Physical Activity and Mortality: A Prospective Study Among Women

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ABSTRACT

Objectives. This study examined the association between recreational physical activity and mortality in middle-aged and older women and the possibility that physical activity serves as an important marker of health.

Methods. Analyses were conducted among participants in the Nurses' Health Study. Levels of physical activity were assessed by questionnaire in 1980 and updated every 2 to 4 years.

Results. Levels of physical activity were inversely associated with mortality risk; however, each activity level above the reference level had approximately the same level of risk reduction (20%–30%). The inverse association was stronger for cardiovascular deaths than for cancer deaths and was strongest for respiratory deaths. Women who died of noncardiovascular, noncancer causes were more likely to have reported that poor health limited their physical activity than were women who died of other causes or who remained alive.

Conclusions. Part of the link between physical activity and mortality risk is probably spurious and difficult to remove analytically; however, on the basis of epidemiologic evidence, much of the health benefit of activity is real. (*Am J Public Health.* 2001;91:578–583)

Benefits of physical activity include reductions in risks of coronary heart disease, stroke, type 2 diabetes mellitus, certain cancers, and osteoporosis.[1] The relationship between physical activity and all-cause mortality has been examined in several prospective studies, and virtually all have indicated a reduction in risk.[2–8]

Reverse causation—that is, serious disease causing low physical activity rather than vice versa—could contribute to an association between low physical activity level and elevated mortality risk. In most previous prospective studies of physical activity and mortality, the possibility of spurious associations due to reverse causation has not been adequately discussed, despite attempts to begin with "healthy" cohorts at baseline and the exclusion of deaths during the first several years of follow-up. Reverse causation is particularly likely for diseases with a long natural history preceding death and for diseases for which physical activity is unlikely to be causally protective. Such diseases include chronic obstructive pulmonary disease, cirrhosis, and dementia.

In this study, we examined the association between recreational physical activity and mortality in the Nurses' Health Study cohort. We considered both total mortality and mortality due to selected major diseases, including those with plausible causal mechanisms related to physical activity and those for which there was no clear biological causal hypothesis. We examined the effects of total recreational activity, as well as the separate effects of walking and more vigorous activities, using repeated measures of physical activity.

To decrease the magnitude of potentially spurious associations, we excluded all women at baseline who reported a history of cancer (except nonmelanoma skin cancer) or cardiovascular disease (coronary heart disease, stroke, or angina), and we ceased updating physical activity level when a woman developed either of these conditions during the course of follow-up. Finally, to explore the possible spurious nature of certain physical activity–mortality associations, we examined whether inactive women who died of causes other than cardiovascular disease and cancer were more likely to have reported major activity limitations as an explanation for their inactivity than were inactive women who died from cardiovascular disease or cancer.

In all of our analyses, we examined physical activity in units of hours per week rather than in metabolic equivalent task units (METs).[9] Recent US federal guidelines regarding physical activity from the Centers for Disease Control and Prevention and the American College of Sports Medicine,[10] as well as the surgeon general's report on physical activity and health,[1] are stated in terms of units of time; these guidelines all endorse at least 30 minutes of moderate-intensity physical activity on most, and preferably all, days of the week. Furthermore, most individuals are accustomed to thinking of physical activity in terms of the time devoted to it rather than in terms of energy expenditure per episode.

Methods

Study Population

The Nurses' Health Study is a prospective cohort study that was established in 1976 when 121 701 female registered nurses aged 30 to 55 years returned a mailed questionnaire about their medical histories and lifestyles. Subsequent questionnaires requesting updated information on risk factors and medical events have been mailed every 2 years. The follow-up rate in this cohort between 1976 and 1996 was 95% of potential person-time (2 410 451 of 2 532 807 person-years). The protocol for the study was approved by the Human Research Committee of the Brigham and Women's Hospital. Because physical activity questions were first asked in the 1980 questionnaire, our baseline cohort consisted of the women who returned the 1980 questionnaire and answered the physical activity questions (n = 85 326). We excluded women at baseline with a history of cardiovascular disease or cancer (n = 4978); as a result, 80 348 women were included in analyses that began in 1980.

