A Prospective Study of Weight Training and Risk of Type 2 Diabetes Mellitus in Men

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Background: The role of weight training in the primary prevention of type 2 diabetes mellitus (T2DM) is largely unknown.

Methods: To examine the association of weight training with risk of T2DM in US men and to assess the influence of combining weight training and aerobic exercise, we performed a prospective cohort study of 32,002 men from the Health Professionals Follow-up Study observed from 1990 to 2008. Weekly time spent on weight training and aerobic exercise (including brisk walking, jogging, running, bicycling, swimming, tennis, squash, and calisthenics/rowing) was obtained from questionnaires at baseline and biennially during follow-up.

Results: During 308,332 person-years of follow-up (18 years), we documented 2278 new cases of T2DM. In multivariable-adjusted models, we observed a dose-response relationship between an increasing amount of time spent on weight training or aerobic exercise and lower risk of T2DM (P<.001 for trend). Engaging in weight training or aerobic exercise for at least 150 minutes per week was independently associated with a lower risk of T2DM of 34% (95% CI, 7%-54%) and 52% (95% CI, 45%-58%), respectively. Men who engaged in aerobic exercise and weight training for at least 150 minutes per week had the greatest reduction in T2DM risk (59%; 95% CI, 39%-73%).

Conclusions: Weight training was associated with a significantly lower risk of T2DM, independent of aerobic exercise. Combined weight training and aerobic exercise conferred a greater benefit.


See also pages 1283 and 1285

Regular Physical Activity (PA) is a cornerstone in the prevention and management of type 2 diabetes mellitus (T2DM). Achieving a daily amount of moderate or vigorous PA of at least 30 minutes per day is associated with a substantial reduction in the risk of T2DM. This is broadly consistent with the current recommendations regarding PA in adults. More recently, evidence from randomized controlled trials has shown that resistance training can improve glycemic control in patients with T2DM, even in the absence of aerobic training. This has led to the recommendation for resistance training 3 times per week in individuals with T2DM. However, whereas the evidence that regular aerobic exercise can prevent T2DM is compelling, to our knowledge, no studies have examined the role of weight training in the primary prevention of T2DM.

In this study, we examined the association of weight training with the risk of T2DM in men observed biennially for 18 years in the Health Professionals Follow-up Study (HPFS). In particular, we examined whether the influence of weight training is independent of aerobic exercise and assessed the combined influence of weight training and aerobic exercise on T2DM risk.

Methods

Study Population

The HPFS is an ongoing prospective cohort study of 51,529 male health professionals aged 40 to 75 years at baseline in 1986. Every 2 years, the cohort participants are sent a questionnaire about diseases and personal and lifestyle characteristics, such as height, weight,
smoking status, dietary intake (food frequency questionnaire), and PA. Ninety-four percent of the cohort has completed at least 1 follow-up questionnaire. For this analysis, we excluded men who reported a history of diabetes, cancer, myocardial infarction, angina, coronary artery bypass graft, other heart conditions, stroke, or pulmonary embolism on the baseline questionnaire (1986), in 1988, and in 1990, leaving a study population of 32,002 participants with information on exposures and covariates. This study was approved by the Harvard School of Public Health institutional review board.

ASSESSMENT OF WEIGHT TRAINING, OTHER PA, AND TELEVISION VIEWING

From 1990 and onward, participants reported their average weekly amount of weight training, other PA, and television viewing biennially. Other PAs included walking, jogging, running, bicycling, swimming, tennis, squash, calisthenics/rowing, and heavy outdoor work. There were 13 response categories ranging from none to greater than 40 hours per week for weight training and other PAs. Participants were also asked about the daily number of flights of stairs climbed and usual walking pace. Of these other PAs, brisk walking, jogging, running, bicycling, swimming, tennis, squash, and calisthenics/rowing were considered aerobic exercises of at least moderate intensity (∼3 metabolic equivalent tasks). We used these activities because they are often performed repetitively and produce dynamic contractions of large muscle groups for an extended period. We calculated the total time spent on aerobic exercise of at least moderate intensity (∼3 metabolic equivalent tasks) and grouped participants into 4 categories: 0, 1 to 59, 60 to 149, and at least 150 minutes per week. We grouped participants in the same categories for weight training. We also constructed a variable representing unstructured PA of at least moderate intensity consisting of metabolic equivalent task–hours per week of heavy outdoor work and stair climbing, as previously described. Reproducibility and validity of the PA questionnaire have been assessed in a subsample of the HPFS participants. The Pearson correlation between PA of vigorous intensity from diaries for 4 weeks across different seasons and from the questionnaire was 0.58. For weight training, the correlation was 0.79. Reproducibility from 2 questionnaires was 0.52 for vigorous PAs and 0.50 for weight training. Another study reported a correlation of 0.54 between PA score obtained from a similar questionnaire and maximum oxygen uptake.

