American Journal of Epidemiology
Vol. 158, No. 7
Printed in U.S.A.
DOI: 10.1093/aje/kwg191

Physical Activity, Obesity, and the Incidence of Type 2 Diabetes in a High-Risk Population

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Received for publication October 23, 2002; accepted for publication April 7, 2003.

This study, examining the longitudinal relation among physical activity, body mass index, and development of type 2 diabetes in a high-risk population, is unique because diabetes was determined by oral glucose tolerance testing rather than by self-report. A physical activity questionnaire assessing past year leisure and occupational activity was administered to 1,728 nondiabetic Pima individuals aged 15–59 years as part of a series of clinic examinations in the Gila River Indian Community from 1987 to 2000. During an average follow-up period of 6 years, 346 subjects developed diabetes. Using time-dependent Cox proportional hazards modeling adjusting for age, the authors found that total activity was related to diabetes incidence in women and men ($p < 0.05$ in women only). After additional adjustment for body mass index, the relation between activity and diabetes incidence was weakened in both men and women. When the age-adjusted diabetes incidence rates were examined by levels of activity stratified by tertile of body mass index, the diabetes incidence rate remained lower in more active than in less active men and women from all body mass index groups, with the exception of the middle body mass index tertile in men ($p < 0.05$ in women only). These results suggest that the adoption and maintenance of a physically active lifestyle can play a significant role in preventing type 2 diabetes.

diabetes mellitus; exercise; incidence; motor activity; obesity

Abbreviation: MET, metabolic equivalent.

It has been suggested in a variety of observational and experimental epidemiologic studies that physical activity may play a significant role in the prevention of type 2 diabetes mellitus. Recent findings of the clinical trials in this area provide the most convincing evidence that physical activity, in conjunction with diet and weight loss, can prevent diabetes in a variety of populations and age groups (1–3). Specifically, studies in men and women with impaired glucose tolerance at baseline from a variety of racial and ethnic backgrounds in the United States, along with men and women from China and Finland, demonstrated a decrease in the incidence of type 2 diabetes as the result of interventions that included physical activity (1–3). However, with the exception of the Chinese study, which was randomized by clinic, all of these intervention trials combined physical activity with weight loss and diet in their intervention scheme. In other words, the independent effect of physical activity intervention was not tested directly.

It is likely that physical activity can play an independent role in the prevention of type 2 diabetes separately from its effect on weight loss and body composition. Exercise training studies have supported the contention that physical activity improves insulin sensitivity independently of any effect of activity on weight loss and fat distribution (4). Likewise, in a recent cross-sectional population study, physical activity was shown to be negatively associated with insulin concentrations in two populations at high risk for diabetes that differed greatly by body mass index (5). The fact that the relation between physical activity and insulin sensitivity was similar in both the Pima Indians, among whom the prevalence of obesity is quite high, and the Mauritians, who are leaner, suggests a beneficial role of physical activity on

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insulin sensitivity, and therefore perhaps even on the prevention of diabetes, that is separate from any influence of physical activity on body composition (5).

Pima Indians of the Gila River Indian Community of Arizona have one of the world's highest documented incidence rates of type 2 diabetes mellitus, and they have a high prevalence of obesity (6, 7). Physical activity levels have been assessed in this population using the original version of the same activity questionnaire that is being used in a number of epidemiologic studies of diabetes worldwide (8, 9). The present study examined the role of physical activity and obesity in the development of type 2 diabetes in Pima Indians. The information gained from examining the longitudinal relation among physical activity, body mass index, and development of diabetes in this high-risk population is unique, because diabetes is determined objectively by oral glucose tolerance testing rather than by subjective reporting of the clinical diagnosis of diabetes.

MATERIALS AND METHODS

Study description

Pima Indians of the Gila River Indian Community of Arizona have participated in a longitudinal population-based diabetes research study conducted by the National Institute of Diabetes and Digestive and Kidney Diseases since 1965. Individuals over the age of 5 years who currently live in a designated part of the community are invited to participate.