Identification of Deaths

In primary analyses, we lagged deaths by 2 years; thus, only deaths that occurred after the completion of the 1982 survey and before July 1996 were included. Most deaths were reported by the participants' families. We also searched the National Death Index to identify deaths among nonrespondents; mortality follow-up was more than 98% complete.[11] For all deaths, we sought death certificates and, when appropriate, requested permission from the next of kin to review medical records (subject to state regulations). Underlying cause of death was assigned according to the *International Classification of Diseases, Eighth Revision* (*ICD-8*). The primary endpoint in this analysis was death from any cause; we also examined deaths due to cardiovascular disease (*ICD-8* codes 410.0–414.9, 430.0–438.9, 443.0–443.9, 450.0–450.9, and 795.0–795.9), all cancers (codes 140.0–207.9), and all other nonaccidental causes. Between July 1982 and June 1996, 4746 deaths occurred among women who provided information on physical activity and on relevant covariates used in multivariate models.

Assessment of Physical Activity

Women were first asked about physical activity on the 1980 questionnaire. We used a single question about the average number of hours spent each week during the previous year on such activities as heavy gardening, vigorous sports, jogging, walking or striding, bicycling, or heavy housework. On the 1982 question-naire, women were asked a slightly different question: "For how many hours per week, on average, do you engage in activity strenuous enough to build up a sweat?"

In 1986, 1988, and 1992, the physical activity questions were more detailed (there were no physical activity questions on the 1990 survey); women were asked to report the average time spent per week during the previous year on each of the following activities: walking or hiking outdoors, jogging (slower than 10 minutes per mile), running (10 minutes per mile or faster), bicycling (including use of a stationary bicycle), swimming, playing tennis or squash, and participating in calisthenics, aerobics, or aerobic dance or using a rowing machine. Each woman also reported her usual walking pace: easy (less than 2 miles [3.2 km] per hour), normal (2–2.9 miles per hour), brisk (3–3.9 miles per hour), or very brisk (4 miles per hour or faster). Thus, for 1980, 1982, 1986, 1988, and 1992, we had a measure of average hours per week of physical activity. For 1986, 1988, and 1992, we also created variables representing average hours per week of walking and of more vigorous (nonwalking) physical activity.

To represent long-term physical activity levels of individual women as accurately as possible, we created measures of cumulative average physical activity level (in units of hours per week) from all available questionnaires up to the start of each 2-year follow-up interval. As stated earlier, we used a 2-year lag in our analyses; thus, deaths in the first 2-year period (July 1980–June 1982) were not included in analyses. (Lagging deaths by 2 years produced relative risks that were modestly attenuated in comparison with those produced in an unlagged analysis, as expected.)

Because lagging deaths by more than 2 years produced results nearly identical to those corresponding to a 2-year lag, we used the 2-year lag to include the largest number of events. For example, mortality from July 1982 to June 1984 was examined in relation to physical activity level reported on the 1980 questionnaire, mortality from July 1984 to June 1986 was examined in relation to the average physical activity level calculated from the 1980 and 1982 questionnaires, and so forth. Because there was no measure of physical activity in 1984, mortality from July 1986 to June 1988 was examined in relation to the same average physical activity level calculated from the 1980 and 1982 questionnaires. Mortality in the final 2-year period, July 1994 to June 1996, was examined in relation to average physical activity level computed from all surveys up to and including the 1992 survey.

We ceased updating of average activity level for all women who developed cardiovascular disease or cancer during follow-up. For instance, if a woman reported on the 1988 survey that she had been diagnosed with coronary heart disease in the previous 2 years, the average of her 1980, 1982, and 1986 physical activity levels was retained as her "average" activity level for analyses in all time periods subsequent to 1986. We used the continuous values of hours per week to compute the cumulative averages at each time period; we then categorized hours per week into 5 levels (less than 1 [referent], 1–1.9, 2–3.9, 4–6.9, and 7 or more hours per week) after averaging.

