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

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## ABSTRACT

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

**Methods:** We aimed to include all cohort studies in adult populations with a sample size >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, including 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 hours per week (equivalent to 30 minutes 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% CI 15% to 24%), while 7 hours per week of moderate activity compared with no activity reduced the mortality risk by 24% (95% CI 19% to 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

- 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 hours per week of moderate intensity activity would achieve a 19% reduction in mortality. Increasing this to one-hour session seven days a week (7 hours per 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.

**Introduction**

Non-vigorous physical activity is a central focus of health promotion.<sup>1-2</sup> 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.<sup>3-6</sup> We aimed to quantify and characterise the nature of the association between non-vigorous physical activity and all-cause mortality.<sup>7</sup>

Active travel is frequently recommended as a way to increase physical activity; and walking is the most popular form of physical activity.<sup>1</sup> Therefore, in addition to studies looking at multiple aspects of non-vigorous activity we looked for studies that estimated the exclusive effect 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 1) prospective cohort study in a healthy/general population with more than 10,000 people at baseline; 2) measure of light or moderate physical activity (either in terms of duration, frequency, distance or a combination); 3) association with all cause mortality. We excluded studies that only measured work related activity. We only included studies of physical activity not physical fitness. We only included studies that compared more than two exposure levels.

**Search strategy**

We searched Medline, Embase, Cochrane (DARE), Web of Science, 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 "On line Appendix: Search strategy". Mesh headings included, "Exercise", "Exercise Therapy", "Physical Fitness", and "Exertion". We

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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 of February 2009 for unpublished studies. All remaining references were assessed by two independent reviewers (JW and OHF) and any disagreements 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 exclusively of walking or cycling. If multiple publications were available on the same cohort 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, combining both intensity and duration of activity. The intensity of activities can be categorised according to subjective exertion or with a fixed measure for each activity, usually measured as METs (Metabolic Equivalent Tasks). A MET is a unit of energy expenditure adjusted for mass, with the reference category of 1 MET being the typical energy expenditure of an individual at rest, (4.18 kilojoules/kilogram/hour).<sup>8</sup> Activities below 6 METs are generally defined as moderate and those below 3 METs as light for adults under 65 years.<sup>2</sup> The intensity of selected activities were based on the compendium of physical activities from Ainsworth 2000.<sup>8</sup> We did not include study results based on activities of greater intensity than 6 METs. Time spent in activities of different intensity over a week can be combined to give an estimate of total MET hours per week. The measure of MET hours per week incorporates both the intensity and the total time per week spent on physical activity.

**Quality assessment**

We assessed the quality of the studies using the Newcastle Ottawa Scale.<sup>9</sup> 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<sup>10</sup>, 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.<sup>11-</sup>

<sup>12</sup> This method allows estimation of the dose response gradient of mortality risk across studies taking into account non-independent relative risks presented within a single study. For each study we assigned the midpoint of each exposure interval as the median dose corresponding to the relative risk. 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<sup>8</sup> that 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 a number of sessions an average duration of 0.5 hours 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 data available and calibrated all other estimates to this. If the reference category was high activity we used the method suggested by Hamling<sup>13</sup> to convert the reference category to the lowest exposure category. If information on person-years of follow-up and deaths per group were 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.<sup>14</sup> Small study effects were assessed by the Egger's regression asymmetry test<sup>15</sup> 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 per week).<sup>16</sup> We used the Akaike's information criterion (AIC, a summary measure that combine fit and complexity) to choose the model that best (lowest AIC value) fitted the data.<sup>17</sup>

### **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 to 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 2-sided.

Results

Search results

We retrieved 6210 records. Initial screening of title and abstract excluded 5725, see Figure 1. No additional reports were retrieved from searching reference lists. We identified one additional report from personal communication.<sup>18</sup> We retrieved 42 reports for further inspection. We excluded 13 reports on examination of full text, including three for not assessing the exposure and outcome in at least 10,000 participants,<sup>19-23</sup> five for not providing an estimate for non-vigorous activity<sup>24-28</sup>, three for not reporting on all-cause mortality<sup>29-31</sup>, and one for only comparing two exposure levels<sup>32</sup>. Contact with one author produced additional data on hazard ratios for physical activity categories.<sup>6</sup>

Table 1 presents the characteristics of the 22 independent studies<sup>3-6, 33-51</sup> reported in 30 reports.<sup>18, 52-58</sup> The studies included nearly 1 million participants (977,925), with more women (643,187) than men (334,738). The cohort studies were conducted in Europe (8 studies), North America (8 studies), East Asia (5 studies), and Australasia (1 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, see Table 1. Mean age at baseline ranged from 38<sup>48</sup> to 72<sup>41</sup>. Estimated exposure in the studies and the associated relative risks and CIs are presented in web only Table 2.

Quality

Out of a maximum of 9 stars, we found that the median and mean number of stars awarded to a study was 6. The highest score was 8 stars (2 studies<sup>3, 37</sup>) and the lowest score was 4 stars (3 studies<sup>40, 50-51</sup>) (Table 3).

The majority of the included studies were of the general population of men or women from a geographically defined area<sup>3-6, 33-39, 59-60</sup> and all selected controls from the same population. Most studies excluded or adjusted 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 (7 studies<sup>3, 33, 38, 40-41, 50-51</sup>) to current smoking status plus pack years<sup>4, 6, 48</sup>. Three studies presented equivalent data suitable for inclusion both with and without exclusion of deaths in the first years.<sup>33, 43, 50</sup> Four studies only provided suitable data after excluding deaths that occurred soon after measurement of baseline data<sup>6, 40, 46, 48</sup>, four studies said excluding such deaths did not substantially alter the effect estimate but did not provide the numbers.<sup>4, 36, 38-39</sup>. Six studies adjusted for physical activity in other domains.<sup>34-35, 38-39, 44, 47</sup>

Assessment of physical activity

The studies used a range of methods to assess and then to combine physical activity (Table 4). Four studies<sup>3, 33, 38, 41</sup> used an interview, while the rest used a self-completed questionnaire. Only one study included a repeat assessment of physical activity.<sup>46</sup>

Of the included studies most looked at time or frequency of bouts of activity but three studies estimated total MET hours over 24 hrs<sup>3, 6, 40</sup>, three presented results on walking alone<sup>34, 38, 47</sup>, two on active commuting<sup>44-45</sup>, two on cycling alone<sup>34, 38</sup>, one on walking and cycling combined<sup>34</sup> and 11 included different kinds of activities measured by duration, frequency and intensity<sup>4-5, 33, 36-37, 40-41, 44, 47-48, 50-51, 61</sup>. All but one<sup>33</sup> specifically mentioned walking (recorded as either transport, work or leisure). One study excluded non-brisk



walking<sup>39</sup>, one study only included 'long walks'<sup>50</sup> and one study only included sessions of activity of a least 30 minutes. 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 more information.<sup>48-49</sup> The highest exposure in our dataset was estimated to be 145 MET hours/wk (equating to 32 hours of moderate activity).<sup>38</sup>

## 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 (0 MET-hours/week) individuals 11 MET hours of non-vigorous physical activity per week (about 2.5 hours per week) of moderate physical activity was associated with a 19% reduction in the mortality rate (95% CI 15 to 24%, heterogeneity  $Q = 196.77$ ,  $I^2 = 85.8\%$ ). Compared with inactive individuals 31 MET hours per week, about 7 hours per week of light and moderate activity, was associated with 22% (95% CI 17 to 26%) and 24% (95% CI 19 to 29%) lower mortality rates respectively (see web-only Table 5).

