade, systolic blood pressure, cholesterol, BMI, glucose intolerance, FEV1. Smoking: yes, no
Rockhill *et al.*[46]	Nurses' Health Study, USA	16	80 348	F	34–59	Age, sex, socio-economic status, ever use of alcohol. Smoking: ever, never
Lee and Paffenbarger[47]	Harvard Alumni Health Study, USA	15	13 485	M	Mean 57.5	Age, BMI, alcohol intake, and early parental death. Smoking: no, current 1–20/day, current >20/day
Kujala *et al.*[48]	Finnish Twin Cohort	17	15 902	F/M	25–64	Age, sex, occupational group, alcohol use. Smoking: pack years/yes, no
Villeneuve *et al.*[5]	Canada Fitness Survey	7	14 442	F/M	20–69	Age. Smoking: never, former, current
Kushi *et al.*[50]	MRFIT, USA	16	12 138	M	35–57	Age, intervention group, years of education, serum cholesterol, diastolic blood pressure and BMI. Smoking: cigarettes/day
Leon *et al.*[49]	Iowa Women's Health Study, USA	7	40 417	F	55–69	Age, age at menarche, age at menopause, age at first live birth, parity, alcohol and energy intake, oestrogen use, BMI, first degree relative with cancer, high blood pressure, diabetes, education, marital status. Smoking: yes/no
Kampert *et al.*[51]	TX, USA	Average 8	29 903	F/M	20–88	Age, examination year, chronic illnesses, and electrocardiogram abnormalities. Smoking: yes/no

BMI = body mass index; F = female; M = male; NHANES = national health and examination survey; FEV1 = forced expiratory volume in one second; FINMONICA = Finland multinational monitoring of trends and determinants in cardiovascular disease; MRFIT = multiple risk factor intervention trial.

Table 2 Quality assessment of the included studies (Newcastle Ottowa Scale)

Study	**Selection**				**Comparability (on design or analysis)**		**Outcome**			**Stars**
	Representativeness of cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at start	Smoking	Other	Assessment	Follow-up length	Attrition	
Hayasaka *et al.*[3]	B*	A*	B*	2*	D	A*	B*	A*	B*	8
Arrieta and Russell[33]	B*	A*	B*	0	D	A*	B*	A*	B*	7
Besson *et al.*[34]	B*	A*	C	0	C	A*	B*	A*	B*	6
Ford *et al.*[37]	B*	A*	C	2*	B*	A*	B*	A*	B*	8
Inoue *et al.*[35]	B*	A*	C	1	D	A*	B*	A*	B*	7
Orsini[6]	B*	A*	C	2*	A*	A*	B*	A*	D	7
Pedersen *et al.*[36]	B*	A*	C	1	C	A*	B*	A*	B*	6
Leitzmann *et al.*[39]	B*	A*	C	1.5*	C	A*	B*	A*	C	6
Matthews *et al.*[38]	B*	A*	B*	1	D	A*	B*	A*	B*	7
Carlsson *et al.*[40]	C	A*	C	0	D	A*	B*	A*	D	4
Schooling *et al.*[41]	B*	A*	C	2*	D	A*	B*	A*	D	6
Trolle-Lagerros *et al.*[4]	B*	A*	C	1	A*	A*	B*	A*	B*	7
Barengo *et al.*[44]	B*	A*	C	2*	D	A*	B*	A*	D	6
Fujita *et al.*[43]	B*	A*	C	1	C	A*	B*	A*	B*	6
Batty *et al.*[45]	C	A*	C	2	D	A*	B*	A*	B*	5
Rockhill *et al.*[46]	C	A*	C	2*	D	A*	B*	A*	B*	6
Lee and Paffenbarger[47]	C	A*	C	1.5*	D	A*	B*	A*	B*	6
Kujala *et al.*[48]	C	A*	C	1.5*	A*	A*	B*	A*	D	6
Villeneuve *et al.*[5]	B*	A*	C	0.5	C	B	B*	A*	D	4
Kushi *et al.*[50]	C	A*	C	0.5	D	A*	B*	A*	D	4
Leon *et al.*[49]	C	A*	C	2*	C	A*	B*	A*	A*	6
Kampert *et al.*[51]	C	A*	C	0	D	A*	B*	A*	D	4

Selection:
Representativeness of cohort—B*: somewhat representative of the general non-morbid population; C: selected group of users, e.g. nurses, volunteers.
Selection of the non-exposed cohort—A*: drawn from the same community as the exposed cohort. Ascertainment of exposure—B*: structured interview; C: written self report.
Outcome not present at start— >1*:cancer: 0.5 self recorded, 1 if clinical assessment; cardiovascular disease: 0.5 self recorded, 1 if clinical assessment; other serious condition: 0.5 self recorded, 1 if clinical assessment; additional 1 point awarded for other relevant exclusions.
Comparability:
Smoking—assessed four categories: A*: pack years and current smoking or excluding ever smokers; B*: quit length; C: never/past/current; D: yes/no.
Other—A*: Study stratifies or controls for important additional factors; B: study does not stratify or control for important additional factors.
Outcome:
Assessment of outcome—B*: Record linkage. **Follow-up length** (was follow-up long enough for outcomes to occur?) — A*: yes (minimum 2 years); B: no (<2 years).
Attrition—A*: complete follow up; B*: >95% follow up, or description provided of those lost; C: follow-up rate <95% and no description of those lost; D: no statement.