We also evaluated the joint effects of walking and more vigorous nonwalking physical activities on mortality risk. For these analyses, the women who responded to the 1986 questionnaire constituted the baseline cohort, because information on specific types of activities was first collected on this survey. Thus, for these analyses, 8 years of mortality follow-up (1988–1996) were examined. Again, we created cumulative average measures of hours per week spent walking and hours spent doing more vigorous activities, and we lagged deaths by 2 years. In this analysis, women with both less than 1 hour per week of walking and less than 1 hour per week of more strenuous activities composed the reference group. As before, we excluded women with a history of cancer or cardiovascular disease at baseline (1986), and we ceased updating activity levels for women developing these conditions during follow-up.

On the 1992 questionnaire, women were asked whether their health limited their ability to engage in vigorous activities, such as running, heavy lifting, or participating in strenuous sports, and moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. Women were also asked whether their health limited their ability to climb stairs or to walk several blocks. Among the most inactive women, we analyzed responses to these questions according to 1992 to 1996 follow-up status (i.e., remained alive in 1996, died of cancer or cardiovascular disease between 1992 and 1996, or died of other causes). A finding that women who died of other causes were much more likely to report previous activity limitations owing to poor health would lend support to the argument that observed associations between physical activity and these other causes of death are at least partly spurious.

Statistical Analysis

We used multivariate pooled logistic regression[12] with 2-year time intervals to approximate the Cox proportional hazards model. With these regression equations, we modeled the risk of death over the follow-up period according to level of cumulative average physical activity level. Each woman contributed person-time from the time the initial questionnaire

containing the exposure information of interest was returned until the end of follow-up (June 1, 1996), death, or loss to follow-up. In these models, the numbers of cases and person-years that accrued at each exposure level within each stratum were counted. For time-varying covariates, including body mass index (BMI), cigarette smoking, parity, alcohol consumption, and menopausal status/use of postmenopausal hormones, cases and person-time were reassigned every 2 years according to the updated exposure values reported on each of the biennial questionnaires.

From these summary tables, we calculated mortality rates as the sum of cases divided by the sum of person-time observed, for each exposure level. We calculated rate ratios (relative risks) for each physical activity level by dividing the rate for that level by the rate for the reference level. We used SAS[13] in conducting all statistical analyses.

We present both age-adjusted relative risks and relative risks adjusted simultaneously for the following factors: age at baseline (continuous), BMI (in approximate quintiles; ≤21.0 kg/m^2, 21.1–22.5 kg/m^2, 22.6–24.3 kg/m^2, 24.4–27.5 kg/m^2, or >27.5 kg/m^2), height (≤59 in [150 cm], 59.1–62 in, 62.1–65 in, 65.1–68 in, or >68 in), cigarette smoking (never smoker, past smoker who quit >5 years previously, past smoker who quit within past 5 years, currently smoking 1–14 cigarettes per day, currently smoking 15–24 cigarettes per day, or currently smoking ≥25 cigarettes per day), alcohol consumption (0, 0.1–4.9, 5.0–14.9, or 15 or more grams per week), and menopausal status or postmenopausal hormone use (premenopausal, postmenopausal with no history of hormone use, postmenopausal with past use of hormones for <5 years, postmenopausal with past use of hormones for ≥5 years, postmenopausal with current use of hormones for <5 years, or post-

menopausal with current use of hormones for ≥5 years). Adjustment for other factors, including dietary intake of various macronutrients and micronutrients, did not change the results; thus, to obtain models as parsimonious as possible, we did not include these factors.

BMI probably acts, in part, as an intermediate variable through which physical activity influences disease and mortality risk. However, in these data, controlling for BMI, singly and in combination with other covariates, did not appreciably alter relative risk estimates for any of the physical activity variables. Therefore, to be consistent with many of the previously published analyses, we included BMI in models.