Only three<sup>41, 44-45</sup> out of the 29 sets of relative risks arising 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 higher than 67.5 MET hours (equivalent to 15 h/wk of moderate intensity activity)<sup>3, 35, 38, 40</sup> 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<sup>34, 38, 43, 46-47</sup>, and one that measured walking and standing time.<sup>35</sup> 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 hour of brisk walking per week (approximately 11 MET hours per week) was associated with a  $RR=0.89$  (95% CI 0.82 to 0.96). Even among the estimates that of walking alone there remained considerable heterogeneity ( $Q = 15.85$ ,  $P$ -heterogeneity = 0.003,  $I^2 = 74.8\%$ ), see Figure 6.

The study of walking and standing found a similar effect to the studies specifically on walking (results not shown)<sup>35</sup>. The two studies that provided estimates based on active commuting alone (excluding walking and cycling for other reasons)<sup>44-45</sup> did not find evidence of an



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effect. Of the two studies that provided point estimates specifically based on cycling<sup>34, 38</sup>, one suggested a substantial benefit<sup>38</sup>, while the other found no evidence of an effect.<sup>34</sup>

**Subgroup/Sensitivity analyses**

In all the following subgroup and sensitivity analyses we fitted a power 0.25 transformation of the exposure variable. 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 hours per week RR 0.79 vs RR 0.83).

We found that excluding deaths that occurred soon after measurement of baseline data randomisation had little effect on the results<sup>33, 43, 50</sup> (11 MET hours/wk 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 hours p/wk RR 0.80 studies with ≥6 stars vs RR 0.83 studies with <6 stars). In one large study<sup>39</sup> 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.<sup>50</sup> Excluding these studies did not change the size of the effect (11 MET hours/wk 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 both sexes. We found a slightly larger effect in women than in men (11 MET hours/wk 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 pre 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 and older (11 MET hours/wk 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) 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 hours per week of moderate intensity activity would reduce mortality by 19%. Increasing this to one hour session seven days a week (7 hours per 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.

**Strengths and weaknesses**

This systematic review benefits from the inclusion of large recently published cohort studies,<sup>3, 6, 33-36</sup> 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 to us over or under estimating the dose response relationship. Reasons for over-estimating the effect include any remaining

publication bias or outcome reporting bias and residual confounding. Although all the studies 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 under-estimating 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,<sup>62</sup> and a larger effect on all-cause mortality from objectively measured physical fitness than recalled physical activity.<sup>63</sup> There is also a high probability of unrecorded change in exposure over time, given the length of follow up (25 year in the longest study<sup>45</sup>) and the lack of repeat measures of exposure. These issues might not just affect the strength of association observed but also the shape of the dose response relationship. The small difference in the AIC result between the 0.25 power transformation and the 0.375 power exposure transformation models, further limits our confidence 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, there could be confounding at the study level. We only found a slightly larger effect in women than among men. This contrasts with a previous systematic review that found a notably larger effect in women.<sup>63</sup> Compared with this review our meta-analysis had the strength of only including studies that reported stratified results for men and for women, which should reduce 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.<sup>63</sup> 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.<sup>64</sup> It suggested energy expenditure of about 4200 kilojoules per week would reduce mortality by 20 to 30%. A more recent review reporting median results suggested a curvilinear relationship.<sup>65</sup> It found an approximate reduction of 20% in the risk of all cause mortality from 1.5 hours per week of moderate to vigorous activity, and a further 20% reduction for 7 hours 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 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.

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One recent systematic review (search dates 2007)<sup>66</sup> looked at walking and all-cause mortality. It reported a 20% risk reduction for an estimated exposure approximately equivalent to 3 hours per week at 3 km per hour. 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<sup>38</sup> study from China, which found a large effect, and the Besson study from England<sup>34</sup>, which found no evidence of an effect, both came with considerable statistical uncertainty. The two studies of active commuting did not find evidence of an effect in men.<sup>44-45</sup> 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 categorised as more vigorous than walking<sup>8</sup> and, until more robust evidence is available, it may be reasonable to assume 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 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<sup>5</sup> 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 standardising measures of physical activity, the most promising measure being the International Physical Activity Questionnaire.<sup>67</sup> We encourage cohort investigators<sup>7</sup> 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.

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Table 1: Summary of studies

Author	Study name	Follow up length	Number in cohort	Sex	Age at baseline (years)	Adjustments
Hayasaka 2009 (3)	Jichi Medical School Cohort Study, Japan	12 years	10,831	F/M	Mean 55	Age, area, BMI, systolic blood pressure, and total cholesterol. Smoking: yes/ no
Arrieta 2008 (33)	NHANES I (NHEFS for follow up), USA	20 years	10,474	F/M	35 to 74	Age (years), female, black race, smoking, BMI, systolic blood pressure, total cholesterol, education and chronic conditions. Smoking: yes/no
Besson 2008 (34)	European Prospective Investigation into Cancer in Norfolk , UK	7 years	14,903	F/M	49 to 83	Age, sex, social class, alcohol consumption, diabetes, cancer, cardiovascular disease, and stroke. Smoking: never, former, current
Ford 2008 (37)	Australian Longitudinal Study on Women's Health	9 years	12,422	F	70 to 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 Age (5-year age categories), area, occupation, diabetes, alcohol intake status , BMI (3 groups), and total energy intake
Inoue 2008 (35)	Japan Public Health Center-based Prospective Study, Japan	Mean 8. 7 years	83,034	F/M	45 to 74	Smoking: never, former, current.
Orsini 2008 (6)	Cohort of Swedish Men, Sweden	9.7 years	37,633	M	45 to 79	Age, alcohol consumption, educational level, parental history of coronary heart disease and cancer. Excluded current & former smokers.
Pedersen 2008 (36)	Copenhagen City Heart study, Denmark	>= 11 years	11 ,914	F/M	>= 20	Age, BMI, education, marital status, known diabetes, and alcohol intake. Smoking: never, former, 1-14 g/d, >14 g/d