Assessment of physical activity

The studies used a range of methods to assess and then to combine physical activity (Table 3). Four studies[3,33,38,41] used an interview, whereas the rest used a self-completed questionnaire. Only one study included a repeat assessment of physical activity.[46]

Of the included studies, most looked at time or frequency of bouts of activity but 3 studies estimated total MET-hours over 24 h,[3,6,40] 3 presented results on walking alone,[34,38,47] 2 on active commuting,[44,45] 2 on cycling alone,[34,38] 1 on walking and cycling combined[34] and 11 included different kinds of activities measured by duration, frequency and intensity.[4,5,33,36,37,40,41,44,47,48,50,51,61] All but one[33] specifically mentioned walking (recorded as transport, work or leisure) in the interview or questionnaire. One study excluded non-brisk walking,[39] one study only included 'long walks'[50] and one study only included sessions of activity of ⩾30 min. Most studies specifically included cycling as a moderate intensity activity.

For all studies the median exposure in each category had to be estimated. In 20 studies the highest exposure category was defined as greater than a given value, with only two studies providing further information.[48,49] The highest exposure in our dataset was estimated to be 145 MET-h/week (equating to 32 h of moderate activity).[38]

Effect of non-vigorous physical activity on all-cause mortality

We first assessed possible non-linearity between non-vigorous physical activity as measured in MET-hours per week and all-cause mortality risk. We found that the power 0.25 model for physical activity, as measured in MET-hours/week, has a better fit (smaller AIC) compared with other power transformations as well as the simple linear trend (linear AIC 142.12, log AIC 40.40, power 0.75 AIC 94.86, power 0.5 AIC 49.69, power 0.375 AIC 36.45, power 0.25 AIC 35.69). The relationship is presented graphically in Figure 2.

Compared with inactive individuals (0 MET-h/week), 11 MET-h of non-vigorous physical activity per week (∼2.5 h/week) of moderate physical activity was associated with a 19% reduction in the mortality rate [95% CI 15–24, heterogeneity $Q = 196.77$, $I^2 = 85.8\%$]. Compared with inactive individuals, 31 MET-h/week, ∼7 h/week of light and moderate activity, was associated with 22% (95% CI 17–26) and 24% (95% CI 19–29) lower mortality rates respectively (see Supplementary Table 2 available as Supplementary data at *IJE* online).

Only 2[41,44] out of the 29 sets of RRs selected from 22 studies did not find a trend towards lower mortality with increased physical activity (Figure 3). The Egger's regression asymmetry test did not detect strong evidence of publication bias or small-study effects ($P = 0.053$), as shown in the funnel plot in Figure 4. In their most comprehensive assessment of physical activity, four studies provided estimates of exposure >67.5 MET-h (equivalent to 15 h/week of moderate intensity activity)[3,35,38,40] and three of these studies found increasing benefit at all levels of energy expenditure.

Walking and cycling

We identified five studies that provided estimates based on walking exposure alone,[34,38,43,46,47] and one that measured walking and standing time.[35] In the assessment of possible non-linearity, we found that the power 0.375 model for walking as measured in MET-hours per week, presented graphically in Figure 5, has a better fit compared with other power transformations as well as the simple linear trend (power 0.25 AIC –33.70, power 0.375 AIC –34.01, power 0.5 AIC –33.98, power 0.75 AIC –33.01, log AIC –33.78, linear AIC –31.05).

Compared with no walking per week, 2.5 h of brisk walking per week (∼11 MET-h/week) was associated with an RR of 0.89 (95% CI 0.82–0.96). Even among the estimates of walking alone, there remained considerable heterogeneity ($Q = 15.85$, P-heterogeneity = 0.003, $I^2 = 74.8\%$) (Figure 6).

The study of walking and standing found a similar effect to the studies specifically on walking (results not shown).[35] The two studies that provided estimates based on active commuting alone (excluding walking and cycling for other reasons)[44,45] did not find evidence of an effect. Of the two studies that provided point estimates specifically based on cycling,[34,38] one suggested a substantial benefit,[38] whereas the other found no evidence of an effect.[34]

Subgroup/sensitivity analyses

In all the following subgroup and sensitivity analyses we fitted a power 0.25 transformation of non–vigorous physical activity as measured in MET–hours/week. We found a larger effect in those studies that adjusted for more metabolic variables compared with those that adjusted for fewer metabolic variables (11 MET-h/week; RR 0.79 vs 0.83).

