Changes in Vigorous Physical Activity and Incident Diabetes in Male Runners

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OBJECTIVE — We examined the relationship between changes in reported vigorous exercise and self-reported physician-diagnosed diabetes in 25,988 active men.

RESEARCH DESIGN AND METHODS — The dose-response relationship between changes in reported vigorous exercise (running distance, change in kilometers per week) and self-reported physician-diagnosed diabetes was followed prospectively for 7.8 ± 1.8 years (means ± SD).

RESULTS — Logistic regression analyses showed that the log odds for diabetes declined significantly in relation to men's change in running distance (coefficient ± SE: −0.012 ± 0.004, $P < 0.01$), which remained significant when adjusted for BMI (−0.018 ± 0.003, $P < 0.0001$). The decline in the log odds for diabetes was related to the distance run at the end of follow-up when adjusted for baseline distance, with (−0.024 ± 0.005, $P < 0.0001$) or without (−0.027 ± 0.005, $P < 0.0001$) adjustment for BMI. Baseline distance was unrelated to diabetes incidence when adjusted for the distance at the end of follow-up. Compared with men who ran <8 km/week at the end of follow-up, incidence rates in those who ran ≥8 km/week were 95% lower between 35 and 44 years of age ($P < 0.0001$), 92% lower between 45 and 54 ($P < 0.0001$), 87% lower between 55 and 64 ($P < 0.0001$), and 46% lower between 65 and 75 ($P = 0.30$). For the subset of 6,208 men who maintained the same running distance during follow-up (±5 km/week), the log odds for diabetes declined with weekly distance run (−0.024 ± 0.010, $P = 0.02$) but not when adjusted for BMI (−0.005 ± 0.010, $P = 0.65$).

CONCLUSIONS — Vigorous exercise significantly reduces diabetes incidence, due in part to the prevention of age-related weight gain and in part to other exercise effects.

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Physical activity decreases the risk of type 2 diabetes (1–9). Moderate and vigorous exercise are purported to produce comparable reductions in diabetes risk if the energy expenditure is the same (2,3). The optimal physical activity dose remains unclear, however, with some (4–7) but not all studies (1,8,9) showing continued reduction in diabetes for high versus intermediate energy expenditures.

The National Runners' Health Study (10–18) is unique among population cohorts in its focus on the health effect of higher doses of vigorously intense physical activity (i.e., sixfold or more the metabolic rate at rest). This study was specifically designed to evaluate the dose-response relationship between vigorous physical activity and health for intensities and durations that exceed current physical activity recommendations (19–21). One specific hypothesis is whether changes in vigorous physical activity affect the risk for developing diabetes. Although women were surveyed and followed up, only 23 developed diabetes; therefore, limited statistical power exists to establish significance in these women. Our analyses of diabetes and vigorous exercise are therefore restricted to men.

This article relates running distance at baseline and at the end of follow-up to self-reported physician-diagnosed diabetes in vigorously active men who were generally lean and ostensibly at low diabetes risk. The benefits of increased vigorous exercise are relevant to the 27% of U.S. women and 34% of U.S. men who meet or exceed the more general exercise recommendations for health benefits (22). Specific issues to be addressed are whether maintenance of the same level of vigorous exercise over time reduces the risk of incident diabetes in relation to the exercise dose, whether men who decrease their activity increase their risk for developing diabetes, and whether running distances at the conclusion of follow-up are more predictive of diabetes than baseline distances, suggesting a causal, acute effect. We have shown previously that greater body weight is related to a lack of vigorous exercise (11–13) and increases the risk for diabetes even among generally lean vigorously active men (10). In runners, leanness may result from exercise or from initially lean men choosing to run further (16). Therefore, we also tested whether body weight mediates the effects of vigorous exercise on diabetes and whether this may result from self-selection.

