EDITOR'S CHOICE

Physical activity, cardiorespiratory fitness and the incidence of type 2 diabetes in a prospective study of men

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ABSTRACT

Objective To assess the independent and joint associations between self-reported physical activity (PA) and objectively measured cardiorespiratory fitness (CRF) from a maximal treadmill exercise test and the development of type 2 diabetes mellitus in a large cohort of men.

Methods Participants for the current analysis were 23 444 men aged 20–85 years free of cardiovascular disease (CVD), cancer or diabetes at baseline. Incident diabetes were identified from mail-back surveys. Cox regression analysis was used to estimate hazard ratios (HRs), 95% confidence intervals (CIs) and diabetes incidence rates (per 10 000 man-years) according to exposure categories.

Results During an average of 18 years of follow-up, 589 incident cases of diabetes were identified. After adjusting for age, examination year, survey response pattern, body mass index, smoking, drinking, fasting glucose, chronic diseases and family history of CVD or diabetes, the walking/jogging/running (WJR) and sport/fitness groups had a 40% and 28% lower risk of developing diabetes compared with the sedentary men, respectively (both $p < 0.05$). For CRF, diabetes incidence rates were 31.9, 14.5 and 6.5 for low-, moderate- and high-fitness groups, respectively. After adjustment for the above covariables, moderate and high CRF had a 38% and 63% lower risk of developing diabetes compared with the low CRF group (p trend<0.0001).

Conclusion Our findings showed a lower risk of developing diabetes for men who participated in a WJR programme or sport/fitness activity, compared with those who were sedentary. Higher levels of fitness were associated with an inverse gradient of incident diabetes.

Type 2 diabetes is a major public health problem. The American Diabetes Association (ADA) reported in 2006 that 9.3% of the US population have diabetes, where 2.8% were undiagnosed.[1] The 2007 estimated direct and indirect cost of diabetes in the US was $178 billion in medical expenses, lost productivity and disability. People with diagnosed diabetes have medical expenditures that are approximately 2.3 times higher per year than those without.[2] Mounting evidence has suggested that physical activity (PA) or cardiorespiratory fitness (CRF) has protective influences on hyperglycaemia[3] and incident diabetes.[3–17] The significance of the evidence has led several organisations, including the American Heart Association, the ADA and the US Department of Health and Human Services to include PA in their recommendations and guidelines.[18 19]

Studies have shown that participation in PA produces multiple health benefits and is inversely associated with incident diabetes.[4 7–12 14] This is inclusive for all activity levels from moderate[6] to vigorous (eg, brisk walking to running).[7] While most studies have been based on self-reported PA, self-reported measures correlate only modestly with objective measures obtained using criterion methods.[20–24] Thus, the true effects of PA on diabetes may not have been fully captured. To overcome the shortcomings of previous studies, we need to examine not only the self-reported PA but also objective exposures such as CRF.[22 25] CRF, an objective reproducible measure that reflects the functional consequences of recent PA habits, disease and genetics,[26] may have different effects on the incidence of diabetes.

Previous studies have reported an inverse association between the fitness level and incident diabetes.[3 4 8 10 15–17] However, very few prospective epidemiological studies have simultaneously examined both CRF and PA and incident diabetes in adults.[16 27] Because CRF and PA are correlated only modestly, more studies are needed to examine the interaction of PA and CRF on incident diabetes to explain these protective influences. Therefore, we set forth to assess the independent and joint associations between PA and CRF and the development of type 2 diabetes mellitus in a large cohort of men from the Aerobics Center Longitudinal Study (ACLS).

METHODS

Participants

The ACLS is a prospective epidemiological study of the health effects of PA and fitness. Data were obtained from a population of patients at the Cooper Clinic, a preventive medicine clinic in Dallas, Texas, USA. Participants came to the clinic for periodic preventive health examinations and for counselling regarding diet, exercise and other lifestyle factors associated with increased risk of chronic disease. Participants thus were volunteers, were not paid and were not recruited specifically to the study, as would be the case for a clinical trial. Many were sent by their employers for the examination, some were referred by their physicians, and others were self-referred. Participants for the current analysis were 23 444 men aged 20–85 years who completed a clinical examination during 1970–2003 and had no

history of known cardiovascular disease (CVD) or cancer. They also reported no physician diagnosis of diabetes, were not taking insulin and had a fasting blood glucose of <126 mg/dl at baseline. The men were predominantly white, well educated and from middle to upper socio-economic strata. All participants provided written consent to participate in the examination and in the follow-up research. The study protocol was reviewed and approved annually by the Cooper Institute Institutional Review Board.

