A systematic review of the evidence for Canada’s Physical Activity Guidelines for Adults

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Abstract

This systematic review examines critically the scientific basis for Canada’s Physical Activity Guide for Healthy Active Living for adults. Particular reference is given to the dose-response relationship between physical activity and premature all-cause mortality and seven chronic diseases (cardiovascular disease, stroke, hypertension, colon cancer, breast cancer, type 2 diabetes (diabetes mellitus) and osteoporosis). The strength of the relationship between physical activity and specific health outcomes is evaluated critically. Literature was obtained through searching electronic databases (e.g., MEDLINE, EMBASE), cross-referencing, and through the authors’ knowledge of the area. For inclusion in our systematic review articles must have at least 3 levels of physical activity and the concomitant risk for each chronic disease. The quality of included studies was appraised using a modified Downs and Black tool. Through this search we identified a total of 254 articles that met the eligibility criteria related to premature all-cause mortality (N = 70), cardiovascular disease (N = 49), stroke (N = 25), hypertension (N = 12), colon cancer (N = 33), breast cancer (N = 43), type 2 diabetes (N = 20), and osteoporosis (N = 2). Overall, the current literature supports clearly the dose-response relationship between physical activity and the seven chronic conditions identified. Moreover, higher levels of physical activity reduce the risk for premature all-cause mortality. The current Canadian guidelines appear to be appropriate to reduce the risk for the seven chronic conditions identified above and all-cause mortality.

Introduction

There is considerable literature supporting the importance of habitual physical activity in the primary and secondary prevention of varied chronic conditions [1-16]. Routine physical activity is thought to be of benefit for over 25 chronic conditions [17]. Seven chronic diseases in particular have been associated with a physically inactive lifestyle including coronary artery disease, stroke, hypertension, colon cancer, breast cancer, type 2 diabetes (diabetes mellitus) and osteoporosis [18-20].

Canada has played a leading role in the development of physical activity guidelines for individuals across the lifespan. This includes the development (in 1998) of “Canada’s Physical Activity Guide to Healthy Active Living” for adults between the ages of 20 and 55 yr [21], which was followed by “Canada’s Physical Activity Guide to Healthy Active Living for Older Adults” [22], and “Canada’s Physical Activity Guide to Healthy Active Living for Children and Youth” [23]. The adult guidelines (which are now approximately 10 years old) state generally that 20-55 yr adults should accumulate 60 min of daily physical activity or 30 min of moderate to vigorous exercise on at least 4 days a week [18,19].

We reported recently that Canada’s adult guidelines were consistent with other international guidelines and were supported by a compelling body of literature [18,19]. We revealed strong evidence that routine physical activity was effective in the primary prevention of cardiovascular disease, stroke, hypertension, breast cancer, colon cancer, type 2 diabetes and osteoporosis. Moreover, physical activity appears to play an important role in the prevention of obesity and obesity-related co-morbidities. However, implicit in the adult guidelines is the belief that there is a dose-response relationship between physical activity and the associated health benefits. Moreover, a central belief in these guidelines and most international physical activity guidelines is that the dose-response relationship is curvilinear with the greatest health benefits seen in physically inactive individuals who become “more physically active.” In fact, a consistent pattern (shown in Figure 1) has been hypothesized, wherein
there are marked changes in health status with relatively minor increments in physical activity/fitness in individuals that are the least active/fit. Generally, the health benefits have been thought to level off at the upper end of the physical activity/fitness continuum (Figure 1). However, recent work (such as that provided by Gledhill and Jamnik in the Canadian Physical Activity and Lifestyle Approach) has speculated that there are likely multiple dose-response curves for various endpoints [24].

The primary purpose of this systematic review was to examine critically the current literature to determine whether or not a dose-response relationship exists between habitual physical activity and chronic disease. In particular, we sought to determine whether the key messaging “Every little bit counts, but more is even better - everyone can do it!” of the adult physical activity guidelines is supported by a strong body of evidence.

Due to the breadth of literature, we have chosen to focus on the relationship between physical activity and all-cause mortality, and the seven chronic conditions that are thought to be reduced greatly with habitual physical activity and chronic disease. In particular, we sought to determine whether the key messaging “Every little bit counts, but more is even better - everyone can do it!” of the adult physical activity guidelines is supported by a strong body of evidence.

Table 1 Relative risks (RR) and population attributable risks (PAR%) for physical inactivity in Canada, Australia, and the USA.

| Disease        | Canada RR | PA (%) | Australia RR | PA (%) | USA RR | PA (%) |
|----------------|-----------|--------|--------------|--------|--------|--------|
| CHD            | 1.45      | 19.4   | 1.5          | 18     | 2.0    | 22     |
| Stroke         | 1.60      | 24.3   | 2.0          | 16     | na     | Na     |
| Hypertension   | 1.30      | 13.8   | na           | na     | 1.5    | 12     |
| Colon Cancer   | 1.41      | 18.0   | 1.5          | 19     | 2.0    | 22     |
| Breast Cancer  | 1.31      | 14.2   | 1.1          | 9      | 1.2    | 5      |
| Type 2 Diabetes| 1.50      | 21.1   | 1.3          | 13     | 1.5    | 12     |
| Osteoporosis   | 1.59      | 24.0   | 14*          | 18*    | 2.0    | 18*    |

Source: Canadian Data [20]; Australian Data [161]; US Data: [162]. *Evaluated the incidence of falls/fractures.

**Methods**

Criteria for considering studies for this review

Our research team utilized a rigorous, systematic, and evidence-based approach to examine critically the levels of evidence on physical activity and the risk for premature mortality and chronic disease. Any studies that evaluated the relationship between at least three different levels of physical activity and mortality or incidence of chronic disease were eligible for inclusion. Therefore, excluded studies included those that examined only the most active versus least active populations (e.g., sedentary/inactive vs. physically active). Any form of physical activity/exercise measurement (e.g., self-report, pedometer, accelerometer, maximal aerobic power (VO2 max)) was eligible for inclusion. The key outcomes were mortality and incidence of chronic disease. Only published, English language studies examining adults (e.g., 19-65 yr) were included. Participants must have previously been healthy (asymptomatic) adults without established chronic disease. There was no restriction according to study design.

To examine the relative risk reductions associated with physical activity, we calculated the mean and median risk reductions across studies focusing on the highest level versus the lowest level of physical activity/fitness. For each study we also determined whether or not a dose-response relationship was present (i.e., reflecting a progressive decrease in the risk with increasing physical activity/fitness levels).

**Search strategy**

Literature searches were conducted in the following electronic bibliographical databases:

- MEDLINE (1950-March 2008, OVID Interface);
- EMBASE (1980- March 2008, OVID Interface);
- CINAHL (1982- March 2008, OVID Interface);
PsycINFO (1840- March 2008, Scholars Portal Interface);
Cochrane Library (-March 2008),
SPORTDiscus (-March 2008).

The Medical Subject Headings (MeSH) were kept broad. See tables 2, 3, 4, 5, 6, 7, 8, and 9 for the complete search strategy and keywords used. The electronic search strategies were created and carried out by researchers experienced with systematic reviews of the literature (DW and LN). The citations and applicable electronic versions of the article (where available) were downloaded to an online research management system (RefWorks, Bethesda, Maryland, USA).

Screening
Two reviewers (LN and SC) screened independently the title and abstract of the citations to identify potential articles for inclusion. Duplicate citations were removed. The reviewers were not blinded to the authors or journals. Biographies of key studies and reviews in the field were also cross-referenced for further articles. For those articles that appeared relevant, the full text was obtained and data was extracted using a common template. In cases of disagreement, discussion with a third reviewer (DW) was used to achieve consensus. Full (100%) consensus was achieved. All studies that were excluded during the citation and full-article screening processes were recorded along with the reasons for exclusion.

### Table 2 Results of the MEDLINE literature search regarding all-cause mortality.

| # Searches (28 Feb 2008) | Results |
|--------------------------|---------|
| 1 exp Physical Fitness/   | 15236   |
| 2 Motor Activity/        | 49721   |
| 3 exp Physical Endurance/| 15383   |
| 4 exp Exercise/          | 57742   |
| 5 exp Exertion/          | 88903   |
| 6 exp Sports/            | 71887   |
| 7 exp exercise therapy/  | 17231   |
| 8 exp exercise tolerance/| 4192    |
| 9 exp health behaviour/  | 59409   |
| 10 leisure time physical activity.mp | 996 |
| 11 occupational physical activity.mp | 190 |
| 12 exp Fliability/       | 2279    |
| 13 exp Muscle Strength/  | 5717    |
| 14 musc$ power.mp        | 965     |
| 15 exp Back/             | 12821   |
| 16 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 | 291635 |
| 17 dose-response.mp      | 321096  |
| 18 intensity.mp          | 142881  |
| 19 volume.mp             | 298471  |
| 20 exp Energy Metabolism/| 206808  |
| 21 exp oxygen consumption/| 83387  |
| 22 exp time factors/     | 764091  |
| 23 17 or 18 or 19 or 20 or 21 or 22 | 1652372 |
| 24 16 and 23             | 67760   |
| 25 exp Cardiovascular Diseases/ | 1411730 |
| 26 exp Heart diseases/   | 675083  |
| 27 exp Myocardial infarction/ | 116070 |
| 28 exp Death, Sudden Cardiac/ | 6772   |
| 29 exp Coronary Artery Disease/ | 18137  |
| 30 exp Coronary Disease/  | 144236  |
| 31 exp Vascular Diseases/ | 1018275 |
| 32 25 or 26 or 27 or 28 or 29 or 30 or 31 | 1411730 |
| 33 24 and 32             | 9603    |
| 34 limit 33 to (english language and humans and "all adult (19 plus years") | 5544 |

### Table 3 Results of the MEDLINE literature search regarding cardiovascular disease.

| Search # | Searches (3 Mar 2008) | Results |
|----------|-----------------------|---------|
| 1        | exp Physical Fitness/  | 15244   |
| 2        | Motor Activity/       | 49751   |
| 3        | exp Physical Endurance/ | 15408  |
| 4        | exp Exercise/         | 57806   |
| 5        | exp Exertion/         | 88967   |
| 6        | exp Sports/           | 71931   |
| 7        | exp exercise therapy/ | 17243   |
| 8        | exp exercise tolerance/ | 4205   |
| 9        | exp health behaviour/ | 59467   |
| 10       | leisure time physical activity.mp | 998 |
| 11       | occupational physical activity.mp | 191 |
| 12       | exp Fliability/       | 2289    |
| 13       | exp Muscle Strength/  | 5731    |
| 14       | musc$ power.mp       | 965     |
| 15       | exp Back/             | 12822   |
| 16        | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 | 291817 |
| 17       | dose-response.mp     | 321198  |
| 18       | intensity.mp         | 142955  |
| 19       | volume.mp            | 298620  |
| 20       | exp Energy Metabolism/ | 206886 |
| 21       | exp oxygen consumption/ | 83387 |
| 22       | exp time factors/    | 764091  |
| 23       | 17 or 18 or 19 or 20 or 21 or 22 | 1652372 |
| 24       | 16 and 23            | 67760   |
| 25       | exp Cardiovascular Diseases/ | 1411730 |
| 26       | exp Heart diseases/  | 675083  |
| 27       | exp Myocardial infarction/ | 116070 |
| 28       | exp Death, Sudden Cardiac/ | 6772   |
| 29       | exp Coronary Artery Disease/ | 18137  |
| 30       | exp Coronary Disease/ | 144236  |
| 31       | exp Vascular Diseases/ | 1018275 |
| 32       | 25 or 26 or 27 or 28 or 29 or 30 or 31 | 1411730 |
| 33       | 24 and 32            | 9603    |
| 34       | limit 33 to (english language and humans and "all adult (19 plus years") | 5544 |

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Data Extraction

Two reviewers (LN and SC) completed standardized data extraction forms, which were verified by two other reviewers (DW and SB). We extracted information regarding the study design, the country where the study was conducted, the participant characteristics, the sample size, the objectives of the study, the methodologies employed, the major outcomes (i.e., mortality, incidence of chronic disease, physical activity levels/classifications), and the comments and conclusions made based on the findings of the study. The reviewers were not blinded to the journal or the author names when extracting information from the articles.

Level of Evidence

The approach used to establish the level and grade of evidence was consistent with that used during creation of the “Canadian clinical practice guidelines on the management and prevention of obesity in adults and children” [25]. The level of evidence provides information regarding the strength of the evidence in favour of physical activity/exercise in the primary prevention of premature mortality and the seven chronic diseases of primary interest. This evaluation process is based on a pre-defined and objective criteria (see Table 10).

The grade for each article provides information regarding whether physical activity is effective in the primary prevention of the varied conditions evaluated (Table 10). Where applicable this grade informs the reader about the potential risk of the physical activity. A study that receives the highest grading would indicate
that the benefits clearly outweigh the risks and receive a strong recommendation.

Quality Assessment
The quality of each study was also established using the procedures of Gorber et al. [26]. Owing to the fact that only observational study designs were included in our systematic review, we used the Downs and Black [27] scale to assess the quality of non-randomized investigations. Similar to the work of Prince et al. [28] we chose to include the most relevant components of the scoring tool. Therefore, a modified version of the Downs and Black checklist was used with the final checklist consisting of 15 items with a maximum score of 15 points. Higher points reflected a superior quality of investigation.

Results
Physical Inactivity and All-Cause Mortality
A total of 2040 citations were identified during the electronic database search (Figure 2). Of these citations, 288 were identified in MEDLINE, 222 in EMBASE, 496 in Cochrane, and 1034 in the CINAHL/SportDiscus/PsychInfo search. A total of 167 duplicates were found, leaving a total of 1873 unique citations. A total of 1696 articles were excluded after scanning, leaving a total of 177 articles for full review. From these articles 130 were excluded after full review leaving 47 articles for inclusion in the systematic review. An additional 23 articles were added to the review based on the authors’ knowledge of the area. The reasons for exclusion included review articles (n = 26), commentary (n = 10), did not report 3 levels of physical activity (n = 24), no objective measure of physical activity (n = 2), report (n = 15), not a formal study (n = 11), not related to all-cause mortality (n = 27), the participants were too young (n = 1), not able to retrieve articles (n = 7), and other (n = 7). Therefore, a total of 70 articles were included in the
systematic review of the literature regarding the relationship between physical activity and premature mortality.

The majority of the studies included in our systematic review were prospective cohort investigations (Table 11). These studies involved a total of 1,525,377 participants; averaging 21,791 participants per study (range 302-252,925). There were a total of 111,125 reported cases of premature all-cause mortality (ranging per study from 43-10,952). The total length of study follow-up for the prospective cohort studies averaged 11.1 yr (ranging from 0.5-28 yr). The articles were published over a 22 yr period ranging from 1985 to 2007. These studies involved large samples of men and women from regions throughout the world.

We observed a mean 31% lower risk for all-cause mortality in the most active individuals. The median risk reduction was 32%. It is important to highlight that many of these studies included women, with sub-analyses that revealed similar risk reductions between sexes. Our findings are consistent with previous reports [15,16,29-31]. The majority (90%) of the studies supported the health benefits of physical activity demonstrating a significant risk reduction in physically active individuals.

The level of evidence would be considered to be a Level 2A based on the presence of overwhelming evidence from observational trials. The studies examined were generally of a good quality with a mean (and median) score of 12 out of 15 (range 10-14).
A clear dose-response relationship was also observed with marked reductions in the risk for all-cause mortality occurring with relatively small increments in physical activity (Figure 3). To examine more closely the temporal relationship between physical activity and all-cause mortality we calculated the (unadjusted) relative risks associated with incremental levels of physical activity/fitness using the reported cases of all-cause mortality and the number of participants (per group) in each investigation. In some instances, we were required to calculate the number of participants based on the reported incidence rates and person years, or based on data obtained directly from the authors (2 investigations). We were not able to obtain this information in 18 investigations, and as such this analysis was restricted to the remaining 52 investigations. There was considerable variability in the methods of classifying the physical activity/fitness levels of the participants. Accordingly, Figure 3 illustrates the mean relative risk reduction according to three separate study types including those that subdivided participants into tertiles, quartiles and quintiles, respectively. This figure demonstrates clearly the dose-response relationship between physical activity and all-cause mortality. Collectively, the literature is consistent indicating that the current Canadian guidelines (approximately 4.2 MJ/wk, 1000 kcal/wk) are associated with a 20-30% lower risk for premature all-cause mortality, with greater health benefits with high volumes and/or intensities of activity. In our analyses it was apparent that the greatest differences in risk occurred between the lowest adjacent activity/fitness categories, suggesting that sedentary individuals can markedly reduce their risk for all-cause mortality with relatively minor increments in physical activity. This is consistent with the current messaging of Canada’s physical activity guidelines.

The strength of the relationship between physical fitness and premature mortality has been well-established [6,32,33]. In our analyses there were greater risk reductions in studies that took objective measures of physical fitness. We observed an average risk reduction of approximately 45%, which was consistent between men and women. A risk reduction of greater than 50% was not uncommon in these studies. For instance, Myers et al. (2004) reported that being fit or physically active was associated with greater than 50% lower mortality risk in men. They also noted that a 4.2 MJ/wk (1000 kcal/wk) increase in physical activity, or a 1 metabolic equivalent (MET) higher physical fitness level was associated with a mortality benefit of around 20%. It is also important to highlight that longitudinal studies evaluating changes in physical activity or fitness have revealed a lower premature mortality risk [16,34-41]. As we previously reported, routine physical activity or elevated physical fitness also appears to reduce the risk for premature mortality in individuals with risk factors for chronic disease [42,43].

**Implications**

Since the seminal work of Morris and colleagues (in the 1950s [44,45]) and the early work of Paffenbarger (in the 1970s [46,47]) there has been considerable research (especially epidemiological evidence) documenting the health benefits of engaging in routine physical activity and/or being physically fit [17,48]. Both physical activity
(a behaviour) and physical fitness (an attained state) appear to be related to health status in a dose-dependent fashion, with physical fitness demonstrating the strongest relationship [18,19]. Numerous reports indicate that physical inactivity and/or low physical fitness are associated with an increased risk for chronic disease and premature all-cause and disease-specific mortality [2,43,49-51]. Some of the most compelling research includes the relationship between physical activity/fitness and all-cause mortality. As demonstrated below and in Table 11 and Figure 1, this literature is extensive.

The assessment of the relationship between all-cause mortality is complicated by the inclusion of deaths related to suicides, homicide, and accidents [18,19,52]. Nonetheless, the available evidence is incontrovertible; individuals who are habitually physically active and/or physically fit are at a markedly reduced risk for premature all-cause mortality [15,16,18,19]. In Canada, physical inactivity is a major cause of premature mortality from diseases of the cardiovascular system (33.3%), cancers (29.1%), and type 2 diabetes (3.5%) [53]. Globally, physical inactivity has been linked with 2 million premature deaths per year, including 22% of cases of coronary heart disease, and 10-16% of cases of breast cancer, colon cancer, rectal cancer and type 2 diabetes [54]. As such, the promotion of the health benefits of physical activity is of paramount importance for the effective prevention of chronic disease and premature mortality on a national and international scale.

In summary, there is a clear dose-response relationship between physical activity and premature all-cause mortality. Physically active individuals have an approximate risk reduction of 31% in comparison to physically inactive individuals. When objective measures of aerobic fitness are taken the risk reductions are even greater approximating 45%.

**Recommendation #1**

For a reduced risk for premature mortality, it is recommended that individuals should participate in 30 min or more of moderate to vigorous exercise on most days of the week. Greater health benefits appear to occur with higher volumes and/or intensities of activity. [Level 2, Grade A]

**Primary Prevention of Cardiovascular Disease**

In our systematic search of the literature, a total of 9408 citations were identified during the electronic database search (Figure 4). Of these citations, 5973 were identified in MEDLINE, 2561 in EMBASE, 193 in Cochrane, and 681 in the CINAHL/SportDiscus/PsychInfo search. A total of 923 duplicates were found, leaving a total of 8485 unique citations. A total of 8138 articles were excluded after scanning, leaving a total of 347 articles for full review. An additional 20 articles were added through cross-referencing. From these articles 319 were excluded after full review leaving 33 articles for inclusion in the systematic review. The reasons for exclusion included non-experimental studies (n = 45), only effect on cardiovascular disease risk factors (n = 115), did not report 3 levels of physical activity (n = 12), subjects less than 18 yr of age (n = 4), reviews, summaries, dissertations, thesis, and abstracts (n = 30), clinical population (n = 14), not on cardiovascular disease or did not fit...
| Publication       | Objective                                                                 | Population                                                                 | Methods                                                                 | Outcome   | Comments and Conclusions                                                   |
|-------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------------------------------------------------|-----------|---------------------------------------------------------------------------|
| Blair et al 1989  | To study physical fitness (PF) and risk of all-cause mortality in men and women. | n = 13,344 (10,224 men; 3,120 women)                                        | Baseline and 8 year follow-up                                          | 283 deaths| Low levels of PF increase the risk for premature mortality.              |
|                  |                                                                          | • Sex: Men and women                                                        |                                                                       |           |                                                                            |
|                  |                                                                          | • Age: 20-60 years (yr)                                                     | PF assessment: Maximal treadmill exercise test.                        |           |                                                                            |
|                  |                                                                          | • Characteristics: Participants were given a preventative Medicine examination including maximal treadmill exercise test |                                                                       |           |                                                                            |
|                  |                                                                          | Fitness categorized into quintiles: Men                                    |                                                                       |           |                                                                            |
|                  |                                                                          | Q1 = least fit                                                              | Q1 = 3.44 (2.05-5.77)                                                 |           |                                                                            |
|                  |                                                                          | Q2                                                                         | Q2 = 1.37 (0.76-2.50)                                                 |           |                                                                            |
|                  |                                                                          | Q3                                                                         | Q3 = 1.46 (0.81-2.63)                                                 |           |                                                                            |
|                  |                                                                          | Q4                                                                         | Q4 = 1.17 (0.63-2.17)                                                 |           |                                                                            |
|                  |                                                                          | Q5 = most fit                                                               | Q5 = 1.00 (referent)                                                 |           |                                                                            |
| Myers et al 2004  | To determine the effects of PF and physical activity (PA) on all-cause mortality. | n = 6,213                                                                  | Baseline and mean 5.5 ± 2.0 year follow-Up                            | 1,256 deaths| Being fit or active is associated with >50% reductions in mortality risk. |
|                  |                                                                          | • Sex: Men                                                                  |                                                                       |           |                                                                            |
|                  |                                                                          | • Age: Mean 59.0 ± 112 yr                                                   | PF Level hazard ratio (HR) (95% CI)                                   |           |                                                                            |
|                  |                                                                          | • Characteristics: Men referred for exercise testing                        | G1 = 1.00 (referent)                                                 |           |                                                                            |
|                  |                                                                          | PF assessment: Treadmill test to measure VO2 peak                           | G2 = 0.59 (0.52-0.68)                                                 |           |                                                                            |
|                  |                                                                          |                                                                            | G3 = 0.46 (0.39-0.55)                                                 |           |                                                                            |
|                  |                                                                          |                                                                            | G4 = 0.28 (0.23-0.34)                                                 |           |                                                                            |
|                  |                                                                          |                                                                            | PF predicted mortality more strongly than PA.                         |           |                                                                            |
|                  |                                                                          |                                                                            | Increasing PA (by 1000 kcal/wk or 1 MET) confers a mortality benefit of 20% |           |                                                                            |
|                  |                                                                          |                                                                            |                                                                       |           |                                                                            |
| Warburton et al.  | To determine the effects of PF and physical activity (PA) on all-cause mortality. | n = 13,344 (10,224 men; 3,120 women)                                        | PA assessment: Self reported PA divided into 4 groups                   |           |                                                                            |
|                  |                                                                          | • Sex: Men                                                                  |                                                                       |           |                                                                            |
|                  |                                                                          | • Age: 59.0 ± 112 yr                                                        |                                                                         |           |                                                                            |
|                  |                                                                          | • Characteristics: None                                                     |                                                                         |           |                                                                            |
|                  |                                                                          | PA Level HR (95% CI)                                                       | G1 = Lowest level                                                    |           |                                                                            |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | n | Year Follow-up | Deaths | Results |
|-------|-----------|---|----------------|--------|---------|
| Blair et al 1995 [36] | To evaluate the relationship between changes in PF and risk of mortality in men. | 9,777 | 4.9 year mean follow-up | 223 | Men who maintained or increased adequate PF had a reduced risk for all-cause mortality than individuals who were consistently unfit. |
| USA | Prospective cohort | | | | G2 = 0.63 (0.36-1.10) G3 = 0.42 (0.23-0.78) G4 = 0.38 (0.19-0.73) |
| Bijnen et al 1999 [37] | To examine the association of PA at baseline and 5 years | 472 | 1985 and 1990 | 118 | Recent levels of PA were more important for mortality risk than PA 5 years previously. |
| Netherlands | Retrospective cohort | | | | G1 = unfit to unfit G2 = unfit to fit G3 = fit to unfit G4 = fit to fit |
| Zutphen Elderly Study | | | | | G1 = 1.00 (referent) G2 = 0.96 (0.41-0.75) G3 = 0.52 (0.38-0.70) G4 = 0.33 (0.23-0.47) |
| | | | | | Total activity = 1.25 (0.79-1.99) Walking = 0.97 (0.60-1.57) Bike = 0.97 (0.59-1.57) Gardening = 0.66 (0.39-1.10) Other = 1.08 (0.66-1.78) Heavy activity = 0.73 (0.45-1.17) Non heavy activity = 0.89 (0.57-1.40) |
|                  | Highest tertile                                                                 | Middle tertile                                                                    | Lowest tertile = 1.00 (referent) |
|------------------|---------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|----------------------------------|
|                  | Total activity = 1.25 (0.73-2.12)                                              | Total activity = 0.56 (0.35-0.89)                                                | PA in 1990:                      |
|                  | Walking = 0.94 (0.58-1.55)                                                      | Walking = 0.82 (0.51-1.32)                                                       |                                  |
|                  | Bike = 1.07 (0.61-1.88)                                                         | Bike = 0.49 (0.29-0.82)                                                          |                                  |
|                  | Gardening = 0.77 (0.42-1.39)                                                    | Gardening = 1.67 (1.00-2.79)                                                     |                                  |
|                  | Other = 1.24 (0.74-2.07)                                                        | Other = 0.93 (0.53-1.69)                                                         |                                  |
|                  | Heavy activity = 0.76 (0.44-1.32)                                               | Heavy activity = 1.19 (0.73-1.92)                                               |                                  |
|                  | Non heavy activity = 0.94 (0.58-1.53)                                           | Non heavy activity = 0.61 (0.38-0.99)                                            |                                  |
|                  | Heavy activity = 0.72 (0.40-1.31)                                               | Non heavy activity = 0.65 (0.40-1.05)                                            |                                  |

Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Design | Cohort Details | Outcome | Findings |
|-------|--------|----------------|---------|----------|
| Gregg et al 2003 [39] | Prospective cohort | n = 9,518 Baseline (1986-1988) and median 10.6 year follow-up (1992-1994) | 2,218 deaths | Increasing and maintaining PA levels could lengthen life for older women but appears to provide less benefit for women aged at least 75 years and those with poor health status. |
| USA | Prospective cohort | n = 9,518 Baseline (1986-1988) and median 10.6 year follow-up (1992-1994) | 2,218 deaths | Increasing and maintaining PA levels could lengthen life for older women but appears to provide less benefit for women aged at least 75 years and those with poor health status. |
| Age: ≥ 65 yr | Multivariate adjusted HRR (95% CI): Quintiles of total PA |
| Prospective cohort | Q1 = <163 | Q2 = 163-503 | Q3 = 504-1045 | Q4 = 1046-1906 | Q5 = ≥ 1907 |
| Walking HRR (95% CI) | Q1 = 1.00 (referent) | Q2 = 0.73 (0.64-0.82) | Q3 = 0.77 (0.68-0.87) | Q4 = 0.62 (0.54-0.71) | Q5 = 0.68 (0.59-0.78) |
| Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39 | Wannamethee et al 1998 [40] | To study the relationship between heart rate, PA and all-cause mortality. | n = 5,934 Baseline (1978-1980) and 12-14 year follow-up | 219 deaths | Maintaining or taking up light or moderate PA reduces mortality in older men. |
| Prospective cohort | Q1 = <70 | Q2 = 70-186 | Q3 = 187-419 | Q4 = 420-897 | Q5 = 898 |
| Multivariate adjusted HRR (95% CI) | Change in activity level: Sedentary at baseline |
| Prospective cohort | Staying sedentary = 1.00 (referent) | Became active = 0.52 (0.40-0.69) |
| Prospective cohort | Became sedentary = 0.92 (0.77-1.09) | Stayed active = 0.68 (0.56-0.82) |
### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Characteristics | PA assessment | Multivariate adjusted RR (95% CI) |
|-------|-----------------|---------------|----------------------------------|
| UK    | Healthy, sedentary (4,311 were considered "healthy" in 1992) | Questionnaire, split into groups | G1 = 1.00 (referent) G2 = 0.61 (0.43-0.86) G3 = 0.90 (0.31-0.79) |
| Prospective cohort | The British Regional Heart Study | PA score | G4 = 0.65 (0.45-0.94) |
| D & B score = 12 | PA assessment | G1 = Inactive/occasional | G2 = Light |
|       |      | G3 = Moderate | G4 = Moderately vigorous/Vigorous |
|       |      | G5 = Regular walking (min/d) | G1 = 0 Recreational activity |
|       |      | G2 = <20 | G3 = 21-40 |
|       |      | G4 = 41-60 | G5 = ≥ 60 |
|       |      | G1 = Inactive/fairly inactive | G2 = Average 4 hr/weekend |
|       |      | G3 = Fairly active >4 hr/weekend | G4 = Very active Sporting activity, 3 Groups |
|       |      | G1 = None | G2 = Occasional |
|       |      | G3 = >1 time/month | G3 = >1 time/month |

**Paffenbarger et al 1986 [63]**
To examine the PA and life-style characteristics of Harvard alumni for the relationship with all-cause mortality.

- **n = 16,936**
- **12-16 year follow-up (1962 to 1978)**
- **1,413 deaths**
- **The findings suggest a protective effect of exercise against all-cause mortality.**

- **Sex: Men**
- **Age: 35-74**

**USA**
- **Characteristics: Harvard alumni**
- **Records of freshman year physical examinations and records of intercollegiate sport**
- **Those who walked**
- **Age adjusted RR (95% CI):**
- **G1 = 1.00 (referent)**
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study                                                                 | Sample Characteristics                                                                 | Duration and Intensity | Mortality | Relative Intensity | Duration | Effect of Walking | Findings |
|----------------------------------------------------------------------|----------------------------------------------------------------------------------------|------------------------|-----------|--------------------|----------|-------------------|----------|
| Schnohr et al 2007 [64]                                             | To determine the impact of walking duration and intensity on all-cause mortality.       | Baseline and an average of 12 year | 1,391 deaths | The findings indicate that the relative intensity and not duration of walking is the most important in relation to all-cause mortality. |
| Denmark                                                             | n = 7,308 (3,204 male; 4,104 female)                                                  |                        |           |                    |          |                   |          |
| Prospective cohort                                                  | Sex: Male and female                                                                   |                        |           |                    |          |                   |          |
|                                                                     | Age: 20-93 yr                                                                          |                        |           |                    |          |                   |          |
| D & B score = 12                                                     | The Copenhagen City Heart Study                                                         |                        |           |                    |          |                   |          |

PA assessment: Mailed questionnaires surveying post college

Physical Activity Index (95% CI):

- G1 = 1.00 (referent)
- G2 = 0.78
- G3 = 0.73
- G4 = 0.68

Exercise reported: Walking (miles/wk) 3 groups

- G5 = 0.62
- G6 = 0.52
- G7 = 0.46
- G8 = 0.62

Trend p = <0.0001

PA index (kcal/wk) 3 groups:

- G1 = <500
- G2 = 500-999
- G3 = 1000-1499
- G4 = 1500-1999
- G5 = 2000-2499
- G6 = 2500-2999
- G7 = 3000-3499
- G8 = >3500

Cox proportional hazard models

Trend p = 0.0009

PA = 0.85
G3 = 0.79
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Duration (hours/day) | G3 = 0.38 (0.18-0.79) |
|----------------------|------------------------|
| 1 = <0.5             | G4 = 0.69 (0.44-1.07) |
| 2 = 0.5-1            | G5 = 0.37 (0.26-0.54) |
| 3 = 1-2              | G6 = 0.33 (0.18-0.61) |
| 4 = >2               | G7 = 0.78 (0.50-1.23) |
|                      | G8 = 0.41 (0.29-0.59) |
|                      | G9 = 0.33 (0.20-0.54) |
| Intensity            | G10 = 0.48 (0.22-0.82) |
| Slow intensity (SI)  | G11 = 0.42 (0.29-0.60) |
| Average intensity (AI)| G12 = 0.28 (0.16-0.48) |
| Fast intensity (FI)  | G13 = 0.38 (0.21-0.69) |

Kushi et al 1997 [65] To evaluate the association between PA and all-cause mortality in postmenopausal women. 7 year follow-up 2,260 deaths The results demonstrate a graded inverse association between PA and all-cause mortality in postmenopausal women.

- Sex: Women
- Age: 55-69 yr
- Characteristics: Postmenopausal Iowa women
- USA
- Prospective cohort
- D & B score = 13
- Multivariate adjusted frequency of moderate and vigorous LTPA
- Divided by frequency/week

| Characteristics: Postmenopausal Iowa women | Women |
|-------------------------------------------|-------|
| G1 = 1.00 (referent)                      | G1 = 1.00 (referent) |
| G2 = 0.82 (0.52-1.29)                     | G2 = 0.82 (0.52-1.29) |
| G3 = 0.78 (0.52-2.21)                     | G3 = 0.78 (0.52-2.21) |
| G4 = 1.22 (0.82-1.81)                     | G4 = 1.22 (0.82-1.81) |
| G5 = 0.74 (0.52-1.05)                     | G5 = 0.74 (0.52-1.05) |
| G6 = 0.96 (0.33-0.96)                     | G6 = 0.96 (0.33-0.96) |
| G7 = 0.94 (0.60-1.47)                     | G7 = 0.94 (0.60-1.47) |
| G8 = 0.87 (0.61-1.23)                     | G8 = 0.87 (0.61-1.23) |
| G9 = 0.48 (0.28-0.83)                     | G9 = 0.48 (0.28-0.83) |
| G10 = 0.88 (0.40-1.88)                    | G10 = 0.88 (0.40-1.88) |
| G11 = 0.64 (0.44-0.95)                    | G11 = 0.64 (0.44-0.95) |
| G12 = 0.38 (0.21-0.69)                    | G12 = 0.38 (0.21-0.69) |
### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Frequency of vigorous PA per week | Activity index |
|-----------------------------------|----------------|
| G1 = Rarely/never                  | G1 = Low       |
| G2 = 1 time/week to a few times/month | G2 = Medium   |
| G3 = 2-4 times/week               | G3 = High      |
| G4 = >4 times/week                | G4 = High      |

**Paffenbarger et al 1993 [67]**

To analyze changes in the lifestyles of Harvard College alumni and the association of these changes with mortality.  

- **n = 10,269**
- **Baseline (1977) and 8 year follow-up (1985)**
- **476 deaths**
- **Sex: Men**
- **Age: 45-84 yr (in 1977)**
- **USA**
- **Prospective cohort**
- **D & B score = 13**

Beginning moderately vigorous sports activity was associated with lower rates of death from all causes among middle aged and older men.

Beginning moderately vigorous sports activity was associated with 23% lower risk of death (95% CI 4%-42%, \( p = 0.015 \)) than those not taking up moderate activity.

- **Characteristics: Participants with no reported life-threatening disease**
- **PA Assessment: Questionnaire – blocks walked daily, stairs climbed daily and type, frequency and duration of weekly sports and recreational activities**
- **Physical activity index (kcal/Wk)**
- **Sports and recreational activities**
  - Light <4.5 METs
  - Moderate >4.5 METs
- **Weekly lists of deaths were obtained from the Harvard college alumni office**
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | Sample Size | Baseline (1981) | Follow-up | Cox proportional hazard ratio model |
|-------|-----------|-------------|-----------------|-----------|--------------------------------------|
| Katzmarzyk and Craig 2002 [154] | To quantify the relationship between musculoskeletal fitness and all-cause mortality. | n = 8,116 (3,933 male; 4,183 female) | 13 year follow-up | RR (95% CI) adjusted for age, smoking status, body mass and $VO_{2\text{max}}$ | South (1990) and 
- Age: 20-69 yr 
- Sex: Men and women 
- Characteristic: Participants who had musculoskeletal fitness measurements taken 
- D & B score = 11 
- Canadian Fitness Survey | 
- Q1 = lowest Sit ups 
- Q2 = Men 
- Q3 
- Q4 = highest 
- $Q_1 = 1.61$ (0.90-2.87) 
- $Q_4 = 1.00$ (referent) 
- Canadian Fitness Survey 
- Cox proportional hazard ratio model 
- Q1 = 2.26 (1.15-4.43) 
- Q2 = 2.24 (1.07-4.67) 
- Q3 = 1.27 (0.59-2.72) 
- Q4 = 1.00 (referent) Push-ups 
- Men 
- Q1 = 1.25 (0.77-2.05) 
- Q2 = 1.17 (0.71-1.90) 
- Q3 = 0.94 (0.55-1.62) 
- Q4 = 1.00 (referent) Grip strength (kg) 
- Men 
- Q1 = 1.49 (0.86-2.59) 
- Canadian Fitness Survey 
- Cox proportional hazard ratio model 
- Q1 = 2.26 (1.15-4.43) 
- Q2 = 2.24 (1.07-4.67) 
- Q3 = 1.27 (0.59-2.72) 
- Q4 = 1.00 (referent) Push-ups 
- Men 
- Q1 = 1.25 (0.77-2.05) 
- Q2 = 1.17 (0.71-1.90) 
- Q3 = 0.94 (0.55-1.62) 
- Q4 = 1.00 (referent) Grip strength (kg) 
- Men 
- Q1 = 1.49 (0.86-2.59) |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Population | Methodology | Outcome | Results |
|-------|------------|-------------|---------|---------|
| Andersen et al 2000 [163] | Denmark | Prospective cohort | Incidence of all-cause mortality and PA | LTPA was inversely associated with all-cause mortality in both men and women in all age groups. |
| | | To evaluate the relationship between levels of OPA, LTPA, cycling to work and sports participation and all-cause mortality. | PA assessment: Questionnaire for LTPA, divided into: | |
| | | | Multivariate adjusted RR (95% CI) | |
| | | | G1 = Low | G2 = Moderate |
| | | | Age 20-33 years | Age 20-44 yr |
| | | | Men | Men |
| | | | D & B score = 13 | |
### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Description | Sex | Age | Characteristics | PA assessment | LTPA | HRR (95% CI) | Notes |
|-------|-------------|-----|-----|-----------------|---------------|------|--------------|-------|
| Barengo et al 2004 [164] | To investigate whether moderate or high LTPA are associated with reduced CVD and all-cause mortality, independent of CVD risk factors and other forms of PA in men and women. | • n = 31,677 (15,853 men; 16,824 women) | • Age: 30-59 yr | • Characteristics: Participants from eastern and south-western Finland | • PA assessment: Questionnaire self administered to measure OPA, LTPA and commuting activity | | Moderate and high levels of LTPA and OPA are associated with reduced premature all-cause mortality. |

| | | Men | | | | | |
|---|---|---|---|---|---|---|---|
| | | G1 = 1.00 (referent) | G2 = 0.73 (0.65-0.83) | G3 = 0.66 (0.56-0.77) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.62 (0.53-0.73) | G3 = 0.60 (0.50-0.72) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.52 (0.45-0.61) | G3 = 0.49 (0.39-0.61) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.72 (0.66-0.78) | G3 = 0.71 (0.65-0.78) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.65 (0.60-0.71) | G3 = 0.59 (0.52-0.67) | | | |
| | | G2 = 0.75 (0.54-1.04) | G3 = 0.66 (0.42-1.05) | | | | |
| | | G1 = 1.00 (referent) | G2 = 0.75 (0.67-0.84) | G3 = 0.75 (0.67-0.85) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.73 (0.65-0.83) | G3 = 0.66 (0.56-0.77) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.62 (0.53-0.73) | G3 = 0.60 (0.50-0.72) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.52 (0.45-0.61) | G3 = 0.49 (0.39-0.61) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.72 (0.66-0.78) | G3 = 0.71 (0.65-0.78) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.65 (0.60-0.71) | G3 = 0.59 (0.52-0.67) | | | |

**Finland**

20 year follow-up

| | | Women | | | | | |
|---|---|---|---|---|---|---|---|
| | | G1 = 1.00 (referent) | G2 = 0.72 (0.66-0.78) | G3 = 0.71 (0.65-0.78) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.65 (0.60-0.71) | G3 = 0.59 (0.52-0.67) | | | |
| | | G2 = 0.75 (0.54-1.04) | G3 = 0.66 (0.42-1.05) | | | | |
| | | G1 = 1.00 (referent) | G2 = 0.75 (0.67-0.84) | G3 = 0.75 (0.67-0.85) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.73 (0.65-0.83) | G3 = 0.66 (0.56-0.77) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.62 (0.53-0.73) | G3 = 0.60 (0.50-0.72) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.52 (0.45-0.61) | G3 = 0.49 (0.39-0.61) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.72 (0.66-0.78) | G3 = 0.71 (0.65-0.78) | | | |
| | | G1 = 1.00 (referent) | G2 = 0.65 (0.60-0.71) | G3 = 0.59 (0.52-0.67) | | | |

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Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Prospective cohort | Men | Women |
|--------------------|-----|-------|
| D & B score = 14 | 0.79 (0.70-0.90) = high, Men | 0.89 (0.81-0.98) = mod, women |
|                  | 0.98 (0.83-1.16) = high, women | 0.75 (0.68-0.83) = mod, men |
|                  | 0.77 (0.71-0.84) = active, men | 0.79 (0.70-0.89) = mod, women |
|                  | 0.78 (0.70-0.87) = active, women | 0.77 (0.71-0.84) = active, men |

**Bath 2003 [165]**

- **To examine differences between older men and women on the self-rated health mortality relationship.**
- **n = 1,042 (406 men; 636 women at baseline)**
- **General physical health 14-item health index (Ebrahim et al 1987) scoring from 0-14 (no health problems – multiple health problems)**
- **Multivariate adjusted HR (95% CI)**
- **Number of deaths: At 4 years 242 (106 men; 136 women)**
- **The self-rated health-mortality relationship can be explained by health and related factors among older men and women.**

**UK**

- **Sex: Men and women**
- **At 12 years 665 (287 men; 378 women)**

**Prospective cohort**

- **Age: >65 yr**
- **Characteristics: Community-dwelling Elderly**
- **General physical health 14-item health index (Ebrahim et al 1987) scoring from 0-14 (no health problems – multiple health problems)**
- **Multivariate adjusted HR (95% CI)**
- **Men after 4 years**
  - **High = 1.00 (referent)**
  - **Med = 1.19 (0.61-2.33)**

- **Low = 1.51 (0.75-3.03)**
- **Women after 4 years**
  - **High = 1.00 (referent)**
  - **Med = 1.03 (0.58-1.82)**

- **PA assessment: Self-rated health surveys, divided into 3 levels of PA:**
  - **High**
  - **Medium**
  - **Low**
- **Men after 12 years**
  - **Low = 1.51 (0.86-2.67)**
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Country | Participants | Follow-up | Deaths | Findings |
|-------|---------|--------------|-----------|--------|----------|
| Bijnen et al 1998 [166] | Netherlands | n = 802 | 10 year follow-up | 373 deaths | PA may protect against all-cause mortality in elderly men |
| Prospective cohort | | | | | |
| | | | | | |
| Blair et al 1993 [167] | USA | n = 3,120 | Baseline and 8 year follow-up | 43 deaths | There is a graded inverse relationship between PF and all-cause mortality in women. |
| Prospective | | | | | |
| | | | | | |

Note: D & B score = 12

PA assessment: Questionnaire, divided into groups
Multivariate adjusted RR (95% CI)

Sex: Men
Age: 64-84 yr

Characteristics: Retired Dutch men

Low Fitness = 40
High Fitness = 16
Mod Fitness = 7

The lack of relationship between PA and death rate was believed to be due to an inadequate assessment of PA.
### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | Design | Characteristics | Sex: Men and women | Age: 20-80 yr (mean 43 yr) | PF assessment: Treadmill test; duration was used to assign participants to sex specific groups: | HR for all-cause mortality |
|-------|-----------|--------|-----------------|----------------------|-----------------------------|---------------------------------------------------------------------------------|-----------------------------|
| Blair et al 1996 [168] | To review the association of PF to all-cause and CVD mortality. | Prospective cohort | • n = 32,421 (25,341 men; 7,080 women) | Men | Baseline and average 8 year follow-up (range 0.1-19.1 years) | • 601 deaths in men | The study observed a steep inverse gradient of death rates across low, moderate and high PF levels. The association was strong and remained after adjustment for potential confounding factors. |
| USA | | | | | | • 89 deaths in women | |
| | | | • Characteristics: Participants were excluded if they did not reach 85% of their age predicted maximal heart rate on the maximal exercise treadmill test | | | | |
| | | | | | | | |
| Boyle et al 2007 [169] | To examine the association between PA and the risk of incident disability, including impairment in activities of daily living and instrumental activities of daily living in community based older persons free from dementia. | Prospective cohort | • n = 1,020 | Men | 2.6 year follow-up | • 156 deaths | The risk of death decreased 11% with each hour of PA/wk. |
| | | | | | | | |
| | | | | | | | |

**Proportional hazard modeling**
- Low (least fit 20%): Men Low = 49
- Med = 27
- High = 23

- Women: Low = 29
- Med = 13
- High = 14

**Incidence of all-cause mortality**
- USA
- Women: Low = 29
- Med = 13
- High = 14
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Characteristics | Prospective cohort | Follow-up | Deaths | RR (95% CI) for achieving recommended PA vs. not achieving recommendation |
|-------|-----------------|--------------------|-----------|--------|--------------------------------------------------------------------------------|
| USA   | Participants from 40 retirement communities across Chicago | D & B score = 13 | Baseline (1984-1986) and 12-14 yr follow-up (1998) | 943 deaths | Participants who achieved recommended amounts of MPA or VPA were at a significantly lower risk of death than their sedentary counterparts. |
| Rush Memory and Aging Project | 7,187 (3,742 men; 3,445 women) | To examine the effect of moderately intense PA on all-cause mortality. | | | Sex: Men and women |
|       | n = 7,187 (3,742 men; 3,445 women) | | | | Women |
|       | Baseline (1984-1986) and 12-14 yr | | | | MPA = 0.65 (0.51-0.82) |
| Germany | Participants were healthy and physically active during leisure time | Prospective cohort | | | VPA = 0.78 (0.57-1.08) |
| Germany | Age: 30-69 yr | | | | MPA or VPA = 0.60 (0.47-0.75) |
|        | Characteristics: Participants were healthy and physically active during leisure time | D & B score = 13 | | | Women |
|        | PA assessment: Questionnaire (Minnesota Leisure Time Physical Activity questionnaire) divided into groups based on: Achieving recommended amount of MPA (30 min, 5 d/wk (≥ 2.5 h/wk)) | | | | MPA = 0.90 (0.77-1.01) |
|        | | | | | VPA = 0.74 (0.61-0.90) |
|        | | | | | MPA or VPA = 0.80 (0.68-0.94) |
| | | | | | p < 0.001 |
| | | | | | RR (95% CI) for volume of lifestyle activities (kcal/kg/wk) |
| | | | | | Women |
| | | | | | G1 = 0 |
| | | | | | G2 = 0.79 (0.57-1.08) |
| | | | | | G2 = 0.79 (0.57-1.08) |
| | | | | | G3 = 0.68 (0.50-0.94) |
| | | | | | G4 = 0.57 (0.41-0.79) |
| | | | | | p < 0.001 |
| | | | | | Men |
| | | | | | G1 = 0.79 (0.57-1.08) |
| | | | | | G2 = 0.74 (0.61-0.90) |
| | | | | | G3 = 0.68 (0.50-0.94) |
| | | | | | G4 = 0.57 (0.41-0.79) |
| | | | | | p < 0.001 |
| | | | | | G1 = 1.00 (referent)
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | Participants | Follow-up | RR (95% CI) | Notes |
|-------|-----------|--------------|-----------|-------------|-------|
| Bucksch and Helmert 2004 [171] | To examine LTPA and premature death in the general population of former West Germany. | \( n = 7,187 \) (3,742 men; 3,445 women) | Baseline (1984-1986) and 12-14 year follow-up (1998) | 943 deaths | LTPA is inversely associated with all-cause mortality in men and women. |
| Germany | | | | | |
| Prospective cohort | | | | | |
| D & B score = 14 | | | | | |
| The National Health Survey of the German Federal Institute of Population Research (1984-1998) | | | | | |
| G1 = 0 | G1 = 100 (referent) | | | | |
| G2 = <1 | G2 = 0.92 (0.70-1.23) | | | | |
| G3 = 1-2 | G3 = 0.89 (0.69-1.17) | | | | |
| G4 = >2 | G4 = 0.61 (0.44-0.84) | | | | |
| p <0.01 | | | | | |
| The LTSA-index (kcal/kg/wk) | | | | | |
| G1 = 0 | Women, LTPA | | | | |
| G2 = 1-10 | G1 = 100 (referent) | | | | |
| G3 = 10-25 | G2 = 0.93 (0.82-1.04) | | | | |
| G4 = >25 | G3 = 0.69 (0.48-0.98) | | | | |
| p <0.01 | G4 = 0.57 (0.35-0.94) | | | | |

Adjusted for age, other recommendation, social class, smoking, BMI, cardio risk factor index, alcohol intake, chronic disease index and dietary factors.
| Study | Key Points |
|-------|------------|
| Carlsson et al, 2006 [172] | To investigate the association between PA and mortality in post-menopausal women.  
- **n = 27,734**  
- **Baseline (1997) and 2-7 year follow-up (1999-2004)**  
- **Sex: Women**  
- **Age: 51-83 yr**  
- **Characteristics:** Women who participated in a population based screening programme in 1987  
- **Prospective cohort**  
- **PA assessment:** Questionnaires for: METs/day, different PA (walking/biking), LTPA, OPA, household PA, TV watching and reading  
- **PA (METs/day):**  
  - >50 = 1.00 (referent)  
  - 45-50 = 1.05 (0.77-1.42)  
  - 40-45 s = 1.09 (0.81-1.46)  
  - 45-40 = 1.26 (0.94-1.70)  
  - <35 = 2.56 (1.85-3.53)  
  - Almost never = 1.94 (1.51-2.50)  
- **Mortality – Records from the National Population Register** |
| Sweden |  
- **Characteristics:** Women who participated in a population based screening programme in 1987  
- **Prospective cohort**  
- **PA assessment:** Questionnaires for: METs/day, different PA (walking/biking), LTPA, OPA, household PA, TV watching and reading  
- **PA (METs/day):**  
  - >50 = 1.00 (referent)  
  - 60-90 = 1.01 (0.76-1.34)  
  - 40-60 = 0.92 (0.70-1.20)  
  - 20-40 = 0.96 (0.75-1.23)  
  - <20 = 1.16 (0.90-1.50)  
  - Almost never = 1.94 (1.51-2.50)  
- **D & B score = 12** |
| Cox proportional hazard regression model |  
- **G2 = 0.68 (0.45-1.01)**  
- **G3 = 0.79 (0.51-1.21)**  
- **G4 = 0.46 (0.25-0.85)**  
- **p < 0.01**  
- Adjusted for age, social class, smoking, BMI, cardio risk factor index, alcohol intake, chronic disease index and dietary factors |
| The study indicates that even fairly small amounts of activity will reduce mortality in older women. |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. *(Continued)*

| Study | Population | Sample Size | Follow-up | Cause of Death | Methodology | Odds Ratio (95% CI) | Adjusted for Age |
|-------|------------|-------------|-----------|----------------|-------------|---------------------|-----------------|
| Crespo et al 2002 [173] | Puerto Rico | n = 9,136 (1962-1965) | Baseline and 12 year follow-up | 1,445 deaths | Multivariate OR (95% CI) adjusted for age | LTPA (hr/wk) |
| | | | | | | • >5 = 1.00 (referent) |
| | | | | | | • 4-5 = 0.95 (0.74-1.22) |
| | | | | | | • 2-3 = 1.02 (0.83-1.26) |
| | | | | | | • 1 = 1.09 (0.88-1.36) |
| | | | | | | • <1 = 1.91 (1.56-2.35) |
| | | | | | | OPA |
| | | | | | | • Heavy manual labour = 1.00 (referent) |
| | | | | | | • Walking/lifting/ a lot carrying = 0.96 (0.55-1.70) |
| | | | | | | • Walking/lifting/ not a lot carrying = 1.00 (0.60-1.68) |
| | | | | | | • Mostly standing = 0.91 (0.52-1.61) |
| | | | | | | • Seated 50% of time = 0.97 (0.58-1.62) |
| | | | | | | • Mostly sedentary = 1.93 (1.15-3.25) |
| | | | | | | Household work (hr/d) |
| | | | | | | • >8 h/d = 1.00 (referent) |
| | | | | | | • 7-8 = 0.68 (0.49-0.93) |
| | | | | | | • 5-6 = 0.66 (0.51-0.87) |
| | | | | | | • 3-4 = 0.83 (0.64-1.06) |
| | | | | | | • 1-2 = 0.89 (0.69-1.15) |
| | | | | | | • <1 = 1.73 (1.30-2.32) |

Some PA is better than none in protecting against all-cause mortality. The benefits are independent of body weight.