RESEARCH DESIGN AND METHODS

The survey instruments and baseline characteristics of the National Runners' Health Survey are described elsewhere (10–18). Briefly, a two-page questionnaire, distributed nationally at races and to subscribers of a popular running magazine (*Runners' World*, Emmaus, PA), solicited information on demographics, running history, weight history, smoking habits, previous history of heart attack and cancer, and medications for blood pressure, thyroid conditions, high cholesterol, and diabetes. Recruitment took place between 1991 and 1994 (primarily 1993) and follow-up between 1999 and 2002. All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The study protocol was approved by the University of California Committee for the Protection of Human Subjects, and all participants signed committee-approved informed consents.

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Characteristics of men who increased, maintained, or decreased weekly running distance*

	Increased or maintained distance		Decreased distance		
	>8 km/week	8 to 0 km/week	0 to −8 km/week	−8 to −24 km/week	Less than −24 km/week
n	3,560	4,450	2,609	8,612	6,756
Diabetes	11 (0.31)	28 (0.63)	25 (0.96)	54 (0.63)	55 (0.81)
Follow-up duration (years)	7.42 ± 1.86	7.47 ± 1.80	7.39 ± 1.83	7.82 ± 1.75	8.32 ± 1.72
Age (years)	46.62 ± 9.77	48.78 ± 9.95	49.83 ± 9.94	49.22 ± 10.01	47.64 ± 10.87
Change in distance run (km/week)	17.89 ± 14.72	1.30 ± 2.06	−4.12 ± 1.66	−13.38 ± 4.43	−37.97 ± 6.11
Average distance run (km/week)	38.55 ± 20.80	29.37 ± 20.09	23.50 ± 17.16	30.28 ± 19.11	34.30 ± 19.27
ΔBMI (kg/m^2)	0.40 ± 1.42	0.73 ± 1.44	0.86 ± 1.38	1.20 ± 1.60	1.82 ± 1.97
Education (years)	16.58 ± 2.45	16.68 ± 2.41	16.77 ± 2.41	16.55 ± 2.41	16.26 ± 2.49
Meat (servings/week)	2.87 ± 3.29	2.99 ± 3.18	2.93 ± 3.07	2.92 ± 3.16	2.99 ± 3.56
Fish (servings/week)	1.58 ± 1.28	1.58 ± 1.28	1.53 ± 1.22	1.58 ± 1.36	1.56 ± 1.27
Fruit (servings/week)	11.09 ± 8.02	10.72 ± 7.74	10.29 ± 7.27	10.44 ± 7.30	10.73 ± 7.75
Alcohol (ml/week)	77.93 ± 100.77	85.84 ± 105.64	85.82 ± 108.34	88.32 ± 105.15	87.08 ± 111.26

Data are *n* (%) or means ± SD unless otherwise indicated.

BMI was calculated as weight in kilograms divided by the square of height in meters. We have previously reported the strong correlations between self-reported and clinically measured heights ($r = 0.96$) and weights ($r = 0.96$) (17) and for self-reported running distances versus self-reported BMIs in cross-sectional analyses (18). Repeat questionnaires in 110 men also showed that self-reported body weights at the start of running ≥12 miles/week had a correlation of 0.97. Physical activity was reported as average distance run per week. Although other leisure-time physical activities were not recorded for this cohort, data from runners recruited after 1998 (when the survey question was introduced) show that running represented (mean ± SD) 91.5 ± 19.1% of all vigorously intense activity and 73.5 ± 23.7% of total reported leisure-time physical activity. Self-reported distance run has been found to be reliable (test-retest correlations: $r = 0.89$ [17]). Eighty percent of the 54,956 participants in the National Runners' Health Study provided follow-up information or were known to be deceased.

Participants reported whether a physician had told them they had diabetes since their baseline questionnaire and whether they took medications for diabetes at baseline and the end of follow-up. Incident diabetes is defined as physician diagnosis or starting medications for this condition subsequent to participants' baseline questionnaire.