Leitzmann 2007 (39)	National Institutes of Health- American Association of Retired Persons Diet and Health Study, USA	Around 5 years	252,925	F/M	50 to 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/d, past >=20/d, current 1-19/d, current >-20/d
Matthews 2007 (38)	Shanghai Women's Health Study, China	Mean 5.7 years.	67,143	F	40 to 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 & hypertension). Smoking: never, ever
Carlsson 2006 (40)	Swedish Mammography Cohort, Sweden	5 years	27,734	F	51 to 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
Schooling 2006 (41)	Hong Kong, China	Average 4.1 years	54,088	F/M	>=65	Age, sex, socioeconomic status, ever use of alcohol. Smoking: ever, never
Trolle- Lagerros 2006 (4)	Women's Lifestyle and Health cohort, Norway and Sweden	Average 11.4 years	99,099	F	30 to 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 2004 (43)	Miyagi, Japan	11 years	41,163	F/M	40 to 64	Age, education, marital status, past history of diseases, drinking, BMI (grouped), and dietary variables. Smoking: never, former, current 1-19/d, >20/d

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Barengo 2004 (44)	North Karelia project & FINMONICA/ Finrisk studies, Finland	20 years	32,677	F/M	30 to 59 years	Age, study year, BMI, systolic blood pressure, cholesterol, and education. Work and leisure physical activity. Smoking: never, former, current
Batty 2001 (45)	Whitehall Study, UK	25 years	12,552	M	40 to 64	Age, employment grade, systolic blood pressure, cholesterol, BMI, glucose intolerance, FEV1. Smoking: yes, no
Rockhill 2001 (46)	Nurses' Health Study, USA	16 years	80,348	F	34 to 59 years	Age, sex, socioeconomic status, ever use of alcohol. Smoking: ever, never
Lee 2000 (47)	Harvard Alumni Health Study, USA	15 years	13,485	M	Mean age, 57.5	Age, BMI, alcohol intake, and early parental death. Smoking: no, current 1-20/d, current >20/d
Kujala 1998 (48)	Finnish Twin Cohort	17 years	15,902	F/M	25 to 64	Age, sex, occupational group, alcohol use. Smoking: pack years/ yes, no
Villeneuve 1998 (5)	Canada Fitness Survey	7 years	14,442	F/M	20 to 69	Age. Smoking: never, former, current
Kushi 1997 (50)	MRFIT, USA	16 years	12,138	M	35 to 57	Age, intervention group, years of education, serum cholesterol, diastolic blood pressure, and BMI. Smoking: cigarettes/d
Leon 1997 (49)	Iowa Women's Health Study, USA	7 years	40, 417	F	55 to 69	Age, age at menarche, age at menopause, age at first live birth, parity, alcohol & energy intake, estrogen use, BMI, first degree relative with cancer, high blood pressure, diabetes, education, marital status. Smoking: yes/no
Kampert 1996 (51)	Texas, USA	Average 8 years	29,903	F/M	20 to 88	Age, examination year, chronic illnesses, and electrocardiogram abnormalities. Smoking: yes/no

**Web Table 2: Strength of association in each study used in the main analysis**

Author	Study name	Exposure (METs/wk) RR (95% confidence interval)					
Hayasaka 2009 (3)	Jichi Medical School Cohort Study, Japan	Exposure	0.0	36.4	70.0	101.3	
		RR (men)	1.0	0.69 (0.55-0.88)	0.59 (0.45-0.76)	0.75 (0.55-1.04)	
		RR (women)	1.0	0.79 (0.58-1.08)	0.90 (0.66-1.22)	0.83 (0.59-1.16)	
Arrieta 2008 (33)	NHANES I (NHEFS for follow up), USA	Adults Exposure	0.0	13.5	27		
		RR	1.0	0.67 (0.54-0.83)	0.57 (0.47-0.69)		
		Elderly Exposure	0.0	10.5	21		
		RR	1.0	0.72(0.58-0.89)	0.63 (0.51-0.78)		
Besson 2008 (34)	European Prospective Investigation into Cancer in Norfolk , UK	Exposure	0.0	1.8	5.5	13.8	
		RR	1.0	0.96 (0.79-1.17)	0.99 (0.82-1.21)	0.82 (0.67-1.0)	
Ford 2008 (37)	Australian Longitudinal Study on Women's Health	Exposure	1.1	6.8	14.6	25.1	
		RR	1.0	0.86 (0.7-1.05)	0.69 (0.55-0.86)	0.70(0.53-0.91)	
Inoue 2008 (35)	Japan Public Health Center-based Prospective Study, Japan	Men Exposure	7.0	27.0	91.4		
		RR	1.0	0.90 (0.81-0.99)	0.80 (0.73-0.88)		
		Women Exposure	7.0	27.0	105.7		
		RR	1.0	0.86 (0.74-0.99)	0.64 (0.55-0.73)		
Orsini 2008 (6)	Cohort of Swedish Men, Sweden	Exposure	3.6	6.6	9.7		
		RR	1.0	0.83 (0.69-0.99)	0.63 (0.51-0.77)		
Pedersen 2008 (36)	Copenhagen City Heart study,	Men	3.5	10.5	18.4		

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	Denmark	Exposure					
		RR	1.0	0.79 (0.72-0.88)	0.73 (0.66-0.81)		
		Women					
		Exposure	3.5	10.5	18.4		
Leitzmann 2007 (39)	National Institutes of Health-American Association of Retired Persons Diet and Health Study, USA	RR	1.0	0.74 (0.68-0.81)	0.75 (0.68-0.83)		
		Exposure	0.0	3.4	9.0	24.8	40.6
		RR	1.0	0.85 (0.79-0.93)	0.79 (0.74-0.85)	0.76 (0.71-0.82)	0.68 (0.63-0.74)
		Exposure	34.7	82.3	110.6	145.4	
Matthews 2007 (38)	Shanghai Women's Health Study, China	RR	1.0	0.81 (0.69-0.94)	0.63 (0.53-0.75)	0.66 (0.55-0.79)	
Carlsson 2006 (40)	Swedish Mammography Cohort, Sweden	Exposure	0.0	56	91	126	151.4
		RR	1.0	0.49 (0.32-0.76)	0.43 (0.28-0.65)	0.41 (0.27-0.65)	0.39 (0.28-0.54)
Schooling 2006 (41)	Hong Kong, China	Exposure	0.0	7.0	37.6		
		RR	1.0	1.24 (0.71-2.19)	1.15 (0.66-1.99)		
Trolle-Lagerros 2006 (4)	Women's Lifestyle and Health cohort, Norway and Sweden	Exposure	0.0	3.5	7.0	22.5	35.0
		RR	1.0	0.78 (0.61-1.00)	0.62 (0.49-0.78)	0.58 (0.44-0.75)	0.46 (0.33-0.65)
Barengo 2004 (44)	Miyagi, Japan	Exposure	6.1	18.4	24.5		
		RR	1.0	0.91 (0.84-1.07)	0.86 (0.77-0.96)		
Fujita 2004 (43)	North Karelia project & FINMONICA/ Finrisk studies, Finland	Men	3.4	10.3	38.5		
		Exposure					
		RR	1.0	1.01 (0.92-1.11)	1.07 (0.98-1.17)		
		Women	3.4	10.3	38.5		
Batty 2001 (45)	Whitehall Study, UK	Exposure	4.1	8.7	12.8		
		RR	1.0	0.98 (0.89-1.09)	1.0 (0.90-1.11)		
Rockhill 2001 (46)	Nurses' Health Study, USA	Exposure	1.8	6.8	10.5		
		RR	1.0	0.81 (0.70-0.88)	0.79 (0.75-0.89)		
Lee 2000 (47)	Harvard Alumni Health Study, USA	Exposure	1.9	5.6	11.3		