Clinical examination

The comprehensive health evaluation was completed following a minimum 12 h fast and has been described in detail elsewhere.[28 29] Briefly, information pertaining to personal and family health histories, personal health habits and demographic information was obtained from standardised medical history questionnaires. Body mass index (BMI) was calculated from measured height and weight as kg/m^2. Resting blood pressure was recorded as the first and fifth Korotkoff sounds using auscultation methods.[30] An antecubital venous blood sample was obtained, and plasma concentrations of lipids and glucose were determined with standardised automated bioassays at the Cooper Clinic Laboratory, which participated in and met quality control criteria of the Centers for Disease Control and Prevention Lipid Standardization Program. Hypertension was defined as a resting blood pressure of 140/90 mm Hg or greater, or a history of physician diagnosis. Hypercholesterolaemia was defined as a total cholesterol of 240 mg/dl or greater. Personal history of CVD (myocardial infarction or stroke), information on smoking habits (never, former or current smoker), alcohol intake (drinks per week), family (from parents and siblings, ie, first-degree relatives) history of CVD or diabetes, and PA habits (sedentary, walking/jogging/running (WJR) and sport/fitness activity) were obtained from a standardised questionnaire.

Physical activity

PA status was categorised into three mutually exclusive groups according to the usual type of PA reported in the last 3 months.[31 32] Sedentary individuals were those participants who answered 'no' to all activity questions (walking, jogging, running, bicycling, swimming, racquet sports and other strenuous sports). WJR participants were those who answered 'yes' to the question, 'Have you participated in a walk/jog/run programme in the last 3 months?'; and 'no' to the other activities. Sport/fitness activity participants were those who answered 'no' to the walk/jog/run question, but 'yes' to a series of questions about participation in racquet sports, cycling, swimming, or other strenuous sports (football, basketball, softball, etc).

Cardiorespiratory fitness

We assessed CRF with a symptom-limited maximal treadmill exercise test using a modified Balke protocol.[28 33] The treadmill test began with the patient walking 88 m/min at 0% grade. At the end of the first minute, the elevation was increased to 2% and thereafter increased 1% per minute until the 25th minute. For those who were able to continue past 25 min, the treadmill speed was increased by 5.4 m/min for each min after the 25th. Exercise duration on this protocol is highly correlated with measured maximal oxygen uptake in men (r=0.92).[34] The test end point was volitional exhaustion or termination by the supervising physician. Maximal metabolic equivalents (METs, 1 MET=3.5 ml O_2 uptake/kg/min) were estimated from the final treadmill speed and grade.[35] Previous ACLS reports have shown that low CRF is an independent predictor of mortality and non-fatal disease.[15 28 29] We defined low, moderate and high CRF exposures according to the lowest 20%, the next 40% and the upper 40%, respectively, of the age-specific distribution of treadmill duration in the overall ACLS population.[15] We used the above approach to maintain consistency in our study methods and because a widely accepted clinical categorisation of CRF does not exist.

Morbidity surveillance

The incidence of diabetes was ascertained from responses to mail-back health surveys in 1982, 1986, 1990, 1999 and 2004. The aggregate survey response rate across all survey periods in the ACLS is ≈ 65%. Non-response bias is a concern in epidemiological studies. This issue has been investigated in the ACLS[36] and found not to present a major source of bias. Baseline health histories and clinical measures were similar between responders and non-responders, and between early and late responders.[36] The end point was defined as a participant report of a physician diagnosis of diabetes and has been described in detail elsewhere.[8 15 37] We previously verified the accuracy of self-reported, physician-diagnosed diabetes in this cohort and observed a 92% agreement between reported events and medical record review.[15] Our methods of case ascertainment are similar to those used in other established epidemiological studies on diabetes.[16 38 39] Though we cannot verify that the participants had type 2 rather than type 1 diabetes due to the self-report nature, based on the current literature, >90% of adults with diabetes are estimated to have type 2 diabetes.[40]

