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Physical Activity of Moderate Intensity and Risk of Type 2 Diabetes

A systematic review

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OBJECTIVE — To systematically evaluate the evidence for an association between physical activity of moderate intensity and risk of type 2 diabetes.

RESEARCH DESIGN AND METHODS — We searched EMBASE and Medline through March 2006 and examined reference lists of retrieved articles. We excluded studies that did not assess physical activity of moderate intensity independent of activities of vigorous intensity (more than six times the resting metabolic rate). Information on study design, participant characteristics, assessment of physical activity, and outcomes and estimates of associations were extracted independently by two investigators. We calculated summary relative risks (RRs) using a random-effects model for the highest versus the lowest reported duration of activities.

RESULTS — We identified 10 prospective cohort studies of physical activity of moderate intensity and type 2 diabetes, including a total of 301,221 participants and 9,367 incident cases. Five of these studies specifically investigated the role of walking. The summary RR of type 2 diabetes was 0.69 (95% CI 0.58–0.83) for regular participation in physical activity of moderate intensity as compared with being sedentary. Similarly, the RR was 0.70 (0.58–0.84) for regular walking (typically ≥2.5 h/week brisk walking) as compared with almost no walking. The associations remained significant after adjustment for BMI. Similar associations were observed in men and women and in the U.S. and Europe.

CONCLUSIONS — These findings indicate that adherence to recommendations to participate in physical activities of moderate intensity such as brisk walking can substantially reduce the risk of type 2 diabetes.

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The prevalence of type 2 diabetes is high and expected to increase dramatically in the U.S. and worldwide (1). Type 2 diabetes is a chronic disease associated with premature mortality and various debilitating complications (2). Intensive treatment regimens can prevent some but not all complications (3). Therefore, primary prevention efforts are clearly needed.

Moderately intense physical activities, such as walking and gardening, are the most common forms of activity among adults in the U.S. (4) and may be an easily adoptable, relatively safe means to reduce the risk of type 2 diabetes. Randomized trials have shown that physical activity alone or in conjunction with dietary changes can reduce the incidence of type 2 diabetes (5–8). However, the intensity of activity required remains unclear because the independent role of moderately intense activities has not been directly examined in these trials.

Observational studies have consistently reported an inverse association between physical activity and type 2 diabetes, but most of these studies focused on vigorous activities or physical activity of various intensities combined (e.g., 9,10). In this article, we systematically review the epidemiological evidence on the association between physical activity of moderate intensity and risk of type 2 diabetes.

RESEARCH DESIGN AND METHODS

We searched EMBASE and Medline through March 2006 for prospective cohort and cross-sectional studies investigating the association between moderately intense physical activity and incidence and prevalence of type 2 diabetes. The search terms "physical activity," "exercise," and "walking" were used in combination with "noninsulin dependent diabetes mellitus," "NIDDM," and "type 2 diabetes," and references lists of retrieved articles were examined. Physical activity of moderate intensity was defined as requiring a metabolic equivalent task (MET) score of 3.0–6.0 (11). One MET corresponds to the energy expenditure during rest (quiet sitting). A typical activity of moderate intensity is "brisk" walking at 5.6 km/h (3.5 miles/h) on a flat surface requiring 3.8 MET (12). Other common activities of moderate intensity include playing golf, leisure bicycling at <16 km/h (10 miles/h), and gardening (12).

The EMBASE and Medline searches were performed independently by two investigators (C.Y.J. and R.P.L.), yielding 491 and 488 articles, respectively. Two additional relevant articles were found by examination of reference lists of retrieved articles. Studies were excluded if they did not involve human subjects, did not present age-adjusted estimates, involved study populations overlapping with other studies, or combined moderately intense activity with strenuous or light activity. Ten prospective cohort studies (13–22) and six cross-sectional studies (23–28) were eligible. Because of the large heterogeneity in exposure and outcome measures for the cross-sectional studies, a

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Abbreviations: MET, metabolic equivalent task.

