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Physical Fitness Among Swedish Military Conscripts and Long-Term Risk for Type 2 Diabetes Mellitus

A Cohort Study

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Background: Early-life physical fitness has rarely been examined in relation to type 2 diabetes mellitus (DM) in adulthood because of the lengthy follow-up required. Elucidation of modifiable risk factors at young ages may help facilitate earlier and more effective interventions.

Objective: To examine aerobic capacity and muscle strength at age 18 years in relation to risk for type 2 DM in adulthood.

Design: National cohort study.

Setting: Sweden.

Participants: 1 534 425 military conscripts from 1969 to 1997 (97% to 98% of all men aged 18 years nationwide) without prior type 2 DM.

Measurements: Aerobic capacity and muscle strength (measured in watts and newtons per kilogram of body weight, respectively) were examined in relation to type 2 DM identified from outpatient and inpatient diagnoses from 1987 to 2012 (maximum age, 62 years).

Results: 34 008 men were diagnosed with type 2 DM in 39.4 million person-years of follow-up. Low aerobic capacity and muscle strength were independently associated with increased risk for type 2 DM. The absolute difference in cumulative incidence of type 2 DM between the lowest and highest tertiles of both aerobic capacity and strength was 0.22% at 20 years of follow-up (95% CI, 0.20% to 0.25%), 0.76% at 30 years (CI, 0.71% to 0.81%), and 3.97% at 40 years (CI, 3.87% to 4.06%). Overall, the combination of low aerobic capacity and muscle strength was associated with a 3-fold risk for type 2 DM (adjusted hazard ratio, 3.07 [CI, 2.88 to 3.27]; $P < 0.001$), with a positive additive interaction ($P < 0.001$). These associations were seen even among men with normal body mass index.

Limitation: This cohort did not include women and did not measure physical fitness at older ages.

Conclusion: In this large cohort of Swedish male military conscripts, low aerobic capacity and muscle strength at age 18 years were associated with increased long-term risk for type 2 DM, even among those with normal body mass index.

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Type 2 diabetes mellitus (DM) affects more than 300 million persons worldwide and, along with increasing rates of obesity and sedentary lifestyle, has more than doubled in prevalence over the past 3 decades (1). Economic costs of type 2 DM and its complications exceed $200 billion annually in the United States (2). Although physical inactivity is a well-established risk factor, few studies have examined objective measurements of physical fitness in relation to type 2 DM. Physical fitness (which includes both aerobic capacity and muscle strength) may be a more informative risk factor because it can be measured more objectively and is a better indicator of habitual physical activity than self-reported activity (3). Most studies of physical fitness have examined aerobic but not muscle fitness and have focused on adults but lacked data on younger persons with sufficient follow-up to examine the long-term risk for type 2 DM. Therefore, the relative effects of aerobic capacity and muscle strength and their effects at younger ages on long-term type 2 DM risk are still unknown. Elucidation of these risk factors in young persons may help facilitate earlier and more effective preventive interventions.

We analyzed data from a national cohort of military conscripts to examine aerobic capacity and muscle strength at age 18 years in relation to risk for type 2 DM in adulthood. We assessed aerobic capacity and muscle strength using standardized tests in approximately 1.5 million male military conscripts in Sweden who were followed up to a maximum age of 62 years. We aimed to examine whether low aerobic capacity and muscle strength at age 18 years were associated with long-term risk for type 2 DM.

Methods

Study Population

We identified 1 547 478 men (age 18 years) who had a military conscription examination in Sweden between 1969 and 1997. This examination was compulsory for all men aged 18 years nationally each year except for 2% to 3% who either were incarcerated or had severe chronic medical conditions or disabilities documented by a physician. We excluded 13 053 (0.8%) men who had a prior inpatient diagnosis of DM. A total of 1 534 425 (99.2% of the original cohort) remained for inclusion in the study.

See also:

Editorial comment 1
Summary for Patients 2

EDITORS' NOTES

Context

The relationship between physical fitness in late adolescence and long-term risk for type 2 diabetes mellitus (DM) during adulthood is uncertain.