We found that excluding deaths that occurred soon after measurement of baseline data randomization had little effect on the results[33,43,50] (11 MET-h/week; RR 0.72 excluding early deaths vs RR 0.73 not excluding early deaths). We found a larger benefit in the higher quality studies (11 MET-h/week; RR 0.80 studies with six or more stars vs RR 0.83 studies with fewer than six stars). In one large study[39] a minimum threshold of moderate activity was set, excluding non-brisk walking and other light activities. In one other study only 'long walks' were included.[50] Excluding these studies did not change the size of the effect (11 MET-h/week; RR 0.81).

We next investigated if there was evidence of a difference in effect between men and women, using the seven studies that presented separate estimates for

Table 3 Physical activity assessment

Study	Physical activity domain	Physical activity measure	Assessment of physical activity	Walking specified/ minimum walking intensity	Physical activity other domains	Physical activity instrument name and validation	Questionnaire or examination
Hayasaka *et al.*[3]	All activities over 24 h	METs (quartiles)	Time spent in sleeping, working and in leisure with activities grouped into five exertion levels.	Yes/any	All included	Based on Framingham criteria	Face-to-face questionnaire
Arrieta and Russell[33]	Non-leisure	Qualitative (three bands)	'In your usual day, aside from recreation, are you physically very active, moderately active, or quite inactive?'	No/unclear	No adjustment	Not specified	Physician examination, laboratory tests, and medical history interview
Besson *et al.*[34]	Walking/ cycling	METs	• Inactive (0 MET-h/week) • Moderately inactive (0–2 MET-h/ week) • Moderately active (3–8 MET-h/week) • Active (⩾8 MET-h/week)	Yes/any	Adjusted for activity at home, for sport or exercise and at work	Study-specific plus EPAQ2 'EPAQ' was validated against repeated measures of free-living energy expenditure estimated from a 4-day individually calibrated minute-by-minute heart rate monitoring throughout the year suggesting that the questionnaire is valid for ranking individuals	Questionnaire and clinical visit
	Walking	Duration	• Non-walkers • Walking ⩽90 min/week • Walking >90 min/week	Yes/any	Adjusted for activity at home, for sport or exercise, at work and cycling		
	Cycling	Duration	• Non-cyclists • Cycling ⩽30 min/week • Cycling >30 min/week	NA	Adjusted for activity at home, for sport or exercise, at work and walking		
Ford *et al.*[37]	Exercise	Sessions/ intensity	• No physical activity or moderate 1/week • Moderate 2–4/week or vigorous 1–2/ week • Moderate 5–8/week or vigorous 3–5/ week • Moderate >8/week or vigorous >5/week	Yes/exercise	No adjustment	Adapted from 1980–89 Australian National Heart Foundation Risk Factor Prevalence Studies. Validation not mentioned	Mailed questionnaire
Inoue *et al.*[35]	Walking/ standing	Duration	• <1 h/day • 1–3 h/day • >3 h/day	Yes/standing included	Adjusted for heavy physical work or strenuous exercise, sedentary activities and leisure-time exercise	Not specified	Mailed questionnaire
Orsini *et al.*[6]	All activities over 24 h	METs (tertiles)	Five to six pre-defined activity levels for each of work, home, walking/cycling, inactive leisure time and exercising, plus time sleeping	Yes/any	Excluded manual workers	Not specified. 'The PA questions have been validated using two 7-day activity records that were performed 6 months apart in a group of Swedish men 44–78 years of age and were show to correlate with total PA (Spearman's rank correlation between the questionnaire and PA records was 0.6).'	Mailed questionnaire

(continued)