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

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Table 1—*Cohort studies of moderately intense physical activity and risk of type 2 diabetes*

Lead author, year (ref.)	Country	Sex	Age (years)	*N*/*n* cases	Moderate-intensity activity	Diabetes assessment	Follow-up (years)	Adjustments
Helmrich, 1991 (13)	U.S.	M	39–68	5,990/202	Nonvigorous (∼5 MET h) sports only vs. no sports participation; walking: ≥15 vs. <5 blocks/day	Self-report of physician diagnosis	14	Age
Lynch, 1996 (14)	Finland	M	42–60	897/46	Activities requiring <5.5 MET h for at least 2 h/week (yes vs. no)	OGTT or self-report of antidiabetes medication	4.2	Age, BMI, baseline glucose level, duration of vigorous activities
Hu FB, 1999 (15)	U.S.	F	40–65	70,912/1,419	Walking in MET h/week among those who did not perform vigorous activities (highest [≥10 MET h/week] vs. lowest [≤0.5 MET h/week] quintile)	Self-report of physician diagnosis (validated)	8	Age, BMI, smoking, menopausal status, hormone therapy, parental history of diabetes, alcohol use, hypertension, hypercholesterolemia
Folsom, 2000 (16)	U.S.	F	55–69	34,257/1,997	Frequency of activities ≤6.0 MET h (>4 times/week vs. rare or never)	Self-report of physician diagnosis	12	Age, BMI, waist-to-hip ratio, education, smoking, alcohol use, hormone therapy use, family history of diabetes, dietary factors
Okada, 2000 (17)	Japan	M	35–60	6,013/444	Weekend leisure-time activity (gardening, home repairs, shopping) vs. being sedentary during weekends	OGTT	10	Age, BMI, alcohol use, smoking status, hypertension, parental history of diabetes, weekday physical activity
Wannamethee, 2000 (18)	U.K.	M	40–59	5,159/196	Regular walking or recreational activities (gardening and home repairs) vs. sedentary	Primary care records	16.9	Age, BMI, smoking, alcohol use, social class, preexisting coronary heart disease
Hu FB, 2001 (19)	U.S.	M	40–75	37,918/1,058	Walking in MET h/week (highest vs. lowest quintile)	Self-report of physician diagnosis (validated)	10	Age, smoking, parental history of diabetes, hypertension, BMI, dietary factors, vigorous exercise
Hu G, 2003 (20)	Finland	M/F	35–64	14,290/373	Leisure-time physical activity (walking, cycling, light gardening) >4 h/week vs. less	National registries	12	Age, BMI, study year, systolic blood pressure, smoking status, education, other physical activity
Weinstein, 2004 (21)	U.S.	F	≥45	37,878/1,361	Walking (≥4 h/week vs. none)	Self-report of physician diagnosis (validated)	6.9	Age, BMI, family history of diabetes, alcohol use, smoking, hormone therapy, hypertension, hypercholesterolemia, dietary factors, treatment group, other physical activity
Hsia, 2005 (22)	U.S.	F	Post-menopausal	87,907/2,271	Walking (highest [>10 MET h/week] vs. lowest [0 MET h/week] quintile)	Self-report of antidiabetes medicaton	5.1	Age, BMI, alcohol use, education, smoking status, hypertension, hypercholesterolemia, dietary factors

MET = work metabolic rate/resting metabolic rate. OGTT, oral glucose tolerance test.

meta-analysis was only conducted for the cohort studies.

Information on study design, participant characteristics, definition of moderately intense physical activity, adjustments for potential confounders, and estimates of associations were abstracted independently by two investigators (C.Y.J. and R.P.L.). In all studies, estimates of relative risks (RRs) with information about their variance were reported. For studies that reported more than one level of moderately intense activity, the RR for the highest as compared with the lowest level of activity was abstracted.

Statistical analysis

We used STATA version 9.1 (STATA, College Station, TX) for all statistical analyses. Summary measures were calculated using random-effects models, which allow each of the studies to estimate a different effect size (29). *P* values for heterogeneity of study results were calculated using Cochran's Q test (30). When available, we separately analyzed BMI-unadjusted and -adjusted results from the original studies to assess the role of physical activity independent of its association with weight. To examine sources of heterogeneity, we conducted metaregression analysis with the log RR of studies as dependent variable and country (U.S./other) and sex (male/female) as independent variables. We assessed potential publication bias using funnel plots, plots of RRs versus precision, and the Begg (31) and Egger (32) tests.

