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Using Longitudinal Data to Estimate the Effect of Starting to Exercise on the Health of Sedentary Older Adults

Paula Diehr
University of Washington, pdiehr@u.washington.edu

Calvin Hirsch
chhirsch@ucdavis.edu

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Paula Diehr Ph.D[1]. and Calvin H. Hirsch M.D[2].

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1 Depts. of Biostatistics and Health Services, University of Washington, Seattle, WA 98195. Ph: 206-543-8004; Fx: 206-543-3286 E-mail: pdiehr@u.washington.edu

2 Depts. of Medicine and Public Health Sciences, Div. of General Medicine, University of California, Davis Medical Center, PSSB-2400, Sacramento, CA 95817. Ph: 916-734-7005; Fx: 916-734-2732. E-mail: chhirsch@ucdavis.edu

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Abstract

Background
It is difficult to estimate the effect of exercise on future health from observational data because exercising may be both a cause and an effect of health status. Unadjusted analyses suffer from selection bias (healthier persons more likely to exercise), while adjusted analyses may adjust away some of the benefits of exercise.

Objective
To obtain a "low-bias" interpretable estimate of the effect of exercise on future health.

Methods
We used data from the Cardiovascular Health Study, a longitudinal study of 5,888 older adults. The number of blocks walked in the previous week, collected annually, were classified as Sedentary (less than 7 blocks per week), Moderate, or Active (28 or more blocks per week). The primary "low bias" analysis was restricted to persons who were both Sedentary and Healthy (in Excellent, Very Good, or Good self-reported health) in the two years before baseline. Self-reported health status (Healthy versus Sick or Dead) at follow-up was regressed on the level of exercise at baseline, variously including or excluding demographics, health prior to baseline, and health at baseline.

Findings
Exercise trends were associated as expected with age, sex, and race. Healthy persons were more likely than Sick to start to exercise, and Sick Active persons were more likely to become Healthy than Sick Sedentary persons. In the total sample, 77% of persons who were Active at baseline were Healthy at follow-up, as compared with 49% of Sedentary persons, a difference of 28 percentage points that is difficult to interpret. In the subset who were both Sedentary and Healthy in the two years before baseline, the difference was only 14 percentage points. That difference declined to 12 points after adjustment for demographics, and to 9 points after adjusting for other health variables measured prior to baseline. After adjustment for health variables measured at baseline (possibly in the causal pathway) the difference dropped to 7 points and was no longer significantly different from zero. Similar findings occurred when survival was the outcome. The apparent effect of exercise on health was substantially smaller if persons who were Dead at follow-up were excluded.

Conclusion
At least a third of the apparent benefit of exercise could be explained by selection bias. Where possible, observational studies of the effects of exercise should measure exercise at every period instead of just at enrollment. This permits incorporating exercise and health data prior to baseline. Analysis should also allow for the benefits of exercise on survival. The "low-bias" estimate of the benefit to a Healthy Sedentary older adult of becoming Active (walking 28 or more blocks per week, median = 48) was 7 percentage points for being alive 2 years later, and 9 percentage points for being alive and healthy. A modest program of walking may confer modest health benefits.

Using longitudinal data to estimate the effect of starting to exercise on the health of Sedentary older adults

1.0 Introduction

Physical activity is recommended for persons of all ages, but there have been relatively few long-term randomized trials of the effects of exercise on the health of older adults, and their results were equivocal. [1] [2] Observational data have been used to address this gap. Some studies have examined the association of exercise with mortality for older adults. [3] [4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [14] Other studies have examined the association of exercise with function and disability [hirvensalo], [15] [16] [17] [18] [19] [20] [21] [22] [23]

The use of observational data to estimate the effect of exercise on health outcomes suffers from three potential biases. The first is selection bias. Health status may contribute to exercise behavior, instead of the other way around. When selection bias is present, the apparent effect of exercise will usually be over-estimated. A second potential bias is that correcting for selection bias, by removing sick persons or adjusting for health-related variables at baseline, may lead to under-estimation of the effect of exercise if the health-related variables lie in the causal pathway between exercise and the outcome. A third possible bias occurs in the treatment of death. It is common to study health status only in persons alive at follow-up, which removes any potential benefits of exercise on preventing mortality. Analyses that exclude persons who die are not prospective, because a person's survival status at follow-up is not known at baseline, and results are likely to be biased in favor of the group with more deaths. Another problem is the difficulty of interpreting such regression results, since the population to which they apply is often unclear.

This paper will use longitudinal data on the number of blocks walked in a week to study the relationship between exercise on future health. We will describe exercise patterns in the sample, propose a discussion model of how exercise affects health, propose a “low-bias” design that minimizes the three types of bias mentioned above while making the results more interpretable, estimate the effect of exercise on health using the low-bias design, and analyze the same data using other approaches.

1.1 Discussion model of the relation of exercise to health

Consider a simple model of the effect of exercise on health, for the purpose of discussion only. Let the level of exercise be binary, Active or Sedentary, and assume that each person has a natural or “latent” health status: Excellent, Very Good, Good, Fair, or Poor. Next, we will assume that changing from Sedentary to Active causes persons to improve health one level above their latent health (e.g., from Good to Very Good), and that stopping exercise will cause a person to decline 1 level in health. This model is partly illustrated in Figure 1. The current status of persons whose latent health is Fair is either Good (if they are Active—box 1), or Fair (if they are Sedentary-box 2), and persons with latent Good health can be in either Very Good or Good health depending on their activity. The future status of persons in box 1 may be either Active and in Good health, or Sedentary and in Fair health (boxes 5 and 6). (The future states for boxes 2 and 3 are not shown). The numbers in parentheses for the current status represent a hypothetical population of 10,000 persons, distributed approximately proportional to prevalence data from the study described below.