ASSESSMENT OF T2DM AND DEATH

We ascertained T2DM that occurred between return of the questionnaire in 1990 and January 31, 2008. Men who reported a diagnosis of T2DM in the biennial follow-up questionnaires were sent a supplementary questionnaire to confirm the diagnosis and obtain information on symptoms, treatment, and diagnostic test results. Between 1990 and 1996, the criteria from the National Diabetes Data Group were used to confirm self-reported diagnosis of T2DM, and from 1998 onward we used the American Diabetes Association criteria. Ninety-seven percent of self-reported T2DM cases (57 of 59) were confirmed by means of medical record review in a validation study in a subgroup of HPFS participants. We identified deaths by searching the National Death Index, from next of kin, or from postal authorities. Death due to cardiovascular disease was classified using the International Classification of Diseases, Eighth Revision. The National Death Index has an estimated sensitivity of at least 98%.

ASSESSMENT OF COVARIATES

Family history of T2DM was assessed at baseline by self-report. Smoking status and body mass index (calculated as weight in kilograms divided by height in meters squared) were assessed at baseline and biannually thereafter. Dietary factors were assessed in 1990, 1994, 1998, 2002, and 2006 using a 131-item validated food frequency questionnaire. Daily intake of total energy (calories per day), saturated fat to polyunsaturated fat ratio, trans fat (percentage of total energy), alcohol intake, coffee intake, cereal fiber (grams per day), whole grains (grams per day), and glycemic load were considered covariates in the analyses. We also calculated a dietary index composed of polyunsaturated fat to saturated fat ratio, trans fat (inverted), cereal fiber, whole grains, and glycemic load (inverted) by standardizing and summarizing the respective continuously scaled dietary variables.

STATISTICAL ANALYSIS

Person-time at risk was calculated from the return of the 1990 questionnaire (until January 31, 2008), death, or loss to follow-up, whichever occurred first. Relative risks (RRs) of T2DM by categories of weight training and aerobic exercise were estimated using time-dependent Cox proportional hazards regression. To control for calendar time and age, the analyses were stratified jointly by age (in months) at the start of follow-up and the year of questionnaire return. We calculated cumulative averages of weight training and aerobic PA from baseline (1990) to censoring time to minimize measurement error and to characterize long-term exposure status. In multivariable analysis, we additionally adjusted for aerobic exercise, other PA, television viewing, alcohol intake, coffee intake, smoking, ethnicity, family history of diabetes, and the dietary variables total calorie intake, saturated fat to polyunsaturated fat ratio, trans fat, cereal fiber, whole grains, and glycemic load. Tests for trend were performed by assigning the median value of each category of the exposure and treating this variable as continuous. To examine the combined association of weight training and aerobic exercise, we constructed a joint variable of weight training (4 categories) and aerobic exercise (2 categories representing adherence to current recommendations) and associated that with T2DM risk. A test for multiplicative interaction was performed using the likelihood ratio test by comparing models with main effects and interaction terms and models containing only main effects. We did not see indications that the proportional hazard assumption was violated based on the interaction test between follow-up time and weight training.