Results

Women with higher physical activity levels in 1980 tended to be younger, leaner, less likely to smoke, and more likely to drink alcohol than those who were less active (Table 1). Table 2 shows relative risks for total mortality according to level of total physical activity. There was an inverse relationship, and the dose–response trend was significant ($P<.0001$ for trend in multivariate analysis); however, the greatest decrease in risk occurred with an increase in the amount of activity from less than 1 hour per week to 1 to 1.9 hours per week. The remaining decreases in risk with increasing activity level were relatively minor. We also evaluated the relationship between total physical activity, categorized in quintiles of MET hours, and mortality, beginning with physical activity level in 1986 (this was the first year in which activity information was collected in a manner allowing conversion into MET hours). The pattern and magnitude of relative risks in this MET hours analysis were quite similar to those of the relative risks reported in Table 2.

Table 3 presents data on the joint classification of walking and more vigorous activities and mortality risk. Relative to the reference group with less than 1 hour of walking and less than 1 hour of more vigorous activities each week, all other groups were at reduced mortality risk. Again, the magnitude of risk reduction for these various activity levels was similar, with no clear pattern apparent in the relative risks. Among women walking less than 1 hour per week, any amount of more vigorous activity involving more than 1 hour per week was associated with a moderate (approximately 20%–25%) reduction in mortality risk. For a given amount of time spent walking, an increase in amount of more vigorous activity tended to be associated with a modest reduction in risk of mortality, although the pattern was not consistent. The relationships between physical activity and mortality depicted in Tables 2 and 3 did not differ meaningfully across levels of various covariates, including smoking status (never, past, current), BMI (in tertiles), postmenopausal hormone use (never, past, current), and level of alcohol consumption (none, low/moderate, high).

Overall, in this cohort, 19.5% of deaths occurring between 1982 and 1996 were due to cardiovascular diseases, 57.5% were due to cancer, and 23.0% were due to all other causes. (The preponderance of cancer deaths over cardiovascular deaths may have been due to the age of the cohort; the deaths analyzed here occurred among women aged 34 to 75 years over the 1980 to 1996 time period.) Deaths among women at the lowest activity level were more likely due to noncancer, noncardiovascular causes than were deaths among women at the highest activity level: approximately 29% of women with an average of less than 1 hour per week of activity who died during follow-up died from noncancer, noncardiovascular causes,

TABLE 1—Baseline (1980) Characteristics of Participants According to Hours per Week of Physical Activity in 1980: Nurses' Health Study

Characteristic	<1.0 h/wk (n=20568)	1.0–1.9 h/wk (n=23071)	2.0–3.9 h/wk (n=13499)	4.0–6.9 h/wk (n=13475)	≥7.0 h/wk (n=9735)
Mean age, y (SD)	48.1 (±6.9)	46.2 (±7.1)	47.1 (±7.2)	46.1 (±7.4)	44.0 (±6.8)
Menarche before 12 years, %	22.5	22.6	23.1	22.5	21.0
Nulliparous, %	7.0	6.5	6.8	7.5	6.4
Postmenopausal, %	42.1	31.7	37.4	33.7	22.2
Ever used postmenopausal hormones,[a] %	46.1	47.2	48.0	50.6	50.0
Current smoker, %	31.8	29.7	30.8	26.0	22.2
Past smoker, %	25.8	25.8	25.4	29.3	35.2
Nonconsumer of alcohol, %	35.2	33.3	34.8	29.9	21.0
Mean BMI at the age of 18 y (SD)	21.4 (±3.1)	21.5 (±3.0)	21.5 (±3.1)	21.4 (±2.9)	21.0 (±2.4)
Mean BMI in 1980 (SD)	25.1 (±5.0)	24.7 (±4.7)	24.7 (±4.5)	23.9 (±3.9)	22.8 (±3.3)
Weight change >10 kg, age of 18 y to 1980, %	40.4	36.8	36.7	29.6	19.0
Height >67 in (170 cm), %	10.3	10.9	10.2	10.9	11.3

Note. BMI=body mass index.
[a] Among postmenopausal women only.