[Figure 1 about here]

Further, assume that Sedentary persons whose health improves one level will begin to exercise. (They may of course also start to exercise for non-health-related reasons). The model is specific so that the effect of various study designs can be described. It is surely over-simplifed, but if we relaxed the “exactly” to “on average” the discussion model might be approximately applicable to a real study population.

1.2 Possible analytical designs

1.2.1 Analytic design that favors the Active group

Consider a design in which exercise status is ascertained at baseline, and health status is determined at follow-up. The treatment group is then the currently Active (box 1 + box 3 in Figure 1) while the control group is the Sedentary (box 2 + box 4). The treatment group is thus made up of persons whose current health is either Good or Very Good, while the controls’ current status is either Fair or Good. The latent health status of 60% of the treatment group is “Good” as compared with 54% of the controls. In terms of either current or latent health status, the treatment group is likely to be healthier at follow-up than the control group because it was healthier to start with, even if exercise did not improve their health. Such a design, rarely used, is likely to be biased in favor of exercise. .

1.2.2 Analytic design that favors the Sedentary group

In one commonly used design, analysis is restricted to persons with “Good” health at baseline. (This is conceptually similar to adjusting for baseline health by regression). The health of the Active and Sedentary persons is compared at follow-up. This design is appealing because, as in a randomized trial, health is uncorrelated with exercise at baseline (as everyone is in “Good” health). In Figure 1, the treatment and control groups are boxes 1 and 4, respectively. Unfortunately, all persons in the treatment group have Fair latent health while the controls have Good latent health. Further, persons in box 1 (treatment group) will have either Good or Fair health in the future (boxs 5 and 6) while the controls (box 4) may be either Very Good or Good (boxes 7 and 8). Based on either the latent health or the future trajectory, this analysis is clearly biased against the treatment group, which has worse latent health and can not improve in health, while the controls can improve. Considered this way, this design seems both illogical and biased against showing an effect of exercise.

1.2.3 A "low-bias" analytical design

A randomized trial of exercise might randomize Sedentary persons initially in Good latent health (Box 4 of Figure 1) to treatment or control status. After a while, most persons in the treatment group will move to box 7 and controls will move to box 8. Comparing the health of these two groups will give the correct estimate of the effect of starting to exercise on Sedentary persons in Good health (i.e., that health improves one level).

In cross-sectional studies, there is no way to estimate latent health, but longitudinal health and exercise data may be useful. For example, if the discussion model holds approximately, the latent health status of a person who has been Sedentary for several years is likely to be the same as his latent health. Here, we used 5 sequential years of longitudinal health and exercise data for the same person, in years referred to here as -2, -1, 0, +1, and +2. These 5-year sequences are referred to as "quintets" of data. Analysis will be restricted to the quintets in which a person was Sedentary and in "Good" health in years -2 and -1. The dependent variable is health status at year +2 (follow-up), coded as a binary variable (Excellent, Very Good, Good = 1; Fair, Poor, Dead = 0). The treatment subjects are those who became Active at baseline, while the controls remained Sedentary. Table 1 illustrates this design. Cells marked X denote health data that are available but not part of the formal design. The analysis will estimate the effect of exercise at baseline (year 0) on health at follow-up, controlled by subject selection for prior exercise and health, and also controlling by regression for age, sex, race, and other health variables measured in years -1 and -2.

[Table 1 about here]

The proposed design should have little selection bias because it controls for health variables prior to baseline. It does not specifically control for health status at baseline, and so does not run the risk of adjusting away the benefits of exercise. The outcome is interpretable as the effect of starting to exercise for sedentary, healthy older adults. And finally, because the dependent variable includes death (coded as 0 for "Not Healthy"), persons who die are not removed from the analysis.

One unresolved issue is exactly when persons in the treatment (Active) group actually started exercising. We know only that exercise started between year -1 (when they reported being Sedentary) and baseline (when they reported being Active). Fortunately, the available dataset includes a measure of self-rated health 6 months before baseline, which may help to control for benefits of early exercise in that period.

2. Methods

2.1 Data

Data came from the Cardiovascular Health Study (CHS), a population-based longitudinal study of risk factors for heart disease and stroke in 5888 adults aged 65 and older at baseline.[24] Participants were recruited from a random sample of Medicare eligibles in four U.S. communities, and extensive data were collected during annual clinic visits and telephone calls. Members of the original cohort of 5201 participants, recruited in about 1990, had up to ten annual clinic examinations. A supplemental cohort of 687 African Americans, recruited in about 1993, had up to seven annual examinations. Follow-up for cardiovascular events was virtually complete for surviving participants.[25] Additional data on health status and events were collected by telephone 6 months after each clinic visit.

"Exercise**"** is based on the reported number of "city blocks or the equivalent" walked in the previous week, which was collected in 1990 and annually from 1992 to 1999. Walking is a major component of physical exercise as measured in the Minnesota Leisure Time Activities questionnaire,[26] which was administered at enrollment. The two measures are highly correlated (data not shown). The blocks data were coded into approximate tertiles as low/Sedentary (<7 blocks per week), Moderate (7-27 blocks), and high/Active (28 or more blocks per week). We used three exercise categories rather than the 2 in the discussion model to permit ascertainment of monotonic trends (dose effects).

Other health-related variables that were collected every year included body mass index (BMI) - measured weight in kilograms divided by height in meters squared; the Modified Mini Mental State Examination score (3MSE); [24] activities and instrumental activities of daily living (ADL and IADL); the Center for Epidemiologic Studies Depression score (CESD); [25] number of bed days in the previous two weeks; whether the person was hospitalized in the prior six months; the measured time it took to walk 15 feet; whether the person had been hospitalized in the previous year. Finally, we noted whether the person had cardiovascular disease (CVD), defined as having angina, coronary heart disease, congestive heart failure, claudication, myocardial infarction, stroke, transient ischemic attack, angioplasty, or coronary artery bypass surgery at the survey time or earlier. A person who is sick by this definition (has CVD) cannot become healthy (no CVD) in the future. All of these variables were dichotomized with favorable values coded as 1, and less favorable values or death coded as 0, as indicated in Table 3 and Appendix Table A and explained in more detail elsewhere. [27]

Data missing between a person's first and last observed measures were imputed from a person-specific regression of the variable on the log of time from the last known measure. Approximately 5% of the relevant data were imputed.