Statistical analysis

Baseline characteristics of the population were estimated by PA and CRF categories. Differences in covariates were tested using ANOVA tests for continuous variables and χ^2 tests for categorical variables. Cox proportional hazards regression analysis was used to estimate hazard ratios (HRs), 95% confidence intervals (CIs) and diabetes incidence rates (per 10 000 man-years) according to exposure categories. Multivariable analyses included controls for baseline measures: age (in years), BMI (kg/m^2), smoking status (never, former or current smoker), alcohol intake (drinks per week), fasting glucose (mg/dl), medical conditions (the presence or absence, separately measured, of hypertension or hypercholesterolaemia) and family history of CVD or diabetes (present or not for each). We also constructed indicator variables (yes/no) for each survey period to account for differences in survey response patterns in order to reduce the influence of ascertainment bias.[15 41] To standardise for surveillance period and length of follow-up, we entered these variables, as well as the year of the baseline examination, into our analyses as covariables. Cumulative hazard plots grouped by exposure suggested no appreciable violations of the proportional hazards assumption. Next, we examined the joint effects of PA (sedentary, WJR and sport/fitness) and CRF (low, moderate and high) on incident diabetes. For this analysis, we created nine activity–fitness combination categories. We compared the effect of each combination of activity and fitness status (sedentary–low; sedentary–moderate; sedentary–high; WJR–low; WJR–moderate; WJR–high; sport/fitness–low; sport/fitness–moderate; and sport/fitness–high) with the referent group (sedentary–low). Finally, we conducted Cox regression analyses of CRF stratified by baseline glucose levels (fasting

glucose <100 mg/dl and 100–125 mg/dl) to assess whether the associations were stronger in particular subgroups. All p values were calculated assuming two-sided alternative hypotheses; p values <0.05 were taken to indicate statistically significant comparisons. All analyses were performed using SAS statistical software, version 9.1 (SAS, Cary, North Carolina).

RESULTS

Tables 1 and 2 show the baseline characteristics of the participants by PA and CRF, respectively. In table 1, sedentary men in general had a lower fitness and higher BMI, were more likely to be current smokers, and had more unfavourable lipid profiles and CVD risk factors, such as hypercholesterolaemia or high blood pressure, than those in the WJR or Sport/Fitness groups. In table 2, participants with lower CRF values tended to be younger, were less active and were more likely to have hypercholesterolaemia or hypertension.

During an average 18 years of follow-up and 424 336 man-years of observation, 589 incident cases of diabetes were identified. Table 3 shows the relative risk of diabetes across PA and CRF groups. The incidence rates were 20.1, 9.6 and 12.4 across the sedentary, WJR and sport/fitness groups, respectively. After adjusting for age, examination year and survey response pattern, the WJR and sport/fitness groups had a 56% and 40% lower risk of developing diabetes compared with the sedentary men, respectively (both p<0.05). Further adjusting for BMI, smoking, drinking, fasting glucose, hypercholesterolaemia, hypertension and family history of diabetes or CVD did not change the associations significantly. After additional adjusting for CRF, the WJR group remained at a lower risk of diabetes than the sedentary group. The sport/fitness group was no longer significantly different from the sedentary group, but still showed a 19% reduction in diabetes risk.

For CRF, diabetes incidence rates were 31.9, 14.5 and 6.5 across low, moderate and high-fitness groups. This presented an inverse gradient of incident diabetes across the incremental CRF groups (p trend <0.0001). After adjustment for the covariables in Model 2, the moderate and high CRF groups had a 38% and 63% lower risk of developing diabetes compared with the low CRF group (p trend <0.0001). Additional adjusting for PA did not change the inverse association between CRF and diabetes.

Next, we examined the joint associations of PA (sedentary, WJR and sport/fitness activity) and CRF (low, moderate and high) on the risk of diabetes (figure 1). The results show the age- and examination year-adjusted diabetes incidence rates per 10 000 man-years among the nine activity–fitness combination categories. The lowest event-rate was the category consisting of high CRF and the sport/fitness PA group. Sedentary and low-fitness men had more than a sixfold higher risk of diabetes compared with high-fitness men who participated in sports/fitness activities. The adjusted incident rate was inversely related to CRF within each of the PA groups (all p trend <0.0001). There was no association between WJR or sport/fitness activity group and outcome within any of the fitness groups, compared with the sedentary men (all p>0.05).