RESULTS

Cohort studies

We identified 10 cohort studies on physical activity of moderate intensity and risk of type 2 diabetes, including a total of 301,221 participants and 9,367 incident cases. Table 1 shows the characteristics of the included studies. Fig. 1 shows the results for moderately intense physical activity and risk of type 2 diabetes with and without adjustment for BMI. For one study only BMI-unadjusted (13) and for one study only BMI-adjusted estimates were presented (22). The summary RR of type 2 diabetes without BMI adjustment was 0.69 (95% CI 0.58–0.83) for the highest as compared with the lowest category of moderate-intensity physical activity. The BMI-adjusted RR of diabetes was 0.83 (0.76–0.90). The *P* value for heterogeneity in study results was <0.001 for the BMI-unadjusted and 0.24 for the BMI-adjusted estimates.

In five of the cohort studies the specific role of walking was examined (13,15,19,21,22). Figure 2 shows the results for walking and risk of type 2 diabetes. The BMI-unadjusted summary RR comparing the highest with the lowest walking level was 0.70 (95% CI 0.58–0.84), and the BMI-adjusted RR was 0.83 (0.75–0.91). *P* values for heterogeneity were 0.08 for the BMI-unadjusted and 0.68 for the BMI-adjusted estimates. The reported amount of walking for the reference category was minimal, and the amount in the highest category was at least 10 MET h/week (15,22), which is equivalent to ~2.5 h/week of brisk walking. Amounts of walking of 2–3 h/week (21), 2.1–3.8 MET h/week (15), and 5.1–10.0 MET h/week (22) have also been associated with a significantly lower risk of type 2 diabetes as compared with being sedentary.

All but two studies (16,22) considered confounding by vigorous physical activity by adjusting for vigorous activity or excluding participants that engaged in vigorous activities. The studies that did not consider potential confounding by vigorous activity did not consistently report stronger or weaker associations than the other studies.

The Egger and Begg tests provided no evidence for publication bias for the BMI-unadjusted ($P = 0.63$ and $P = 0.84$, respectively) and BMI-adjusted ($P = 0.83$ and $P = 0.40$) association between moderately intense physical activity and risk of type 2 diabetes.

Characteristics of the study population

The inverse association between moderately intense physical activity and type 2 diabetes was observed in populations from the U.S., Finland, and the U.K. (Table 1). In the Japanese study by Okada et al. (17), no inverse association was observed, but this may have been due to the moderate-intensity activity definition that was restricted to weekends, included relatively light-intensity activities, and did not consider duration. We conducted a metaregression analysis for the association between moderate-intensity physical activity and did not find significant differences in results between U.S. and non-U.S. populations ($P = 0.20$). The summary RR for the U.S. studies was 0.68 (95% CI 0.56–0.81), while that of the non-U.S. studies was 0.75 (0.56–1.00). After excluding the study by Okada et al. (17), the RR for non-U.S. studies was 0.66 (0.54–0.80) and the *P* value for difference by region 0.96. For the BMI-adjusted RRs, the *P* values for difference by region was 0.07 before and 0.75 after exclusion of the study by Okada et al. We also evaluated potential differences by sex. The BMI-unadjusted association between moderate-intensity physical activity and diabetes risk was significantly stronger for female (RR 0.58 [95% CI 0.51–0.65]) than for male (0.82 [0.70–0.96]) cohorts ($P = 0.04$). However, after excluding the study by Okada et al., the RR for male cohorts became 0.77 (95% CI 0.67–0.88) and the difference with the female cohorts no longer statistically significant ($P = 0.36$). For the BMI-adjusted RRs, the *P* values for differences between male and female cohorts was 0.17 before and 0.81 after exclusion of the study by Okada et al.

Cross-sectional studies

Six cross-sectional studies that examined the association between moderately intense activities and type 2 diabetes or impaired glucose tolerance (Table 2) were identified. Results from two Dutch studies suggested inverse associations for gardening and bicycling (which tends to be of easy pace in this population) but not for walking (24,26). In a French study, participation in moderately intense household activities was inversely associated with type 2 diabetes (25). Two other studies were consistent with an inverse association between moderately intense activities and type 2 diabetes, but CIs were wide (23,27). In an Australian study, 2.5 h/week of moderately intense activities as compared with less time spent on these activities tended to be associated with a lower prevalence of abnormal glucose metabolism in women but not in men (28).