TABLE 2—Hours per Week of Physical Activity (Updated Every 2 Years, 1980–1992) and Relative Risks of All-Cause Mortality, 1982–1996: Nurses' Health Study

Physical Activity, h/wk	Person-Years of Observation (n = 1 270 498)	No. of Cases, 1982–1996 (n = 4746)	Age-Adjusted RR (95% CI)	Multivariate-Adjusted[a] RR (95% CI)
<1	263 918	1333	1.0	1.0
1–1.9	332 359	1203	0.76 (0.70, 0.82)	0.82 (0.76, 0.89)
2–3.9	346 025	1204	0.66 (0.61, 0.71)	0.75 (0.69, 0.81)
4–6.9	255 543	790	0.64 (0.58, 0.70)	0.74 (0.68, 0.81)
≥7	72 653	216	0.62 (0.54, 0.72)	0.71 (0.61, 0.82)

Note. RR = relative risk; CI = confidence interval.
[a]Adjusted for age at baseline, smoking status, recent alcohol consumption, height, body mass index, and postmenopausal hormone use (*P* for trend in multivariate-adjusted RRs: <.001).

TABLE 3—Hours per Week of Walking and More Vigorous Activities and Relative Risks of All-Cause Mortality, 1988–1996: Nurses' Health Study

Physical Activity h/wk	Person-Years of Observation (n = 588 426)	No. of Outcomes, 1988–1996 (n = 2470)	Age-Adjusted RR (95% CI)	Multivariate-Adjusted[a] RR (95% CI)
Less than 1 hour walking				
<1	207 542	1064	1.0	1.0
1–2.9	34 278	101	0.62 (0.51, 0.77)	0.72 (0.59, 0.89)
≥3	10 532	36	0.73 (0.52, 1.02)	0.84 (0.60, 1.17)
1–2.9 hours walking				
<1	130 657	527	0.73 (0.66, 0.81)	0.80 (0.72, 0.89)
1–2.9	61 340	188	0.58 (0.50, 0.68)	0.68 (0.58, 0.80)
≥3	22 219	66	0.60 (0.47, 0.77)	0.71 (0.55, 0.92)
3 or more hours walking				
<1	65 627	288	0.72 (0.63, 0.82)	0.80 (0.70, 0.91)
1–2.9	33 351	130	0.64 (0.53, 0.77)	0.78 (0.65, 0.94)
≥3	22 880	70	0.53 (0.41, 0.67)	0.63 (0.49, 0.80)

Note. RR = relative risk; CI = confidence interval.
[a]Adjusted for age at baseline, smoking status, recent alcohol consumption, height, body mass index, and postmenopausal hormone use.

whereas 20% of women with 7 or more hours of activity per week who died succumbed to these causes. The leading specific causes of mortality in this category of noncardiovascular, noncancer deaths (across all categories of physical activity) were chronic obstructive pulmonary disease and emphysema (15.7% of "other" deaths), cirrhosis (8.4%), type 2 diabetes mellitus (5.7%), and so-called ill-defined causes (5.6%).

Table 4 presents data on the association between average physical activity level (beginning in 1980) and cause-specific mortality. Higher levels of physical activity were associated with very modestly reduced risks of cancer mortality, and the dose–response trend was not significant. The inverse association with cardiovascular disease was stronger. Although the inverse dose–response trend was statistically significant, the relative risks did not decrease monotonically.

Low levels of physical activity are hypothesized to be causally related to risk of diabetes, and thus diabetes ideally should not be grouped with other leading causes of noncancer, noncardiovascular deaths. Therefore, we also examined the association between physical activity and noncancer, noncardiovascular, nondiabetes causes of death. There was a strong inverse association, stronger than either of the associations with cancer or cardiovascular disease.

The single leading contributor to deaths not due to cancer, cardiovascular disease, or diabetes was the category of respiratory deaths (*ICD-8* codes 460–519.9). As can be seen in Table 4, relative risks relating physical activity and respiratory deaths were the most strongly inverse of all associations in our analyses (relative risk of 0.23 for the most active vs the least active group). We could not evaluate this relationship in those with no history of tobacco use,

because there were no deaths from these respiratory causes in the most active groups of non-smokers. (Nonsmokers who died of causes other than cancer, cardiovascular disease, or diabetes died predominantly of cirrhosis and dementia.)