Finally, we examined the influence of baseline fasting glucose on the association between fitness and diabetes risk (figure 2). There was an inverse gradient for the risk of diabetes across levels of fitness in normal glucose (<100 mg/dl) (p_{trend}=0.008) and impaired fasting glucose (IFG: 100–125 mg/dl) (p_{trend}<0.001) groups. Among men with normal glucose, risk was lower in the moderate- (HR 0.53 (95% CI 0.33 to 0.84)) and high- (HR 0.45 (95% CI 0.26 to 0.81)) CRF groups. In individuals with IFG, risk was lower in both the moderate- (HR 0.70 (95% CI 0.53 to 0.92)) and high- (HR 0.43 (95% CI 0.29 to 0.63)) CRF groups.

DISCUSSION

Our primary findings indicate that both CRF and PA are inversely associated with the risk of developing diabetes. The inverse association between fitness and incident diabetes was strong, even after adjustment for PA. We also found that doing any PA, including walking/jogging/running, or any sport-related fitness activity, is protective. Our findings confirm previous reports that both CRF and PA are independent factors for diabetes in men.[13] We previously reported that low fitness is a risk factor for diabetes in men.[8 42] Since the ACLS concurrently measured objective fitness and self-reported subjective PA, this allowed us to evaluate these exposures separately and jointly.

Our findings are also consistent with other large epidemiological studies that examined CRF and diabetes risk.[8 15 27 39] Sawada *et al* reported in a cohort study of 4747 Japanese men, aged 20–40 at baseline, in which 280 developed type 2 diabetes. An inverse association of incident type 2 diabetes (p trend <0.001) was shown across incremental quartiles of CRF.[39] Lynch *et al* studied 897 middle-aged Finnish men, aged 42–60, in a 4-year prospective study. Forty-six cases of diabetes were identified from 2 h postload glucose concentrations. CRF was assessed by respiratory gas exchange on a maximal bicycle ergometry test. They reported that those in the lowest quartile compared with the highest quartile had a fivefold higher risk of diabetes after adjustment for confounding factors.[27] Overall, these studies, including our own, show a strong inverse association between CRF and diabetes incidence.

Previous studies, including the Alumni of the University of Pennsylvania Study, the Nurses' Health Study, the US Physicians' Health Study, the British Regional Heart Study and the Population Sample from Northeast Finland, have all shown an inverse association between moderate or high intensity PA and the risk of type 2 diabetes.[6 10] One exception is with the Japanese study by Okada *et al*.[11] where 444 of the 6013 Japanese men developed type 2 diabetes. This may be attributed to the fact that they were studying leisure-time activity on the weekends instead of more frequent bouts throughout the week. Even so, men who engaged in PA at least once a week had a 25% lower risk of developing diabetes compared with those who exercised less often. More bouts of exercise during the weekend reduced the risk further.[11] In our study, the WJR and sports groups were not differentiated by intensity, and the risk of type 2 diabetes was similar in the two groups. In the US Physicians Health Study, 21 271 men aged 40–84 were followed for 5 years. Men who exercised vigorously at least once a week had a 29% lower risk of diabetes compared with those who exercised less than once a week. Our findings correlate with previous findings that participation in PA has a protective effect on developing type 2 diabetes.

It is true that engaging in PA will influence CRF to improve health.[43] Therefore, looking at both PA and CRF together needs attention. Data on joint associations of PA and CRF on diabetes are scant.[16] Lynch *et al*. reported that PA and CRF independently protected people from developing diabetes when they performed 40 min or more of PA at or above 5.5 METS.[27] In the Canadian Physical Activity Longitudinal Study (PALS), 709 men and 834 women were followed for about 15 years. They

Table 1 Baseline characteristics of study participants by physical activity categories, Aerobics Center Longitudinal Study, 1970–2003