CONCLUSIONS — In our meta-analysis of 10 prospective cohort studies, a substantial inverse association was observed between physical activity of moderate intensity and risk of type 2 diabetes. Those who regularly engaged in physical activity of moderate intensity had ~30% lower risk of type 2 diabetes as compared with sedentary individuals. A similar decrease in diabetes risk was observed when we specifically examined regular walking. After adjustment for BMI, the reduction in diabetes risk remained substantial (17%)

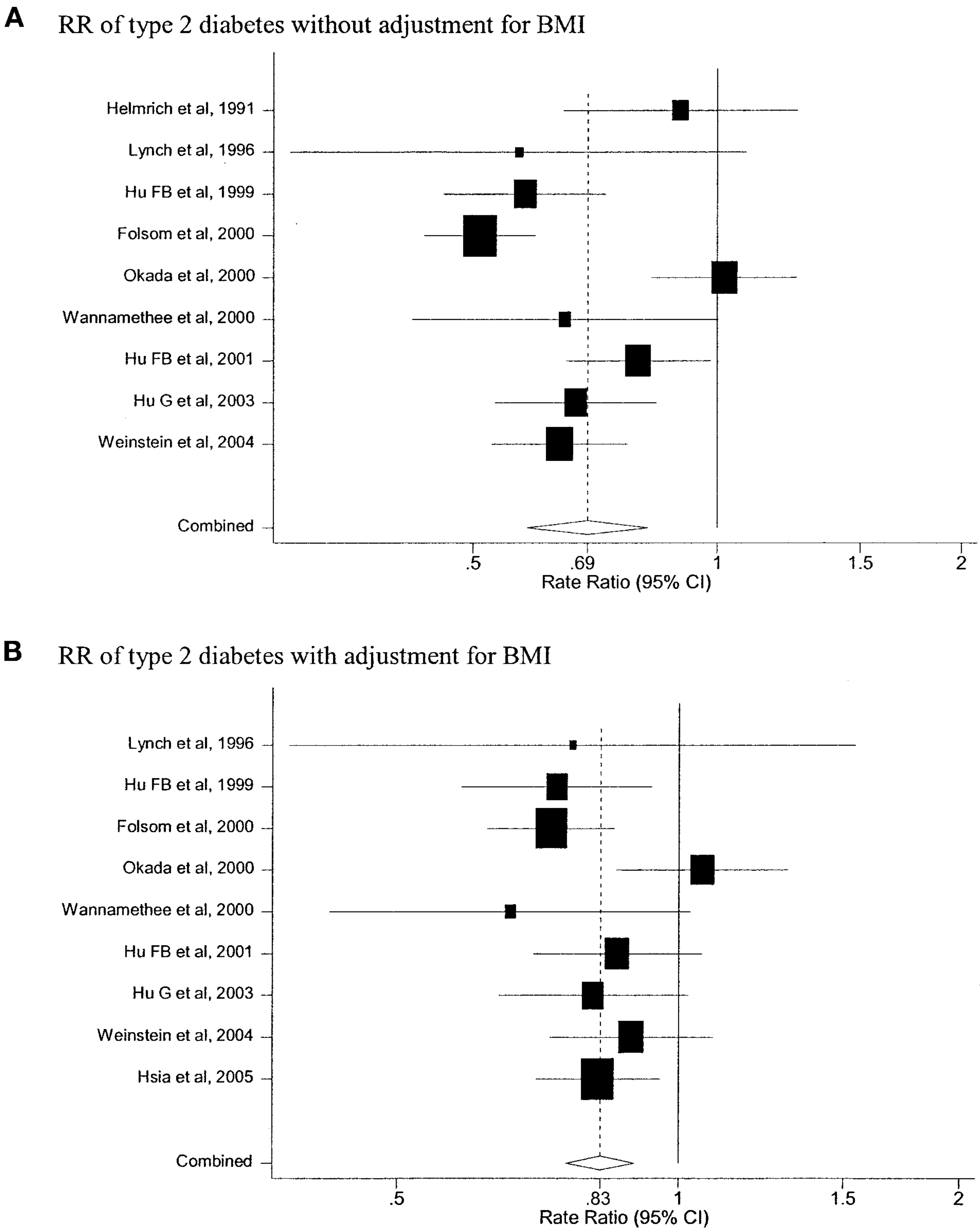

Figure 1—*RRs for total physical activity of moderate intensity and incidence of type 2 diabetes for individual cohort studies and all studies combined without adjustment for BMI (A) and with adjustment for BMI (B). RR comparing the highest with the lowest reported level of moderate-intensity activity are shown in Table 1. Filled bars and open diamonds indicate 95% CIs. The size of the squares corresponds to the weight of the study in the meta-analysis.*

for both regular moderately intense activity and walking.