		RR	1.0	0.91 (0.82-1.02)	0.92 (0.83-1.01)	21.6 (0.84-0.75)	
Kujala 1998 (48)	Finnish Twin Cohort	Exposure	3.5	14	49		
		RR	1.0	0.80 (0.69-0.91)	0.76 (0.59-0.76)		
Villeneuve 1998 (5)	Canada Fitness Survey	Men					
		Exposure	1.8	7	15.8	30.4	
		RR	1.0	0.97 (0.69-1.36)	0.87 (0.57-1.33)	0.72 (0.43-1.21)	
		Women					
		Exposure	1.8	7	15.8	30.4	
		RR	1.0	0.81 (0.56-1.17)	0.70 (0.44-1.13)	0.82 (0.53-1.27)	
Kushi 1997 (50)	MRFIT, USA	RR	1.8	9.5	22.8	49.7	
		Exposure	1.0	0.85 (0.73-0.99)	0.87 (0.75-1.02)	0.83 (0.71-0.97)	
Leon 1997 (49)	Iowa Women's Health Study, USA	RR	0	2.3	6.8	23.1	
		Exposure	1.0	0.73 (0.62-0.84)	0.68 (0.58-0.80)	0.67 (0.56-0.80)	
Kampert 1996 (51)	Texas, USA	Men					
		Exposure	0	6.6	18.6	36.6	56.5
		RR	1.0	0.71 (0.58-0.87)	0.83 (0.59-1.16)	0.57 (0.30-1.08)	0.92 (0.29-2.88)
		Women	0	6.6	18.6	28.9	
		Exposure					
		RR	1.0	0.68 (0.39-1.17)	0.39 (0.09-1.65)	1.14 (0.27-4.80)	

Table 3: Quality

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 >1 scores *	Smoking	Other	Assessment	Follow up length	Attrition	

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Hayasaka 2009 (3)	B*	A*	B*	2*	D	A*	B*	A*	B*	8
Arrieta 2008 (33)	B*	A*	B*	0	D	A*	B*	A*	B*	7
Besson 2008 (34)	B*	A*	C	0	C	A*	B*	A*	B*	6
Ford 2008 (37)	B*	A*	C	2*	B*	A*	B*	A*	B*	8
Inoue 2008 (35)	B*	A*	C	1	D	A*	B*	A*	B*	7
Orsini 2008 (6)	B*	A*	C	2*	A*	A*	B*	A*	D	7
Pedersen 2008 (36)	B*	A*	C	1	C	A*	B*	A*	B*	6
Leitzmann 2007 (39)	B*	A*	C	1.5*	C	A*	B*	A*	C	6
Matthews 2007 (38)	B*	A*	B*	1	D	A*	B*	A*	B*	7
Carlsson 2006 (40)	C	A*	C	0	D	A*	B*	A*	D	4
Schooling 2006 (41)	B*	A*	C	2*	D	A*	B*	A*	D	6
Trolle-Lagerros 2006 (4)	B*	A*	C	1	A*	A*	B*	A*	B*	7
Barengo 2004 (44)	B*	A*	C	2*	D	A*	B*	A*	D	6
Fujita 2004 (43)	B*	A*	C	1	C	A*	B*	A*	B*	6
Batty 2001 (45)	C	A*	C	2	D	A*	B*	A*	B*	5
Rockhill 2001 (46)	C	A*	C	2*	D	A*	B*	A*	B*	6
Lee 2000 (47)	C	A*	C	1.5*	D	A*	B*	A*	B*	6
Kujala 1998 (48)	C	A*	C	1.5*	A*	A*	B*	A*	D	6
Villeneuve 1998 (5)	B*	A*	C	0.5	C	A*	B*	A*	D	5
Kushi 1997 (50)	C	A*	C	0.5	D	A*	B*	A*	D	4
Leon 1997 (49)	C	A*	C	2*	C	A*	B*	A*	A*	6
Kampert 1996 (51)	C	A*	C	0	D	A*	B*	A*	D	4

<b>Representativeness of cohort:</b>
B* Somewhat representative of the general non-morbid population
C Selected group of users e.g., nurses, volunteers
<b>Selection of the non exposed cohort</b>
A* Drawn from the same community as the exposed cohort
<b>Ascertainment of exposure</b>
B* Structured interview

C	Written self report
<b>Outcome not present at start</b>	
Cancer	0.5 self recorded, 1 if clinical assessment
CVD	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	
<b>Comparability</b>	
<b>Smoking assessed 4 categories:</b>	
A*	Pack years & current smoking or excluding ever smokers
B*	Quit length
C	Never/past/current
D	Yes/no
<b>Other</b>	
A*	Study controls for important other additional factors
<b>Outcome</b>	
Assessment of outcome	
B*	Record linkage
<b>Was follow-up long enough for outcomes to occur?</b>	
A*	Yes (minimum 2 years)
B	No (less than 2 years)
<b>Adequacy of follow up of cohorts</b>	
A*	Complete follow up - all subjects accounted for
B*	Participants lost to follow up unlikely to introduce bias : > 95 % follow up, or description provided of those lost
C	Follow up rate < 95% and no description of those lost
D	No statement



Table 4: Physical activity assessment							
Study	Physical activity domain	Physical activity metric	Assessment of physical activity	Walking specified / minimum walking intensity	Physical activity other domains	Physical activity instrument name and validation	Questionnaire or examination
Hayasaka 2009 (3)	All (24 hours)	METs (quartiles)	Time spent sleeping, working and in leisure with activities grouped into 5 exertion levels.	Yes/any	All included	Based on Framingham criteria	Face to face questionnaire
Arrieta 2008 (33)	Non-leisure	Qualitative (3 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, lab tests, and medical history interview
Besson 2008 (34)	Walking/ cycling	METs	<ul style="list-style-type: none"><li>Inactive (0 MET h/wk)</li><li>Moderately inactive (0 – MET h/wk)</li><li>Moderately active (3-8 MET h/wk)</li><li>Active (&gt;=8 MET h/wk)</li></ul>	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-d 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	Hours	<ul style="list-style-type: none"><li>Non-walkers</li><li>Walking &lt;= 90 m/wk</li><li>Walking &gt;90 m/wk</li></ul>	Yes/any	Adjusted for activity at home, for sport or exercise, at work and cycling.		
	Cycling	Hours	<ul style="list-style-type: none"><li>Non-cyclists</li><li>Cycling &lt;= 30 m/wk</li><li>Cycling &gt;30 m/wk</li></ul>	NA	Adjusted for activity at home, for sport or exercise, at work and cycling.		