Statistics

We used logistic regression analyses to test whether changes in distance run per week were related to the incidence of diabetes (JMP version 5.1; SAS Institute, Cary, NC). The results are presented simultaneously adjusted for BMI at the end of follow-up and at baseline ($BMI_{exercise}$) and adjusted for BMI when participants began running ≥12 miles/week ($BMI_{preexercise}$). Adjustment for $BMI_{preexercise}$ was compared with adjustment for $BMI_{exercise}$ to assess whether the attenuating effect of the adjustment reflects BMI as a mediator (independent of $BMI_{preexercise}$) or as a self-selection effect (entirely due to $BMI_{preexercise}$). All results (except the descriptive results of Table 1) include adjustment for the average age during follow-up (age and age^2), follow-up duration, and the average weekly intakes of alcohol, meat, fish, and fruit at baseline and at the end of follow-up. We also used logistic regression analyses to estimate the incidence of diabetes within five age intervals (25–34, 35–44, 45–54, 55–64, and 65–74 years). Incident diabetes was used as the dependent variable and age intervals as the independent variables in zero-intercept logistic regression analyses, in which an individual's log odds for developing diabetes was the sum of the time spent within each interval between baseline and the end of the follow-up survey (13).

RESULTS — A total of 29,140 men who were nonsmokers, nonvegetarian, and nondiabetic at baseline provided running distance, height, and weight measures. From these, we excluded 2,020 men who completed only one side of their follow-up survey questionnaire, 844 men who did not provide their end-of-follow-up running distance (which probably implies they had stopped running), and 288 men who did not report their end-of-follow-up BMI. Relative to the entire baseline cohort, those who were excluded ran similar weekly baseline distances (excluded versus included means ± SE: 39.0 ± 0.4 vs. 37.7 ± 0.1 km/week) and weighed the same (23.9 ± 0.04 vs. 23.9 ± 0.02 kg/m^2) as those included in the analyses but were significantly older (aged 47.7 ± 0.2 vs. 44.6 ± 0.1 years) and had run more years at baseline (13.8 ± 0.1 vs. 13.1 ± 0.1 years). The characteristics of the remaining sample are presented in Table 1, which shows that changes in weekly distance run were inversely associated with changes in BMI and the incidence of diabetes.

Table 2 shows that change in running distance was inversely related to the log odds for developing diabetes (model 1). Adjustment for $BMI_{preexercise}$ had little effect. The greater the decline in running distance, the greater the increase in incidence. When adjusted for $BMI_{exercise}$, men who decreased their weekly running distance were at significantly greater odds for developing diabetes than those who increased their distance by ≥8 km/week (Fig. 1*A*).

A total of 6,208 men who maintained their running distance within ±5 km/week during follow-up were included in these analyses. The log odds for incident diabetes in this group declined in proportion to average weekly kilometers run (regression coefficient ± SE: −0.024 ± 0.010, $P < 0.05$), even in the absence of any change in distance. The coefficient became nonsignificant when adjusted for

Table 2—*Logistic regression analyses of incident diabetes by running distance*

	Model 1 (coefficients ± SE)			Model 2 (coefficients ± SE)		
	Intercept	Δkm/week	Average km/week	Intercept	Baseline km/week	Follow-up km/week
Unadjusted	−4.354	−0.012 ± 0.004†	−0.029 ± 0.005§	−4.354	−0.002 ± 0.005	−0.027 ± 0.005§
$BMI_{exercise}$ adjusted	−5.380	−0.018 ± 0.003§	−0.012 ± 0.005*	−5.380	0.013 ± 0.004†	−0.024 ± 0.005§
$BMI_{preexercise}$ adjusted	−4.689	−0.009 ± 0.004*	−0.025 ± 0.005§	−4.689	−0.004 ± 0.005	−0.022 ± 0.005§

Models 1 and 2 represent two approaches to entering the baseline and follow-up distances into the model, either separately as recorded or reexpressed as their difference and average. The intercept term includes adjustment to the mean age, follow-up duration, and reported intakes of meat, fish, fruit, and alcohol. (Note: Because the two models differ only in their expression of the baseline and follow-up values, the same intercept applies to both.) Additional adjustment for $BMI_{preexercise}$ (i.e., when participants began running ≥12 km/week) and $BMI_{exercise}$ (both baseline and end of follow-up BMI) as indicated. Significance levels for logistic regression coefficients: *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$; §$P < 0.0001$.