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### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study                        | Population                                                                 | Follow-up                                                                 | Mortality | Findings                                                                 |
|------------------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------|-----------|--------------------------------------------------------------------------|
| The Puerto Rico Heart Health Program | • The Puerto Rico Heart Health Program                                        | • C3 = 0.63 (0.54-0.74)                                                 | 926 deaths| In the study, an inverse association of both LTPA and walking pace with mortality from all-causes was seen. |
|                              | • C4 = 0.54 (0.46-0.64)                                                    |                                                                           |           |                                                                          |
|                              | p < 0.0001                                                                 |                                                                           |           |                                                                          |
|                              | Multivariate adjusted OR (95% CI)                                           |                                                                           |           |                                                                          |
|                              | • C1 = 1.00 (referent)                                                     |                                                                           |           |                                                                          |
|                              | • C2 = 0.68 (0.58-0.79)                                                    |                                                                           |           |                                                                          |
|                              | • C3 = 0.63 (0.54-0.75)                                                    |                                                                           |           |                                                                          |
|                              | • C4 = 0.55 (0.46-0.65)                                                    |                                                                           |           |                                                                          |
|                              | p < 0.0001                                                                 |                                                                           |           |                                                                          |
| Davey Smith et al 2000 [174]  | To examine the relationship of PA and various causes of death.             | • n = 6,702 (at baseline)                                                | Baseline |                                                                         |
|                              | • Sex: Men                                                                 | Baseline (1969-1970) and 25 year follow-up                                |           |                                                                         |
|                              | • Age: 40-64 yr                                                            |                                                                           |           |                                                                         |
|                              | • Characteristics: Participants from rural northern Japan                    |                                                                           |           |                                                                         |
|                              | • Whitehall study                                                          |                                                                           |           |                                                                         |
|                              | PA assessment: Questionnaire with 3 groups for walking pace (Slower, same, faster) and 3 groups for LTPA (inactive, moderately active, active) | Age adjusted RR (95% CI) for walking pace                                 |           |                                                                         |
|                              | • Slower = 2.47 (2.2-2.8)                                                   |                                                                           |           |                                                                         |
|                              | • Same = 1.35 (1.2-1.5)                                                    |                                                                           |           |                                                                         |
|                              | • Faster = 1.00 (referent)                                                 |                                                                           |           |                                                                         |
|                              | p < 0.001                                                                 |                                                                           |           |                                                                         |
|                              | Fully adjusted RR (95% CI) for walking pace                                |                                                                           |           |                                                                         |
|                              | • Slower = 1.87 (1.6-2.1)                                                   |                                                                           |           |                                                                         |
|                              | • Same = 1.21 (1.1-1.3)                                                    |                                                                           |           |                                                                         |
|                              | • Faster = 1.00 (referent)                                                 |                                                                           |           |                                                                         |
|                              | p < 0.001                                                                 |                                                                           |           |                                                                         |
|                              | Age adjusted RR (95% CI) for LTPA                                          |                                                                           |           |                                                                         |
|                              | • Inactive = 1.44 (1.3-1.6)                                                |                                                                           |           |                                                                         |
|                              | • Mod = 1.13 (1.0-1.2)                                                     |                                                                           |           |                                                                         |
|                              | • Active = 1.00 (referent)                                                 |                                                                           |           |                                                                         |
|                              | p < 0.001                                                                 |                                                                           |           |                                                                         |
|                              | Fully adjusted RR (95% CI) for LTPA                                        |                                                                           |           |                                                                         |
|                              | • Inactive = 1.20 (1.1-1.3)                                                |                                                                           |           |                                                                         |
|                              | • Mod = 1.07 (1.0-1.2)                                                     |                                                                           |           |                                                                         |
|                              | • Active = 1.00 (referent)                                                 |                                                                           |           |                                                                         |
|                              | p < 0.001                                                                 |                                                                           |           |                                                                         |
| Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued) |
| --- |
| Eaton et al 1995 [175] | To determine whether self-reported PA predicts a decreased rate of CHD and all-cause mortality in middle aged men. |
| Europe, Israel, mid-eastern Asia, Northern Africa | n = 8,463 21 year follow-up | n = 2,593 deaths |
| Prospective cohort | D & B score = 12 | | |
| | | PA assessment: Questionnaire for LTPA | Age adjusted RR (95% CI) |
| | | Sex: Men | LTPA |
| | | Age: ≥40 yr | G1 = Sedentary |
| | | Characteristics: Government employees without known CVD | G2 = Light |
| | | | G3 = Light daily |
| | | | G4 = Heavy |
| | | | G5 = Physical labour |
| | | | G1 = 1.00 (referent) |
| | | | G2 = 0.84 (0.74-0.94) |
| | | | G3 = 0.81 (0.73-0.90) |
| | | | G4 = 0.84 (0.72-0.98) |
| | | | G5 = 0.56 (0.43-0.74) |
| | | | p < 0.005 |

| Fang et al 2005 [176] | To assess the association of exercise and CVD outcome among persons with different blood pressure status. |
| USA | n = 9,791 (3,819 men; 5,972 women) 17 year follow-up | Incidence of all-cause mortality and PA |
| Prospective cohort | D & B score = 12 | A significant effect of exercise on mortality in normotensive subjects was not found. |
| | | | |
| | | | PA assessment: Questionnaire with 3 groups |
| | | | Multivariate adjusted HR (95% CI) |
| | | | G1 = Least exercise |
| | | | G2 = Moderate exercise |
| | | | G3 = Most exercise |
| | | | G1 = 1.00 (referent) |
| | | | G2 = 0.75 (0.53-1.05) |
| | | | G3 = 0.71 (0.45-1.12) |

| Fried et al 1998 [177] | To determine the disease, functional and personal characteristics that jointly predict mortality. |
| USA | n = 5,886 5 year follow-up | 646 deaths |
| Prospective cohort | D & B score = 11 | PA was a predictor of 5-year mortality. |
| | | | |
| | | | PA assessment: Self reported exercise (5 groups) |
| | | | Incidence of all-cause mortality and PA |
| | | | MPA or VPA (kJ/wk) |
| | | | Multivariate adjusted RR (95% CI) |
| | | | G1 = ≤282 |
| | | | G2 = 283-1789 |
| | | | G3 = 1790-4100 |
| | | | G4 = 4101-7908 |
| | | | G5 = >7908 |
| | | | G1 = 1.00 (referent) |
| | | | G2 = 0.78 (0.60-1.00) |
| | | | G3 = 0.81 (0.63-1.05) |
| | | | G4 = 0.72 (0.55-0.93) |
| | | | G5 = 0.56 (0.43-0.74) |
| | | | p < 0.005 |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study          | Country       | Number of Participants | Duration | Follow-up | Mortality | Physical Activity Assessment | Method                                      | Adjusted RR (95% CI)                     | Significance |
|---------------|---------------|------------------------|----------|-----------|-----------|-------------------------------|---------------------------------------------|-----------------|
| Fujita et al 2004 [178] | Japan        | n = 41,163 (20,004 men; 21,159 women) | Baseline (1990) and 11 year follow-up (2001) | 1,879 deaths | Time spent walking was associated with a reduced risk for all-cause mortality. |
|               | Prospective cohort | D & B score = 13   | Age and sex adjusted RR (95% CI) for time spent walking (hr/d) |                                     |                                     |
|               | Japan         |                        | G1 = ≤ 30 min | G2 = 30 min to 1 hr | G3 = ≥ 1 hr | Age and sex adjusted RR (95% CI) for time spent walking (hr/d) |                                     |                                     |
|               |               |                        | RR (95% CI) for time spent walking (hr/d) (adjusted for age, education, marital status, past history of diseases, smoking, drinking, BMI and dietary variables) |                                     |                                     |
|               |               | Whole group            | G1 = 1.22 (1.09-1.35) | G2 = 1.09 (0.95-1.22) | G3 = 1.00 (referent) | p < 0.001 | Men only | G1 = 1.14 (1.00-1.30) | G2 = 1.03 (0.90-1.19) | G3 = 1.00 (referent) | p = 0.006 |
|               |               | Women only             | G1 = 1.40 (1.16-1.68) | G2 = 1.23 (1.01-1.49) | G3 = 1.00 (referent) | p < 0.001 | RR (95% CI) for time spent walking (hr/d) (adjusted for age, education, marital status, past history of diseases, smoking, drinking, BMI and dietary variables) | Whole group | G1 = 1.17 (1.04-1.31) | G2 = 1.06 (0.93-1.20) | G3 = 1.00 (referent) | p = 0.011 |
|               |               | Men                    | G1 = 1.08 (0.94-1.25) | G2 = 0.98 (0.84-1.14) | G3 = 1.00 (referent) | p = 0.318 | Women | G1 = 1.38 (1.12-1.70) |                                     |                                     |
|               |               | Women                  | G1 = 1.38 (1.12-1.70) |                                     |                                     |                                     |                                     |                                     |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Population | Methods | Results | Conclusion |
|-------|------------|---------|---------|------------|
| Glass et al 1999 [179] | To examine any association between social activity, productive activity and PA and mortality in older people. | n = 2,761 (1,169 men; 1,143 women) | 13 year follow-up | Incidence of all-cause mortality by fitness activity quartile | More active elderly people were less likely to die than those who were less active. |
| USA | | | | | |
| Prospective cohort | | | | | |
| D & B score = 12 | | | | | |
| | | | | | |
| Gulati et al 2003 [180] | To determine whether exercise capacity is a predictor for all-cause mortality in asymptomatic women. | n = 5,721 | Baseline (1992) and 8 year follow-up (2000) | 180 deaths | This study confirmed that exercise capacity is an independent predictor of death in asymptomatic women, greater than what has been previously established among men. |
| USA | | | | | |
| Prospective cohort | | | | | |
| D & B score = 11 | | | | | |
| | | | | | |
| Haapanen et al 1996 [181] | To examine the association between LTPA and all-cause mortality. | n = 1,072 | Baseline and a 10 yr 10 month follow-up | 168 deaths | Low PA is a risk factor for all-cause mortality. |
| Finland | | | | | |
| | | | | | |
| | | | | | |

For every 1 MET increase there was a reduced death risk of 17% ($p < 0.001$)
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Design | Characteristics | Sample Size | Follow-up | Measurements | Findings |
|-------|--------|-----------------|-------------|-----------|--------------|----------|
| Hakim et al 1998 [182] | Prospective cohort | Age: 35-63 yr, Healthy, sedentary | n = 707 | Baseline and 12 yr follow-up | Mortality–National Death Index search, Cox proportional HR | G1 = 2.74 (1.46-5.14) G2 = 1.10 (0.55-2.21) G3 = 1.74 (0.87-3.50) G4 = 1.00 (referent) | USA 
To examine the association between walking and mortality in retired men. 
208 deaths The findings in older physically capable men indicate that regular walking is associated with a lower overall mortality rate. |
| Hillsdon et al 2004 [183] | Prospective cohort | Age: 61-81 yr, Retired non-smoking men who were physically capable of participating in low intensity activities on a daily basis | n = 10,522 (4,929 men; 5,593 women) | >10 year follow-up | PA assessment: Questionnaire for frequency of VPA | G1 vs. G3 = 1.8 (1.2-2.7) G1 vs. G2 = 1.5 (1.1-2.1) G2 vs. G3 = 1.1 (0.8-1.7) Trend p = 0.01 | UK 
To examine whether VPA is associated with all-cause mortality. 
825 deaths Questionnaire respondents who reported engaging in VPA less than twice a week experienced a 37% reduced risk of all-cause mortality compared with respondents who reported a lower frequency of VPA. |

Prospective cohort
D & B score = 14
- Characteristics: Healthy, sedentary
- Mortality–National Death Index search
- Cox proportional HR

Prospective cohort
D & B score = 12
- Characteristics: Retired non-smoking men who were physically capable of participating in low intensity activities on a daily basis
- PA assessment: Questionnaire for frequency of VPA
- Honolulu Heart Program

Prospective Cohort
D & B score = 11
- Characteristics: Healthy, sedentary
- OXCHECK study
- Fully adjusted RR (99% CI)
- Mortality – Recorded from the Office of National Statistics

D & B score = 14
- Characteristics: Healthy, sedentary
- Mortality–National Death Index search
- Cox proportional HR

D & B score = 12
- Characteristics: Retired non-smoking men who were physically capable of participating in low intensity activities on a daily basis
- PA assessment: Questionnaire for frequency of VPA
- Honolulu Heart Program

D & B score = 11
- Characteristics: Healthy, sedentary
- OXCHECK study
- Fully adjusted RR (99% CI)
- Mortality – Recorded from the Office of National Statistics

Hakim et al 1998 [182] 
To examine the association between walking and mortality in retired men. 
USA 
208 deaths The findings in older physically capable men indicate that regular walking is associated with a lower overall mortality rate. |

Hillsdon et al 2004 [183] 
To examine whether VPA is associated with all-cause mortality. 
UK 
825 deaths Questionnaire respondents who reported engaging in VPA less than twice a week experienced a 37% reduced risk of all-cause mortality compared with respondents who reported a lower frequency of VPA. |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Year | Objective | Design | Sample Size | Follow-up | Deaths | Findings |
|-------|------|-----------|--------|-------------|-----------|--------|----------|
| Hu et al 2005 [184] | To examine the association of PA and BMI and their combined effect with the risk of total, CVD and cancer mortality. | Prospective cohort | Men and women | 47,212 (22,528 men, 24,684 women) | 17.7 year follow-up | 7,394 deaths | Regular PA is an important indicator for decreased risk of all-cause mortality. PA has a strong independent effect on mortality. |
| | | Finland | Age 25-64 yr | | | | |
| | | Characteristics: Participants from eastern Finland | | | | |
| | | PA assessment: Questionnaire for PA level, divided into 3 groups | | | Adjusted HR (95% CI) | |
| | | Men | G1 = 1.00 (referent) | | | G1 = Low |
| | | | G2 = 0.74 (0.68-0.81) | | | G2 = Moderate |
| | | | G3 = 0.63 (0.58-0.70) | | | G3 = High |
| | | | Trend p = <0.001 | | | |
| | | Women | G1 = 1.00 (referent) | | | G1 = Low |
| | | | G2 = 0.64 (0.58-0.70) | | | G2 = Moderate |
| | | | G3 = 0.58 (0.52-0.64) | | | G3 = High |
| | | | Trend p = <0.001 | | | |
| Hu et al 2004 [185] | To examine the association of BMI and PA with death. | Prospective cohort | Women | 116,564 | 24 year follow-up | 10,282 deaths | Reduced PA is a strong and independent predictor of death. |
| | | USA | Age: 30-55 yr | | | | |
| | | Characteristics: Females free of known CVD and cancer | | | | |
| | | PA assessment: Questionnaire for PA level, divided into 3 groups (hr/week) | | | Multivariate RR (95% CI) by PA (hr/wk) | |
| | | | G1 = ≥ 3.5 | | | G1 = 1.00 (referent) |
| | | | G2 = 1.0-3.4 | | | G2 = 1.18 (1.10-1.26) |
| | | | G3 = <1.0 | | | G3 = 1.52 (1.41-1.63) |
| | | BMI (kg/m²) | G1 = <25 | | | G1 = 1.00 (referent) |
| | | | G2 = 25-29 | | | G2 = 1.14 (1.06-1.22) |
| | | | G3 = 30 | | | G3 = 1.44 (1.34-1.55) |
| Kampert et al 1996 [186] | To examine PF and PA in relation to all-cause and cancer mortality. | Prospective cohort | | 32,421 (25,341 men, 7,080 women) | Baseline (1970) and ~8 year follow-up (1989) | 690 deaths | The data support the hypothesis that an active and fit way of life delays death. |

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http://www.ijbnpa.org/content/7/1/39
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Characteristics | Study Design | PA Assessment | Outcome | Results |
|-------|-----------------|--------------|---------------|---------|---------|
| Kaplan et al 1996 [187] | Sex: Men and women | USA | Prospective cohort | Age: 20-88 yr (mean ~43) | Incidence of all-cause mortality and PA | Cox proportional HR |
| | USA | Prospective cohort | Age: 16-94 yr | Characteristics: Northern Californian adults | Death rates/1000 person years | Men, Women |
| | USA | Prospective cohort | | | Death rates/1000 person years | Men, Women |

**Men**

- Sedentary = 1.00 (referent)
- C1-2 = 0.71 (0.58-0.97)
- C3 = 0.83 (0.59-1.16)
- C4 = 0.57 (0.30-1.08)
- C5 = 0.92 (0.29-2.88)

**Women**

- Sedentary = 1.00 (referent)
- C1-2 = 0.68 (0.39-1.17)
- C3 = 0.39 (0.09-1.65)
- C4-5 = 1.14 (0.27-4.80)

**Sedentary = 855**

**C1-2 = 1,072**

**C3 = 1,292**

**C4 = 1,453**

**C5 = 1,601**

**Sedentary = 605**

**C1-2 = 792**

**C3 = 979**

**C4-5 = 1,158**

**Cox proportional HR**

**T1 = 24.68**

**T2 = 11.37**

**T3 = 7.59**

**T1 = 18.03**

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Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | Participants | Methods | Follow-up | Outcomes | Findings |
|-------|-----------|--------------|---------|-----------|----------|----------|
| Khaw et al 2006 [188] | To examine the relationship between PA patterns over 1 year and total mortality. | n = 22,191 (9,984 men; 12,207 women) | UK | 8 year follow-up | 1,553 deaths | Even very moderate levels of usual PA are associated with reductions in mortality. |
| | | | | | | |
| Prospective cohort | | | | | | |
| | | | | | | |
| D & B score = 13 | | | | | | |
| | | | | | | |
| Kohl et al 1996 [189] | To determine the association of maximal exercise hemodynamic responses with risk of all-cause mortality. | n = 26,621 (20,387 men; 6,234 women) | USA | Average 8.1 year follow-up | 348 deaths in men and 66 in women | The results suggest an exaggerated SBP or an attenuated heart rate response to maximal exercise may indicate an elevated risk for mortality. |
| | | | | | | |
| Prospective cohort | | | | | | |
| | | | | | | |
| D & B score = 12 | | | | | | |

**Notes:**
- T2 = 7.66
- T3 = 3.88

**Risks:**
- Incidence of all-cause mortality and PA
- Adjusted RR (95% CI)
- All

**Characteristics:** Community living participants

**PA assessment:** Questionnaire, divided into 4 groups of PA

**PF assessment:** Maximal exercise test HR (bpm), divided into 4 Groups:
- Q1 = 1.00 (referent)
- Q2 = 0.61 (0.44-0.85)
- Q3 = 0.69 (0.51-0.93)
- Q4 = 0.60 (0.41-0.87)

**Age:** Male mean 42.2 yr; female mean 41.9 Yr

**Characteristics:** Apparently healthy patients of a preventive medicine centre
### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | Study Population | Baseline and Outcomes | Findings |
|-------|-----------|------------------|-----------------------|----------|
| Kujala et al 1998 [190] | To investigate LTPA and mortality in a cohort of twins. | • Finland, Age: 25-64 yr, Characteristics: Healthy, Finnish same sex twins | • Baseline 1975 and death outcome from 1977-1994 | **Women**<br>• Q1 = 1.00 (referent)<br>• Q2 = 1.23 (0.65-2.32)<br>• Q3 = 0.69 (0.30-1.63)<br>• Q4 = 0.71 (0.22-2.24)<br>Trend p>0.05 | LTPA is associated with reduced mortality, even after genetic and other familial factors are taken into account. |

**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex<br>**Prospective cohort**<br>• The Finnish Twin Cohort<br>D & B score = 13<br>Baseline 1975 and death outcome from 1977-1994<br>1,253 deaths<br>**Women**<br>• Sex: Men and women<br>• Age: 25-64 yr<br>• Characteristics: Healthy, Finnish same sex twins<br>PA assessment: Questionnaire, quintiles of fitness in MET hours/day<br>Adjusted for age and sex

[190] Kujala et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39

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Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study                  | Objective                                                                 | Sample Size | Follow-up | RR (95% CI) by category of walking |
|------------------------|---------------------------------------------------------------------------|-------------|-----------|-----------------------------------|
| LaCroix et al 1996     | To determine whether walking is associated with a reduced risk of CVD hospitalization and death in older adults. | n = 1,645 (615 men; 1030 women) | 4.2 year follow-up | Walking more than 4 hr/wk was associated with a reduced risk of mortality from all-causes. |
| USA                    |                                                         |             |           |                                   |
| Prospective cohort     |                                                         |             |           |                                   |
| D & B score = 12       |                                                         |             |           |                                   |

- CE = 0.44 (0.23-0.83)
  Trend p = 0.005
  Adjusted for smoking
  - Sedentary = 1.00 (referent)
  - OE = 0.70 (0.48-1.01)
  - CE = 0.56 (0.29-1.09)
  Trend p = 0.004
  Adjusted for smoking, occupational group, alcohol
  - Sedentary = 1.00 (referent)
  - OE = 0.73 (0.50-1.07)
  - CE = 0.56 (0.29-1.11)
  Trend p = 0.06
  OR (95% CI) in quintiles among 434 same sex twin pairs compared with sedentary category in 1975
  - Q1 = 1.00 (referent)
  - Q2 = 0.85
  - Q3 = 0.72
  - Q4 = 0.68
  - Q5 = 0.60

LaCroix et al 1996
[191]

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### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | Sample Size | Methods | Results |
|-------|-----------|-------------|---------|---------|
| Lam et al 2004 [192] | To investigate the relationship between LTPA and mortality in Hong Kong | n = 24,079 cases (13,778 men; 10,301 women); n = 13,054 controls (3,918 men; 9,136 women) | PA assessment: Questionnaire for LTPA, divided into 3 groups | Multivariate adjusted OR (95% CI) by LTPA frequency: Men: G1 = 1.00 (referent); G2 = 0.60 (0.54-0.67); G3 = 0.66 (0.60-0.73) Women: G1 = 1.00 (referent); G2 = 0.73 (0.68-0.79); G3 = 0.66 (0.60-0.73) | The data confirm and extend previous findings in Caucasian populations on the association between LTPA and longevity. |
| | | 10 years prior | | | |
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| Lan et al 2006 [193] | To investigate the relationship between exercise and all-cause mortality. | n = 2,113 (1,081 men; 1,032 women) | PA assessment: Questionnaire for LTPA (frequency/wk) | HR (95% CI) by LTPA frequency: Men: G1 = 1.00 (referent); G2 = 0.49 (0.36-0.67); G3 = 0.20 (0.09-0.46) Women: G1 = 1.00 (referent); G2 = 0.60 (0.42-0.85); G3 = 0.48 (0.32-0.73) | Older persons are recommended to expend at least 1000 kcal/wk through regular exercise for mortality reduction. |
| | | Baseline and 2 year follow-up | | | |
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Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Laukkanen et al 2001 [194] | Questionnaire for EE (kcal/wk), divided into 5 groups: | Trend p = <0.001 |
|----------------------------|------------------------------------------------------|------------------|
|                             | G1 = Sedentary                                       | Multivariate adjusted |
|                             | G2 = <500                                            | • G1 = 1.00 (referent) |
|                             | G3 = 500-999                                         | • G2 = 0.70 (0.50-0.98) |
|                             | G4 = 1000-1999                                       | • G3 = 0.35 (0.15-0.82) |
|                             | G5 = ≥2000                                           | Trend p = 0.014 |
|                             |                                                      | HR (95% CI) by EE |
|                             |                                                      | Adjusted for age and sex |
|                             |                                                      | • G1 = 1.00 (referent) |
|                             |                                                      | • G2 = 0.64 (0.41-1.01) |
|                             |                                                      | • G3 = 0.55 (0.35-0.85) |
|                             |                                                      | • G4 = 0.30 (0.17-0.53) |
|                             |                                                      | • G5 = 0.24 (0.12-0.48) |
|                             |                                                      | Trend p <0.001 |
|                             |                                                      | Multivariate adjusted |
|                             |                                                      | • G1 = 1.00 (referent) |
|                             |                                                      | • G2 = 0.80 (0.49-1.30) |
|                             |                                                      | • G3 = 0.74 (0.46-1.17) |
|                             |                                                      | • G4 = 0.50 (0.27-0.90) |
|                             |                                                      | • G5 = 0.43 (0.21-0.87) |
|                             |                                                      | Trend p = 0.043 |
|                             | To examine the relationship between maximal oxygen    | 124 deaths |
|                             | uptake and overall mortality.                        | PF has a strong, graded, inverse association with overall mortality. |
|                             | • n = 1,294                                          | Baseline and 10.7 year follow-up |
|                             |                                                      | • Age: 42.0-61.3 yr (mean 52.1) |
|                             |                                                      | • Characteristics: Men free from OVD, COPD, and cancer at baseline |
|                             |                                                      | PF assessment: Exercise tolerance test, 4 groups by maximal oxygen uptake (ml/kg/min) |
|                             |                                                      | Maximal oxygen uptake |
|                             |                                                      | • G1 = 1.00 (referent) |
|                             |                                                      | • G2 = 1.47 (0.71-3.01) |
|                             |                                                      | • G3 = 2.79 (1.44-5.39) |
|                             |                                                      | • G4 = 3.85 (2.02-7.32) |
|                             |                                                      | • G5 = 7.3 (3.65-14.6) |
|                             |                                                      | Linear trend p = <0.001 |
| Finnish                    |                                                      |                           |
| Prospective cohort          |                                                      |                           |
| D & B score = 14            |                                                      |                           |
| Study                          | Design/Methodology                                                                 | Outcomes                                                                                                           | Findings                                                                                                                                 |
|-------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Lee and Paffenbarger 2000 [195] | To compare various levels of PA with mortality.                                    | RR (95% CI) 2,539 deaths                                                                                         | The study provides some support for recommendations that emphasize MPA. A benefit of VPA is also evident.                                |
| USA                           | Prospective cohort The Harvard Alumni Health Study                                  | RR (95% CI)                                                                                                       |                                                                                                                                         |
|                               | D & B score = 12                                                                  | RR (95% CI)                                                                                                       |                                                                                                                                         |
| Lee et al 1995 [196]          | To examine the independent association of vigorous and non-vigorous PA with longevity. | RR (95% CI) 3,728 deaths                                                                                         | There is a graded inverse relationship between PA and mortality. Vigorous, but not non-vigorous activities are associated with longevity. |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| USA | Characteristics: Harvard University alumni, without self-reported physician diagnosed cardiovascular disease, cancer or chronic obstructive pulmonary disease |
|-----|----------------------------------|
|     | Prospective cohort Q1 = ≤ 630 |
|     | Q2 = 630-1680 Q3 = 1680-3150    |
|     | Q4 = 3150-6300 Q5 = >6300       |
| D & B score = 12 | RR (95% CI) by EE (Vigorous activity, kJ/wk) |
|     | Q1 = 1.00 (referent) Q2 = 0.94 (0.86-1.04) |
|     | Q3 = 0.95 (0.86-1.05) Q4 = 0.91 (0.83-1.01) |
|     | Q5 = 0.91 (0.82-1.00)          |
|     | D & B score = 12 Q4 = 3150-6300 |
|     | Q5 = >6300 RR (95% CI) by EE (Vigorous activity, kJ/wk) |
|     | Q1 = 1.00 (referent) Q2 = 0.88 (0.82-0.96) |
|     | Q3 = 0.92 (0.82-1.02) Q4 = 0.87 (0.77-0.99) |
|     | Q5 = 0.87 (0.78-0.97)          |
| Lee et al 2004 [197] | To investigate the effect of various PA patterns on all-cause mortality. |
|     | n = 8,421 Baseline 1988 and follow-up 1993 |
|     | 1,234 deaths The results suggest that regular PA generating 1000 kcal/wk or more should be recommended for lowering mortality rates. Among those with no major risk factors, even 1-2 episodes per week generating 1000 kcal or more can postpone mortality. |
|     | Sex: Men |
|     | Age: Mean 66 yr |
|     | USA | Characteristics: Participants free of major chronic disease |
| Prospective cohort | PA assessment: Questionnaire for PA (kcal/wk), 4 groups |
|     | G1 = 1.00 (referent) G2 = 0.75 (0.63-0.90) |
|     | G3 = 0.82 (0.63-1.07) G4 = 0.61 (0.53-0.69) |
| D & B score = 11 | Multivariate adjusted |
|     | G2 = 500-999 (Insufficiently active) |
|     | G3 = ≥ 1000 (Weekend warrior) |
|     | G4 = Regularly active |
|     | G1 = 1.00 (referent) G2 = 0.75 (0.62-0.91) |
|     | G3 = 0.85 (0.65-1.11) |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Participants | Design | Methods | Follow-up | Outcomes | Findings |
|-------|-------------|--------|---------|-----------|----------|----------|
| Leitzmann et al 2007 [198] | n = 252,925 (142,828 male; 110,097 women) | Prospective cohort | PA assessment: Questionnaire for MPA and VPA, 5 groups each MPA (h/wk) | Baseline and 6 month follow-up | 7,900 deaths | Following PA guidelines is associated with lower risk of death. Mortality benefit may also be achieved by engaging in less than recommended activity levels. |
| USA | | | Multivariate adjusted RR (95% CI) according to activity | | | |
| | | | G1 = 1.00 (referent) | G2 = 0.85 (0.79-0.93) | G3 = 0.79 (0.74-0.85) | G4 = 0.76 (0.71-0.82) | G5 = 0.68 (0.63-0.73) |
| D & B score = 13 | | | | | | |
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| Leon et al 1997 [199] | n = 12,138 | Prospective cohort | PA assessment: Minnesota LTPA questionnaire, categorized by frequency/month and average duration, deciles (min/d) | 16 year follow-up | 1,904 deaths | The data suggest that a relatively small amount of daily moderate intensity LTPA can reduce premature mortality in middle-aged and older men at high risk for CHD. |
| | | | Multivariate adjusted RR (95% CI) by deciles of LTPA | | | |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Country       | Study Details                                                                 | Results                                                                 |
|---------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| USA           | Prospective cohort: Men who at entry to the study were free of clinical evidence of CHD or other serious medical problems but were at the upper 10%-15% of a CHD probability score distribution derived from the FHS data. | Cox proportional HR                                                     |
|               | D & B score = 12                                                              | D1 = 1.00 (referent)                                                   |
|               | D2-4 = 0.85 (0.73-0.99)                                                       | D5-7 = 0.87 (0.75-1.02)                                                |
|               | D8-10 = 0.83 (0.71-0.97)                                                      | D1 = 4.9                                                               |
|               | D2-4 = 22.7                                                                  | D5-7 = 53.9                                                            |
|               | D8-10 = 140.4                                                                 |                                                                 |
| Sweden        | Prospective cohort: Free from major disease at baseline PA assessment: Questionnaire for OPA and LTPA, 3 groups | Cox proportional HR                                                     |
|               | Sex: Women                                                                    | RR (95% CI) by LTPA                                                    |
|               | Age: 38-60 yr                                                                 | Low = 1.00 (referent)                                                  |
|               | LTPA during age 20-38 years                                                   | Med = 0.66 (0.34-1.26)                                                |
|               | LTPA during the past 12 months                                                | High = 0.46 (0.21-1.01)                                               |
|               | 20 year follow-up                                                             |                                                                 |
| Lissner et al 1996 [200] | To examine the relationship of OPA and LTPA on all-cause mortality in women. | Cox proportional HR                                                     |
|               | n = 1,405                                                                     | 277 deaths                                                             |
|               | Baseline and 20 year follow-up                                                | Decreases in PA as well as low initial levels are strong risk factors for mortality. |
|               | Sex: Women                                                                    | RR (95% CI) by LTPA                                                    |
|               | Age: 38-60 yr                                                                 | Low = 1.00 (referent)                                                  |
|               | LTPA during age 20-38 years                                                   | Med = 0.56 (0.35-0.90)                                                |
|               | LTPA during the past 12 months                                                | High = 0.44 (0.22-0.91)                                               |
|               | 20 year follow-up                                                             |                                                                 |
| The Gothenburg Prospective Study of Women | OPA assessment: Questionnaire for OPA and LTPA, 3 groups | Proportional hazard regression                                           |
|               | G1 = Low                                                                       | Low = 1.00 (referent)                                                  |
|               | G2 = Medium                                                                    | Med = 0.56 (0.39-0.82)                                                |
|               | G3 = High                                                                       | High = 0.43 (0.24-0.88)                                               |
|               | 20 year follow-up                                                             |                                                                 |
|               | OPA during age 20-38 years                                                    |                                                                 |

LTPA: Leisure-Time Physical Activity; OPA: Occupational Physical Activity; D & B score: Risk score derived from the D & B study; CHD: Coronary Heart Disease; FHS: Framingham Heart Study; RR: Risk Ratio; CI: Confidence Interval.
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | Participants | Design | Measured PA | Follow-up | Outcomes |
|-------|-----------|--------------|--------|-------------|-----------|----------|
| Manini et al 2006 [201] | To determine whether energy expenditure is associated with all-cause mortality in older adults. | • n = 302 (150 men, 152 women) | Prospective cohort | • Sex: Men and women | Mean follow-up of 6.15 years | • 55 deaths |
| USA | Age: 70-82 yr | PA assessment: Questionnaire, divided into tertiles of PA EE (kcal/d) | Adjusted for age, sex, race and study site | | Free-living activity EE was strongly associated with lower risk of mortality. |
| D & B score = 13 | Characteristics: High-functioning community dwelling elders | | | | |
| | | T1 = <521 | • T1 = 1.00 (referent) |
| | | T2 = 521-770 | • T2 = 0.63 (0.63-1.18) |
| | | T3 = >770 | • T3 = 0.37 (0.15-0.76) |

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Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study Details | Outcome | Follow-up | Mortality | Methodology |
|---------------|---------|-----------|-----------|-------------|
| Matthews et al 2007 [202] | To determine the effects of exercise and non-exercise PA on mortality. | n = 67,143 | Baseline and an average of 5.7 year follow-up | Overall mortality is an important indicator of longevity. |
| China | Characteristics: Women without heart disease, stroke or cancer | PA assessment: Interview to report (MET hr/d), 4 groups Overall activity | Multivariate adjustment | |
| Prospective cohort | | | | |
| D & B score = 12 | | | | |
| Menotti and Seccareccia 1985 [203] | To investigate the relationship between OPA and all-cause mortality. | n = 99,029 | Baseline and 5 year follow-up | The results suggest that PA may play a role in the prediction of fatal events. |
| Italy | Characteristics: Men employed on the Italian railway system | PA assessment: Questionnaire Men at risk classified by 3 levels of PA and 3 levels of job responsibility, combined to create 8 groups of PA-job responsibility | Age adjusted death rates per 1000 over 5 years classified by PA only | |
| | | | | | Sedentary = 26.20 |
| | | | | | Moderate = 27.05 |
| | | | | | Heavy = 27.35 |
| Study | Design | Characteristics | 5-8 year follow-up | Incidence of all-cause mortality and PA | An inverse relation of PA and total mortality |
|-------|--------|-----------------|-------------------|---------------------------------------|------------------------------------------|
| Mensink et al 1996 [204] | Germany | - Sex: Men and women | Total activity, 3 groups | Adjusted RR (95% CI) | |
| Prospective cohort | - Age: 25-69 yr | - Characteristics: Participants from communities in Western Germany | Total activity, men | | |
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| D & B score = 12 | | | | | |
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| Study                          | Objective                                                                 | Sample Size | Follow-up | Incidence of all-cause mortality and PA | Conditioning activity, women |
|-------------------------------|----------------------------------------------------------------------------|-------------|-----------|----------------------------------------|------------------------------|
| Morgan and Clarke 1997 [205]  | To assess the value of broadly based customary PA scores in predicting 10-year mortality in elderly people. | n = 1,042 (407 men, 635 women) | 10 year follow-up | Incidence of all-cause mortality and PA | Conditioning activity, women |
|                              | • Sex: Men and women PA assessment: Questionnaire for PA, 3 groups         |             |           |                                         | Conditioning activity, women |
|                              | • Age: ≥65 yr                                                              |             |           |                                         | Conditioning activity, women |
|                              | • Characteristics: British elders                                          |             |           |                                         | Conditioning activity, women |
|                              | D & B score = 12                                                           |             |           |                                         | Conditioning activity, women |
|                              | Prospective cohort                                                        |             |           |                                         | Conditioning activity, women |
|                              | • Nottingham Longitudinal Study of Activity and Aging                     |             |           |                                         | Conditioning activity, women |
|                              | G1 = Low                                                                   |             |           |                                         | Conditioning activity, women |
|                              | G2 = Intermediate                                                          |             |           |                                         | Conditioning activity, women |
|                              | G3 = High                                                                  |             |           |                                         | Conditioning activity, women |
|                              | Men                                                                        |             |           |                                         | Conditioning activity, women |
|                              | Women                                                                      |             |           |                                         | Conditioning activity, women |
| Myers et al 2002 [206]        | To compare PF and PA levels with all-cause mortality.                      | n = 6,213   | Baseline and mean 6.2 ± 3.7 year         | 1,256 deaths                | Exercise capacity is a more powerful predictor of mortality among men than other established risk factors for CVD. |
|                              | • Sex: Men                                                                 |             | follow-up |                                         | Conditioning activity, women |
|                              | • Age: Mean 59 ± 11 yr                                                    |             |           |                                         | Conditioning activity, women |

*HR (95% CI)*
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| USA | • Characteristics: Participants with a normal exercise test result (n = 2,534) and participants with an abnormal exercise test or CVD or both (n = 3,679) | PF assessment: Treadmill test for VO\textsubscript{2} peak, divided into quintiles (METs) | • Q1 = 4.5 (3.0-6.8) |
| Prospective cohort | | • Q2 = 2.4 (1.5-3.8) | • Q3 = 1.7 (1.1-2.8) | • Q4 = 1.3 (0.7-2.2) |
| D & B score = 12 | Q1 = Lowest level \(1.0-5.9\) | Q2 \(\geq 13.0\) | Q3 = 1.00 (referent) |

Ostbye et al 2002 [207] To analyze the effect of smoking and other modifiable risk factors on ill health, defined in a multidimensional fashion. | • n = 12,956 | 6 year follow-up | • 782 deaths |
| | • Sex: Men and women | | Quitting smoking and increasing exercise levels are the lifestyle interventions most likely to improve overall health. |
| | • Age: 50-60 yr | | |
| USA | • Characteristics: Participants from the Health and Retirement Study (HRS) only | PA assessment: Questionnaire for PA, 4 groups | Incidence of all-cause mortality and PA |
| Prospective cohort | | | |
| D & B score = 13 | G1 = Sedentary | Death rates (95% CI) per 1000 population/yr | |
| | G2 = Light | \(\text{G1} = 20.6 \ (17.8-24.0)\) | |
| | G3 = Moderate | \(\text{G2} = 9.1 \ (8.1-9.5)\) | |
| | G4 = Heavy | \(\text{G3} = 8.3 \ (7.5-9.2)\) | |
| | | \(\text{G4} = 4.4 \ (3.5-5.6)\) | |

Paffenbarger et al 1994 [208] To study the adoption or maintenance of PA and other optional lifestyle patterns for their influence on mortality rates of Harvard College alumni. | • n = 14,786 | Follow-up between 1977 and 1988 | • 2,343 deaths |
| | • Sex: Men | | Adopting a physically active lifestyle delays mortality and extends longevity. |
| | • Age: 45-84 yr (in 1977) | | |

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Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| USA | Characteristics: Harvard College alumni | D & B score = 14 |
|-----|-----------------------------------------|-----------------|
| Prospective cohort Physical activity index (kcal/wk) | • G1 = 1.00 (referent) |
| | • G2 = 1.13 (1.01-1.26) |
| | • G3 = 0.72 (0.64-0.82) |
| | • G4 = 0.77 (0.69-0.85) |
| USA | Physical activity index (kcal/wk) Walking (km/wk) | Adjusted for potential confounding influences |
| Prospective cohort | Physical activity index (kcal/wk) Sports and recreational activities were scored according to intensity and duration |
| | • G1 = 1.00 (referent) |
| | • G2 = 1.21 (1.08-1.35) |
| | • G3 = 0.94 (0.83-1.07) |
| | • G4 = 0.89 (0.78-1.01) |
| | Moderately vigorous sports play (METs) |
| | • G1 = 1.00 (referent) |
| | • G2 = 1.11 (0.93-1.33) |
| | • G3 = 0.73 (0.65-0.81) |
| | • G4 = 0.72 (0.64-0.80) |
| Richardson et al 2004 [209] | To investigate the impact of a sedentary lifestyle on all-cause mortality. | Baseline (1992) and 8 year follow-up |
| | • n = 9,611 (4,642 men; 4,969 women) | • 810 deaths |
| | • Sex: Men and women | A sedentary lifestyle is associated with a higher risk of death in pre-retirement aged adults. |
| | • Age: 51-61 yr | OR (95% CI) |
| | • Characteristics: Participants born between 1931-1941 and who not institutionalized in 1992 | • G1 = 1.00 (referent) |
| | PA assessment: Questionnaire for PA, 3 groups: | • G2 = 0.64 (0.52-0.81) |
| | G1 = Sedentary | • G3 = 0.62 (0.44-0.85) |
| | G2 = occasional or light | • G4 = 0.72 (0.57-0.91) |
| | G3 = Regular MVPA | p = 0.01 |

USA D & B score = 13
| Study                                      | Objective                                                                 | N and follow-up                                                                 | Deaths | Mortality Risk                                                                 |
|-------------------------------------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------|--------------------------------------------------------------------------------|
| Health and Retirement Study               | To determine the association between recreational PA and mortality in women | n = 80,348 Baseline (1980) and follow-up between 1982-1996                     | 4,871  | People who are more physically active are at reduced mortality risk relative to those who are less active. |
| USA                                       | Sex: Women                                                               |                                                                                  |        |                                                                                  |
|                                           | Age: 30-55 yr                                                            |                                                                                  |        |                                                                                  |
|                                           | Characteristics: Free from CVD or cancer at baseline                      |                                                                                  |        |                                                                                  |
|                                           | Nurses Health Study                                                     | PA assessment: Questionnaire in 1980 and updated every 2-4 years, 5 groups of PA (hr/wk) |        |                                                                                  |
|                                           | G1 = 1.00 (referent)                                                    |                                                                                  |        |                                                                                  |
|                                           | G2 = 0.82 (0.76-0.89)                                                   |                                                                                  |        |                                                                                  |
|                                           | G3 = 0.75 (0.69-0.81)                                                   |                                                                                  |        |                                                                                  |
|                                           | G4 = 0.74 (0.68-0.81)                                                   |                                                                                  |        |                                                                                  |
|                                           | G5 = 0.71 (0.61-0.82)                                                   |                                                                                  |        |                                                                                  |
|                                           | p<0.001                                                                  |                                                                                  |        |                                                                                  |
| Prospective cohort                        |                                                                          |                                                                                  |        |                                                                                  |
| D & B score = 11                          |                                                                          |                                                                                  |        |                                                                                  |
|                                          | Sweden                                                                   |                                                                                  |        |                                                                                  |
|                                           | Sex: Men                                                                 |                                                                                  |        |                                                                                  |
|                                           | Age: 47-55 yr                                                            |                                                                                  |        |                                                                                  |
|                                           | Characteristics: Without symptomatic CHD                                  |                                                                                  |        |                                                                                  |
|                                           | PA assessment: Postal questionnaires, 3 groups:                          |                                                                                  |        |                                                                                  |
|                                           | G1 = Sedentary                                                           |                                                                                  |        |                                                                                  |
|                                           | G2 = Moderately active                                                   |                                                                                  |        |                                                                                  |
|                                           | G3 = Regular exercise                                                   |                                                                                  |        |                                                                                  |
|                                           | Unadjusted RR (95% CI)                                                  |                                                                                  |        |                                                                                  |
|                                           | G1 = 1.00 (referent)                                                    |                                                                                  |        |                                                                                  |
|                                           | G2 = 0.74 (0.68-0.82)                                                   |                                                                                  |        |                                                                                  |
|                                           | G3 = 0.73 (0.68-0.79)                                                   |                                                                                  |        |                                                                                  |
|                                           | Multivariate adjustment                                                  |                                                                                  |        |                                                                                  |
|                                           | G1 = 1.00 (referent)                                                    |                                                                                  |        |                                                                                  |
|                                           | G2 = 0.84 (0.77-0.93)                                                   |                                                                                  |        |                                                                                  |
|                                           | G3 = 0.83 (0.77-0.90)                                                   |                                                                                  |        |                                                                                  |

To investigate the effect of OPA and LTPA on risk of death.
| Study                  | Objective                                                                 | Sample Size                                     | Follow-up Period | Deaths | Key Findings                                                                 |
|-----------------------|---------------------------------------------------------------------------|-------------------------------------------------|------------------|--------|------------------------------------------------------------------------------|
| Schnohr et al 2003    | To assess the associations of regular LTPA and changes in LTPA with risk of death. | \( n = 7,023 \) (4,471 men; 5,676 women)       | 18 year          | 2,725  | Maintaining or adopting a moderate or high degree of PA was associated with lower risk of death. |
| Denmark               | - Sex: Men and women                                                      | - PA assessment: Questionnaire, 9 groups         |                  |        |                                                                               |
|                       | - Age: 20-79 yr                                                           | - Characteristics: Participants from the Copenhagen City Heart Registered Population |                  |        |                                                                               |
|                       | Prospective cohort                                                       | G1 = Low–low                                    |                  |        |                                                                               |
|                       |                                                                         | G2 = Low–moderate                               |                  |        |                                                                               |
|                       |                                                                         | G3 = Low–high                                   |                  |        |                                                                               |
|                       |                                                                         | G4 = Moderate–low                               |                  |        |                                                                               |
|                       |                                                                         | G5 = Moderate–Moderate                           |                  |        |                                                                               |
|                       |                                                                         | G6 = Moderate–high                              |                  |        |                                                                               |
|                       |                                                                         | G7 = High–low                                   |                  |        |                                                                               |
|                       |                                                                         | G8 = High–moderate                              |                  |        |                                                                               |
|                       |                                                                         | G9 = High–high                                  |                  |        |                                                                               |
|                       | G1 = 1.00 (referent)                                                     | G2 = 0.64 (0.49-0.83)                           |                  |        |                                                                               |
|                       | G3 = 0.64 (0.47-0.87)                                                    | G4 = 0.73 (0.56-0.96)                           |                  |        |                                                                               |
|                       | G5 = 0.71 (0.57-0.88)                                                    | G6 = 0.64 (0.51-0.81)                           |                  |        |                                                                               |
|                       | G7 = 1.11 (0.76-1.62)                                                    | G8 = 0.66 (0.51-0.85)                           |                  |        |                                                                               |
|                       | G9 = 0.61 (0.48-0.76)                                                    |                                                 |                  |        |                                                                               |
|                       | Women                                                                     | G1 = 1.00 (referent)                            |                  |        |                                                                               |
|                       |                                                                         | G2 = 0.75 (0.57-0.97)                           |                  |        |                                                                               |
|                       |                                                                         | G3 = 0.72 (0.50-1.05)                           |                  |        |                                                                               |
|                       |                                                                         | G4 = 0.70 (0.54-0.91)                           |                  |        |                                                                               |
|                       |                                                                         | G5 = 0.64 (0.52-0.79)                           |                  |        |                                                                               |
|                       |                                                                         | G6 = 0.58 (0.45-0.73)                           |                  |        |                                                                               |
|                       |                                                                         | G7 = 0.72 (0.48-1.07)                           |                  |        |                                                                               |
|                       |                                                                         | G8 = 0.61 (0.47-0.80)                           |                  |        |                                                                               |
|                       |                                                                         | G9 = 0.66 (0.51-0.85)                           |                  |        |                                                                               |
| Schnohr et al 2004    | To examine whether the relationship between established risk factors and mortality differs with socioeconomic status as measured by level of education. | \( n = 30,635 \) (16,236 men; 14,399 women)   | 16 year          | 10,952 | The study shows the strong predictive effect of PA on mortality is independent of education level. |
|                       |                                                                         | 18 year follow-up                               |                  |        |                                                                               |
|                       |                                                                         | 10,952 deaths                                   |                  |        |                                                                               |

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Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

- **Denmark**
  - Age: 20-93 yr
  - Characteristics: Participants from the Copenhagen City Heart Registered Population
  - **Prospective cohort**
  - D & B score = 12

| Characteristics | Incidence of all-cause mortality and PA stratified by years of education |
|-----------------|------------------------------------------------------------------------|
|                  | Deaths <8 years of education                                           |
|                  | Men                                                                     |
|                  | G1 = 916                                                               |
|                  | G2 = 1693                                                              |
|                  | G3 = 1012                                                              |
|                  | G4 = 67                                                                |
|                  | Women                                                                  |
|                  | • G1 = 872                                                             |
|                  | • G2 = 1298                                                            |
|                  | • G3 = 346                                                             |
|                  | • G4 = 10                                                              |
|                  | 8-11 years of education                                                |
|                  | Men                                                                     |
|                  | • G1 = 432                                                             |
|                  | • G2 = 1040                                                            |
|                  | • G3 = 616                                                             |
|                  | • G4 = 33                                                              |
|                  | Women                                                                   |
|                  | • G1 = 363                                                             |
|                  | • G2 = 852                                                             |
|                  | • G3 = 268                                                             |
|                  | • G4 = 10                                                              |
|                  | >11 years of education                                                 |
|                  | Men                                                                     |
|                  | • G1 = 104                                                             |
|                  | • G2 = 302                                                             |
|                  | • G3 = 182                                                             |
|                  | • G4 = 11                                                              |
|                  | Women                                                                   |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study Authors, Year | Objective | Sample Size (Men; Women) | Baseline and Follow-up Details | Deaths | Findings |
|---------------------|-----------|--------------------------|--------------------------------|--------|----------|
| Schnohr et al 2006 [214] | To investigate the association between LTPA and mortality. | n = 4,894 (2,136; 2,758) | Baseline (1976) and start of follow-up in 1981-1983 (to 2000) | 1,787 | Long-term moderate or high PA was associated with significantly lower mortality in men and women. |
|                      | Denmark | Prospective cohort | PA assessment: Survey for LTPA, 3 groups: | | |
|                      | | | G1 = 1.00 (referent) | | |
|                      | | | G2 = 0.64 (0.56-0.73) | | |
|                      | | | G3 = 0.56 (0.48-0.65) | | |
|                      | | | The Copenhagen City Heart Study | | |
|                      | | | D & B score = 13 | | |
|                      | | | Unadjusted | | |
|                      | | | Multivariate adjustment | | |
|                      | | | G1 = 1.00 (referent) | | |
|                      | | | G2 = 0.78 (0.68-0.89) | | |
|                      | | | G3 = 0.75 (0.64-0.87) | | |
|                      | | | Trend p < 0.001 | | |
| Schooling et al 2006 [215] | To examine how a Comprehensive assessment of baseline health status affects the relationship between obesity or PA and mortality. | n = 54,088 (17,849; 36,239) | 4.1 year follow-up | 3,819 | PA, which normally has a negative relationship with adiposity, had the largest impact on survival for the health states, with the strongest inverse relationship between BMI and mortality. |
|                      | Hong Kong | Prospective cohort | PA assessment: Interview for PA min/d, 3 groups | | |
|                      | | | G1 = None | | |
|                      | | | G2 = ≤ 30 min/d | | |
|                      | | | G3 = ≥ 30 min/d | | |
|                      | | | Incidence of all-cause mortality and PA | | |
|                      | | | Adjusted HR (95% CI) | | |
|                      | | | G1 = 1.00 (referent) | | |
|                      | | | G2 = 0.83 (0.76-0.91) | | |
|                      | | | G3 = 0.73 (0.67-0.80) | | |
|                      | | | Trend p = 0.001 | | |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Study | Objective | n | Baseline and follow-up | Outcome | Findings |
|-------|-----------|---|------------------------|---------|----------|
| Sundquist et al 2004 [216] | To study the association between varying levels of PA and all-cause mortality in the elderly. | - n = 3,306 (1,414 men; 1,792 women) | - Baseline (1988-1989) and follow-up in 2000 | - 1,806 deaths | Even occasional PA decreases the risk of mortality among elderly people. |
| Sex: Men and women | Age ≥65 yr | Characteristics: Non-institutionalized elders | Age-adjusted HR (95% CI) | |
| | | | Sweden | |
| | | | Prospective cohort | |
| | | | The Swedish Annual Level-of-Living Survey (Statistics Sweden) | |
| | | | G1 = none | |
| | | | G2 = occasionally | |
| | | | G3 = once per week | |
| | | | G4 = twice per week | |
| | | | G5 = vigorously at least twice per week | |
| | | | Men and women | |
| | | | D & B score = 12 | |
| | | | Cox proportional HR | |
| Talbot et al 2007 [217] | To investigate how changes in LTPA affect all-cause mortality. | - n = 2,092 (1,316 men; 776 women) | - Baseline in 1958 for males and in 1978 for females and an average follow-up of 21.2 ± 94 years for men and 10.2 ± 56 years for women | - 628 deaths (538 male; 90 female) | Greater declines in total and high-intensity LTPA are independent predictors of all-cause mortality. |
| Sex: Men and women | Age: 19-<90 yr | | | | |
| | | | USA | | |
### Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Prospective cohort | Characteristics: Community residents, generally with above average income, high education and with good or excellent self-related health | If RR is <1 then a SD increase is associated with decrease in mortality. If RR is >1, then a SD increase is associated with increase in mortality |
|--------------------|-------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| D & B score = 13   | PA assessment: Questionnaire for LTPA (METs min/24 h), 3 groups |                                                                                                                                  |
|                    | The Baltimore Longitudinal Study of Aging                                                      |                                                                                                                                  |
|                    | G1 = low                                          | Multivariate adjustment                                                                                                         |
|                    | G2 = medium                                       | Men <70 years                                                                                                                   |
|                    | G3 = high                                         | • G1 = 0.96 (0.84-1.08)                                                                                                         |
| Rate of change (ROC)|                                                                                                    | • G2 = 0.91 (0.79-1.04)                                                                                                         |
|                    |                                                                                                   | • G3 = 0.42 (0.33-0.53)                                                                                                         |
|                    |                                                                                                   | • ROC low = 0.90 (0.80-1.01)                                                                                                     |
|                    |                                                                                                   | • ROC med = 1.01 (0.90-1.14)                                                                                                     |
|                    |                                                                                                   | • ROC high = 0.78 (0.65-0.94)                                                                                                    |
|                    |                                                                                                   | Men >70 years                                                                                                                    |
|                    |                                                                                                   | • G1 = 0.95 (0.82-1.10)                                                                                                         |
|                    |                                                                                                   | • G2 = 0.89 (0.76-1.05)                                                                                                         |
|                    |                                                                                                   | • G3 = 0.78 (0.62-0.97)                                                                                                         |
|                    |                                                                                                   | • ROC low = 1.07 (0.93-1.24)                                                                                                     |
|                    |                                                                                                   | • ROC med = 1.13 (1.00-1.27)                                                                                                     |
|                    |                                                                                                   | • ROC high = 0.91 (0.75-1.12)                                                                                                    |
|                    |                                                                                                   | Women <70 years                                                                                                                  |
|                    |                                                                                                   | • G1 = 0.75 (0.53-1.07)                                                                                                         |
|                    |                                                                                                   | • G2 = 0.61 (0.36-1.03)                                                                                                         |
|                    |                                                                                                   | • G3 = 0.80 (0.50-1.30)                                                                                                         |
|                    |                                                                                                   | • ROC low = 1.02 (0.74-1.40)                                                                                                     |
|                    |                                                                                                   | • ROC med = 1.38 (0.86-2.28)                                                                                                     |
|                    |                                                                                                   | • ROC high = 0.90 (0.63-1.27)                                                                                                    |
|                    |                                                                                                   | Women >70 years                                                                                                                  |
|                    |                                                                                                   | • G1 = 0.85 (0.63-1.15)                                                                                                         |
|                    |                                                                                                   | • G2 = 0.78 (0.39-1.59)                                                                                                         |
|                    |                                                                                                   | • G3 = 0.62 (0.32-1.22)                                                                                                         |
|                    |                                                                                                   | • ROC low = 1.10 (0.85-1.42)                                                                                                     |
|                    |                                                                                                   | • ROC med = 0.96 (0.46-2.03)                                                                                                     |
|                    |                                                                                                   | • ROC high = 0.70 (0.40-1.22)                                                                                                    |
| Study | Year | Title | Country | Follow-up | Sex | Age | PA Assessment | Incidence of all-cause mortality and PA past and current | Study Results |
|-------|------|-------|---------|-----------|-----|-----|---------------|--------------------------------------------------------|---------------|
| Trolle-Lagerros et al 2005 [218] | To quantify the effect of PA on overall mortality in younger women and to assess the effect of past versus current activity. | • n = 99,099 | 11.4 year follow-up | • 1,313 deaths | • Sex: Women | • Age: 30-49 yr | PA assessment: Questionnaire using a 5 point scale, 5 groups | • Characteristics: Participants from Norway and one region of Sweden | Current PA substantially reduces mortality among women. The association is observed even with low levels of PA and is accentuated with increased PA. |
| Villeneuve et al 1998 [219] | To examine the relationship between PF, PA and all-cause mortality. | • n = 14,442 (6,246 men; 8,196 women) | Baseline (1981) and 7 year follow-up | RR (95% CI) by EE, multivariate adjustment | • Sex: Men and women | • Age: 20-69 yr | PA assessment: Questionnaire for EE (kcal/kg/day), 5 groups | There was a reduction in mortality risk associated with even modest participation in activities of low intensity. |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Prospective cohort | Canadian Fitness Survey | D & B score = 11 |
|--------------------|-------------------------|-----------------|
|                    | G1 = 1.00 (referent)    |                 |
| Characteristics: Asymptomatic for CVD |                           |                 |
| G2 = 0.81 (0.59-1.11) |                           |                 |
| G3 = 0.79 (0.54-1.13) |                           |                 |
| G4 = 0.86 (0.61-1.22) |                           |                 |
| G5 = 0.82 (0.65-1.04)* |                           |                 |
| G2 = 0.81 (0.56-1.17) |                           |                 |
| G3 = 0.70 (0.44-1.13) |                           |                 |
| G4 = 0.82 (0.53-1.27) |                           |                 |
| G5 = 0.78 (0.59-1.04)* |                           |                 |

D & B score = 11

Canadian Fitness Survey

| G1 = 0-<0.5 | G2 = 0.81 (0.56-1.17) | G3 = 0.70 (0.44-1.13) | G4 = 0.82 (0.53-1.27) | G5 = 0.78 (0.59-1.04)* |
| G2 = 0.5-<1.5 |                           |                     |                       |                    |
| G3 = 1.5-<3.0 |                           |                     |                       |                    |
| G4 = ≥ 3.0 | Non vigorous LTPA, men |                           |                     |                    |
| G5 = ≥ 0.5 |                           |                     |                       |                    |
| PF levels: |                           |                     |                       |                    |
| Recommended | G1 = 1.00 (referent)    |                           |                     |                    |
| Minimum     | G1 = 1.00 (referent)    |                           |                     |                    |
|             | G2 = 0.81 (0.56-1.17) |                           |                     |                    |
|             | G3 = 0.70 (0.44-1.13) |                           |                     |                    |
|             | G4 = 0.82 (0.53-1.27) |                           |                     |                    |
|             | G5 = 0.78 (0.59-1.04)* |                           |                     |                    |

Undesirable Refusal

LTPA, women

Multivariate Poisson regression analysis

| G1 = 1.00 (referent)    |                           |                     |                    |
| G2 = 0.94 (0.69-1.30) |                           |                     |                    |
| G3 = 0.92 (0.64-1.34) |                           |                     |                    |
| G4 = 0.71 (0.45-1.11) |                           |                     |                    |
| G5 = 0.88 (0.68-1.04)* |                           |                     |                    |

Non vigorous LTPA, women

| G1 = 1.00 (referent)    |                           |                     |                    |
| G2 = 0.97 (0.69-1.36) |                           |                     |                    |
| G3 = 0.87 (0.57-1.33) |                           |                     |                    |
| G4 = 0.72 (0.43-1.21) |                           |                     |                    |
| G5 = 0.89 (0.67-1.17)* |                           |                     |                    |

RR (95% CI) by fitness levels, adjusted for age, sex and smoking

Recommended = 1.00 (referent)

| Minimum = 1.02 (0.69-1.51) |                           |                     |                    |
| Undesirable = 1.52 (0.72-3.18) |                           |                     |                    |
| Refusal = 1.04 (0.45-2.39) |                           |                     |                    |

Weller and Corey 1998 [220]

To study the relationship between PA and mortality in women.

| n = 6,620 | Baseline and 7 year follow-up | 449 deaths | PA is inversely associated with risk of death in women. |
|-----------|-------------------------------|------------|------------------------------------------------------|
| Sex: Women | Age: ≥30 yr                  |            | OR (95% CI)                                          |
Table 11: Studies examining the relationship between physical activity and all-cause mortality. (Continued)

| Country | Characteristics: Without known heart disease | PA assessment: Questionnaires for: EE (kcal/kg/d), quartiles | EE (kcal/kg/d) |
|---------|---------------------------------------------|---------------------------------------------------|---------------|
| Prospective cohort | Canadian Fitness Survey | Q1 = lowest | Q1 = 1.00 (referent) |
| | D & B score = 11 | Q2 = | Q2 = 0.91 (0.66-1.23) |
| | | Q3 = | Q3 = 0.94 (0.72-1.23) |
| | | Q4 = highest | Q4 = 0.89 (0.67-1.17) |

Yu et al 2003 [221] To examine the relationship between LTPA and all-cause mortality.

| UK | Characteristics: Without a history of CHD at baseline | PA assessment: Questionnaire (Minnesota LTPA index, kcal/d), 3 group | Age adjusted HR (95% CI) |
|---|-----------------------------------------------------|-----------------------------------------------------------------|------------------------|
| Prospective cohort | Sex: Men Age: 49-64 yr | | G1 = 1.00 (referent) |
| | | | G2 = 0.73 (0.54-0.99) |
| | | | G3 = 0.74 (0.55-1.04) |
| | | Trend $p = 0.046$ | |
| D & B score = 11 | G1 = Light to no activity | Multivariate adjusted | G1 = 1.00 (referent) |
| | G2 = Moderate activity | | G2 = 0.79 (0.58-1.08) |
| | G3 = Heavy activity | | G3 = 0.76 (0.56-1.04) |
| | | Trend $p = 0.083$ | |

Yu et al 2003 [221] To examine the relationship between LTPA and all-cause mortality.