Ford 2008 (37)	Exercise	Sessions/intensity	<ul style="list-style-type: none"> <li>No physical activity or moderate 1 per wk</li> <li>Moderate 2-4 per wk or vigorous 1-2 per wk</li> <li>Moderate 5-8 per wk or vigorous 3-5 per wk</li> <li>Moderate 8+ per wk or vigorous 5+ per wk</li> </ul>	Yes/Exercise	No adjustment	Adapted from 1980-89 Australian National Heart Foundation Risk Factor Prevalence Studies. Validation not mentioned	Mailed questionnaire
Inoue 2008 (35)	Walking/standing	Hours	<ul style="list-style-type: none"> <li>&lt;1 h/d</li> <li>1-3 h/d</li> <li>&gt;3 h/d</li> </ul>	Yes/standing included	Adjusted for heavy physical work or strenuous exercise, sedentary activities and leisure-time exercise	Not specified	Mailed questionnaire
Orsini 2008 (6)	All (24 hours)	METs (tertiles)	Five to six pre-defined activity levels for each of work, home, walking/bicycling, 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 shown to correlate with total PA (Spearman's rank correlation between the questionnaire and PA records was 0.6)."	Mailed questionnaire
Pedersen 2008 (36)	Leisure time (including commuting)	Hours/intensity	<ul style="list-style-type: none"> <li>Almost entirely inactive or engaging in light physical activity &lt;2 h/wk</li> <li>Light physical activity for 2-4 h/wk (e.g. walking, cycling, light gardening, light physical exercise)</li> <li>Light physical activity for &gt;4</li> </ul>	Yes/ Any	No adjustment	Saltin & Grimby 1968	Examination & self administered questionnaire

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			<p>h per week or more vigorous activity for 2–4 h/wk (e.g. brisk walking, fast cycling, heavy gardening)</p> <ul style="list-style-type: none"><li>• Vigorous physical activity for &gt;4 h/wk</li></ul>				
Leitzmann 2007 (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 2 administrations of the questionnaire mailed 3 to 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 2007 (38)	Non-exercise	METs	Walking, cycling, household, stair climbing (walking = 3.3 METs, cycling 4.0 METs) <ul style="list-style-type: none"><li>• &lt;9.9</li><li>• 10.0 to 13.6</li><li>• 13.7 to 18.0</li><li>• &gt;=18.1</li></ul>	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=-.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 <ul style="list-style-type: none"><li>• 0 to 3.4</li><li>• 3.5 to 7.0</li><li>• 7.1 to 10.0</li><li>• &gt;=10.1</li></ul>	Functional	Adjusted for other physical activity		
	Cycling	METs	Cycling but not for exercise <ul style="list-style-type: none"><li>• 0</li></ul>	NA	Adjusted for other physical activity		

			<ul style="list-style-type: none"> <li>• 0.1 to 3.4</li> <li>• <math>\geq 3.5</math></li> </ul>				
Carlsson 2006 (40)	All (24 hours)	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 seven-day activity record was 0.56 and that the reproducibility to a second questionnaire performed six months later was 0.65."	Mailed questionnaire
Schooling 2006 (41)	Leisure (retired)	Duration	i. None ii. $\leq 30$ min per day iii. $> 30$ min per day $> 85\%$ reported relatively low-intensity exercise such as stretching exercise, walking slowly, or traditional Chinese exercises	Yes/ Any	Not adjusted	Not specified, "simple questions can maximise reliability and validity of physical activity assessment."	Structured interviews and clinical examination
Trolle-Lagerros 2006 (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 2004 (44)	Active commuting	Duration	<ul style="list-style-type: none"> <li>• <math>&lt; 15</math> min/d</li> <li>• 15 to 29 min/d</li> <li>• <math>\geq 30</math> min/d</li> </ul>	None	Adjusted & unadjusted presented	"questions were similar to those used and validate in the 'Seven Countries Study'.	Questionnaire and clinical examination
Fujita 2004 (43)	Walking	Duration	<ul style="list-style-type: none"> <li>• <math>\leq 0.5</math> h/d</li> <li>• 0.5 to 1 h/d</li> <li>• <math>\geq 1</math> h/d</li> </ul>	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	Questionnaire

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Batty 2001 (45)	Active commuting	Duration	<ul style="list-style-type: none"><li>• 0-9 min/d</li><li>• 10-19 min/d</li><li>• &gt;=20 min/d</li></ul>	None	Not adjusted	Not stated	Questionnaire
Rockhill 2001 (46)	Walking	Duration	<ul style="list-style-type: none"><li>• &lt; 1h/wk</li><li>• 1-2.9 h/wk</li><li>• &gt;=3 h/wk</li></ul>	None	Not adjusted	Not stated	Questionnaire
Lee 2000 (47)	Walking	kJ/wk	Summed energy expenditure from walking, stair climbing and sports/ recreation kJ/week <ul style="list-style-type: none"><li>• &lt;4200</li><li>• 4200 &lt; 8400</li><li>• 8400 &lt; 12600</li><li>• 12600&lt;16800</li><li>• &gt;=16800</li></ul>	Yes/ All	Adjusted for other 4 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 1998 (48)	Leisure	Sessions/ intensity	<ul style="list-style-type: none"><li>• Sedentary: no leisure activity</li><li>• Occasional: in between</li><li>• Conditioning: Exercising at 6 times a month for mean duration 30 min and at least vigorous walking</li></ul>	Yes/ Leisure only	No	Not specified	Mailed questionnaire
Villeneuve 1998 (5)	Non vigorous leisure & household chores	Kilocalorie s/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 Questionnaire	Questionnaire and clinical examination of 7916/14442

Kushi 1997 (50)	Moderate leisure	Sessions	<p>"Aside from work or home, do you do anything daily that keeps you physically fit?"</p> <p>Separate questions on frequency of participation in moderate pa (e.g. bowling, golf, gardening or taking long walks)</p> <ul style="list-style-type: none"> <li>• Rarely/ never</li> <li>• 1 wk to few a month</li> <li>• 2 to 4/ wk</li> <li>• &gt; 4/ wk</li> </ul>	Yes/ Long walks only	No	Not specified	Questionnaire
Leon 1997 (49)	Leisure	Duration	<ul style="list-style-type: none"> <li>• Mean minutes per day</li> <li>• 4.9 min/ d leisure time pa (0-9 mins)</li> <li>• 22.7 min/ d (range 10-36 min)</li> <li>• 53.9 min/d (range 37-75 min/d)</li> <li>• 140.4 min/d (range 76-359 min/d)</li> </ul>	Yes/ All	No	MLTPA	Questionnaire and clinical examination
Kampert 1996 (51)	Walking/ running	Distance	<ul style="list-style-type: none"> <li>• Sedentary</li> <li>• 1-10 miles/wk ( or who participated in other sporting or leisure time activities were classified as moderately active)</li> <li>• 11-20 miles/wk</li> <li>• 21-40 miles/wk</li> <li>• &gt;=40 miles/wk</li> </ul>	All	Not adjusted	Not specified	Questionnaire

Abbreviations: M, male; F, female; g/d, grams per day; h/d, hours per day; min/d, minutes per day; kj/week, kilojoules per week; miles/wk, miles per week; METs, metabolic equivalent tasks; METs,