Table 3 Continued

Study	Physical activity domain	Physical activity measure	Assessment of physical activity	Walking specified/ minimum walking intensity	Physical activity other domains	Physical activity instrument name and validation	Questionnaire or examination
Pedersen *et al.*[36]	Leisure time (including commuting)	Duration/ intensity	• Almost entirely inactive or engaging in light physical activity <2 h/week • Light physical activity for 2–4 h/week (e.g. walking, cycling, light gardening, light physical exercise) • Light physical activity for >4 h/week or more vigorous activity for 2–4 h/week (e.g. brisk walking, fast cycling, heavy gardening) • Vigorous physical activity for >4 h/week	Yes/any	No adjustment	Saltin and Grimby[68]	Examination and self-administered questionnaire
Leitzmann *et al.*[39]	All	Duration	Activities of moderate intensity in banded hours per week	Yes/brisk walking	Adjusted for vigorous activity	'Contains important elements of the Physical Activity Scale for the Elderly (PASE), which showed an interclass correlation coefficient of 0.84 for two administrations of the questionnaire mailed 3–7 weeks apart and a correlation coefficient of 0.58 comparing activity energy expenditure as assessed by the questionnaire with that using the doubly labelled water method.'	Questionnaire
Matthews *et al.*[38]	Non-exercise	METs	Walking, cycling, household, stair climbing (walking = 3.3 METs, cycling 4.0 METs) • <9.9 • 10.0–13.6 • 13.7–18.0 • ⩾18.1	Yes/functional	Adjusted for other physical activity	Not specified. 'Spearman's correlations for each activity type, compared with repeated 7-day recalls obtained over 12 months, were as follows: adult exercise (r = –0.62); walking and cycling to and from work (r = 0.67 and 0.66, respectively); walking and cycling for other reasons (r = 0.33 and 0.66, respectively); stair climbing (r = 0.73); and household activities (r = 0.46).'	Interview
	Walking	METs	Walking but not for exercise • 0–3.4 METs/day • 3.5–7.0 METs/day • 7.1–10.0 METs/day • ⩾10.1 METs/day	Functional	Adjusted for other physical activity		
	Cycling	METs	Cycling but not for exercise • 0.00 METs/day • 0.1–3.4 METs/day • ⩾3.5 METs/day	NA	Adjusted for other physical activity		
Carlsson *et al.*[40]	All activities over 24 h	METs	Activities in banded hours per day: Household work, walking and bicycling, work, television watching and reading, exercise during leisure time, and open question on sleep	Yes/any	Not applicable	'Norman *et al*. indicated that the correlation between total daily activity score estimated from the questionnaire and from a 7-day activity record was 0.56 and that the reproducibility to a second questionnaire performed 6 months later was 0.65.'	Mailed questionnaire
Schooling *et al.*[41]	Leisure (retired)	Duration	• None • ⩽30 min/day	Yes/any	Not adjusted		Structured interviews

(continued)

Table 3 Continued

Study	Physical activity domain	Physical activity measure	Assessment of physical activity	Walking specified/ minimum walking intensity	Physical activity other domains	Physical activity instrument name and validation	Questionnaire or examination
			• >30 min/day >85% reported relatively low-intensity exercise such as stretching exercise, walking slowly or traditional Chinese exercises			Not specified, 'simple questions can maximize reliability and validity of physical activity assessment.'	and clinical examination
Trolle-Lagerros *et al.*[4]	All	Sessions	None: sedentary; moderate: e.g. a few walks a week; vigorous: e.g. sports/ jogging several times a week	Yes/any	Not adjusted	Not specified	Questionnaire
Barengo *et al.*[44]	Active commuting	Duration	• <15 min/day • 15–29 min/day • ⩾30 min/day	None	Adjusted and unadjusted presented	'Questions were similar to those used and validate in the Seven Countries Study.'	Questionnaire and clinical examination
Fujita *et al.*[43]	Walking	Duration	• ⩽0.5 h/day • 0.5–1 h/day • ⩾1 h/day	None	Not adjusted	106 people completed questionnaire 5 times and on the fourth time used a pedometer. Sex and age adjusted daily steps by category were 5857, 7047 and 7621	Questionnaire
Batty *et al.*[45]	Active commuting	Duration	• 0–9 min/day • 10–19 min/day • ⩾20 min/day	None	Not adjusted	Not stated	Questionnaire
Rockhill *et al.* [46]	Walking	Duration	• <1 h/week • 1–2.9 h/week • ⩾3 h/week	None	Not adjusted	Not stated	Questionnaire
Lee and Paffenbarger[47]	Walking	kJ/week	Summed energy expenditure from walking, stair climbing and sports/ recreation, kJ/week • <4200 • 4200 < 8400 • 8400 < 12600 • 12600<16800 • ⩾16800	Yes/all	Adjusted for other four components	Not specified. 'This activity assessment is reasonably reliable and valid; for example, for energy expenditure, the test-retest correlation over 1 month was 0.72, while the correlation for questionnaire estimates and estimates from activity records was 0.65.'	Questionnaire
Kujala *et al.*[48]	Leisure	Sessions/ intensity	• Sedentary: no leisure activity • Occasional: in between sedentary and conditioning • Conditioning: exercising 6 times a month for mean duration 30 min and at least vigorous walking	Yes/leisure only	No	Not specified	Mailed questionnaire
Villeneuve *et al.*[5]	Non-vigorous leisure and household chores	kcal/kg	Leisure time PA (including type, frequency, duration and intensity)	Yes/leisure only	People doing vigorous activity excluded	Modelled on Minnesota Leisure Time Physical Activity (MLTPA) Questionnaire	Questionnaire and clinical examination of 7916/14 442
Kushi *et al.*[50]	Moderate leisure	Sessions	'Aside from work or home, do you do anything daily that keeps you physically fit?' Separate questions on frequency of participation in moderate pa (e.g. bowling, golf, gardening or taking long walks)	Yes/long walks only	No	Not specified	Questionnaire

(continued)