We examined whether, among the least active group of women (those reporting less than 1 hour of any activity per week), those who remained alive or subsequently died of cancer, cardiovascular disease, or diabetes were less likely to report major activity limitations than those who subsequently died of other causes. Among women who reported less than 1 hour of activity on the 1992 questionnaire, those who remained alive were less likely than those who died of other causes to have reported that their health limited their ability to engage in vigorous and moderate activities and to climb stairs and walk several blocks. For instance, 57.5% of sedentary women in 1992 who subsequently died of "other" causes of death had reported major limitations with moderate activities; the corresponding percentages were 31.8%, 23.7%, and 7.2%, respectively, for similarly sedentary women who died of cardiovascular disease or cancer or who remained alive.

Discussion

To our knowledge, this is the largest, and one of the longest, prospective studies of recreational physical activity and mortality in women. We collected repeated, detailed information on types of activities. It is likely that the use of repeated measures of physical activity provided a more accurate estimate of average activity level than a single baseline measure, as used in most other prospective studies of physical activity and mortality. We also gathered detailed information on a large number of potentially confounding variables, and our follow-up rate was high (more than 95% of potential person-time).

Our findings are in agreement with the well-known observation that people who are more physically active are at reduced mortality risk relative to those who are less active. We found, similar to Kushi et al.,[4] that moderate recreational activity (primarily walking, in the Nurses' Health Study cohort) conveys approximately the same mortality benefit as more vigorous activities, at least among middle-aged and older women. Our results are also in accord with analyses of specific disease outcomes in this cohort, as discussed subsequently. We were unable to address the role of specific sports or activities other than walking because of the small proportion of women in the cohort who regularly engaged in a specific nonwalking activity.

We found strong evidence of a spurious component in the physical activity–mortality

TABLE 4—Hours per Week of Physical Activity and Adjusted Relative Risks of Mortality From Specific Causes, 1982–1996: Nurses' Health Study

Physical Activity, h/wk	Relative Risk (95% Confidence Interval)			
	Cardiovascular Deaths[a] (n = 923)	Cancer Deaths[b] (n = 2727)	Noncancer, Noncardiovascular, Nondiabetes Causes of Death[c] (n = 1040)	Respiratory Deaths (n = 181)
<1	1.0	1.0	1.0	1.0
1–1.9	0.80 (0.68, 0.96)	0.92 (0.83, 1.02)	0.65 (0.56, 0.77)	0.42 (0.30, 0.57)
2–3.9	0.74 (0.62, 0.88)	0.85 (0.76, 0.94)	0.57 (0.48, 0.67)	0.46 (0.34, 0.63)
4–6.9	0.62 (0.50, 0.77)	0.95 (0.85, 1.07)	0.47 (0.38, 0.57)	0.29 (0.19, 0.44)
≥7	0.69 (0.49, 0.97)	0.87 (0.72, 1.04)	0.46 (0.33, 0.64)	0.23 (0.11, 0.50)

Note. Estimates were adjusted for age at baseline, smoking status, recent alcohol consumption, height, body mass index, and postmenopausal hormone use.
[a]*P* for trend < .001.
[b]*P* for trend = .25.
[c]Leading causes of death in this category: chronic obstructive pulmonary disease and emphysema (17.0%), cirrhosis (9.1%), and dementia (4.4%).

association. This spuriousness is impossible to remove through conventional analytic approaches, including controlling for confounding variables such as smoking and alcohol consumption, restricting the baseline cohort to an allegedly healthy group free of cardiovascular disease and cancer, lagging deaths by several years, and ceasing the updating of physical activity data once an individual is diagnosed with one of these conditions. Our baseline questionnaire did not enable us to identify women with cognitive decline, cirrhosis, or respiratory problems at study initiation (whether or not these conditions had been formally diagnosed by a physician), and thus we were unable to remove them to create a truly "healthy" initial cohort. In addition, we could not cease the updating of physical activity for women who developed such conditions over the course of follow-up, because we did not collect "incidence" data on these conditions until relatively late in follow-up. In any case, because there may not be an isolated "date" of onset of certain of the conditions (e.g., dementia, respiratory disease), physical activity is probably often curtailed before a clinical diagnosis is made.