$BMI_{exercise}$ (−0.005 ± 0.010), whereas it remained essentially unchanged when adjusted for $BMI_{preexercise}$ (−0.022 ± 0.010), suggesting mediation rather than self-selection.

An alternative formulation of the logistic regression used in Table 2 is considered in model 2 of Table 2. Model 2 includes baseline and end–of–follow-up running distances directly, rather than their reexpression as average and difference. The significance levels refer to the significance of the end–of–follow-up distance (in kilometers) run per week when adjusted for baseline distance and the significance of the baseline distance run per week when adjusted for the end–of–follow-up distance. The incidence of diabetes was inversely related to running distance at end of follow-up but not at baseline. Adjusting the end–of–follow-up distance for $BMI_{exercise}$ or $BMI_{preexercise}$ had little effect on the coefficient. Figure 1*B* shows that end–of–follow-up distances of ≥8 km/week were associated with a 50% reduction in the odds of developing diabetes compared with shorter distances.

Finally, the data were analyzed to assess the progressive increase in the risk of developing diabetes with age. The data were stratified by running distances at the end of follow-up to test whether the incidence for running <8 km/week was different from that at ≥8 km/week. Running distances ≥8 km/week were combined because their graphs were largely overlapping. The log odds for incident diabetes for men <35, 35–44, 45–54, and 55–64 years of age were calculated within each stratum, as described in RESEARCH DESIGN AND METHODS. These are presented in Fig. 2 as incidence rates per 1,000 person-years. Among men aged ≥35 years, diabetes incidence was significantly lower for those who ran >8 km/week compared with those who ran less. The lack of significance in men <35 years of age reflects the smaller sample size and limited statistical power to detect differences.

CONCLUSIONS — These analyses demonstrate that the odds for developing diabetes were significantly related to changes in weekly distance run in men. Men who increased their running distance by an average of 18 km/week (i.e., the average distance run within the >8 km/week category of Fig. 1*A*) had significantly lower odds of developing diabetes than those who decreased their distance run. The odds for developing diabetes appeared to be related to distances run at the end of the follow-up period only, suggesting that the effect of distance run on diabetes (or the converse) is acute. Because