Significant inverse associations were observed in both men and women and in both U.S. and Northern European cohorts. Most studies were conducted in predominantly white populations. No significant association between moderate-intensity physical activity and type 2 diabetes was observed in the two studies that reported results for other ethnic groups, but this may have been due to the "light"

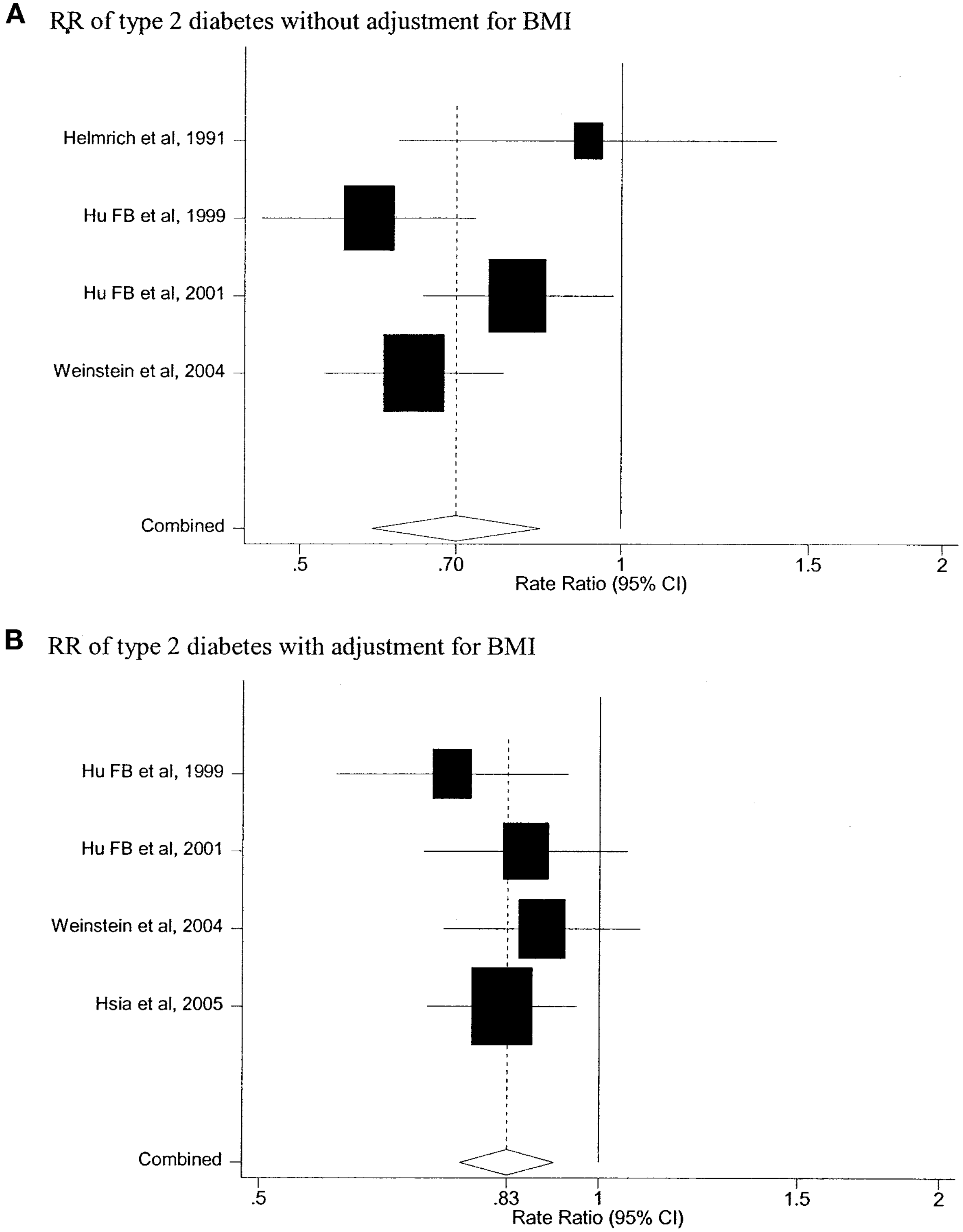

Figure 2—*RRs for walking and incidence of type 2 diabetes for individual cohort studies and all studies combined without adjustment for BMI* (A) *and with adjustment for BMI* (B). *RR comparing the highest with the lowest reported level of walking are shown in Table 1. Filled bars and open diamonds indicate 95% CIs. The size of the squares corresponds to the weight of the study in the meta-analysis.*

definition of activity (17) and limited statistical power as a result of lower numbers for nonwhites (22). In the Diabetes Prevention Program, the lifestyle intervention that focused on both diet and physical activity resulted in a similar reduction in incidence of type 2 diabetes in participants of African-American, Hispanic, American-Indian, and Asian ethnicity as compared with whites (6,33).