Contribution

In this cohort of 1.5 million male military conscripts who had a standardized physical fitness assessment at age 18 years, low aerobic capacity and muscle strength were associated with an increased long-term risk for type 2 DM, even among those with normal body mass index (BMI).

Caution

Follow-up measurements of physical fitness and BMI were not available.

Implication

Poor physical fitness levels during late adolescence may be a modifiable risk factor for type 2 DM later in life.

Physical Fitness Ascertainment

We evaluated aerobic capacity and muscle strength using the Swedish Military Conscription Registry, which contains information from a required 2-day, standardized physical and psychological examination for all conscripts after 1969. We measured aerobic capacity as the maximal aerobic workload in watts with a standard, well-validated, ergometer test using a stationary bicycle with electric brakes, as previously described (4). Maximal aerobic workload is highly correlated with maximal oxygen uptake (correlation of approximately 0.9) (5), and the bicycle ergometer test yields highly reproducible results, with a test–retest correlation of 0.95 (6). We measured muscle strength as the weighted sum of maximal knee extension (weighted × 1.3), elbow flexion (weighted × 0.8), and hand grip (weighted × 1.7), measured in newtons, using standard, well-validated isometric dynamometer tests (7). Each test was done 3 times. Maximum value was recorded for analysis except when the last value was the highest, in which case testing was repeated until strength values stopped increasing. All testing equipment was calibrated daily (7). In the present study, aerobic capacity and muscle strength were standardized per kilogram of body weight and examined alternatively as continuous linear variables, as categorical variables in tertiles (aerobic capacity: low [<3.58 watts/kg], medium [3.58 to 4.17 watts/kg], or high [≥4.18 watts/kg]; muscle strength: low [<28.23 newtons/kg], medium [28.23 to 32.12 newtons/kg], or high [≥32.13 newtons/kg]), and by using cubic spline curves.

Type 2 DM Ascertainment

The study cohort was followed up for type 2 DM from the time of the military conscription examination through 31 December 2012. We identified type 2 DM using International Classification of Diseases (ICD) diagnosis codes in the Swedish Hospital Registry and Swedish Outpatient Registry. The former registry contains all primary and secondary hospital discharge diagnoses from 6 populous counties in southern Sweden starting in 1964, with nationwide coverage starting in 1987, and the latter registry contains outpatient diagnoses nationwide starting in 2001. Diagnoses in the Swedish Hospital Registry are greater than 99% complete and have a reported positive predictive value of 85% to 95% (8). Because earlier ICD versions did not distinguish between type 1 and type 2 DM, we ascertained type 2 DM using ICD, Ninth Revision, code 250 (excluding codes 250.X1 and 250.X3) between 1987 and 1996 and ICD, 10th Revision, code E11 between

Table 1. Physical Fitness and Other Characteristics Among Men Aged 18 y Who Did or Did Not Develop Type 2 DM*

Characteristic	Type 2 DM	
	Yes (*n* = 34 008)	**No (*n* = 1 500 417)**
Aerobic capacity		
Low	22 878 (67.3)	489 539 (32.6)
Medium	7604 (22.4)	499 672 (33.3)
High	3526 (10.4)	511 206 (34.1)
Mean (SD), *watts/kg*	3.3 (0.7)	3.9 (0.7)
Muscle strength		
Low	15 887 (46.7)	498 406 (33.2)
Medium	10 751 (31.6)	501 151 (33.4)
High	7370 (21.7)	500 860 (33.4)
Mean (SD), *newtons/kg*	28.4 (5.0)	29.2 (6.5)
BMI		
Normal	25 918 (76.2)	1 388 856 (92.6)
Overweight or obese	8090 (23.8)	111 561 (7.4)
Mean (SD), *kg/m²*	23.3 (4.3)	21.6 (2.8)
Height		
<175 cm	9552 (28.1)	336 657 (22.4)
175–184 cm	18 684 (54.9)	883 191 (58.9)
≥185 cm	5772 (17.0)	280 569 (18.7)
Mean (SD), *cm*	177.6 (7.4)	178.0 (7.5)
Weight		
<60 kg	3694 (10.9)	187 755 (12.5)
60–79 kg	20 543 (60.4)	1 115 921 (74.4)
≥80 kg	9771 (28.7)	196 741 (13.1)
Mean (SD), *kg*	73.5 (14.3)	68.8 (10.3)
Family history of diabetes		
No	18 251 (53.7)	1 164 670 (77.6)
Yes	15 757 (46.3)	335 747 (22.4)
Education		
<12 y	8247 (24.2)	225 154 (15.0)
12–14 y	16 177 (47.6)	662 094 (44.1)
≥15 y	9584 (28.2)	613 169 (40.9)
Neighborhood SES		
Low	7864 (23.1)	231 265 (15.4)
Medium	21 166 (62.2)	988 613 (65.9)
High	4978 (14.6)	280 539 (18.7)