	Physical activity categories			
	Sedentary	Walker/jogger/runner	Sport/fitness	p Value
N	7158	11 478	4808	
Age (mean±SD, years)	44.7±9.7	44.9±9.8	45.5±9.9	<0.0001
Body mass index (mean±SD, kg/m^2)	26.7±3.8	25.7±3.3	26.4±3.7	<0.0001
Exercise tolerance (mean±SD, maximal metabolic equivalents achieved during the treadmill test)	10.4±2.0	12.7±2.5	11.5±2.2	<0.0001
Treadmill test duration (mean±SD, min)	15.2±4.2	20.1±4.8	17.6±4.5	<0.0001
Lipids (mean±SD, mg/dl)				
Total cholesterol	216.1±39.9	204.6±37.8	206.9±38.8	<0.0001
High-density lipoprotein cholesterol	43.8±11.4	47.6±12.2	46.2±11.9	<0.0001
Triglycerides	147.8±107.6	119.5±82.1	134.1± 107.0	<0.0001
Fasting blood glucose (mean±SD, mg/dl)	99.6±10.0	98.2±9.2	98.2±9.1	<0.0001
Blood pressure (mean±SD, mm Hg)				
Systolic	123±14	122±14	121±13	<0.0001
Diastolic	82±10	81±9	81±9	<0.0001
Smoking status (%)				<0.0001
Never smoker	50.9	52.5	53.9	
Past smoker	27.4	36.8	29.8	
Current smoker	21.7	10.8	16.4	
Alcohol consumption (mean±SD, drinks/week)	8.4±11.8	7.9±12.5	8.1±12.6	0.12
Hypercholesterolaemia (%)	24.4	15.5	17.4	<0.0001
Hypertension (%)	33.9	29.6	30.7	<0.0001
Family history of diabetes (%)	4.3	6.2	7.1	<0.0001
Family history of cardiovascular disease (%)	3.7	5.5	5.5	<0.0001

SI conversion factors: to convert total cholesterol and high-density lipoprotein cholesterol values to mmol/l, multiply by 0.0259; triglycerides values to mmol/l, by 0.0113; glucose values to mmol/l, by 0.0555.

Table 2 Baseline characteristics of study participants by cardiorespiratory fitness categories, Aerobics Center Longitudinal Study, 1970–2003

	Cardiorespiratory fitness categories			
	Low	Moderate	High	p Value
N	3301	9101	11042	
Age (mean±SD, years)	44.2±9.5	45.0±9.6	45.1±9.9	<0.0001
Body mass index (mean±SD, kg/m^2)	28.8±5.0	26.6±3.3	24.9±2.6	<0.0001
Exercise tolerance (mean±SD, maximal metabolic equivalents achieved during the treadmill test)	8.5±1.3	10.7±1.2	13.6±2.0	<0.0001
Treadmill test duration (mean±SD, min)	11.2±2.7	15.9±2.5	22.1±3.6	<0.0001
Lipids (mean±SD, mg/dl)				
Total cholesterol	218.5±41.2	212.1±39.0	202.6±37.3	<0.0001
High-density lipoprotein cholesterol	40.9±10.8	44.0±11.0	49.3±12.2	<0.0001
Triglycerides	176.3±129.0	144.2 ±104.5	106.6±66.7	<0.0001
Fasting blood glucose (mean±SD, mg/dl)	100.3±10.1	99.1± 9.6	97.7±8.9	<0.0001
Blood pressure (mean±SD, mm Hg)				
Systolic	125±15	122±13	121±13	<0.0001
Diastolic	84±10	82±10	80±9	<0.0001
Physical activity (%)				<0.0001
Sedentary	63.9	40.2	12.6	
Walker/jogger/runner	19.1	36.2	68.4	
Sport/fitness	17.0	23.6	19.0	
Smoking status (%)				<0.0001
Never smoker	40.8	50.0	57.6	
Past smoker	31.0	32.0	33.3	
Current smoker	28.3	18.0	9.2	
Alcohol consumption (mean±SD, drinks/week)	8.8±12.3	8.4±12.6	7.6±12.1	<0.0001
Hypercholesterolaemia (%)	26.9	21.2	14.1	<0.0001
Hypertension (%)	44.0	33.5	25.3	<0.0001
Family history of diabetes (%)	4.5	5.9	6.1	<0.003
Family history of cardiovascular disease (%)	3.9	4.5	5.6	<0.0001

SI conversion factors: To convert total cholesterol and high-density lipoprotein cholesterol values to mmol/l, multiply by 0.0259; triglycerides values to mmol/l, by 0.0113; glucose values to mmol/l, by 0.0555.