At intervals of approximately 2 years, each subject is invited for a comprehensive examination conducted at the study clinic located in the community (6, 7). At each examination, a 75-g oral glucose tolerance test is performed, in which venous serum insulin and plasma glucose concentrations are determined after an overnight fast and 2 hours postload. Diabetes is diagnosed if the 2-hour postload plasma glucose concentration is at least 11.1 mmol/liter (200 mg/dl) at this examination or if a diagnosis is made during the course of routine medical care (7, 10). The examination also includes a medical history, physical examination, and measurement of height and weight (with light indoor clothing but without shoes). Obesity is estimated by the body mass index (weight (kg)/height $(m)^2$).

Physical activity interview

Since September 1987, a physical activity questionnaire has been administered by trained interviewers to individuals between the ages of 15 and 60 years who take part in these examinations. The activity questionnaire, interviewer's instructions, and questionnaire calculations have been described previously (8, 9, 11). This questionnaire was shown previously to be both feasible and reliable in this population, with a test-retest correlation of 0.89 for total physical activity over an interval period of 1–3 weeks (8). The validity of this questionnaire has also been demonstrated with objective measures of physical activity including doubly labeled water (12) and the Caltrac activity monitor (8).

The physical activity questionnaire assesses both leisure and occupational physical activity over the past year. Only physical activities that demand energy expenditure greater than that required by activities of daily living (such as bathing, grooming, and feeding) are assessed. For the leisure section of the questionnaire, individuals were presented with a list of common local activities and asked to report the activities that they had participated in during the past 12 months. They were then asked to estimate the frequency and duration for each activity identified. For occupational activity, individuals were asked to list all jobs held during the past 12 months. For each job entry, data were collected for time spent walking or cycling to work per day, as well as the average job schedule (months per year, days per week, and hours per day worked). Activity on the job was determined by the number of hours spent sitting at work and the most common physical activities performed when not sitting.

Estimates of leisure and occupational activity were calculated separately as hours per week averaged over the past year. Each activity was also weighted by its relative metabolic cost, referred to as a metabolic equivalent (MET), thereby deriving MET-hours per week as the final unit of expression. One MET represents the energy expenditure for an individual at rest, whereas a 10-MET activity requires 10 times the resting energy expenditure (13). (As an example, brisk walking is estimated to be about 3.5–4.0 METs, whereas jogging/running would be ≥7 METs).

A subjective determination was made by the interviewer whether or not the participant was capable of correctly answering the activity questions during the activity interview. Interviews judged not reliable by the trained interviewer were omitted from the analyses (8). Less than 3 percent of the interviews were excluded because they were judged to be "not reliable" by the interviewers. In addition, pregnant women were excluded from all analyses.

Statistical analysis

Spearman rank-order correlation coefficients were determined to assess the bivariate associations between the various physical activity estimates over time among all nondiabetic individuals.

Physical activity was categorized into two groups for each sex at a cutoff of 16 MET-hours per week, which is crudely equivalent to a brisk walk for one-half hour every day. This cutoff is consistent with the Surgeon General's activity recommendations for the general public. Moving the cutoff point a few MET-hours per week higher or lower did not change the overall interpretation of the results. Body mass index tertiles were based upon the distribution of the body mass index values of the individuals who were nondiabetic at baseline.

Subjects had to have both a baseline physical activity measure and at least one follow-up examination at which time diabetes status was determined in order to be included in analyses of diabetes incidence. Person-time was calculated from the baseline examination until diabetes developed or until the last examination, whichever came first. Incidence rates (new cases per 1,000 person-years) were calculated for

TABLE 1. Baseline characteristics of the 1,728 nondiabetic individuals, Gila River Indian Community, 1987–2000†

	Low activity (<16 MET‡-hours/week)	High activity (≥16 MET-hours/week)
Men	(*n* = 122)	(*n* = 554)
Activity (MET-hours/week)*	1–11 (5)	52–184 (112)
Age (years)*	31 (12)	27 (10)
Body mass index (kg/m^2)*	34 (9)	31 (7)
Fasting glucose (mg/dl)	98 (9)	97 (10)
2-hour glucose (mg/dl)**	113 (30)	106 (29)
Women	(*n* = 439)	(*n* = 613)
Activity (MET-hours/week)*	0–10 (5)	30–108 (53)
Age (years)*	30 (11)	27 (10)
Body mass index (kg/m^2)	34 (9)	33 (8)
Fasting glucose (mg/dl)**	95 (10)	94 (10)
2-hour glucose (mg/dl)**	120 (29)	116 (27)