2.2 **Analysis**

The primary analysis used the low-bias design described above to estimate the effect of exercise on Sedentary older adults who were earlier in "Good" health. We also examined other designs that have been used in the literature. The primary dependent variable was a binary variable representing "Alive and Healthy at follow-up"and the independent variable of interest was the exercise category at baseline. Ordinary least squares regression was used rather than logistic regression so that coefficients could be interpreted as the amount of increase in the proportion Alive and Healthy at follow-up. This is appropriate when the outcome is not rare.[28] In the designs that we examined, analyses may or may not include the health information prior to baseline or at baseline, and may or may not include the deaths in the outcome variable.

The primary outcome, measured two years after baseline, was whether the person was Healthy (Excellent, Very Good, or Good self-reported health) or Not Healthy (Fair, Poor, or Dead). Dichotomizing the health status information may lose some information. (For example, boxes 7 and 8 for Figure 1, both groups would be classified as "Healthy" on the dichotomized variable and no exercise effect on health would be detected). To explore this consideration more fully we repeated the analyses coding the Excellent to Poor categories as .95, .90, .80, .30, and .15, respectively. The interpretation of this recoded variable is the approximate probability that a person with this level of self-reported health will be Healthy one year in the future (PHF), as verified in several different data sets. [29] Because Dead persons can not be Healthy in the future, persons who are Dead receive a zero on this measure. PHF was used as an alternative outcome. Other alternative outcomes were health with the deaths excluded, and survival. A robust standard error was used to account for correlation among the quintets, because some persons contributed an eligible quintet to more than one exercise group.

Under the assumption that the low-bias analysis gives an approximately unbiased estimate of the treatment effect, we hypothesized that analyses that do not control for prior health and exercise will over-estimate the effects of exercise, and that analyses that adjust for baseline health or that exclude the deaths will under-estimate the exercise effect.

3. Findings.

3.1 Exercise Categories over 7 years: natural history

Figure 2 shows the patterns of exercise from 1993 to 1999 for the 5555 persons alive in 1993, by ethnicity and gender. In each column, activity level is represented by shading. For example, in 1993, 48% of the white men (upper-right panel) were in the high/Active exercise category, and 24% were in the low/Sedentary category. (There is also a “missing” category which represents the few missing observations that were not imputed because there were no data the year before or after).

[Figure 2 about here]

Over time, the percentage of Active persons grew smaller while the percent Dead increased and the percent in the Moderate and Sedentary categories stayed about the same. Even though the death rate was higher for men, proportionately more women were Sedentary and fewer were Active compared to men, and blacks were more Sedentary and less Active than whites. There were some small differences in age and health in 1993: for white women, mean age was 75.2, and 78% were Healthy; for white men, the values were 76.0 and 80%; for black women 73.92 and 58%; for black men 73.3 and 62%. Blacks had slightly lower mortality than whites because of the age differences.

3.2 Probabilities of Transition

Table 2 shows one-year probabilities of transition among states by age (under 75 versus 75-100) and sex, for blacks and whites combined. The unit of analysis is the transition pair, defined as two measures for the same person one year apart. A person could contribute up to 6 transition pairs to this table. The first line shows information for 709 women who were aged 65-74, were Sick (in Fair or Poor health), and were Sedentary (<7 blocks per week) at time 1. One year later, at time 2, 4.9% had died, 56.8% were still Sick and Sedentary, and 1.7% had become Healthy and Active.

[Table 2 about here]

Table 2 shows that most of the CHS enrollees (technically, transition pairs) were Healthy. Most (the plurality) of the Healthy persons were Active and most of the Sick persons were inactive. Mortality was related to age, sex, and exercise group in predictable ways, and there was substantial transition among the health states. There is evidence that feeling Healthy "causes" exercise, because the probability of moving from Sedentary to Active in one year was higher for Healthy persons than for Sick persons. Further, Active Sick persons were more likely to become Sedentary than were Active Healthy persons. Alternatively, exercise could be said to "cause" health, because the probability that a Sick person is Healthy one year later was higher for Active than for Sedentary persons.

3.3 Patterns over time in the low-bias analysis sample

To implement the design in Table 1, we identified a subset of 678 CHS participants who were Sedentary and had "Good" self-reported health in both year -2 and year -1. At baseline (year 0), 427 were still Sedentary while 185 had transitioned to Moderate, and 66 to Active. Table 3 shows descriptive statistics for these persons as a function of their exercise category at year 0 (baseline).

[Table 3 about here]

Two years before baseline, all were in exercise category 1 (Sedentary), by design. At baseline the three groups were in category 1, 2, or 3 respectively, by design, and the "average category" was different at follow-up. More meaningfully, the following line shows that the median number of blocks walked in each period was consistent with the exercise category on the previous line. Note that the median number of blocks in the Active category dropped from 48 at baseline to 10 at follow-up.

The percentage who were Healthy (Excellent, Very Good, or Good health, as opposed to Fair, Poor or Dead) 2 years before baseline was 100%, because all were in "Good" health by design. At baseline, those percentages had dropped to 76.6% 82.7%, and 87.9% for the 3 exercise groups respectively. That is, at baseline there was already a monotonic relationship (dose effect) between health and exercise category, which might have represented selection bias or might have represented the early benefit of exercise, since persons could have started to exercise any time in the year prior to baseline. There is a similar relationship at follow-up. The following line shows the percentage who were Healthy six months before baseline. The data suggest that some of the high exercisers may have started to exercise in the first 6 months of the period, and had already experienced the benefits.