- Characteristics: Without known heart disease
- Canadian Fitness Survey
- Prospective cohort
- D & B score = 11

Yu et al 2003 [221] To examine the relationship between LTPA and all-cause mortality.

- n = 1,975 Baseline and 10 year follow-up
- Q2 = 0.91 (0.66-1.23)
- Q3 = 0.94 (0.72-1.23)
- Q4 = 0.89 (0.67-1.17)
- G1 = 1.00 (referent)
- G2 = 0.73 (0.54-0.99)
- G3 = 0.74 (0.55-1.04)
- Trend $p = 0.046$

The study found a strong inverse association between heavy LTPA and all-cause mortality.
definition of cardiovascular disease ($n = 78$), and other ($n = 19$). Therefore, a total of 49 articles were included in the systematic review of the literature regarding the relationship between physical activity and the incidence of cardiovascular disease.

The majority of the studies included in our systematic review were prospective cohort investigations (Table 12). These studies involved a total of 726,474 participants; averaging 12,313 participants per study (range 680-88,393). There were a total of 34,815 reported cases of cardiovascular disease (ranging per study from 42-2,596). The total length of study follow-up for the prospective cohort studies averaged 14.1 yr (ranging from 2-29 yr). The articles were published over a 32 yr period ranging from 1975 to 2007. These studies involved large samples of men and women from regions throughout the world.

Similar to the all-cause mortality data, the risk for cardiovascular disease demonstrates a graded inverse dose-response relationship to physical activity and fitness. The relative reduction in the incidence of cardiovascular disease averages 33% (median risk reduction of 36%), with greater risk reductions in studies that employed objective measures of aerobic fitness. It is not uncommon for studies to demonstrate a 50% or higher risk reduction when an objective measure of physical fitness was taken (Table 12). The importance of physical activity may actually be underestimated owing to multivariate control for many confounding factors (as discussed previously) and the fact that effects of within-person variation in physical activity are often not considered [55]. The relative risk reduction appears to be similar for men and women, and also appear to extend to non-Caucasian populations [56]. Some evidence also exists indicating that small amounts of physical activity are associated with lower cardiovascular-disease related mortality [57,58]. Similar to all-cause mortality, physical activity confers health benefits independent of other known risk factors [42,59]. Collectively, the level of evidence would be considered to be Level 2A based on the presence of overwhelming evidence from observational trials. The quality of the investigations was generally high with a mean (and median) Downs and Black score of 12 (range 9-14).
Implications

Research in the field began with the landmark work of Morris and colleagues, which demonstrated that men in physically demanding occupations (bus conductors and postmen) had a significantly lower risk of heart disease than individuals who worked in less demanding jobs (bus drivers and office workers) [45]. Since then considerable research has examined the relationship between physical activity and the risk for cardiovascular disease. In fact, several systematic reviews of the literature have been developed regarding the role of habitual physical activity in the primary and secondary prevention of cardiovascular disease [33,60-62]. The research to date has been consistent and compelling, habitual physical activity reduces markedly the risk for cardiovascular disease.

Based on the available literature, there is compelling evidence that the recommendation of 30 min of moderate intensity exercise on most days of the week (equivalent to 4.2 MJ/wk or 1000 kcal/wk) reaches a threshold associated with significant reductions in cardiovascular-related mortality [32,63]. Brisk walking has also been shown to be preferable to a slower pace [64]. However, weekly exercise volumes of less than 4.2 MJ (1000 kcal) may be cardio-protective [14,59,65-67]. For instance, Lee et al. (2001) found that as little as 1 hr/wk of walking was associated with a 50% lower cardiovascular disease mortality in one sample of women. Wisloff et al. [58] reported that a single weekly bout of self-reported high intensity exercise was associated with a lower risk of cardiovascular death relative to those reporting no activity in both men (RR = 0.61, 95% CI = 0.49-0.75), and women (RR = 0.49, 95% CI = 0.27-0.89). Moreover, no additional benefit was seen with higher durations or frequency of exercise sessions [58]. The authors stated that this evidence challenges “current recommendations that require at least 1000 kcal of caloric expenditure per week to achieve exercise-induced protection against premature cardiovascular death.” However, this research is in fact supportive of the Canadian guidelines which recognize the potential health benefits of low volumes of physical activity as reflected by the statement “Every little bit counts, but more is even better - everyone can do it!” It however should be noted that the statement “more is even better” is supported by a strong evidence base.

Recommendation #2

For a reduced risk for cardiovascular disease-related events and mortality, it is recommended that individuals participate in 30 min or more of moderate to vigorous exercise on most days of the week. Greater health benefits appear to occur with high volume and/or intensities of activity. Health benefits may also occur with as little as one hr of brisk walking per week. [Level 2, Grade A]

The Primary Prevention of Stroke

Stroke affects a significant proportion of Canadian society with approximately 50,000 new cases each year [68]. The relationship between physical activity and the risk for stroke is compelling, supporting at least a 25-
Table 12 Studies examining the relationship between physical activity and cardiovascular disease.

| Publication | Objective | Population | Methods | Outcome | Comments and Conclusions |
|-------------|-----------|------------|---------|---------|-------------------------|
| Paffenbarger and Hale 1975 [47] USA | To evaluate the role of PA in reducing coronary mortality among longshoreman | n = 6,351 | 22 years of follow up, or until reached the age of 75 yr | RR (95% CI) Sudden death | VPA is associated with reduced risk of coronary mortality, particularly sudden cardiac death. |
| D & B score = 12 | | | | | |
| | | | | | |
| Manson et al 2002 [56] USA | To compare the roles of walking and vigorous exercise in the prevention of CV events in a large, ethnically diverse cohort of postmenopausal women. | n = 73,743 | Enrolment from 1994-98 Clinic visit for baseline screening, | Number of New Cases: 345 | Both walking and VPA are associated with substantial reductions in the incidence of CHD events. |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Walking (MET-hr/wk) | D & B score = 12 |
|---------------------|------------------|
| G3 = 7.3-13.4       | G4 = 13.5-23.3    |
| G5 = ≥ 23.4         | G3 = 0.69 (0.51-0.95) |
|                      | G4 = 0.68 (0.50-0.93) |
|                      | G5 = 0.47 (0.33-0.67) |
|                      | p = <0.001       |

Walking (MET-hr/wk) | Multivariate RR (95% CI) |
---------------------|--------------------------|
| G1 = None           | Q1 = None                |
| G2 = 0.1-2.5        | Q2 = 0.56 (0.32-0.98)    |
| G3 = 2.6-5.0        | Q3 = 0.73 (0.48-1.25)    |
| G4 = 5.1-100        | Q4 = 0.58 (0.34-0.99)    |
| G5 > 10             | Q5 = 1.00 (referent)     |
|                      | p = 0.004               |

Time for VPA (min)   | Vigorous exercise       |
---------------------|--------------------------|
| G1 = None           | G1 = 1.00 (referent)     |
| G2 = 1-60           | G2 = 1.12 (0.79-1.60)    |
| G3 = 61-100         | G3 = 0.56 (0.32-0.98)    |
| G4 = 101-150        | G4 = 0.73 (0.48-1.25)    |
| G5 > 150            | G5 = 0.58 (0.34-0.99)    |
|                      | p = 0.008               |

Norway

- Sex: Men and women
- Age: ≥ 20 yr
- Characteristics: Free form CVD
- HUNT study

Men and women who exercise to a moderate degree and spend less than the recommended energy (< 1000 kcal/wk) are at lower risk of dying from heart disease than those who never exercise.

Wisloff et al 2006 [58] To study the association between the amount and intensity of exercise and CVD mortality.

- n = 56,072 (27,143 men; 28,929 women)
- Length of follow-up: 16 ± 4 yr
- Number of Cases: 1,603 male; 1,993 female

PA assessment: Questionnaire for LTPA, 4 groups

Multivariate RR (95% CI)

- Q1 = 1.00 (referent)
- Q2 = 0.66 (0.50-0.87)
- Q3 = 0.83 (0.65-1.06)
- Q4 = 0.57 (0.39-0.84)
- Q5 = 1.00 (referent)
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Women | Outcome Measure: Ischaemic heart disease mortality | Cox proportional HR |
|-------|-------|----------------------------------------------------|---------------------|
| Lee et al 2001 [59] | Q2 = 0.63 (0.31-1.29) |  |  |
|  | Q3 = 0.66 (0.32-1.34) |  |  |
|  | Q4 = 0.86 (0.45-1.62) |  |  |
|  | Q2 = 1/wk ≤ 30 min low |  |  |
|  | Q3 = 1/wk ≤ 30 min high |  |  |
|  | Q4 = 2-3/wk ≤ 30 min low |  |  |
|  | Sex: Women |  |  |
|  | Age: ≥ 45 yr |  |  |
|  | Characteristics: Healthy |  |  |
|  | Women’s Health Study |  |  |
|  | Recruitment of Participants: Sept 1992-May 1995 |  |  |
|  | n = 39,372 |  |  |
|  | Number of Cases: 244 |  |  |
|  | USA and Puerto Rico |  |  |
|  | D & B score = 12 |  |  |
|  | Multivariate RR (95% CI) Time spent walking |  |  |
|  | G1 = 1.00 (referent) |  |  |
|  | G2 = 0.86 (0.57-1.29) |  |  |
|  | G3 = 0.49 (0.28-0.86) |  |  |
|  | G4 = 0.48 (0.29-0.78) |  |  |
|  | p < 0.001 |  |  |
|  | As little as 1 hour of walking per week predicted lower risk |  |  |
|  | Time spent walking |  |  |
|  | G1 = No regular walking |  |  |
|  | G2 = 1-59 min/wk |  |  |
|  | G3 = 1.0-1.5 h/wk |  |  |
|  | G4 = ≥ 2.0 h/wk |  |  |
|  | Walking pace (km/h) |  |  |
|  | G1 = No regular walking |  |  |
|  | G2 = 3.2 |  |  |
|  | G3 = 3.2-4.7 |  |  |
|  | G4 = ≥ 4.8 |  |  |
|  | EE (kcal/wk) |  |  |
|  | G1 = 100 (referent) |  |  |
|  | EE (kcal/wk) |  |  |
|  | G2 = 200 |  |  |
|  | G3 = 200-599 |  |  |
|  | G4 = 0.75 (0.50-1.12) |  |  |
### Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| G1 = No vigorous, <200 kcal/wk | G2 = No vigorous, ≥ 200 kcal/wk | G3 = Vigorous, 1-199 kcal/wk | G4 = Vigorous, 200-499 kcal/wk | G5 = Vigorous, ≥ 500 kcal/wk |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| n = 10,269                    | Baseline measure in 1962 or 1967 with a follow up in 1977 | Alumni who increased their PA index to 2000 kcal or more per week had a 17% lower risk of death from CHD than those who were sedentary (p = 0.507) | Moderately vigorous sports activity was associated with lower rates of death from CHD among middle aged and older men |

#### Paffenbarger et al. 1993 [67]
- To analyze changes in the lifestyle of Harvard Alumni and the associations of these changes to mortality.
- **Sex**: Men
- **Age**: 45-84 yr
- **Characteristics**: Health, Harvard College Alumni
- **USA**
- **Prospective cohort**
- **D & B score = 13**
- **PA assessment**: Mailed questionnaires included questions on type, duration, intensity, frequency of PA.
- **Men who took up moderate activity had a 41% lower risk than those who continued not to engage in such activity (p = 0.044)**
- **Outcome Measure**: CHD deaths between 1977 and 1985
- **Cox proportional hazards model**
- **Poisson regression methods**
- **The Mantel extension of the Mantel-Haenszel test**

#### Haapanen et al. 1997 [77]
- To examine the association between duration and intensity of LTPA and the risk of CHD.
- **n = 2,840 (1,500 men; 1,340 women)**
- **Length of Follow-up**: 10 yrs
- **Incident Rates (per 1000 person-years) for CHD = 108 for men and 75 for women.**
- **Total EE had an inverse and independent association with risk of CHD in middle aged Finnish men but not among women.**
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Finland Prospective cohort | Sex: Men and women | PA assessment: Questionnaire for LTPA EE (kcal/wk) | Multivariate RR (95% CI) LTPA and CHD mortality |
|----------------------------|--------------------|--------------------------------------------------|-----------------------------------------------|
| D & B score = 13           | Age: 35-63 yr      | Men                                              |                                               |
|                            | Characteristics: Healthy |                                                |                                               |
|                            | G1 = Low activity   | Men                                              |                                               |
|                            | G2 = Moderate activity |                                                 |                                               |
|                            | G3 = High activity   | Women                                            |                                               |
|                            |                      |                                                  |                                               |
| Barengo et al 2004 [164]  | To investigate whether moderate or high LTPA are associated with a reduced CVD and all-cause mortality, independent of CVD risk factors and other forms of PA in men and women. | n = 31,677 (15,853 men; 16,824 women) | 20 year follow-up | Moderate and high levels of LTPA and OPA are associated with reduced CVD mortality. |
|                            | Number of Cases (Men): 1,661 |                                                | Number of Cases (Women): 778                  |
|                            |                      |                                                  |                                               |
| Finland Prospective cohort | Sex: Men and women | PA assessment: Questionnaire for LTPA and OPA, 3 groups | HR (95% CI) LTPA, men |
| D & B score = 14           | Age: 30-59          | G1 = Low activity                                | G1 = 1.00 (referent) |
|                            | Characteristics: Participant from eastern and south-western Finland | G2 = Moderate activity                          | G2 = 0.91 (0.82-1.00) |
|                            |                      | G3 = High activity                               | G3 = 0.83 (0.69-0.99) |
|                            |                      | LTPA, women (referent)                           |                                               |
|                            |                      | G1 = 1.00                                        |                                               |
|                            |                      | G2 = 0.83 (0.71-0.96)                            |                                               |
|                            |                      | G3 = 0.89 (0.68-1.18)                            |                                               |
|                            |                      | OPA, men                                          |                                               |
|                            |                      | G1 = 1.00 (referent)                             |                                               |
|                            |                      | G2 = 0.75 (0.64-0.87)                            |                                               |
|                            |                      | G3 = 0.77 (0.69-0.87)                            |                                               |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Description | N | Length of Follow-up | Number of Cases | Outcome Measure | RR (95% CI) | Additional Information |
|-------|-------------|---|---------------------|----------------|----------------|-------------|-----------------------|
| Bijnen et al 1998 [166] | To describe the association between the PA pattern of elderly men and CHD mortality. | 802 | 10 yrs | 90 | PA did not show a protective effect on death from CHD. | • G1 = 1.00 (referent)  
• G2 = 0.73 (0.60-0.88)  
• G3 = 0.77 (0.65-0.91) | Netherlands  
• Characteristics: Free from Serious Illness  
• Ethnicity: Dutch  
• Zutphen Elderly Study  
D&B score = 13 |
| Davey-Smith et al 2000 [174] | To examine the association between two measures of physical activity (LTPA and usual walking pace) with cause specific mortality (CHD). | 6,702 | 25 yrs | 955 | Inverse associations of both LTPA and walking pace with mortality from CHD were seen. | • G1 = 1.45 (0.9-2.2)  
• G2 = 1.30 (1.1-1.6)  
• G3 = 1.00  
p < 0.01 | England  
• Characteristics: Whitehall Study  
• Ethnicity: White  
• Sex: Men  
• Age: 40-64 yr  
D&B score = 11 |
| Study | Objective | Participants | Outcome | Follow-up | Cases | Baseline levels of self-reported LTPA predicted a decreased rate of CHD. |
|-------|-----------|--------------|---------|-----------|-------|---------------------------------------------------------------------|
| Eaton et al 1995 [175] | To determine whether self reported PA predicts a decreased risk of CHD. | n = 8,463 (LTPA), 8,418 (OPA) | Length of Follow-up: 21 yrs | Number of Cases: 709 | Age adjusted RR (95% CI) by LTPA level |
| USA | • Sex: Men | PA assessment: Interview | • G1 = 1.00 (referent) | • G2 = 0.79 (0.63-0.99) |
| Prospective cohort | • Age: 40 yr | LTPA | • G3 = 0.73 (0.59-0.89) | • G4 = 0.71 (0.52-0.98) |
| D & B score = 11 | • Characteristics: Healthy, free of CHD | G1 = Sedentary | G2 = Light | G3 = Light Daily | G4 = Heavy |
| | Ethnicity: Israeli | G1 = Sitting | G2 = Physical Labour | G3 = Walking | G4 = Physical Labour |
| | | | | | Outcome Measure: CHD Death |
| | | Cox Proportional HR | | | |
| Hillardon et al 2004 [183] | To examine whether a short, easily administered measure of PA is associated with the risk of death from all causes and specific causes. | n = 10,522 (4,929 men; 5,593 women) | Length of Follow-up: > 10 yrs | Number of Cases: 155 | Multivariate RR (95% CI) by PA level |
| UK | • Sex: Men and women | PA assessment: Questionnaire, 3 groups: | • G1 = 1.00 (referent) | • G2 = 0.99 (0.75-1.18) | Self reported VPA is associated with the risk of future mortality. |
| Prospective cohort | • Age: 35-64 yr | G1 = Never / <1 time/month | G2 = <2 times/wk | G3 = ≥ 2 times/wk |
| D & B score = 11 | • Characteristics: no history of chest pain | | | | |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study                          | Duration and Setting | Outcome Measure: IHD mortality | Cox proportional HR | Follow up for 16 years | Age Adjusted RR (95% CI) | A relatively small amount (10-36 min/d) of daily moderate intensity LTPA can significantly reduce premature mortality from CHD in middle aged men at high risk for CHD. |
|-------------------------------|----------------------|---------------------------------|---------------------|-----------------------|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Leon et al 1997 [199]         | USA                  | Sex: Men Age: 35-57 yr          | PA assessment: Questionnaire at baseline (Minnesota LTPA questionnaire), divided/ grouped into deciles of LTPA (min/d) | n = 12,138 Follow up for 16 years | G1 = 1.00 (referent)  | G2 = 0.71 (0.56-0.91)  | G3 = 0.75 (0.59-0.96)  | G4 = 0.69 (0.54-0.96)  |
| Prospective cohort            |                      |                                 |                     |                       | D & B score = 11         | G1 = 1.00 (referent)  | G2 = 0.75 (0.54-0.96)  | G3 = 0.84 (0.64-1.04)  | G4 = 0.75 (0.59-0.96)  |
| Rosengren et al 1997 [211]    | Sweden               | Sex: Men Age: 47-55 yr          | PA assessment: Questionnaire for LTPA, 3 groups | n = 7,142 Length of Follow-up: 20 yrs | Number of Cases: 684 | Multivariate adjusted RR (95% CI) for LTPA | G1 = 1.00 (referent)  | G2 = 0.84 (0.71-1.00)  | G3 = 0.84 (0.73-0.96)  |
| Prospective cohort            |                      |                                 |                     |                       |                         | G1 = Sedentary          | G2 = Moderately active |                      |                         |

To study the relationship of PA to CHD in a well defined population at above average risk for CHD over a 16 yr observation period. There appears to be a protective effect of LTPA on CHD-related death.
### Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Objective | Sample Size | Follow-up | Number of Cases | LTPA and CHD-related mortality | Adjusted RR (95% CI) | Sex | Age | Characteristics | PA assessment | OR (95% CI) by LTPA |
|-------|-----------|-------------|-----------|----------------|--------------------------------|----------------------|-----|-----|----------------|---------------|----------------------|
| Schnohr et al 2006 [214] | To describe the associations between different levels of LTPA and subsequent causes of death. | n = 4,894 (2,136 men; 2,758 women) | 5 years | Number of Cases: 292 | There was an inverse and significant dose-response association between LTPA and CHD-related mortality. | Adjusted RR (95% CI) Whole group | Denmark | Age 20–79 yr | • Sex: Men and women | Questionnaire LTPA | • G1 = referent |
| | | | | | | | Prospective cohort | | | • Characteristics: Healthy | | • G1 = 1.00 (referent) |
| | | | | | | | | | | Cox proportional HR | • G2 = 0.71 (0.51-0.99) |
| | | | | | | | | | | | • G3 = 0.56 (0.38-0.82) |
| Weller et al 1998 [220] | To examine the relationship between PA and mortality. | n = 6,620 | 7 yrs | Number of Cases: 109 | LTPA is inversely associated with risk of fatal MI. | OR (95% CI) by LTPA | Canada | Age ≥ 30 yr | • Sex: Women | Questionnaire, 4 groups for LTPA (kcal/kg/day) and non-LTPA (kcal/kg/day) |
| | | | | | | | Prospective cohort | | | • Characteristics: Canadian Women | | • Q1 = 1.00 (referent) |
| | | | | | | | | | | | • Q2 = 0.61 (0.07-1.19) |
| | | | | | | | | | | | • Q3 = 0.84 (0.52-1.37) |
| | | | | | | | | | | | • Q4 = 0.63 (0.36-1.09) |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Characteristics | Outcome Measure | PA assessment | Number of Cases | Results |
|-------|-----------------|----------------|---------------|-----------------|---------|
| Yu et al 2003 [221] | To examine the optimal intensity of LTPA to decrease the risk of CHD mortality in middle aged British men. | Q1 = ≥ 0 | Multivariate adjusted HR (95% CI) | 82 | Strong significant inverse relationship between heavy LTPA and CHD mortality. |
| | • n = 1,975 | Q2 = ≥ 0.1 | | | |
| | • Age: 49-64 yr | Q3 = ≥ 0.5 | | | |
| | • Characteristics: Healthy, no previous history of CHD | Q4 = ≥ 1.6 | | | |
| | • Sec: Men | | | | |
| | | | | | |
| | UK | | | | |
| | Prospective cohort | Total activity level (kcal/day) | | | |
| | • Caerphilly collaborative heart study | G1 = 0.0 - 161.6 | | | |
| | | G2 = 161.8 - 395.3 | | | |
| | | G3 = 395.5 - 2,747.2 | | | |
| | | Cox proportional HR | | | |
| | D & B score = 11 | | | | |
| Altieri et al 2004 [222] | To assess the possible protective role of PA on CHD. | Q1 = lowest | OR (95% CI) for CHD and OPA | 507 | LTPA from 15-19 yrs as well as OPA from 30 - 39 yrs both have a significant inverse relationship with risk of non fatal acute MI. |
| | • n = 985 (507 men; 478 women) | Q2 | | | |
| | • Age: < 79 yr | Q3 | | | |
| | • Sex: Men and women | | | | |
| | | | | | |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Characteristics | Outcome Measure | HR (95% CI) for CHD and LTPA | Adjusted OR (95% CI) |
|-------|----------------|----------------|-----------------------------|---------------------|
| Batty et al 2003 [223] | Case: Patients admitted to Hospital with non-fatal Acute MI. Controls: Patients admitted to hospital for acute condition unrelated to known or potential risk factors for acute MI | Non Fatal acute MI | Q4 = highest | Q4 = 0.57 (0.34-0.95) |
| | | | | p = 0.045 |
| | | | | A suggestion that the symptomatic nature of ischemia appeared to modify the affects of |
| | | | | p = 0.045 |
| | | | | PA on total and CHD mortality. |
| | | | | PA on total and CHD mortality. |
| | | | | Regular and at least MPA can be beneficial to heart health. |

| Canada | Characteristics: Healthy and free from heart disease | | G1 = 5.0 (1.84-13.59) |
|-------|-----------------------------------------------------|----------------|---------------------|
|       |                                                     |               | G2 = 3.7 (1.26-10.67) |
|       |                                                     |               | G3 = 1.00 (referent) |

| UK | Prospective cohort | Characteristics: British civil servants who underwent a resting ECG | | |
|----|--------------------|-------------------------------------------------|----------------|---------------------|
|    | D & B score = 11 | | G1 = Inactive | G1 = 1.14 (0.9-1.4) |
|    |                    | | G2 = Moderate | G2 = 0.94 (0.8-1.1) |
|    |                    | | G3 = Active | G3 = 1.00 (referent) |

| Chen and Millar [224] | To examine the potential protective effect of LTPA on the incidence of heart disease and depression. | | |
|----------------------|---------------------------------------------------------------|----------------|---------------------|
|                      | Characteristics: Healthy and free from heart disease          |               | G1 = 5.0 (1.84-13.59) |
|                      | PA assessment: EE from self administered questionnaire, 4 groups (kcal/kg/day) |               | G2 = 3.7 (1.26-10.67) |
|                      |                  |               | G3 = 1.00 (referent) |

Batty et al [223]  To examine the relationship between physical activity and three mortality endpoints in healthy persons.  

- * n = 6,474  
- * Sex: Men  
- * Age: 40-64 yr  
- PA assessment: Questionnaire for LTPA, divided into 3 groups:  
  - G1 = Inactive  
  - G2 = Moderate  
  - G3 = Active  
  
Chen and Millar [224]  To examine the potential protective effect of LTPA on the incidence of heart disease and depression.  

- * n = 15,670  
- * Sex: Men and women  
- * Age: ≥ 20 yr  
- PA assessment: EE from self administered questionnaire, 4 groups (kcal/kg/day)  
  
D & B score = 11  

Outcome Measure: Non Fatal acute MI  
Unconditional logistic regression  

Number of Cases: 837  
Number of Dropouts: 158  

D & B score = 13  

Outcome Measure: CHD mortality  
Cox Proportional HR  

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| Study                                                                 | Design          | National Population Health Survey | Outcome Measure: CHD incidence | G1 = Sedentary | G2 = Light (<1.5) | G3 = Moderate (1.5-2.9) | G4 = Active (≥ 3) | Odds Ratio (95% CI) | D & B score |
|----------------------------------------------------------------------|-----------------|-----------------------------------|--------------------------------|----------------|-------------------|-----------------------|-------------------|---------------------|-------------|
| Conroy et al 2005 [225]                                             | Cohort study    |                                   | Multivariate RR (95% CI)       | G1 = 1.00 (referent) | G2 = 0.62 (0.48-0.80) | G3 = 0.61 (0.48-0.79) | G4 = 0.61 (0.46-0.81) | PA and incidence of CHD | 11          |
|                                                                     |                 |                                   |                                |                |                   |                       |                   |                     |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | Baseline PA (kcal/wk) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G4 = 0.61 (0.46-0.81) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G1 = <200            | <0.001      |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G3 = 600-1499        | <0.001      |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G1 = 1.00 (referent)  |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G2 = 0.76 (0.57-1.02) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G3 = 0.61 (0.46-0.79) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G5 = 0.81 (0.58-1.14) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | Past PA              |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G1 = 1.00 (referent)  |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G2 = 0.76 (0.57-1.02) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G3 = 0.61 (0.46-0.79) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G4 = 0.61 (0.46-0.81) |             |
|                                                                     |                 |                                   |                                |                |                   |                       |                   | G5 = 0.81 (0.58-1.14) |             |

* n = 37,169
* Length of Follow-up: 9 yrs
* Number of Cases: 477
* PA during middle age predicts lower risk of CHD

* Women's Health Study
* Characteristics: Healthy women health professionals
* PA assessment: Questionnaire for EE (kcal/wk) and months/yr
* Sex: Women
* Age: ≥ 45 yr

* Multivariate RR (95% CI)
* Baseline PA and incidence of CHD

* D & B score = 11
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Objective | Population | Length of Follow-up | Number of Cases | Outcome Measure | Multivariate RR (95% CI) for PAI |
|-------|-----------|------------|---------------------|-----------------|----------------|----------------------------------|
| Dorn et al 1999 [226] | To examine the long-term relationships between total PA and mortality from all causes and CHD in the general population. | USA | Prospective cohort | n = 1,461 (698 men, 763 women) | Multivariate RR (95% CI) for PAI | 0.40 (0.19-0.88) for 1 kcal/kg/h |
|          |           |           |                      |     29 years     |    | in non-obese men                |
|          |           |           |                      |     109 men, 81 women |    | PA favorably influences mortality risks in non-obese men and younger women. |
|          |           |           |                      |                  |    | PA assessment: Questionnaire     |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | in obese men                     |
|          |           |           |                      |                  |    | Healthy, free from CHD, diabetes, and Stroke. |
|          |           |           |                      |                  |    | Sex: Men and women               |
|          |           |           |                      |                  |    | Outcome Measure: CHD Mortality    |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | Characteristics: D&B score = 11   |
|          |           |           |                      |                  |    | Cox Proportional Hazard Ratio   |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | in women < 60 yrs                 |
|          |           |           |                      |                  |    | 0.42 (0.11-1.52) for 1 kcal/kg/h  |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | in women > 60 yrs                 |
|          |           |           |                      |                  |    | 0.83 (0.51-1.36) for 1 kcal/kg/h  |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | Ethnicity: White.                |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | Ethnicity: Black and non Black    |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for LTPA |
|          |           |           |                      |                  |    | Atherosclerosis Risk in Communities Study |
|          |           |           |                      |                  |    | Q1 = Low                         |
|          |           |           |                      |                  |    | LTPA, women                       |
|          |           |           |                      |                  |    | Q1 = 1.00 (referent)              |
|          |           |           |                      |                  |    | Q2 = 0.74 (0.42-1.31)             |
|          |           |           |                      |                  |    | Q3 = 1.07 (0.55-2.09)             |

Folsom et al 1997 [227] | To examine the association of PA at baseline with CHD incidence. | USA | Prospective cohort | n = 13,999 (6,166 men, 7,833 women) | Multivariate RR (95% CI) for PAI | 0.83 (0.51-1.36) for 1 kcal/kg/h |
|          |           |           |                      |     4-7 yrs    |    | in non-obese men                 |
|          |           |           |                      |     223 men, 97 women |    | PA favorably influences mortality risks in non-obese men and younger women. |
|          |           |           |                      |                  |    | PA assessment: Questionnaire during home interview, divided into quartiles of LTPA and sports activity |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | in women < 60 yrs                 |
|          |           |           |                      |                  |    | 0.42 (0.11-1.52) for 1 kcal/kg/h  |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | in women > 60 yrs                 |
|          |           |           |                      |                  |    | 0.78 (0.41-1.47) for 1 kcal/kg/h  |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for PAI |
|          |           |           |                      |                  |    | Ethnicity: Black and non Black    |
|          |           |           |                      |                  |    | Multivariate RR (95% CI) for LTPA |
|          |           |           |                      |                  |    | Q1 = Low                         |
|          |           |           |                      |                  |    | LTPA, women                       |
|          |           |           |                      |                  |    | Q1 = 1.00 (referent)              |
|          |           |           |                      |                  |    | Q2 = 0.74 (0.42-1.31)             |
|          |           |           |                      |                  |    | Q3 = 1.07 (0.55-2.09)             |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. *(Continued)*

| Outcome Measure: CHD incidence Poisson Regression | Multivariate RR (95% CI) Sports, men |
|--------------------------------------------------|-------------------------------------|
| Q4 = 0.64 (0.34-1.24)                            | Q1 = 1.00 (referent)                |
|                                                  | Q2 = 1.15 (0.79-1.68)              |
|                                                  | Q3 = 1.03 (0.68-1.54)              |
|                                                  | Q4 = 0.83 (0.56-1.23)              |

Sports, women

| Q1 = 1.00 (referent) | Q2 = 0.99 (0.58-1.67) | Q3 = 0.64 (0.32-1.27) | Q4 = 0.72 (0.37-1.38) |

Fransson et al 2004 [228] To estimate the influence of LTPA and OPA on acute MI.

- **n = 4069 (2,742 men; 1,327 women)**
- **Sex: Men and Women**
  - G1 = Seldom
  - G2 = Sometimes

**Case Control**

- **Age: 45-70 yr**
- **Characteristics: Cases: Diagnosed with acute MI**
  - G3 = 1x/wk
  - G4 = 2-3x/wk
  - G5 = >3x/wk

**D & B score = 12**

- **Number of Cases: 1,204 men, 550 women**
  - Exercise seems to reduce the risk of MI.

**Sweden**

- **PA assessment:** Questionnaire for LTPA, 5 groups
  - LTPA, men
  - G1 = 1.00 (referent)
  - G2 = 0.76 (0.61-0.95)
  - G3 = 0.67 (0.51-0.88)
  - G4 = 0.63 (0.49-0.83)
  - G5 = 0.53 (0.38-0.73)

- **Stockholm Heart Epidemiology**
  - Questionnaire for total physical activity, 3 groups
    - LTPA, women
    - G1 = 1.00 (referent)
    - G2 = 0.69 (0.49-0.98)
    - G3 = 0.38 (0.25-0.58)
    - G4 = 0.62 (0.38-1.01)
    - G5 = 0.31 (0.15-0.66)

- **Total physical activity, men**
  - G1 = 1.00 (referent)
  - G2 = 0.66 (0.47-0.94)
| Study | Country | Study Design | Sex | Age | Characteristics | Outcome Measure: Acute MI | Number of Cases | Number of Subjects | Primary Findings |
|-------|---------|-------------|-----|-----|----------------|---------------------------|----------------|------------------|-----------------|
| Fransson et al 2006 [229] | Sweden | Case Control | Men and women | 45-70 yr | Characteristics: Cases had acute MI | G3 = Twice per week or more | 1204 men, 550 women | 4069 (2,742 men; 1,327 women) | Regular LTPA seems to provide protection against MI and non-fatal MI. |
| | | | | | | G1 = Very little /occasional walks | Multivariate OR (95% CI) for acute MI | | |
| | | | | | G2 = Occasional / once per week | LTPA, men | | |
| | | | | | G3 = Twice per week or more | Multivariate OR (95% CI) for non-fatal MI | | |

Outcome Measure: Acute MI
- **G3** = 0.46 (0.31-0.69)
- **G1** = 1.00 (referent)
- **G2** = 0.34 (0.22-0.53)
- **G3** = 0.16 (0.07-0.37)
- **G1** = 1.00 (referent)
- **G2** = 0.91 (0.73-1.15)
- **G3** = 0.90 (0.72-1.12)
- **G1** = 1.00 (referent)
- **G2** = 0.77 (0.51-1.17)
- **G3** = 0.47 (0.31-0.69)
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study            | To investigate the independent associations and the possible interaction of BMI, LTPA, and perceived physical performance and functional capacity with the risk of mortality. | Length of Follow-up: 16 yrs | Number of Cases: 208 all cause deaths, 54% of those CVD. 73% of CVD deaths due to CHD | Increase perceived PF is associated with a reduced risk of CHD mortality in men. |
|------------------|---------------------------------------------------------------------------------------------------------------------------------|-----------------------------|--------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Haapanen-Niemi 2000 [230] | n = 2,212 (1,090 men; 1,122 women) | Multivariate RR (95% CI) | Multivariate RR (95% CI) | Total LTPA EE index and CHD mortality, men |
| Finland Prospective cohort | Age: 35-63 yr | Total LTPA energy expenditure (kcal/wk) | Total LTPA EE index and CHD mortality, men | Total LTPA EE index and CHD mortality, women |
| D & B score = 13 | Characteristics: Healthy | G1 = High | G2 = Moderate | G3 = Low | Multivariate RR (95% CI) | Multivariate RR (95% CI) | Multivariate RR (95% CI) | Multivariate RR (95% CI) | Total LTPA EE index and CHD mortality, women |
|                  | Ethnicity: Finnish | G1 = Better | G2 = Similar | G3 = Worse | Perceived physical fitness compared to age-mates | Perceived physical fitness, men | Perceived physical fitness, women |
|                  | Sex: Men and women | PA assessment: Postal Survey | Multivariate RR (95% CI) | Perceived physical fitness, women |
|                  |                   | G1 = 1.00 (referent) | G2 = 0.88 (0.44-1.76) | G3 = 1.70 (0.90-3.21) | p = 0.056 |
|                  |                   | G2 = 0.88 (0.44-1.76) | G3 = 1.70 (0.90-3.21) | G1 = 1.00 (referent) | p = 0.011 |
|                  |                   | G2 = 2.82 (1.06-7.46) | G3 = 4.64 (1.56-13.84) | G1 = 1.00 (referent) | p = 0.046 |
|                  |                   | G3 = 1.17 (0.51-2.68) |                          | G1 = 1.00 (referent) |                          |
|                  |                   |                          |                          | G2 = 0.43 (0.16-1.16) |                          |
|                  |                   |                          |                          | G3 = 1.17 (0.51-2.68) |                          |
|                  |                   |                          |                          | p = 0.046 |                          |
|                  |                   |                          |                          | Multivariate RR (95% CI) |                          |
|                  |                   |                          |                          | Perceived physical fitness, women |                          |
|                  |                   |                          |                          | G1 = 1.00 (referent) |                          |
|                  |                   |                          |                          | G2 = 0.82 (0.32-2.16) |                          |
|                  |                   |                          |                          | G3 = 1.89 (0.57-6.27) |                          |
|                  |                   |                          |                          | p = 0.154 |                          |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. *(Continued)*

| Study               | Objective                                                                 | **n** | **Length of Follow-up** | **Number of Cases** | **Rate of CHD Mortality and Morbidity** |
|---------------------|---------------------------------------------------------------------------|-------|-------------------------|---------------------|-----------------------------------------|
| Kannel et al 1986 [231] | To examine the role of low levels of OPA and LTPA in the development of CV morbidity and mortality over the short and long term. | 1,166 | 24 yrs                  | 220 mortality, 371 morbidity | Rate of CHD Mortality and Morbidity decreases with increased level of PA but no association was found with physical demand of work |
| USA Prospective cohort | D & B score = 11                                                         |       |                         |                     |                                         |
|                     | PA assessment: Questionnaire during examination                           |       |                         |                     |                                         |
|                     | Cumulative 24 year age adjusted rate per 1000 people                      |       |                         |                     |                                         |
|                     | 24 hr PA index for LTPA CHD mortality                                      |       |                         |                     |                                         |
|                     | PA index: 24 hr PA index for LTPA CHD incidence                            |       |                         |                     |                                         |
|                     | G1 = Sedentary                                                             | 255   |                         |                     |                                         |
|                     | G2 = Light                                                                 | 184   |                         |                     |                                         |
|                     | G3 = Medium                                                                | 152   |                         |                     |                                         |
|                     | G4 = Heavy                                                                 |       |                         |                     |                                         |
|                     | Physical demand of work                                                    |       |                         |                     |                                         |
|                     | 24 hr PA index for LTPA CHD incidence                                      |       |                         |                     |                                         |
|                     | G1 = Sedentary                                                             | 414   |                         |                     |                                         |
|                     | G2 = Light                                                                 | 353   |                         |                     |                                         |
|                     | G3 = Medium                                                                | 311   |                         |                     |                                         |
|                     | G4 = Heavy                                                                 |       |                         |                     |                                         |
|                     | Outcome Measure: CHD mortality and Morbidity                               |       |                         |                     |                                         |
|                     | Physical demand of work and CHD mortality                                  |       |                         |                     |                                         |
|                     | Cox proportional HR                                                       |       |                         |                     |                                         |
|                     | Physical demand of work and CHD incidence                                  |       |                         |                     |                                         |
| Kaprio et al 2000 [232] | To examine the contribution of genetic and other familial factors to the relationship between LTPA and CHD. | 8,205 | 18 yrs                  | 723                 | LTPA compared to being sedentary helps prevent CHD in men. |
| Finland             | PA assessment: Questionnaire for LTPA, 3 groups                            |       |                         |                     |                                         |
|                     | Multivariate RR (95% CI)                                                  |       |                         |                     |                                         |
|                     | G1 = 1.00 (referent)                                                      |       |                         |                     |                                         |
### Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Design | Sample Size | Characteristics | Outcome Event | Cox Proportional HR (95% CI) by VO\textsubscript{2} max |
|-------|--------|-------------|-----------------|---------------|-----------------------------------------------------|
| Lakka et al 1994 [233] | Prospective cohort | n = 1,166 | Finland | To investigate the independent associations of LTPA and maximal oxygen uptake with the risk of acute MI | Baseline examination: 1984-1989 |
| | | | | | Adjusted RH (95% CI) by conditioning PA level |
| | | | | | G1 = Sedentary PA, G2 = Occasional PA, G3 = Conditioning PA |
| | | | | | G1 = <0.7 |
| | | | | | G2 = 0.7 |
| | | | | | G3 = >2.2 |
| | | | | | G1 = 1.00 (referent) |
| | | | | | G2 = 1.11 (0.98-1.21) |
| | | | | | G3 = 0.31 (0.12-0.85) |

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Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study                                | Objective                                                                 | Methodology                                                                 | Results                                                                                                                                   |
|--------------------------------------|---------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Laukkanen et al. 2004 [234]          | To determine whether VO₂peak predicts CVD morbidity and mortality in a sample of men as related to conventional risk factors, medications or underlying chronic disease. | VO₂peak (ml/kg/min) measured by exercise test with an electrically braked cycle ergometer, divided into quartiles. |
| Finland                              | • Sex: Men                                                                | Healthy men with low VO₂ peak (lowest quartile) had an increased risk.        |
| Prospective cohort                   | • Age: 42-60 yr                                                           | Unfit men with unfavorable risk profiles are the risk group that would benefit the most from preventative measures. |
| D & B score = 11                     | • Characteristics: Healthy and not healthy participants                 |                                                                              |
| Lee et al. 2000 [235]                | To investigate whether different durations of exercise episode are associated with different risk of CHD. | PA assessment: Survey for EE (kJ/wk), divided into 5 groups and episodes of PA (min), divided into 6 groups. |
| USA                                  | • Sex: Men                                                                | Multivariate adjusted RR (95% CI) by EE.                                      |
| USA                                  | • Age: Mean 66.1 ± 7.5                                                    |                                                                               |
| USA                                  | • Characteristics: Healthy                                                |                                                                               |
| Prospective cohort                   | • Harvard Alumni Study                                                   |                                                                               |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Participants | Energy expenditure (kJ/wk) | Multivariate adjusted RR (95% CI) by duration of PA episode | Duration of PA episode (min) |
|-------|--------------|-----------------------------|-------------------------------------------------------------|-----------------------------|
| D & B | G1 = <4,200  | G2 = 4,200-8,399             | G3 = 8,400-12,599                                           | G1 = None                    |
|       | G4 = 12,600-16,799 | G5 = ≥ 16,800 | • G1 = 1.00 (referent)                                      | • G1 = None                    |
|       | G2 = 4,200-8,399 | G3 = 12,600-16,799 | G5 = ≥ 16,800 | • G2 = 1.15 (0.70-1.87)                                      | • G2 = 1-15                  |
|       | G3 = 8,400-12,599 | G4 = 12,600-16,799 | G5 = ≥ 16,800 | • G3 = 1.01 (0.68-1.51)                                      | • G3 = 16-30                 |
|       | G4 = 12,600-16,799 | G5 = ≥ 16,800 | G5 = ≥ 16,800 | • G4 = 1.11 (0.67-1.84)                                      | • G4 = 31-45                 |
|       | G5 = ≥ 16,800 | G6 = >60                    | G6 = >60         | • G5 = 1.18 (0.77-1.80)                                      | • G5 = >60                   |
|       |               |                            | G6 = >60         | • G6 = 1.25 (0.83-1.87)                                      |                             |

As long as the total EE is similar, more frequent shorter bouts or longer less frequent bouts have an equivalent reduction in CHD risk.

Lee et al. 2003 [236] To investigate whether moderate-intensity exercise is associated with reduced CHD: • n = 7,337 | PA assessment: Survey rating usual level of exertion when exercising, divided into tertiles | Number of Cases: 551 | Inverse association between relative intensity of PA and the risk of CHD.