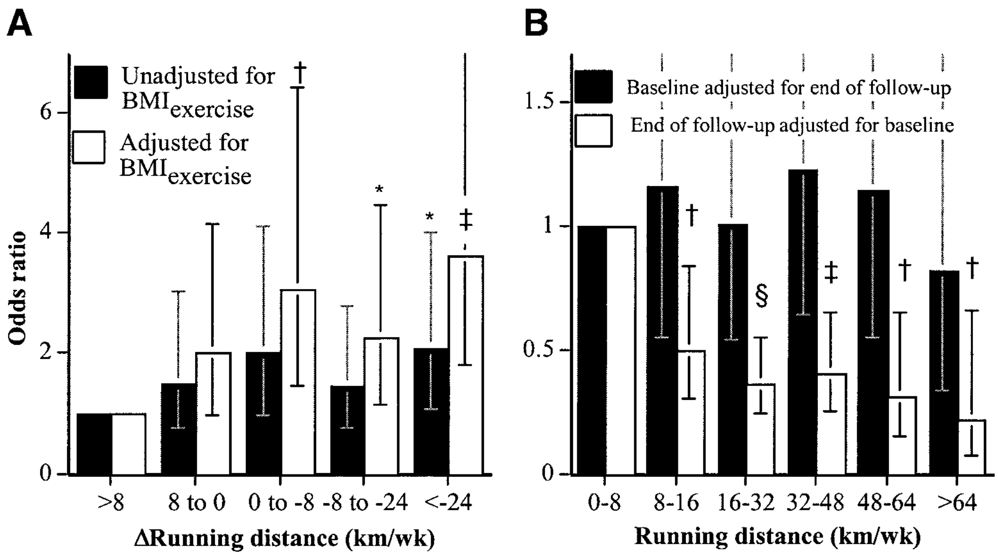

Figure 1—*Odds ratio of incident diabetes in relation to concurrent changes in weekly running distance* (A) *and baseline and follow-up distance* (B) *in 25,988 men during 7.8 years of follow-up. Adjusted for follow-up duration, average age (age and age*^{2}*), and average weekly intakes of meat, fish, and fruit during follow-up. Additional adjustment for* $BMI_{exercise}$ *(BMI at baseline and end of follow-up) where indicated. Significant odds reductions relative to men whose distance increaded >8 km/week* (A) *or who averaged 0–8 km/week* (B)*:* *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$; §$P < 0.0001$.

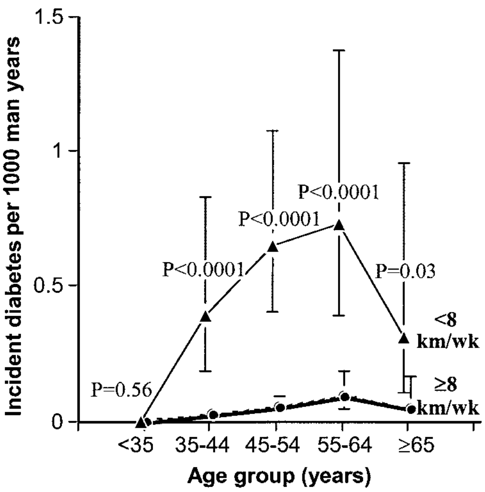

Figure 2—*Incidence of diabetes by age classes and stratified by reported running distance (kilometers per week) at the end of follow-up. Person-years of follow-up for men who ran <8 km/week and ≥8 km/week were 645 and 1,416 between ages 25 and 34 years, 12,703 and 45,603 between ages 35 and 44 years, 17,651 and 57,406 between ages 45 and 54 years, 9,939 and 27,417 between ages 55 and 64 years, and 3,469 and 7,532 between ages 65 and 74 years, respectively.*

these analyses examine concurrent changes in vigorous exercise with diabetes incidence, they do not distinguish between whether running affects diabetes risk or, conversely, whether diabetes affects the ability to run. However, among the 6,208 men who maintained the same level of vigorous exercise during follow-up, the odds for developing diabetes declined in association with running distance. Table 2 and Fig. 1*B* appear to negate the possibility that the effect is due to self-selection (i.e., men who are at higher risk for diabetes choose to run shorter distances) because this would be expected to affect baseline as well as follow-up running distances. This latter observation is important given our previous observations that 26% of the association between body weight and running distance, and all of the association between weight and cardiovascular fitness, can be ascribed to initially leaner men choosing to run further and faster (16).

Fig. 1*A* suggests that running as little as 8–16 km/week reduces the odds for developing diabetes. This agrees with other studies showing that subjects who had intermediate physical activity levels were at lower risk than the most sedentary individuals (1–9). Over the past decade, physical activity guidelines of the Centers for Disease Control and Prevention, the National Institutes of Health, and the American Heart Association have emphasized the health benefits of walking 2 miles (3.2 km) briskly on most days of the week (19–21). A 2-mile brisk walk 5 days per week is the energy equivalent of running 10.9 km/week (23); thus, these recommendations are consistent with Fig. 2, which also suggests that further reductions in the odds for developing diabetes accrue at even higher amounts of vigorous exercise.