BMI = body mass index; DM = diabetes mellitus; SES = socioeconomic status.
* Values are numbers (percentages) except where indicated. Percentages may not sum to 100 due to rounding.

Table 2. Cumulative Incidence of Type 2 Diabetes mellitus by Aerobic Capacity and Muscle Strength in Men Aged 18 y

Muscle Strength (Tertiles), by Follow-up	Aerobic Capacity (Tertiles)					
	High			Medium		
	Cumulative Incidence (95% CI), %	Risk Difference (95% CI), %	*P* Value	Cumulative Incidence (95% CI), %	Risk Difference (95% CI), %	*P* Value
10 y						
High	0.01 (0 to 0.01)	Reference	–	0.01 (0.01 to 0.02)	0.01 (0 to 0.01)	0.050
Medium	0 (0 to 0.01)	0 (−0.01 to 0)	0.060	0.02 (0.01 to 0.03)	0.01 (0.01 to 0.02)	<0.001
Low	0 (0 to 0.01)	0 (−0.01 to 0)	0.53	0.01 (0 to 0.01)	0 (0 to 0.01)	0.46
20 y						
High	0.06 (0.05 to 0.07)	Reference	–	0.11 (0.10 to 0.12)	0.05 (0.03 to 0.07)	<0.001
Medium	0.05 (0.04 to 0.06)	−0.01 (−0.03 to 0)	0.150	0.14 (0.12 to 0.16)	0.08 (0.06 to 0.10)	<0.001
Low	0.04 (0.03 to 0.06)	−0.02 (−0.03 to 0)	0.030	0.09 (0.07 to 0.11)	0.03 (0.01 to 0.05)	0.003
30 y						
High	0.19 (0.18 to 0.22)	Reference	–	0.26 (0.24 to 0.28)	0.06 (0.03 to 0.09)	<0.001
Medium	0.20 (0.18 to 0.22)	0.01 (−0.02 to 0.03)	0.70	0.36 (0.33 to 0.39)	0.16 (0.13 to 0.20)	<0.001
Low	0.15 (0.13 to 0.17)	−0.05 (−0.08 to −0.02)	0.001	0.28 (0.25 to 0.31)	0.08 (0.05 to 0.12)	<0.001
40 y						
High	0.48 (0.45 to 0.52)	Reference	–	0.92 (0.88 to 0.97)	0.43 (0.37 to 0.48)	<0.001
Medium	0.55 (0.52 to 0.59)	0.07 (0.02 to 0.11)	0.006	1.35 (1.29 to 1.41)	0.88 (0.81 to 0.95)	<0.001
Low	0.51 (0.48 to 0.55)	0.03 (−0.02 to 0.08)	0.39	1.22 (1.16 to 1.28)	0.74 (0.67 to 0.80)	

1997 and 2012. We did a sensitivity analysis that further included all DM diagnoses from 1969 to 1986 using ICD, Eighth Revision, code 250 from hospital discharge records (before outpatient data were available). Among men without type 2 DM diagnoses between 1987 and 2012, a total of 542 was diagnosed with DM between 1969 and 1986, of which most would be expected to have type 2 DM (for example, among men with the same age distribution, 75% of inpatient DM diagnoses between 1987 and 2012 had type 2 DM).