We also examined the nature of the possible dose-response relationship between weight training and T2DM by using restricted cubic spline regression with 4 knots. Deviation from linearity was tested using the likelihood ratio test by comparing models with cubic spline terms and models containing only the linear term. We performed several sensitivity analyses to assess the robustness of the results. First, we used the simple update and the baseline information, respectively, on weight training as an alternative to the cumulative average. Second, we performed an analysis using a 4-year lag in exposure classification to assess the possibility of reverse causality. Third, we included confounding variables assessed on the continuous scale in this form in the models to address the possibility of residual confounding. Fourth, we repeated the analysis with death from all causes treated as a competing risk according to the method of Fine and Gray. All the analyses were conducted using a commercially available software package (SAS, version 9.2; SAS Institute, Inc.).
RESULTS

During 508 332 person-years of follow-up (18 years), we documented 2278 new cases of T2DM. Table 1 provides the baseline characteristics of the study population by level of weight training per week. Fourteen percent of men reported weight training at baseline. Whereas the age-adjusted percentage of men who engaged in weight training increased with time to 29% in 2006, the average time spent weight training in these individuals seemed stable over time (Figure 1). Men who reported weight training at least 150 minutes per week at baseline performed more aerobic exercise, viewed less television, drank less alcohol, were less likely to smoke, and had a healthier dietary intake profile (except for glycemic load) compared with men reporting no weight training.

Table 1 examines the association of weight training and aerobic exercise with the risk of T2DM. In multivariable-adjusted analysis including aerobic exercise, men performing weight training 1 to 59, 60 to 149, and at least 150 minutes per week had RRs of 0.88, 0.75, and 0.66 for lower risk of T2DM (P < .001 for trend), respectively, compared with men reporting no weight training. The RRs of T2DM for men performing 1 to 59, 60 to 149, and at least 150 minutes per week of aerobic exercise compared with men reporting no aerobic exercise were 0.93, 0.69, and 0.48 respectively (P < .001 for trend), in multivariable-adjusted analysis. Using the baseline information only or the simple updated information on weight training (instead of the cumulative updated information), results modestly attenuated (baseline: multivariable-adjusted RR = 0.67; 95% CI, 0.51-0.88; and simple updated: multivariable-adjusted RR = 0.75; 95% CI, 0.60-0.94 for the highest categories of weight training). Using a 4-year lag in exposure classification strengthened the association (multivariable-adjusted RR = 0.50; 95% CI, 0.33-0.76 for the highest category of weight training). To assess the possibility of residual confounding, we included covariates as continuous variables where possible, but this did not materially change the results. To further address the possibility that the association of weight training with risk of T2DM was due to confounding by aerobic exercise, we restricted the analysis to men who reported no aerobic exercise. This analysis showed that any weight training was associated with 48% (95% CI, 1%-72%) lower risk compared with no weight training in multivariable-adjusted analysis. In a secondary analysis, we also analyzed whether weight training was associated with mor-
For each 60 minutes of weight training per week, the risk of type 2 diabetes mellitus decreased by 13% (95% CI, 6%-19%; P < .001). For aerobic exercise, the relationship clearly seemed nonlinear, with the strongest association at the lower level of aerobic exercise (P < .001 for the nonlinear response) (Figure 2).

### Table 2. Weight Training, Aerobic Exercise, and Risk of Type 2 Diabetes Mellitus in Men From the Health Professionals Follow-up Study (1990-2008)^a

<table>
<thead>
<tr>
<th>Variable</th>
<th>Activity, min/wk</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1-59</td>
</tr>
<tr>
<td>Weight training</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median time, min/wk</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>No. of cases</td>
<td>1630</td>
<td>507</td>
</tr>
<tr>
<td>Person-y</td>
<td>322,964</td>
<td>130,190</td>
</tr>
<tr>
<td>Age adjusted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable-adjusted model 1b</td>
<td>1 [Reference]</td>
<td>0.72 (0.65-0.80)</td>
</tr>
<tr>
<td>Multivariable-adjusted model 2c</td>
<td>1 [Reference]</td>
<td>0.78 (0.71-0.87)</td>
</tr>
<tr>
<td>Multivariable-adjusted model 3d</td>
<td>1 [Reference]</td>
<td>0.88 (0.79-0.98)</td>
</tr>
<tr>
<td>Multivariable-adjusted model 3d</td>
<td>1 [Reference]</td>
<td>0.82 (0.72-1.02)</td>
</tr>
<tr>
<td>Aerobic exercise^e</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median time, min/wk</td>
<td>0</td>
<td>27</td>
</tr>
<tr>
<td>No. of cases</td>
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<td>589</td>
</tr>
<tr>
<td>Person-y</td>
<td>56,897</td>
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</tr>
<tr>
<td>Age adjusted</td>
<td></td>
<td></td>
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<tr>
<td>Multivariable-adjusted model 1b</td>
<td>1 [Reference]</td>
<td>0.93 (0.79-1.03)</td>
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<tr>
<td>Multivariable-adjusted model 2c</td>
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<tr>
<td>Multivariable-adjusted model 3d</td>
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<td>0.93 (0.81-1.06)</td>
</tr>
<tr>
<td>Multivariable-adjusted model 3d</td>
<td>1 [Reference]</td>
<td>1.00 (0.88-1.15)</td>
</tr>
</tbody>
</table>

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^aData are given as relative risk (95% CI) except where indicated otherwise.