The age-specific analyses of Fig. 2 shows significantly less diabetes in those who ran >8 km/week (average 33 km/week) compared with less active men throughout middle age and older. Men >35 years of age who were vigorously active had rates of incident diabetes comparable to young men. For diabetes and other cardiovascular risk factors (18), the benefits of vigorous exercise do not appear to be substantially diminished with age. In Fig. 2, the decrease in diabetes incidence among 65- to 75-year-old men compared with younger men who ran <8 km/week could result from the greater imprecision of the estimate due to the small sample size, as reflected in the broad CI.

One assumption of the traditional prospective design is that the probability of the event remains constant. As shown in Table 1, the majority of men decreased their activity during follow-up. Our analyses of the 6,208 men who maintained the same level of activity throughout follow-up represents the idealized prospective cohort study design. The decline in their log odds for diabetes per weekly kilometers run (-0.024 ± 0.010 per km) was 71% larger than the logistic regression coefficient for the entire sample without regard to changes in running distance during follow-up (-0.014 ± 0.004, $P < 0.001$) (unpublished observation). This suggests that prospective studies of physical activity and diabetes may underestimate the true benefit of physical activity (1–9).

Although adjustment for BMI only moderately affected the relationships of Table 2, the adjustment did eliminate the relationship between diabetes and distance run among men who ran consistently during follow-up. Others also report that BMI adjustment attenuates the relationship between physical activity and diabetes (2). We have previously demonstrated in this same cohort of men that baseline BMI predicts de novo diabetes during follow-up (10). Normal-weight men who were diagnosed for diabetes during follow-up had higher BMIs and larger waist circumferences at baseline than those who remained nondiabetic (10). Although the odds for diabetes accelerated much more dramatically at higher BMI levels, men with BMIs between 22.5 and 25.0 kg/m^2 were more than twice as likely to develop diabetes as leaner men (10). At higher levels, the odds for diabetes tripled for each 2.5 kg/m^2 increment. Other published findings by us show that vigorous exercise attenuates age-related weight gain in men and appears to be particularly efficacious in the prevention of more extreme weight gain (13). Changes in exercise levels in men also produce acute changes in body weight from increases and decreases in energy expenditure (12).

The principal limitations of these analyses are their reliance on self-reported diabetes, weekly running distances, and body weights. The self-reported distance and weights appear reliable, as indicated by their test-retest correlations (17) and their consistent relationships to other variables in this cohort (10–18). The sample is generally college educated and therefore probably reliable in reporting physician diagnosis or medication use for diabetes. Hu et al. (2) reported that 88.6% of the self-reported diabetes diagnoses in the Nurses' Health Study were valid, as determined from additional questions on classic symptoms, plasma glucose concentrations, or medication use to confirm type 2 diabetes. This validity rate for the nurses may represent an upper bound on the error rate for our sample, who, though educated, are not generally medically trained. Evolving criteria for physician diagnosis of diabetes during the follow-up may affect incidence rates, individuals may underreport diagnosis due to privacy concerns, and the reliability of self-reported weight or exercise could have changed with age or over time; however, we expect that such biases would be similar between high- and low-mileage runners and therefore not affect the analyses. We have also reported that fasting plasma glucose levels from the medical records of 8,283 male runners declined significantly with distance run when compared cross-sectionally (15). Presumably few, if any, of the incident cases of diabetes were type 1 because those using medication for diabetes at baseline were excluded from the analyses. Although insulin use was reported by some runners who developed diabetes, this would not necessarily be indicative of type 1 diabetes.

In summary, current public health guidelines are oriented on motivating sedentary and inadequately active men and women to include 30 min of moderately intense physical activity in their daily routine (19–21). These recommendations appear apropos to the prevention of diabetes; however, greater exercise doses confer even greater health benefits. Other studies show that exercise does not need to be vigorous to be beneficial; a growing body of evidence from randomized controlled studies involving men and women with pre-diabetes status shows that accumulation of 150 min/week of routine, lifestyle physical activity (particularly walking) can reduce type 2 diabetes risk (24–26). Future guidelines should discuss the health consequences of reducing activity in those who currently meet or exceed recommendations.

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