Adjustment Variables

Other variables that may be associated with type 2 DM were obtained from the Swedish Military Conscription Registry and national census data, which were linked via an anonymous personal identification number. Adjustment variables include the following: year of the military conscription examination modeled simultaneously as continuous and categorical variables (1969 to 1979, 1980 to 1989, or 1990 to 1997); body mass index (BMI) in kg/m^2 modeled simultaneously as continuous and categorical variables ("overweight or obesity" is defined as ≥85th percentile on the Centers for Disease Control and Prevention's 2000 growth charts that categorize BMI by sex and age for children and adolescents aged 2 to 19 years, which corresponds to BMI ≥25.6 kg/m^2 for men aged 18 years [9]); and family history of DM in a parent or sibling (yes or no, identified from diagnoses in the Swedish Hospital Registry from 1964 to 2012 and the Swedish Outpatient Registry from 2001 to 2012; not self-reported, thus enabling unbiased ascertainment). Variables also included highest education level attained during the study period (<12, 12 to 14, or ≥15 years) and neighborhood socioeconomic status at baseline (included because neighborhood socioeconomic characteristics have been associated with type 2 DM [10, 11] as well as physical activity and BMI [12]). Socioeconomic status is measured according to an index that includes low education level, low income, unemployment, and social welfare receipt (13) and is categorized as low (<−1 SD from the mean), medium (≥−1 SD and ≤1 SD), or high (>1 SD). Height and weight were examined in a separate model as alternatives to BMI and were modeled simultaneously as continuous and categorical variables (height: <175, 175 to 184, or ≥185 cm; weight: <60, 60 to 79, or ≥80 kg) (9).

We imputed missing data for each variable using a standard multiple imputation procedure based on the variable's relationship with all other covariates and type 2 DM (14). Missing data were relatively infrequent for aerobic capacity (5.7%), muscle strength (5.0%), height (7.2%), weight (7.3%), education level (0.4%), and neighborhood socioeconomic status (9.1%). As an alternative to multiple imputation, sensitivity analyses were done after restricting to persons with complete data for all variables (n = 1 361 083 [88.0%]).

Statistical Analysis

We calculated absolute time-to-event measures using the cumulative incidence function for type 2 DM. We generated covariate-standardized cumulative incidence curves for type 2 DM using the method of Simon and Makuch (15). We also used Cox proportional hazards regression to estimate the relative hazard of type 2 DM for different levels of aerobic capacity and muscle strength. The Cox model scale was years elapsed since the military conscription examination (which also corresponds to attained age because baseline age was the same [18 years] for all conscripts). Persons were censored at emigration (n = 112 158 [7.3%]) or death (n = 58 835 [3.8%]). The proportional hazards assumption was evaluated by graphical assessment of log–log plots and was met in all models. Interactions between

Table 2–Continued

Aerobic Capacity (Tertiles)		
Low		
Cumulative Incidence (95% CI), %	**Risk Difference (95% CI), %**	***P* Value**
0.14 (0.12 to 0.17)	0.14 (0.11 to 0.16)	<0.001
0.08 (0.07 to 0.09)	0.07 (0.06 to 0.09)	<0.001
0.05 (0.04 to 0.05)	0.04 (0.03 to 0.05)	<0.001
0.41 (0.37 to 0.45)	0.35 (0.31 to 0.39)	<0.001
0.33 (0.31 to 0.36)	0.27 (0.24 to 0.30)	<0.001
0.28 (0.26 to 0.31)	0.22 (0.20 to 0.25)	<0.001
0.80 (0.75 to 0.85)	0.61 (0.55 to 0.66)	<0.001
0.78 (0.74 to 0.82)	0.58 (0.53 to 0.63)	<0.001
0.96 (0.92 to 1.00)	0.76 (0.71 to 0.81)	<0.001
2.69 (2.59 to 2.79)	2.21 (2.10 to 2.31)	<0.001
2.98 (2.89 to 3.06)	2.50 (2.41 to 2.59)	<0.001
4.45 (4.36 to 4.54)	3.97 (3.87 to 4.06)	<0.001

aerobic capacity and muscle strength were examined on either the additive or multiplicative scale. We assessed additive interactions using relative excess risk due to interaction (RERI), which is computed for binary variables as the following: $RERI_{HR\ (hazard\ ratio)} = HR_{11} - HR_{10} - HR_{01} + 1$ (16, 17). We assessed multiplicative interactions using the ratio of HRs, $HR_{11} \div (HR_{10} \times HR_{01})$. We also examined interactions graphically using cubic spline curves.