The survival rate at follow-up was monotone in the amount of exercise at baseline. Active persons were slightly more likely than the Sedentary to be overweight or obese. There were small differences among the exercise groups in age, sex, and race (with more men in the Active group). The final lines show that at all 3 time periods, Active persons, compared to Sedentary persons, had less ADL and IADL impairment, scored higher on the 3MSE, and spent fewer days in bed. At follow-up, more Active than Sedentary participants could walk 15 feet in less than 10 seconds in the timed walk test. People who started to exercise were more likely to have avoided being in the hospital, and substantially more likely to be free of cardiovascular disease, even 2 years before they started to exercise.

The exercise groups thus differed on the health variables at baseline, in part because they were different 2 years before baseline, and perhaps in part because there was a change in health from Year - 1 to baseline (either before or after the choice to exercise more). There was often a "dose response", with a monotonic relation between the variable and the exercise category. To increase the sample size for the regression analyses we included a second group of 285 persons (quintets) who were Sedentary and either in Excellent or Very Good health in both of the two years before baseline. The trends over time for that cohort are in Appendix Table B .

3.4 Regressions with Trajectory Matching

We regressed health at follow-up on exercise at baseline, and controlled sequentially for other covariates in Table 3. Column 1 of Table 4 shows the results of the primary analysis. “Sedentary” is the reference category, and only the coefficients for the Active group are shown. Asterisks denote whether regression coefficients were significant at the .01, .05, or .10 two-tailed level of significance.

[Table 4 about here]

Step 1 shows that, with only the baseline exercise category in the regression (plus a dummy variable denoting whether the health during the 2 pre-baseline years was Good both years or Very Good/Excellent both years), the proportion alive and Healthy at follow-up in the Active group was 0.136 higher (13.6 percentage points higher) than in the Sedentary group. This difference was statistically significant at the .01 level. The regression coefficients for the Moderate exercise group were usually smaller and less significant than those for the Active group (a dose-response effect), and are shown in Appendix Table C.

Step 2 added age, sex, and race, which decreased the coefficient (effect of exercise) slightly. Step 3 added the other health variables that were measured in the year before baseline, and is what we call the “low-bias” analysis. Step 3 could not have controlled for any variables in the causal pathway (i.e., that were “caused” by exercise) because the variables were measured while everyone was sedentary. Step 4 added health status measured 6 months before baseline (when some unknown proportion, of those who were Active at baseline had already become Active, and some may have already achieved their exercise benefit). The coefficients did not change much at this step. Step 5 added self-rated health at baseline, a variable that is probably in the causal pathway, and step 6 added the remainder of the baseline health variables. At every step, the estimated effect of becoming Active became smaller and less significant. Interactions of the exercise category with age, sex, race, and whether the prior health pattern was Good both years or Excellent/Very both years were examined (not shown). There were no consistent results and these interactions were not considered further.

The low-bias estimate of the effect of becoming Active, using the binary outcome, was thus **.088** (95% c.i. .008, .176). We also used the PHF coding of the outcome as described above. The 6 regression coefficients, shown in more detail in Appendix Table D were: .108, .093, .079, .081, .068, .060, where **.079** (95% c.i. .024, .134) is the "low-bias" estimate of the effect of exercise on the probability of being Healthy one year after follow-up. All estimates were significantly different from zero. A further set of analyses was performed with 2-year survival as the outcome. The 6 regression coefficients were .091, .080, .073, .074, .068, .062, and at the first 4 steps were significantly different from zero. The low-bias estimate of the effect of becoming Active on 2-year mortality is thus **.073** (95% c.i. .022, .124). Additional results are in Appendix Table E.

3.5 Alternative regressions

Table 4 shows some alternative regression analyses. For column 2, we removed the health constraints in the 2 years prior to baseline, requiring only that persons be Sedentary in both years. The available sample size nearly doubled, and the effect size at

Step 2 was nearly twice that in column 1. However, in Step 3 and following, where the measures of health in the year before baseline were added, the effect size became similar to column 1, though more significant because of the larger sample size.

Column 3 shows results for the analysis that also removed the restrictions on prior exercise. This again doubled the sample size, and gave a somewhat larger exercise effect, which was always significant due to the larger sample size. The fourth column shows the results of the most typical analysis, in which the health and exercise information prior to baseline is unavailable, and only the baseline health variables were used for adjustment. Effect sizes in columns 3 and 4 were somewhat higher than those in columns 1 and 2, in part because the population is quite different.

3.6 Remove the Deaths

As mentioned above, eliminating the possible effect of exercise on survival not only makes the design retrospective but is also biased against finding an effect of exercise, even if the original study is a randomized controlled trial. Results of a similar set of regressions are shown in columns 3 and 4 of Appendix Table C, conducted after removing persons who were Dead at follow-up. The regression coefficients for the Active group were as follows: .067, .056, .036, .039, .026, and .020, none significantly different from zero. The estimated effects of exercise were thus smaller and the results less significant, as compared with columns 1 of Table 4.

4.0 Summary and Discussion

This paper has presented new information about exercise over time, and about one-year transitions among health and activity states, that were different by age, for men and women, and for blacks and whites. These findings are not the main topic of this paper and are not addressed further. The interested reader may multiply the percent in each column of Table 2 by the row total (divided by 100) to recreate the original counts. Although the discussion model in Figure 1 ignores many factors that relate to changes in exercise and health, it illustrates the types of biases inherent to different designs.