USA • Sex: Male | Multivariate adjustment RR (95% CI) • T1 = 1.00 (referent) | • T2 = 0.87 (0.70-1.09) | • T3 = 0.92 (0.75-1.14)

• Age: Mean 66.1 yr

• Characteristics: Healthy

Prospective cohort Energy expenditure (kcal/wk)

Harvard Alumni Study T1 = <1000

T2 = 1000-2499

T3 = ≥ 2500

Cox proportional HR
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study                         | Objective                                                                 | n: Cases/Controls | PA assessment | Risk Factors | Case control details                                                                 | Risk Measure                                                                 |
|-------------------------------|---------------------------------------------------------------------------|-------------------|---------------|--------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Lemaitre et al 1999 [237]     | To investigate whether regular participation in moderate intensity activity confers overall protection from sudden primary cardiac arrest. | 355/503          | Interview (with spouses) for LTPA, 7 groups | Sex: Men and women, Age: 25-74 yr, Characteristics: Previously healthy prior to primary cardiac arrest. | Case control individually matched to case patients on age (within 7 years) and sex at a ratio of about 2:1 were randomly selected from community by random-digit dialing. | Participation in moderate intensity LTPA was associated with a decreased risk of primary cardiac arrest. |
| USA                           |                                                                           |                   |               | G1 = No activity, G2 = Gardening only ≤ 60 min/wk, G3 = Gardening only > 60 min/wk | Sex: Men and women, Age: 25-74 yr, Characteristics: Previously healthy prior to primary cardiac arrest. | RR (95% CI) G1 = 1.00 (referent), G2 = 0.52 (0.21-1.28), G3 = 0.34 (0.13 0.89). |
| Case control                  |                                                                           |                   |               | G4 = Walking ≤ 60 min/wk, G5 = Walking > 60 min/wk, G6 = Moderate intensity LTPA (not walking or gardening), G7 = High intensity LTPA | Sex: Men and women, Age: Mean 67 yr, Characteristics: Postmenopausal women, Cases: Diagnosed with non-fatal MI Controls: free from MI | Logistic regression analysis. G4 = 0.45 (0.17-1.19), G5 = 0.27 (0.11-0.67), G6 = 0.31 (0.13-0.74), G7 = 0.34 (0.16-0.75). |
| D & B score = 11              |                                                                           |                   |               |                                                                                   |                                                                                   |
| Lemaitre et al 1995 [238]     | To examine whether LTPA decreases the risk of MI in postmenopausal women. | 1,193/1,193       | Phone interview for LTPA, divided into quartiles of EE (mean kcal/wk) | Sex: Women, Age: Mean 67 yr, Characteristics: Postmenopausal women, Cases: Diagnosed with non-fatal MI Controls: free from MI | Number of Cases: 268 Risk of MI among postmenopausal women is decreased by 50% with modest LT energy expenditures, equivalent to 30-45 min of walking for exercise three times per week. | Logistic regression analysis. Q1 = 1.00 (referent), Q2 = 0.52 (0.34-0.80). |
| USA                           |                                                                           |                   |               | Q1 = 71, Q2 = 472, Q3 = 1183, Q4 = 3576 | Sex: Women, Age: Mean 67 yr, Characteristics: Postmenopausal women, Cases: Diagnosed with non-fatal MI Controls: free from MI | Multivariate RR (95% CI) Q1 = 1.00 (referent), Q2 = 0.34 (0.26-0.63), Q3 = 0.40 (0.25-0.63), Q4 = 0.40 (0.25-0.63). p = <0.001. |
| Case control                  |                                                                           |                   |               |                                                                                   |                                                                                   |
| D & B score = 11              |                                                                           |                   |               |                                                                                   |                                                                                   |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Design | Country | Sample Size and Characteristics | Measures of PA | Follow-up | Number of Cases | Physical Activity and Cardiovascular Disease |
|-------|--------|---------|---------------------------------|----------------|-----------|-----------------|-----------------------------------------------|
| Li et al 2006 [239] | Prospective cohort | USA | n = 88,393 | Nurses’ Health Study | Multivariate HR (99% CI) | 20 yrs | 2,358 | Physical inactivity independently contributes to the development of CHD in women. |
| | | | | PA assessment: Questionnaire for LTPA (hr/wk), 3 groups | | | | |
| | | | | Prospective cohort | | | | |
| | | | | Age: 34-59 yr | | | | |
| | | | | Characteristics: Nurses | | | | |
| | | | | Outcome Measure: CHD incidence | | | | |
| | | | | Cox proportional HR | | | | |
| | | | | | | | | |
| Lemaitre et al 1995 [240] | Case control | Portugal | n = 1,107 (726 controls, 381 cases) | PA assessment: Questionnaire, 3-5 groups depending on variable | OR (95% CI) | | PA level was inversely associated with occurrence of MI in both sexes, although the association presented a significant linear trend only for women; in men it suggested a u-shaped relation. |
| | | | | Total PA, men | | | | |
| | | | | Age: ≥ 40 yr | | | | |
| | | | | Characteristics: Case: Admitted to Hospital and diagnosed with first episode of MI Control: Healthy, no history of CHD | | | | |
| | | | | G1 = 28.3-32.1 | | | | |
| | | | | G2 = 32.2-33.3 | | | | |
| | | | | G3 = 33.4-36.5 | | | | |
| | | | | G4 = 36.6-40.3 | | | | |
| | | | | G5 = 40.4-83.1 | | | | |

Note: CHD = coronary heart disease; LTPA = leisure-time physical activity; OR = odds ratio; CI = confidence interval; HR = hazard ratio; D&B score = Drosdorfer-Burkholder score.
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study                  | Design       | Outcome measure                  | Time engaged in LTPA, even non strenuous LTPA was associated with a lower risk of MI, and the shape of this relationship was non-linear |
|------------------------|--------------|-----------------------------------|-------------------------------------------------------------------------------------------------------------------------------|
| Lovasi et al 2007 [241]| Case control | LTPA                              | USA LTPA and non fatal CHD                                                                                                       |
|                        |              | • n = 4,094                        | • Sex: Men and women                                                                                                              |
|                        |              | • PA assessment Telephone interview (Minnesota LTPA Questionnaire)                                                                 |
|                        |              | • Number of Cases: 697             | • Age: 64 ± 9 yr                                                                                                                 |
|                        |              | • Characteristics: Group Health Cooperative Members | • Characteristics: Group Health Cooperative Members                                                                                  |
|                        |              |                                   | • G1 = 1.00 (referent)                                                                                                           |
|                        |              |                                   | • G2 = 0.88 (0.66-1.17)                                                                                                          |
|                        |              |                                   | • G1 = None                                                                                                                      |
|                        |              |                                   | • G2 = <2                                                                                                                         |
|                        |              |                                   | • G3 = 2-5                                                                                                                        |
|                        |              |                                   | • G4 = 5-9                                                                                                                        |
|                        |              |                                   | • G5 = >9 h/wk                                                                                                                    |
|                        |              |                                   | • Sex: Men and women                                                                                                              |
|                        |              |                                   | • Number of Cases: 697                                                                                                           |
|                        |              |                                   | • Age: 64 ± 9 yr                                                                                                                 |
|                        |              |                                   | • Characteristics: Group Health Cooperative Members                                                                                  |
|                        |              |                                   | • G1 = 1.00 (referent)                                                                                                           |
|                        |              |                                   | • G2 = 0.76 (0.59-0.99)                                                                                                          |
|                        |              |                                   | • G1 = None                                                                                                                      |
|                        |              |                                   | • G2 = non strenuous LTPA                                                                                                         |
|                        |              |                                   | • G3 = Any Strenuous LTPA                                                                                                        |
|                        |              |                                   | • Outcome measure: non fatal CHD                                                                                                  |
|                        |              |                                   | • Logistic regression                                                                                                           |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study                  | Participants | Methods | Outcomes | Results |
|------------------------|--------------|---------|----------|---------|
| Manson et al 1999 [242]| n = 72,488   | Questionnaire with detailed information on PA | Number of Cases: 645 coronary events | Both walking and VPA are associated with a substantial reductions in incidence of CHD. Risk reductions for each were similar when total PAy was similar. Walking 3 or more hours per week could reduce the risk of CHD by 30-40%. |
|                        |              |         |          |         |
| USA                    |              |         |          |         |
| Prospective cohort     |              |         |          |         |
| Nurses’ Health Study   |              |         |          |         |
| D & B score = 12       |              |         |          |         |
| Total PA score         | G1 = 1.00 (referent) | G2 = 0.88 (0.71-1.10) | G3 = 0.81 (0.64-1.02) | G4 = 0.74 (0.58-0.95) | G5 = 0.66 (0.51-0.86) | p = 0.002 |
| G1 = 1.0-2.0           |              |         |          |         |
| G2 = 2.1-4.6           |              |         |          |         |
| G3 = 4.7-104           |              |         |          |         |
| G4 = 10.5-217          |              |         |          |         |
| G5 = >21.7             |              |         |          |         |
| Multivariate RR (95% CI) by walking activity | G1 = 1.00 (referent) | G2 = 0.78 (0.57-1.06) | G3 = 0.88 (0.65-1.21) | G4 = 0.70 (0.51-0.95) | G5 = 0.65 (0.47-0.91) | p = 0.02 |
| Walking, in those who did not participate in VPA: (MET hr/wk) | G1 = 0.5 | G2 = 0.6-2.0 | G3 = 2.1-3.8 | G4 = 3.9-9.9 | G5 = ≥ 10 |         |
| G1 = 0.5              |              |         |          |         |
| G2 = 0.6-2.0          |              |         |          |         |
| G3 = 2.1-3.8          |              |         |          |         |
| G4 = 3.9-9.9          |              |         |          |         |
| G5 = ≥ 10             |              |         |          |         |
| Multivariate RR (95% CI) by walking pace | 1.00 (referent) | 0.75 (0.59-0.96) | 0.64 (0.47-0.88) |         |         |
| Walking pace (mph)    | G1 = <2.0 | G2 = 2.0-2.9 | G3 = ≥ 3.0 |         |         |
| Study | Authors | Year | Sample Size | Follow Up | Number of Cases | Findings |
|-------|---------|------|-------------|-----------|----------------|----------|
| Mora et al 2007 [243] | Mora et al | 2007 | 27,055 | 10.9 ± 16 yr | 640 | There remained a borderline significant inverse association between PA and risk of CHD after adjustment for all sets of risk factors. |
| | | | | | | - Sex: Women<br>- Age: ≥ 45 yr<br>- PA assessment: Questionnaires at study entry for categories of EE from PA (kcal/wk), 4 groups<br>- Characteristics: Healthy<br>- Women's health study<br>- Number of Cases: 640<br>- USA<br>- Prospective cohort<br>- G1 = 1.00 (referent)<br>- G2 = 0.84 (0.67-1.06)<br>- G3 = 0.76 (0.61-0.96)<br>- G4 = 0.62 (0.48-0.82)<br>- HR (95% CI), basic model |
| O'Connor et al 1995 [244] | O'Connor et al | 1995 | 680 (532 men and 148 women) | | 340 | Significant inverse association between PA level and the risk of non-fatal MI in men, which persisted after adjustment for other risk factors. |
| | | | | | | - Sex: Men and women<br>- Age: < 76 yr<br>- Characteristics: Cases: Diagnosed MI (non-fatal), no previous history of CHD. Controls: no history of CHD.<br>- Outcome measure: non-fatal MI<br>- USA<br>- Case control<br>- Q1 = Lowest<br>- Q2 = 0.60 (0.32-1.13)<br>- Q3 = 0.41 (0.21-0.78)<br>- Q4 = 0.41 (0.22-0.77)<br>- Adjusted OR (95% CI) by PA level, men<br>- Q1 = 1.00 (referent)<br>- Q2 = 0.60 (0.32-1.13)<br>- Q3 = 0.41 (0.21-0.78)<br>- Q4 = 0.41 (0.22-0.77)<br>- p = 0.003 |
| | | | | | | - Sex: Men and women<br>- Age: < 76 yr<br>- Characteristics: Cases: Diagnosed MI (non-fatal), no previous history of CHD. Controls: no history of CHD.<br>- Outcome measure: non-fatal MI<br>- USA<br>- Case control<br>- Q1 = Lowest<br>- Q2 = 0.60 (0.32-1.13)<br>- Q3 = 0.41 (0.21-0.78)<br>- Q4 = 0.41 (0.22-0.77)<br>- Adjusted OR (95% CI) by PA level, women<br>- Q1 = 1.00 (referent)
### Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Country | Sample Size | Sex | Age | Characteristics | Case Definition | Control Definition | OR (95% CI) by Physical Activity | P-value |
|-------|---------|-------------|-----|-----|-----------------|----------------|-----------------|---------------------------------|---------|
| Rastogi et al 2004 [245] | India | 1,050 | Men and women | 21-74 yr | Cases: Diagnosed with MI (non-fatal) | Non-cardiac patients | | Adjusted OR (95% CI) by LTPA | 0.001 |
| | USA | | | | | | | Multivariate OR (95% CI) by Sedentary Time | | | | | | | | | |

#### Moderate-vigorous sports

| Category | OR (95% CI) | P-value |
|----------|-------------|---------|
| Q1 (Lowest) | 1.00 (referent) | |
| Q2 | 1.12 (0.60-2.10) | 0.02 |
| Q3 | 0.61 (0.30-1.24) | |
| Q4 (Highest) | 0.43 (0.20-0.92) | |
| Adjusted OR (95% CI) by moderate-vigorous sports | | |

**Notes:**
- LTPA = Leisure-time physical activity
- MI = Myocardial infarction
- Sedentary time = Time spent sitting or lying down
- Multivariate OR = Adjusted for age, sex, and other potential confounders.
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Outcome Measure: Non-fatal MI | p | Conditional logistic regression |
|-------|-------------------------------|---|--------------------------------|
| Rodriguez et al 1994 [246] | • n = 7,074 | 0.02 | To examine the relationship between PA and 23 yr incidence of CHD morbidity and mortality. |
|       | • Sex: Men | | |
|       | • Age: 45-64 yr | | |
| USA   | • Characteristics: Japanese- American living in Oahu, Hawaii in 1965, < 65 years to reduce effect of retirement on PA levels | | |
|       | • T1 = 1.00 (referent) | | T1 = Low |
|       | • T2 = 1.01 (0.86-1.19) | | T2 = Moderate |
|       | • T3 = 0.83 (0.86-1.19) | | T3 = High |
|       | Multivariate adjusted RR (95% CI), CHD incidence | | Cox proportional regression model |
|       | • T1 = 1.00 (referent) | | |
|       | • T2 = 1.07 (0.90-1.26) | | These data support the hypothesis that PA is associated with a favorable profile of CVD risk factors. |
|       | • T3 = 0.95 (0.80-1.14) | | This study did not show a dose-response relationship since the medium tertile of PA showed increased rates of CHD compared to the inactive group. |
|       | The Honolulu Heart Program | | |
|       | • T3 = 0.95 (0.80-1.14) | | Age adjusted RR (99% CI), CHD mortality |
|       | • T1 = 1.00 (referent) | | Multivariate adjusted RR (95% CI) |
|       | • T2 = 1.12 (0.88-1.44) | | • T1 = 1.00 (referent) |
|       | • T3 = 0.74 (0.56-0.97) | | • T2 = 1.19 (0.93-1.53) |
| D & B | | | • T3 = 0.85 (0.65-1.13) |
| Study | Design | Objective | Methodology | Population | Follow-up | Cases | Findings |
|-------|--------|-----------|-------------|------------|-----------|-------|----------|
| Rothenbacher et al 2003 [247] | Case control | To estimate the risk for CHD associated with LTPA | Interview | Germany | n = 791 (312 cases, 479 controls) | LTPA (h/wk) | Multivariate OR (95% CI), LTPA | LTPA showed a clear inverse association with risk of CHD. |
| | | | | | | G1 = 0 | Multivariate OR (95% CI), LTPA | |
| | | | | | G2 = <1 | Winter | |
| | | | | | G3 = 1-2 | | |
| | | | | | G4 = >2 | | |
| | | | | | | G1 = 1.00 (referent) | |
| | | | | | | G2 = 0.48 (0.27-0.84) | |
| | | | | | | G3 = 0.54 (0.369-0.82) | |
| | | | | | | G4 = 0.27 (0.19-0.47) | |
| | | | | | | | | |
| Seccareccia and Menotti 1992 [248] | Prospective cohort | To examine the relationship between OPA and the risk of CHD death. | Questionnaire for OPA (kcal/d), 3 groups | Italy | n = 1,621 | 25 year of follow-up | Age Standardized CHD and deaths rates: |
| | | | | | | | G1 = 18.9 ± 3.1 |
| | | | | | | | G2 = 13.1 ± 1.7 |
| | | | | | | | G3 = 11.0 ± 0.9 |
| | | | | | | | G1 = Sedentary, < 2400 |
| | | | | | | | G2 = Moderate, 2400-3199 |
| | | | | | | | G3 = Heavy ≥ 3200 |
| Study | Design | Population | Method of PA assessment | Number of Cases | End Point | Findings |
|-------|--------|------------|-------------------------|----------------|-----------|----------|
| Sesso et al 2000 [249] | Prospective cohort | USA | Questionnaire | 2,135 | L-shaped association between PA and the risk of CHD, with a reduction in CHD risk of approximately 20% for total PA levels >4200 kJ/wk | *Sex: Men*<br>*Age: 39-88 yr*<br>*Characteristics: Healthy*<br>PA Index (kJ/wk)<br>G1 = <2100<br>G2 = 2100-4199<br>G3 = 4200-8399<br>G4 = 8400-12599<br>G5 = >12600 | Multivariate HR (99% CI)<br>G1 = 1.00 (referent)<br>G2 = 0.90 (0.79-1.03)<br>G3 = 0.81 (0.71-0.92)<br>G4 = 0.81 (0.71-0.94)<br>G5 = >12600<br>*p* = 0.003 |
| Sundquist et al 2005 [250] | Prospective cohort | Sweden | Questionnaire | 2,135 | Positive long term effect of LTPA on CHD risk among men and women. | *Sex: Men and women*<br>*Age: 35-74 yr*<br>*Characteristics: Those not hospitalized for CHD in the last 2 years and those who rate their general health as poor were excluded*<br>PA Index (kJ/wk)<br>Q1 = None<br>Q2 = Occasionally<br>Q3 = 1-2 times per week<br>Q4 = Vigorous ≥2 times per week | Multivariate adjusted RR (99% CI)<br>Q1 = 1.00 (referent)<br>Q2 = 0.76 (0.55-1.07)<br>Q3 = 0.74 (0.53-1.04)<br>Q4 = 0.59 (0.37-0.95) |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study Authors | Hypothesis | Sample Size | Study Design | Measurement | Results |
|---------------|------------|-------------|--------------|-------------|---------|
| Talbot et al. 2002 [251] | To examine the contributions of LTPA and aerobic fitness to the risk of coronary events in healthy younger and older adults. | *n* = 689 | Prospective cohort; D&B score = 12 | Surveys began in 1960 and were completed on every visit | In younger men PF predicts a reduced risk of CHD but not LTPA. |
|                |            |             | USA          | After adjusting for coronary risk factors there was: | In older men, high intensity LTPA and PF appear to be of similar importance in reducing CHD risk. |
|                |            |             |              | RR: 0.53 (p < 0.001) and RR: 0.61 (p = 0.034) in older men. | |
|                |            |             |              | Total LTPA was unrelated to coronary risk in either age group. With 3 levels of LTPA intensity substituted for total LTPA: | |
|                |            |             |              | RR = 0.39 for tertile 3 vs. tertile 1 | |
| Tanasescu et al. 2002 [252] | To assess the amount, type and intensity of PA in relation to risk of CHD in men. | *n* = 44,452 | Prospective cohort; D&B score = 11 | PA assessment: Questionnaire, Total PA (MET hr/wk); Exercise intensity (METs). Age adjusted HR (95% CI) by total PA. | Total PA, running, weight training, and walking were associated with a reduced risk for CVD. |
|                |            |             | USA          | Age adjusted HR (95% CI) by total PA | |
|                |            |             |              | Q1 = 1.00 (referent) | The average exercise intensity was associated with a reduced risk (independent of total PA). |
|                | Sex: Men   | Age: 40-75 yr |              | Q2 = 0.85 (0.74-0.98) | |
|                | Characteristics: Health professionals, no history of CHD and in good health | Total PA (MET hr/wk) |              | Q3 = 0.78 (0.67-0.92) | |
|                | Q1 = 0.632 | Q2 = 6.33-14.49 |              | Q4 = 0.72 (0.62-0.83) | |
|                | Q3 = 14.50-25.08 | Q4 = 25.09-41.98 |              | Q5 = 0.58 (0.49-0.68) | |
|                | Q5 = > 41.99 |            |              | *p* = .001 | |
|                | Health Professionals follow-up study | Exercise intensity (METs) | | *G1 = Low-1.4* | |
|                |            |             |              | Age adjusted HR (95% CI) by exercise intensity | |
|                |            |             |              | *G1 = .00* (referent) | |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study | Objective | Participants | Length of Follow-up | Number of Cases | Outcome Measure | Multivariate HR (99% CI), men | Multivariate HR (99% CI), women |
|-------|-----------|--------------|---------------------|-----------------|----------------|-----------------------------|--------------------------------|
| Vatten et al 2006 [253] | To investigate whether obesity-related CV mortality could be modified by PA. | n = 54,284 (27,769 men; 26,515 women) | 16 years | 2,462 | Increased PA reduces the risk of death in women, but not in men. | Age adjusted HR (95% CI) | Cox proportional HR |
| Norway | | | | | | p = 0.02 | |
| Prospective cohort | Sex: Men and women | | | | | Q1 = 1.00 (referent) | |
| | PA assessment | | | | | Q2 = 1.01 (0.89-1.16) | |
| | Questionnaire | | | | | Q3 = 0.98 (0.84-1.14) | |
| | Age ≥ 20 yr | | | | | Q4 = 1.18 (1.00-1.38) | |
| | Divided into 4 groups | | | | | p = 0.11 | |
| | Characteristic: Free from CVD at baseline | | | | | Q1 = High | |
| | Q2 = Medium | | | | | Q3 = Low | |
| | Q4 = Never | | | | | p <0.001 | |
| D & B score = 12 | HUNT study | | | | | Multivariate HR (99% CI), women | |
| | | | | | | Outcome Measure: Ischemic heart disease mortality | |
| | | | | | | Q1 = 1.00 (referent) | |
| | | | | | | Q2 = 1.23 (1.01-1.51) | |
| | | | | | | Q3 = 1.54 (1.24-1.91) | |
| | | | | | | Q4 = 1.52 (1.23-1.88) | |
| | | | | | | Cox proportional HR | p <0.001 | |
Table 12: Studies examining the relationship between physical activity and cardiovascular disease. (Continued)

| Study            | Objective                                                                 | Sample Size | Follow-up | Number of Cases | Outcome Measure                                                                 |
|------------------|---------------------------------------------------------------------------|-------------|------------|-----------------|--------------------------------------------------------------------------------|
| Wagner et al 2002 [254] | To investigate if the association between PA patterns and incidence of coronary events could explain the gradient in CHD observed between 2 countries. | n = 9,758   | 5 yrs      | 167 hard CHD, 154 angina events | Beneficial effect of LTPA EE on hard CHD incidence in middle aged men |
|                  | • Sex: Men and women                                                      |             |            | Number of Dropouts: < 2% |                                                         |
|                  | • Age: 50-59 yr                                                           |             |            |                  |                                                         |
|                  | • Characteristics: Healthy at Baseline                                    |             |            |                  |                                                         |
|                  | Prospective cohort                                                       |             |            |                  |                                                          |
|                  | G1 = Lowest                                                               |             |            |                  |                                                          |
|                  | G2 = Middle                                                               |             |            |                  |                                                          |
|                  | G3 = Highest                                                              |             |            |                  |                                                          |
|                  | Outcome Measure: CHD hard events and Angina                              |             |            |                  |                                                          |
|                  | G1 = 1.00 (referent)                                                      |             |            |                  |                                                          |
|                  | G2 = 0.73 (0.51-1.05)                                                    |             |            |                  |                                                          |
|                  | G3 = 0.66 (0.46-0.96)                                                    |             |            |                  |                                                          |
|                  | HR (95% CI), hard events                                                 |             |            | p = 0.04         |                                                          |
|                  | HR (95% CI), angina                                                      |             |            |                  |                                                          |
|                  | G1 = 1.00 (referent)                                                      |             |            |                  |                                                          |
|                  | G2 = 0.83 (0.55-1.25)                                                    |             |            | p = 0.10         |                                                          |
|                  | G3 = 1.28 (0.88-1.86)                                                    |             |            |                  |                                                          |

D & B score, Downs and Black quality score; YR, years; G, groups; CHD, coronary heart disease; RR, risk ratio; 95% CI, 95% confidence interval; PA, physical activity; VPA, vigorous physical activity; CV, cardio vascular; MET, metabolic equivalent; kcal/wk, kilocalories per week; Q, quartile or quintile; km/h, kilometers per hour; LTPA, leisure-time physical activity; HR, hazard ratio; OPA, occupational physical activity; kcal/kg/day kilocalories per kilogram per day; MI, myocardial infarction; ECG, electrocardiogram; kcal/kg/h kilocalories per kilogram per hour; mph, miles per hour; CVD, cardiovascular disease.
30% risk reduction in the most active individuals [31]. In fact, in a review of the literature Katzmarzyk and Janssen [20] reported that lack of physical activity carried a relative risk of 1.60 (95% CI = 1.42-1.80) for stroke, similar to or higher than that for coronary heart disease (1.45), hypertension (1.30), colon cancer (1.41), breast cancer (1.31), type 2 diabetes (1.50), and osteoporosis (1.59).

In our systematic review of the literature, a total of 1104 citations were identified during the electronic database search (Figure 5). Of these citations, 405 were identified in MEDLINE, 183 in EMBASE, 227 in Cochrane, and 289 in the CINAHL/SportDiscus/PsychInfo search. A total of 13 duplicates were found, leaving a total of 1091 unique citations. A total of 1011 articles were excluded after scanning, leaving a total of 80 articles for full review. An additional 9 articles were retrieved through cross-referencing and the authors’ knowledge of the field. From these articles 64 were excluded after full review leaving 25 articles for inclusion in the systematic review. The reasons for exclusion included non-experimental/weak design (poor execution introducing bias) (n = 16), did not contain three levels of physical activity or not possible to determine dose-response relationship (n = 14), reviews, summaries, meta-analyses (n = 17), dissertations, thesis, abstracts (n = 8), and other (n = 9). Therefore, a total of 25 articles were included in the systematic review of the literature regarding the relationship between physical activity and the primary prevention of stroke (Table 13).

The data providing dose-response information is all observational in nature, involving both case control and cohort investigations. These studies (predominantly prospective cohort designs) included a total of 479,336 participants; averaging 17,753 subjects per study (range 428-73,265). There were a total of 12,361 reported cases of stroke (ranging per study from 32-2,863). The total length of study follow-up for the prospective cohort studies averaged 13.2 yr (ranging from 6-26 yr). The articles were published over a 14 yr period ranging from 1993 to 2007. These studies involved large samples of men and women from regions throughout the world including studies from the USA (11), UK (2), Iceland (1), Denmark (2), Norway (4), Netherlands (1), Finland (2), Japan (1), Australia (1) and Greece (1). Very few studies [69,70] examined non-Caucasian participants. We found strong evidence that physical activity was associated with a reduced risk for stroke. The level of evidence was consistent with a Level 3A classification. We observed an average risk reduction of 31% across all studies (median = 29%). In comparison to cardiovascular disease, there was more variability in the risk reductions in stroke in the highest activity/fitness group. The quality of the investigations was also generally quite good with a mean (and median) Downs and Black score of 13 (range 11-15).

The risk reductions appear to be even greater in studies that assessed physical fitness directly. For instance, in data from the Aerobics Center Longitudinal Study [71] the high fitness group (estimated peak METs = 13.1) and the moderate fitness group (estimated peak METs 10.5) had significantly lower risks of stroke mortality (68 and 63%, respectively) than the least fit men (estimated peak METs 8.5).

A dose-response relationship did emerge when examining the literature. However, as illustrated by others this was extremely variable amongst studies and varied
| Publication | Objective | Population | Methods | Outcome | Comments and Conclusions |
|-------------|-----------|------------|---------|---------|---------------------------|
| Wisloff et al 2006 [58] | To assess exercise amount and intensity in relation to subsequent CVD mortality (including stroke). | n = 27,143 men, 28,929 women | 16 year follow up | Multivariate adjusted RR (95% CI) | Both high and low-intensity exercise may be associated with a reduced risk of stroke in both men and women. |
| Norway | Sex: Men and women | PA Assessment: Questionnaire | G1 = 1.00 (referent) | |
| | Age: ≥ 20 yr | PA | G2 = 0.90 (0.70-1.17) | |
| | Characteristics: free from CVD | | G3a = 0.90 (0.64-1.26) | |
| | HUNT Study | G1 = None | G3b = 0.59 (0.27-1.27) | |
| | | G2 = <1/wk | G3c = 0.62 (0.40-0.95) | |
| | | G3a = 1/wk ≤ 30 min low | G3d = 0.51 (0.31-0.86) | |
| | | G3b = 1/wk ≤ 30 min high | G4a = 0.72 (0.49-1.05) | |
| | | G3c = 1/wk > 30 min low | G4b = 0.63 (0.31-1.30) | |
| | | G3d = 1/wk > 30 min high | G4c = 1.02 (0.72-1.44) | |
| Prospective cohort | | G4a = 2-3/wk ≤ 30 min low | G4d = 0.59 (0.37-0.92) | |
| | | G4b = 2-3/wk ≤ 30 min high | G5a = 0.97 (0.70-1.36) | |
| | | G4c = 2-3/wk > 30 min low | G5b = 0.68 (0.27-1.66) | |
| | | G4d = 2-3/wk > 30 min high | G5c = 0.81 (0.65-1.20) | |
| | | G5a = ≥ 4/wk ≤ 30 min low | G5d = 0.67 (0.49-1.11) | |
| | | G5b = ≥ 4/wk ≤ 30 min high | | |
| | | G5c = ≥ 4/wk > 30 min low | RR (95% CI) Women | |
| | | G5d = ≥ 4/wk > 30 min high | G1 = 1.00 (referent) | |
| | Outcome Measure: IHD mortality | Cox proportional HR | G2 = 1.01 (0.81-1.25) | |
| | | | G3a = 0.88 (0.68-1.15) | |
| | | | G3b = 0.98 (0.46-2.10) | |
| | | | G3c = 0.63 (0.42-0.94) | |
| | | | G3d = 1.00 (0.50-1.98) | |
| | | | G4a = 0.91 (0.70-1.17) | |
| | | | G4b = 1.44 (0.78-2.62) | |
| | | | G4c = 0.62 (0.44-0.88) | |
| | | | G4d = 0.77 (0.36-1.66) | |
| | | | G5a = 0.74 (0.56-0.99) | |
| | | | G5b = 0.40 (0.10-1.62) | |
| | | | G5c = 0.63 (0.45-0.89) | |
| | | | G5d = 0.51 (0.21-1.26) | |
### Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Participants | Follow-up | Incidence Rates per 1000 of Stroke | Protective Effect of PA on Reducing Risk of Stroke with Age |
|-------|--------------|-----------|------------------------------------|----------------------------------------------------------|
| Abbott et al 2003 [69] | USA | Sex: Men, Age: 45-93 yr | Incidence rates per 1000 of stroke increased with age. PA assessment: Using PA index over a 24 hour period PA information collected at study enrolment (1965-1968) and updated at physical examinations that occurred at 6, 15, and 26 years into follow-up. | n = 7,589, 6, 15, and 26 year follow up |
| Gillium et al 1996 [70] | USA | Sex: Men and women, Age: 45-74 yr | Incidence of stroke event increased with advancing age p < 0.001. | n = 2,368 men, 2,713 women |

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**Abbott et al 2003**

To examine the way in which risk factor effects on the incidence of thromboembolic and hemorrhagic stroke can change over a broad range of ages.

- **n = 7,589**
- **6, 15 and 26 year follow up**
- **Incidence rates per 1000 of stroke:** The protective effect of PA on reducing risk of stroke increased with age.

**Prospective cohort**

- Characteristics: Free from CHD and stroke at enrolment; Japanese ancestry living on the island of Oahu, Hawaii.
- Grouped into 4 age groups, yr:
  - **G1 = 9.0 (49)**
  - **G2 = 17.8 (124)**

**D & B score = 14**

- **Honolulu Heart Program**
  - **G1 = 45-54**
  - **G2 = 55-64**
  - **G3 = 65-74**
  - **G4 = 75-93**
  - **Outcome Measure:** diagnosis of fatal and non fatal stroke during 26 years of follow-up
  - **Cox proportional HR**

**Gillum et al 1996**

To examine the relationship between recreational and non-recreational PA and risk of stroke.

- **n = 2,368 men, 2,713 women**
- **11.6 year follow up**
- **Number of Cases:** 249 white women, 270 white men, 104 black
- **Sedentary behaviour was found to be associated with increased risk of stroke.**

**Addendum:**

- **Prospective cohort**
  - Ethnicity: Black and white
  - **T2 = Medium**
  - **T3 = High**
  - **Outcome Measure:** Total Stroke
  - **Cox proportional HR**

- **D & B score = 12**
  - **NHANES I**
  - **T1 = Low**
  - **T2 = Medium**
  - **T3 = High**
  - **Outcome Measure:** Total Stroke
  - **Cox proportional HR**

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  - [http://www.ijbnpa.org/content/7/1/39](http://www.ijbnpa.org/content/7/1/39)
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| RR (95% CI) | White men age 45-64 | White women age 45-64 | White men age 65-74 | White women age 65-75 |
|-------------|---------------------|-----------------------|---------------------|-----------------------|
| **Recreational PA** |                     |                       |                     |                       |
| RR (95% CI) | White men age 45-64 | White women age 45-64 | White men age 65-74 | White women age 65-75 |
| **Non-recreational PA** |                     |                       |                     |                       |

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### Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Objective | Participants | Methods | Outcome Measures | Results |
|-------|-----------|--------------|---------|------------------|---------|
| Lee and Blair 2002 [71] | To examine the association between PF and stroke mortality in men. | n = 16,878, Baseline medical evaluation between 1971 and 1994 with average follow-up period of 10 years | Average estimated maximal METs, T1 = 8.5 MET, T2 = 10.5 MET, T3 = 13.1 MET | T1, T2, T3 and D & B score, Cox proportional HR, RR (95% CI) adjusted for age and exam year, Trend p = 0.005 | Moderate and high levels of PF were associated with lower risk of stroke mortality in men. |
| USA | Prospective cohort | PF assessment: Maximal exercise tolerance test, divided into tertiles | RR (95% CI) adjusted for age and exam year | T1 = Low, T2 = Moderate, T3 = High | |
| D & B score = 13 | | | | | |
| Hu et al 2000 [72] | To examine the association between PA and risk of total stroke and stroke sub-types in women. | n = 72,488, Baseline measurement in 1986 with follow-up questionnaire in 1988 and 1992 | 407 cases of stroke (258 ischemic strokes, 67 subarachnoid hemorrhages, 42 intracerebral hemorrhages, and 40 strokes of unknown type) | PA, including moderate-intensity exercise such as walking, is associated with a substantial reduction in risk of total and ischemic stroke in a dose-response manner. | Multivariate RR (95% CI) for total stroke by total PA level, Multivariate RR (95% CI) for ischemic Stroke by total PA level |
| USA | Prospective cohort | PA assessment: Questionnaire for total PA (MET h/wk), divided into quintiles, walking activity (MET h/wk), divided into quintiles and walking pace | Multivariate RR (95% CI) for total stroke by total PA level | Q1 = 1.00 (referent), Q2 = 0.98, Q3 = 0.82, Q4 = 0.74, Q5 = 0.66 | Total PA (MET h/wk) p = 0.005 |
| D & B score = 13 | | | | | Q1 = 0 - 2.0, Q2 = 2.1 - 4.6, Q3 = 4.7 - 10.4, Q4 = 10.5-21.7 |
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Walking activity (MET h/wk) | Multivariate RR (95% CI) for total stroke by walking activity |
|-----------------------------|-------------------------------------------------------------|
| Q5 = > 21.7                | Q1 = 1.00 (referent)                                       |
| Q1 = 05                     | Q2 = 0.87                                                  |
| Q2 = 0.6 - 2.0              | Q3 = 0.83                                                  |
| Q3 = 2.1 - 3.8              | Q4 = 0.76                                                  |
| Q4 = 3.9 - 10               | Q5 = 0.52                                                  |
| Q5 = 10                     | p = 0.003                                                  |

| Walking pace (mph)          | Outcome measure: Stroke incidence p = 0.01                 |
|-----------------------------|-------------------------------------------------------------|
| G1 < 2.0                    | Multivariate RR (95% CI) for ischemic stroke by walking activity |
| G2 = 2-2.9                  | Q1 = 1.00 (referent)                                       |
| G3 = 3.0                    | Q2 = 0.76                                                  |
| G4 = 3.9 - 10               | Q3 = 0.78                                                  |
| G5 = 10                     | Q4 = 0.70                                                  |
|                              | Q5 = 0.66                                                  |

Pooled logistic regression
Cox proportional HR

| Walking activity (MET h/wk) | Multivariate RR (95% CI) for total stroke by usual Walking Pace |
|-----------------------------|-----------------------------------------------------------------|
| Q5 = > 21.7                 | Q1 = 1.00 (referent)                                           |
| Q1 = 05                     | Q2 = 0.77                                                      |
| Q2 = 0.6 - 2.0              | Q3 = 0.75                                                      |
| Q3 = 2.1 - 3.8              | Q4 = 0.69                                                      |
| Q4 = 3.9 - 10               | Q5 = 0.60                                                      |
| Q5 = 10                     | p = 0.02                                                        |

Multivariate RR (95% CI) for ischemic stroke by usual walking pace

| Walking pace (mph)          | Multivariate RR (95% CI) for ischemic stroke by usual walking pace |
|-----------------------------|-----------------------------------------------------------------|
| G1 < 2.0                    | Q1 = 1.00 (referent)                                           |
| G2 = 2-2.9                  | Q2 = 0.71                                                      |
| G3 = 3.0                    | Q3 = 0.47                                                      |
| G4 = 3.9 - 10               | p < 0.001                                                       |

p < 0.001

Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39
http://www.ijbnpa.org/content/7/1/39
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study            | Aim                                                                 | n = 21,823 | 11.1 year follow up | Number of Cases: 533 | VPA is associated with a decreased risk of stroke in men. |
|------------------|----------------------------------------------------------------------|------------|---------------------|----------------------|----------------------------------------------------------|
| Lee et al 1999   | To examine the association between exercise and stroke risk.         |            |                     |                      |                                                          |
|                  | • Sex: Men                                                           |            |                     |                      |                                                          |
|                  | • Age: 40-84 yr                                                      |            |                     |                      |                                                          |
|                  | PA assessment: Questionnaire for frequency of VPA, divided into 4 groups |            |                     |                      |                                                          |
|                  | Multivariate RR1 (95% CI) for total stroke by VPA                   |            |                     |                      |                                                          |
| USA              |                                                                      |            |                     |                      |                                                          |
|                  | Prospective cohort                                                  |            |                     |                      |                                                          |
|                  | D & B score = 13                                                     |            |                     |                      |                                                          |
|                  |                                                                      |            |                     |                      |                                                          |
|                  | G1 < 1 time/week                                                     |            |                     |                      |                                                          |
|                  | G2 = 1 time/week                                                     |            |                     |                      |                                                          |
|                  | G3 = 2-4 times/week                                                  |            |                     |                      |                                                          |
|                  | G4 ≥ 5 times/week                                                    |            |                     |                      |                                                          |
|                  | p = 0.04                                                             |            |                     |                      |                                                          |
|                  | RR1 = adjusted for smoking, alcohol consumption, history of angina and parental history of MI at <60 years |            |                     |                      |                                                          |
|                  | RR2 (95% CI) for total stroke by VPA                                 |            |                     |                      |                                                          |
|                  | RR2 = adjusted for all of the above plus, BMI, history of, hypertension, high cholesterol and diabetes |            |                     |                      |                                                          |
|                  | VPA                                                                 |            |                     |                      |                                                          |
|                  | RR2 (95% CI) for hemorrhagic stroke by VPA                           |            |                     |                      |                                                          |
|                  | Cox proportional HR                                                  |            |                     |                      |                                                          |
|                  | Outcome Measure: Total Stroke (Ischemic and Hemorrhagic)            |            |                     |                      |                                                          |
|                  | p = 0.81                                                             |            |                     |                      |                                                          |
|                  | RR2 (95% CI) for hemorrhagic stroke by VPA                           |            |                     |                      |                                                          |
|                  | p = 0.10                                                             |            |                     |                      |                                                          |
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Objective | Sample | Methods | Key Findings |
|-------|-----------|--------|---------|--------------|
| Bijnen et al 1998 [166] | To describe the association between the PA patterns of elderly men and stroke mortality. | *n* = 802 | 10 year follow up | Number of Cases: 47 | No significant finding |
| | | Denmark | Prospective cohort | | |
| | | | | | | \( \text{D & B score} = 15 \) |
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| Schnohr et al 2006 [214] | To describe the association between different levels of LTPA and subsequent causes of death (stroke). | *n* = 2136 men, 2758 women | 5 year follow up | RR (99% CI), univariate | Although RR for of death from stroke was below 1 for both moderate and high compared with low PA, this association did not reach the level of statistical significance. |
| | | Copenhagen | Prospective cohort | | |
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Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Characteristics | PA assessment | Multivariate HR (95% CI), men | Multivariate HR (95% CI), women |
|-------|-----------------|---------------|-------------------------------|-------------------------------|
| Norway | Age: 20 yr | Questionnaire for total amount of PA, divided into 4 groups | | |
|        | Sex: Men and women | | | |
|        | HUNT study | G1 = High | Q1 = 1.00 (referent) | Q1 = 1.00 (referent) |
|        |          | G2 = medium | Q2 = 1.05 (0.85-1.30) | Q2 = 1.00 (referent) |
|        |          | G3 = low   | Q3 = 1.21 (0.95-1.54) | Q3 = 1.16 (0.93-1.45) |
|        |          | G4 = never | Q4 = 1.35 (1.05-1.74) | Q4 = 1.45 (1.14-1.83) |
|        | Characteristics: Free from CVD at baseline | | | |
|        | Prospective cohort | | | |
| Iceland | Age: 45-80 | Questionnaire for LTPA (h/wk) and type of activity (intensity), each divided into 3 groups | | |
|        | Sex: Men | | | |
|        | Characteristics: no history of Stroke | | | |
|        | Prospective cohort | Reykjavik Study | | |
|        | D & B score = 14 | | | |
|        | D & B score = 13 | | | |
|        | LTPA summer/winter | | | |
|        | G1 = none | | | |
|        | G2 = ≤ 5 h/wk | | | |
|        | G3 = ≥ 6 h/wk | | | |
|        | Type of Activity | | | |
|        | Agnarsson et al 1999 [255] | To examine the association of LTPA and pulmonary function with the risk of stroke. | | |
|        | n = 4,484 | Length of Follow-up: 10.6 ± 3.6 years | Number of Cases: 249 | Apparent protective effect of regular continued LTPA in middle age men on the risk of ischemic stroke. |
|        | | | | |
|        | Adjusted for age and smoking RR (95% CI) for total stroke by LTPA level | | | |
|        | Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39 | http://www.ijbnpa.org/content/7/1/39 | | |
| Study | Objective | Participants | Design | Methods | Outcome Measure | RR (95% CI) for total stroke by type of activity | RR (95% CI) for ischemic stroke by type of activity |
|-------|-----------|--------------|--------|---------|----------------|-----------------------------------------------|-----------------------------------------------|
| Ellekjaer et al 2000 [256] | To examine the association between different levels of LTPA and stroke mortality in middle-aged and elderly women | n = 14,101 | Baseline 1984-1986: 2 self administered questionnaires and clinical measurements included in the screening program | Number of cases: 457 | This study demonstrates a consistent, negative association between PA and stroke mortality in women. | Multivariate RR (95% CI), all age groups | Multivariate RR (95% CI), age 70-79 years |
| G1 = none | G2 = low intensity | G3 = high intensity | RR (95% CI) for total stroke by type of activity | | | |
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Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Objective | Sample Size | Follow-up | Number of Cases | Outcome Measure: Ischemic Stroke | Multivariate adjusted RR (95% CI) by PA assessment:
|-------|-----------|-------------|-----------|----------------|---------------------------------|-------------------------------------------------------------|
| Evenson et al 1999 [257] | To examine the relationship between PA and ischemic stroke risk | n = 14,575 | 7.2 year follow up | Number of Cases: 189 | USA Atherosclerosis Risk in Communities Study PA assessment: Questionnaire (Baecke questionnaire) | Multivariate Poisson and Cox proportional HR

| Outcome Measure: Ischemic Stroke | Multivariate adjusted RR (95% CI) by LTPA | Multivariate adjusted RR (95% CI) by OPA |
|---------------------------------|---------------------------------|---------------------------------|
| Q1 = 1.00 (referent) | Q2 = | Q3 = 0.83 (0.52-1.32) |
| Q1 = 1.00 (referent) | Q2 = | Q3 = 0.69 (0.47-1.00) |

PA was weakly associated with a reduced risk of ischemic stroke among middle aged adults.

| Study | Objective | Sample Size | Baseline Screening from May 1972-December 1973. | HR (95% CI) for stroke incidence | Increased LTPA is associated with a reduced risk of stroke incidence but not mortality. |
|-------|-----------|-------------|-----------------------------------------------|-------------------------------|-----------------------------------------------------|
| Haheim et al 1993 [258] | To determine the risk factors of stroke incidence and mortality. | n = 14,403 | Baseline Screening from May 1972-December 1973. | G1 = 1.00 (referent) | G2 = 0.64 (0.38-1.08) |

| Sex: Men | Age: 40-49 yr | Sex: Men | Age: 40-49 yr |
|---------|---------------|---------|---------------|
| Q1 = 1.00 (referent) | Q2 = | Q3 = 0.89 (0.57-1.37) |
| Q1 = 1.00 (referent) | Q2 = | Q3 = 0.69 (0.47-1.00) |

Using a Cox proportional hazards model, the authors estimated the risk of ischemic stroke among middle aged adults. The results showed a weak association between PA and ischemic stroke risk, with hazard ratios ranging from 0.79 to 0.56 for different levels of PA. These findings suggest that increased PA may reduce the risk of ischemic stroke in middle aged adults.
Table 13: Studies examining the relationship between physical activity and stroke. *(Continued)*

| Country       | PA assessment: Questionnaire for LTPA, divided into groups | D & B score | Outcome Measure: Incidence of stroke morbidity and mortality until study end date, December 31, 1984. Cox proportional HR |
|---------------|----------------------------------------------------------|-------------|-------------------------------------------------------------------------------------------------------------------------------------|
| Norway        |                                                          | 14          |                                                                                                                                       |
| Prospective   |                                                          |             |                                                                                                                                       |
| cohort        |                                                          |             |                                                                                                                                       |
| D & B score   |                                                          | 14          |                                                                                                                                       |
| Norway        |                                                          |             |                                                                                                                                       |
| Prospective   |                                                          |             |                                                                                                                                       |
| cohort        |                                                          |             |                                                                                                                                       |
| D & B score   |                                                          | 14          |                                                                                                                                       |
| Finland       |                                                          |             |                                                                                                                                       |
| Prospective   |                                                          | 13          |                                                                                                                                       |
| cohort        |                                                          |             |                                                                                                                                       |
| D & B score   |                                                          | 13          |                                                                                                                                       |

**Hu et al 2005**

To assess the relationship of different types of PA with total and type-specific stroke risk.

- *n = 47,721*
- **Sex:** Men and women
- **Age:** 25-64
- **Characteristics:** Healthy at baseline

PA assessment: Mailed questionnaire for LTPA, OPA and commuting PA, divided into groups as follows:

- **LTPA levels:**
  - G1 = Low
  - G2 = Moderate
  - G3 = High
  - *G1 = 1.00 (referent)*
  - *G2 = 0.85*
  - *G3 = 0.75*
  - *p = 0.007*

- **OPA:**
  - G1 = Light
  - G2 = Moderate
  - G3 = Hard
  - *G1 = 1.00 (referent)*
  - *G2 = 0.85*

- **Commuting PA:**
  - G1 = Motorized or no work
  - G2 = walking or cycling 1-29 min
  - G3 = walking or cycling ≥ 30 min
  - *G1 = 1.00 (referent)*
  - *G2 = 0.85*
  - *G3 = 0.73*
  - *p < 0.001*

- **RR (95% CI) by LTPA, men and women:**
  - G1 = Low
  - G2 = Moderate
  - G3 = High
  - *G1 = 1.00 (referent)*
  - *G2 = 0.72*
  - *p < 0.001*

- **RR (95% CI) by OPA, men and women:**
  - Not significant

**Hu et al 2005**

To assess the relationship of different types of PA with total and type-specific stroke risk.

- *n = 47,721*
- **Sex:** Men and women
- **Age:** 25-64
- **Characteristics:** Healthy at baseline

PA assessment: Mailed questionnaire for LTPA, OPA and commuting PA, divided into groups as follows:

- **LTPA levels:**
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  - G2 = Moderate
  - G3 = High
  - *G1 = 1.00 (referent)*
  - *G2 = 0.85*
  - *G3 = 0.75*
  - *p = 0.007*

- **OPA:**
  - G1 = Light
  - G2 = Moderate
  - G3 = Hard
  - *G1 = 1.00 (referent)*
  - *G2 = 0.85*

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  - G1 = Motorized or no work
  - G2 = walking or cycling 1-29 min
  - G3 = walking or cycling ≥ 30 min
  - *G1 = 1.00 (referent)*
  - *G2 = 0.85*
  - *G3 = 0.73*
  - *p < 0.001*

- **RR (95% CI) by OPA, men and women:**
  - Not significant
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Outcome Measure: Incidence of fatal or non-fatal stroke occurring during follow-up until end of 2003. Mean follow-up of 19 years. |
|-------|----------------------------------------------------------------------------------------------------------------------------------|
| Kiely et al 1994 [260] | RR (95% CI) by OPA, women  
- Not significant 
RR (95% CI) by OPA, men and women  
- G1 = 1.00 (referent)  
- G2 = 0.90  
- G3 = 0.87  
* p = 0.007 
RR (95% CI) by commuting PA, men  
- G1 = 1.00 (referent)  
- G2 = 0.91  
- G3 = 0.85  
* p = 0.047 
RR (95% CI) by commuting PA, women  
- G1 = 1.00 (referent)  
- G2 = 0.86  
- G3 = 0.85  
* p = 0.018 
RR (95% CI) by commuting PA, men and women  
- G1 = 1.00 (referent)  
- G2 = 0.89  
- G3 = 0.85  
* p = 0.002 |
| USA | To examine the influence of increased PA on stroke risk in members of the Framingham study cohort.  
- n = 1,897 men 2,299 women  
- Sex: Men and women  
- Age: 28-62 yr  
- Characteristics: Free from stroke  
- Baseline measurement in 1954-1955 and follow up in either 1968-1969 or 1971-1972  
- Multivariate adjusted RR (95% CI) at first examination, men (mean age 50 years)  
- Medium and high levels of PA among men are protective against stroke relative to low levels.  
- PA assessment: Questionnaire for metabolic work done during a typical 24 hr period, divided into 3 groups  
- G1 = 1.00 (referent)  
- G2 = 0.90 (0.62-1.31) * p = 0.59  
- G3 = 0.84 (0.59-1.18) * p = 0.31 |
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Methodology | Participants | Outcome Measure | Multivariate adjusted RR (95% CI) at first examination, women (mean age 50 years) | Protective effect of PA was slightly less for high levels of PA compared to medium levels for older men. |
|-------|-------------|--------------|----------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| -     | -           | -            | -              | -                                                                               | -                                                                                                 |

D & B score = 12

| G1 | Low | G2 | Medium | G3 | High |
|----|-----|----|--------|----|------|
|    | 1.00 (referent) | 1.21 (0.89-1.63) | 0.89 (0.60-1.31) | 0.54 |

Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up.

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Multivariate adjusted RR (95% CI) at second examination, men (mean age 63 years) | Cox proportional HR |
|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------|
| -                                                                                | -                                                                               | -                 |

| G1 | Low | G2 | Medium | G3 | High |
|----|-----|----|--------|----|------|
|    | 1.00 (referent) | 0.41 (0.24-0.89) | 0.53 (0.34-0.84) | 0.0007 |
|    |                  |                  | p = 0.0007           |          |

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Multivariate adjusted RR (95% CI) at second examination, women (mean age 64 years) | Cox proportional HR |
|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------|
| -                                                                                | -                                                                               | -                 |

| G1 | Low | G2 | Medium | G3 | High |
|----|-----|----|--------|----|------|
|    | 1.00 (referent) | 0.97 (0.64-1.47) | 1.21 (0.75-1.96) | 0.43 |
|    |                  |                  | p = 0.67           |          |

Krarup et al 2007 [261]

To compare the reported level of PA performed during the week preceding an ischemic stroke with that of community controls.

- n = 127 cases 301 controls

PA assessment:

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Univariate OR (95% CI) | Stroke patients are less physically active in the week preceding an ischemic stroke when compared to age and sex-matched controls. Increasing PASE score was inversely, log-linearly and significantly associated with OR for ischemic stroke. |
|--------------------------------------------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| -                                                                                | -                     | -                                                                                                                                        |

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Univariate OR (95% CI) | Stroke patients are less physically active in the week preceding an ischemic stroke when compared to age and sex-matched controls. Increasing PASE score was inversely, log-linearly and significantly associated with OR for ischemic stroke. |
|--------------------------------------------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| -                                                                                | -                     | -                                                                                                                                        |

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Univariate OR (95% CI) | Stroke patients are less physically active in the week preceding an ischemic stroke when compared to age and sex-matched controls. Increasing PASE score was inversely, log-linearly and significantly associated with OR for ischemic stroke. |
|--------------------------------------------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| -                                                                                | -                     | -                                                                                                                                        |

Krarup et al 2007 [261]

To compare the reported level of PA performed during the week preceding an ischemic stroke with that of community controls.

- n = 127 cases 301 controls

PA assessment:

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Univariate OR (95% CI) | Stroke patients are less physically active in the week preceding an ischemic stroke when compared to age and sex-matched controls. Increasing PASE score was inversely, log-linearly and significantly associated with OR for ischemic stroke. |
|--------------------------------------------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| -                                                                                | -                     | -                                                                                                                                        |

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Univariate OR (95% CI) | Stroke patients are less physically active in the week preceding an ischemic stroke when compared to age and sex-matched controls. Increasing PASE score was inversely, log-linearly and significantly associated with OR for ischemic stroke. |
|--------------------------------------------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| -                                                                                | -                     | -                                                                                                                                        |

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Univariate OR (95% CI) | Stroke patients are less physically active in the week preceding an ischemic stroke when compared to age and sex-matched controls. Increasing PASE score was inversely, log-linearly and significantly associated with OR for ischemic stroke. |
|--------------------------------------------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| -                                                                                | -                     | -                                                                                                                                        |

| Outcome Measure: Incidence of stroke, as defined by the first occurrence of atherothrombotic brain infarctions, cerebral embolism or other type of stroke, during 32 years of follow-up. | Univariate OR (95% CI) | Stroke patients are less physically active in the week preceding an ischemic stroke when compared to age and sex-matched controls. Increasing PASE score was inversely, log-linearly and significantly associated with OR for ischemic stroke. |
|--------------------------------------------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| -                                                                                | -                     | -                                                                                                                                        |

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http://www.ijbnpa.org/content/7/1/39
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Case control | Characteristics: Case: Stroke Patients (20% had history of Stroke), Controls: 4% had history of stroke | Multivariate OR (95% CI) PASE Score |
|--------------|---------------------------------------------------------------------------------------------------------|-----------------------------------|
| D & B score = 14 | Q1 = 0-49, Q2 = 50-99, Q3 = 100-149, Q4 = 150+ | Q1 = 1.00 (referent) |
|              | Outcome measure: Ischemic stroke | Q2 = 0.53 (0.26-1.08) |
|              | Chi squared Kruskal-Wallis Statistics | Q3 = 0.27 (0.12-0.59) |
|              | Multivariate conditional logistic regression | Q4 = 0.09 (0.03-0.25) |

Kurl et al 2003

- To examine the relationship of PF with subsequent incidence of stroke. Also to compare PF with conventional risk factors as a predictor for future stroke.
- n = 2,011 Baseline examinations conducted between March 1984 and December 1989 with average follow up period of 11 years
- Finland
  - Characteristics: Free from stroke or pulmonary disease
  - Kuopio Ischaemic Heart Disease Risk Factor Study

- Sex: Men
- Age: 42, 48, 54 or 60 yrs

- Multivariate HR (95% CI), any stroke
- Low PF was associated with an increased risk of any stroke and ischemic stroke.