* $p < 0.01$; ** $p < 0.05$.
† Values are the mean (standard deviation), except for "activity," which is the 25th–75th percentile (median).
‡ MET, metabolic equivalent.

strata defined by age, sex, physical activity, and body mass index. When a person changed age, body mass index, or physical activity categories (e.g., on the basis of a more recent examination), person-years were apportioned accordingly (i.e., in a time-dependent fashion). Age-standardized incidence rates were calculated by the direct method (based on the 1980 Pima census) as described previously (7). Statistical significance of the difference in diabetes incidence rates between physically active and physically inactive individuals, controlled for age group, was assessed with a modified Mantel-Haenszel procedure.

The Cox proportional hazards model was used to estimate the effects of physical activity and body mass index on the development of diabetes in the individuals who were nondiabetic at baseline. Physical activity and body mass index were included as time-dependent variables in these models, along with age at baseline. This model allows the use of all of the available data for each subject, from the first nondiabetic examination to either the onset of diabetes or the last examination. We used a quadratic term to adjust for age in the Cox proportional hazards model to allow for the nonlinear effect of age on the incidence of diabetes. All analyses were performed separately for men and women.

RESULTS

From the time the activity questionnaire was incorporated into the clinic examinations in September 1987, physical activity interviews were completed on 3,690 men and women aged 15–59 years whose heritage was at least half Pima, Tohono-O'odham, or a combination of these two closely related tribes. Among these individuals, 1,728 were nondiabetic at baseline and had at least one follow-up examination. Most of the cases of diabetes (63 percent) were identified for the first time at follow-up examinations offered every 2 years at the clinic. The method of identification of cases of diabetes did not appear to vary by activity group (low active = 60 percent, high active = 65 percent).

The baseline characteristics of these 1,728 individuals are presented in table 1. The mean body mass index values were extremely high compared with those of most other populations, as shown previously (14).

In general, leisure physical activity was the largest contributor to total physical activity levels for most of the men and women, although occupational activity was the largest contributor among the few individuals (mostly younger men) who had physically active jobs (data not shown). Likewise, leisure physical activity levels decreased with age and were higher in men than in women (data not shown), again as shown previously (11).

Spearman's rank order correlations between leisure and occupational physical activities over increasing time intervals were examined to determine the consistency of these measures. Not surprisingly, as the time period between examinations is extended from less than 3 years, to 3–6 years, and to greater than 6 years, the correlations for both leisure and occupational activities decreased over time. Spearman's rank order correlations among these three time periods for leisure activity were 0.48, 0.41, and 0.36 for men and 0.49, 0.41, and 0.26 for women; for occupational activity, they were 0.26, 0.18, and 0.15 for men and 0.21, 0.15, and 0.15 for women. Interestingly, the correlations for occupational activity were lower than those for leisure activity at all time points.

During an average follow-up period of 6 years (ranging from 1 to 13 years), 346 subjects developed type 2 diabetes. Diabetes incidence rates are presented in figure 1 by levels of total (leisure and occupational) physical activity. In general, for most age/sex groups, the diabetes incidence rate was lower in the more active than in the less active individuals,