Results from cross-sectional studies were generally consistent with an inverse association between moderately intense physical activity and type 2 diabetes. Results were more heterogeneous than for

Table 2—*Cross-sectional studies of moderately intense physical activity and risk of type 2 diabetes*

Lead author, year (ref.)	Country	Sex	Age (years)	*N*/*n* cases	Outcome assessment	Classification moderate-intensity activity	OR (95% CI)	Adjustments
James, 1998 (23)	U.S.	M/F	30–55	916/78	Type 2 diabetes: FBG or use of antidiabetes medication	Walking for ≥15 min at a time or home maintenance/gardening vs. inactive	0.51 (0.20–1.28)	Age, sex, education, BMI, waist-to-hip ratio
Baan, 1999 (24)	Netherlands	M	55–75	503/69	Type 2 diabetes: 2-h postload glucose or use of antidiabetes medication	Walking (≥285 vs. <60 min/week)	1.45 (0.63–3.32)	Age, BMI, waist-to-hip ratio, family history of diabetes, smoking
						Bicycling (yes vs. no)	0.26 (0.14–0.49)	
						Gardening (yes vs. no)	0.56 (0.29–1.06)	
		F	55–75	513/49	Same as male participants	Walking (≥270 vs. <45 min/week)	1.05 (0.47–2.36)	Same as male participants
						Bicycling (yes vs. no)	0.37 (0.18–0.78)	
						Gardening (yes vs. no)	0.46 (0.21–1.01)	
Defay, 2001 (25)	France	M	>60	1,113/213	Type 2 diabetes: FBG or use of antidiabetes medication	Usual intensity of household activities (moderate vs. light)	0.67 (0.48–0.94)	None
		F	>60	1,419/132	Same as male participants	Usual intensity of household activities (moderate vs. light)	0.61 (0.40–0.95)	None
van Dam, 2002 (26)	Netherlands	M	69–89	424/90	IGT or newly detected type 2 diabetes: OGTT	Taking walks (>20 min/day vs. none)	0.92 (0.46–1.88)	Age, other physical activities
						Bicycling (>20 min/day vs. none)	0.37 (0.20–0.70)	
						Gardening (>20 min/day vs. none)	0.33 (0.16–0.66)	
Combe, 2004 (27)	France	M	20–74	3,759/299	Newly detected type 2 diabetes: FBG	Walking >1 h/day (yes vs. no)	0.81 (0.64–1.04)	None
Dunstan, 2004 (28)	Australia	M	≥25	8,299/1,555 (men and women)	IFG, IGT, or newly detected type 2 diabetes: OGTT	Walking and "other" moderate-intensity activities (≥2.5 vs. <2.5 h/week)	0.96 (0.66–1.40)	Age, sex, education, family history of diabetes, smoking, dietary factors, TV watching, waist circumference
		F	≥25		Same as male participants	Walking and "other" moderate-intensity activities (≥2.5 vs. <2.5 h/week)	0.73 (0.53–1.01)	Same as male participants

FBP, fasting blood glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

the prospective studies, possibly as a result of the smaller study sizes and differences in the activity classification. In two cross-sectional studies of Dutch elderly, no association was observed for walking, whereas other moderately intense activities were inversely association with type 2 diabetes (24,26). This lack of association for walking may have reflected a lower average walking pace in these elderly populations. A brisk usual walking pace was associated with a substantially lower risk of type 2 diabetes compared with an easy pace in two U.S. studies (15,19).

Strengths and limitations of the data

Because our meta-analysis included only observational studies, it is possible that the summary estimates were influenced by confounding and other biases. Although all studies adjusted for age, not all adjusted for known or suspected diabetes risk factors such as dietary factors, alcohol consumption, cigarette smoking, and waist-to-hip ratio. The inverse association was similar in studies with the most complete adjustment for confounding, but we cannot fully exclude residual confounding by unmeasured or imprecisely measured diabetes risk factors. Lack of adjustment for light-intensity physical activity or sedentary activities may also have resulted in residual confounding (15,19). Furthermore, the included studies mostly focused on leisure time physical activity, but commuting and occupational activities can also contribute importantly to the accumulation of moderately intense physical activity for the reduction of diabetes risk (20,34).