We did sensitivity analyses that included only men with at least 30 years of follow-up (n = 686 964 [44.4%]) or that evaluated the effect of unmeasured confounders (such as smoking) using external adjustment (18). We performed 10 000 model simulations to analyze smoking, assuming 2 uniform independent distributions for smoking prevalence among exposed and unexposed persons between 0.2 and 0.4 (19) and a log-normal distribution for the smoking–type 2 DM relative hazard that implies a mean relative hazard of 1.5 (SD, 0.4) (20). All statistical tests were 2-sided and used an α-level of 0.05, and all analyses were done using Stata, version 13.0 (StataCorp).

This study was approved by the Regional Ethics Committee of Lund University, Malmö, Sweden.

Role of the Funding Source

This study was funded by the National Heart, Lung, and Blood Institute, National Institutes of Health; the Swedish Research Council; and Region Skåne/Lund University. The funding source had no role in the study design, conduct, or reporting.

RESULTS

Among the 1 534 425 men in this cohort, 34 008 (2.2%) were subsequently diagnosed with type 2 DM in 39.4 million person-years of follow-up (mean follow-up, 25.7 years). The median age at the end of follow-up was 46.1 years (mean, 45.9 years [SD, 8.9] [range, 19.0 to 62.0]), and the median age at diagnosis was 46.8 years (mean, 44.7 years [SD, 9.9] [range, 18.0 to 62.0]). **Table 1** shows aerobic capacity, muscle strength, and other characteristics among men aged 18 years who did or did not subsequently develop type 2 DM.

Table 2 shows the covariate-standardized cumulative incidence of type 2 DM at 10, 20, 30, and 40 years of follow-up by aerobic capacity and muscle strength at age 18 years. Low aerobic capacity was associated with significantly increased cumulative incidence at each of these follow-up times, regardless of muscle strength level. Low muscle strength was associated with increased cumulative incidence after 40 years of follow-up among men with low or medium aerobic capacity. The combination of low aerobic capacity and muscle strength was associated with the highest cumulative incidence, which reached 4.45% at 40 years of follow-up (risk difference relative to high aerobic capacity and muscle strength, 3.97% [95% CI, 3.87% to 4.06%]; $P < 0.001$). The **Figure** shows cumulative incidence curves for type 2 DM by aerobic capacity and muscle strength.

Table 3 summarizes the adjusted relative hazards of type 2 DM across the entire follow-up by aerobic capacity and muscle strength at age 18 years. Low aerobic capacity and muscle strength were independently associated with a higher risk for type 2 DM, although low aerobic capacity was a stronger risk factor ($P_{heterogeneity} < 0.001$). The combination of low aerobic capacity and muscle strength was associated with the highest risk for type 2 DM (HR, 3.07 [CI, 2.88 to 3.27]; $P < 0.001$). For the lowest compared with the highest tertiles, aerobic capacity and muscle strength had a positive interaction on the additive scale ($P_{interaction} < 0.001$) but not the multiplicative scale ($P_{interaction} = 0.62$). The same additive interaction was found when examined at 30 or 40 years of

Figure. Cumulative incidence of type 2 diabetes mellitus, by aerobic capacity and muscle strength in men aged 18 years with a maximum follow-up of 44 years.