Table 3 Continued

Study	Physical activity domain	Physical activity measure	Assessment of physical activity	Walking specified/ minimum walking intensity	Physical activity other domains	Physical activity instrument name and validation	Questionnaire or examination
			• Rarely/never • 1/week to few a month • 2–4/week • >4/week				
Leon *et al.* [49]	Leisure	Duration	• Mean minutes per day • 4.9 min/day leisure time pa (0–9 min) • 22.7 min/day (range 10–36 min) • 53.9 min/day (range 37–75 min/day) • 140.4 min/day (range 76–359 min/day)	Yes/all	No	MLTPA	Questionnaire and clinical examination
Kampert *et al.* [51]	Walking/ running	Distance	• Sedentary • 1–10 miles/week (or who participated in other sporting or leisure time activities) • 11–20 miles/week • 21–40 miles/week • ⩾40 miles/week	All	Not adjusted	Not specified	Questionnaire

mins = minutes; h = hours; EPAQ2 = EPIC physical activity questionnaire 2; EPIC = European prospective investigation into cancer study; NA = not applicable; PA = physical activity; MLTPA = Minnesota leisure time physical activity questionnaire.

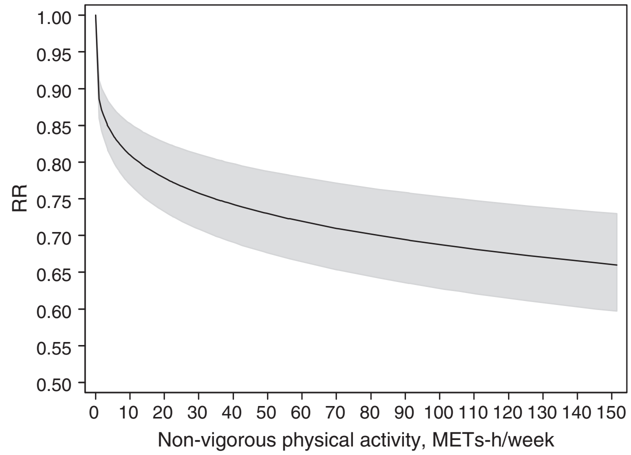

Figure 2 Association between MET-hours/week of non-vigorous physical activity and RR for all-cause mortality. In total, 29 estimates from 22 studies, 52 294 deaths, and 7 569 742 person years of follow-up, were taken. Data were fitted with a random-effect model including a power transformation of 0.25 for MET-hours/week. Shaded areas represent 95% CIs

both genders. We found a slightly larger effect in women than in men (11 MET-h/week; RR 0.85 for men and 0.83 for women). The effect in the group of studies that presented separate results by sex was smaller than in the overall analysis. We found little difference between the older studies compared with more recent studies (mid-year of study before 1991 RR 0.80 vs, mid-year of study post-1990 RR 0.81). We found a larger reduction in mortality from lower physical activity doses in adults aged ⩾65 years (11 MET-h/week; RR 0.78 for older adults vs 0.81 for younger adults).

Discussion

In the meta-analysis we found an inverse association between physical activity (measured as MET-hours/week) and the risk for all-cause mortality. This study is the first systematic review to estimate the dose–response effect of non-vigorous intensity physical activity on all-cause mortality. Based on these findings, in populations with low levels of activity 2.5 h/week of moderate intensity activity would reduce mortality by 19%. Increasing this to a 1 h session 7 days a week (7 h/week) of activity could increase the benefit to 24%. Evidence on the dose–response function allows estimation of the marginal benefits for groups with different levels of activity. Our analysis suggests a non-linear relationship with the greatest benefit appearing in the process of changing from a sedentary lifestyle to low levels of activity and smaller additional benefits from higher levels of activity. We found that walking reduces all-cause mortality but the effect was smaller than in studies that looked across activities in different domains.