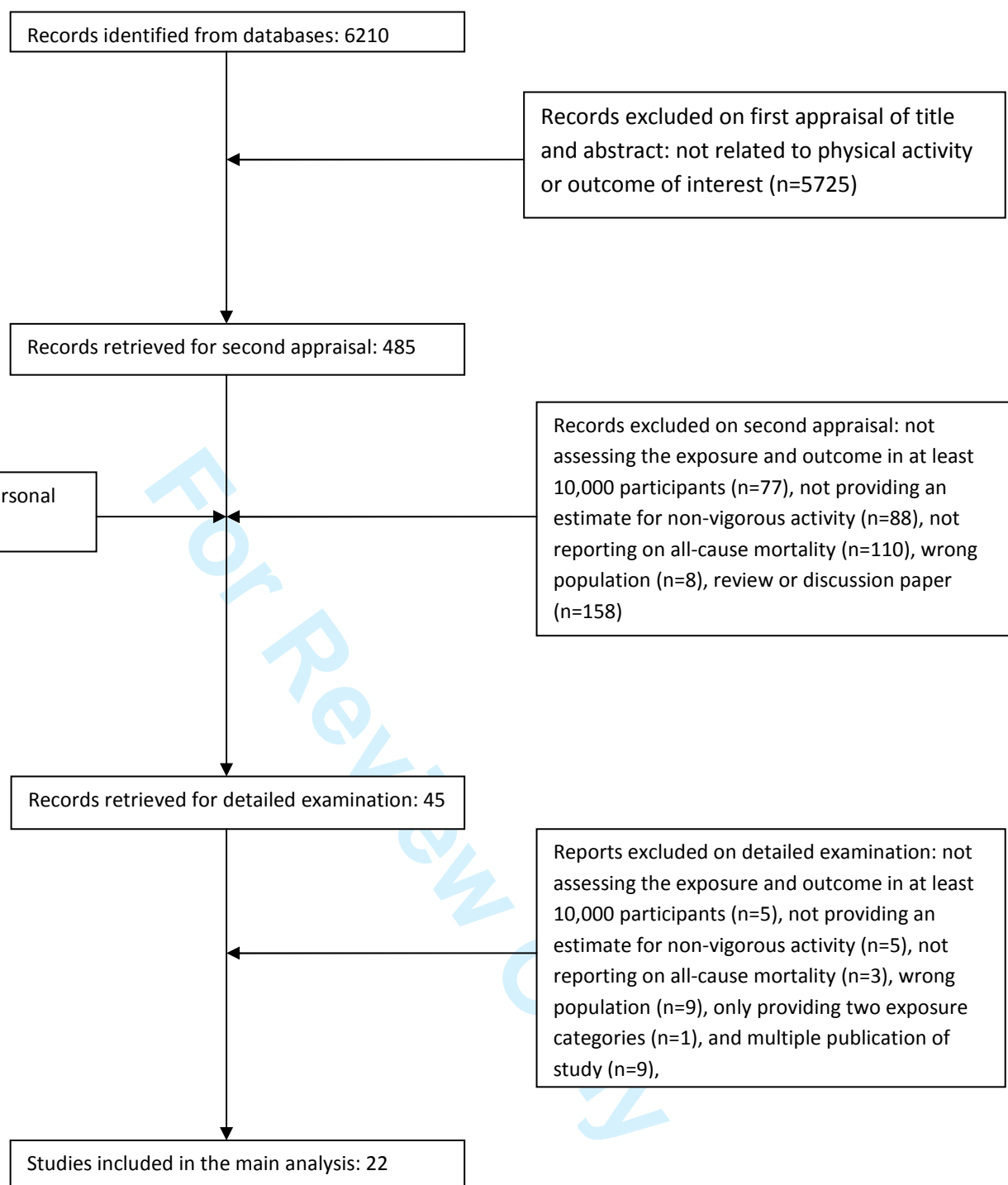
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\*Metabolic variables include blood glucose, BMI, blood pressure and cholesterol. Score is based on 1 point for every metabolic variable adjusted for as continuous and 0.5 for every variable adjusted for as discrete, every variable excluded on and every variable stratified by.

Web Table 5: Association between hours of light and moderate physical activity and RR (Relative Risk) for all cause mortality		
	Light activity*	Moderate activity**
Hours week	RR (95% CI)	RR (95% CI)
0	1.00 (Referent)	1.00 (Referent)
1	0.86 (0.83-0.89)	0.84 (0.81-0.88)
2.5	0.83 (0.79-0.87)	0.81 (0.76-0.85)
5	0.80 (0.76-0.84)	0.77 (0.73-0.82)
7	0.78 (0.74-0.83)	0.76 (0.71-0.81)
10	0.77 (0.72-0.82)	0.74 (0.68-0.79)
14	0.75 (0.70-0.80)	0.72 (0.66-0.78)

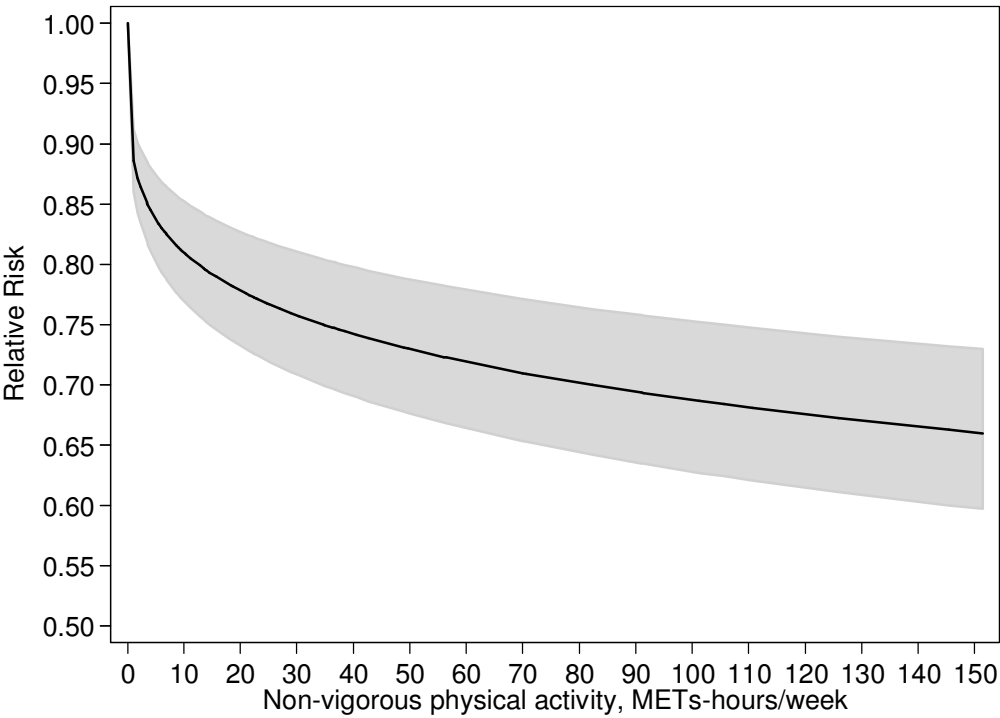
\*An activity of approximately 2.5 METs such as walking at 3.2 kilometres per hour  
\*\* An activity of approximately 4.5 METs such as 5.6 kilometres per hour carrying less than 11 kilograms