- Multivariate HR (95% CI), ischemic stroke

| Prospective cohort | Baseline examinations conducted between March 1984 and December 1989 with average follow up period of 11 years |
|--------------------|---------------------------------------------------------------------------------------------------------|

| D & B score = 14 | PF assessment: Maximal exercise test on cycle ergometer. VO2 max (ml/kg/min) divided into quartiles |
|------------------|-----------------------------------------------------------------------------------------------------|
|                  | Multivariate HR (95% CI), ischemic stroke |

|                  | Trend p = 0.01 |
|                  | Multivariate HR (95% CI), ischemic stroke |

- Q1 = >35.3
- Q2 = 30.3-35.3
- Q3 = 25.2-30.2
| Study                     | Objective                                                                 | Sample Size | Baseline Measurement | Model A: All 4 Categories of PA | Higher Levels of PA Assessed Using a Single Simple Pragmatic Tool Based on Both OPA and LTPA | Significant Risk Reduction |
|--------------------------|---------------------------------------------------------------------------|-------------|----------------------|--------------------------------|----------------------------------------------------------------------------------|---------------------------|
| Myint et al 2006 [263]   | To examine the association between a combination of OPA and LTPA with risk of subsequent stroke | n = 22,602  | 1993-1997            | HR (95% CI), men and women    | G1 = 1.00 (referent)                                                             | G1 = 25.2                 |
|                          |                                                                           |             |                      |                                 | G2 = 0.78 (0.61-1.00)                                                          |                           |
|                          |                                                                           |             |                      |                                 | G3 = 0.66 (0.49-0.91)                                                          |                           |
|                          |                                                                           |             |                      |                                 | G4 = 0.70 (0.49-0.99)                                                          |                           |
|                          |                                                                           |             |                      |                                 | p = 0.024                                                                      |                           |
|                          |                                                                           |             |                      |                                 | G1 = 0.75 (0.52-1.09)                                                          |                           |
|                          |                                                                           |             |                      |                                 | G2 = 0.55 (0.35-0.86)                                                          |                           |
|                          |                                                                           |             |                      |                                 | G3 = 0.67 (0.43-1.05)                                                          |                           |
|                          |                                                                           |             |                      |                                 | p = 0.41                                                                       |                           |
|                          |                                                                           |             |                      |                                 | Women not significant p = 0.50                                                  |                           |
|                          |                                                                           |             |                      |                                 | G1 = 0.61 (0.43-0.86)                                                          |                           |
|                          |                                                                           |             |                      |                                 | G2 = 0.67 (0.43-1.05)                                                          |                           |

Outcome Measure: Incidence of fatal and non-fatal stroke.
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Objective | Sample | Duration | Number of Cases | Sex: Men and Women | PA Assessment | Number of Dropouts | Multivariate Adjusted HR (95% CI) by Duration of Walking PA, Men | Multivariate Adjusted HR (95% CI) by Duration of Walking PA, Women | Outcome Measure | Cox Proportional HR |
|-------|-----------|--------|----------|-----------------|-------------------|---------------|-------------------|----------------------------------------------------------------------|----------------------------------------------------------------------|----------------|-------------------|
| Noda et al 2005 [264] | To examine the impact of exercise on CVD (stroke) mortality in Asian populations. | n = 31,023 men, 42,242 women | 9.7 year follow up | Number of Cases: 186 men, 141 women | PA through walking and sports participation may reduce the risk of mortality from ischemic stroke | Multivariate adjusted HR (95% CI) by duration of walking PA, men | Number of Dropouts: 3.4% | Multivariate adjusted HR (95% CI) by duration of walking PA, women | Multivariate adjusted HR (95% CI) by sport PA, men | Multivariate adjusted HR (95% CI) by sport PA, women |
|      | Japan     |        |          |                 |                   |               |                   |                                                                      |                                                                      |                |                   |
|      | Prospective cohort |        |          |                 |                   |               |                   | Q1 = <0.5                                                                 | Q1 = 1.38 (0.82-2.33)                                                      |                   |                   |
|      | D & B score = 13 |        |          |                 |                   |               |                   | Q2 = 0.05                                                                  | Q2 = 1.00 (referent)                                                        |                   |                   |
|      |            |        |          |                 |                   |               |                   | Q3 = 0.6-0.9                                                                | Q3 = 0.56 (0.35-0.91)                                                       |                   |                   |
|      |            |        |          |                 |                   |               |                   | Q4 = >1.0                                                                  | Q4 = 0.71 (0.49-1.02)                                                       |                   |                   |

Outcome Measure: Death from ischemic stroke

Cox proportional HR

Multivariate adjusted HR (95% CI) by sport PA, men

- Q1 = 1.34 (0.86-2.08)
- Q2 = 1.00 (referent)
- Q3 = 1.22 (0.66-2.25)
- Q4 = 0.84 (0.45-1.57)

Multivariate adjusted HR (95% CI) by sport PA, women

- Q1 = 1.07 (0.64-1.77)
- Q2 = 1.00 (referent)
- Q3 = 0.62 (0.25-1.58)
- Q4 = 0.73 (0.31-1.70)
Table 13: Studies examining the relationship between physical activity and stroke. (Continued)

| Study | Objective | Population | Methods | Measures | Findings | Notes |
|-------|-----------|------------|---------|----------|----------|-------|
| Paganini-Hill and Barreto 2001 [265] | To identify risk factors and preventative measures for stroke in elderly men and women. | • n = 4,722 men, 8,532 women | Baseline survey in 1981-1982. | Multivariate adjusted RR (95% CI) for total hemorrhagic occlusion by exercise, men | Emphasized role of lifestyle modification in the primary prevention of stroke. | USA Age: 44-101 yr • Characteristics: no previous history of stroke. Residence of a retirement community in Southern California |
| Prospective cohort | | | PA assessment: Questionnaire on amount of hours per day of exercise | G1 = <0.5 • Q1 = 1.00 (referent) G2 = <0.1 G3 = 1+ Multivariate adjusted RR (95% CI) for total hemorrhagic occlusion by exercise, women | | |
| D & B score = 13 | | | | | |
| Pitsavos et al 2004 [266] | To investigate the interaction between PA in men with LVH on stroke mortality. | • n = 489 | | | | USA Age: 40-59 yr • Characteristics: Those without LVH Corfu Cohort (Greece) from Seven Countries Study D & B score = 12 | PA assessment: Questionnaire RR (99% CI) G1 = Sedentary G1 = 1.00 (referent) G2 = Moderate G2 = 0.64 (0.45-0.91) G3 = Hard G3 = 0.72 (0.51-1.02) | Outcome Measure: Incidence of hemorrhagic occlusion strokes up until December 31, 1998. Cox proportional HR | | |
| Study                          | Objective                                                                 | Sample Size | Methodology                                                                 | Results                                                                 |
|-------------------------------|---------------------------------------------------------------------------|-------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------|
| Sacco et al 1998 [267]         | To investigate the association between LTPA and ischemic stroke.          | n = 369     | Case Subjects were recruited during hospitalization, self referral or from monitoring non hospitalized stroke. Controls were eligible if they had never been diagnosed with stroke and were >39 years. | LTPA was related to a decreased occurrence of ischemic stroke in elderly, multiethnic, urban subjects. |
|                               |                                                                           | 678 control | USA                                                                         |                                                                        |
|                               |                                                                           | n = 369     | Case Subjects: Diagnosed with first cerebral infarction after July 1, 1993. Control Subjects: Never diagnosed with stroke |                                                                        |
|                               |                                                                           | 678 control | Case control                                                                |                                                                        |
|                               |                                                                           |             | Multivariate conditional logistic regression Baseline data collection from 1982-1983 in East Boston (MA), New Haven (CT) and Iowa and Washington counties (IA). |                                                                        |
|                               |                                                                           |             | PA assessment: Questionnaire Divided into duration of LTPA (h/wk)             |                                                                        |
|                               |                                                                           |             | • Northern Manhattan Stroke Study                                            |                                                                        |
|                               |                                                                           |             | • Sex: Men and women                                                         |                                                                        |
|                               |                                                                           |             | • Age: > 39 yr                                                               |                                                                        |
|                               |                                                                           |             | • Characteristics: Case Subjects: Diagnosed with first cerebral infarction after July 1, 1993. Control Subjects: Never diagnosed with stroke |                                                                        |
|                               |                                                                           |             | • G1 = 100 (referent)                                                       |                                                                        |
|                               |                                                                           |             | • G2 = 042                                                                  |                                                                        |
|                               |                                                                           |             | • G3 = 035                                                                  |                                                                        |
|                               |                                                                           |             | • G4 = 031                                                                  |                                                                        |
|                               |                                                                           |             | PA assessment: Questionnaire Divided into duration of LTPA (h/wk)             |                                                                        |
|                               |                                                                           |             | • Northern Manhattan Stroke Study                                            |                                                                        |
|                               |                                                                           |             | • Sex: Men and women                                                         |                                                                        |
|                               |                                                                           |             | • Age: ≥ 65 yrs                                                             |                                                                        |
| Simonsick et al 1993 [268]     | To examine the association between recreational PA among physically capable older adults and incidence of selected chronic diseases and mortality over 3 and 6 years. | n = 1,815 | After 3 years Iowa. No consistent relationship between PA and stroke was found after 3 or 6 years across all 3 population cohorts. |                                                                        |
|                               |                                                                           |             |                                                                           |                                                                        |
| Location | Physical Activity Level | OR (95% CI) Stroke and activity level | Analysis Method |
|----------|-------------------------|--------------------------------------|----------------|
| USA      | Characteristics: Physically capable to do heavy work around the house, walk up and down a flight of stairs and walk a half mile without help. | - T1 = 0.22 (0.08-0.61) | Logistic Regression |
| Prospective cohort | D & B score = 12 | - T2 = 1.05 (0.60-1.84) | Prospective cohort |
| New Haven | OR (95% CI) Stroke and activity level | - T3 = 1.00 (Referent) | New Haven |
| East Boston | OR (95% CI) Stroke and activity level | - T1 = 1.05 (0.56-2.12) | East Boston |
| Iowa      | OR (95% CI) Stroke and activity level | - T2 = 1.29 (0.72-2.32) | Iowa |
| New Haven | OR (95% CI) Stroke and activity level | - T3 = 1.00 (Referent) | New Haven |
| East Boston | OR (95% CI) Stroke and activity level | - T1 = 1.21 (0.56-2.61) | East Boston |
Table 13: Studies examining the relationship between physical activity and stroke. *(Continued)*

| Study | To examine whether intracerebral hemorrhage is associated with dynamic or static exercise. | Number of Cases: 331 | Findings not significant after multivariate analysis. |
|-------|------------------------------------------------------------------------------------------|----------------------|------------------------------------------------------|
| Thrift et al 2002 [269] | *n = 662* PA assessment: Interview, divided into 3 groups: frequency of vigorous activity | | |
| | • Sex: Men and women | • G1 = 1.00 (referent) | |
| | • Age: 18-80 yr | • G2 = 0.68 (0.36-1.27) | p = 0.773 |
| | Australia | • G3 = 0.66 (0.39-1.11) | |
| | Case control | G1 = Never | G1 = 1.00 (referent) |
| | | G2 = Rarely | G2 = 0.94 (0.59-1.48), p = 0.773 |
| | | G3 = Once or more per month | G3 = 1.18 (0.57-2.46), p = 0.0650 |
| | D & B score = 14 | | |
| | OPA level | Multivariate OR (95% CI) by OPA level | |
| | G1 = Sedentary | • G1 = 1.00 (referent) | |
| | | G2 = Light to moderate | G2 = 0.94 (0.59-1.48), p = 0.773 |
| | | G3 = Heavy | G3 = 1.18 (0.57-2.46), p = 0.0650 |
| | Outcome Measure: Intracerebral hemorrhage | | |
| | | Multiple logistic regression | |

D & B score, Downs and Black quality score; YR, years; wk, week; CVD, cardiovascular disease; G, groups; PA, physical activity; CHD, coronary heart disease; RR, risk ratio; 95% CI, 95% confidence interval; T, tertile; PF, physical fitness; MET, metabolic equivalent; Q, quartile or quintile; OPA, occupational physical activity; LTPA, leisure-time physical activity; HR, hazard ratio; VPA, vigorous physical activity; LVH, left ventricular hypertrophy.
according to the type of stroke (ischemic or haemorrhagic) [52]. For instance, 12 studies (46%) revealed a dose-response relationship in one or more measures of occupational and/or leisure-time physical activity and the risk for stroke. It is difficult to determine the minimal and optimal physical activity dosage for the prevention of stroke. Brisk walking has been associated with a lower risk of total and ischemic stroke [72]. In the Harvard Alumni study, the risk of stroke was lower at a weekly energy expenditure of 4.2-8.4 MJ/wk (1000-1999 kcal/wk) (RR = 0.76 (95% CI, 0.59 to 0.98)). With expenditures of 8.4-12.6 MJ/wk (2000-2999 kcal/wk) the RR dropped to 0.54 (0.38 to 0.76) [73]. Thus, the recommended daily expenditure of Canada’s physical activity guidelines is sufficient to reduce the risk for stroke. Further research is required to clearly determine the risk reductions at exercise volumes less than 4.2 MJ/wk (1000 kcal/wk).

In summary, the results of these studies (taken as a whole) indicate that occupation- and leisure time-related physical activity are inversely related to the risk for stroke. Both physically active men and women have a lower risk of stroke, and it appears that this benefit may be present for both ischemic and haemorrhagic stroke [74]. The relationship between physical activity and stroke appears to be consistent between men and women. Unfortunately, relatively limited data exists in non-Caucasian populations.

**Recommendation #3**

*For a reduced risk of stroke, it is recommended that individuals should participate in 30 min or more of moderate to vigorous exercise on most days of the week. Brisk walking appears to be protective against the development of stroke. It remains to be determined whether lower volumes of physical activity lead to a reduced risk for stroke.* [Level 3, Grade A]

### Primary Prevention of Hypertension

A total of 6287 citations were identified during the electronic database search (Figure 6). Of these citations, 4054 were identified in MEDLINE, 1360 in EMBASE, 253 in Cochrane, and 620 in the CINAHL/SportDiscus/PsychInfo search. A total of 40 duplicates were found, leaving a total of 6247 unique citations. A total of 6167 articles were excluded after scanning, leaving a total of 80 articles for full review. An additional five articles were found through cross-referencing and the reviewers’ personal files. From these articles 72 were excluded after full review for the following reasons: weak design (n = 4), did not contain three levels of physical activity or not possible to determine dose-response relationship (n = 19), reviews, summaries, meta-analyses (n = 8), not dealing with hypertension (n = 2), only reported on changes in blood pressure (n = 27), clinical population (n = 7), and other (n = 6). Therefore, a total of 12 articles were included in the systematic review of the literature regarding the relationship between physical activity and the primary prevention of hypertension. The majority of the literature examining the dose-response (for at least three levels of physical activity/fitness) involved prospective cohort analyses (83%).

As shown in Table 14, 12 investigations examined the dose-response (i.e., three or more levels) relationship between physical activity and the incidence of hypertension. This involved a total of 112,636 participants, averaging 10,240 subjects per study (range 1,243-41,837).
| Publication Country Study Design Quality Score | Objective | Population | Methods | Outcome | Comments and Conclusions |
|-----------------------------------------------|-----------|------------|---------|---------|--------------------------|
| Rankinen et al 2007 [75]                      | To investigate the contributions of DNA sequence variation in candidate genes, PF and BMI, as well as their interactions to the incidence of hypertension. | n = 629 cases; 605 controls | 10 year follow up | PF showed the strongest association with HTN risk among all subjects as well as sex-specific models. Each 1-MET increment in PF was associated with 19% (12-14%), 16% (9-22%), 32% (17-45%) risk reduction in all subjects, men and women respectively. | PF is a significant predictor of the risk of hypertension. |
| USA Case control                              | All subjects required to have 2 clinic visits at least 2 years apart. D&B score = 13 | Age: Case: 43.3 (9.2) yr Control: 42.7 (8.9) yr | PF assessment: treadmill test (Blake protocol) | When divided into quartiles on the basis of sex specific MET cut-offs, the third and fourth quartiles had a 58% (41-71%) and 63% (47-75%) lower risk of hypertension compared to the 1st quartile. |
| Pereira et al 1999 [76]                       | To examine PA and incident hypertension in men and women. | n = 7,459 | PA Assessment: Questionnaire for leisure, sport and work index, divided into quartiles | White Men | There is an inverse association between PA and incident hypertension in White middle aged men. White men in the highest quartiles of sport and leisure activity had statistically significant reductions in the odds of developing hypertension of 23 and 34% respectively, compared to men in the lower quartiles. |
| USA Prospective cohort                        | All subjects required to have 2 clinic visits at least 2 years apart. D&B score = 12 | Age: 45-65 yr | Leisure Index Model 1 | Q1 = Lowest Q2 | Q1 = 1.00 (referent) Q2 = 0.95 (0.70-1.28) |
| D & B score = 12                              | Characteristics: No history of angina, MI, evidence of MI, angioplasty or other CV surgery or hypertension | Q3 = Highest | Q4 = Highest | Model 1 adjusted for: Age, education, baseline BP and study centre | Q3 = 0.83 (0.63-1.09) Q4 = 0.64 (0.46-0.89) |
Table 14: Studies examining the relationship between physical activity and hypertension. (Continued)

| Study                          | Sample Size          | Follow-up Period | Incidence Rates of Hypertension | Odds Ratios | Trend p |
|--------------------------------|----------------------|------------------|---------------------------------|-------------|---------|
| Haapanen et al 1997 [77]       | n = 732 men; 796 women | 10 year follow up (1980 baseline) | Age-adjusted incidence rates of hypertension | Total energy expenditure High as referent: | Increased EE during LTPA and increased intensity of these activities were associated with reduced risk for incident hypertension (age adjusted) in men but not women. |

Model 2 adjusted for: Covariates in model 1 and smoking, alcohol consumption, parental history of hypertension, energy, sodium, potassium and caffeine intake, BMI, waist to hip ratio, menopausal status and hormone use.

Outcome Measure: Incidence of hypertension as defined as a SBP 140 mmHg and/or a DBP 90 mmHg or use of antihypertensive medications.

Unconditional logistic regression

Orthogonal polynomial coefficients

| Leisure Index Model 2 | Women | Men |
|----------------------|-------|-----|
| Q1 = 1.00 (referent)  |       |     |
| Q2 = 0.99 (0.72-1.35) |       |     |
| Q3 = 0.86 (0.65-1.13) |       |     |
| Q4 = 0.66 (0.47-0.94) |       |     |
| Trend p = 0.01       |       |     |

| Sport Index Model 1   | Women | Men |
|-----------------------|-------|-----|
| Q1 = 1.00 (referent)  |       |     |
| Q2 = 1.26 (0.78-2.05) |       |     |
| Q3 = 1.06 (0.61-1.84) |       |     |
| Q4 = 1.92 (1.12-3.29) |       |     |
| Trend p = 0.04        |       |     |

| Sport Index Model 2   | Women | Men |
|-----------------------|-------|-----|
| Q1 = 1.00 (referent)  |       |     |
| Q2 = 1.23 (0.91-1.66) |       |     |
| Q3 = 0.92 (0.70-1.22) |       |     |
| Q4 = 0.74 (0.54-1.02) |       |     |
| Trend p = 0.02        |       |     |

| Sport Index Model 2   | Women | Men |
|-----------------------|-------|-----|
| Q1 = 1.00 (referent)  |       |     |
| Q2 = 1.26 (0.93-1.71) |       |     |
| Q3 = 0.95 (0.71-1.26) |       |     |
| Q4 = 0.77 (0.55-1.08) |       |     |
| Trend p = 0.05        |       |     |
### Table 14: Studies examining the relationship between physical activity and hypertension. (Continued)

| Country | Sex | Age | Study Overview | Outcome Measure | Risk Estimates |
|---------|-----|-----|----------------|----------------|---------------|
| Finland | Men and women | 35-65 yrs | Prospective cohort | PA assessment: Questionnaire for EE (kcal/wk), divided into tertiles | Male: T1 = Low = 0-1100, T2 = Medium = 1101-1900, T3 = High >1900 |
| D & B score = 11 | | | | | Female: T1 = Low = 0-900, T2 = Medium = 901-1500, T3 = High >1500 |
| | | | | | Trend p = 0.021 |
| USA | Men | 35-74 yrs | Prospective cohort | PA assessment: Questionnaire for PA based on number of stairs ascended, blocks walked and hours per week of light and vigorous sports play, yard work etc. | Risk estimates: RR = 1.35 Trend p = <0.001 |
| D & B score = 12 | | | | | Multivariate estimates: MM 50% of men who engaged in vigorous sports were at 35% greater risk of hypertension than the 41% who did not. RR = 1.35 Trend p = <0.001 |

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**Paffenbarger et al. 1983 [78]**

- **To examine the relationship of student and alumnus PA patterns and other characteristics with incident hypertension.**
- **Study Overview:** PA assessment: Questionnaire for PA, based on number of stairs ascended, blocks walked and hours per week of light and vigorous sports play, yard work etc.
- **Outcome Measure:** Diagnosis of Hypertension by physicians using criteria of SBP > 160 mmHg and/or DBP > 95 mmHg.
- **Risk Estimates:** There was no significantly reduced risk for hypertension in men who climbed 50 plus stairs per day (compared to < 50 stairs), who walked 5 plus blocks per day (compared to < 5 blocks), or who played light sports (compared to those who did not). Contemporary vigorous exercise was inversely related to hypertension risk.

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Table 14: Studies examining the relationship between physical activity and hypertension. (Continued)

| Study | Country | Objective | Design | Sample Size | Methods | Exposure | Outcome | Follow-up | RR (95% CI) | Additional Details |
|-------|---------|-----------|--------|-------------|---------|----------|---------|-----------|-------------|-------------------|
| Paffenbarger et al 1997 [79] | USA | To investigate the quantity and intensity of energy expenditure required to delay hypertension and prevent premature death. | Prospective cohort | n = 6,390 | PA Assessment: Questionnaire for weekly sports play, divided into tertiles | RR (95% CI) | Lack of vigorous sports play independently increased the risk of developing hypertension. |  | - T1 = 1.00 (referent) |  |
| | USA | | D & B score = 12 | | | | | | - T2 = 1.04 (0.77-1.40) |  |
| Hu et al 2004 [81] | Finland | To discover whether regular PA can reduce the risk of hypertension in normal weight and overweight men and women. | Prospective cohort | n = 8,302 men; 9,139 women | PA assessment: Questionnaire for OPA, LTPA, and commuting PA, divided into tertiles | Multivariate adjusted HR (95% CI), men | Regular PA can reduce the risk of hypertension. The protective effect of PA was observed in both sexes regardless of level of obesity. | 11 year follow up | - T1 = 1.00 (referent) |  |
| | Finland | | D & B score = 13 | | | | | | - T2 = 0.63 |  |
| Gu et al 2007 [82] | China | To determine the 8-year incidence of HTN and its risk factors among Chinese adults. | Prospective cohort | n = 10,325 | Baseline Examination in 1991 with 8 year follow up | RR (95% CI), men | Increasing PA has the potential to reduce incidence of hypertension. |  | - G1 = 1.00 (referent) |  |
| | China | | D & B score = 13 | | | | | | - G2 = 1.12 (0.86-1.46) |  |
Table 14: Studies examining the relationship between physical activity and hypertension. (Continued)

| Study | Outcome measure: HTN as defined at SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or current use of antihypertensive medication t-tests, chi squared tests, Cochran-Armitage modeling, Modified Poisson approach | RR (95% CI) Frequency walk time to work (minutes) | Trend p | The duration of walk to work was associated with a decreased risk of hypertension even after adjustment. Regular PA (at least once weekly) was inversely related to the risk of incident hypertension |
|-------|---------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|---------|-------------------------------------------------------------------------------------------------------------------------------------|
| Hayashi et al 1999 [83] | n = 6,017 PA assessment: Questionnaire on health related behaviours and exercise Walk time to work | T1 = 0-10 min T2 = 11-20 min T3 = ≥ 21 min | T1 = 1.00 (referent) T2 = 0.65 (0.47-0.90) T3 = 0.72 (0.59-0.88) | | The rate of rise in both SBP and DBP in each follow-up year decreased with higher EE and that the risk of developing hypertension decreased in a dose dependent manner with higher daily life activity level. Analysis stratified by the presence of or absence of a risk factor showed the negative association of daily life activity with the risk of developing hypertension for men at both low and high risk. This tendency was also observed among men in all 3 categories of normotension. |
| Nakanishi et al 2005 [84] | n = 2,548 7 year follow up Multivariate adjusted RR (95% CI) by PA level only | | Q1 = 1.00 (referent) Q2 = 0.84 (0.72-0.98) | | |
Table 14: Studies examining the relationship between physical activity and hypertension. (Continued)

| Study            | Characteristics | Participants | Unadjusted OR (95% CI) |
|------------------|-----------------|--------------|------------------------|
| D & B score = 12 | Healthy at baseline: No hypertension or CHD. All office workers for a Japanese company | 1,599 | Q1 = 0.75 (0.63-0.88) |
|                  | Q2 = 33.3-369   |              | Q4 = 0.54 (0.45-0.64)  |
|                  | Q3 = 37.0-403   |              | Trend p = < 0.001      |
|                  | Q4 = 40.4       |              | Multivariate adjusted RR (95% CI) by PA level, low normal BP |
|                  |                  |              | Q1 = 1.00 (referent)   |
|                  | 3 categories of normotensive BP |              | Q2 = 0.70 (0.47-1.05)  |
|                  | Low Normal: SBP < 120, DBP < 80 |              | Q3 = 0.55 (0.37-0.83)  |
|                  | Normal: SBP 120-130, DBP 80-85 |              | Q4 = 0.43 (0.28-0.65)  |
|                  | High Normal: SBP 130-139 |              | Trend p = < 0.001      |
|                  | DBP 85-89       |              | Multivariate adjusted RR (95% CI) by PA level, normal BP |
|                  |                  |              | Q1 = 1.00 (referent)   |
|                  |                  |              | Q2 = 0.89 (0.68-1.16)  |
|                  |                  |              | Q3 = 0.69 (0.52-0.91)  |
|                  |                  |              | Q4 = 0.50 (0.37-0.68)  |
|                  |                  |              | Trend p = < 0.001      |
|                  |                  |              | Multivariate adjusted RR (95% CI) by PA level, high normal BP |
|                  |                  |              | Q1 = 1.00 (referent)   |
|                  |                  |              | Q2 = 0.86 (0.69-1.07)  |
|                  |                  |              | Q3 = 0.88 (0.69-1.11)  |
|                  |                  |              | Q4 = 0.60 (0.46-0.78)  |
|                  |                  |              | Trend p = 0.001        |
| Foy et al 2006 [85] | To examine whether insulin resistance is associated with the effect of vigorous or moderate PA on baseline BP. | Baseline examination in 1992-1993 | Participants who meet or exceed current caloric expenditure recommendations for VPA demonstrate significantly less hypertension than do sedentary or underactive individuals.
Table 14: Studies examining the relationship between physical activity and hypertension. (Continued)

| Country | Study Title | Study Design | Participants | Physical Activity Assessment | Outcome Measure | Results |
|---------|-------------|--------------|--------------|------------------------------|-----------------|---------|
| USA     | Folsom et al 1990 [270] | prospective cohort | n = 41,837 | Questionnaire for LTPA | Baseline mailed survey in 1986 | • n = 978 cases | High PA reduced the risk of hypertension only before adjusting for other factors. |
| USA     | Levenstein et al 2001 [271] | prospective cohort | n = 1,031 men, 1,326 women | Questionnaires in 1965 and 1974, cohort followed until 1994 | LTPA predictor of hypertension OR (95% CI) | Risk of HTN was reduced with increases in LTPA in women. |

**Notes:**
- **Sex:** Men and women
- **PA assessment:** VPA over the past year was determined via a 1-year recall of physical activity (kcal/d), divided into 3 groups
- **T1 = 1.00 (referent)**
- **T2 = 0.69 (0.53-0.88)**
- **T3 = 0.57 (0.45-0.74)**
- **Trend p = < 0.001**
- **Adjusted OR (95% CI)**
  - **T1 = 1.00 (referent)**
  - **T2 = 0.82 (0.62-1.09)**
  - **T3 = 0.73 (0.55-0.98)**
  - **Trend p = 0.004**
- **Study Characteristics:** Community dwelling adults
- **Characteristics:** Levenstein et al 2001 [271]
- **Outcome measure:** Incidence of hypertension (defined as those who are taking antihypertensive medications)
- **Logistic regression analysis**
- **Men: 0.98 (0.94-1.02)**
- **Women: 0.90 (0.87-0.94)**
- **PA assessment:** LTPA rated on a scale of 0-16 points and analysed as a continuous variable
- **All Subjects: 0.94 (0.91-0.97)**
- **Outcome measure:** Incidence of hypertension defined as those who are taking antihypertensive medications
- **Men: 0.98 (0.94-1.02)**
- **Women: 0.90 (0.87-0.94)**

**Variables:**
- **D & B score:** Downs and Black quality score; YR, years; PF, physical fitness; BMI, body mass index; MET, metabolic equivalent; PA, physical activity; MI, myocardial infarction; G, groups; Q, quartile or quintile; 95% CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; EE, energy expenditure; kcal/wk, kilocalories per week; T, tertile; RR, risk ratio; HR, hazard ratio; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; OPA, occupational physical activity; LTPA, leisure-time physical activity; BP, blood pressure; kcal/day, kilocalories per day.
There were a total of 11,441 reported cases of hypertension (ranging per study from 118-2,936). The total length of study follow-up averaged 8.6 yr (ranging from 0-16 yr). The articles were published over a 24 yr period ranging from 1983 to 2007.

All studies reviewed demonstrated positive effects of physical activity on the risk for hypertension. Of these studies all (7; 58%) revealed an inverse and graded relationship between hypertension and at least one measure of physical activity or fitness. Across all studies, when comparing the most active/fit group versus the least active/fit group we found an average RR of 0.68 (median = 0.70, range 0.37 to 0.90). Therefore, we observed that physical activity/fitness was associated with an average risk reduction of 32% for hypertension. It should be noted that the study [75] demonstrating the largest risk reduction (63%) evaluated cardiorespiratory fitness directly during a maximal treadmill test. This supports research (as discussed previously) which indicates that physical fitness is a better predictor of chronic disease than physical activity [6,18,19,32,33]. *Taken as a whole, the level of evidence can be classified as Level 3A*. The quality of studies was generally good with a mean Downs and Black score of 11 (median = 11, range = 10-12).

Five studies showed variable results (i.e., no clearly defined dose-response) while generally supporting the inverse relationship between physical activity/fitness and hypertension [76-80]. The variability in the response appears to be the result of different activity/fitness classifications and/or differing subject populations. For instance, some studies revealed that the dose-response relationships differed between genders and/or ethnicities [76,77]. Pereira et al. [76] revealed a 30% reduction in the risk for hypertension in the most active white men. There were graded dose-response relationships between indices of both leisure and sport activities in the white men.

However, there was a lack of association between physical activity and hypertension in white women and African American men and women. Similarly, Haapenen et al. [77] revealed a stronger association in men than in women. However, it should be noted clearly that other studies included in this systematic review evaluated women demonstrating a graded response [81]. Moreover, several studies were conducted with non-Caucasian populations and demonstrated a dose-dependent benefit [82-85]. In fact, data was obtained from varied regions of the world including USA (7), Japan (2), China (1), and Finland (1). Therefore, there is evidence to suggest that the protective effects of physical activity with respect to hypertension are transferable to women and non-Caucasian populations. However, further research is clearly warranted that examines the relationship between physical activity and hypertension in persons of different ethnicities. Moreover, further research is needed to determine the effects of impact of socio-economic status on the observed relationships.

Some studies have indicated that vigorous activity is required to reduce the risk for hypertension. For instance, Paffenbarger [78] revealed that Harvard Alumni who did not engage in vigorous sports play were at a 35% higher risk for developing hypertension. However, there was no difference in the risk for hypertension in men who climbed >50 stairs per day, walked more than 5 city blocks daily, or engaged in light sports only. Similarly, the Paffenbarger and Lee [79] study revealed that moderately vigorous sports play was associated with a lower risk for hypertension, but physical activity (kcal/wk), walking distance (km/wk) and the amount of stairs climbed (floors/wk) were not significant predictors of the risk for hypertension. Collectively, this research group concluded that these findings highlighted the importance of the intensity of effort.

However, it should be noted that many of the studies in our systematic review observed the protective effect with moderate intensity physical activities. Findings from randomized controlled trials have also provided strong evidence that moderate intensity aerobic exercise is sufficient to reduce blood pressure and the risk for hypertension, particularly in at risk individuals [86,87]. The American College of Sports Medicine [88] recently advocated that to prevent hypertension, individuals should exercise on most, and preferably all, days of the week at a moderate intensity, for 30 min or more per day (continuous or accumulated). They also recommended supplementing endurance type activities with resistance exercise. This is supported by research indicating that moderate intensity resistance training can reduce blood pressure [89]. Collectively, this research and our current summary of the dose-response literature indicates that physical activity levels that are of a moderate to vigorous intensity are sufficient to lead to marked reductions in the risk for hypertension.

**Implications**

The impact of hypertension on North American society is enormous. In the US, 31% of non-institutionalized adults over the ages of 20 are currently thought to have hypertension [90]. In Canada, approximately 20% of adults report a diagnosis of hypertension including over 4 million Canadians [91-93]. It has been estimated that a 55 yr old Canadian with normal blood pressure has a greater than 90% chance of developing hypertension before the age of 80 yr [92]. The primary prevention of hypertension is of paramount importance to the attenuation of the risks and costs associated with hypertension and related comorbidities.

There is clear evidence that routine physical activity and/or increased physical fitness reduce greatly the risk...
for hypertension in both normotensive and hypertensive individuals [18,19]. Extensive research has been conducted in the area including numerous prospective trials and various randomized controlled trials. Numerous reviews of the literature (of epidemiological and randomized controlled trials) have supported an inverse relationship between physical activity/fitness and the incidence of hypertension [20,87,89,94-102]. In a recent systematic review of the prospective literature, Katzmarzyk and Janssen (2004) calculated that physically inactive individuals were at a 30% higher risk for hypertension (RR = 1.30 (95% CI = 1.16-1.46)) with a population attributable risk of 13.8% in Canada [20]. Acute bouts of exercise have also been shown to lead to transient changes in blood pressure that are potentially of health benefit [98]. For instance, blood pressure is often reduced after a single exercise session for 12-22 hr [88,103].

It is clear that routine physical activity is effective in both the primary and secondary prevention of hypertension. However, the optimal dosage of physical activity/exercise remains somewhat unclear. Our review of the literature examined critically the relationship between multiple levels of physical activity/fitness and the incidence of hypertension (in individuals without diagnosed hypertension). As identified above this evidence was compelling supporting the protective effects of habitual physical activity in the primary prevention of hypertension.

Recommendation #4
For a reduced risk for hypertension, it is recommended that individuals should participate in 30 min or more of moderate to vigorous exercise on most days of the week. [Level 3, Grade A]

Primary Prevention of Colon and Breast Cancer

Colon Cancer

In our systematic search of the colon cancer literature, a total of 252 citations were identified during the electronic database search (Figure 7). Of these citations, 83 were identified in MEDLINE, 44 in EMBASE, 25 in Cochrane, and 100 in the CINAHL/SportDiscus/PsychInfo search. A total of 15 duplicates were found, leaving a total of 237 unique citations. A total of 164 articles were excluded after screening, leaving a total of 73 articles for full review. From these articles 47 were excluded after full-text review leaving 26 articles for inclusion, and an additional 7 articles were added from the authors’ personal files. The reasons for exclusion included non-experimental/weak design (n = 8), reviews, summaries, meta-analyses (n = 13), editorial/comment (n = 4), did not contain three levels of physical activity or not possible to determine dose-response relationship (n = 9), and other (n = 10). Therefore, a total of 33 articles were included in the systematic review of the literature regarding the relationship between physical activity and the primary prevention of colon cancer.

These studies involved a total of 1,433,103 participants; averaging 43,427 participants per study (range 142-413,044). There were a total of 17,959 reported cases of colon cancer (ranging per study from 93-1,993). The total length of study follow-up for the prospective cohort studies averaged 10.7 yr (ranging from 4-26 yr). The articles were published over a 23 yr period ranging from 1985 to 2008. These studies involved large samples of men and women from regions throughout the world.

A dose-dependency of this relationship was present in the majority of the studies. When comparing the most...
active/fit group versus the least active/fit group we found a mean risk reduction of 30% (median = 32%) across all studies. The most compelling literature was that which evaluated the relationship between moderate-to-vigorous leisure time physical activity. Based on the literature reviewed and the volume of activity assessed it would appear that Canada’s guidelines for physical activity are sufficient to lower the risk for the development of colon cancer in asymptomatic adults. The level of evidence would be considered to be Level 2A. The studies were generally of a higher quality with a mean Downs and Black score of 13 (median = 14, range = 11-15).

It should be noted that there was considerable variability in the findings and conclusions of the studies (Table 15). As discussed later, the literature was further confounded by the fact that the relative risks associated with physical activity were often controlled (through multivariate analyses) for various potential confounding factors, which may actually inappropriately decrease the level of risk reduction associated with physical activity [31]. Moreover, similar to other chronic conditions this literature was limited greatly by the lack of consistent physical activity assessment and description. In many instances, it was difficult to determine the actual absolute volume and/or intensity of activity for each category of comparison. However, despite these limitations the results of these studies (taken as a whole) indicate that both occupation- and leisure time-related physical activity are inversely related to the risk of colon cancer.

**Breast Cancer**

As reviewed eloquently by others, the epidemiological evidence relating physical activity to a decreased incidence of breast cancer is persuasive. A recent systematic review of the literature found that more than 60 observational trials have examined the relationship between physical activity and breast cancer [31]. Previous reviews of the literature have revealed compelling and consistent findings indicating that habitual physical activity is associated with a reduced risk for breast cancer ranging from 20-80% [31,104].

Various investigations have attempted to evaluate the dose-response relationship between physical activity and the incidence of breast cancer (Table 16). Despite the volume of evidence available questions still remain regarding the minimal and optimal volume of exercise required to reduce the risk for breast cancer. As discussed by others [31,104] the findings are as varied as the investigations.

In our systematic search of the literature, a total of 571 citations were identified during the electronic database search (Figure 8). Of these citations, 228 were identified in MEDLINE, 89 in EMBASE, 56 in Cochrane, and 198 in the CINAHL/SportDiscus/PsychInfo search. A total of 46 duplicates were found, leaving a total of 571 unique citations. A total of 411 articles were excluded after scanning, leaving a total of 114 articles for full review. From these articles 77 were excluded after full review leaving 37 articles for inclusion in the systematic review. An additional 6 articles were found through the reviewers’ personal files. The reasons for exclusion included not containing three levels of physical activity or not possible to determine dose-response relationship (n = 1), reviews, summaries, meta-analyses (n = 20), report (n = 5), editorial/comment (n = 21), not a research article (N = 11), not dealing specifically with breast cancer (n = 4), not relevant (n = 5), not primary prevention (n = 3), and other (n = 10). Therefore, a total of 43 articles were included in the systematic review of the literature regarding the relationship between physical activity and the primary prevention of breast cancer.

The data providing dose-response information is all observational in nature, involving both case control and cohort investigations. These studies involved a total of 1,861,707 participants averaging 44,326 subjects per study (range 526-680,000). There were a total of 80,247 reported cases of breast cancer (ranging per study from 109-17,986). The total length of study follow-up for the prospective cohort studies averaged 10.5 yr (ranging from 4-31 yr). The articles were published over a 14 yr period ranging from 1993-2007. These studies involved large samples of men and women from regions throughout the world.

The literature with respect to the primary prevention of breast cancer is as compelling as that found with respect to colon cancer. There is strong evidence that routine physical activity is associated with a reduced risk for the development of breast cancer. However, this literature is also confounded by many shortcomings (similar to other cancer literature) including considerable variability in the statistical analyses employed, the physical activity measurement tools used, and the experimental designs.

The overall risk reduction for breast cancer for individuals that are habitually physically active (at or above Canada’s guidelines for physical activity) is thought to approximate 20-40% [31,105]. In our analyses, we found very similar findings. When comparing the most active group versus the least active group we found a mean (and median) risk reduction of 20% across all studies. The level of evidence would be considered to be Level 2A. Generally, the articles were of high quality with a mean Downs and Black score of 13 (median = 13, range = 9-14).

A dose-dependency of this relationship is also generally present in the majority of the studies. For instance, greater than 50% studies revealed a dose-response
Table 15 Studies examining the relationship between physical activity and colon cancer.

| Publication | Objective | Population | Methods | Outcome | Comments and Conclusions |
|-------------|-----------|------------|---------|---------|--------------------------|
| Hou et al 2004 [272] | To examine the effect of various forms of PA on colon cancer risk, with particular attention to commuting PA | • n = 931 case, 1,552 control | PA assessment: Interview for the following variables | • Number of cases: 931 | Regular frequent PA over a long period of time reduces risk of CC. |
| China | Case control | • Sex: Men and women | OPA (kJ/min) | Multivariate OR (95% CI) by OPA, men: | |
| | | • Age: 30-74 yr | G1 = <8 | • G1 = 1.00 (referent) | p = 0.10 |
| | | • Characteristics: Case: diagnosed with CC. Controls: selected randomly from residents of urban Shanghai. | G2 = 8-12 | • G2 = 1.23 (0.93-1.64) | |
| | | | G3 = >12 | • G3 = 0.81 (0.59-1.19) | |
| | | | Commuting PA (MET hr/wk) | Multivariate OR (95% CI) by OPA, women: | |
| | | | G1 = <48.3 | • G1 = 1.00 (referent) | |
| | | | G2 = 48.3-94.3 | • G2 = 0.96 (0.69-1.61) | |
| | | | G3 = >94.3 | • G3 = 0.64 (0.39-1.02) | p = 0.009 |
| | | | LTPA (MET hr/wk) | Multivariate OR (95% CI) Commuting PA, men: | |
| | | | G1 = < 9.2 | • G1 = 1.00 (referent) | |
| | | | G2 = 9.2-13.6 | • G2 = 1.11 (0.31-1.23) | |
| | | | G3 = >13.6 | • G3 = 0.52 (0.27-0.87) | p = 0.007 |
| | | | Outcome Measure: incident CC | Multivariate OR (95% CI) Commuting PA, women: | |
| | | | | • G1 = 1.00 (referent) | |
| | | | | • G2 = 0.87 (0.42-1.52) | |
| | | | | • G3 = 0.56 (0.21-0.91) | p = 0.007 |
| | | | | Multivariate OR (95% CI) LTPA, men: | |
| | | | | • G1 = 1.00 (referent) | |
| | | | | • G2 = 1.17 (0.13-1.95) | |
| | | | | • G3 = 0.72 (0.41-1.07) | p = 0.06 |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study | Objective | Design | PA assessment | Number of cases | Outcome Measure | Findings |
|-------|-----------|--------|---------------|----------------|----------------|----------|
| Boutron-Ruault et al 2001 [273] | To determine which step of the adenoma-carcinoma pathway was influenced by OPA and recreational PA. | Case control | Questionnaire and classified into 3 groups | 171 | Incident CC | Multivariate OR (95% CI) LTPA, women<br> G1 = 1.00 (referent)<br> G2 = 1.03 (0.41-1.59)<br> G3 = 0.84 (0.13-2.25)<br> p = 0.15 | Multivariate OR (95% CI) LTPA, women<br> G1 = 1.00 (referent)<br> G2 = 1.03 (0.41-1.59)<br> G3 = 0.84 (0.13-2.25)<br> p = 0.15 | A sedentary lifestyle was associated with a high risk of CC. |
| France | Sex: Men and women | Age: 30-79 years | Characteristics: Cases had diagnosis of colorectal adenoma, controls were polyp free. | | | |
| Brownson et al 1991 [274] | To investigate the risks of 16 cancer types in relation to OPA. | Case control | Medical records and classified into 3 groups | 1,838 | Incidence CC | Multivariate OR (95% CI) LTPA<br> G1 = 1.00 (referent)<br> G2 = 0.7 (0.4-1.1)<br> G3 = 0.3 (0.2-0.5)<br> p = <0.0001 | Multivariate OR (95% CI) LTPA<br> G1 = 1.00 (referent)<br> G2 = 0.7 (0.4-1.1)<br> G3 = 0.3 (0.2-0.5)<br> p = <0.0001 | OPA is inversely related to risk of CC. |
| USA | Sex: Men | Age: ≥ 20 yr | Characteristics: White, working | | | |
| Case control | G2 = Moderate - Activity required 20-80% of time | G3 = 1.1 (1.0-1.3) | | | | |
| D & B score = 15 | G3 = High - Activity required >80% of time | $p = 0.05$ |
|------------------|---------------------------------------------|---------|
| Studies examining the relationship between physical activity and colon cancer. | Outcome Measure: CC | Maximum likelihood estimates |
| Calton et al 2006 [275] | n = 31,783 | 11 year follow up |
| USA | Sex: Women | Number of cases: 243 |
| Prospective cohort | Age: 61.1 yr | Results do not support the hypothesis that PA is related to a lower incidence of CC in women. |
| D & B score = 12 | Characteristics: Free from cancer at baseline | Multivariate RR (95% CI), TPA |

- **TPA (MET h/d)**
  - $G1 = 340-48.5$
  - $G2 = 485-54.3$
  - $G3 = 543-59.0$
  - $G4 = 591-64.9$
  - $G5 = 650-98.1$

  - $p = 0.77$

- **MPA (h/d)**
  - $G1 = 0-3.0$
  - $G2 = 3.0-5.0$
  - $G3 = 5.0-6.70$
  - $G4 = 6.71-8.14$
  - $G5 = 8.15-18.0$

  - $p = 0.80$

- **VPA (h/d)**
  - $Q1 = 0$
  - $Q2 = 0.1-1.0$

  - $Q1 = 1.00$ (referent)
  - $Q2 = 1.19$ (0.85-1.66)
  - $Q3 = 0.87$ (0.59-1.29)
  - $Q4 = 1.10$ (0.78-1.55)
  - $Q5 = 0.94$ (0.61-1.46)
  - $Q6 = 1.07$ (0.70-1.62)

  - $p = 0.80$
| Study | Objective | Population | Methodology | Results | Conclusions |
|-------|-----------|------------|-------------|---------|-------------|
| Chao et al. 2004 [276] | To examine how the characteristics of recreational PA affect its association with colon cancer incidence among older. | USA | Sex: Men and women | Multivariate RR (95% CI) by recreational PA, men | Increased amounts of time spent in recreational PA is associated with substantially lower risk of CC. |
| | | Prospective cohort | Age: mean 63 yr | Multivariate RR (95% CI) by recreational PA, men | |
| | | D & B score = 12 | Cancer prevention study II Nutrition Cohort | Multivariate RR (95% CI) by recreational PA, women | |

**Outcome Measure:** Incidence of CC

**Cox proportional HR**

**Q3 = 1.1-2.0**

**Q4 = 2.1-14.0**
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Activities (h/wk) | Men        | p   | Women       | p   | Men and Women | p   |
|------------------|------------|-----|-------------|-----|---------------|-----|
| Q1 = None        | G1 = 1.00  |     | G1 = 1.00   |     | G1 = 1.00     |     |
| Q2 = <4          | G2 = 0.90  | 0.68-1.18 | G2 = 1.02 | 0.71-1.46 | G2 = 0.93 | 0.75-1.16 |
| Q3 = 4-6         | G3 = 0.83  | 0.59-1.16 | G3 = 0.98 | 0.65-1.47 | G3 = 0.88 | 0.68-1.13 |
| Q4 = ≥ 7         | G4 = 0.75  | 0.55-1.01 | G4 = 1.0  | 0.68-1.47 | G4 = 0.84 | 0.66-1.06 |
|                  | G5 = 0.86  | 0.63-1.19 | G5 = 0.89 | 0.68-1.15 | G5 = 0.89 | 0.68-1.15 |
|                  | G6 = 0.60  | 0.41-0.87 | G6 = 0.65 | 0.49-0.87 | G6 = 0.65 | 0.49-0.87 |

Outcome Measure: Incidence of CC

Cox proportional HR

Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39
http://www.ijbnpa.org/content/7/1/39
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study | n | Sex | Age | PA assessment | Characteristics | OPA | OPA LTPA | Multivariate RR (95% CI) by OPA | Multivariate RR (95% CI) by LTPA |
|-------|---|-----|-----|---------------|----------------|-----|---------|--------------------------------|---------------------------------|
| Colbert et al 2001 [277] | 29,133 | Men | 50-69 yr | Interview for OPA and LTPA | Smokers | G1 = 0.61 (0.39-0.98) | G2 = 1.00 (referent) | G3 = 0.60 (0.34-1.04) | G4 = 0.45 (0.26-0.78) |
| USA Prospective cohort | | | | | Alpha- Tocopherol, Beta-Carotene Cancer Prevention Study | OPAs | Sedentary | Sedentary | Sedentary | Sedentary | Sedentary |
| Multivariate RR (95% CI) by walking, women | | | | | | | | | | |
| Q1 = 1.00 (referent) | | | | | | | | | | |
| Q2 = 0.73 (0.53-1.02) | | | | | | | | | | |
| Q3 = 0.95 (0.58-1.47) | | | | | | | | | | |
| Q4 = 0.53 (0.36-0.78) | | | | | | | | | | |
| p = 0.02 | | | | | | | | | | |
| Multivariate RR (95% CI) by walking plus other activities, men | | | | | | | | | | |
| Q1 = 1.00 (referent) | | | | | | | | | | |
| Q2 = 0.73 (0.53-1.02) | | | | | | | | | | |
| Q3 = 0.95 (0.58-1.47) | | | | | | | | | | |
| Q4 = 0.53 (0.36-0.78) | | | | | | | | | | |
| p = 0.02 | | | | | | | | | | |
| Multivariate RR (95% CI) by walking plus other activities, women | | | | | | | | | | |
| Q1 = 1.00 (referent) | | | | | | | | | | |
| Q2 = 0.73 (0.53-1.02) | | | | | | | | | | |
| Q3 = 0.95 (0.58-1.47) | | | | | | | | | | |
| Q4 = 0.53 (0.36-0.78) | | | | | | | | | | |
| p = 0.02 | | | | | | | | | | |
| Colbert et al 2001 [277] | | | | | | | | | | |
| To examine the association between OPA and LTPA and colon cancer in male smokers | | | | | | | | | | |
| USA | | | | | | | | | | |
| D & B score = 13 | | | | | | | | | | |

OPA is protective against CC in a dose-response manner.
### Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study | Objective | Participants | Methods | Results |
|-------|-----------|--------------|---------|---------|
| Dosemeci et al 1993 [278] | To examine associations between PA and cancer sites among workers in Turkey | n = 6,236 (3,486 cases in men and 379 cases in women; 2,127 control men and 244 control women) | PA assessment: Stanford Occupational Classification code system. | Occupational EE is inversely related to risk of CC. |
| Turkey | n = 93 cases for CC | | | |
| Case control | Sex: Men and women | | Sex: Men and women | Multivariate OR (95% CI) by total occupational EE |
| Case control | Age: not indicated | | Age: not indicated | |
| Case control | Characteristics: All hospitalized cases diagnosed with CC. Controls: included subjects diagnosed as non-cancers and cancers which there is no suggestion of an association with PA. | | | |
| | Sitting time at work (h/d) Levels: G1 = <8 | | Sitting time at work (h/d) Levels: | G1 = <8 |
| | G2 = 8-12 | | G2 = 8-12 | G2 = 8-12 |
| | G3 = >12 | | G3 = >12 | G3 = >12 |
| | p = 0.04 | | p = 0.04 | |
| Friedeneich et al 2006 [279] | To investigate the role of PA in the development of colon cancer. | n = 413,044 | 4 year follow-up | Inverse association between PA and risk of CC, particularly for right sided tumours. |
| UK | Sex: Men and women | PA assessment: modified Baedle Questionnaire | Q1 = 1.00 (referent) | |
| Prospective cohort | Age: 35-70 yr | | Q2 = 0.92 (0.76-1.12) | |
| Prospective cohort | Characteristics: Free of cancer at baseline | | Q3 = 0.86 (0.70-1.04) | |
| Prospective cohort | European Prospective Investigation into Nutrition and Cancer (EPIC) | TPA | Q4 = 0.78 (0.59-1.08) | |
| Prospective cohort | Q1 = Inactive | | Q1 = Inactive | Q1 = Inactive |
| Prospective cohort | p = 0.04 | | p = 0.04 | |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study                                    | Design/Population | Activity Measure | Outcome Measure | HR (95% CI) |
|------------------------------------------|-------------------|------------------|-----------------|-------------|
| Giovannucci et al 1995 [280]             | Prospective cohort | Household PA     | Incidence of colon cancer | Q1 = 1.00 (referent) |
| D & B score = 14                         |                   | Q2 = Moderately inactive | Multivariate RR (95% CI), TPA and right sided CC | Q2 = 0.65 (0.43-1.00) |
|                                         |                   | Q3 = Moderately active |                  |             |
|                                         |                   | Q4 = Active        |                  |             |
|                                         |                   | Q1 = <19.5         |                  |             |
|                                         |                   | Q2 = 19.5-396      |                  |             |
|                                         |                   | Q3 = 39.6-739      |                  |             |
|                                         |                   | Q4 = ≥ 739         |                  |             |
| Isomura et al 2006 [281]                 | Case control      | OPA, LTPA, commuting, housework and shopping | Incidence of colorectal cancer | Q1 = 1.00 (referent) |
| D & B score = 12                         |                   |                  | Multivariate OR (95% CI) for all CC by OPA, men | Q2 = 0.9 (0.6-1.4) |
|                                         |                   |                  |                  |             |

Giovannucci et al 1995 [280]: To examine the association between PA and colon cancer. n = 47,723 6 year follow-up Multivariate RR (95% CI) A moderate level of PA was related to a substantially lower risk of CC in this cohort of middle age to elderly men.

USA: Characteristics: Health professionals Age: 40-75 yr PA assessment: Questionnaire

Propective cohort: Health Professionals Follow-up Study Outcome Measure: Incidence of colorectal cancer

Isomura et al 2006 [281]: To examine the relationship of OPA, LTPA, commuting, housework and shopping with colorectal cancer risk. n = 1545 (778 cases, 767 controls) PA assessment: Questionnaire and interview for the following variables Number of cases: 778 Adds to the evidence that PA confers decreased risk of CC, especially of distal CC in both men and women.