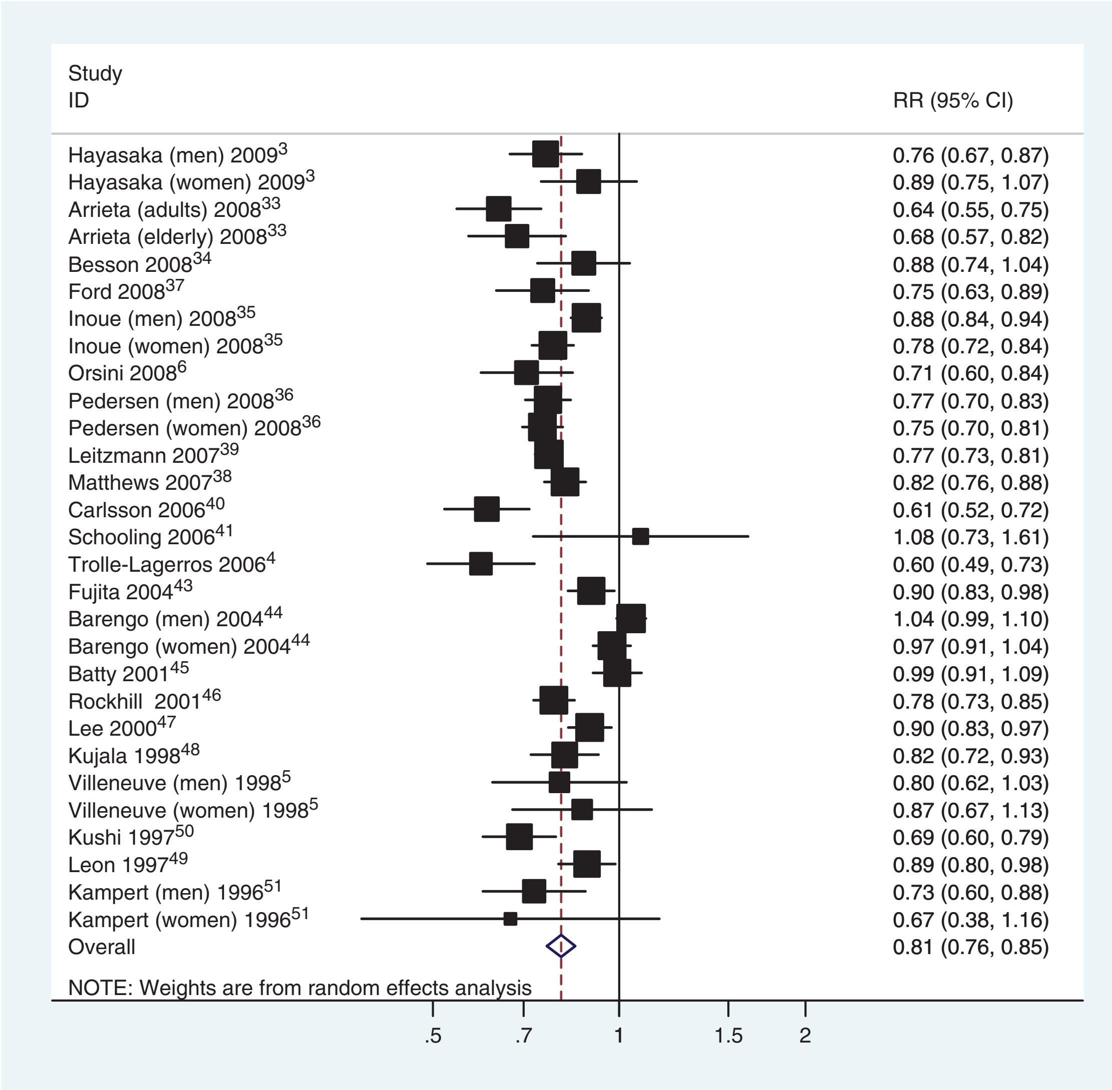

Figure 3 Adjusted RR of all-cause mortality for 11 vs 0 MET-h/week of moderate non-vigorous physical activity. The size of each square is proportional to the study's weight (inverse of variance). Data were fitted with a random-effect model including a power transformation of 0.25 for non-vigorous physical activity ($Q = 196.77$, $P < 0.001$, $I^2 = 86\%$)

Strengths and weaknesses

This systematic review benefits from the inclusion of large recently published cohort studies,[3,6,33–36] in total representing nearly 1 million people. We sought unbiased estimates from large studies and were not short of power for the overall analysis. The analyses included study populations from Europe, North America, East Asia and Australasia. However, the studies were highly heterogeneous in their methods and their findings.

There are a number of factors that may have led us to over- or underestimate the dose–response relationship. Reasons for overestimating the effect include any remaining publication bias or outcome reporting bias and residual confounding. Although all studies were adjusted for multiple potential confounders (see Table 1), there are likely to remain potentially important confounding differences (such as in dietary factors) between people with higher and lower levels of physical activity that could substantially affect the results. Reasons for underestimating the effect include the exclusion of people with existing disease, which might have been caused by lack of activity and misclassification of exposure, both at baseline and over time. Previous research has found a low to moderate correlation between self-reported and objectively measured physical activity,[62] and a larger effect on all-cause mortality from objectively measured physical fitness than recalled physical activity.[63] There is also a high probability of unrecorded change in exposure over time, given the length of follow up (25 years in the longest study[45]) and the lack of repeat measures of exposure.

These issues might not only affect the strength of association observed, but also the shape of the

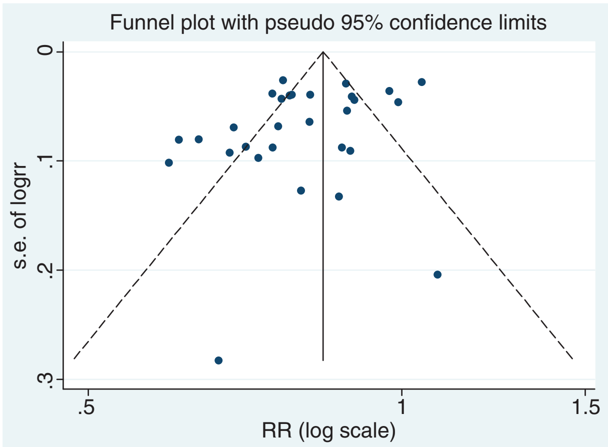

Figure 4 Funnel plot with pseudo 95% CIs for the association between 11 MET-h/week of non-vigorous physical activity and all-cause mortality in each of the studies. In total, 29 estimates were taken from 22 studies. Data were fitted with a power transformation of 0.25 for non-vigorous physical activity