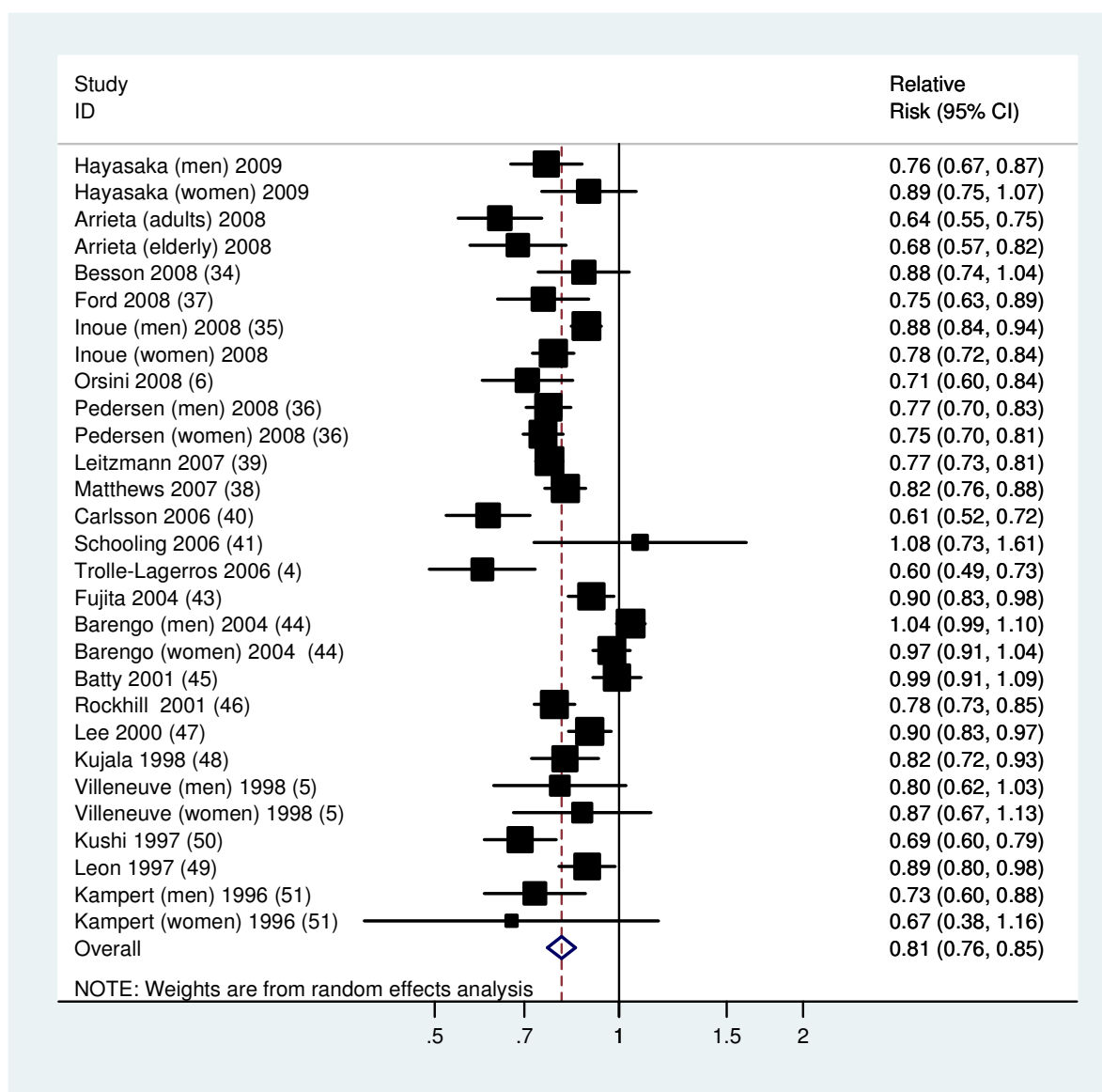
**Figure 1.** Flow chart for selection of studies

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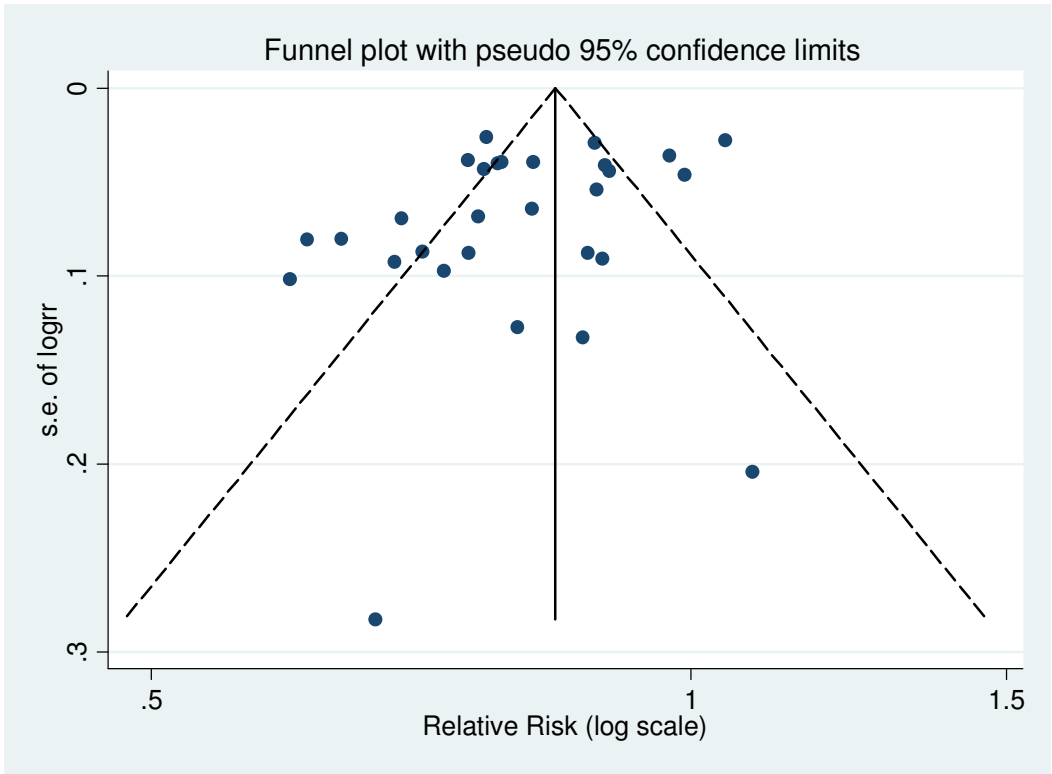
**Figure 2.** Association between MET hours per week of non-vigorous physical activity and relative risk for all cause mortality

29 estimates from 22 studies, 52,294 deaths, and 7,569,742 person years of follow up. Data were fitted with a random-effect model including a power transformation of 0.25 for MET-hours/week. Shaded areas represent 95% confidence intervals.