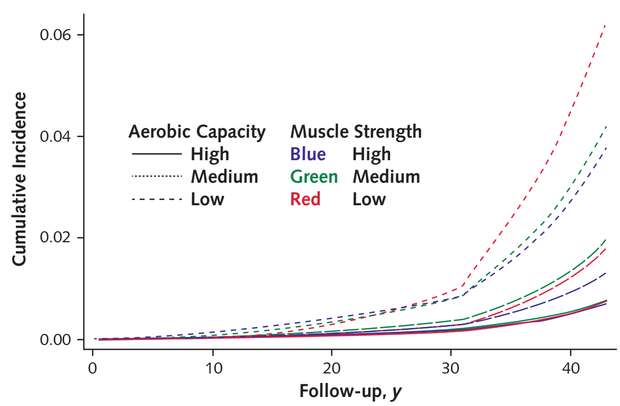

Table 3. **Interactions Between Aerobic Capacity and Muscle Strength Among Men Aged 18 y in Relation to Subsequent Risk for Type 2 Diabetes Mellitus***

Variable	Aerobic Capacity (Tertiles)					
	High			Medium		
	Cases, *n/N*	HR (95% CI)	*P* Value	Cases, *n/N*	HR (95% CI)	*P* Value
Muscle strength (tertiles)						
High	1252/195 299	1.00		2371/202 217	1.08 (1.01–1.16)	0.028
Medium	1268/173644	1.19 (1.10–1.29)	<0.001	2893/162 087	1.60 (1.49–1.71)	<0.001
Low	1006/145 789	1.58 (1.45–1.72)	<0.001	2340/142 972	1.92 (1.79–2.06)	<0.001
HR (95% CI) for medium muscle strength within strata of aerobic capacity	–	1.19 (1.10–1.29)	<0.001	–	1.48 (1.39–1.56)	<0.001
HR (95% CI) for low muscle strength within strata of aerobic capacity	–	1.58 (1.45–1.72)	<0.001	–	1.78 (1.67–1.88)	<0.001
Interaction on additive scale, lowest vs. highest tertiles: RERI (95% CI)	–	–		–	–	
Interaction on multiplicative scale, lowest vs. highest tertiles: ratio of HRs (95% CIs)	–	–		–	–	

HR = hazard ratio; RERI = relative excess risk due to interaction.
* HRs are adjusted for year of the military conscription examination, body mass index, family history of diabetes, education, and neighborhood socioeconomic status.

follow-up ($P_{interaction}$ < 0.001) but not at earlier times ($P_{interaction}$ > 0.05).

Appendix Table 1 (available at www.annals.org) shows the univariate effects of aerobic capacity, muscle strength, BMI, and other variables associated with type 2 DM. In secondary analyses, we found positive additive—but not multiplicative—interactions between either low aerobic capacity or muscle strength and high BMI in relation to type 2 DM (P < 0.001) (Appendix Tables 2 and 3, available at www.annals.org). Low aerobic capacity and muscle strength were associated with a higher risk for type 2 DM, even among men with normal BMI. In sensitivity analyses that included DM diagnoses from 1969 to 1986 (for which type 1 and type 2 DM could not be distinguished), were restricted to men with no missing data, or included only men with at least 30 years of follow-up, all risk estimates were very similar to the main results (data not shown). External adjustment for smoking yielded risk estimates for association between low aerobic capacity or muscle strength and type 2 DM that were 9% lower and remained highly significant (P < 0.001), which suggests that unmeasured confounding had little influence on our main findings.

Discussion

In this large, national cohort study, low aerobic capacity and muscle strength in men aged 18 years were associated with a higher risk for type 2 DM in adulthood, independent of BMI, family history, or socioeconomic factors. A combination of low aerobic capacity and muscle strength was associated with the highest risk, although aerobic capacity had a stronger influence. Furthermore, both factors were associated with increased risk for type 2 DM, even among men with normal BMI. Positive additive interactions were found between low aerobic capacity and muscle strength, which suggests that interventions to improve aerobic capacity would have the greatest public health effect on type 2 DM among men with low muscle strength if the associations are causal.

Most previous studies have examined physical fitness only in adulthood (21–29). The largest of these was a U.S. study of 46 979 middle-aged adults with a median follow-up of 5 years, which reported that higher physical fitness levels based on a treadmill stress test were independently protective against DM (P_{trend} < 0.001) (26). Fewer studies have examined physical fitness early in life, and none examined physical fitness in adolescence in relation to the long-term risk for type 2 DM. Our findings suggest that low aerobic capacity at age 18 years is strongly associated with higher risk for type 2 DM later in life, regardless of baseline muscle strength or BMI, after maximum follow-up to age 62 years.