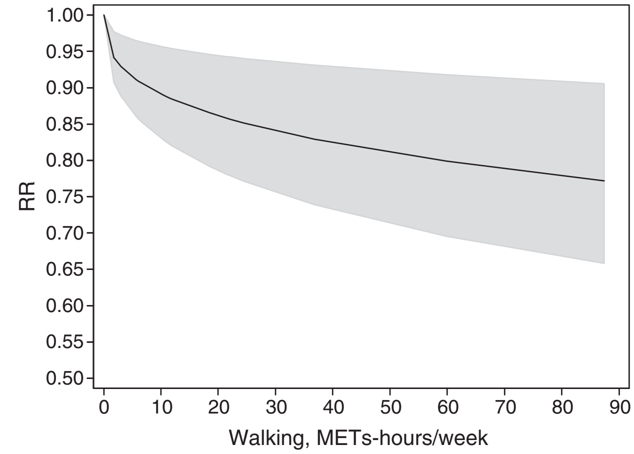

Figure 5 Association between MET-h/week of non-vigorous physical activity and adjusted RR for all-cause mortality in the studies of walking alone. In total, five estimates from five studies, 22 882 deaths and 1 581 769 person years of follow up, were taken. Shaded area represents 95% CIs. Data were fitted with a random-effects model including a power transformation of 0.375 for walking MET-hours/week

dose–response relationship, if confounding varied by exposure level. The small difference in the AIC result between the 0.25 power transformation and the 0.375 power exposure transformation models further limits our surety in the precise nature of the relationship.

Surprisingly, we found a larger effect in those studies that adjusted for more cardio-metabolic at baseline. This finding could indicate that the benefits of physical activity on mortality occur largely independent of the effect on metabolic variables. However, these could be confounding at the study level. We found only a slightly larger effect among women than men. This contrasts with a previous systematic review that found a notably larger effect in women.[63] Compared with that review our meta-analysis had the strength of only including studies that reported stratified results for men and women, which should have reduced the impact of study-level confounding.

Effect estimates from previous reviews

A recent systematic review (search date 2007) and meta-analysis, including studies with more than 5000 people, found a 29% reduction in all-cause mortality from self-reported physical activity, between the least and most active groups.[63] This review did not suggest the shape of the dose–response relationship. An earlier review proposed an inverse linear dose–response across studies but did not undertake a meta-analysis.[64] It suggested energy expenditure of ~4200 kJ/week would reduce mortality by 20–30%. A more recent review reporting median results suggested a curvilinear relationship.[65] It found an approximate reduction of 20% in the risk of all-cause mortality from 1.5 h/week of moderate to vigorous activity, and a further 20% reduction for 7 h of activity. Our results suggest a smaller benefit and a more clearly non-linear relationship than that identified by these earlier reviews. It is possible that these differences could be explained because the earlier reviews included smaller studies which found a larger effect. Alternatively, our selection of point estimates specifically relating to non-vigorous activities of daily living may have led to a smaller effect estimate.

Walking and cycling

We found a smaller effect in those studies that included walking alone. If the people in the walking studies were active in other domains then this smaller effect would be expected with a non-linear relationship between total physical activity and all-cause mortality. However, it could be the case that even within light and moderate activities, activities of greater intensity than walking may bring additional benefit beyond the increase in MET-hours. Furthermore, our confidence in the exact nature of the exposure–response relationship between walking and mortality is limited by the small differences in the AIC between the different exposure transformations.

One recent systematic review (search dates 2007)[66] looked at walking and all-cause mortality. It reported a 20% risk reduction for an estimated exposure approximately equivalent to 3 h/week at 3 km/h. This is notably larger than our observed association. However, their analysis combined results from studies comparing different walking speeds as well as different walking durations or distances.

We found limited evidence on cycling. Estimates from both the Matthews[38] study from China, which