Table 3 Hazard ratios (HR) for developing diabetes, according to baseline physical activity and cardiorespiratory fitness category

	Cases	Man-years	Rate*	Model 1† HR (95% CI)	Model 2‡ HR (95% CI)	Model 3§ HR (95% CI)
Physical activity						
Sedentary	300	152 680	20.1	1.0 (referent)	1.0 (referent)	1.0 (referent)
Walker/jogger/runner	195	198 569	9.6	0.44 (0.37 to 0.53)	0.60 (0.48 to 0.74)	0.76 (0.60 to 0.96)
Sport/fitness	94	73 178	12.4	0.60 (0.47 to 0.76)	0.72 (0.55 to 0.94)	0.81 (0.62 to 1.07)
Cardiorespiratory fitness						
Low	214	69 387	31.9	1.0 (referent)	1.0 (referent)	1.0 (referent)
Moderate	250	170 553	14.5	0.42 (0.35 to 0.51)	0.62 (0.49 to 0.78)	0.65 (0.51 to 0.82)
High	125	184 401	6.5	0.18 (0.14 to 0.23)	0.37 (0.28 to 0.50)	0.43 (0.31 to 0.60)
p Value for linear trend			<0.0001	<0.0001	<0.0001	<0.0001

*Rate per 10 000 man-years adjusted for age and examination year.
†Model 1: adjusted for baseline age, examination year and survey response pattern.
‡Model 2: adjusted for all variables in Model 1 plus body mass index (kg/m^2), smoking status (never, former and current), alcohol intake (drinks per week), fasting glucose (mg/dl), hypercholesterolaemia (yes or no), hypertension (yes or not), family history of diabetes (present or not) and family history of cardiovascular disease (present or not).
§Model 3: adjusted for all variables in Model 2 plus physical activity or cardiorespiratory fitness.

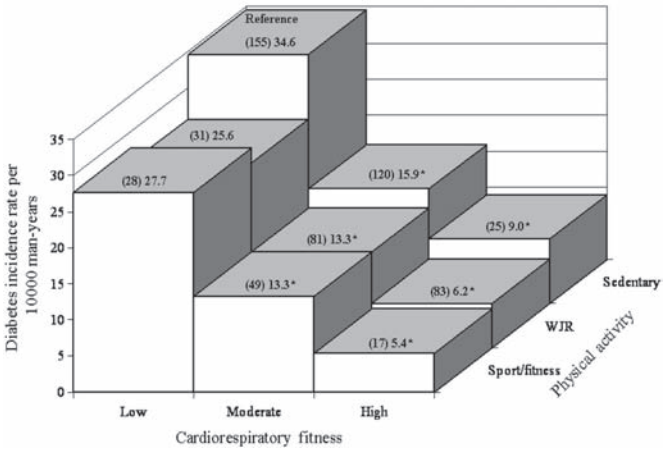

Figure 1 Total number of cases (N) and age- and examination year-adjusted diabetes incidence rates per 10 000 man-years according to cardiorespiratory fitness (CRF) and physical activity (PA) categories. The adjusted incidence rate was inversely related to CRF within each of the PA groups (all p<0.0001 for trend); however, there was no association between walking/jogging/running or sport/fitness activity group and outcome within any of the fitness groups, compared with the sedentary men (all p>0.05). *Significant difference compared with the reference.

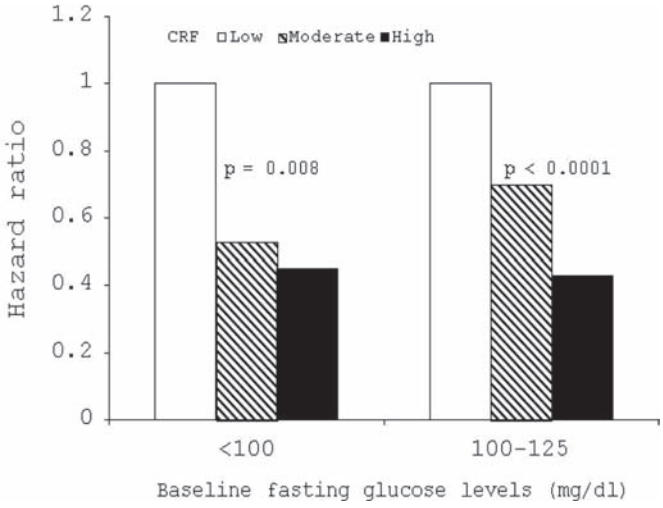

Figure 2 Multivariate-adjusted hazard ratios for cardiorespiratory fitness (CRF) and incident diabetes by baseline glucose levels. The height of bars represent HRs adjusted for age, examination year, body mass index (kg/m^2), smoking status (never, former and current), alcohol intake (drinks per week), fasting glucose (mg/dl), hypercholesterolaemia (yes or no), hypertension (yes or not), family history of diabetes (present or not), family history of cardiovascular disease (present or not) and physical activity.