We also found that low muscle strength was an independent risk factor for type 2 DM later in life, although it was less influential than aerobic capacity. These findings are broadly consistent with previously reported associations between muscle strength among adults and reduced risk for metabolic syndrome (30, 31), between resistance training among adults and reduced risk for type 2 DM (32, 33), and between resistance training and improved glycemic control among adults with type 2 DM (34). The overall evidence to date suggests that high muscle strength and resistance training improve glycemic control and are protective against type 2 DM, independent of aerobic capacity. However, the combination of high muscle strength and aerobic capacity is associated with the greatest protective benefit (32, 33).

Obesity is a strong, well-established risk factor for type 2 DM (35–37). Of note, we found that low aerobic capacity and muscle strength were long-term risk factors for type 2 DM, even among men with normal BMI. Other cohort studies have reported that low aerobic capacity is associated with type 2 DM, even among nonobese adults, without examining muscle strength (21, 26, 29). Overall, these findings suggest that physical fitness has important health benefits for all, even for persons who are not overweight or obese.

Table 3—Continued

Aerobic Capacity (Tertiles)			HR (95% CI) for Aerobic Capacity Within Strata of Muscle Strength			
Low			Medium Aerobic Capacity	*P* Value	Low Aerobic Capacity	*P* Value
Cases, *n/N*	HR (95% CI)	*P* Value				
3747/110 714	1.90 (1.77–2.03)	<0.001	1.08 (1.01–1.16)	0.028	1.90 (1.77–2.03)	<0.001
6590/176 171	2.25 (2.11–2.39)	<0.001	1.35 (1.25–1.44)	<0.001	1.89 (1.77–2.01)	<0.001
12 541/225 532	3.07 (2.88–3.27)	<0.001	1.22 (1.13–1.31)	<0.001	1.94 (1.81–2.08)	<0.001
–	1.19 (1.14–1.23)	<0.001	–		–	
–	1.62 (1.55–1.68)	<0.001	–		–	
–	0.59 (0.45–0.73)	<0.001	–		–	
–	1.02 (0.93–1.12)	0.62	–		–	

There are several mechanisms by which aerobic and muscle fitness may enhance glycemic control (38, 39). Aerobic exercise is known to increase mitochondrial density and oxidative enzyme activity, which promotes fatty acid oxidation and insulin sensitivity (40). Strength training augments type 2 muscle fiber growth, which increases glucose use capacity (40), and may upregulate proteins in the insulin-signaling cascade, which increases insulin activity and further enhances glucose use (41). Both aerobic exercise and strength training help reduce adiposity, a known risk factor for type 2 DM (42).

Strengths of our study include its large, national cohort design and prospective ascertainment of aerobic capacity, muscle strength, BMI, and type 2 DM diagnoses. The design prevented selection bias, and the use of registry data with prospectively measured exposures prevented self-reporting bias. We examined objective, well-validated measures of aerobic capacity and muscle strength, which are probably better indicators of habitual physical activity than self-reported activity (3). We were able to adjust for other strong risk factors for type 2 DM, including BMI, family history, and socioeconomic factors, which were also prospectively ascertained and not self-reported.

Limitations include the measurement of physical fitness and BMI at only one age (18 years), which rendered us unable to examine changes in these factors over time. Because this study was based on Swedish military conscripts, the cohort consisted entirely of men. Other studies have reported similar associations between low physical fitness levels and risk for type 2 DM in women (21, 28). Outpatient diagnoses in the present study were available only starting in 2001; therefore, type 2 DM before this period was underreported. However, this underreporting is expected to be nondifferential with respect to physical fitness and thus would influence results toward the null hypothesis. In addition, diagnoses before 1987 were excluded from the main analyses because they did not distinguish between type 1 and type 2 DM. However, sensitivity analyses that included all DM diagnoses before 1987 (of which most were likely type 2 DM) yielded results very similar to our main findings. Last, this was a relatively young cohort in Sweden. Additional studies will be needed in other populations, in diverse ethnic groups, and with follow-up to older ages.