There are 2 lines of evidence in this analysis that suggest the spuriousness of a component of the physical activity–mortality association. First, the strongest physical activity–mortality associations in the Nurses' Health Study cohort involved causes of death other than cancer, cardiovascular disease, and diabetes. It is likely, although not provable, that the strong inverse associations between physical activity and these other causes of death were largely spurious. Etiologic knowledge of many of these diseases does not support a strong causal role for physical activity. Because death from these conditions usually occurs many years after initial diagnosis, women in the Nurses' Health Study cohort who died from such causes probably were in poor health, and

thus inactive, for at least several years before death. Women who died of these causes were more likely to have reported major activity limitations than were women who died of cancer or cardiovascular disease, which lends support to the intuition that these diseases often cause severe reductions in physical activity. Without the ability to remove women with cognitive decline, cirrhosis, or respiratory disease from the cohort, it is impossible to remove the strong "reverse causation" association between low physical activity and high risk of death from these causes.

Similarly, in the Iowa Women's Health Study, in which the researchers excluded the first 3 years of death after the baseline activity measurement,[4] the strongest inverse association still was found between physical activity and death from respiratory causes. The study authors also noted that, unlike the situation with cancer or heart disease, they had no baseline information on history of respiratory illnesses among the study participants.

A second piece of evidence suggesting spuriousness is the sharp decrease in mortality risk seen among those with only 1 to 1.9 hours per week of physical activity, a decrease similar in magnitude to that observed in more active categories. On the basis of epidemiologic evidence regarding the effect of physical activity on the incidence of major chronic diseases, it is unlikely that 1 to 1.9 hours of recreational physical activity per week offers the same degree of benefit in reducing mortality risk as do higher levels of activity. If, however, individuals who are sedentary because of ill health and high risk of imminent death compose a portion of the reference group, all relative risks computed with regard to this reference group will be more strongly inverse than otherwise, and this spurious effect might be large enough to overshadow a truly inverse causal gradient.

The probable existence of spurious associations between physical activity and some major causes of death illustrates the problematic nature of studying all-cause mortality as an outcome and of attempting to quantify the precise magnitude of protection against premature mortality that is causally conveyed by physical activity. In this cohort, we conducted additional analyses of change in physical activity and found, as expected, that those who were consistently active, or who increased their physical activity level over time, were at reduced mortality risk relative to those who were consistently inactive or who decreased their physical activity level. We did not report these analyses here, however, because an analysis of change in physical activity level and mortality risk among older persons is especially likely to be plagued by the problem of reverse causation.

Despite the existence of a spurious component in the relationship between physical activity and mortality, there is a large body of evidence supporting the plausibility of benefits of physical activity. Randomized controlled trials have shown the beneficial effects of physical activity on blood pressure,[14,15] blood lipids,[16,17] and insulin sensitivity.[18–20] Observational studies of disease incidence, which are less susceptible to the effects of reverse causation than are studies of total mortality, have also consistently shown benefits. In the Nurses' Health Study cohort, previous studies of recreational physical activity and risk of various chronic diseases that are leading causes of death have shown that more active women are at lower risk of coronary heart disease,[21] stroke,[22] type 2 diabetes,[23] colon cancer,[24] and breast cancer[25] than less active women. □