Japan: Sex: Men and women OPA, men

Case control: Age: 20-74 yr OPA, men

Cox proportional HR Mantel-Haenszel estimator and logistic regression

D & B score = 12

p = 0.03
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

- Characteristics: Free from cancer at baseline
  - G1 = Sedentary
  - G2 = Moderate
  - G3 = Hard

D & B score = 12

- Fukuoka colorectal cancer study
  - Multivariate OR (95% CI) for proximal OPA, women
    - G1 = Sedentary
      - G1 = 1.00 (referent)
    - G2 = Active
      - G2 = 1.2 (0.6-2.2)
      - G3 = 0.7 (0.4-1.4)
    - G3 = Hard
      - G3 = 0.7 (0.4-1.0)

  - Multivariate OR (95% CI) for proximal OPA, men
    - G1 = Sedentary
      - G1 = 1.00 (referent)
    - G2 = Active
      - G2 = 1.2 (0.6-2.2)
      - G3 = 0.7 (0.4-1.4)
    - G3 = Hard
      - G3 = 0.7 (0.4-1.0)

  - Multivariate OR (95% CI) for distal CC by OPA, men
    - G1 = 0.0
      - G1 = 1.00 (referent)
    - G2 = 0.1-15.9
      - G2 = 0.8 (0.4-1.4)
      - G3 = 0.6 (0.4-1.0)
    - G3 = 16.0
      - G3 = 0.6 (0.4-1.0)

  - Multivariate OR (95% CI) for all CC by non-OPA, men
    - Moderate or hard non-OPA, men (MET hr/wk)
      - G1 = 1.00 (referent)
      - G2 = 0.1-14.9
      - G3 = 15.0
      - G3 = ≥15.0
      - p = 0.22
      - Multivariate OR (95% CI) for proximal CC by non-OPA, men
        - G1 = 1.00 (referent)
        - G2 = 1.2 (0.6-2.1)
        - G3 = 0.9 (0.5-1.7)
      - p = 0.69

  - Multivariate OR (95% CI) for distal CC by non-OPA, men
    - G1 = 1.00 (referent)
    - G2 = 0.8 (0.5-1.3)
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

- G3 = 0.7 (0.4-1.1)
  \( p = 0.19 \)

Multivariate OR (95% CI) for all CC by non-OPA, women
- G1 = 1.00 (referent)
- G2 = 0.9 (0.5-1.5)
- G3 = 0.8 (0.5-1.4)
  \( p = 0.45 \)

Multivariate OR (95% CI) for proximal CC by non-OPA, women
- G1 = 1.00 (referent)
- G2 = 1.5 (0.7-3.3)
- G3 = 1.6 (0.7-3.6)
  \( p = 0.41 \)

Multivariate OR (95% CI) for distal CC by non-OPA, women
- G1 = 1.00 (referent)
- G2 = 0.7 (0.4-1.3)
- G3 = 0.6 (0.3-1.1)
  \( p = 0.12 \)

Multivariate OR (95% CI) for all CC by moderate or hard non-OPA, men
- G1 = 1.00 (referent)
- G2 = 0.8 (0.6-1.2)
- G3 = 0.8 (0.5-1.1)
  \( p = 0.24 \)

Multivariate OR (95% CI) for proximal CC by moderate or hard non-OPA, men
- G1 = 1.00 (referent)
- G2 = 1.1 (0.6-2.1)
- G3 = 1.0 (0.6-1.8)
  \( p = 0.99 \)

Multivariate OR (95% CI) for distal CC by moderate or hard non-OPA, men
- G1 = 1.00 (referent)
- G2 = 0.7 (0.4-1.1)
- G3 = 0.7 (0.4-1.0)
  \( p = 0.12 \)
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study | Objective | Follow-up | Number of cases | Support for hypothesis |
|-------|-----------|-----------|-----------------|------------------------|
| Johnsen et al. 2006 [282] | To investigate the effects of OPA on colon cancer incidence. | 76 year follow-up | Number of cases: 140 women, 157 men | No support for the hypothesis that OPA measured by MET-score may be associated with a lower risk of CC. |

**Multivariate OR (95% CI) for all CC by moderate or hard non-OPA, women**
- G1 = 1.00 (referent)
- G2 = 1.0 (0.6-1.6)
- G3 = 0.8 (0.5-1.4)

\[ p = 0.35 \]

**Multivariate OR (95% CI) for proximal CC by moderate or hard non-OPA, women**
- G1 = 1.00 (referent)
- G2 = 1.3 (0.6-2.5)
- G3 = 1.3 (0.6-2.7)

\[ p = 0.59 \]

**Multivariate OR (95% CI) for distal CC by moderate or hard non-OPA, women**
- G1 = 1.00 (referent)
- G2 = 0.8 (0.5-1.5)
- G3 = 0.5 (0.3-1.1)

\[ p = 0.41 \]
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study              | Purpose                                                                 | n | PA assessment | Number of cases | Outcome Measure          | Findings                                                                 |
|--------------------|-------------------------------------------------------------------------|---|---------------|-----------------|--------------------------|--------------------------------------------------------------------------|
| Larssen et al 2006 | To examine the relationship between PA and colorectal cancer.          | 6,961 | Questionnaire scored from 2-12, divided into quartiles | 108             | Inactivity was not a significant risk factor for advanced colonic neoplasia. |
| Norway             | Sex: Men and women, Age: 50-64, Characteristics: No history of colorectal surgery, radiotherapy, cardiopulmonary disease, anticoagulant therapy, coronary episode |     | Q1 = 2-4      | Q2 = 0.61 (0.32-1.16) | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    | Cross-sectional evaluation within a randomized controlled trial         |     | Q2 = 5        | Q3 = 0.75 (0.45-1.26) | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    | D & B score = 13                                                        |     | Q3 = 6        | Q4 = 0.56 (0.34-0.92) | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    |                                                                        |     | Q4 = 7-12     | p = 0.04         | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    |                                                                        |     | Q4 = 30-59    | p = 0.23         | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    |                                                                        |     | Q4 = 30-59    | p = 0.23         | RR (95% CI) Q1 = 1.00 (referent)                                          |
| Larsson et al 2006 | To investigate the association between PA and colorectal cancer.        | 45,906 | Questionnaire for the following variables | 309 (133 proximal, 138 distal) | Results support a role of PA in reducing the risk of CC                   |
| Sweden             | Sex: Men, Age: 45-79 yr                                                 |     |               |                 | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    | Characteristics: Free of cancer at baseline                            |     |               |                 | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    | Prospective cohort                                                     |     |               |                 | RR (95% CI) Q1 = 1.00 (referent)                                          |
|                    | LTPA (min/day)                                                         |     |               |                 | RR (95% CI) Q1 = 1.00 (referent)                                          |
| D & B score = 14   |                                                                        |     |               |                 | RR (95% CI) Q1 = 1.00 (referent)                                          |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Outcome Measure | Incidence of Proximal CC (h/day) | Multivariate HR (95% CI) for distal CC by LTPA | Cox proportional HR for proximal CC by home/housework PA |
|-----------------|----------------------------------|-----------------------------------------------|--------------------------------------------------------|
| Q4 = ≥ 60       | Multivariate HR (95% CI) by home/housework PA |                                   |                                                        |
| Home/housework PA (h/day) | • Q1 = 1.00 (referent) | • Q1 = 1.00 (referent) | • G1 = 1.00 (referent) |
| Q1 = none       | • Q2 = 0.75 (0.58-0.97) | • Q2 = 0.51 (0.28-0.93) | • G2 = 0.78 (0.53-1.14) |
| Q2 = <1         | • Q3 = 0.75 (0.58-0.97) | • Q3 = 0.50 (0.29-0.87) | • G3 = 0.50 (0.29-0.89) |
| Q3 = 1-2        | • Q4 = 0.68 (0.48-0.96) | • Q4 = 0.40 (0.22-0.70) | • G3 = 0.50 (0.29-0.89) |
| Q4 = ≥ 3        | p = 0.01                          | p = 0.01                                       | p = 0.02                                               |
| Incidence of Proximal CC (h/day) | • G1 = <1 | • G1 = 1.00 (referent) | • G1 = 1.00 (referent) |
| G1 = <1         | • G2 = 1.07 (0.81-1.42) | • G2 = 1.07 (0.81-1.42) | • G2 = 1.07 (0.81-1.42) |
| G2 = 1-2        | • G3 = 1.08 (0.81-1.46) | • G3 = 1.08 (0.81-1.46) | • G3 = 1.08 (0.81-1.46) |
| G3 = ≥ 3        | p = 0.58                          | p = 0.58                                       | p = 0.58                                               |

Lee and Paffenbarger 1994 [285]

To predict cancer risk using prospective assessments of PA.

- n = 17,607
- Sex: Men
- Age: 30-79 yr
- Number of dropouts: 14%
- Number of cases: 280
- USA
- Characteristics: Healthy at baseline
- Harvard College Alumni
- PA assessment: Questionnaire for PA level (kcal/wk)
- Multivariate RR (95% CI), Model A: PA in 1962/1966 and updated in 1977
- Prospective cohort
- D & B score = 13

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- Multivariate RR (95% CI), Model A: PA in 1962/1966 and updated in 1977
- Prospective cohort
- D & B score = 13

Found a trend, of borderline statistical significance toward decreasing CC risk with increasing PA.
| Study | Methodology | Outcome Measure | Multivariate RR (95% CI) | Data Interpretation |
|-------|-------------|-----------------|--------------------------|---------------------|
| Lee et al. 1997 [286] | Prospective cohort | Incidence of fatal and non-fatal CC | G1 = 1.00 (referent), G2 = 0.75 (0.42-1.35), G3 = 0.94 (0.54-1.64), p = 0.76 | Does not support the hypothesis that PA is related inversely to risk of developing CC. |
| USA Physicians Health Study | Prospective cohort | Frequency of PA at baseline | G1 = 1.00 (referent), G2 = 1.1 (0.7-1.7), G3 = 1.2 (0.8-1.6), G4 = 1.1 (0.7-1.6), p = 0.6 | |

USA: Characteristics Physicians, free of cancer at baseline

D & B score = 15

Outcome Measure: Incidence of fatal and non-fatal CC

Cox proportional HR
| Study                        | Objective                                                                 | Data Description                                                                 | Findings                                                                 |
|------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Lee et al 2007 [287]         | To examine the association between PA and the risk of developing CRC in Japanese men and women. | n = 65,022 6 year follow-up Number of cases: 154 proximal CC, 166 distal CC 6 | PA may prevent CC among Japanese men.                                      |
|                              |                                                                           | Sex: Men and women Age: 40-69 yr                                                |                                                                          |
|                              |                                                                           | Multivariate RR (95% CI) for CC men                                             |                                                                          |
|                              |                                                                           | Q1 = 1.00 (referent)                                                            |                                                                          |
| Japan                        |                                                                           | Q2 = 0.87 (0.61-1.26)                                                           |                                                                          |
|                              |                                                                           | Q3 = 0.62 (0.41-0.95)                                                           |                                                                          |
|                              |                                                                           | Q4 = 0.58 (0.39-0.87)                                                           |                                                                          |
| Prospective cohort           |                                                                           | PA assessment: Questionnaire for PA level (median MET hr/d)                      |                                                                          |
|                              |                                                                           | Q1 = 28.25                                                                      |                                                                          |
|                              |                                                                           | Q2 = 33.25                                                                      |                                                                          |
|                              |                                                                           | Q3 = 35.25                                                                      |                                                                          |
|                              |                                                                           | Q4 = 43.75                                                                      |                                                                          |
|                              |                                                                           | Multivariate RR (95% CI) for proximal CC men                                     |                                                                          |
|                              |                                                                           | Q1 = 1.00 (referent)                                                            |                                                                          |
|                              |                                                                           | Q2 = 0.89 (0.52-1.51)                                                           |                                                                          |
|                              |                                                                           | Q3 = 0.44 (0.22-0.86)                                                           |                                                                          |
|                              |                                                                           | Q4 = 0.29 (0.14-0.60)                                                           |                                                                          |
|                              |                                                                           | p = 0.001                                                                       |                                                                          |
|                              |                                                                           | Multivariate RR (95% CI) for distal CC Men                                       |                                                                          |
|                              |                                                                           | Q1 = 1.00 (referent)                                                            |                                                                          |
|                              |                                                                           | Q2 = 0.92 (0.54-1.54)                                                           |                                                                          |
|                              |                                                                           | Q3 = 0.75 (0.42-1.33)                                                           |                                                                          |
|                              |                                                                           | Q4 = 0.89 (0.53-1.51)                                                           |                                                                          |
|                              |                                                                           | p = 0.685                                                                       |                                                                          |
|                              |                                                                           | PA level and incidence of CC women                                              |                                                                          |
|                              |                                                                           | Q1 = 1.00 (referent)                                                            |                                                                          |
|                              |                                                                           | Q2 = 1.03 (0.65-1.64)                                                           |                                                                          |
|                              |                                                                           | Q3 = 0.91 (0.57-1.47)                                                           |                                                                          |
|                              |                                                                           | Q4 = 0.89 (0.54-1.49)                                                           |                                                                          |
|                              |                                                                           | p = 0.610                                                                       |                                                                          |
|                              |                                                                           | Multivariate RR (95% CI) for proximal CC women                                  |                                                                          |
|                              |                                                                           | Q1 = 1.00 (referent)                                                            |                                                                          |
|                              |                                                                           | Q2 = 1.14 (0.61-2.12)                                                           |                                                                          |
|                              |                                                                           | Q3 = 1.01 (0.53-1.80)                                                           |                                                                          |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study | Population | Method | Data | Results |
|-------|------------|--------|------|---------|
| Longnecker et al 1995 [288] | USA | To examine the relationship between OPA and vigorous LTPA and the risk of cancer of the right colon and rectum. | • n = 242 rectal cancer and 703 controls | Number of cases: 163 The amount of time spent at vigorous LTPA was associated with a decreased risk of cancer of the right colon. |
| | | | PA assessment: Interview for vigorous LTPA and OPA (coded and self-reported), divided into groups: | |
| | | | | • Sec. Men |
| | | | | • Age: ≥ 31 yr |
| | | | | • Characteristics Case: Diagnosed with adenocarcinoma of the right colon or rectum. Controls: Both community and hospital. No history of large bowel cancer. |
| | | | Number of cases: 163 | RR (95% CI) by vigorous LTPA |
| | | | Case control | • G1 = 1.00 (referent) |
| | | | | • G2 = 0.73 (0.23-2.29) |
| | | | Vigorous LTPA (h/wk) | • G3 = 0.47 (0.16-1.36) |
| | | | | • G4 = 0.60 (0.35-1.00) |
| | | | D & B score = 14 | Multivariate OR (95% CI) by vigorous LTPA |
| | | | | • G1 = 1.00 (referent) |
| | | | | • G2 = 0.81 (0.26-2.54) |
| | | | | • G3 = 0.36 (0.11-1.14) |
| | | | | • G4 = 0.57 (0.33-0.97) |
| | | | | • G5 = 0.57 (0.33-0.97) |
| | | | | • G6 = 0.99 (0.30-3.22) |
| | | | | | • G7 = 1.00 (referent) |
| | | | | | • G8 = 0.79 (0.39-1.61) |
| | | | | | • G9 = 0.79 (0.36-1.74) |
| | | | | | • G10 = 0.99 (0.30-3.22) |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study                      | Objective                                                                 | n     | Follow-up | Cases   | Description                                                                 |
|----------------------------|---------------------------------------------------------------------------|-------|-----------|---------|-----------------------------------------------------------------------------|
| Mai et al. 2007 [289]      | To examine in detail the relationship between recreational PA and invasive CC among women. | 120,147 | 7 year    | 395     | Modest inverse association between recreational PA and CC                  |
|                            | Sex: Women                                                                |       |follow-up  |         |                                                                             |
|                            | Age: 22-84 yr                                                             |       |           |         |                                                                             |
|                            | USA                                                                       |       |           |         |                                                                             |
|                            | Characteristics: no prior history of CC                                    |       |           |         |                                                                             |
|                            | PA assessment: Questionnaire                                               |       |           |         |                                                                             |
|                            | RR (95% CI) by MPA over past 3 years                                       |       |           |         |                                                                             |
|                            | G1 = 1.00 (referent)                                                      |       |           |         |                                                                             |
|                            | G2 = 0.95 (0.72-1.24)                                                     |       |           |         |                                                                             |
|                            | G3 = 0.78 (0.62-0.97)                                                     |       |           |         |                                                                             |
|                            | p = 0.02                                                                  |       |           |         |                                                                             |
|                            | D & B score = 15                                                          |       |           |         |                                                                             |
| Martinez et al. 1997 [290]| To examine whether LTPA could significantly influence the risk of CC in women. | 89,448 | 6 year    | 212     | Significant inverse association between LTPA and incidence of CC in women. |
|                            | Sex: Women                                                                |       |follow-up  |         |                                                                             |

Outcome Measure: Diagnosed with CC
Conditional Logistic Regression

Multivariate OR (95% CI) by self-reported lifetime OPA

- G1 = 1.00 (referent)
- G2 = 0.85 (0.41-1.76)
- G3 = 0.68 (0.31-1.52)

p = 0.42
| Study | Characteristics | Age | PA assessment | Multivariate RR (95% CI) for all CC | p |
|-------|-----------------|-----|---------------|-----------------------------------|---|
| USA   | Nurses, free from cancer at baseline | 30-55 yr | Questionnaire for LTPA | G1 = 1.00 (referent) | G1 = <2, G2 = 2-4, G3 = 5-10, G4 = 11-21, G5 = >21 |
|       | Prospective cohort |       |               | G1 = 1.00 (referent) | G2 = 0.71 (0.44-1.15), G3 = 0.78 (0.50-1.20), G4 = 0.67 (0.42-1.07), G5 = 0.54 (0.33-0.90) |
|       | D & B score = 14 |       |               | G1 = 1.00 (referent) | G2 = 0.71 (0.36-1.41), G3 = 0.81 (0.43-1.55), G4 = 0.79 (0.40-1.56), G5 = 0.77 (0.38-1.58) |
|       | n = 59,369 |       |               | G1 = 1.00 (referent) | G2 = 0.84 (0.60-1.19) |

Nilsen et al 2008 [291] To study the separate associations of recreational PA with the incidence of and mortality from cancer in the ascending, transverse, descending and sigmoid segments of the colon.

- Sex: Men and women
- PA assessment: Questionnaire for frequency and duration of recreational PA
- Number of cases: 736
- 17 year follow-up
- Strong inverse associations between recreational PA and risk of cancer morbidity and mortality of the transverse and sigmoid colon but no association for cancer in the ascending and descending colon.
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Frequency of Recreational PA (times per week) | G1 = none | G2 = <1 | G3 = 1 | G4 = 2-3 | G5 = ≥ 4 |
|---------------------------------------------|-----------|---------|--------|---------|---------|
| D & B score = 14                            | p = 0.18  | HR (95% CI) by frequency of recreational PA, women |
|                                             | G1 = 1.00 (referent) | G2 = 0.91 (0.66-1.25) | G3 = 0.79 (0.57-1.09) |
| Duration of recreational PA (min per exercise) | G4 = 0.66 (0.47-0.92) |
|                                             | G1 = 1.00 (referent) | G2 = 1.07 (0.71-1.60) |
|                                             | G3 = 0.80 (0.57-1.12) |
| Intensity of recreational PA                 | G4 = 0.68 (0.48-0.97) |
|                                             | G1 = 1.00 (referent) | G2 = 0.74 (0.50-1.08) |
|                                             | G3 = Moderate/High | G4 = 0.73 (0.53-1.01) |
|                                             | G5 = 0.64 (0.53-1.34) |
| Summary score for recreational PA            | G1 = 1.00 (referent) |
|                                             | G2 = 0.85 (0.59-1.23) |
|                                             | G3 = 0.81 (0.60-1.09) |
|                                             | G4 = 0.73 (0.53-1.01) |
| By subsite-specific (transverse colon, decending colon, sigmoid colon) CC | G5 = 0.64 (0.53-1.34) |

Levels of REC PA:

- Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39
  http://www.ijbnpa.org/content/7/1/39
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Level | Description | HR (95% CI) by intensity of recreational PA, women | p value | HR (95% CI) by summary score for recreational PA, men | p value | HR (95% CI) by summary score for recreational PA, women | p value | HR (95% CI) by total CC and recreational PA, incidence | p value | HR (95% CI) by subsite specific CC and recreational PA, death | p value | HR (95% CI) for transverse CC incidence and recreational PA | p value |
|-------|-------------|--------------------------------------------------|---------|--------------------------------------------------|---------|--------------------------------------------------|---------|--------------------------------------------------|---------|--------------------------------------------------|---------|--------------------------------------------------|---------|
| G1    | None        | • G1 = 1.00 (referent)                           |         | • G1 = 1.00 (referent)                           |         | • G1 = 1.00 (referent)                           |         | • G1 = 1.00 (referent)                           |         | • G1 = 1.00 (referent)                           |         | • G1 = 1.00 (referent)                           |         |
| G2    | < 1 x/wk    | • G2 = 0.83 (0.62-1.12)                          |         | • G2 = 0.85 (0.62-1.16)                          |         | • G2 = 0.86 (0.64-1.01)                          |         | • G2 = 0.87 (0.70-1.12)                          |         | • G2 = 0.87 (0.64-1.18)                          |         | • G2 = 0.87 (0.64-1.18)                          |         |
| G3    | low score   | • G3 = 0.74 (0.52-1.06)                          |         | • G3 = 0.69 (0.48-0.98)                          |         | • G3 = 0.72 (0.53-0.98)                          |         | • G3 = 0.87 (0.70-1.08)                          |         | • G3 = 0.79 (0.59-1.04)                          |         | • G3 = 0.56 (0.41-0.78)                          |         |
| G4    | high score  |                                             |         |                                             | p = 0.11|                                             |         |                                             |         |                                             |         |                                             |         |
| Outcome Measure: | HR (95% CI) by intensity of recreational PA, women |         |                                             |         |                                             |         |                                             |         |                                             |         |                                             |         |

Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39
http://www.ijbnpa.org/content/7/1/39
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

Schnohr et al 2005 [292] To assess the association between LTPA and incidence of cancer in the general population.  • n = 28,259 (15,043 men, 13,216 women) 14 year follow-up  • Number of cases: 215 men, 108 women  For the most active men, VPA was associated with a non-significant lower risk of CC.

- G1 = Low
- G2 = Moderate
- G3 = Vigorous
- G4 = Free from cancer at baseline

Prospective cohort:  • Age: 20-98 yr
- Characteristics: Free from cancer at baseline

PA assessment: Questionnaire for LTPA
- Multivariate RR (95% CI), men
  - G1 = 1.00 (referent)
  - G2 = 1.08 (0.74-1.57)
  - G3 = 0.72 (0.47-1.11)
  - G4 = 0.29 (0.15-0.56)

p <0.001

D & B score = 13

Multivariate RR (95% CI), women
- G1 = 1.00 (referent)

HR (95% CI) for transverse CC death and recreational PA
- G1 = 1.00 (referent)
- G2 = 0.75 (0.44-1.28)
- G3 = 0.66 (0.41-1.08)
- G4 = 0.44 (0.25-0.78)

p = 0.004

HR (95% CI) for sigmoid CC incidence and recreational PA
- G1 = 1.00 (referent)
- G2 = 0.73 (0.36-1.49)
- G3 = 0.40 (0.190.82)
- G4 = 0.33 (0.14-0.76)

p = 0.002

HR (95% CI) for sigmoid CC death and recreational PA
- G1 = 1.00 (referent)
- G2 = 0.78 (0.45-1.35)
- G3 = 0.51 (0.30-0.87)
- G4 = 0.29 (0.15-0.56)

p <0.001

Denmark

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| Study          | Setting                  | Case-control Study | Outcome Measure                           | Cox proportional HR |
|---------------|--------------------------|--------------------|-------------------------------------------|---------------------|
| Slattery et al 1988 [293] | USA                      | Case control       | Number of cases: 229                      | $G_2 = 1.02$ (0.70-1.50) $G_3 = 0.90$ (0.56-1.46) $p = 0.68$ |
|               |                          | Interview for the following variables | Multivariate OR (95% CI) by TPA, men | Q1 = 1.00 (referent) Q2 = 1.19 (0.67-2.13) |
|               |                          | PA assessment      | Multivariate OR (95% CI) by intense PA, men | Q1 = Low Q2 = 0.83 (0.40-1.75) Q3 = 0.27 (0.11-0.65) Q4 = 0.08 (0.02-0.32) |
|               |                          |                    | Multivariate OR (95% CI) by non-intense PA, men | Q1 = Low Q2 = 1.00 (referent) Q3 = 0.42 (0.24-0.74) Q4 = 0.25 (0.12-0.55) |
|               |                          |                    | Multivariate OR (95% CI) by intense PA, women | G1 = 1.00 (referent) G2 = 0.55 (0.23-1.34) |
|               |                          |                    | Multivariate OR (95% CI) by non-intense PA, women | Q1 = 1.00 (referent) Q2 = 1.40 (0.76-2.67) Q3 = 0.93 (0.51-1.72) Q4 = 1.25 (0.68-2.39) |
|               |                          |                    | PA shows an inverse relationship with incidence of CC. | Q1 = 1.00 (referent) Q2 = 1.09 (0.62-1.90) |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study | Objective | Participants | Methods | Findings |
|-------|-----------|--------------|---------|----------|
| Slattery et al 1997 [294] | To examine the relationship between weekly PA patterns (source, duration and frequency) and CC. | n = 1,993 cases, 2,410 controls | PA Assessment: Interview, adapted CARENA PA history | Number of cases: 1,993 High level of leisure time VPA during the past 20 yrs was associated with a reduced risk of CC in both men and women. The same associations were not observed with leisure time MPA. |
| USA | | | | |
| Case control | Sex: Men and women | Recent leisure time VPA | Multivariate OR (95% CI) by recent leisure time VPA, men |
| | Age: 30-79 yr | Q1 = 1.00 (referent) Q2 = 0.80 (0.64-1.01) Q3 = 0.84 (0.66-1.05) Q4 = 0.69 (0.55-0.87) | |
| | Characteristics: Cases: diagnosed with first primary CC. Controls: no history of CC | Q1 = None Q2 = Low Q3 Q4 = High | |
| The Three Centered Diet, Activity and Lifestyle Colon Cancer Study | Leisure time VPA | Multivariate OR (95% CI) by leisure time VPA, men |
| | Q1 = Low Q2 = 30-60 Q3 = ≥ 60 Q4 = High | Q1 = 1.00 (referent) Q2 = 0.79 (0.61-1.02) Q3 = 0.83 (0.64-1.07) Q4 = 0.86 (0.67-1.10) | |
| | Current PA (min) | Multivariate OR (95% CI) by leisure time VPA, women |
| | LTPA (ranked by time per session) | Q1 = None Q2 = Low - <30 min Q3 = moderate - 30-60 min Q4 = high ->60 min | Q1 = 1.00 (referent) Q2 = 0.75 (0.59-0.95) Q3 = 0.68 (0.53-0.87) Q4 = 0.63 (0.48-0.83) | |
| | Number of activity session per week | | | |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| G1 = None | Multivariate OR (95% CI) by current MPA time per week |
|-----------|-----------------------------------------------------|
| G2 = 1    | - Q1 = 1.00 (referent)                              |
| G3 = 2-4  | - Q2 = 1.00 (0.83-1.21)                              |
| G4 = 5-7  | - Q3 = 0.90 (0.76-1.07)                              |
| G5 = >7   | - Q4 = 0.92 (0.77-1.10)                              |

Outcome Measure: Diagnosed with CC

Unconditional regression models

| G1 = None | Multivariate OR (95% CI) by current VPA time per week |
|-----------|-----------------------------------------------------|
| G2 = 1    | - Q1 = 1.00 (referent)                              |
| G3 = 2-4  | - Q2 = 0.90 (0.73-1.12)                              |
| G4 = 5-7  | - Q3 = 0.89 (0.71-1.10)                              |
| G5 = >7   | - Q4 = 0.83 (0.69-0.98)                              |

Multivariate OR (95% CI) by current MPA time per session

| G1 = None | - Q1 = 1.00 (referent)                              |
| G2 = 1    | - Q2 = 1.20 (0.91-1.59)                              |
| G3 = 2-4  | - Q3 = 1.09 (0.83-1.42)                              |
| G4 = 5-7  | - Q4 = 1.08 (0.82-1.42)                              |

Multivariate OR (95% CI) by leisure time MPA time per session

| G1 = None | - Q1 = 0.86 (0.74-0.99)                              |
| G2 = 1    | - Q2 = 0.76 (0.64-0.90)                              |
| G3 = 2-4  | - Q3 = 0.68 (0.52-0.87)                              |

Multivariate OR (95% CI) by leisure time VPA time per session

| G1 = None | - Q1 = 1.00 (referent)                              |
| G2 = 1    | - Q2 = 0.72 (0.56-0.92)                              |
| G3 = 2-4  | - Q3 = 0.87 (0.73-1.03)                              |
| G4 = 5-7  | - Q5 = 1.00 (0.81-1.25)                              |

Multivariate OR (95% CI) by number of MPA sessions/wk

| G1 = None | - G1 = 1.00 (referent)                              |
| G2 = 1    | - G2 = 1.02 (0.79-1.30)                              |
| G3 = 2-4  | - G3 = 0.86 (0.72-1.02)                              |
| G4 = 5-7  | - G4 = 0.91 (0.81-1.14)                              |
| G5 = >7   | - G5 = 1.02 (0.82-1.27)                              |

Multivariate OR (95% CI) by number of VPA sessions/wk

| G1 = None | - G1 = 1.00 (referent)                              |
| G2 = 1    | - G2 = 0.72 (0.56-0.92)                              |
| G3 = 2-4  | - G3 = 0.87 (0.73-1.03)                              |
| G4 = 5-7  | - G5 = 1.00 (0.81-1.25)                              |
| G5 = >7   | - G5 = 0.84 (0.61-1.15)                              |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Slattery et al 1997 [295] | To determine how physical inactivity interacts with other components of energy balance in determining risk of CC. | • n = 1,993 cases, 2,410 controls | PA Assessment: Interview for lifetime VPA (PA index) | Number of cases: 1,993 | These results support previous findings that physical inactivity is associated with an increased risk of developing CC. |
|-------------------------|----------------------------------------------------------------------------------------------------------------|----------------------------------|-------------------------------------------------|---------------------|---------------------------------------------------------------------------------------------------------------------------------|
| USA                     | • Sex: Men and women | Q1 = 10-12 | Multivariate OR (95% CI), men | • Q1 = 1.00 (referent) | |
|                         | • Age: 30-79 yr | Q2 = 7-9 | • Q2 = 1.60 (1.11-1.75) | |
|                         | • Characteristics: Cases: diagnosed with first primary CC. Controls: no history of CC | Q3 = 4-6 | Multivariate OR (95% CI), women | • Q3 = 1.59 (1.26-2.01) | |
|                         | Case control: The Three Centered Diet, Activity and Lifestyle Colon Cancer Study | Q4 = <4 | Multivariate OR (95% CI), women | • Q4 = 1.68 (1.26-2.12) | |
|                         | D & B score = 14 | | | | |
|                         | | | | | |
| Takahashi et al 2007 [296] | To investigate the association between time spent walking each day and the risk of CRC. | • n = 20,519 men, 21,469 women | 7 year follow-up | Number of cases: 101 | Time spent walking per day was associated with a lower risk of colon cancer in men but not in women. |
| Japan                   | • Sex: Men and women | PA assessment: Questionnaire for time spent walking (h/day) | • Number of dropouts: 3.5% | Multivariate RR (95% CI), men | • G1 = 1.00 (referent) |
|                         | • Age: 40-64 yr | | | | |
|                         | • Characteristics: Free from cancer at baseline | G1 = <0.5 | Multivariate RR (95% CI), men | • G2 = 0.72 (0.43-1.21) | |
|                         | | G2 = 0.5-1 | • G3 = 0.38 (0.22-0.64) | | |
|                         | | G3 = >1 | p < 0.001 | | |
|                         | D & B score = 12 | Outcome Measure: Incidence of CC | Multivariate RR (95% CI), women | | |
|                         | | | • G1 = 1.00 | | |
|                         | | | • G2 = 2.68 (0.94-7.68) | | |
|                         | | | • G3 = 1.79 (0.64-4.96) | | |
|                         | | | p = 0.42 | | |
| Study                          | Objective                                                                 | Participants                                                                 | PA assessment                                                                                      | Multivariate RR (95% CI)                                                                 | Notes                                                                 |
|-------------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Tang et al 1999               | To investigate the association between PA, water intake and risk of CRC in a hospital-based case controlled study. | n = 163 cases, 163 controls                                                   | Interview                                                                                           | G1 = 1.00 (referent) G2 = 2.22 (0.68-7.21) G3 = 0.19 (0.05-0.77)                                    | Found a negative association between LTPA and the risk of CC among men. |
|                              |                                                                           | Case control                                                                 |                                                                                                      |                                                                                                  |                                                                     |
|                              |                                                                           | Number of cases: 163                                                          |                                                                                                      |                                                                                                  |                                                                     |
| Taiwan                       |                                                                           | Sex: Men and women                                                           |                                                                                                      |                                                                                                  |                                                                     |
|                              |                                                                           | Age: 33-80 yr                                                                |                                                                                                      |                                                                                                  |                                                                     |
|                              |                                                                           | Characteristics Cases: Hospital patients diagnosed with colorectal cancer. Controls: Hospital patients in hospital for other reasons, free of CRC. |                                                                                                      |                                                                                                  |                                                                     |
|                              |                                                                           | D & B score = 14                                                             |                                                                                                      |                                                                                                  |                                                                     |
| Tavani et al 1999            | To investigate the relationship between PA and risk of CC in both sexes at different ages. | n = 5,379 (1,225 cases and 4,154 controls)                                     | PA assessment: Questionnaire on activity at work and during leisure time                               | G1 = 1.00 (referent) G2 = 0.89 (0.64-1.23) G3 = 0.72 (0.54-0.97) G4 = 0.54 (0.40-0.74) G5 = 0.47 (0.31-0.71) | The study confirms that OPA is protective against CC.              |
|                              |                                                                           | Sex: Men and women                                                           |                                                                                                      |                                                                                                  |                                                                     |
|                              |                                                                           | Age: 19-74 yr                                                                |                                                                                                      |                                                                                                  |                                                                     |
|                              |                                                                           | D & B score = 13                                                             |                                                                                                      |                                                                                                  |                                                                     |
| Warburton et al 2010          |                                                                            |                                                                             |                                                                                                      |                                                                                                  |                                                                     |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Unconditional multiple Logistic Regression | $p < 0.05$ |
|------------------------------------------|-----------|
| Multivariate OR (95% CI) for CC by OPA at age 30-39 yr, men |
| - G1 = 1.00 (referent) |
| - G2 = 1.01 (0.75-1.37) |
| - G3 = 0.79 (0.59-1.06) |
| - G4 = 0.71 (0.52-0.97) |
| - G5 = 0.64 (0.44-0.93) |
| $p < 0.01$ |
| Multivariate OR (95% CI) for CC by OPA at age 30-39 yr, women |
| - G1 = 1.00 (referent) |
| - G2 = 0.65 (0.46-0.93) |
| - G3 = 0.57 (0.41-0.79) |
| - G4 = 0.49 (0.33-0.72) |
| $p < 0.01$ |
| Multivariate OR (95% CI) for CC by OPA at age 50-59 yr, men |
| - G1 = 1.00 (referent) |
| - G2 = 1.06 (0.78-1.43) |
| - G3 = 0.85 (0.63-1.14) |
| - G4 = 0.68 (0.49-0.95) |
| - G5 = 0.69 (0.45-1.05) |
| $p < 0.01$ |
| Multivariate OR (95% CI) for CC by OPA at age 50-59 yr, women |
| - G1 = 1.00 (referent) |
| - G2 = 0.69 (0.47-1.00) |
| - G3 = 0.68 (0.46-1.00) |
| - G4 = 0.75 (0.47-1.20) |
| $p = > 0.05$ |
| Multivariate OR (95% CI) for ascending CC by OPA at age 30-39 yr No significant associations for men or women |
| Multivariate OR (95% CI) for transverse and descending CC by OPA at age 30-39 yr, men |
| - Q1 = 1.00 (referent) |
| - Q2 = 0.92 (0.51-1.67) |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

- Q3 = 0.76 (0.43-1.37)
- Q4 = 0.46 (0.24-0.87)

\( p < 0.05 \)

Multivariate OR (95% CI) for transverse and descending CC by OPA at age 30-39 yr, women

- Q1 = 1.00 (referent)
- Q2 = 0.51 (0.23-1.10)
- Q3 = 0.39 (0.19-0.80)
- Q4 = 0.29 (0.12-0.71)

\( p < 0.01 \)

Multivariate OR (95% CI) for sigmoid CC by OPA at age 30-39 yr, men

- Q1 = 1.00 (referent)
- Q2 = 1.02 (0.65-1.57)
- Q3 = 0.78 (0.51-1.20)
- Q4 = 0.54 (0.34-0.85)

\( p < 0.01 \)

Multivariate OR (95% CI) for sigmoid CC by OPA at age 30-39 yr, women

- Q1 = 1.00 (referent)
- Q2 = 0.62 (0.36-1.05)
- Q3 = 0.71 (0.44-1.15)
- Q4 = 0.58 (0.32-1.03)

\( p > 0.05 \)

To examine the association between self-reported OPA and LTPA and the subsequent risk of CC.

- \( n = 81,516 \) (53,242 men, 28,274 women)

163 year follow up

Number of cases: 236 men, 99 women

An inverse dose-response relationship between TPA and risk of CC was observed in women. In men this inverse dose-response was found only for those 45 yrs or older at study entry.

Thune et al 1996 [299]

Norway

Prospective cohort

PA assessment:
Questionnaire for TPA (OPA plus recreational PA (combined))

Multivariate RR (95% CI) for total CC, men

- Sex: Men and women
- Age: 20-49 yr
- Characteristics: Free from cancer at baseline

D & B score = 14

\( p = 0.49 \)
| Outcome Measure | Multivariate RR (95% CI) for total CC, women |
|-----------------|--------------------------------------------|
| Incidence of CC | • G1 = 1.00 (referent)                      |
|                 | • G2 = 0.97 (0.33-2.77)                     |
|                 | • G3 = 0.63 (0.39-1.04)                     |
|                 | p = 0.04                                   |
| Cox proportional HR | Multivariate RR (95% CI) for proximal CC, men |
|                 | • G1 = 1.00 (referent)                      |
|                 | • G2 = 1.16 (0.57-2.34)                     |
|                 | • G3 = 0.96 (0.47-1.93)                     |
|                 | p = 0.64                                   |
|                 | Multivariate RR (95% CI) for proximal CC, women |
|                 | • G1 = 1.00 (referent)                      |
|                 | • G2 = 1.22 (0.51-2.94)                     |
|                 | • G3 = 0.62 (0.30-1.28)                     |
|                 | p = 0.10                                   |
|                 | Multivariate RR (95% CI) for distal CC, men |
|                 | • G1 = 1.00 (referent)                      |
|                 | • G2 = 1.29 (0.72-2.33)                     |
|                 | • G3 = 0.99 (0.55-1.80)                     |
|                 | p = 0.53                                   |
|                 | Multivariate RR (95% CI) for distal CC, women |
|                 | • G1 = 1.00 (referent)                      |
|                 | • G2 = 0.84 (0.32-2.17)                     |
|                 | • G3 = 0.61 (0.30-1.23)                     |
|                 | p = 0.15                                   |
|                 | Multivariate RR (95% CI) for total CC, men < 45 yrs at entry |
|                 | • G1 = 1.00 (referent)                      |
|                 | • G2 = 2.02 (0.78-5.21)                     |
|                 | • G3 = 2.23 (0.88-5.66)                     |
|                 | p = 0.13                                   |
|                 | Multivariate RR (95% CI) for total CC, women < 45 yrs at entry |
|                 | • G1 = 1.00 (referent)                      |
|                 | • G2 = 0.96 (0.39-2.40)                     |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study | Population | Methodology | Cases | Controls | OR (95% CI) by number of work years in jobs with sedentary or light work (yr) | OR (95% CI) by proportion of years in jobs with sedentary or light work |
|-------|------------|-------------|-------|----------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Vena et al 1985 [300] | To assess the relationship between lifetime OPA and the risk of CC. | Questionnaire | 210 | 1,431 | • Sex: Men<br>• Age: 30-79 yr<br>• Characteristics: Cases: admitted to hospital. Diagnosis of CC Controls: Admitted to hospital. Diagnosed with non-neoplastic non-digestive diseases | • OR (95% CI) by number of work years in jobs with sedentary or light work (yr)<br>• G1 = None<br>• G2 = 1-20<br>• G3 = >20<br>• OR (95% CI) by proportion of years in jobs with sedentary or light work<br>• G1 = 1.00 (referent)<br>• G2 = 1.53<br>• G3 = 1.97<br>• G4 = 1.49 |
| USA | | | | | • G1 = 1.00 (referent)<br>• G2 = 0.96 (0.39-1.58)<br>• G3 = 0.66 (0.40-1.10) | • OR (95% CI) by proportion of life in jobs with sedentary or light work<br>• G1 = 1.00 (referent)<br>• G2 = 0.99 (0.41-2.39)<br>• G3 = 0.66 (0.33-1.33) |
| Study                  | Objective                                                                 | Case control | D & B score | USA | Sex: Men and women | Number of cases: 87 men, 13 women | Outcome Measure: Diagnosed with CC | Proportion of life in jobs with sedentary or light work |
|-----------------------|---------------------------------------------------------------------------|--------------|-------------|-----|--------------------|-----------------------------------|-----------------------------------|----------------------------------------------------------|
| Vetter et al 1992     | To investigate the influence of OPA on the risk of CC in a developing country. | Case control | 11          | USA | Men and women      | 87                   | CC                                | G1 = 1.00 (referent)                                      |
| White et al 1996      | To assess the relationship between PA and CC among men and women.          | Case control | 14          | USA | Men and women      | 251 men & 194 women          | CC                                | G1 = 1.00 (referent)                                      |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Characteristics | Cases: Diagnosed with CC, no previous history or CC or inflammatory bowel |
|-----------------|--------------------------------------------------------------------------|
|                 | G5 = ≥ 4                                                                 |
|                 | • G5 = 0.57 (0.40-1.11)                                                 |

Moderate-high intensity PA (episodes/wk)

| G1 = 0          | RR (95% CI) by total PA, women  |
|-----------------|---------------------------------|
| G2 = <1         | • G1 = 1.00 (referent)          |
| G3 = 1-<2       | • G2 = 1.17 (0.57-2.40)         |
| G4 = ≥ 2        | • G3 = 1.27 (0.65-2.45)         |
|                 | p = 0.03                        |

Controls: No history of CC or inflammatory bowel

| G1 = 0          | RR (95% CI) by total PA, men and women |
|-----------------|----------------------------------------|
| G2 = <1         | • G1 = 1.00 (referent)                  |
| G3 = ≥ 1        | • G2 = 0.94 (0.60-1.47)                |
| METS/wk         | • G3 = 0.77 (0.50-1.19)                |
| Q1 = 0          | • G4 = 0.57 (0.39-0.85)                |
| Q2 = <7.30      | • G5 = 0.83 (0.57-1.22)                |
| Q3 = 7.30-17.88 | • G6 = 0.66 (0.41-1.05)                |
| Q4 = ≥ 17.88    | p = 0.04                               |
|                 | RR (95% CI) by moderate-high intensity PA, men |
|                 | • G1 = 1.00 (referent)                 |
|                 | • G2 = 0.84 (0.49-1.43)                |
|                 | • Q3 = 0.75 (0.42-1.36)                |
|                 | • Q4 = 0.66 (0.41-1.05)                |
|                 | p = 0.07                               |

Unconditional logistic regression

| G1 = 1.00 (referent) |
|----------------------|
| G2 = 1.07 (0.58-1.97) |
| G3 = 1.00 (0.51-1.98) |
| G4 = 0.74 (0.42-1.29) |
| p = 0.37              |

Outcome Measure: Diagnosed with CC

RR (95% CI) by moderate-high intensity PA, women

| G1 = 1.00 (referent) |
|----------------------|
| G2 = 0.74 (0.42-1.29) |
| p = 0.37              |

RR (95% CI) by moderate-high intensity PA, men and women
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

|   | RR (95% CI) by high intensity PA, men |   | RR (95% CI) by high intensity PA, women |   | RR (95% CI) by high intensity PA, men and women |   | RR (95% CI) by METs/wk, men |   | RR (95% CI) by METs/wk, women |   | RR (95% CI) by METs/wk, women |
|---|--------------------------------------|---|----------------------------------------|---|---------------------------------------------|---|-------------------------------|---|-------------------------------|---|-------------------------------|
|   | Q1 = 1.00 (referent)                 |   | G1 = 1.00 (referent)                   |   | G1 = 1.00 (referent)                        |   | Q1 = 1.00 (referent)           |   | Q1 = 1.00 (referent)           |   | Q1 = 1.00 (referent)           |
|   | Q2 = 0.99 (0.62-1.59)                |   | G2 = 0.85 (0.48-1.52)                 |   | G2 = 0.93 (0.59-1.44)                       |   | Q2 = 0.64 (0.38-1.07)          |   | Q2 = 0.87 (0.51-1.49)          |   | Q2 = 0.73 (0.50-1.06)          |
|   | Q3 = 0.86 (0.55-1.34)                |   | G3 = 0.57 (0.35-0.92)                 |   | G3 = 0.64 (0.45-0.92)                       |   | Q3 = 0.59 (0.37-0.96)          |   | Q3 = 1.20 (0.69-2.08)          |   | Q3 = 0.80 (0.56-1.16)          |
|   | Q4 = 0.70 (0.49-1.00)                |   |                                         |   |                                         |   | Q4 = 0.69 (0.42-1.13)          |   | Q4 = 0.74 (0.41-1.34)          |   | Q4 = 0.73 (0.50-1.06)          |

\( p = 0.05 \)
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study                          | Objective                                                                 | Population Details                                                                 | Methodology                                                                 | Findings                                                                                   |
|-------------------------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| Wolin et al 2007 [303]        | To assess the relationship between PA and risk of CC in women.            | n = 79,295, 16-year follow-up                                                     | Number of cases: 547 (245 distal, 302 proximal) Number of dropouts: 10% | A significant inverse association exists between PA, including moderate intensity, such as walking, and risk of CC in women that is more pronounced for distal tumours. |
|                              | • Sex: Women                                                              | PA assessment: Questionnaire                                                       | USA                                                                        |                                                                                           |
|                              | • Age: 40-65 yr                                                            |                                                                                   | Prospectively cohort study                                                 |                                                                                           |
|                              | • Characteristics: Nurses, no history of CC, ulcerative colitis, and Crohn’s disease |                                                                                   | D & B score = 14                                                           |                                                                                           |
|                              |                                                                           |                                                                                   | Nurses’ Health Study                                                        |                                                                                           |
|                              | Level of PA                                                               | Multivariate RR (95% CI) for distal CC by level of PA                              | G1 = <2                                                                    | G1 = 1.00 (referent)                                                                 |
|                              | G2 = 2.1-4.5                                                              | G2 = 0.93 (0.64-1.36)                                                             | G3 = 4.6-10.3                                                              | G3 = 0.99 (0.68-1.44)                                                                 |
|                              | G4 = 10.4-21.4                                                            | G4 = 0.87 (0.59-1.29)                                                             | G5 = ≥ 21.5                                                                | G5 = 0.54 (0.34-0.84)                                                                 |
|                              | MPA or VPA (hr/wk)                                                        | p = 0.004                                                                         |                                                                                           |                                                                                           |
|                              | G1 = 0                                                                    | Multivariate RR (95% CI) for proximal CC by level of PA not significant p = 0.77  |                                                                                           |                                                                                           |
|                              |                                                                               |                                                                                   | G2 = <1                                                                    |                                                                                           |
|                              | G3 = 1-1.9                                                                |                                                                                   | G4 = ≥ 4                                                                   |                                                                                           |
|                              | G4 = 2-3.9                                                                |                                                                                   | G5 = ≥ 4                                                                   |                                                                                           |
|                              | MPA or VPA (hr/wk)                                                        |                                                                                   | G1 = 1.00 (referent)                                                       | Multivariate RR (95% CI) for all CC by MPA or VPA                                       |
|                              |                                                                               |                                                                                   | G2 = 0.85 (0.64-1.14)                                                      |                                                                                           |
|                              |                                                                               |                                                                                   | G3 = 0.74 (0.53-1.04)                                                      |                                                                                           |
|                              |                                                                               |                                                                                   | G4 = 0.56 (0.33-0.94)                                                      |                                                                                           |
|                              |                                                                               |                                                                                   | p = 0.01                                                                  | Multivariate RR (95% CI) for distal CC by MPA or VPA                                     |
|                              |                                                                               |                                                                                   | G1 = 1.00 (referent)                                                       |                                                                                           |
|                              |                                                                               |                                                                                   | G2 = 1.10 (0.73-1.66)                                                      |                                                                                           |
|                              |                                                                               |                                                                                   | G3 = 0.63 (0.36-1.10)                                                      |                                                                                           |
|                              |                                                                               |                                                                                   | G4 = 0.51 (0.22-1.17)                                                      |                                                                                           |
|                              |                                                                               |                                                                                   | p = 0.04                                                                  | Multivariate RR (95% CI) for proximal CC by MPA or VPA not significant p = 0.12           |
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

| Study                        | Setting     | Case-control design | Characteristics | Outcome Measure | Methodology                        | Findings |
|------------------------------|-------------|---------------------|-----------------|-----------------|-----------------------------------|----------|
| Zhang et al 2006 [304]       | USA         | Case control        | Sex: Men and women | CC              | Multivariate OR (95% CI)          | Found a significant inverse association between reported LTPA and risk of CC with a slightly stronger association for the right colon than the left in both men and women. |
|                              |             |                     | Age: 40-85 yr    |                 | Multivariate OR (95% CI)          |          |
|                              |             |                     | G1 = <1 month    |                 | G1 = 1.00 (referent)              |          |
|                              |             |                     | G2 = 1-4 months  |                 | G2 = 0.7 (0.5-1.1)                |          |
|                              |             |                     | G3 = ≥ 2 weeks   |                 | G3 = 0.6 (0.4-0.8)                |          |
|                              |             |                     |                 |                 | \(p = 0.003\)                     |          |
|                              |             |                     |                 |                 | Multivariate OR (95% CI)          |          |
|                              |             |                     | Outcome Measure: | CC              | CC                                 |          |
|                              |             |                     | G1 = 1.00 (referent) |               | G1 = 1.00 (referent)              |          |
|                              |             |                     | G2 = 0.9 (0.5-1.7)|               | G2 = 0.9 (0.5-1.7)                |          |
|                              |             |                     | G3 = 0.5 (0.3-0.9)|               | G3 = 0.5 (0.3-0.9)                |          |
|                              |             |                     | \(p = 0.02\)     |                 |                                   |          |
|                              |             |                     |                 |                 | Multivariate OR (95% CI)          |          |
|                              |             |                     |                 |                 | Multivariate OR (95% CI)          |          |
|                              |             |                     |                 |                 | Multivariate OR (95% CI)          |          |

Note: LTPA = Leisure Time Physical Activity; OPA = Occupational Physical Activity; CC = Colon Cancer; CI = Confidence Interval; D & B score = Delphi & Bresnahan score; G1 = Group 1 (referent); G2 = Group 2; G3 = Group 3; \(p\) = p-value.
Table 15: Studies examining the relationship between physical activity and colon cancer. (Continued)

- G3 = 0.8 (0.6-1.2)  
  $p = 0.55$
  Multivariate OR (95% CI) by moderate-strenuous LTPA, women
  - G1 = 1.00 (referent)
  - G2 = 0.6 (0.3-1.1)
  - G3 = 0.8 (0.5-1.2)  
  $p = 0.62$
  Multivariate OR (95% CI) by moderate-strenuous LTPA and OPA, OPA-Low
  - G1 = 1.00 ( Referent )
  - G2 = 0.5 (0.3-0.9)
  - G3 = 0.8 (0.5-1.2)  
  $p = 0.41$
  Multivariate OR (95% CI) by moderate-strenuous LTPA and OPA, OPA-Medium
  - G1 = 0.7 (0.5-1.1)
  - G2 = 0.7 (0.4-1.3)
  - G3 = 0.5 (0.3-0.8)  
  $p = 0.04$
  Multivariate OR (95% CI) by moderate-strenuous LTPA and OPA, OPA-High
  - G1 = 0.9 (0.5-1.6)
  - G2 = 0.6 (0.3-1.3)
  - G3 = 0.5 (0.3-0.8)