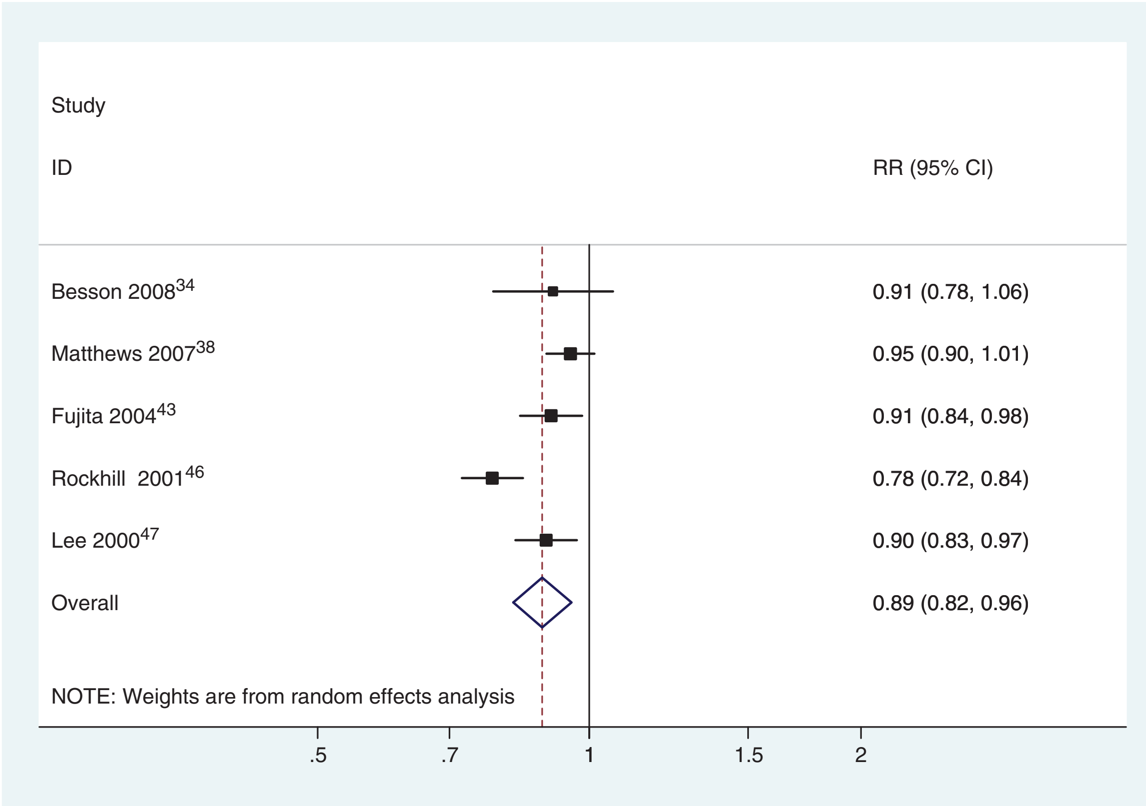

Figure 6 Adjusted RR of all-cause mortality for 11 vs 0 MET-h/week of walking. The size of each square is proportional to the study's weight (inverse of variance). Data were fitted with a random-effect model including a power transformation of 0.375 for walking MET-hours/week ($Q = 15.85$, $P = 0.003$, $I^2 = 75\%$)

found a large effect and the Besson study from England,[34] which found no evidence of an effect, came with considerable statistical uncertainty. The two studies of active commuting did not find evidence of an effect.[44,45] In the first study, the lack of association might be partly explained by the high levels of work-related activity amongst the study population. In the second study, the length of follow up, at 25 years, may have led to a high degree of misclassification of exposure over time. Cycling is usually categorized as more vigorous than walking,[8] and until more robust evidence is available, it may be reasonable to assume that the benefit is similar to the overall benefit from moderate intensity activity, if applied to a given baseline level of activity.

Future research

Further research should investigate how different approaches to increasing activity in one domain (such as walking) impacts on activities in other domains (such as leisure activity) and on other health behaviours, in particular diet and smoking.

The finding of a strongly non-linear relationship means that estimates of additional benefit from increasing activity will be strongly sensitive to assumptions on baseline activity levels. Health promotion recommendations for increasing moderate physical activity are primarily targeted at populations with low levels of vigorous activity. Although many of the studies included in our meta-analysis adjusted for vigorous activity, only one study[5] presented stratified results for people engaging and not engaging in vigorous physical activity. We recommend that future cohort investigators provide analyses stratified by time spent in vigorous activity, in addition to providing estimates controlling for other kinds of activity.

We recommend standardizing measures of physical activity, the most promising measure being the International Physical Activity Questionnaire.[67] We encourage cohort investigators[7] to report the information required for meta-analysis of the dose response; in particular, reporting the median exposure dose for each exposure interval not just the range.

Conclusion

Our systematic review and meta-analysis shows that non-vigorous physical activity has a dose–response protection effect against all-cause mortality. The largest benefit was found in moving from sedentary behaviour to low levels of activity, but even at high levels of activity benefits accrue from additional activity.

Supplementary data

Supplementary data are available at *IJE* online.

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Conflict of interest: None declared.

KEY MESSAGES

- Physical activity reduces mortality. The greater the amount of activity the larger the mortality reduction. The greatest mortality reduction from increasing physical activity is found amongst the least active.
- We found that populations with low levels of activity 2.5 h/week of moderate intensity activity would achieve a 19% reduction in mortality. Increasing this to a 1 h session 7 days a week (7 h/week) of activity might increase the benefit to 24%.
- We found substantial heterogeneity in the studies both in terms of measure of physical activity and results.

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