found that physical fitness, not PA, was an important predictor independent of other risk factors. They explained that some of the discrepant results for the influence of PA may be related to the measures of PA versus physical fitness.[16] We found that both PA and fitness affected incidence diabetes, even after adjusting for each other. Some of the possible explanations about the different findings from PALS are as follows. They modelled their questionnaire after the Minnesota Leisure Time PA questionnaire, which collects information over the previous 12 months. In our study, we only collected activity data over the previous 3 months. PALS calculated the average daily leisure-time activity energy expenditure; however, we have no such data available. Insufficient sample size in PALS and differences in population age may also play a role.

The effect of CRF or PA on incident diabetes may be explained by several pathways. Upregulation of glucose from enhanced skeletal muscle mitochondria enzyme activity may be the contributor enhanced in those participating in PA. Decrease in insulin resistance and increase in insulin sensitivity[44] of skeletal muscle may be due to increased activity for physical demands. Although CRF has a genetic component (25–40%),[45 46] it is clear that usual PA habits are the primary determinant of fitness. In the current study, PA and CRF were only weakly associated (r=0.26). Finally, greater activity may improve one's concurrent conditions such as hypertension, dyslipidaemia and abdominal obesity, where the body is reacting to chronic systemic inflammation.[3]

Strengths of this study include the extensive baseline examination, the large size of the cohort, the long follow-up period and the objective laboratory treadmill testing for quantifying CRF. There are several limitations that need to be considered

when interpreting these data. Recall bias might lead to the misclassification of the PA groups. In terms of exposure assessment, we classified men at study enrolment, but in the present analysis, we were unable to evaluate the effect of changes in PA and fitness over time on our diabetes outcomes. It is possible that sedentary or low-fitness men increased their activity or fitness levels at some point in the follow-up interval. Additionally, others may have experienced decreases in these characteristics. Such misclassification of exposure would likely underestimate the magnitude of the association observed in the present study. Other risk factors might also change during the long period of follow-up. Most of the men were white and from middle-to-upper socio-economic strata, which may limit the generalizability but should not affect the internal validity. Furthermore, the activity intensity of the WJR group and sports/fitness groups was not distinguished. We have no data from the oral glucose tolerance test (OGTT). It is likely that OGTT would have identified some of the men as having diabetes at baseline, and this could have influenced the results. Since we are only counting those diagnosed as having diabetes from the returned surveys, it is possible that those undiagnosed cases may be misclassified. However, our methods of case ascertainment should not be less valid than those of other epidemiological studies[16 38 39] in which self-reported diabetes were used. Finally, there is no sufficient diet or medication information available to include in the analysis.

CONCLUSION

In conclusion, our prospective findings show a lower risk of developing diabetes if men participated in WJR or some type of sport activity rather than being sedentary. CRF had a strong inverse association with incident diabetes. The joint association of either WJR or sport/fitness combined with a high level of CRF provided the higher protective influence on type 2 diabetes, compared with a sedentary lifestyle. Even with overwhelming evidence that it is important to stay physically active and to improve CRF, less than 40% of adults with diabetes reported being regularly engaged in moderate or vigorous PA.[12] Therefore, health professionals should actively advise the general public as well as people with diabetes to lead an active lifestyle and improve their fitness level.

What is already known on this topic

- Although the independent effects of physical activity or cardiorespiratory fitness on incident diabetes are well established, additional studies are needed on the combined association and relative contributions of physical activity and fitness to diabetes prevention.

What this study adds

- Being active and fit provided a higher protective influence on type 2 diabetes. The much stronger inverse association for fitness compared with activity suggests that earlier studies on activity and diabetes may have underestimated the true association. We hope our findings will encourage health professionals to promote physical activity and actively advise all patients to improve their fitness level.

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Competing interests None.

Ethics approval Ethics approval was provided by the The Cooper Institute IRB.

Provenance and peer review Not commissioned; externally peer reviewed.

Detail has been removed from these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

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