D & B score, Downs and Black quality score; YR, years; PA, physical activity; OPA, occupational physical activity; kJ/min, kilojoules per minute; G, groups; MET, metabolic equivalent; HR, hazard ratio; RR, risk ratio; OR, odds ratio; 95% CI, confidence interval; LTPA, leisure-time physical activity; CC, colon cancer; TPA, total physical activity; MDA, moderate physical activity; h/d, hours per day; VPA, vigorous physical activity; h/wk, hours per week.
| Publication                  | Objective                                                                 | Population            | Methods                                                                 | Outcome                                                                 | Comments and Conclusions                                                                 |
|-----------------------------|----------------------------------------------------------------------------|-----------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Rockhill et al 1999 [106]   | To examine the effect of PA on the risk for BC                             | n = 121,701           | PA assessment: Self-reported LTPA, grouped into hr/wk                    | 3,137 cases of BC                                                       | Women who engaged in 7 or more hours per week of MVPA had a 20% lower risk of BC. An inverse dose-response relationship existed between PA and BC incidence. |
| USA                         | Sex: Women 16-yr follow-up Characteristics: Free of BC                      |                       | RR (95% CI) for BC and LTPA                                             | RR (95% CI) for BC and LTPA                                             |                                                                                          |
| Prospective cohort          | G1 = <1                                                                     |                       | RR (95% CI) for BC and LTPA                                             | RR (95% CI) for BC and LTPA                                             |                                                                                          |
|                            | G2 = 1.0-1.9                                                                |                       | RR (95% CI) for BC and LTPA                                             | RR (95% CI) for BC and LTPA                                             |                                                                                          |
|                            | G3 = 2.0-3.9                                                                |                       | RR (95% CI) for BC and LTPA                                             | RR (95% CI) for BC and LTPA                                             |                                                                                          |
| D & B score = 13            | G4 = 4.0-69                                                                 |                       | RR (95% CI) for BC and LTPA                                             | RR (95% CI) for BC and LTPA                                             |                                                                                          |
| Sesso et al 1998 [107]      | To examine the association between PA and BC among postmenopausal women    | n = 1,566             | 31-yr follow-up                                                        | 109 cases of BC                                                        | There is an inverse relationship between PA and BC in postmenopausal women.               |
| USA                         | Sex: Women 45.5 Age: 45.5 Characteristics: Free of BC                       |                       | PA assessment: Questionnaire at baseline, divided into tertiles (kcal/wk)| RR (95% CI) for BC and PA                                              |                                                                                          |
| Prospective cohort          | T1 = <500                                                                   |                       | RR (95% CI) for BC and PA                                              | RR (95% CI) for BC and PA                                              |                                                                                          |
|                            | T2 = 500-999                                                                |                       | RR (95% CI) for BC and PA                                              | RR (95% CI) for BC and PA                                              |                                                                                          |
|                            | T3 = ≥ 1,000                                                                |                       | RR (95% CI) for BC and PA                                              | RR (95% CI) for BC and PA                                              |                                                                                          |
| D & B score = 14            |                                                                           |                       | RR (95% CI) for BC and PA                                              | RR (95% CI) for BC and PA                                              |                                                                                          |
| Dosemeci et al 1993 [278]   | To conduct a multiple-site case-control study of 15 cancers to examine associations between PA, SES, and these cancer sites among workers. | n = 2,643 control group | Cases obtained from an oncological treatment center from 1979-1984      | 31 men had BC and 241 women had BC                                     | This study shows the sitting-time index showed an elevated risk of female BC for sedentary jobs without SES adjustment. |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Design | Participants | Case Characteristics | Control Characteristics | Adjusted SES OR (95%CI), men | Adjusted SES OR (95%CI), women |
|-------|--------|--------------|----------------------|-------------------------|-----------------------------|-------------------------------|
| Turkey | Case control | n = 2,127 men and n = 244 women | Sex: Men and women | Controls: pulsed from the same hospital as the cases | G1 = 1.40 (0.60-3.90) | G1 = 1.10 (0.60-2.10) |
| Case | D & B score = 12 | PA assessment: OPA (kJ/min) | G1 = <8 | G2 = 1.10 (0.40-3.10) | G2 = 0.90 (0.50-1.80) |
| Case | D & B score = 12 | | G2 = 8-12 | G3 = 1.00 (referent) | G3 = 1.00 (referent) |
| Case | D & B score = 12 | | G3 = >12 | | |
| Bernstein et al 1994 [305] | Case control | n = 1,090 (545 cases; 545 controls) | Sex: Women | G1 = none | G1 = 1.00 (referent) |
| USA | | Age: ≤ 40 yr | | G2 = 0.95 (0.64-1.41) | G2 = 0.90 (0.50-1.80) |
| USA | | Characteristics: White women matched for age and parity | PA assessment: Questionnaire for overall participation in PA after menarche (h/wk), PA within 10 years after menarche (h/wk), each divided into 5 groups | G3 = 0.65 (0.45-0.96) | G3 = 0.54 (0.35-0.80) |
| USA | | | | G4 = 0.08 (0.04-1.78) | G5 = 0.04 (0.02-0.17) |
| USA | | | | G5 = 0.27 (0.06-1.41) | G5 = 0.27 (0.06-1.41) |

The slightly elevated risk of male BC was based on a small number and disappeared when the risk was adjusted for SES.
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study          | Description                                                                 | Participants | Cases | This study supports an inverse association between PA and BC among black women and among white women. |
|----------------|------------------------------------------------------------------------------|--------------|-------|-----------------------------------------------------------------------------------------------|
| Bernstein et al 2005 [306] | To examine the relationship between BC risk and lifetime and time- or age-specific measures of LTPA among white and black women. | n = 9,187 (4,538 cases; 4,649 control) | 4,538 cases of BC |                                                                                              |
|                | • Sex: Women                                                                 |              |       | Multivariate adjusted OR (95%CI) annual MET h/wk, White participants                           |
|                | • Age: 35-64                                                                 |              |       |                                                                                              |
|                | • Ethnicity: White (including Hispanics) or Black                             |              |       |                                                                                              |
|                | Controls: random-digit dialing methods                                        |              |       |                                                                                              |
### Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Characteristics: Case Group: histologically confirmed cases of invasive BC | Control Group: healthy | PA assessment: Questionnaire for lifetime PA (MET h/wk), divided into 5 groups | Multivariate adjusted OR (95%CI) annual MET h/wk, Black participants |
|-------|--------------------------------------------------------------------------|------------------------|--------------------------------------------------------------------------------|------------------------------------------------------------------|
| Carpenter et al. 1999 [307] | To examine whether lifetime exercise activity is related to BC risk in post-menopausal women. | • n = 2,027 (1,123 case; 904 control) | Cases: diagnosed with primary invasive or in situ BC | 1,123 cases of BC |
| USA | • Sex: Women | | | Strenuous exercise appears to reduce BC risk among post-menopausal women who do not gain sizable amounts of weight during adulthood. |
| | • Age: 55-64 yr | | | 1,123 cases of BC |
| | • Ethnicity: White (including Hispanic) | | | | 1,123 cases of BC |
| Case control | • Characteristics: post-menopausal, English-speaking, born in USA, Canada or Western Europe | | | Multivariate adjusted OR (95%CI) |
| D & B score = 15 | | | | 1,123 cases of BC |
| | | | | 1,123 cases of BC |
| | | | | 1,123 cases of BC |

- **Case control**
  - **D & B score = 13**
    - **Characteristics: Case Group:** histologically confirmed cases of invasive BC
    - **Control Group:** healthy
    - **PA assessment:** Questionnaire for lifetime PA (MET h/wk), divided into 5 groups
    - **Unconditional logistic regression modeling**
      - **G1 = Inactive**
        - **G2 = 0.84 (0.71-0.99)**
        - **G3 = 0.89 (0.75-1.04)**
        - **G4 = 0.82 (0.69-0.97)**
        - **G5 = 0.81 (0.69-0.96)**
      - **G2 = ≤ 2.2**
      - **G3 = 2.3-66**
      - **G4 = 6.7-15.1**
      - **G5 = ≥ 15.2**
      - **Trend p = 0.09**
  - **Case control**
    - **D & B score = 15**
      - **Characteristics: Case Group:** histologically confirmed cases of invasive BC
      - **Control Group:** healthy
      - **PA assessment:** Questionnaire for lifetime PA (MET h/wk), divided into 3 groups
      - **Trend p = 0.01**
      - **G1 = no activity**
        - **G2 = 0.1-17.59**
      - **G3 = 0.55 (0.37-0.83)**
      - **G4 = 0.79 (0.63-0.99)**
      - **G5 = 0.77 (0.62-0.95)**
      - **G2 = 0.08 (0.72-1.07)**
      - **G3 = 0.88 (0.72-1.07)**
      - **G4 = 0.55 (0.37-0.83)**
      - **G5 = 1.00 (referent)**
      - **G2 = 1.11 (0.91-1.35)**
      - **G3 = 0.83 (0.67-1.03)**
      - **G4 = 0.77 (0.62-0.95)**
      - **G5 = 0.77 (0.62-0.95)**
      - **Trend p = 0.003**

Carpenter et al. 1999 [307] To examine whether lifetime exercise activity is related to BC risk in post-menopausal women.
| Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued) |
|------------------------------------------------------------------------------------------------|
| **Carpenter et al 2003 [308]** To examine the effects of obesity and lifetime exercise patterns on post-menopausal BC risk according to family history. | G3 = ≥17.6 |
| PA assessment: Interview for the following PA variables | Conditional logistic regression |
| Sex: Women | 1,883 cases of BC |
| Age: 55-72 | Exercise independent of body size seemed to exert a protective effect primarily among women with a negative family history. |
| Characteristics: Postmenopausal Women | USA |
| Lifetime exercise between menarche and reference date (MET hr/wk) | Case control D & B score = 15 |
| G1 = 0 | G1 = 1.00 (referent) |
| G2 = 0.1-3.74 | G2 = 0.85 (0.71-1.03) |
| G3 = 3.75-8.74 | G3 = 0.87 (0.69-1.10) |
| G4 = 8.75-17.59 | G4 = 1.02 (0.79-1.30) |
| G5 = ≥17.60 | G5 = 0.66 (0.48-0.90) |
| Average exercise activity in 10 years prior to reference date (MET hr/wk) | Trend p = 0.07 |
| G1 = 0 | G1 = 1.00 (referent) |
| G2 = 0.1-6.9 | G2 = 0.93 (0.71-1.22) |
| G3 = 7.0-13.9 | G3 = 0.92 (0.70-1.19) |
| G4 = 14.0-24.4 | G4 = 0.86 (0.65-1.11) |
| G5 = ≥24.5 | G5 = 0.75 (0.55-1.02) |
| Trend p = 0.05 |

| **Chang et al 2006 [309]** To address the independent and combined effects of energy intake, BMI, and PA on BC incidence in women. | n = 27,541 |
| 9.3 year follow-up (median 49 yr) | 764 women developed BC |
| The study suggests that energy intake, BMI and physical inactivity are each independently and positively associated with BC risk. |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Design and Key Characteristics | PA Assessment | Multivariate Adjusted RR (95% CI) | Findings |
|-------|-------------------------------|---------------|-----------------------------------|----------|
| **Prospective cohort** | | | | |
| USA | Sex: Women | | | |
| | Age: 55-74 | | | |
| | Characteristics: no history of any cancer (nonmelanoma skin cancer patients were included in the trial) | | | |
| D & B score = 13 | Prostate, Lung, colorectal, and Ovarian Cancer Screening Trial | Questionnaire for vigorous PA (h/wk), divided into 6 groups | G1 = 0 | |
| | | | G2 = 1 | G1 = 1.00 (referent) |
| | | | G3 = 2 | G2 = 0.89 (0.69-1.15) |
| | | | G4 = 3 | G3 = 0.96 (0.73-1.26) |
| | | | G5 = 4 | G4 = 0.90 (0.70-1.16) |
| | | | G6 = ≥5 | G5 = 0.90 (0.70-1.16) |
| | | | Total cases diagnosed n = 849 | G6 = 0.78 (0.61-0.99) |
| | | | Cox proportional HR Trend p = 0.153 | |
| **Colditz et al 2003 [310]** | Sex: Women | | | |
| | Age: 25-42 | | | |
| | Characteristics: pre-menopausal, no history of any cancer other than nonmelanoma skin cancer | | | |
| n = 110,468 | PA assessment: Self report on 8 activities (walking or hiking, jogging (>10 min/mile), running, Biking, racquet sports, lap swimming, calisthenics/aerobics other aerobic activities) to calculate MET scores (MET h/wk), divided into 5 groups | | | |
| USA | | | G1 = <3 | G1 = 1.00 (referent) |
| | | | G2 = 3-8.9 | G2 = 1.05 (0.82-1.34) |
| | | | G3 = 9-17.9 | G3 = 0.96 (0.75-1.23) |
| | | | G4 = 18-269 | G4 = 1.05 (0.80-1.37) |
| | | | G5 = ≥27 | G5 = 1.07 (0.84-1.36) |
| | | | Cox proportional HR Trend p = 0.69 | |
| **Coogan et al 1997 [311]** | Sex: Women | | | |
| | Age: 25-42 | | | |
| | Characteristics: no history of any cancer other than nonmelanoma skin cancer | | | |
| n = 118,646 (4,863 cases and 6,783 controls) | PA assessment: Telephone interview to estimate OPA, divided into tertiles | | | |
| USA | | | 4,863 cases of BC | There was evidence of a graded inverse relationship between the intensity of work related activity and the incidence of BC. |
| | Sex: Women | | | |
| | T1 = Sedentary | | | |
| | T2 = Low activity | | | |
| | T3 = High activity | | | |
| | | | G1 = 1.00 (referent) | |
| Study | Design | Age at BC | Physical Activity | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
|-------|--------|-----------|-------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Coogan and Aschengrau 1999 [312] | Case control | T1 = Exclusively sedentary | Sex: Women | T1 = 1.00 (referent) | | | | | |
| | | T2 = Exclusively light | Ethnicity: White, Black or Other | T2 = 2.01 (0.70-1.90) | | | | | |
| | | T3 = Exclusively medium or heavy | Characteristics: must have worked outside the home | T3 = 0.90 (0.40-1.90) | | | | | |
| | | 233 cases of BC | USA | There was no evidence that holding a job of medium/heavy activity reduced BC. | | | | | |
| Dallal et al 2007 [313] | Case control | Men | Exclusively sedentary | Q1 = 1.00 (referent) | | | | | |
| | | | Q2 = 0.88 (0.78-0.99) | | | | | | |
| | | | Q3 = 0.88 (0.99-0.88) | | | | | | |
| | | | Q4 = 1.02 (0.88-1.18) | | | | | | |
| | | | Q5 = 0.80 (0.69-0.94) | | | | | | |

**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**
**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Objective | Design | Sample Size | Follow-up | Cases of Incident BC | Results |
|-------|-----------|--------|-------------|-----------|----------------------|---------|
| Dirx et al 2001 [314] | To evaluate the relationship between PA and BC risk with specific emphasis on interaction with other aspects of energy balance. | Case study | n = 62,537 | 7.3 yr follow-up | 1,208 cases of incident BC | The current study supports the hypotheses that PA is related inversely to BC risk in postmenopausal women. |
| | | Netherlands | | | | |
| | | | | | Sex: Women |
| | | | | | Age: 55-69 |
| | | | | | Characteristics: healthy, postmenopausal |
| | | | | | Multivariate adjusted RR (95% CI) for in situ BC |
| | | | | | • Q1 = 1.00 (referent) |
| | | | | | • Q2 = 0.96 (0.79-1.17) |
| | | | | | • Q3 = 0.86 (0.67-1.11) |
| | | | | | • Q4 = 0.95 (0.70-1.30) |
| | | | | | • Q5 = 0.69 (0.48-0.98) |
| | | | | | Trend p = 0.02 |
| | | | | | Exponentially distributed failure time regression models |

**Dirx et al 2001**

- **D & B score = 11**
  - Q1 = <30
  - Q2 = 30-60
  - Q3 = 61-90
  - Q4 = >90
  - • Q1 = 1.00 (referent) |
  - • Q2 = 0.84 (0.67-1.07) |
  - • Q3 = 0.78 (0.60-1.00) |
  - • Q4 = 0.76 (0.58-0.99) |

**Dorn et al 2003** [315]

To examine the associations between LTPA and OPA across the lifespan and pre- and post-menopausal BC.

| Study | Objective | Design | Sample Size | Follow-up | Cases of BC | Results |
|-------|-----------|--------|-------------|-----------|-------------|---------|
| Dorn et al 2003 [315] | To examine the associations between LTPA and OPA across the lifespan and pre- and post-menopausal BC. | Case control | n = 1,550 (740 case; 810 control) | | 740 cases of BC | The study supports the hypothesis that strenuous LTPA is associated with a reduced risk of BC risk in both pre- and post-menopausal women. |
| | | USA | | | | |
| | | | | | Sex: Women |
| | | | | | Age: 40-85 |
| | | | | | Characteristics: Case Group – histologically confirmed incidence of BC. Control Group – healthy |
| | | | | | Controls: randomly selected and frequency matched on age and county with the cases. |
| | | | | | • G1 = 1.00 (referent) |
| | | | | | Multivariate adjusted OR (95% CI), pre-menopausal |

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*Note: Adjusted risk ratios are based on multivariate models controlling for other confounding factors.*
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Participants | Activity assessment | OR (95% CI) | Trend p |
|-------|--------------|---------------------|-------------|---------|
| Drake 2001 [316] | n = 4,520 | Self-report of type, intensity, duration and frequency of walking, jogging, biking, stationary biking, swimming, dancing, racket sports, stretching, participating in other exercise, calisthenics, weight-lifting and treadmill exercises, divided into groups | • G1 = 1.00 (referent) • G2 = 0.85 (0.61-1.19) • G3 = 0.73 (0.45-1.17) • G4 = 0.78 (0.47-1.29) Trend p = 0.19 | 
| Prospective cohort | USA | Aerobic Center Longitudinal Study | Activity type | 
| D & B score = 11 | | | • G1 = Aerobic (job, bike, aerobic dance) • G2 = Moderate (golf, walk) • G3 = Weight training • G4 = >546 Logistic regression | 

- **Aerobic Center Longitudinal Study**
- **150 incident cases of breast cancer**
- **Increased frequency of a specific PA (jogging) was found to have an important protective role in BC incidence.**
| Study | Objective | Sample Size | Case Definition | Control Definition | Findings |
|-------|-----------|-------------|-----------------|-------------------|----------|
| Friedenreich et al. 2001 [317] | To examine the type and dose of PA and the time periods in life when PA may be specifically associated with BC risk. | n = 2,470 (1,233 case; 1,237 control) | Cases: in situ and invasive cases of BC from 1995-1997 | OR (95% CI), pre-menopausal | This study provides evidence that lifetime PA reduces risk of post-menopausal BC. |
| Canada | • Sex: Women | Controls: matched to cases on age and place of residence | Q1 = 1.00 (referent) |
| Case Control | • Age ≤ 80 | • Characteristics: Case Group - Alberta residents, English speaking, capable of completing an in-person interview. Control Group – no history of cancer diagnoses excluding nonmelanoma skin cancer | Q2 = 1.15 (0.78, 1.70) |
| Friedenreich et al. 2001 [318] | To examine the influence of frequency, duration, and intensity of PA on risk of BC and to compare BC risks associated with self-reported versus assigned intensity of PA. | n = 2,470 (1,233 case; 1,237 control) | Cases: in situ and invasive cases of BC | OR (95% CI), pre-menopausal | This study found that moderate-intensity activities were the major contributors to the decrease in BC risk found in this study. |
| Canada | • Sex: Women | Controls: matched to cases on age and place of residence | Q1 = 1.00 (referent) |
| Case Control | • Age ≤ 80 | • Characteristics: Case Group - Alberta residents, English speaking, capable of completing an in-person interview. Control Group – no history of cancer diagnoses excluding nonmelanoma skin cancer | Q2 = 1.15 (0.78, 1.70) |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Characteristics | Case Group | Control Group | PA assessment | OR (95% CI) | Trend p |
|-------|----------------|------------|---------------|---------------|-------------|---------|
| Friedenreich and Rohan 1995 [319] | Sex: Women | n = 902 (451 case; 451 control) | Cases: first diagnosis of BC in 1982 and 1984 | Logistic regression | Adjusted OR (95%CI), pre-menopausal | This study found some evidence (of borderline statistical significance) that recreational PA is associated with decreased risk of BC. |
|     | Age: 20-74 yr | Controls: Randomly selected from the electoral roll, matched on date of birth to each case | | | | |
|     | Characteristics: Australian women | | | | | |
| Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39 | | | | | | http://www.ijbnpa.org/content/7/1/39 |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Year | Design | Cases | Control | Sex | Age | Ethnicity | Activity Assessment | Setting | Group Characteristics | Group | Activity Score | Activity Score (95%CI) | OR (95%CI) | Adjusted OR (95%CI) |
|-------|------|--------|-------|---------|-----|-----|-----------|--------------------|---------|----------------------|-------|---------------|----------------------|-----------|------------------|
| Gammon et al 1998 [320] | To examine the association between LTPA and BC among young women. | • n = 3,173 (1,668 case; 1,505 control) | Cases: women diagnosed with BC between 1990-1992 | 1,668 cases of BC | USA | • Sex: Women | • Age: <45 | Controls: were matched to cases by age group and geographic center | • D & B score = 13 | • Characteristics: Case Group – diagnosed with invasive or in situ BC. Control Group – healthy | • Q1 = 1.00 (referent) | • Q2 = 0.79 (0.63-0.98) | • Q3 = 0.98 (0.79-1.22) | • Q4 = 1.01 (0.81-1.25) | Trend p = 0.42 |
| Gilliland et al 2001 [321] | To investigate the relationship of PA with BC risk in Hispanic and non-Hispanic White women | • n = 1,556 (712 case; 844 control) | Cases: diagnosed with BC between 1992-1994 | 712 cases of BC | USA | • Sex: Women | • Age: between 35-74 at diagnosis | Controls: matched on ethnicity, age and seven health planning districts | • D & B score = 13 | • Ethnicity: Hispanic and non-Hispanic White | • Characteristics: Case Group – diagnosed with in situ or invasive BC and residents of New Mexico at time of diagnosis. Control Group – healthy | • G1 = 1.00 (referent) | • G2 = 1.17 (0.53-2.55) | G1 = 1.00 (referent) | G2 = 1.17 (0.53-2.55) | Trend p < 0.001 | G1 = 1.00 (referent) | G2 = 1.35 (0.64-2.85) |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Design | Country | Population | Case-control | Case Group | Control Group | Results |
|-------|--------|---------|------------|--------------|------------|---------------|---------|
| Hsing et al 1998 [322] | Case control | USA | n = 690 (178 case; 512 control) | Cases: selected from 18,733 decedents included in the 1986 NMFS conducted by the US National Center for Health Statistics (NCHS) | Controls: selected from male decedents dying of causes other than BC PA assessment: Questionnaire (frequency and intensity), divided into groups G1 = Regular G2 = Irregular G3 = Hardly any Logistic regression analysis | Adjusted OR (95%CI), post-menopausal Hispanic: G1 = 1.00 (referent) G2 = 0.74 (0.40-1.36) G3 = 0.37 (0.18-0.75) G4 = 0.38 (0.18-0.77) Trend p = 0.741 Adjusted OR (95%CI), post-menopausal non-Hispanic: G1 = 1.00 (referent) G2 = 0.45 (0.26-0.78) G3 = 0.49 (0.28-0.86) G4 = 0.45 (0.24-0.85) Trend p = 0.019 |
| Hu et al 1997 [323] | To study breast cancer focusing on breast-feeding, body weight, and PA as well as reproductive histories on pre- and post-menopausal Japanese women. | Case control | n = 526 (157 case; 369 control) | Cases: Histologically confirmed cases of BC from 1989-1993 | Reduced risk of pre-menopausal BC was associated with high EE in PA during teenage years, although the trend was not statistically significant. |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Country  | Case control | D & B score | Sex: Women | Characteristics: Case Group – histologically confirmed cases of BC and resident of Gifu prefecture at time of diagnosis. Control Group – no breast disease or hormone-related (ovarian, endometrial and thyroid) cancers | Unadjusted RR (95%CI), pre-menopausal | Unadjusted RR (95%CI), post-menopausal |
|----------|--------------|-------------|------------|-----------------------------------------------------------------------------------------------------------------|--------------------------------------|--------------------------------------|
| Japan    | Case control | 13          | Women      | Controls: individuals who had the screening test for BC during the same period | • G1 = 100 (referent)                   | • G1 = 100 (referent)                   |
|          | D & B score  |             | Age: 26-75 | PA assessment: Questionnaire for TPA (kcal/wk), divided into groups | • G2 = 0.74 (0.38-1.44)                | • G2 = 0.74 (0.38-1.44)                |
|          |              |             |            | G1 = 1.00 (referent)                                                                                           |                                      |                                      |
|          |              |             |            | G2 = 0.74 (0.38-1.44)                                                                                           |                                      |                                      |
| USA      | John et al 2003 | [324]      | Women      | This study supports previous reports of a reduced risk of BC in physically active women. | • G3 = 1.01 (0.54-1.87)                | • G3 = 1.01 (0.54-1.87)                |
|          |              |             | Age: 35-79 | PA assessment: In-person interview for lifetime PA (hr/wk), divided into groups | • G3 = 0.73 (0.42-1.28)                | • G3 = 0.73 (0.42-1.28)                |
|          |              |             | Ethnicity: Latina, African-American and White | Controls: randomly selected according race/ethnicity and age distribution of cases | • G1 = 1.00 (referent) G2 = 0.84 (0.49-1.45) | • G1 = 1.00 (referent) G2 = 0.84 (0.49-1.45) |
|          | Case control | 12          |            | Cases: diagnosed between 1995-1998 | • G3 = 0.73 (0.42-1.28)                | • G3 = 0.73 (0.42-1.28)                |
|          |              |             | Age: 26-75 | Logistic regression models | • G3 = 0.73 (0.42-1.28)                | • G3 = 0.73 (0.42-1.28)                |
|          |              |             |            | G1 = 1.00 (referent)                                                                                           |                                      |                                      |
|          |              |             |            | G2 = 0.84 (0.49-1.45)                                                                                           |                                      |                                      |
|          |              |             |            | G3 = 0.73 (0.42-1.28)                                                                                           |                                      |                                      |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Population | Design | Setting | Case Control | PA Assessment | Number of Cases | OR (95%CI) | Trend p |
|-------|------------|--------|---------|-------------|---------------|----------------|------------|---------|
| Kruk 2007 [325] | Poland | Case control | D & B score = 13 | n = 590 (268 case; 322 control) | PA assessment: Questionnaire for lifetime PA (MET hr/wk/yr), divided into groups | 268 cases of BC | Multivariate adjusted OR (95%CI), pre-menopausal Whites | Logistic regression modeling |
| | | | | | | | | |
| | | | | · Sex: Women | | | | Multivariate adjusted OR (95%CI), post-menopausal Whitess |
| | | | | · Age: 35-75 yr | | | | · G1 = 1.00 (referent) |
| | | | | · Characteristics: Polish women. Cases identified from the Szczecin Regional Cancer Registry. Controls matched on age and place of residence | | | | · G2 = 0.94 (0.64-1.37) |
| | | | | | | | | · G3 = 0.91 (0.60-1.41) |
| | | | | | | | | Trend p = 0.042 |
| | | | | | | | | Multivariate adjusted OR (95%CI), post-menopausal African Americans |
| | | | | · G1 = 1.00 (referent) |
| | | | | · G2 = 0.78 (0.52-1.17) |
| | | | | · G3 = 0.71 (0.47-1.07) |
| | | | | | | | | Logistic regression analysis |
| | | | | · G3 = 0.44 (1.14-1.37) |
| | | | | Trend p = 0.42 |

The results of this study provide evidence of an inverse association between PA and the risk of BC.
### Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study                  | Objective                                                                 | Sample Size | Design                                                                 | Outcome Measures                                                                 | Adjusted OR (95% CI)                                                                 | Additional Findings                                                                 |
|------------------------|---------------------------------------------------------------------------|-------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Kruk 2007 [326]        | To examine the relationship between LTPA and BC risk                      | n = 822     | Case control                                                           | PA assessment: Questionnaire for LTPA (METs), divided into groups                | • G1 = 1.00 (referent)                                                          | The findings provide further support to the hypothesis that increased LTPA throughout life is associated with a decreased risk of BC. |
|                        |                                                                           | (cases n = 257, control n = 565) | D & B score = 13                                                        |                                                                                  |                                                                                  |                                                                                  |
| Poland                 |                                                                           |             |                                                                         |                                                                                  |                                                                                  |                                                                                  |
| Case control           |                                                                           |             |                                                                         |                                                                                  |                                                                                  |                                                                                  |
| D & B score = 13       |                                                                           |             |                                                                         |                                                                                  |                                                                                  |                                                                                  |
| Lahmann et al 2007 [327]| To examine the association of PA with pre- and post-menopausal BC risk.   | n = 218,169 | Prospective cohort                                                     | PA assessment: Interviews and questionnaire for TPA and recreational PA, each divided into quartiles | • Q1 = 1.00 (referent)                                                          | Increasing PA reduces BC risk.                                                   |
|                        |                                                                           |             |                                                                         |                                                                                  |                                                                                  |                                                                                  |
|                        |                                                                           |             |                                                                         |                                                                                  |                                                                                  |                                                                                  |
|                        |                                                                           |             |                                                                         |                                                                                  |                                                                                  |                                                                                  |

**Notes:**
- **D & B score:** Design and Bias score.
- **Trend p:** Trend test for non-linearity.
- **Multivariate adjusted HR (95% CI):** Multivariate adjusted hazard ratio and 95% confidence interval.
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Design | Sex | Age | Characteristics | PA assessment | VPA assessment | RR (95% CI) | Trend p |
|-------|--------|-----|-----|-----------------|---------------|----------------|-------------|---------|
| Lee et al 2001 [328] | Prospective cohort | Women | ≥ 45 yr | Healthy women | PA (kJ/wk), divided into quartiles | VPA (kJ/wk), divided into quintiles | Multivariate adjusted RR (95% CI) | Trend p |
| USA | | | | | Q1 = <840 | Q1 = none | | 0.11 |
| | | | | | Q2 = 840-2519 | Q2 = 1-839 | | 0.03 |
| | | | | | Q3 = 2520-6299 | Q3 = 840-2099 | | |
| | | | | | Q4 = ≥ 6300 | Q4 = 2100-4199 | | |
| | | | | | Q5 = ≥ 4200 | | | |
| | | | | | Proportional hazard regression | | | |
| | | | | | Q1 = 1.00 (referent) | Q1 = 1.00 (referent) | | |
| | | | | | Q2 = 1.04 (0.77-1.40) | Q2 = 0.97 (0.68-1.39) | | |
| | | | | | Q3 = 0.86 (0.64-1.17) | Q3 = 0.78 (0.54-1.12) | | |
| | | | | | Q4 = 0.80 (0.58-1.12) | Q4 = 0.67 (0.44-1.02) | | |
| | | | | | Q5 = 1.00 (referent) | Q5 = 0.98 (0.69-1.40) | | |
| | | | | | Multivariate adjusted RR (95% CI) by PA, all women | Multivariate adjusted RR (95% CI) by VPA, all women | | |
| | | | | | Q1 = 1.00 (referent) | Q1 = 1.00 (referent) | | |
| | | | | | Q2 = 1.05 (0.94-1.17) | Q2 = 1.02 (0.70-1.48) | | |
| | | | | | Q3 = 0.92 (0.83-1.03) | Q3 = 1.11 (0.78-1.58) | | |
| | | | | | Q4 = 0.96 (0.85-1.08) | Q4 = 0.97 (0.66-1.44) | | |
| | | | | | Q5 = 0.80 (0.64-1.12) | Q5 = 0.98 (0.69-1.40) | | |
| | | | | | Trend p = 0.176 | Trend p = 0.03 | | |

The data suggest that PA during middle age and older is not uniformly associated with decreased BC risk. Among post-menopausal women only, higher levels of PA may decrease the risk of BC.
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study                          | Country | Design       | Sex       | Age at diagnosis | Physical Activity Assessment | Adjusted RR (95% CI) | Trend p  |
|-------------------------------|---------|--------------|-----------|------------------|-------------------------------|----------------------|----------|
| Magnusson et al 2005 [329]    | UK      | Case control | Women     | Study 1 = 36 yr, study 2 = 36-45 yr, study 3 = 46-54 yr | PA assessment: Interview for sports participation (h/wk in the following age categories (12-14 yr, 16-18 yr, 20-30 yr, 12-30 yr, around age of diagnosis) | An inverse association between body fatness but not PA at a young age and the risk of BC in pre-menopausal women. |
|                               |         |              |           |                  |                               |                      |          |
|                               |         |              |           |                  |                               |                      |          |

- $Q_3 = 0.91$ (0.57-1.47)
- $Q_4 = 0.93$ (0.57-1.50)
- $Q_5 = 0.76$ (0.47-1.24)
- Trend $p = 0.29$
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Objective | Cohort Details | PA Assessment | OR (95% CI) | Results |
|-------|-----------|----------------|---------------|-------------|---------|
| Malin et al 2005 [330] | To evaluate a pattern of behavioral exposures indicating positive energy balance would be associated with increased BC risk. | China | PA assessment: Questionnaire for PA (MET hr/d/yr), divided into groups | G1 = 0 | The study suggests that promotion of behavioral patterns that optimize energy balance maybe a viable option for BC prevention. |
| | | n = 3,015 (1,459 cases; 1,556 control) | | G2 = 0.1-2.92 | |
| | | | | G3 = >2.92 | |
| | | D & B score = 12 | | | |
| | | Characteristics: Residents of urban Shanghai | | | |
| Margolis et al 2005 [331] | To study the association between PA and incident invasive BC. | Norway/Sweden | PA assessment: Questionnaire for PA using a 5 point scale and for competitive PA (years of participation), each divided into groups | Multivariate adjusted RR (95% CI) by PA level, at enrollment | No evidence of a protective effect of PA on BC risk was found. |
| | | n = 99,504 | | | |
| | | Baseline and 9.1 year follow-up | | | |
| | | 1,166 cases of BC | | | |
| | | D & B score = 13 | | | |
| | | Characteristics: Residents of urban Shanghai | | | |
| | | The Norwegian-Swedish Women's Lifestyle and Health Study | | | |
| | | PA level (5 point scale) | | | |
| | | G1 = None | G1 = 1.00 (referent) | | |
| | | G2 = Low | G2 = 1.35 (0.96- 1.90) | | |
| | | G3 = Moderate | G3 = 1.26 (0.91- 1.74) | | |
| | | G4 = High | G4 = 1.19 (0.91- 1.74) | | |
| | | G5 = Vigorous | G5 = 1.24 (0.85- 1.82) | | |
| | | Competitive PA (years) | Trend p = 0.85 | | |
| | | G1 = None | G1 = 1.00 (referent) | | |
| | | G2 = 0-4 | G2 = 0.93 (0.62- 1.39) | | |
| | | G3 ≥ 5 | G3 = 0.94 (0.65- 1.35) | | |
| | | Multivariate adjusted RR (95% CI) by PA level, at age 14 | Trend p = 0.60 | | |
| | | G1 = 1.00 (referent) | G1 = 1.00 (referent) | | |
| | | G2 = 0.93 (0.62- 1.39) | G2 = 0.93 (0.62- 1.39) | | |
| | | G3 = 0.94 (0.65- 1.35) | G3 = 0.94 (0.65- 1.35) | | |
| | | G4 = 1.07 (0.73- 1.55) | G4 = 1.07 (0.73- 1.55) | | |
| | | G5 = 1.05 (0.72- 1.54) | G5 = 1.05 (0.72- 1.54) | | |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Objective | Study Details | Multivariate adjusted RR (95% CI) by years of competitive PA | Adjusted OR (95% CI) by LTPA during adulthood, all ages and menopausal status | Trend p |
|-------|-----------|---------------|-----------------------------------------------------------|------------------------------------------------------------------------------|---------|
| McTiernan et al 1996 [332] | To investigate the relationship between LTPA and BC. | USA |  - n = 1,029 (cases n = 537, controls n = 492) | - PA assessment: Questionnaire (Minnesota LTPA Questionnaire) for LTPA (hr/wk), divided into groups | The results indicate a weak negative association between PA and risk of BC in middle-aged women. |
|     |           |   |   | G1 = None | G1 = 1.00 (referent) |
|     |           |   |   | G2 = 0.1-1.5 | G2 = 1.1 (0.7-1.6) |
|     |           |   |   | G3 = 1.6-2.5 | G3 = 0.7 (0.4-1.1) |
|     |           |   |   | G4 = 2.6-3.5 | G4 = 0.7 (0.4-1.1) |
|     |           |   |   | G5 = 3.6-5.0 | G5 = 0.6 (0.4-0.9) |
|     |           |   |   | G6 = >5 | G6 = 1.1 (0.7-1.6) |
|     |           |   |   | Calculated categories of EE (total time x intensity code) | Trend p = 0.29 |
|     |           |   |   | G1 = Lowest | Adjusted OR (95% CI) by LTPA during adulthood, aged ≥ 55 yr, post-menopausal only |
|     |           |   |   | G2 = 0.1-1.5 | G2 = 0.8 (0.5-1.3) |
|     |           |   |   | G3 = 1.6-2.5 | G3 = 0.5 (0.3-0.9) |
|     |           |   |   | G4 = 2.6-3.5 | G4 = 0.6 (0.4-1.1) |
|     |           |   |   | G5 = 3.6-5.0 | G5 = 0.4 (0.2-0.8) |
|     |           |   |   | G6 = >5 | G6 = 0.8 (0.5-1.3) |
|     |           |   |   | Trend p = 0.03 |
|     |           |   |   | Adjusted OR (95% CI) by category of total EE in adulthood, all ages and menopausal status | Trend p = 0.25 |
|     |           |   |   | G1 = Lowest | Adjusted OR (95% CI) by total EE in adulthood, all ages and menopausal status |
|     |           |   |   | G2 = 0.1-1.5 | G2 = 1.2 (0.8-2.0) |
|     |           |   |   | G3 = 1.6-2.5 | G3 = 0.9 (0.6-1.3) |
|     |           |   |   | G4 = 2.6-3.5 | G4 = 0.6 (0.4-0.9) |
|     |           |   |   | G5 = 3.6-5.0 | G5 = 0.9 (0.6-1.5) |
|     |           |   |   | G6 = >5 | G6 = 0.9 (0.6-1.4) |

Reference: Warburton et al. International Journal of Behavioral Nutrition and Physical Activity 2010, 7:39 http://www.ijbnpa.org/content/7/1/39
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Objective | Population | Follow-up | Cases of BC | Adjusted OR (95% CI) by category of total EE in adulthood, aged ≥ 55 yr, post-menopausal only | Increased PA is associated with reduced risk for BC in post-menopausal women. |
|-------|-----------|------------|-----------|-------------|------------------------------------------------------------------|---------------------------------------------------------------------------------|
| McTiernan et al 2003 [333] | To examine the association between current and past LTPA and incidence of BC in post-menopausal women. | USA | n = 74,171 | 1,780 | • G1 = 1.00 (referent)  
• G2 = 0.8 (0.4-1.4)  
• G3 = 0.7 (0.4-1.2)  
• G4 = 0.5 (0.3-0.8)  
• G5 = 0.8 (0.5-1.3)  
• G6 = 0.6 (0.4-1.0)  
Trend p = 0.009 | Increased PA is associated with reduced risk for BC in post-menopausal women. |
| - Sex: Women | • Age: 50-79 | Prospective cohort | D & B score = 13 | Baseline and mean follow-up of 4.7 years | Adjusted RR (95% CI) by TPA, |
| - Characteristics: Women from the Women's Health Initiative Observational Study | TPA (MET/hr/wk) | G1 = none | G1 = 1.00 (referent) |
| - Moderate or strenuous PA (hr/wk) | G2 = 0.5-5.0 | • G2 = 0.90 (0.77-1.07) |
| - BMI ≤ 1 | G3 = 5.1-10.0 | • G3 = 0.82 (0.68-0.97) |
| - BMI 11-20 | G4 = 10.1-20.0 | • G4 = 0.78 (0.60-1.00) |
| - BMI 21-30 | G5 = 20.1-40 | • G5 = 0.70 (0.51-0.97) |
| - BMI > 40 | G6 = ≥ 40.0 | • G6 = 0.68 (0.51-0.92) |
| - Trend p = 0.03 | Strenuous PA (hr/wk) | G1 = none | G1 = 1.00 (referent) |
| - BMI ≤ 1 | G2 = ≤ 1 | • G2 = 0.78 (0.57-1.10) |
| - BMI 1-20 | G3 = 1.1-20 | • G3 = 0.70 (0.51-0.97) |
| - BMI 21-30 | G4 = 2.1-30 | • G4 = 0.80 (0.60-1.10) |
| - BMI 31-40 | G5 = 3.1-40 | • G5 = 0.68 (0.51-0.92) |
| - BMI > 40 | G6 = ≥ 41.0 | • G6 = 0.63 (0.43-0.93) |
| - Trend p = 0.03 | Strenuous PA (hr/wk) | G1 = none | G1 = 1.00 (referent) |
| - BMI ≤ 1 | G2 = ≤ 10 | • G1 = referent |
| - BMI 11-20 | G3 = 1.1-20 | • G2 = 0.78 (0.57-1.10) |
| - BMI 21-30 | G4 = 2.1-30 | • G3 = 0.70 (0.51-0.97) |
| - BMI 31-40 | G5 = 3.1-40 | • G4 = 0.80 (0.60-1.10) |
| - BMI > 40 | G6 = ≥ 41.0 | • G5 = 0.68 (0.51-0.92) |
| - Trend p = 0.03 | Strenuous PA (hr/wk) | G1 = none | G1 = 1.00 (referent) |
| - BMI ≤ 1 | G2 = ≤ 10 | • G2 = 0.78 (0.57-1.10) |
| - BMI 11-20 | G3 = 1.1-20 | • G3 = 0.70 (0.51-0.97) |
| - BMI 21-30 | G4 = 2.1-30 | • G4 = 0.80 (0.60-1.10) |
| - BMI 31-40 | G5 = 3.1-40 | • G5 = 0.68 (0.51-0.92) |
| - BMI > 40 | G6 = ≥ 41.0 | • G6 = 0.63 (0.43-0.93) |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Country | Sample Size | Follow-up | BC Cases | Analysis | Baseline and 16.4 year follow-up | BC Cases | Analysis |
|-------|---------|-------------|-----------|----------|----------|----------------------------------|----------|----------|
| Navarro Silvera et al 2006 [334] | Canada | n = 40,318 in analysis (49,613 prior to exclusion) | 1,673 cases of BC from the 40,318 included in the analysis (2,545 cases from total prior to exclusion) | The results of the study suggest that BC risk may vary according to various combinations of the components of energy balance. |
| | | Sex: Women | PA assessment: Questionnaire for VPA (min/d), divided into groups | Adjusted HR (95% CI) by VPA |
| | | | | | | | | |

Adjusted RR (95% CI) by TPA, BMI >28.44

- G1 = 1.00 (referent)
- G2 = 1.10 (0.88-1.50)
- G3 = 0.90 (0.67-1.20)
- G4 = 1.00 (0.79-1.30)
- G5 = 0.89 (0.65-1.20)
- G6 = 0.94 (0.57-1.60)

Trend p = 0.30

Adjusted RR (95% CI) by current moderate or strenuous PA

- G1 = 1.00 (referent)
- G2 = 0.92 (0.78-1.10)
- G3 = 0.91 (0.79-1.10)
- G4 = 0.94 (0.81-1.10)
- G5 = 0.99 (0.83-1.20)
- G6 = 0.91 (0.78-1.10)
- G7 = 0.79 (0.63-0.99)

Trend p = 0.12

Adjusted RR (95% CI) by current strenuous PA

- G1 = 1.00 (referent)
- G2 = 0.94 (0.80-1.10)
- G3 = 0.95 (0.80-1.10)
- G4 = 0.93 (0.78-1.10)
- G5 = 0.91 (0.67-1.20)

Trend p = 0.25

| Group | Cox proportional hazard ratio |
|-------|--------------------------------|
| G3 = 1.1-2.0 | G2 = 0.72 (0.53-0.98) |
| G4 = 2.1-4.0 | G3 = 0.78 (0.57-1.10) |
| G5 = >4.0 | G4 = 0.77 (0.58-1.00) |
|       | G5 = 0.85 (0.64-1.10) |
|       | G6 = 0.78 (0.52-1.20) |

Trend p = 0.74
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Prospective cohort | • Age: 40-59 | G1 = none | • G1 = 1.00 (referent) |
|--------------------|-------------|-----------|------------------------|
| D & B score = 13   | • Characteristics: Canadian women with no history of BC | G2 = Any | • G2 = 0.98 (0.85-1.13) |
|                    | • National Breast Screening Study (NBSS) | G3 = 0-30 | • G3 = 1.06 (0.88-1.27) |
|                    |                        | G4 = 30-60 | • G4 = 0.98 (0.83-1.16) |
|                    |                        | G5 > 60 | • G5 = 0.93 (0.78-1.10) |
|                    |                        | Cox proportional hazard ratio | Trend \(p=0.38\) |
|                    |                        |            | Adjusted HR (95\% CI) by VPA, pre-menopausal |
|                    |                        | G1 = none | • G1 = 1.00 (referent) |
|                    |                        | G2 = 0.91 (0.75-1.10) |
|                    |                        | G3 = 1.02 (0.80-1.31) |
|                    |                        | G4 = 0.88 (0.70-1.11) |
|                    |                        | G5 = 0.87 (0.68-1.09) |
|                    |                        | Trend \(p=0.23\) |
|                    |                        | Adjusted HR (95\% CI) by VPA, post- menopausal |
|                    |                        | G1 = none | • G1 = 1.00 (referent) |
|                    |                        | G2 = 1.06 (0.87-1.30) |
|                    |                        | G3 = 1.08 (0.81-1.42) |
|                    |                        | G4 = 1.11 (0.87-1.41) |
|                    |                        | G5 = 1.00 (0.78-1.29) |
|                    |                        | Trend \(p=0.96\) |

Patel et al 2003 [335] To examine the association between various measures of PA and post-menopausal BC risk

USA

• Sex: Women

Prospective cohort

• Age: 50-74

D & B score = 14

• Characteristics: Postmenopausal women

• The American Cancer Society Cancer Prevention Study II (CPS-II) Nutritional Cohort

G1 = none

G2 = 0.1-69

G3 = 7.0-17.5

G4 = 17.6-31.5

G5 = 31.6-42.0

G6 = >42.0

• Baseline and 5 year follow-up

1,520 cases of breast cancer

The study shows a lower risk of post-menopausal BC is associated with regular PA.

Baseline and 5 year follow-up

PA assessment: Questionnaire for LTPA (METs hr/wk) at various times during life, divided into groups

Adjusted RR (95\% CI), LTPA at study entry

http://www.ijbnpa.org/content/7/1/39
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Design | n | PA assessment | Adjusted OR (95% CI) | Findings |
|-------|--------|---|---------------|----------------------|----------|
| Patel et al 2003 [336] | To evaluate the association between lifetime LTPA and BC risk | n = 1,183 (cases n = 616) n = 567, controls n = 616 | PA assessment: Calendar reporting for lifetime exercise activity (MET h/wk), divided into groups | Adjusted OR (95% CI) | The findings suggest that PA may modify the risk of in situ BC particularly in women without a family history of BC. |
| USA | Case control | D & B score = 14 | • Sex: Women | G1 = None | G1 = 1.00 (referent) |
| | | | • Age: 35-64 | G2 = 0.0-30 | G2 = 0.70 (0.48-1.03) |
| | | | • Characteristics: White and Black women | G3 = 3.0-80 | G3 = 0.65 (0.44-0.96) |
| | | | | G4 = 8.0-16.0 | G4 = 0.61 (0.41-0.92) |
| | | | | G5 = 16.0-32.0 | G5 = 0.63 (0.40-0.98) |
| | | | | G6 = >32.0 | G6 = 0.65 (0.39-1.08) |
| | | | Unconditional logistical regression | Trend p = 0.08 (among active women p = 0.03) |
| Rintala et al 2002 [337] | To obtain an estimate of BC incidence in association with self-rated OPA. | n = 680,000 | PA assessment: Self-reported OPA in 5 classes (1=low, 5=high) | 17,986 cases of BC | The results support the hypothesis that OPA, if high enough, markedly reduced BC risk. |
| | | | | 17,986 cases of BC | |
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Country | Sex: Women | Class 1 = Jobs sitting and light hand tasks | Adjusted RR (95% CI), age 25-39 years |
|---------|------------|--------------------------------------------|-------------------------------------|
| Finland | Age: Women born in 1930-1969 | Class 2 = Handling of heavier items (conveyor belt) | C1+2 = 1.00 (referent) |
|         | Characteristics: Finish women | Class 3 = Jobs involving body motion | C3 = 0.99 (0.85-1.17) |
|         |                           | Class 4 = Jobs involving walking up stairs or long distances, bending and carrying | C4 = 0.90 (0.76-1.07) |
|         |                           | Class 5 = Same as class 4 except heavy tasks were performed for most of the day | C5 = 0.68 (0.51-1.93) |
|         |                           | Poisson regression models | |

Trend
Adjusted RR (95% CI), age 40-54 years
- C1+2 = 1.00 (referent)
- C3 = 1.02 (0.94-1.11)
- C4 = 0.99 (0.91-1.09)
- C5 = 0.84 (0.70-1.00)

Trend
Adjusted RR (95% CI), age ≥ 55 years
- C1+2 = 1.00 (referent)
- C3 = 1.01 (0.96-1.07)
- C4 = 1.04 (0.98-1.11)
- C5 = 0.82 (0.71-0.94)

Rockhill et al 1998 [338] To examine the association between PA at two different times in life and BC risk. n = 372 Baseline and 6 year follow-up 372 cases of BC The findings do not support a link between PA in late adolescence or in the recent past and BC risk among young adult women.

USA

| Prospective cohort | Age: 25-42 | Characteristics: Nurses, The Nurses Health Study | Multivariate adjusted RR (95% CI) |
|--------------------|------------|------------------------------------------------|--------------------------------|
| D & B score = 12   |            |                                                | G1 = 1 (referent) |
|                    |            |                                                | G2 = 1.0 (0.8-1.4) |
|                    |            |                                                | G3 = 1.1 (0.8-1.4) |
|                    |            |                                                | G4 = 1.0 (0.7-1.4) |
|                    |            |                                                | G5 = 1.1 (0.8-1.5) |

Logistic regression
| Study                          | Objective                                                                 | N                           | USA                                                                 | Case control                                                                 |
|-------------------------------|---------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Slattery et al 2007 [339]     | To evaluate the BC risk associated with TPA and VPA at ages 15, 30 and 50 years and the referent year prior to diagnosis/selection. | n = 4,850 Non-Hispanic white: n = 3,128 (cases n = 1,527 controls n = 1,601); Hispanic American Indian: n = 1,722 (cases n = 798, controls n = 924) | PA assessment: Questionnaire for TPA (activity score) and lifetime VPA (h/wk) | 1,527 cases of BC (non-Hispanic white), 798 cases of BC (Hispanic American Indian) |
|                              |                                                                           |                              |                                                                     | The data suggest that PA is important in reducing risk of BC in non-Hispanic white and Hispanic American Indian women. |

- Sex: Women
- Age: <50 yr
- Characteristics: Non-Hispanic white and Hispanic American Indian

| PA assessment | TPA score | OR (95% CI) by TPA score, non-Hispanic white |
|---------------|-----------|---------------------------------------------|
|               | G1        | G1 = 1.00 (referent)                        |
|               | G2        | G2 = 0.78 (0.52-1.17)                       |
|               | G3        | G3 = 0.84 (0.57-1.22)                       |
|               | G4        | G4 = 0.70 (0.44-1.12)                       |

Trend p = 0.26

- Lifetime VPA
- G1 = None
- G2 = <1.0
- G3 = 1.0-2.9
- G4 = ≥ 3.0

Multivariable logistic regression

| OR (95% CI) by lifetime VPA, non-Hispanic white |
|------------------------------------------------|
| G1 = 1.00 (referent)                           |
| G2 = 0.66 (0.36-1.23)                          |
| G3 = 0.73 (0.40-1.34)                          |
| G4 = 0.69 (0.37-1.27)                          |

Trend p = 0.68

- Hispanic American Indian
- G1 = 1.00 (referent)
- G2 = 1.15 (0.67-1.96)
- G3 = 1.19 (0.70-2.03)
- G4 = 1.09 (0.62-1.90)

Trend p = 0.84

| Sprague et al 2007 [340]            | To investigate the relationship between LTPA and strenuous OPA and BC risk. | n = 15,710 (1,689 cases in situ, 6,391 invasive and 7,630 controls) | Adjusted OR (95% CI) for in situ BC by lifetime TPA (hr/wk) | The results provide further evidence that for most women, PA may reduce the risk of invasive BC. |
|-----------------------------------|--------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------|---------------------------------------------------------------------------------|
|                                  |                                                                           | PA assessment: Questionnaire for lifetime TPA (hr/wk and MET hr/wk), divided into groups | G1 = 0                                                      |                                                                                  |
|                                  |                                                                           | Lifetime total PA (hr/wk) | G1 = 1.00 (referent)                                       |                                                                                  |
|                                  |                                                                           | G2 = 0.92 (0.72-1.19)      |                                                             |                                                                                  |

- Sex: Women
- Age: 20-69

- Lifetime total PA (hr/wk)
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.