^bAdjusted for age (months), smoking (never, past, or current with cigarette use of 1-14, 15-24, or ≥25 per day), alcohol consumption (0, 1-5, 6-10, 11-15, or >15 g/d), coffee intake (0, <1, 1-3, >3-5, or >5 cups per day), race (white vs nonwhite), family history of diabetes, intake of total energy, trans fat, polyunsaturated fat to saturated fat ratio, cereal fiber, whole grain, and glycemic load (all dietary factors in quintiles).

^cAdditionally adjusted for aerobic exercise (or weight training if aerobic exercise was the exposure), other physical activity of at least moderate intensity (quintiles), and television viewing (quintiles).

^dAdditionally adjusted for body mass index.

^eAerobic exercise consists of walking at a brisk pace, jogging, running, bicycling, swimming, tennis, squash, and calisthenics/rowing.

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**Figure 2.** Dose-response relationship between weight training and risk of type 2 diabetes mellitus. Dotted lines represent 95% CIs for the trend obtained from restricted cubic spline regression (4 knots). The model included the following covariates: age (months), aerobic exercise (0, 1-59, 60-149, or ≥150 minutes per week), other physical activity of at least moderate intensity (quintiles), television viewing (quintiles), smoking (never, past, or current with cigarette use of 1-14, 15-24, or ≥25 per day), alcohol consumption (0, 1-5, 6-10, 11-15, or >15 g/d), coffee intake (0, <1-1.3, >3-5, ≥5 cups per day), race (white vs nonwhite), family history of diabetes, intake of total energy, trans fat, polyunsaturated fat to saturated fat ratio, cereal fiber, whole grain, and glycemic load (all dietary factors in quintiles). The analysis was truncated to men reporting no more than 420 minutes per week. P = .29 for the nonlinear relationship.
We then examined the association of weight training and aerobic exercise stratified by age (<65 vs ≥65 years), body mass index (<30 vs ≥30), family history of T2DM (yes vs no), and dietary index score (below vs above the median) (Table 3 and eTable). The association of weight training with T2DM was stronger in men younger than 65 years (P < .001 for multiplicative interaction). There was also evidence that the association was stronger in men with no family history of T2DM (P = .04 for multiplicative interaction). This was less apparent for aerobic exercise, where associations were fairly similar across these strata (eTable).

In this large prospective cohort study with biannual follow-up for 18 years, men who engaged in weight training had a reduced risk of T2DM. The association was independent of aerobic exercise, and even a modest amount of time engaged in weight training seemed to be beneficial. The risk reduction associated with weight training was comparable in magnitude with that of aerobic exercise, with risk reductions of approximately 35% and 50%, respectively, in men performing at least 150 minutes per week of either weight training or aerobic exercise. These results support that weight training serves as an important alternative for individuals who have difficulty adhering to aerobic exercise, but the combination of weight training with aerobic exercise conferred an even greater benefit.

These findings are in agreement with those from a recent meta-analysis of randomized controlled trials showing that resistance training can improve glycemic control in individuals with T2DM. However, no previous studies, to our knowledge, have examined the association of weight training with the risk of T2DM. A variety of cross-sectional studies have shown that weight training...
ing, muscle strength, or muscle mass is associated with greater insulin sensitivity or prediabetes. In addition, 2 prospective cohort studies\textsuperscript{22,23} have reported that greater muscle strength was associated with a lower risk of incident metabolic syndrome, although association was attenuated with adjustment for aerobic fitness in both studies. Finally, in a study\textsuperscript{24} from the HPFS, we reported an inverse association between weight training and risk of coronary heart disease independent of other PAs. Further studies are needed to examine the associations between weight training and other outcomes, including total and cause-specific mortality.