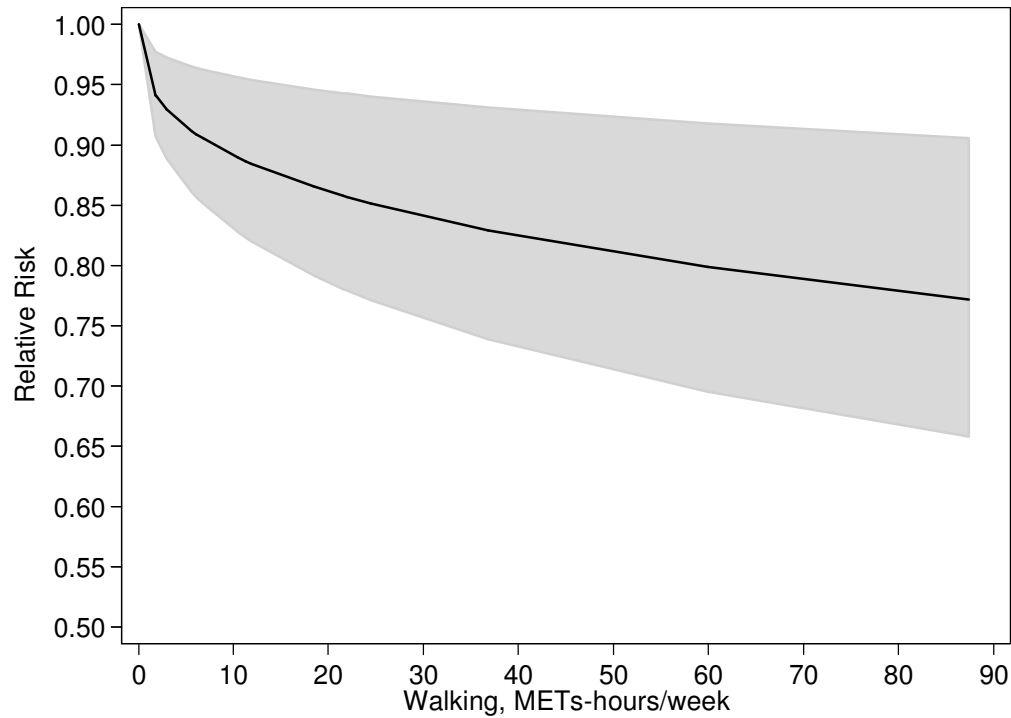
**Figure 3.** Adjusted relative risk of all-cause mortality for 11 vs 0 MET-hours/week of moderate non-vigorous physical activity.

CI indicates confidence interval. 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 ( $Q=196.77$ ,  $p\text{-value} < 0.001$ ,  $I\text{-squared}=86\%$ ).



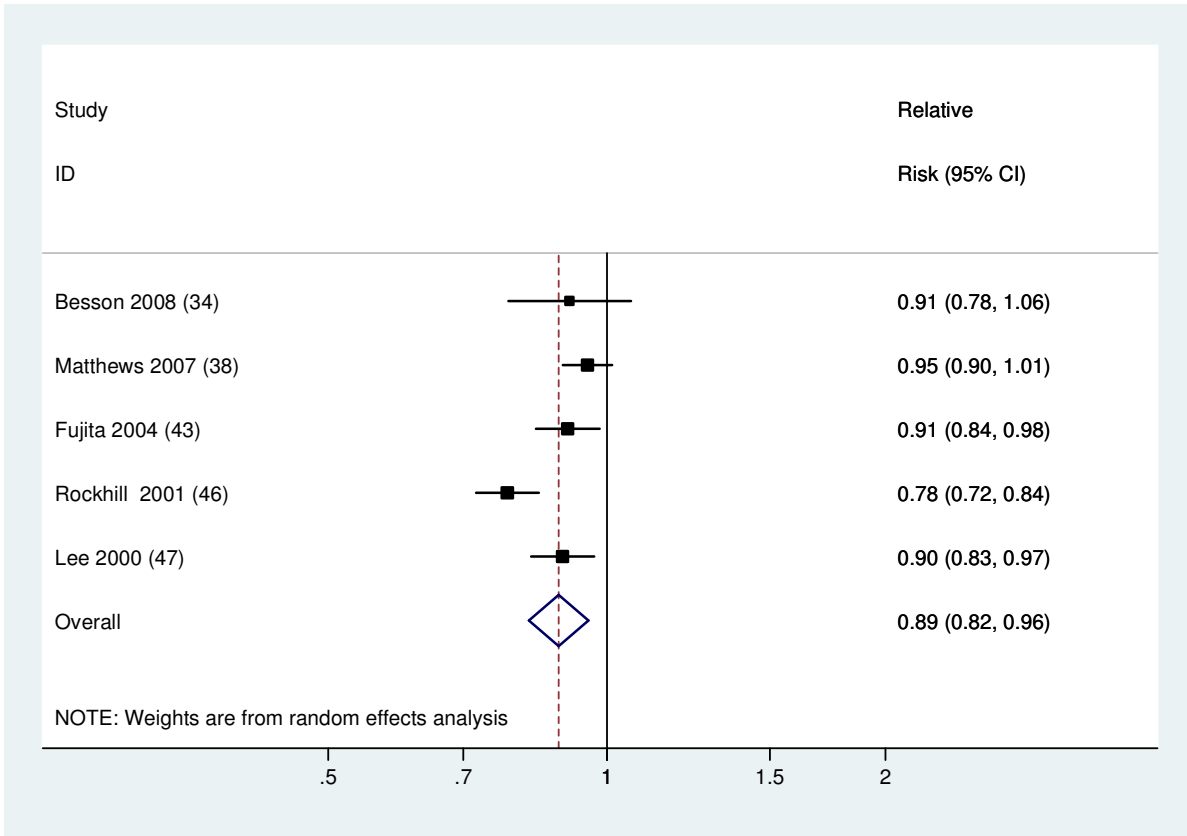
**Figure 4.** Funnel plot with pseudo 95% confidence intervals for the association between 11 MET- hours per week of non-vigorous physical activity and all-cause mortality in each of the studies.

29 estimates from 22 studies. Data were fitted with a power transformation of 0.25 for non-vigorous physical activity.



**Figure 5.** Association between MET hours per week of non-vigorous physical activity and adjusted relative risk for all cause mortality in the studies of walking alone

5 estimates from 5 studies, 22,882 deaths, and 1,581,769 person years of follow up. Shaded area represents 95% confidence intervals. Data were fitted with a random-effect model including a power transformation of 0.375 for walking MET-hours/week.



**Figure 6.** Adjusted relative risk of all-cause mortality for 11 vs 0 MET-hours/week of walking.

CI indicates confidence interval. 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-value = 0.003, I-squared=75%).