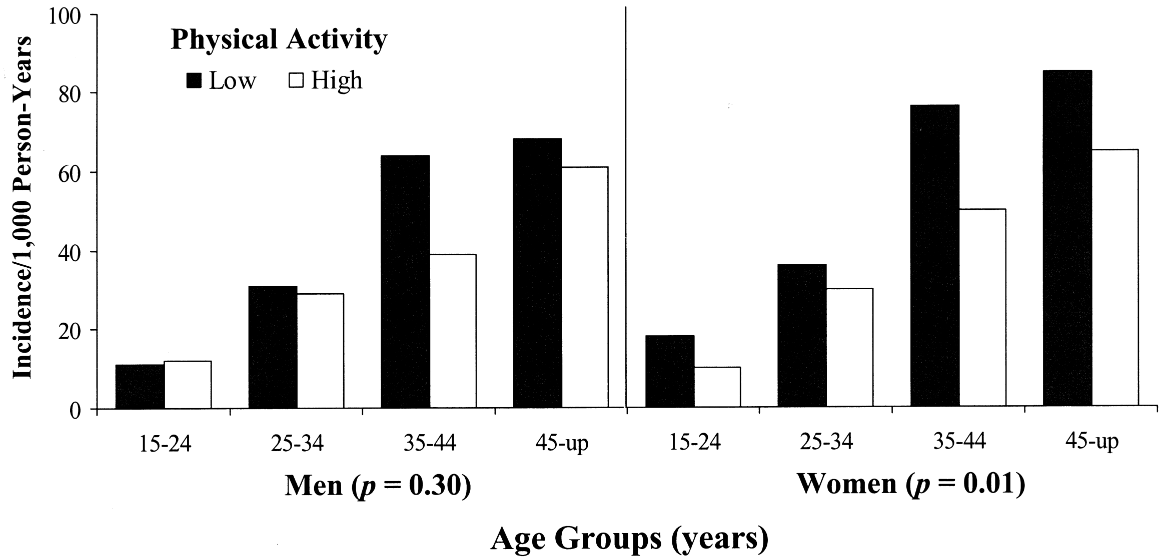

FIGURE 1. Diabetes incidence rates by total physical activity levels in a follow-up of 1,728 Pima Indians without diabetes at baseline, Gila River Indian Community, 1987–2000. Dark bar, low activity; light bar, high activity.

although this difference was statistically significant ($p = 0.01$) only in women. If occupational activity is removed from the physical activity estimate, the relation between physical activity and diabetes incidence is strengthened (data not shown).

The time-dependent Cox proportional hazards model was used to estimate the age-adjusted effect of physical activity on diabetes incidence alone and then with body mass index added to the model (table 2). Consistent with the findings presented in figure 1, total physical activity was significantly ($p < 0.05$) related to diabetes incidence in women but not in men. If occupational activity is removed from the physical activity estimate, the relation between leisure physical activity and diabetes incidence is strengthened, particularly in men. After adjustment for body mass index, the relation between activity and diabetes incidence was weakened in both men and women. Similar results were found if weight was added to the model instead of body mass index.

Diabetes incidence rates for men and women are presented in figure 2 by levels of total (leisure and occupational) physical activity stratified by approximate tertile of body mass index and adjusted for age. (The mean values and range for the three body mass index tertiles for men are 1 = mean of 24 kg/m^2 (ranging from ≥17 to <28), 2 = 31 kg/m^2 (ranging

TABLE 2. Time-dependent proportional hazard regression predicting diabetes incidence by physical activity level (high/low), Gila River Indian Community, 1987–2000*

	Events (no.)/total (no.)	Variable	Hazard ratio	95% confidence interval	*p* value
Men	116/676				
	Controlled for age	Leisure activity	0.66	0.45, 0.99	0.04
		Total activity	0.82	0.51, 1.30	0.4
	Controlled for age and body mass index	Leisure activity	0.88	0.59, 1.34	0.06
		Total activity	1.10	0.67, 1.78	0.7
Women	230/1,052				
	Controlled for age	Leisure activity	0.70	0.53, 0.92	0.01
		Total activity	0.75	0.58, 0.97	0.03
	Controlled for age and body mass index	Leisure activity	0.74	0.56, 0.97	0.03
		Total activity	0.78	0.60, 1.02	0.07

* There were no significant interactions between physical activity and body mass index in any of the eight analyses.