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**Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)**

| Study | Country  | Sex | Age | Case control | PA assessment | TPA at age 12-19 yr | Multivariate adjusted OR (95% CI) by TPA at age 12-19 yr | Trend p  |
|-------|----------|-----|-----|--------------|---------------|--------------------|----------------------------------------------------------|---------|
| Steindorf et al 2003 [341] | Germany | Women | Mean cases 41.9 yr, controls 42.5 yr | | Computer assisted telephone interview for TPA (MET hr/wk) at various ages | | | |
| D & B score = 13 | | | | | | | | |

The data do not suggest an inverse association between PA and BC risk in pre-menopausal women.
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study | Objective | Design | Country | Sample Size | Duration/Assessment | Multivariate adjusted OR (95% CI) by TPA at age 12-30 yr | Trends |
|-------|-----------|--------|---------|-------------|---------------------|----------------------------------------------------------|--------|
| Tehard et al 2006 [342] | To investigate the type, duration, frequency and intensity of PA required to reduce the risk of BC | Prospective cohort | France | 90,509 | Baseline and follow-up every 2 years for 12 years | 3,424 cases of BC | BC risk was reduced, especially with VPA. |

- **n = 90,509**

- **Sex: Women**

- **Age: 40-65**

- **Characteristics: French women insured with Mutuelle Generale de l’Education Nationale**

- **E3N Cohort Study**

| PA Variable | G1 | G2 | G3 | G4 | Trend p |
|-------------|----|----|----|----|---------|
| TPA (MET hr/wk) | 1.00 (referent) | 1.05 (0.93-1.17) | 0.94 (0.83-1.05) | 0.90 (0.80-1.02) | <0.05 |
| Total recreational PA (MET hr/wk) | 1.00 (referent) | 0.88 (0.79-0.98) | 0.84 (0.72-0.95) | 0.81 (0.72-0.92) | <0.01 |
| Walking (min/d) | 1.00 (referent) | 1.03 (0.95-1.11) | | | |
| Study | Country | Cohort | Baseline and mean follow-up | Cases | Controls | PA assessment | Adjusted RR (95% CI) | Adjusted RR (95% CI) by LTPA or OPA | Notes |
|-------|---------|--------|-----------------------------|-------|----------|---------------|---------------------|----------------------------------|-------|
| Thune et al 1997 [343] | Norway | Prospective cohort | n = 25,624 | 351 cases of BC (110 premenopausal and 251 postmenopausal women) | | LTPA and OPA are associated with a reduced risk of BC. | |
|       |         |        | Sex: Women | Baseline and mean follow-up of 14 years | | | | | |
|       |         |        | Age: 20-54 | PA assessment: Self-reported LTPA and OPA, divided into groups | | | | | |
|       |         |        | D & B score = 14 | | | | | | |
| G1 = Sedentary | | | | | | | | | |
| G2 = Moderate | | | | | | | | | |
| G3 = Regular exercise OPA | | | | | | | | | |
| G1 = Sedentary | | | | | | | | | |
| G2 = Walking | | | | | | | | | |
| G3 = Lifting | | | | | | | | | |
| G4 = Heavy manual labor during work | | | | | | | | | |
| Pre-menopausal | | | | | | | | | |
| G1 = Sedentary | | | | | | | | | |
| G2 = Walking | | | | | | | | | |
| G3 = Lifting or heavy manual labor | | | | | | | | | |

Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)
Table 16: Studies examining the relationship between physical activity and breast cancer. (Continued)

| Study                | Objective | n= 3,783 (BC = 2,736) | PA assessment: Interview for OPA, divided into groups | Women with low OPA had an increased risk of BC, the incidence of BC was reduced in women with high-activity jobs. |
|----------------------|-----------|-----------------------|------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| Zheng et al 1993     | To assess the role of OPA in the risk of BC | n= 3,783 (BC = 2,736) | 2,736 cases of BC | 2,736 cases of BC |
|                      | China     | D & B score = 9       | Sex: Women                                           | G1 = Low                                                                                                   |
|                      |           |                       | Age: 30                                              | G2 = Moderate                                                                                              |
|                      |           |                       |                                                     | G3 = High                                                                                                  |

Zheng et al 1993 [344]

D & B score, Downs and Black quality score; YR, years; PA, physical activity; BC, breast cancer; LTPA, leisure-time physical activity; g, group; HR, hazard ratio; RR, risk ratio; OR, odds ratio; 95% CI, confidence interval; T, tertile; MET, metabolic equivalent; MET/wk, metabolic equivalent per week; OPA, occupational physical activity; MET h/wk/yr, metabolic equivalent per hour per week per year; kcal/wk, kilocalories per week; TPA, total physical activity; VPA, vigorous physical activity.
relationship in one or more measures of occupational and/or leisure-time physical activity and the risk for breast cancer. Moreover, the majority of studies demonstrated the greatest risk reduction at the highest activity level. With respect to the minimal and optimal volume of exercise required, Lee [105] stated that 30-60 min/day of moderate-to-vigorous physical activity is required to decrease the risk for breast cancer. This belief is strongly supported by the literature. However, others have shown significant risk reductions at lower exercise volumes. For instance, Rockhill et al. [106] showed significant reductions (12% or greater) in the risk for breast cancer in women who accumulated at least 1 hr of moderate or vigorous physical activity per week. Similarly, Sesso et al. (1998) revealed that there was an 8% reduction in the risk for breast cancer with a relatively small energy expenditure of 500-999 kcal/wk. Further risk reductions were observed with higher energy expenditures (=1000 kcal/wk = 51% reduction in the risk). As discussed above, Monninkhof et al. revealed a 6% decrease in breast cancer risk for each additional hour of physical activity per week [104].

Taken as a whole, it would therefore appear that Canada’s guidelines for physical activity are more than appropriate for reducing the risk for breast cancer. Further research however is required to determine the minimal volume of exercise that is effective in the primary prevention of breast cancer.

Implications

There is a preponderance of data linking physical inactivity to site-specific cancers, particularly of the breast and colon [31,104-109]. The protective effects of physical activity also appear with other forms of cancer (such as endometrial cancer) [110]. In an important review of the literature Lee revealed that physically active women have a 20-30% lower risk of breast cancer, and physically active men and women have a 30-40% lower risk of colon cancer [105]. A more recent systematic review of the literature revealed a 20-80% lower risk of breast cancer in post-menopausal women [104], with a weaker association in pre-menopausal women. Considering data from both pre- and post-menopausal women the authors demonstrated that physically active individuals had a 15-20% lower risk of breast cancer. Monninkhof et al. also reported a 6% lower risk of breast cancer for each additional hour of physical activity per week [104]. This level of risk reduction was also supported by the U.S. Department of Health and Human Services during its recent evaluation of the literature [31].

Our current reviews of the literature support previous work in the field including the finding of a dose-response relationship between physical activity and cancers of the breast and colon [104,105,109]. It would appear that 30-60 min/day of moderate-to-vigorous physical activity is associated with a lower risk of breast and colon cancer.

Recommendation #5

For a reduced risk for site specific cancers (such as colon cancer and breast cancer), it is recommended that individuals should participate in 30 min or more of moderate to vigorous exercise on most days of the week. [Level 2, Grade A]

Primary Prevention of Type 2 Diabetes

In comparison to other chronic conditions, there is relatively limited literature examining the relationship between multiple levels of physical activity/fitness and the incidence of type 2 diabetes. All of the literature...
examining the dose-response (for at least three levels of physical activity/fitness) involved prospective cohort analyses. A total of 3655 citations were identified during the electronic database search (Figure 9). Of these citations, 2038 were identified in MEDLINE, 1116 in EMBASE, 118 in Cochrane, and 372 in the CINAHL/SportDiscus/PsychInfo search. A total of 614 duplicates were found, leaving a total of 3041 unique citations. A total of 2865 articles were excluded after scanning, leaving a total of 176 articles for full review. From these articles 156 were excluded after full review leaving 20 articles for inclusion in the systematic review of the literature regarding the relationship between physical activity and type 2 diabetes. The reasons for exclusion included non-experimental/weak design (N = 18), three levels of physical activity not reported (N = 16), reviews, summaries, or meta-analyses (N = 41), not related to type 2 diabetes (N = 71), and other (N = 10).

As shown in Table 17, 20 investigations examined the dose-response (i.e., three or more levels) relationship between physical activity and the incidence of type 2 diabetes. This involved a total of 624,952 subjects, averaging 32,892 subjects per study (range 1,543-87,907). There were a total of 19,325 cases of type 2 diabetes (ranging per study from 78-4,030). The total length of follow-up averaged 9.3 yr (ranging from 3 -16.8 yr). The articles were published over a 16 yr period ranging from 1991 to 2007.

Of these studies 100% revealed an inverse relationship between type 2 diabetes and levels of physical activity or fitness. When comparing the most active/fit group versus the least active/fit group we found an average risk reduction of 42% (median = 44%). Therefore in our analyses the most physically active/fit had a 42% lower risk of developing type 2 diabetes. The majority (84%) of these studies revealed incremental reductions in the risk for type 2 diabetes with increasing activity/fitness levels. Therefore, the health benefits with respect to type 2 diabetes prevention appear to continue across the physical activity/fitness continuum. Similar to other clinical conditions, the dose-response relationship is such that small changes in activity levels yield marked reductions in the risk for type 2 diabetes. The health benefits of exercise appear to be particularly prevalent in individuals at high risk for developing type 2 diabetes (e.g., those with a high body mass index, the metabolic syndrome, a history of hypertension and/or a family history of type 2 diabetes). The level of evidence relating physical activity to the primary prevention of type 2 diabetes would be considered to be Level 2A. The quality of the investigations was generally high with a mean (and median) Downs and Black score of 13 (range 11-14).

As with other conditions is it difficult to separate the effects of volume and intensity of exercise. However, small changes in activity levels clearly can have a large effect on the risk for and incidence of type 2 diabetes. For instance, Hu and coworkers [111] revealed that nurses (n = 68,497) who engaged in 1 hr/day of brisk walking had 24% less obesity and 34% less type 2 diabetes (over a 6-year follow-up). These authors estimated that approximately 30% of new cases of obesity and 43% of new cases of type 2 diabetes could be prevented by adopting an active lifestyle including less than 10 hr/wk of television watching and ≥ 30 min/d of brisk walking. Similarly, over a 5-year period, male physicians who
| Publication          | Objective                                                                 | Population                          | Methods                                                                 | Outcome              | Comments and Conclusions |
|---------------------|---------------------------------------------------------------------------|-------------------------------------|-------------------------------------------------------------------------|----------------------|--------------------------|
| Haapanen et al 1997 [77] | To examine the association of PA and the risk of CHD, hypertension and T2D. | n = 1,340 men, 1,500 women          | 10 yr follow-up                                                       | Number of cases: 118 | LTPA has a preventive effect on T2D. |
|                     | • Age: 35-63 yr                                                        |                                      | PA assessment: Self-reported                                           |                      |                          |
|                     |                                                            |                                      | LTPA (kcal/wk), divided into groups                                     |                      |                          |
|                     |                                                            |                                      | • G1 = 1.54 (0.83-2.84)                                                 |                      |                          |
|                     |                                                            |                                      | • G2 = 1.21 (0.63-2.31)                                                 |                      |                          |
|                     |                                                            |                                      | • G3 = 1.00 (referent)                                                  |                      |                          |
|                     |                                                            |                                      | p = 0.374                                                              |                      |                          |

| Hu et al 2008 [111] | To examine the relationship between sedentary behaviours (particularly prolonged television watching) and risk of obesity and T2D in women. | n = 68,497 (diabetes specific analyses) | 6 yr follow-up | Number of cases: 1515 | Sedentary behaviours (especially television watching) are associated with an increased risk for obesity and T2D. |
|                     | • n = 50,277 (obesity specific analyses)                             |                                      | PA assessment: Self-reported PA and sedentary behaviour                |                      |                          |
|                     |                                                            |                                      | Outcome measure: onset of obesity and T2D                             |                      |                          |
|                     |                                                            |                                      | Each 2-h/d increment in TV watching was associated with a 23% (95% CI, 17%-30%) increase in obesity and a 14% (95% CI, 9%- 23%) increase in risk of T2D |                      |                          |
|                     |                                                            |                                      | Standing or walking around at home (2 h/d) was associated with a 9% (95% CI, 6%-12%) reduction in obesity and a 12% (95% CI, 7%- 16%) reduction in T2D |                      |                          |
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| Characteristics                                                                 | Each 1 hour per day of brisk walking was associated with a 24% (95% CI, 19%-29%) reduction in obesity and a 34% (95% CI, 27%-41%) reduction in T2D |
|---------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Free of T2D, CVD, or cancer at baseline                                          |                                                                                                                                  |
| Nurses’ Health Study                                                            |                                                                                                                                  |
| Manson et al 1992 [112]                                                        | To examine the association between regular exercise and the subsequent development of T2D.                                      |
| • Sex: Men                                                                      | PA assessment: Questionnaire for VPA (enough to develop sweat)                                                                      |
| • Age: 40-84 yr                                                                 | The age-adjusted incidence of T2D:                                                                                                 |
| • Characteristics                                                               | • 369 cases per 100,000 person-years in men who engaged in VPA less than once weekly                                               |
| USA                                                                              | • 214 cases per 100,000 person-years in those exercising at least five times per week (p trend < 0.001)                              |
| Free of diagnosed diabetes, CVD and cancer at baseline                          |                                                                                                                                  |
| Prospective cohort                                                              |                                                                                                                                  |
| D & B score = 14                                                                | Exercise frequency (times/wk)                                                                                                       |
|                                                                                | G1 = < Weekly                                                                                                                    |
|                                                                                | G2 = At least weekly                                                                                                              |
|                                                                                | Age-adjusted RR (95% CI) by exercise frequency                                                                                      |
| Times per week                                                                  | • G1 = 1.00 (referent)                                                                                                             |
| G1 = 0                                                                          | • G2 = 0.64 (0.51-0.82)                                                                                                           |
| G2 = 1                                                                          | • G3 = 2.4                                                                                                                        |
| G3 = 2-4                                                                        | • G4 = >5                                                                                                                         |
| G4 = >5                                                                         | Age-adjusted RR (95% CI) by exercise frequency                                                                                      |
| Outcome measure: Incidence T2D                                                  | • G1 = 1.00 (referent)                                                                                                             |
|                                                                                | • G2 = 0.77 (0.55-1.07)                                                                                                           |
|                                                                                | • G3 = 0.62 (0.46-0.82)                                                                                                           |
|                                                                                | • G4 = 0.58 (0.40-0.84)                                                                                                           |
|                                                                                | Age- and BMI-adjusted RR (95% CI) by exercise frequency                                                                         |
|                                                                                | • G1 = 1.00 (referent)                                                                                                             |
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| Study | Population | Follow-up | Number of cases | Outcome Measure | Sex | Age | PA Assessment | OR (95% CI) |
|-------|------------|-----------|----------------|----------------|-----|-----|--------------|-------------|
| Hu et al. 2001 [114] | To examine the relationship between dietary and lifestyle factors in relation to the risk for T2D | 16 yr follow-up | 3300 | Incidence of T2D | Women | 40-75 yr | Questionnaire for PA (h/wk), divided into groups | Multivariate-adjusted RR (95%) |
| | USA | | | | | | | Q1 = 1.00 (referent) |
| | Retrospective cohort | Characteristics: participants had no history of diabetes, CVD, or cancer. | | | | | | Q1 = <0.5 |
| | | | | | | | | Q2 = 0.89 (0.77-1.02) |
| | | | | | | | | Q3 = 0.87 (0.75-1.00) |
| | | | | | | | | Q4 = 0.83 (0.71-0.96) |
| | | | | | | | | Q5 = 0.71 (0.56-0.90) |
| Sato et al. 2007 [116] | To examine the relationship between walking to work and the development of T2D | 4 yr follow-up | 878 | Incidence of T2D | Men | 40-55 yr | For time spent walking to work, divided into tertiles | OR (95% CI) |
| | Japan | | | | | | | T1 = 1.00 (referent) |
| | Prospective cohort | Kansai Healthcare Study | | | | | | T2 = 0.86 (0.70-1.06) |
| | | | | | | | | T3 = 0.73 (0.58-0.92) |
| | | | | | | | | Significant difference was seen between ≤ 10 min and ≤ 20 min only (p = 0.007) |
| | | | | | | | | T2 = 11-20 min |
| | | | | | | | | T3 = ≥20 min |

Note: OR = Odds Ratio, CI = Confidence Interval
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| D & B score = 14 | Outcome measure: Incidence of T2D |
|-----------------|-----------------------------------|
| To examine the relationship of OPA, commuting and LTPA with the incidence of T2D. | Multivariate adjusted HR (95% CI) for OPA, men |
| • n = 14,290 | Moderate and high OPA, commuting PA or LTPA significantly reduces risk of T2D in middle aged adults. |
| • Sex: Men and women | |
| Finland | |
| Prospective cohort | An asymptomatic for stroke, CHD, or diabetes at baseline. |
| • Age: 35-64 yr | |
| • Characteristic: OPA | |
| • G1 = Light (sitting) | |
| • G2 = Moderate (standing, walking) | Multivariate adjusted HR (95% CI) for OPA, women |
| • G3 = Active (walking, lifting) | |
| Commuting PA (min/d) | |
| • G1 = None | Multivariate adjusted HR (95% CI) for OPA, men and women |
| • G2 = 1-29 | |
| • G3 = ≥ 30 | |
| LTPA | |
| • G1 = Low (inactive) | |
| • G2 = Moderate (walking, cycling >4 hr/wk) | |
| • G3 = High (running, jogging >3 hr/ wk) | Multivariate adjusted HR (95% CI) for commuting PA, men |
| Outcome measure: incidence of T2D | |
| Cox proportional HR | Multivariate adjusted HR (95% CI) for commuting PA, women |
| • G1 = 1.00 (referent) | |
| • G2 = 1.00 (0.71-1.42) | |
| • G3 = 0.75 (0.46-1.23) |
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| Study                        | Design          | Number of Cases | Multivariate adjusted HR (95% CI) for LTPA, men | Multivariate adjusted HR (95% CI) for LTPA, women | Multivariate adjusted HR (95% CI) for LTPA, men and women |
|------------------------------|-----------------|-----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Hsia et al 2005 [118] USA    | Prospective cohort | 87,907          | G1 = 1.00 (referent)  
G2 = 0.81 (0.64-1.20)  
G3 = 0.84 (0.57-1.25) | G1 = 1.00 (referent)  
G2 = 0.78 (0.57-1.06)  
G3 = 0.64 (0.45-0.92) | G1 = 1.00 (referent)  
G2 = 0.78 (0.57-1.06)  
G3 = 0.64 (0.45-0.92) |

To evaluate the relationship between PA and the incidence of T2D in a large, diverse group of older women.

- n = 87,907
- PA assessment: Questionnaire for frequency and duration of 4 walking speeds and 3 other activities classified by intensity (light, moderate, strenuous)
- Number of cases: 2,271

There is a strong inverse relationship between PA and T2D. There is a stronger relationship between PA and T2D in Caucasian women than in minority women. This may be explained by less precise risk estimates in minority women.
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| Q1 = 1.00 (referent) | Multivariate adjusted HR (95% CI) by TPA, Caucasian |
|----------------------|-----------------------------------------------------|
| Q2 = 0.88 (0.76 - 1.01) |
| Q3 = 0.74 (0.64 - 0.87) |
| Q4 = 0.80 (0.68 - 0.94) |
| Q5 = 0.67 (0.56 - 0.81) | Trend p = 0.002 |

- Characteristics: participants had no history of diabetes, were not on any antidiabetic medications
- Women’s Health Initiative

| Wannamethee et al 2000 [120] | To examine the role of components of the insulin resistance syndrome in the relationship between PA and the incidence of T2D and CHD. |
|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| n = 5,159 | 16.8 yr follow-up |
| Number of cases: 196 |
| The relationship between PA and T2D appears to be mediated by serum insulin and components of the insulin resistance syndrome. However, these factors do not appear to explain the inverse relationship between PA and T2D. |

- Sex: Men
- Age: 40-59 yr
- PA assessment: Questionnaire for TPA
- Physical activity groups were identified and scored:

| Q1 = None | Q5 = 0.46 (0.27 - 0.79) |
| Q2 = Occasional | Q4 = Moderate |
| Q3 = Light | Multivariate adjusted RR (95% CI) |
| Q2 = 0.48 (0.28 - 0.83) |
| Q3 = 0.45 (0.41 - 1.03) |

- Prospective cohort
- D & B score = 14
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| Study | Objective | Design | Sample Size | Follow-up | Number of Cases | Effect Size |
|-------|-----------|--------|-------------|-----------|----------------|-------------|
| Manson et al 1991 [121] | To examine the association between regular VPA and the incidence of T2D. | Prospective cohort | n = 87,253 | 8 yr follow-up | 1303 | RR = 0.66 (0.6-0.75) |
| USA | Prospective cohort | Questionnaire | Frequency of weekly exercise (0-4) | The reduction in risk remained significant after adjustment for BMI | PA assessment: | D & B score = 13 |
| | | | | PA is promising in the primary prevention of T2D. | | |

Q5 = Moderately vigorous/vigorous MPA (sporting activity once a week or frequent lighter-intensity activities such as walking, gardening, do-it-yourself projects) are sufficient to produce a significant reduction in risk of both CHD and T2D.

- Sex: Women
- Age: 34-59 yr
- Characteristics: Free of diagnosed diabetes, cardiovascular disease and cancer

Multivariate adjustments for age, body-mass index, family history of diabetes, and other variables did not alter the reduced risk found with exercise.

Multivariate analysis:
- Family history of diabetes did not modify the effect of exercise, and risk reduction with exercise was evident among both obese and non-obese women.
| Helmrich et al 1994 [122] | To examine the relationship between PA and the development of T2D. | \( n = 5,990 \) | 98,524 man-years of follow-up (1962-1976) | Number of cases: 202 | Increased PA is effective in preventing T2D. |
|--------------------------|---------------------------------------------------------------|-----------------|----------------------------------------|-----------------------|-----------------------------------------------|
| USA                      | Sex: Men                                                       |                 |                                        | RR (95% CI) by blocks walked per day | The protective benefit is especially pronounced in those individuals who have the highest risk of disease. |
|                          | Age: 39-68 yr                                                 |                 |                                        |                       |                                               |
|                          | Characteristics: healthy, asymptomatic                         |                 |                                        |                       |                                               |
|                          | PA assessment: Questionnaire for LTPA (walking, stair climbing, sports etc; kcal/wk) Blocks walked/day |                 |                                        |                       |                                               |
|                          | The protective benefit is especially pronounced in those individuals who have the highest risk of disease. |                 |                                        |                       |                                               |

Further review of the data reported by Helmich et al. 1991

University of Pennsylvania Alumni Health Study

Prospective cohort

D & B score = 14

LTPA (kcal/wk) kcal were assigned to each activity and added together

LTPA was inversely related to the development of T2D

Same findings to that reported in 1991

Helmrich et al 1991 [123] To examine the relationship between PA and the subsequent development of T2D.

\( n = 5,990 \)

98,524 man-years of follow-up (1962-1976)

Number of cases: 202

Increased PA is effective in preventing T2D.

Sex: Men

Age: 39-68 yr

Characteristics: healthy, asymptomatic

PA assessment: Questionnaire for LTPA kcal/wk; stairs climbed/day and blocks walked/day, divided into groups

LTPA was inversely related to the development of type 2 diabetes

The protective benefit is especially pronounced in those individuals who have the highest risk of disease.
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| Prospective cohort | RR (95% CI) by sports played |
|--------------------|------------------------------|
| University of Pennsylvania Alumni Health Study | • G1 = 1.00 (referent) |
| • G2 = 0.90 |
| • G3 = 0.69 |
| • G4 = 0.65 |

| All activities LTPA | Trend p = 0.02 |
|--------------------|----------------|
| Q1 = <500          | RR (95% CI) by Flights of stairs climbed/day |
| Q2 = 500-999       | • T1 = <5 = 1.00 (referent) |
| Q3 = 1000-1499     | • T2 = 0.78 |
| Q4 = 1500-1999     | • T3 = 0.75 |
| Q5 = 2000-2499     | Trend p = 0.07 |
| Q6 = 2500-2999     | RR (95% CI) by Blocks walked/day |
| Q7 = 3000-3499     | • T1 = 1.00 (referent) |
| Q8 = ≥ 3500        | • T2 = 1.31 |

| Sports played |
|---------------|
| G1 = None |
| • G2 = Moderate |
| G3 = Vigorous |
| G4 = Moderate and Vigorous |

| Age adjusted RR (95% CI) by all activities |
|------------------------------------------|
| Stairs climbed per day |
| T1 = <5 |
| • Q1 = 1.00 (referent) |
| T2 = 5-14 |
| • Q2 = 0.94 |
| T3 = ≥ 15 |
| • Q3 = 0.79 |
| • Q4 = 0.78 |
| Blocks walked per day |
| T1 = <5 |
| • Q5 = 0.68 |
| Q6 = 0.90 |
Table 17: The relationship between physical activity and the development of type 2 diabetes. *(Continued)*

| Activity Level | Age Adjusted RR (95% CI) by all activities except vigorous sports | Trend test p-value |
|---------------|---------------------------------------------------------------|-------------------|
| T2 = 5-14     | • Q7 = 0.86                                                    |                   |
| T3 = ≥ 15     | • Q8 = 0.52                                                   |                   |
|               | p = 0.01 for trend                                            |                   |

Cox proportional HR

Age adjusted RR (95% CI) by vigorous sports only

| Activity Level | Age Adjusted RR (95% CI) | Trend test p-value |
|---------------|---------------------------|-------------------|
| T1 = Low      | • Q1 = 1.00 (referent)    |                   |
| T2 = Moderate | • Q2 = 0.97               |                   |
|               | • Q3 = 0.87               |                   |
|               | • Q4 = 0.92               |                   |
|               | • Q5 = 0.75               |                   |
|               | • Q6 = 1.29               |                   |
|               | • Q7 = 1.03               |                   |
|               | • Q8 = 0.48               |                   |

Wei et al 1999

To determine whether PF is associated with risk for impaired fasting glucose and T2D.

- n = 8,633
- 6 yr follow-up
- Number of cases: 149
- High PF is associated with a reduced risk for impaired fasting glucose and T2D.

USA

- Sex: Men
- Age: 43.5 yr
- Characteristics: Non-diabetic men

Prospective cohort

PF assessment: Maximal treadmill exercise test (METs), divided into 3 groups

- 593 patients developed impaired fasting glucose
- OR (95% CI) for developing glucose intolerance

| Category       | OR (95% CI) |
|----------------|-------------|
| T1 = Low       | • T1 = 1.9 (1.5–2.4) |
| T2 = Moderate  | • T2 = 1.5 (1.2–1.8) |
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| D & B score = 12 | T3 = High | Outcome measure: Incidence of impaired fasting glucose and T2D | T3 = 1.00 (referent) OR (95% CI) for developing T2D |
|------------------|-----------|-------------------------------------------------------------|------------------------------------------------------|
|                  |           |                                                             | T1 = 3.7 (2.4 - 5.8)                                  |
|                  |           |                                                             | T2 = 1.7 (1.1 - 2.7)                                  |
|                  |           |                                                             | T3 = 1.00 (referent)                                 |

Statistics: GLM
Katzmarzyk et al 2007 [126] To examine the relationships among adiposity, PA, PF and the development of T2D in a diverse sample of Canadians.

- **n = 1,543 (709 men and 834 women)**
- **6 yr follow-up**
- **Number of cases: 78 (37 in men, 41 in women)**
- Adiposity and PF are important predictors of the development of T2D.

Canada
- **Sex: Men and women**
- **PF assessment: Questionnaire**
- PA was associated with 23% lower odds of developing diabetes and maximal METs was also associated with significantly lower odds of developing diabetes (OR = 0.28)

Prospective cohort
- **Age: 36.8 - 37.5**
- **PA assessment: LTPA Questionnaire**
- **Characteristics: Free of diabetes at baseline**
- **Canadian Physical Activity Longitudinal Study**
- **D & B score = 13**

Burchfiel et al 1995 [345] To examine the relationship between PA and T2D.

- **n = 6,815**
- **6 yr follow-up**
- **Number of cases: 391**
- PA is associated inversely and independently with incident T2D.

USA
- **Sex: Men (Japanese-American)**
- **PA assessment: Questionnaire PA index (based on intensity and duration of activity)**
- **The Honolulu Heart Program**
- **D & B score = 13**
- **Characteristics: Free of diabetes at entry**
- **Levels of activity:**
  - Q1 = Basal - Sleeping reclining
  - Q2 = Sedentary
  - Q3 = Slight - Casual walking
  - Q4 = Moderate - Gardening
  - Q5 = Heavy - Lifting, shoveling
- **Outcome measure: Self-reported T2D (clinically recognized)**

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Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

|Study| Objective| Sample Size| Follow-up| Outcomes| Methods|
|-----|----------|------------|----------|---------|---------|
|Dziura et al 2004 [346]|To determine the prospective relation between reports of habitual PA, 3-year change in body weight, and the subsequent risk of T2D in an older cohort.| n = 2,135| 3 years| 118 cases of T2D| PA assessment: Questionnaire for 4 types of activities (walking, gardening/housework, physical exercises, active sports or swimming) and frequency of participation measured with a PA score. Observation of an inverse relationship between reported PA and rate of T2D.

**USA**
- Sex: Men and women
- Age: ≥ 65 yr
- Ethnicity: 83% White, 15% African American, 2% Non-white

| | Incident density of T2D = 66/1000 person years|
|---|---|
|Prospective cohort| Diabetes (n = 118) PA score: 2.17 ± 1.7 'Some' PA: 78% Subjects reporting some PA at baseline experienced a rate of T2D over 50% lower relative to those reporting no PA.|
|D & B score = 12| Characteristics: Healthy asymptomatic

Subjects reporting 'Some' PA at baseline experienced a rate of T2D over 50% lower relative to those reporting no PA.

| | Non-Diabetes (n = 2017) PA score: 2.34 ± 1.7 'Some' PA: 84% Pearson product moment correlation coefficient and Cox proportional HR
|---|---|
|Hu et al. 1999 [347]|To quantify the dose-response relationship between total PA and incidence of T2D in women. | n = 70,102| 8 yr of follow-up| 1419 cases |

**USA**
- Sex: Women
- Age: 40-65 yr

| | Multivariate-adjusted RR (95% CI) of TPA (MET hr/wk) and VPA (6 METs) by TPA
|---|---|
|Prospective cohort| Characteristics: participants had no history of diabetes, CVD, or cancer

Increased PA is associated with substantial reduction in risk of T2D including PA of moderate intensity and duration. |
|D & B score = 12| Nurses’ Health Study

Q1 = 0-2.0
Q2 = 2.1-4.6
Q3 = 4.7-10.4
Q4 = 10.5-21.7
Q5 = ≥ 21.8

Trend p < 0.001

|Q1 = ≤ 0.5 | Q1 = 1.0 (referent) |
|---|---|
|Q2 = 0.6-2.0 | Q2 = 0.62 (0.57-0.73) |
|Q3 = 2.1-3.8 | Q3 = 0.73 (0.65-0.80) |
|Q4 = 3.9-9.9 | Q4 = 0.69 (0.56-0.86) |
|Q5 = ≥ 10.0 | Q5 = 0.58 (0.46-0.73) |

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### Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| Study | Population | Prolonged TV Watching | Incidence of T2D | Multivariate-adjusted RR (95% CI) by PA | Multivariate-adjusted RR (95% CI) by TV time |
|-------|------------|-----------------------|------------------|----------------------------------------|---------------------------------------------|
| Hu et al 2001 [348] | USA | Men, Age: 40-75 yr | 10 year follow-up | Multivariate-adjusted RR (95% CI) by PA | Time spent watching television per week (h/wk) |
| | | n = 37,918 | 10 year follow-up | Q1 = 0.59 | Q1 = 0.00 (referent) |
| | | | | Q1 = 1.00 (0.66 – 0.93) | |
| | | | | Q2 = 1.66 (1.15 - 2.39) | Q1 = 1.00 (referent) |
| | | | | Q3 = 2.16 (1.45 - 3.22) | Q2 = 1.66 (1.15 - 2.39) |
| | | | | Q4 = 2.57 (1.46 - 5.65) | Q3 = 1.66 (1.15 - 2.39) |
| | | | | Q5 = 3.05 (1.54 - 5.97) | Q4 = 2.16 (1.45 - 3.22) |
| | | | | Trend p < 0.001 | Q5 = 2.87 (1.46 - 5.65) |

### Additional Information
- Increasing PA is associated with a significant reduction in risk for T2D, whereas a sedentary lifestyle indicated by prolonged TV watching is related directly to increased risk.
- This study found that obesity and physical inactivity independently contributed to the development of T2D.
- The benefits of PA were not limited to lean women; among those who were overweight and obese, physically active women tended to be at lower risk for T2D than sedentary women.
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| D & B score = 12 | • Characteristics: No history of diabetes, CVD or cancer | Q1 = <2.1 | Q1 = 2.37 (2.15–2.16) |
|                 | • Nurses’ Health Study | Q2 = 2.1–4.6 | Q2 = 1.92 (1.73–2.13) |
|                 |                     | Q3 = 4.7–10.4 | Q3 = 1.48 (1.34–1.64) |
|                 |                     | Q4 = 10.5–21.7 | Q4 = 1.40 (1.26–1.55) |
|                 |                     | Q5 = ≥ 21.8 | Q5 = 1.00 (referent) |
|                  |                  |               | Trend p < 0.001 |
|                  |                  |               | Cox proportional HR |

Sawada et al 2003 [350] To examine the association between PF and the incidence of T2D.

| Japan | • Sex: Men | • Age: 20–40 yr | PF assessment: Maximal aerobic power estimate ml/kg/min using a submaximal cycle ergometer test, divided into quartiles | Age-adjusted RR (95% CI) |
|       |           |               | Q1 = 32.4 ± 3.1 | Q1 = 1.00 (referent) |

Prospective cohort

| Characteristics: Free of diabetes, CVD, hypertension, tuberculosis, and gastrointestinal disease at baseline | Q2 = 380 ± 2.5 | Q2 = 0.56 (0.42–0.75) |
|                                                                 | Q3 = 424 ± 3.0 | Q3 = 0.35 (0.25–0.50) |
|                                                                 | Q4 = 51.1 ± 6.2 | Q4 = 0.25 (0.17–0.37) |
|                                                                 |              | Trend p < 0.001 |

Outcome measure: Incidence of T2D Multivariate adjusted RR (95% CI)

| Q1 = 1.00 (referent) | Q2 = 0.78 (0.58–1.05) |
| Q3 = 0.63 (0.45–0.89) | Q4 = 0.56 (0.37–0.84) |
|              | Trend p = 0.001 |

Cox proportional HR

Weinstein et al 2004 [351] To examine the relative contributions and joint association of PA and BMI with T2D.

| • n = 37,878 | 6.9 year follow up | Number of cases: 1,361 | Although BMI and physical inactivity are independent predictors of incident diabetes, the magnitude of the association with BMI was greater than with PA in combined analyses. These findings underscore the critical importance of adiposity as a determinant of T2D. |

| Q1 = 2.37 (2.15–2.16) | Q2 = 1.92 (1.73–2.13) |
| Q3 = 1.48 (1.34–1.64) | Q4 = 1.40 (1.26–1.55) |
| Q5 = 1.00 (referent) | |
Table 17: The relationship between physical activity and the development of type 2 diabetes. (Continued)

| USA | Sex: Women | PA assessment: Questionnaire for walking per week (h/wk) and TPA (kcal/wk), divided into groups and quartiles respectively | Multivariate-adjusted HR (95% CI) by time spent walking |
|-----|------------|---------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
|     | Prospective cohort |                                                                                                                                                                           |                                                      |
|     | Age: 45+ years |                                                                                                                                                                           |                                                      |
|     | Health care professionals |                                                                                                                                                                           |                                                      |
|     | Characteristics: No history of CVD, cancer or diabetes |                                                                                                                                                                           |                                                      |
|     | D & B score = 12 |                                                                                                                                                                           |                                                      |
|     | G1 = 1.00 (referent) |                                                                                                                                                                           |                                                      |
|     | G2 = 0.95 (0.82-1.10) |                                                                                                                                                                           |                                                      |
|     | G3 = 0.87 (0.73-1.02) |                                                                                                                                                                           |                                                      |
|     | G4 = 0.66 (0.54-0.81) |                                                                                                                                                                           |                                                      |
|     | G5 = 0.89 (0.73-1.09) |                                                                                                                                                                           |                                                      |

Walking per week (h/wk)
G1 = no walking
G2 = <1
G3 = 1-1.5
G4 = 2-3
G5 = ≥ 4
TPA (kcal/wk)
Q1 < 200
Q2 = 200-599
Q3 = 600-1,499
Q4 ≥ 1,500

Cox proportional HR
Trend p = 0.004
Trend p = 0.001

Cox proportional HR

D & B score, Downs and Black quality score; YR, years; PA, physical activity; CHD, coronary heart disease; T2D, type 2 diabetes; LTPA, leisure-time physical activity; g, group; kcal/wk, kilocalories per week; HR, hazard ratio; RR, risk ratio; OR, odds ratio; 95% CI, confidence interval; CVD, cardiovascular disease; OPA, occupational physical activity; PF, physical fitness; MET, metabolic equivalent; MET/wk, metabolic equivalent per week.
exercised vigorously at least once weekly had a 29% lower incidence of type 2 diabetes than individuals who did not exercise regularly [112]. These authors also revealed that physical activity that was sufficient to cause sweating was associated with a lower incidence of type 2 diabetes. Other research has also demonstrated that moderate-to-vigorous physical activity (≥ 5.5 METs for at least 40 min per week) and/or aerobic fitness levels above 31 mL·kg⁻¹·min⁻¹ are associated with a lower risk of type 2 diabetes in middle-aged men [113] with the effect being the greatest in high-risk individuals. Therefore, it would appear that Canada’s recommendations for physical activity are sufficient to reduce the risk for type 2 diabetes.

In 2001, Hu et al. [114] reported very interesting and compelling research regarding the role of lifestyle factors in the development of type 2 diabetes. Using data from the Nurses’ Health Study, they defined a low-risk group according to five lifestyle factors including BMI, a healthy diet, the participation in moderate-to-vigorous physical activity for at least 30 min per day, no current smoking, and the consumption of an average of at least one-half serving of an alcoholic beverage per day. They revealed that the women in the low risk group had a RR for type 2 diabetes of only 0.09 (CI 0.05-0.17) in comparison to the rest of the cohort. They also found that 91% of the cases of type 2 diabetes in this cohort (CI 83-95%) could be attributed to the five lifestyle factors. This research provided compelling evidence that the majority of type 2 diabetes could be prevented through healthy living [115].

As reviewed in Table 17 there is evidence that leisure-time, occupational and commuting-related leisure time activities significantly reduce the risk for the development of type 2 diabetes. For instance, a recent study by Sato and colleagues [116] revealed that the walking distance to work was directly related to the incidence of type 2 diabetes in 8,576 Japanese men followed for 4 years. The risk reduction was approximately 27% in the participants who walked to work for ≥21 min compared to those who did so for ≥10 min. These findings are similar to that found by Hu et al. who reported that moderate occupational, commuting and leisure-time physical activities all had a significant inverse relationship to risk in middle-aged men and women [117].

Although ethnicity is often not reported in the current research, the studies examined in our systematic review came from a variety of countries and regions. Data was obtained from studies from the USA, Canada, UK, Japan, and Finland. For instance, Hsia et al. (2005) conducted a prospective 5-year study of 87,907 post-menopausal women, finding a strong graded inverse relationship between physical activity and type 2 diabetes. The relationship was stronger in “Caucasian” than in minority (African-American, Hispanic or Asian) women. The authors postulated this finding might reflect less precise risk assessments in minority women [118]. As we have outlined previously, further research is clearly warranted that examines the relationship between physical activity and type 2 diabetes in persons of different ethnicities. Moreover, further research is needed to determine the effects of socio-economic status on the observed relationships. Nonetheless, the research is compelling, habitual physical activity appears to be highly effective in the primary prevention of type 2 diabetes.

Implications

In 1992, the consensus panel from the International Conference on Physical Activity, Fitness and Health (held in Toronto, Canada) [17] indicated that physical activity can effectively reduce the risk for, and incidence of, type 2 diabetes. Over 15 years later, the research is compelling; habitual physical activity is an effective primary preventative strategy against the development of type 2 diabetes [111-113,118-123]. As shown in our analyses, numerous observational studies have revealed that regular physical activity is associated with a lower risk of developing type 2 diabetes [111-113,118-123]. Moreover, increased aerobic fitness is inversely associated with the risk of type 2 diabetes [113,124]. It is also apparent that both aerobic and resistance type activities reduce the risk for type 2 diabetes [125,126].

Although it is difficult to determine the dose-response between physical activity and type 2 diabetes in the majority of the current randomized controlled trials, these trials have revealed important findings. Influential exercise and/or lifestyle intervention trials have demonstrated clearly the health benefits of physical activity/exercise in the prevention of type 2 diabetes. For instance, in the Diabetes Prevention Program (US), 3,234 high-risk participants were randomly assigned to one of three groups: a) a placebo control, b) metformin drug therapy (850 mg twice daily), and c) a lifestyle intervention. The authors revealed that the lifestyle intervention (including physical activity for at least 150 minutes per week) was more effective than metformin (alone) (respective reductions in incidence 58% and 31%) [127]. Similarly, Tuomilehto et al. (2001) conducted a randomized controlled trial with middle-aged, overweight subjects with impaired glucose tolerance (172 males and 350 females). The authors reported a significant reduction in the incidence of type 2 diabetes in the intervention group (which received advice regarding moderate intensity exercise (30 min/day) and dietary control). The lifestyle intervention reduced the risk of type 2 diabetes by approximately 54% in women and 63% in men [128]. In a review of the literature, Williamson et al. revealed modest weight loss via diet and
physical activity reduced the incidence of type 2 diabetes in high risk individuals by 40-60% over a 3-4 year period [129]. Collectively, the epidemiological and randomized controlled trials provide compelling evidence supporting the role of habitual physical activity in the primary prevention of type 2 diabetes.

Recommendation #6
For a reduced risk for type 2 diabetes, it is recommended that individuals should participate in 30 min or more of moderate to vigorous exercise on most days of the week. [Level 2, Grade A]

Primary Prevention of Osteoporosis
The protective effects of physical activity and exercise training on bone health are well documented. In fact, the relationship between indicators of bone health (such as bone mineral density or bone mineral content) and physical activity have been evaluated extensively (see Table 18). Numerous exercise intervention trials have revealed that aerobic and resistance activities have a beneficial effect on bone mineral density across the lifespan [16]. In fact, several systematic reviews of the literature [130-135] and major consensus statements [136] have shown clearly the potential benefits of both aerobic and resistance training on bone health (particularly in post-menopausal women). It has been estimated that exercise interventions prevent or reverse at least 1% of bone loss per year in the lumbar spine and the femoral neck of pre- and post-menopausal women [130,137].

Exercise has also been shown to significantly reduce the risk and/or number of falls in comparison to inactive controls [138-142]. Moreover, fracture risk and/or incidence has been shown to be reduced in active individuals [143-145]. Case-control studies of older persons who suffered a hip fracture have revealed that these individuals had significantly lower physical activity levels throughout adulthood [136,146]. Observational studies have also revealed an inverse relationship between the incidence of fractures and physical activity [147-149]. For instance, Joakimsen et al. revealed lower fracture rates in individuals who performed more weight-bearing activities [148]. Similarly, Kujala et al. [147] in a 21-year prospective study revealed that intense activity was associated with a lower incidence of hip fracture (Hazard Ratio = 0.38, 95% CI = 0.16-0.91). Feskanich et al. (2002) also revealed that moderate physical activity was inversely related to the risk of hip fracture in postmenopausal women [149]. In a review of observational trials, Katzmarzyk and Janssen [20] revealed that the fracture risk was markedly higher in habitually inactive individuals (RR = 1.59 [95% CI = 1.40-1.80]) with a population attributable risk of 24% in Canada.

There is clear evidence that exercise training is of benefit for bone health and accordingly reduces the risk for osteoporosis. However, remarkably limited research has actually examined the relationship between routine physical activity and the prevalence and/or incidence of osteoporosis (Figure 10). In our systematic search of the osteoporosis literature, a total of 3655 citations were identified during the electronic database search (Figure 7). Of these citations, 1888 were identified in MEDLINE, 236 in EMBASE, 82 in Cochrane, and 481 in the CINAHL/SportDiscus/PsychInfo search. A total of 276 duplicates were found, leaving a total of 2411 unique citations. A total of 2059 articles were excluded after screening, leaving a total of 352 articles for full review. From these articles all 352 were excluded after full-text review. The reasons for exclusion included non-experimental/weak design (n = 87), did not contain three levels of physical activity or not possible to determine dose-response relationship (n = 38), reviews, summaries, meta-analyses (n = 39), not dealing specifically with osteoporosis (n = 21), only on change in bone mineral density (N = 123), clinical population (N = 10), bone metabolism (N = 13), fractures (N = 3), population < 18 yrs (N = 11), and other (N = 7). An additional 2 articles were found through the authors’ knowledge of the field.

As identified in our systematic search, the majority of the literature has dealt with the relationship between physical activity and indicators of bone health and/or the incidence of fractures. However, a recent observational trial [150] has provided evidence supporting the ability of physical activity to reduce the incidence of osteoporosis. For instance, Robitaille et al. revealed a dose-response relationship between physical activity level and the prevalence of reported osteoporosis in 8073 women aged ≥ 20 yr in the National Health and Nutrition Examination Survey, 1999-2004 [150]. Those performing no physical activity were at a higher risk than those who engaged in moderate (<30 MET hr/wk) and high (>30 MET hr/wk) levels of physical activity. There was a dose-response relationship with the highest physical activity group having the lowest prevalence of osteoporosis. Similarly, Keramat et al. [151] in a case-control investigation revealed that physical activity was protective against the development of osteoporosis.

At this time it is difficult to define clearly the actual dose-response required to cause a reduction in the incidence of osteoporosis. It is clear that bone adaptations to exercise are load dependent and site specific [9,10,16,152]. As such, physical activities that involve significantly loading/impact are often advocated for the prevention of osteoporosis. It is has been shown that running 15-20 miles per week is associated with bone mineral accrual or maintenance. Longer distances however may be associated with reduced bone mineral density [136].

Feskanich et al. reported that the risk of hip fracture was lowered by 6% for each increase of 3 MET-hours
### Table 18: Studies examining the relationship between physical activity and osteoporosis.

| Publication            | Objective                                                                 | Population               | Methods                      | Outcome                                                                 | Comments and Conclusions                                                                 |
|------------------------|---------------------------------------------------------------------------|--------------------------|------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Robitaille et al 2008  | To assess the relationship between the physician-diagnosed osteoporosis and family history and examine whether osteoporosis risk factors account for this relationship. | *n* = 8,073              | PA assessment: Questionnaire. Level of PA was expressed in MET (hr/wk) | Prevalence of reported osteoporosis in US women by PA level | Prevalence of osteoporosis declines with increasing PA in a dose-response manner. |
| USA                    | Cross-sectional                                                          | USA                      | D & B score = 10             | Muscle strengthening activities were expressed in frequency/Wk Times/week | *

#### Robitaille et al 2008 [150]

- **Objective**: To assess the relationship between the physician-diagnosed osteoporosis and family history and examine whether osteoporosis risk factors account for this relationship.
- **Population**: *n* = 8,073
- **Methods**: PA assessment: Questionnaire. Level of PA was expressed in MET (hr/wk)
- **Outcome**: Prevalence of reported osteoporosis in US women by PA level
- **Comments and Conclusions**: Prevalence of osteoporosis declines with increasing PA in a dose-response manner.

#### Keramat et al 2008 [151]

- **Objective**: To assess risk factors for osteoporosis in postmenopausal women from selected BMD centers in Iran and India.
- **Population**: *n* = 363; 178 cases, 185 controls
- **Methods**: Study period 2002–2005
- **Outcome**: OR (95% CI) of osteoporosis in exercisers vs. non-exercisers. Iran (age adjusted)
- **Comments and Conclusions**: Exercise was shown as a protective factor in both countries and it remained significant after adjustment for age, weight, and height in Iran.
Table 18: Studies examining the relationship between physical activity and osteoporosis. (Continued)

| Study | Characteristics | BMD assessment | PA assessment | PA | Other exercises | Regular Walking |
|-------|----------------|----------------|---------------|----------------|------------------|-----------------|
| India | Sex: Women | BMD assessment: DEXA | PA assessment: Questionnaire. | PA was categorized as exercises, other exercises (e.g., swimming, aerobics, weight training) and walking | Exercises = NS | Other exercises = NS | Regular Walking = NS |
| Iran | Case control | Characteristics: Cases had BMD > 2.5 SD below average of young normal bone density in L1-L4 spine region and/or total femoral region. Controls had BMD < 1 SD below normal | Multinominal logistic regression | Regular Walking = 0.5 (0.3-0.8) | Other exercises = 0.4 (0.2-0.6) | Regular Walking = 0.3 (0.2-0.6) |
| Iran (age, weight, height adjusted) |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| India (age adjusted) |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |

D & B score = 11

Walking and other exercises were shown as protective factors in Iranian subjects.

D & B score, Downs and Black quality score; YR, years; MET/wk, metabolic equivalent per week; G, groups; PA, physical activity; BMD, bone mineral density; SD, standard deviation; DEXA, dual energy x-ray absorptiometry; NS, not significant.
per week of activity (or 1 hr/wk of walking at an average pace) [149]. There was a linear reduction with increasing physical activity level. Walking for at least 4 hr/wk was also associated with a 41% lower risk of hip fracture compared to less than 1 hr/wk [149]. The work of Robitaille et al. also indicated that moderate levels of physical activity are sufficient to reduce the prevalence of osteoporosis [150].

In summary, there is preliminary evidence to indicate that the current Canadian physical activity guidelines are sufficient to maintain and/improve bone health. However, further research is clearly required, in particular research that examines the relationship between physical activity and the incidence of osteoporosis in both men and women from varied ethnic backgrounds. Currently, the level of evidence would be considered to be at a Level 3A. The quality of the investigations was generally low with a mean (and median) Downs and Black score of 11.

**Recommendation #7**

For a reduced risk for osteoporosis, it is recommended that individuals should participate in load bearing activities for 30 min or more on most days of the week. [Level 3, Grade A]

**Other Considerations**

**Musculoskeletal Fitness and Health**

In the present analyses, all indices of physical activity/fitness were incorporated into our systematic reviews. Although the majority of the data is related to aerobic activities, it should be noted that many of these activities also had a significant musculoskeletal component. Moreover, direct measurements of musculoskeletal fitness were included in various studies included in our review. Although there is limited information available (in comparison to aerobic activities) there is compelling evidence that musculoskeletal fitness is also positively associated with health status [9,10,16].

Warburton and colleagues [9,10] in two reviews of the literature reported that enhanced musculoskeletal fitness is associated positively with glucose homeostasis, bone health, functional independence, mobility, psychological well-being, and overall quality of life and negatively associated with fall risk, morbidity and premature mortality. They also reported that interventions that increase musculoskeletal fitness also have a significant positive effect on the health status of the individuals with a low musculoskeletal reserve (e.g., the frail elderly).

In an evaluation of the current literature some key findings emerge. Grip strength has particularly been shown to be inversely related to premature mortality and/or morbidity (e.g., functional limitations) [153-156]. Rantanen et al. (1998) reported that those individuals with the lowest grip strength had a higher rate of mortality at a younger age (over a 27-year period) than their counterparts with higher muscular strength. Furthermore, they revealed that those with a faster rate of decline in muscular strength (>1.5% per year) or a very low grip strength (<21 kg) had a greater incidence of chronic diseases, such as type 2 diabetes, stroke, arthritis, coronary heart disease, and pulmonary disorders. It was shown that those in the lowest grip strength tertile had an 8-fold increased risk for disability. Individuals with high muscular strength have also been shown to develop less functional limitations in comparison to their counterparts with lower strength over a 5-year period [157].

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**Figure 10 Results of the Literature Search for Osteoporosis**

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**Citations from electronic database search:**
- MEDLINE: 1888
- EMBASE: 236
- Cochrane: 82
- CINAHL/SportDiscus/PsycInfo: 481

**Total Citations Downloaded to RefWorks:**
- Total in RefWorks: 2687
- Total with Duplicates Excluded (N=2411)

**Full Articles Assessed for Eligibility after Scanning Titles (N=352)**

**Citations Excluded after Scanning Titles (N=2059)**

**Articles added through referencing (N = 2)**

**Articles Excluded after Full Review (N =352)**
- Reasons: non experimental (N=87); not 3 levels of physical activity (N=38);
- Reviews, summaries, meta-analysis (N=39); not related to osteoporosis (N=21); only on change in bone mineral density (N=123); clinical population (N=10); bone metabolism (N=13); fractures (N=3); population < 18yrs (N=11); other (N=7)

**Articles Included (N=2)**

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Katzmarzyk and colleagues [126,154,158] in Canada have also demonstrated a positive relationship between musculoskeletal fitness and health status. For instance, Katzmarzyk and Craig (2002) revealed that there was a significantly higher risk of premature mortality in the lower quartile of sit-ups in both men (RR = 2.72) and women (RR = 2.26). Grip strength was also predictive of mortality in men (RR = 1.49), but not women. In a recent study, Mason et al. revealed that musculoskeletal fitness was a significant predictor of weight gain over a 20-year period [158]. Importantly, they also reported that individuals with low musculoskeletal fitness had 78% greater odds of significant weight gain (≥ 10 kg) compared to those with high musculoskeletal fitness. These studies provide direct support for the inclusion of resistance and flexibility training in Canada’s physical activity guidelines for adults [3,159].

Recommendation #8
For improved health status and reduced risk for chronic disease and disability, it is recommended that individuals should include daily activities that tax the musculoskeletal system [Level 2, Grade A]

Limitations
It is important to note that for each chronic condition, the methods used to determine the relationship between physical activity and the specific clinical outcome were often quite varied. For instance, early work in the field generally controlled for few confounding variables (such as age). In comparison, current literature often controls for a myriad of potential confounding variables. These discrepancies make the comparison of the relative risk reductions between studies and across clinical conditions more difficult. Moreover, the multivariate analyses (controlling for various potential confounding factors) may inappropriately decrease the level of risk reduction associated with physical activity and the clinical endpoint [31]. This is owing to the fact that some of the health benefits associated with physical activity may be mediated through these variables [31].

There was often considerable variability in the findings and major conclusions of the studies examined. Often the available literature was limited by the lack of a clear standard for assessing physical activity. In many instances, it was extremely difficult to determine the actual dosage of physical activity used to group the participants. This lack of clarity makes it very difficult to clearly define the dose-response relationship between physical activity and various chronic conditions.

Conclusions
There is incontrovertible evidence that regular exercise is an effective preventative strategy against premature mortality, cardiovascular disease, stroke, hypertension, colon cancer, breast cancer, and type 2 diabetes. There is also compelling indirect evidence to support the protective effects of physical activity with respect to osteoporosis. In many instances the dose-response relationship is linear with further health benefits with increasing levels of activity. The current Canadian physical activity guidelines for adults are sufficient to reduce the risk for multiple chronic diseases simultaneously. The acknowledgement that every bit of exercise counts towards health benefits (with greater benefits at higher energy expenditures) is consistent with the literature and a reasonable message to promote to the general population. However, further investigation is likely required to evaluate the relationship between physical activity and health status in non-Caucasian populations.

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Authors’ contributions
DW was responsible for the conceptualization and design of the systematic review, the generation of the systematic review terms, oversaw the data collection, evaluated each article included in the review, and was responsible for creating and revising the manuscript. SC was involved in the data collection, the critical review of the articles, the creation of the tables contained in the article and the revision of the manuscript. AI assisted with the data collection, the critical review of the articles, and the creation and the revision of tables in the manuscript. LN assisted with the generation of the systematic review terms, the retrieval of articles, and the generation and revision of the tables. SB was involved in the conceptualization and design of the systematic review, the generation of the systematic review terms, oversaw the data collection, the review of the articles, and was responsible for creating and revising the manuscript. All authors have read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

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