The regression coefficients at step 3 in Table 4, columns 1 (and 2), show "low-bias" estimates of the effect of Sedentary persons in Good (or average) health becoming Active. Column 3, step 3, which also includes only the data before baseline, may still have controlled away effects of exercise because there is no way of knowing when or why the person started to exercise. Both selection bias and over-adjustment are possible in column 3, and the resulting higher regression coefficient at step 3 may reflect those biases.

The most common analysis of observational data regresses health at follow-up on baseline exercise, controlling for baseline variables, similar to column 4 of Table 4. The very large exercise effect after control for demographics shrinks substantially after control for baseline health variables (steps 5 and 6), some of which may have already been improved by exercise (i.e., may be in the causal pathway). We can be reasonably sure that the exercise effect is no larger than .255 and that perhaps, if there are no unmeasured confounders, it is no smaller than .078. In addition to the unacceptably large range of possible results, the interpretation of this analysis is problematic. The analysis adjusted for baseline health, effectively comparing two equally Healthy groups at baseline, where one is Active and the other Sedentary. As discussed in section 1.2.2, under the discussion model the "latent" health of the Active group may have been lower than the health of the Sedentary, and the controls may have had more opportunity to improve their health than the treatment group. This analysis thus seems likely to understate the effects of exercise, although there is no way to know whether that was the case. Further, the results are generalizable to a population that is difficult to define.

The analysis in column 1 of Table 4 avoids many of these problems, because it matched trajectories on prior exercise and health to specify a typical population of interest: Sedentary, Healthy persons. Up through step 3, no variables in the causal pathway are used, and the analysis at that step can not have over-corrected for health status.

This analysis does, however, suffer from the lack of data on just when, between year -1 and baseline, persons became Active. If they first became Active and then became healthier, this improved health should not be adjusted away. If, on the other hand, their health improved and then they started to exercise, that prior improvement in health should be controlled for. In a supplementary analysis, we pretended that the quintets of data were 6 months rather than 1 year apart, and examined persons who fit the criteria for the Active group at "baseline". As shown in Appendix F, "6 months before baseline"only 9.5% had improved health and only 39% had started to exercise. Nearly 5 times as many people changed to exercise without improving their health as changed their health before starting to exercise. This finding suggests that in the actual study, many more persons in the Active group started to exercise before changing their health than started to exercise because their health had changed. This would make adjustment for health 6 months before baseline inappropriate because most of the changes observed 6 months before baseline would be due to early effects of exercise. Adjusting for it (at step 4) over-adjusted only for persons who started to exercise early on, but correctly adjusted for those who became Healthy first. Fortunately, the results for step 3 and step 4 were quite similar, suggesting that the effect of early exercise were not adjusted away.

In Table 4, trajectory matching only on prior exercise (column 2), gave results comparable to column 1 at step 3. Inclusion of health status 6 months before baseline had more effect under this model, presumably because the population included persons who were Sick before baseline and more change was possible. Either model seems appropriate.

Removing the deaths (Appendix Table C columns 3 and 4) had the expected consequence of under-estimating the effect of exercise, and in a non-prospective way. Exercise studies should attempt to include the possible effect of exercise on survival.

Unfortunately, in many cohort studies, exercise data are collected only at baseline, and no prior information is available to permit trajectory matching. (This could have been remedied by collecting exercise information at every time point instead of just at baseline). In that case, a stepwise approach that first enters variables that are clearly not in the causal pathway, then those that might be in the pathway, and finally those very likely to be in the causal pathway is advised.

This study found, in a low-bias analysis, approximately a 9 percentage point improvement in Sedentary Healthy persons who started to become active compared with those who remained sedentary, even after controlling for a large number of health-related variables measured before baseline. A reason for some of this improvement may be that Active and Sedentary persons evaluate their health differently. Idler and Benyamini have reported on many different interpretations of self-rated health.[30]

Limitations

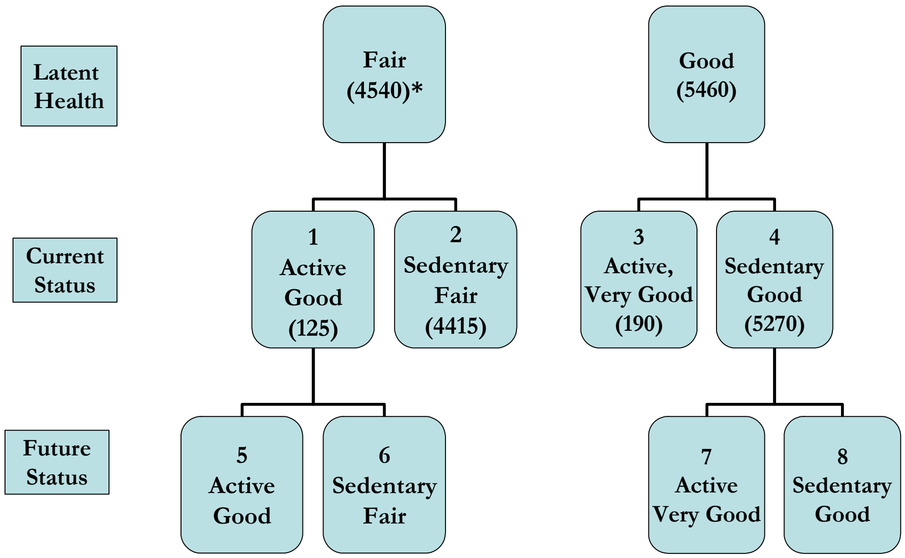
These models have been compared for only one dataset, and need to be verified. It is a limitation that the start of exercise was not known exactly. The number of blocks walked is not a perfect surrogate for exercise, since, for example, a person involved in a vigorous cycling program would have less time available for walking. In addition, the number of blocks walked in a single week may not be typical of the entire year and is highly variable over time. Misclassification when assigning persons to groups usually results in conservative comparisons among the groups. The fact that we have found a significant exercise effect even with these flawed exercise data suggests the effect may be stronger than seen here. We did not have sufficient data to consider the effect of exercise on Sick persons, which would also have been of interest.