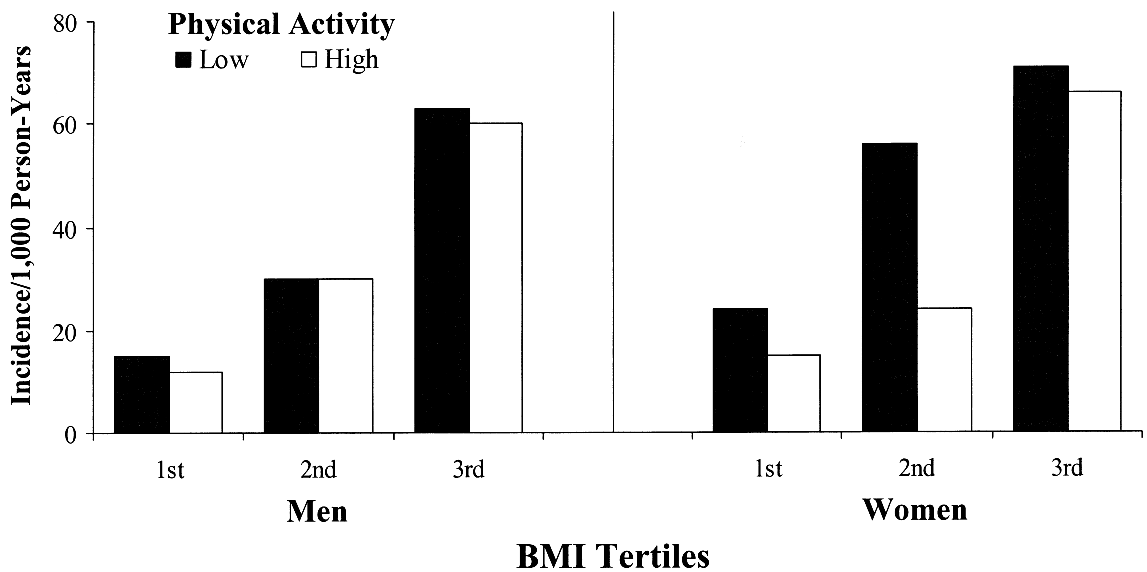

FIGURE 2. Diabetes incidence rates per 1,000 person-years by total physical activity and body mass index (adjusted for age), Gila River Indian Community, 1987–2000. Dark bar, low activity; light bar, high activity. BMI, body mass index.

from ≥28 to <33), and 3 = 40 kg/m^2 (ranging from ≥33 to <66); and for women they are 1 = mean of 24 kg/m^2 (ranging from ≥16 to <30), 2 = 32 (ranging from ≥30 to <36), and 3 = 42 (ranging from ≥36 to <69).) The diabetes incidence rate remained lower in the more active than in the less active individuals in all body mass index groups for both men and women, with the exception of the middle body mass index tertile in men. This relation between physical activity and diabetes incidence adjusted for age and body mass index was statistically significant only in women ($p < 0.01$). There was no significant interaction between age, body mass index, or sex and total physical activity.

DISCUSSION

The finding that a physically active lifestyle is associated with a lower incidence of type 2 diabetes has been shown in several prospective studies. Physical activity was inversely related to the incidence of type 2 diabetes among male alumni from the University of Pennsylvania (15), a relation that was particularly evident in men at high risk for developing diabetes (defined as those with a high body mass index, a history of hypertension, or a parental history of diabetes). In a study of female registered nurses aged 34–59 years at baseline, women who reported engaging in vigorous exercise at least once a week had a lower incidence of self-reported type 2 diabetes during the 8 years of follow-up than did women who did not exercise weekly (16). Similar findings were observed between exercise and incidence of type 2 diabetes in a 5-year prospective study of male physicians aged 40–84 years (17). Likewise, in a large cohort of postmenopausal women aged 55–69 years, the 12-year incidence of diabetes was lower in those women who reported any physical activity compared with the sedentary women (18). In all of these prospective studies, however, the diagnosis of diabetes was based upon self-reported, physician-diagnosed diabetes.

The results of the present study are consistent with those of the other prospective studies in the literature although different from these studies in that diabetes was determined objectively by an oral glucose tolerance test rather than through subjective reporting. Individuals reporting participation in more physical activities were less likely to develop type 2 diabetes over time. Specifically, for most age/sex groups, the diabetes incidence rate was lower in the more active than in the less active individuals, although this difference was statistically significant only in women.