The prospective design of the cohort studies and low loss to follow-up in most studies reduced the likelihood of selection bias. Some misclassification of moderate-intensity physical activity probably occurred, but it seems unlikely that this misclassification differed by future diabetes outcome, and it can thus be expected to have biased estimates of associations toward the null. In the studies that relied upon self-report of a physician's diagnosis of diabetes, differences in detection of diabetes associated with physical activity could have led to diagnostic bias. This is unlikely given that several cross-sectional studies measured glucose concentrations in all participants, and restriction to symptomatic cases did not substantially affect the results in a cohort study (15). We did not find any evidence of publication bias based on the Egger and Begg test and the funnel plot. However, the power of these tests is known to be limited (35), and we cannot fully exclude the possibility that publication bias has affected our results.

Mechanisms

We found a significant inverse association between moderately intense physical activity and type 2 diabetes that persisted after adjustment for BMI. In line with this finding, biological mechanisms have been identified for beneficial effects of physical activity on glucose metabolism independent of body fatness. Exercise has been shown to increase insulin-stimulated glycogen synthesis through an increased rate of insulin-stimulated glucose transport by GLUT4 glucose transporters and increased glycogen synthase activity (36). In addition, elevated capillary proliferation in muscles, increased muscle mass, and a higher proportion of more insulin-sensitive types of muscle fibers may contribute to beneficial effects of physical activity on insulin sensitivity (37).

Findings from intervention studies

No large randomized trials have specifically investigated the effect of increasing physical activity of moderate intensity on incidence of type 2 diabetes. A randomized trial of moderate-intensity physical activity in individuals with a family history of diabetes did not find a significant reduction in incidence of type 2 diabetes after 2 years, but compliance with the program was poor and the number of participants small ($n = 37$ in the exercise program) (38). In a 2-year randomized controlled trial in 179 individuals with type 2 diabetes, counseling to achieve 10 MET h/ week of moderately intense physical activity resulted in significantly reduced body weight and fasting glucose and A1C concentrations (39). In a post hoc analysis, a significant reduction in A1C was observed for participants that increased 11–20 MET h/week, but greater beneficial effects were observed in those who increased their activity with 21–30 MET h/week (39). Several randomized controlled trials tested the effects of brisk walking on glucose metabolism in individuals without diabetes (40–42). Increased walking resulted in reduced plasma insulin (40,41) or glucose (42) concentrations after 12–24 weeks.

A Chinese trial in individuals with impaired glucose tolerance found that those randomized at the clinic level to a combination of moderate and vigorous activities had a 47% reduction in incidence of type 2 diabetes as compared with the control group (7). A post hoc analysis of the Finnish Diabetes Prevention Study examined the association between walking during follow-up and incidence of type 2 diabetes. After adjustment for other activities, dietary factors, and BMI, at least 2.5 h/week of walking for exercise was associated with a 63% lower risk of type 2 diabetes as compared with <1 h/week (43). In addition, an increase in walking intensity was associated with a lower risk of type 2 diabetes.

Recommendations

Our systematic review indicates that regular participation in moderately intense physical activity is associated with a substantially lower risk of type 2 diabetes. The association was partly independent of BMI, suggesting that moderate-intensity physical activity can reduce the risk of type 2 diabetes even in those who do not achieve weight loss. Findings from several prospective studies (15,21,22,43) indicate that 30 min or more of daily moderate-intensity activity, as recommended in multiple U.S. guidelines (11,44), can substantially reduce the risk of type 2 diabetes as compared with being sedentary. Moderately intense activity as defined in guidelines (3.0–6.0 MET h) (11) includes walking at brisk pace but not walking at an easy or casual pace (12), and walking at brisk pace also seems preferable for the prevention of type 2 diabetes (15,19,43). Further studies are needed to define more specifically what combinations and duration and pace are optimal for reducing the risk of type 2 diabetes. However, given that only 31% of adults in the U.S. currently meet the general physical activity recommendations (45), efforts to prevent type 2 diabetes should strongly emphasize the benefit of moderately intense physical activities and encourage wider participation in these activities.

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