Conclusion

The apparent effect of exercise in longitudinal studies is potentially subject to bias. It is desirable to match on the trajectory of prior exercise and health, and to include possible benefits of exercise on survival in the outcome measure. The low-bias analysis estimated a significant effect of a 9.2 percentage point difference (95% c.i. 0.8 to .17.6) in two years between the Active and the Sedentary. For survival, the difference was 7.3 percentage points (95% c.i. 2.2 to 12.4). Those who became Active walked as little as 28 blocks per week (median 48 blocks), suggesting that even small increases in exercise may be beneficial for Sedentary Healthy older adults.

Figure 1

Discussion Model



* Number of subjects in hypothetical population of 10,000, based on the prevalence data for persons who were Sedentary the two previous years and are either in Fair health both previous years (latent Fair health), or in Good health both previous years (latent Good health).

Figure 2

Natural history of exercise in CHS from 1993 to 1999, by Gender and Ethnicity.

Sedentary: walked < 7 blocks in previous week
Active: walked $\geq$ 28 blocks in previous week

Table 1
A Low-bias Design

Year: **Group**		**-2**	**-1**	**-0.5**	**0 (baseline)**	**+1**	**+2 (follow-up)**
Tx	**Activity**	Sedentary	Sedentary		Active		
	EVGGFPD	Good	Good	X	X	X	E/VG/G=1. F/P/D=0
Control	**Activity**	Sedentary	Sedentary		Sedentary		
	EVGGFPD	Good	Good	X	X	X	E/VG/G=1. F/P/D=0

EVGGFPD: Self-rated health (excellent/very good/good/fair/poor / Dead) (EVGGFP)
X: EVGGFP and other health measures were available at this time but not used in the "low bias" analysis.

Table 2
Exercise and Health Transitions by age and sex (up to 9 per person)

Health and Blocks at Time 2 (%) [1]

Age	Sex	Health and Blocks at Time 1 [1]	Dead	Sick Sed	Sick Mod	Sick Active	Healthy Sed	Healthy Mod	Healthy Active	# of Pairs
65-74	**F**	**S Sed**	4.9	56.8	11.3	4.1	18.2	3.0	1.7	709
		S Med	4.3	33.3	24.7	9.0	9.7	13.3	5.7	279
		S Active	2.8	21.6	14.2	35.8	8.0	7.4	10.2	176
		H Sed	1.8	12.7	2.8	1.4	51.5	19.7	10.2	1310
		H Med	0.8	4.7	3.9	1.6	27.5	38.7	22.8	1152
		H Active	0.2	1.8	2.0	2.6	12.2	24.8	56.4	1320
	M	**S Sed**	12.3	49.6	14.6	5.0	11.2	5.0	2.3	260
		S Med	3.9	23.5	30.2	17.9	6.1	12.3	6.1	179
		S Active	9.5	10.9	14.9	33.8	6.0	4.5	20.4	201
		H Sed	2.4	9.3	4.7	2.4	43.8	23.8	13.6	450
		H Med	1.6	4.4	5.4	2.8	19.4	37.8	28.7	614
		H Active	0.9	1.1	1.3	4.7	6.3	18.1	67.6	1138
75-100	**F**	**S Sed**	11.4	60.7	6.1	1.3	16.9	2.7	0.9	2407
		S Med	5.9	35.3	27.3	5.2	10.1	10.7	5.4	572
		S Active	8.8	18.3	19.2	25.0	4.6	9.2	15.0	240
		H Sed	3.2	17.9	2.5	0.6	55.3	15.6	4.9	3217
		H Med	1.5	6.3	4.6	1.3	30.6	39.4	16.2	1894
		H Active	1.3	3.7	2.6	4.0	15.3	23.3	49.8	1606
	M	**S Sed**	19.8	51.1	9.2	3.3	11.1	3.8	1.6	1052
		S Med	14.3	25.8	27.4	10.8	9.2	7.6	4.9	511
		S Active	15.0	15.9	14.1	32.9	3.6	4.8	13.8	441
		H Sed	6.2	15.5	3.2	1.2	45.6	19.1	9.2	1391
		H Med	2.9	5.3	5.6	2.6	23.2	36.4	23.9	1391
		H Active	2.0	2.5	2.9	5.3	11.0	20.5	55.8	2012

1 Low/Sedentary is walking <7 blocks per week; high/Active is walking at least 28 blocks per week. Healthy is Excellent, Very Good, or Fair health; Sick is Fair or Poor health. Time 1 and Time 2 are 1 year apart.

Table 3
Health and demographics
of 678 Persons Sedentary and in "Good Health" in Years -2 and -1
before and after baseline

Column #	1	2	3	4	5	6	7	8	9
	2 yrs before B/L			Baseline			Follow-up [2]		
Exercise Category at Baseline [1]	Sed	Mod	Active	Sed	Mod	Active	Sed	Mod	Active
# of cases	427	185	66	427	185	66	427	185	66
Exer Category [1]	1	1	1	1.0	2.0	3.0	1.2	1.4	1.8
Blocks (Median) [3]	2	3	3	1	12	48	1	4	10
Healthy (%) [1]	100.0	100.0	100.0	76.6	82.7	87.9	64.6	71.9	74.2
Healthy 6 mos prior (%)				81.3	77.8	84.8			
Alive (%)	100.0	100.0	100.0	100.0	100.0	100.0	90.2	93.5	98.5
Age (mean)	76.7	75.3	75.1	78.7	77.3	77.1	80.7	79.3	79.1
Male (%)				27.6	29.2	30.3			
White (%)				85.0	76.8	86.4			
BMI>normal (%) [3]	68.6	65.2	73.4	67.0	60.9	75.0	64.8	60.8	69.8
No ADL	75.4	84.3	93.9	68.4	81.6	84.8	57.8	65.9	78.8
No IADL	59.3	67.6	71.2	49.2	65.4	68.2	39.6	50.8	59.1
CESD < 10	84.5	82.2	90.9	81.0	85.9	90.9	71.7	73.5	75.8
3MSE > 89	85.2	91.9	92.4	82.4	87.6	87.9	70.0	81.1	86.4
No Bed Days	95.8	94.6	97.0	94.1	97.8	97.0	84.5	85.4	95.5
Walk 15' <10 sec	91.5	98.4	97.0	89.1	95.7	98.5	76.1	83.2	95.5
No Hospital days	87.8	91.4	89.4	85.2	88.6	93.9	80.3	84.3	87.9
No CVD	71.7	66.5	86.4	65.3	63.8	84.8	55.7	55.7	80.3