The 2 largest trials\textsuperscript{25,26} of resistance training in individuals with T2DM showed that the combination of aerobic exercise and resistance training conferred further benefit for glycemic control in individuals with T2DM than did either type of exercise alone. We observed that combining aerobic exercise and weight training was associated with the largest reduction in the risk of T2DM. Although we observed that the time spent engaged in weight training provided a fairly comparable reduction in risk compared with the time spent in aerobic exercise, it is unclear whether the total energy expenditure plays the same role for the 2 types of exercise. Because the anaerobic energy expenditure contribution during weight training can be substantial, the energy requirements for weight training may be grossly underestimated compared with that of aerobic exercise using metabolic equivalent task values. Furthermore, we did not obtain specific information about the type and intensity of weight training. Thus, it is uncertain whether the altered daily total energy expenditure from engaging in aerobic exercise is comparable with that from weight training in this study.

Although many of the acute and chronic physiologic responses induced by resistance training and aerobic exercise are similar, there are also distinct effects of each exercise type.\textsuperscript{27} At the cellular level, engagement in aerobic exercise increases mitochondrial density and oxidative enzyme activity, thereby facilitating improved fatty acid oxidation, whereas resistance training increases the glycolytic capacity and promotes type II muscle fiber abundance and growth, which enhances the capacity of glucose use.\textsuperscript{28} In turn, aerobic exercise leads to greater improvements in aerobic fitness, whereas resistance training favors increased lean body mass and muscle strength.\textsuperscript{29,30} Beyond improving glycemic control, both exercise types have been shown to reduce adiposity and improve blood pressure and lipid levels.\textsuperscript{31-34}

We did not observe a strong attenuation of the association with weight training after additional adjustment for body mass index. This may be attributable to weight training being able to increase lean mass and reduce fat mass without a major change in body weight, as previously indicated in trials in individuals with T2DM.\textsuperscript{25,26} However, using waist circumference indicated that part of the beneficial effect of weight training was mediated by abdominal adiposity. In a previous analysis,\textsuperscript{35} weight training was associated with a smaller increase in waist circumference over time in men.

We found that the association of weight training with T2DM risk was attenuated in men 65 years and older and in men with a family history of T2DM. The attenuation of association in these subgroups may be attributed to power. An alternative explanation could be that the intensity of weight training is decreased at older ages. However, we do not have data to test this hypothesis. The possible weakened relationship between weight training and T2DM risk in men with a positive family history deserves more attention in future studies.

The strengths of this study include the large sample size, the long follow-up, and the biannual assessment of exposures and most confounders, including important dietary factors. We also showed that associations were robust to a variety of sensitivity analyses, including an analysis using a 4-year lag in exposure classification. Limitations include that the study comprised only men who were working health professionals and mostly of white race. The findings may, therefore, not be generalizable to women and other ethnic or racial groups of men. Furthermore, we did not explore the importance of type and intensity of weight training as we obtained information only on weekly nonspecific weight training. Finally, there is a possibility of residual and unknown confounding.

Because we observed risk reduction with any weight training in individuals reporting no aerobic exercise, it is unlikely that the association of weight training can be explained by residual confounding by aerobic exercise.

In conclusion, this prospective cohort study showed that weight training was associated with a reduced risk of T2DM in a dose-response manner independent of aerobic exercise level. The magnitude of risk reduction associated with weight training was close to that with aerobic exercise. These results suggest that weight training is a valuable alternative for individuals who have difficulty adhering to aerobic exercise, and adding weight training to aerobic exercise seems to give further protection from T2DM. Further research should examine the effects of duration, type, and intensity of weight training on T2DM risk in greater detail.

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Author Contributions: Mr Grøntved and Dr Hu had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Grøntved and Hu. Acquisition of data: Rimm, Willett, and Hu. Analysis and interpretation of data: Grøntved, Willett, Andersen, and Hu. Drafting of manuscript: Grøntved. Critical revision of manuscript for important intellectual content: Grøntved, Rimm, Willett, Andersen, and Hu. Statistical analysis: Grøntved and Willett. Obtained funding: Hu. Administrative, technical, or material support: Hu. Study supervision: Andersen and Hu.

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Online-Only Material: The eTable and eFigure are available at http://www.archinternmed.com.

REFERENCES