In previous cross-sectional analyses in this population, total physical activity levels (leisure and occupational activities combined) were significantly related to both glucose and insulin concentrations (5, 11). These cross-sectional findings were much stronger in men than in women. Why, then, would the prospective relation between physical activity and the development of type 2 diabetes appear to be stronger in women? Although the effect of physical activity was not statistically stronger in women than in men (i.e., there was no significant sex/activity interaction), a stronger effect in women is plausible because of the lack of consistency of occupational physical activity over time in this population. In the current analyses, a total physical activity estimate was used (representing the combination of occupational and leisure activity). Although leisure physical activity appears to be the larger contributor to total physical activity levels for most Pima men and women (11), occupational activity is a large contributor among the individuals who had physically active jobs. However, many of these physically demanding jobs held by this population are seasonal and are not maintained over the years. This is supported by the finding that, despite the fact that the short-term (2- to 3-week) test-retest correlation was high for both the leisure and occupational estimates of the activity questionnaire (8), the less than 3-year, the 3- to 6-year, and the greater than 6-year correlations were substantially lower for occupational activity than for leisure activity. In other words, the tracking of occupational activity levels over time in this population was much weaker than that of leisure activity. Therefore, the reason that the prospective relation between physical activity and the development of type 2 diabetes may be stronger in women than in men may be due to our assessment of physical activity. Because men in this population held the majority of the occupationally active jobs, the inadequate assessment of occupational activity in the physical activity estimate would be more of an issue in men than in women. This is a limitation of this study that could be corrected in future efforts by more frequent assessments of physical activity throughout the follow-up period.

Finally, although physical activity significantly predicted diabetes, how likely is it that activity can play a role in the prevention of type 2 diabetes independently of its effect on weight loss and body composition? The present effort mirrors the findings of other large prospective studies that have examined the relation of physical activity and the development of diabetes. In general, these findings demonstrate that the relation between activity and diabetes development is attenuated but persists when body mass index is added to the model (15–18). Interestingly, this attenuation was greater for men than women in the present study. Similarly, the incidence of diabetes remained lower in the more active individuals across most categories of body mass index for both men and women in this study and other studies, despite the varied range of body mass index values and the different body mass index groupings used in the various populations examined (16–18). Finally, of the recent clinical trials of type 2 diabetes prevention, the Da Qing Study was the only one that had an exercise-alone arm (1). The decrease in diabetes development in the exercise intervention arm occurred without a significant change in body mass index and was evident in both initially lean (body mass index, <25 kg/m^2) and overweight (body mass index, ≥25 kg/m^2) participants.

To understand the potential contribution of physical activity to the prevention of type 2 diabetes apart from its effect on weight loss and body composition, one must define the physiologic basis underlying the relation between activity and diabetes. Beyond the effect of activity on body mass and composition, physical activity may reduce the risk for type 2 diabetes directly through improvements in insulin sensitivity (4). However, a large portion of the effect of physical activity in decreasing insulin resistance is short lived and may last only a few days (19, 20). Thus, the consistency of an individual's activity throughout the years is a key issue that needs to be measured before one can understand the mechanisms underlying the relation between physical activity and diabetes prevention. This again identifies the need for more frequent measurement of physical activity (ideally with an objective measure) throughout the follow-up period to assess the benefits of activity beyond its effect on body weight. Regardless of whether the effects of physical activity in the prevention of diabetes are independent of its influence on body composition, the available data, including those from the present study, suggest that the adoption and maintenance of a physically active lifestyle can play a significant role in the prevention of type 2 diabetes.

ACKNOWLEDGMENTS

Dr. Kriska was supported in part by grant RO1 DK43394-06A1 from the National Institute of Diabetes and Digestive and Kidney Diseases.

The authors are indebted to the members of the Gila River Indian Community for cooperating with this investigation; to Angelina Barley, Helen Johns, Joy Jones, and Sonja Antone for assisting in the data collection; and to the staff of the Diabetes and Arthritis Epidemiology Section for conducting the examinations. The helpful comments of Dr. Robert G. Nelson are greatly appreciated.

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