1 Low/Sedentary is walking <7 blocks per week; high/Active is walking at least 28 blocks per week. Healthy is Excellent, Very Good, or Fair health; Sick is Fair or Poor health, or (at follow-up) Dead.
2 Follow-up is 2 years after Baseline.
3 BMI and Median Blocks are calculated for living persons only. All other variables code Dead as zero.

Table 4 Alternative Regressions,
Coefficients comparing Active to Sedentary

	Column	PRIMARY 1	2	3	4
	Health yrs -2, -1	**Both G or Both VG**	**Any**	**Any**	**Unknown**
	Activity yrs -2, -1	**Sedentary**	**Sedentary**	**Any**	**Unknown**
N	**N Persons**	1127	2535	5122	5123
	N Clusters				
		988	2144	5122	5123
Step	**Variable added**				
1	Exercise + indicator for prior E/VG (vs G) (column 1 only)	.136 ***	.250 ***	.284 ***	.283 ***
2	+age, sex, race	.116 ***	.232 ***	.256 ***	.255 ***
3[1]	**+ other health vars in year -1**	**.088****	**.089 *****	.117 ***	
4	+E/VG/G in year -0.5	.091 **	.076 **	.098 ***	
5	+E/VG/G at baseline	.074 *	.054 *	.071 ***	.127 ***
6	+other health variables at baseline	.059	.042	.091 ***	.078 ***

***p<.01, 2 tailed, **p<.05 2-tailed,. * p<.10 2-tailed.
1 Line 3 is the “low-bias” estimate for columns 1 and 2

Appendix Table A

Variable Definitions and Symbols

VARIABLE	DEFINITION OF VARIABLE	DEFINITION OF HEALTHY
ACTIVIES OF DAILY LIVING (ADL)	Do you have any difficulty walking around your home? Getting out of bed or a chair? Because of health or physical problems do you have any difficulty or are you unable to ... eat, including feeding yourself? Dress yourself? Bathe or shower? Use the toilet, including getting to the toilet?. # (of 6).	0 ADLs
BED DAYS	Days spent in bed in past 14 days.	0 Days
BLOCKS WALKED	# of blocks walked in last week.	> 9 blocks
BODY MASS INDEX (BMI)	Weight (kg) / ht^2 (meters).	20-30
DEPRESSION (CESD)	CESD has 10 depressive symptoms rated on a scale from 0 to 3. The sum of items has a maximum of 30.	< 10
EVGGFP	Is your health: Excellent, Very Good, Good, Fair, or Poor**)**.	Excellent, Very Good, or Good
HOSPITAL	100 if hospitalized in previous 6, 0 if not	Not hospitalized
INSTRUMENTAL ACTIVITIES OF DAILY LIVING (IADL)	Because of health or physical problems do you have any difficulty or are you unable to ... Do heavy housework like scrubbing floors or washing windows; or yard work, like raking leaves or mowing? Do light housework? Shop for personal items? Prepare your own meals? Manage your money, such as paying bills? Use the telephone? # (of 6).	0 IADLs
MODIFIED MINI MENTAL STATE EXAM (3MSE)	Coded 0 to 100, 100 is best	80-100
SYSTOLIC BLOOD PRESSURE (SBP)	Systolic Blood Pressure	# 125
TIMED WALK	# of Seconds to walk 15 feet.	< 10 seconds

Appendix Table B
Health and demographics
of 285 Persons Sedentary and in "Good Health" in Years -2 and -1
before and after baseline

Descriptive statistics for E/VG E/VG SedSed									
Column #	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
	2 yrs before B/L			**Baseline**			**2 yrs after B/L [2]**		
Exercise Category at Baseline [1]	**Sed**	**Mod**	**Active**	**Sed**	**Mod**	**Active**	**Sed**	**Mod**	**Active**
# of cases	153	92	40	153	92	40	153	92	40
Exer Category [2]	1	1	1	1.0	2.0	3.0	1.3	1.5	1.7
Blocks (Median) [3]	2	3	2	1	12	48	2	5.5	9
Healthy (%) [2]	100.0	100.0	100.0	96.1	97.8	100.0	80.4	89.1	92.5
Healthy 6 mos prior (%)				96.7	94.6	97.5			
Alive (%)	100.0	100.0	100.0	100.0	100.0	100.0	93.5	95.7	100.0
Age (mean)	76.1	75.1	74.4	78.1	77.1	76.4	80.1	79.1	78.4
Male (%)				21.6	29.3	35.0			
White (%)				83.7	85.9	90.0			
BMI>normal (%)	73.2	71.1	47.5	69.4	75.6	47.5	70.3	72.9	47.5
No ADL	93.5	90.2	90.0	86.3	90.2	92.5	76.5	84.8	82.5
No IADL	85.6	81.5	82.5	78.4	79.3	90.0	62.1	72.8	80.0
CESD < 10	95.4	93.5	92.5	90.2	89.1	97.5	82.4	85.9	90.0
3MSE>89	88.2	92.4	97.5	88.2	92.4	95.0	82.4	87.0	90.0
No Bed Days	96.7	98.9	97.5	95.4	100.0	100.0	91.5	92.4	97.5
Walk 15' <10 sec	98.0	98.9	100.0	95.4	96.7	95.0	88.2	91.2	95.0
No Hospital days	95.4	95.7	85.0	93.5	91.3	97.5	81.0	85.9	92.5
No CVD	81.0	82.6	92.5	80.4	81.5	90.0	72.5	76.1	82.5