Contributors

B. Rockhill conceived of specific hypotheses, planned the appropriate analyses, analyzed the data, and wrote

References

1. *Physical Activity and Health: A Report of the Surgeon General*. Atlanta, Ga: National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention; 1996.
2. Kaplan G, Seeman T, Cohen R, Knudsen L, Guralnik J. Mortality among the elderly in the Alameda County Study: behavioral and demographic risk factors. *Am J Public Health*. 1987; 77:307–312.
3. Blair S, Kohl H III, Paffenbarger R Jr, Clark D, Cooper K, Gibbons L. Physical fitness and all-cause mortality: a prospective study of healthy men and women. *JAMA*. 1989;262:2395–2401.
4. Kushi L, Fee R, Folsom A, Mink P, Anderson K, Sellers T. Physical activity and mortality in postmenopausal women. *JAMA*. 1997;277: 1287–1292.
5. Lee I-M, Hsieh C-C, Paffenbarger RS Jr. Exercise intensity and longevity in men: the Harvard Alumni Health Study. *JAMA*. 1995;273: 1179–1184.
6. Paffenbarger RS Jr, Hyde RT, Wing AL, Hsieh C-C. Physical activity, all-cause mortality and longevity of college alumni. *N Engl J Med*. 1986;314:605–613.
7. Sandvik L, Erikssen J, Thaulow E, Erikssen G, Mundal R, Rodahl K. Physical fitness as a predictor of mortality among healthy, middle-aged Norwegian men. *N Engl J Med*. 1993;328: 533–537.
8. Sherman S, D'Agostino R, Cobb J, Kannel W. Physical activity and mortality in women in the Framingham Heart Study. *Am Heart J*. 1994;83: 879–884.
9. Ainsworth B, Haskell W, Leon A, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc*. 1993;25:71–80.
10. Pate R, Pratt M, Blair S, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA*. 1995;273:402–407.
11. Rich-Edwards J, Corsano K, Stampfer MJ. A test of the National Death Index and Equifax Nationwide Death Search. *Am J Epidemiol*. 1994;140:1016–1019.
12. D'Agostino RB, Lee MLT, Belanger AJ, Cupples LA, Anderson K, Kannel WB. Relation of pooled logistic regression to time dependent Cox regression analysis: the Framingham Heart Study. *Stat Med*. 1990;9:1501–1515.
13. *SAS Users Guide, Version 6.12*. Cary, NC: SAS Institute Inc; 1996.
14. Leon A. Recent advances in the management of hypertension. *J Cardiopulm Rehabil*. 1991;11: 182–191.
15. American College of Sports Medicine. Position stand. Physical activity, physical fitness, and hypertension. *Med Sci Sports Exerc*. 1993; 25(10):i–x.
16. Stefanick M, Wood P. Physical activity, lipid and lipoprotein metabolism, and lipid transport. In: Bouchard C, Shephard R, Stephens T, eds. *Physical Activity, Fitness, and Health: International Proceedings and Consensus Statement*. Champaign, Ill: Human Kinetics; 1994:417–431.
17. Durstine J, Haskell W. Effects of exercise training on plasma lipids and lipoproteins. *Exerc Sport Sci Rev*. 1994;22:395–400.
18. Goodyear L, Hirshman M, Horton E. The glucose transport system in skeletal muscle: effects of exercise and insulin. *Med Sport Sci*. 1992;37: 201–215.
19. Henriksson J. Influence of exercise on insulin sensitivity. *J Cardiovasc Risk*. 1995;2: 303–309.
20. Yamanouchi K, Shinozaki T, Chikada K, et al. Daily walking combined with diet therapy is a useful means for obese NIDDM patients not only to reduce body weight but also to improve insulin sensitivity. *Diabetes Care*. 1995;18: 775–778.
21. Manson J, Hu F, Rich-Edwards J, et al. A prospective study of walking compared with vigorous exercise in the prevention of coronary heart disease in women. *N Engl J Med*. 1999; 341:650–658.
22. Hu F, Manson J, Stampfer M, et al. A prospective study of physical activity and risk of stroke in women. *Am J Epidemiol*. 1999;149:S29.
23. Hu F, Sigal R, Rich-Edwards J, et al. Walking compared with vigorous physical activity and risk of type 2 diabetes mellitus in women. *JAMA*. 1999;282:1433–1439.
24. Martinez ME, Giovannucci E, Spiegelman D, et al. Physical activity, body size, and colorectal cancer in women. *Am J Epidemiol*. 1996; 143:S73.
25. Rockhill B, Willett W, Hunter D, Manson J, Hankinson S, Colditz G. A prospective study of recreational physical activity and breast cancer risk. *Arch Intern Med*. 1999;159: 2290–2296.