1 Low/Sedentary is walking <7 blocks per week; high/Active is walking at least 28 blocks per week. Healthy is Excellent, Very Good, or Fair health; Sick is Fair or Poor health, or (at follow-up) Dead.
2 Baseline+2 years is follow-up.
3 BMI and Median Blocks are calculated for living persons only. All other variables include the Dead at follow-up.

Appendix Table C
Primary Analysis for Low-bias Design
Sedentary GG (n=764) + Sedentary (EVG/EVG) n = 370)

		Primary (n=1127)[1]		**Dead Removed (1037)[1]**	
	Column	**1**	**2**	**3**	**4**
		Moderate	**Active**	**Med**	**Active**
N		301	119	285	118
Step	**Variables added**				
1	Exercise +indicator for E/VG (vs G)	.105 ***	.136 ***	.073 **	.067 *
2	+age, sex, race	.088 ***	.116 ***	.061 **	.056
3	+ other health vars in year -1	.078 ***	**.088****	.055 *	.035
4	+E/VG/G in year -0.5	.085 ***	.091 **	.060 **	.038
5	+E/VG/G at baseline	.069 **	.074 *	.051 *	.026
6	+other health variables at baseline	.058 *	.059	.045	.018

Statistical significance:
***p<.01, 2 tailed, **p<.05 2-tailed,. * p<.10 2-tailed.
1 The other health variables are defined in Table 3 and in the text.

Appendix Table D
Other outcome ---- prob(Healthy) or PHF

	Column	**1** [1]	**2**	**3**	**4**
	Health yrs -2 and -1	**G/G or EVG/EVG**	**Any**	**Any**	**Unknown**
	Activity yrs -2 and -1	**Sedentary**	**Sedentary**	**Any**	**Unknown**
N					
Quintets		1127	2535	5124	5124
Persons		988	2149	5124	5124
Step	**Variable added**				
1	Exercise + indicator for prior E/VG (vs G) if needed	10.787***	16.87***	19.884***	19.884***
2	+age, sex, race	9.343***	17.473***	17.976***	17.976***
3	**+ other health vars in year -1**	**7.875*** **	**8.391*** **	**8.914*** **	
4	+E/VG/G in year -0.5	8.043***	7.296***	7.350***	
5	+E/VG/G at baseline	6.809**	5.841***	5.625***	9.615***
6	+other health variables at baseline	5.998**	5.226***	4.999***	6.385***

Statistical significance:
***p<.01, 2 tailed, **p<.05 2-tailed,. * p<.10 2-tailed.
The other health variables are defined in Table 3 and in the text.
[not updated controlling for hosp and cvd]

Appendix Table E
Other outcome (survival)

	Column	1 [1]	2	3	4
	Health yrs -2 and -1	**G/G or EVG/EVG**	**Any**	**Any**	**Unknown**
	Activity yrs -2 and -1	**Sedentary**	**Sedentary**	**Any**	**Unknown**
N					
Quintets		1127	2535	5124	5124
Persons		988	2149	5124	5124
Step	**Variable added**				
1	Exercise + indicator for prior E/VG (vs G) if needed	.091***	.118***	.082***	.082***
2	+age, sex, race	.080***	.110***	.076***	.076***
3	+ other health vars in year -1	.073***	.077***	.042***	
4	+E/VG/G in year -0.5	.074***	.071***	.037***	
5	+E/VG/G at baseline	.068***	.066***	.030***	.050***
6	+other health variables at baseline	.062**	.060***	.029***	.035***

Statistical significance:
***p<.01, 2 tailed, **p<.05 2-tailed,. * p<.10 2-tailed.
The other health variables are defined in Table 3 and in the text.
[not updated using hosp and cvd]

APPENDIX F
CHICKEN AND EGG

To gain some intuition about whether persons were likely to improve health which caused them to exercise, or start to exercise which improved their health, we pretended that the 5 quintile years were actually 6-month periods, and examined the persons who were in Good health and Sedentary 1 and 2 "years" before baseline, but were Active at "baseline". We then looked at the states "6 months" before baseline. (This is a different definition of exercise with only 2 categories, Active (14+ blocks per week) vs. Sedentary (<14 blocks per week).

HEALTH AND EXERCISE "6 MONTHS" BEFORE "BASELINE"

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NEITHER IMPROVED	130	53.9	53.9	53.9
	HEALTH FIRST	18	7.5	7.5	61.4
	EXERCISE FIRST	88	36.5	36.5	97.9
	BOTH IMPROVED	5	2.1	2.1	100.0
	Total	241	100.0	100.0	

There were 241 people who met the criteria (they would be comparable to the baseline "Active" group). Six months before baseline, 53.9% were still Good (or worse) and Sedentary, 2.1% had become both Active and healthier. There is no information about which came first in those cells.

Eighteen people (7.5%) changed their health first (before starting to exercise) while 88 (36.5%) were exercising without having changed their health.

This suggests that
1 Most people (130+18)/241 started to exercise fairly close to baseline.
2 Among discordant pairs, people were 88/18=4.9 times as likely to exercise and then change health as to change health and then start to exercise.

This is for a longer time period than in the real study (years instead of semesters), but it is the only available information.

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