In summary, we found that low aerobic capacity and muscle strength at age 18 years were independently associated with a higher risk for type 2 DM in adulthood among men with either normal or high BMI. These findings suggest that interventions to improve aerobic and muscle fitness levels early in life could help reduce risk for type 2 DM in adulthood. Additional studies with longitudinal measurements of fitness levels will be needed to delineate the most important windows of susceptibility and further inform preventive interventions.

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Reproducible Research Statement: *Study protocol, data set, and statistical code:* Not available.

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Appendix Table 1. Adjusted HRs for Univariate Effects of Physical Fitness or Other Factors Among Men Aged 18 y on Subsequent Risk for Type 2 Diabetes

Characteristic	Adjusted Model 1*			Adjusted Model 2†		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Aerobic capacity in watts per kilogram of body weight (tertiles)						
Low	3.55	3.42–3.70	<0.001	1.72	1.65–1.79	<0.001
Medium	1.49	1.43–1.55	<0.001	1.15	1.11–1.20	<0.001
High	1.00			1.00		
Per 1 unit (trend test)	0.36	0.36–0.37	<0.001	0.65	0.64–0.67	<0.001
Muscle strength in newtons per kilogram of body weight (tertiles)						
Low	2.67	2.60–2.75	<0.001	1.52	1.47–1.56	<0.001
Medium	1.44	1.40–1.49	<0.001	1.25	1.22–1.29	<0.001
High	1.00			1.00		
Per 1 unit (trend test)	0.60	0.59–0.61	<0.001	0.97	0.96–0.97	<0.001
BMI						
Normal	1.00			1.00		
Overweight or obese	4.98	4.85–5.11	<0.001	2.89	2.81–2.98	<0.001
Per 1 BMI unit (trend test)	1.22	1.21–1.22	<0.001	1.15	1.14–1.15	<0.001
Height						
<175 cm (5 ft, 9 in)	1.31	1.28–1.34	<0.001	1.53	1.49–1.58	<0.001
175–184 cm	1.00			1.00		
≥185 cm (6 ft, 1 in)	1.03	1.00–1.06	0.045	0.75	0.73–0.78	<0.001
Per 5 cm (trend test)	0.99	0.98–0.99	0.001	0.87	0.86–0.87	<0.001
Weight						
<60 kg (132 lb)	0.90	0.87–0.93	<0.001	0.81	0.78–0.84	<0.001
60–79 kg	1.00			1.00		
≥80 kg (176 lb)	3.34	3.26–3.42	<0.001	2.36	2.29–2.42	<0.001
Per 5 kg (trend test)	1.28	1.27–1.28	<0.001	1.22	1.21–1.23	<0.001
Family history of diabetes						
No	1.00			1.00		
Yes	2.52	2.47–2.58	<0.001	2.14	2.09–2.19	<0.001
Education						
<12 y	1.14	1.11–1.17	<0.001	1.08	1.05–1.11	<0.001
12–14 y	1.00			1.00		
≥15 y	0.59	0.57–0.60	<0.001	0.70	0.68–0.72	<0.001
Per higher category (trend)	0.71	0.70–0.72	<0.001	0.80	0.79–0.81	<0.001
Neighborhood SES						
Low	1.43	1.39–1.47	<0.001	1.31	1.27–1.34	<0.001
Medium	1.00			1.00		
High	0.98	0.94–1.01	0.119	1.13	1.10–1.17	<0.001
Per higher category (trend)	0.81	0.79–0.82	<0.001	0.90	0.88–0.92	<0.001

BMI = body mass index; HR = hazard ratio; SES = socioeconomic status.
* Adjusted for year of the military conscription examination.
† Adjusted for year of the military conscription examination, aerobic capacity, muscle strength, BMI, family history of diabetes, education, and neighborhood SES. Height and weight were modeled simultaneously as an alternative to BMI in a separate model. The reference category for all variables is indicated by an HR of 1.00.

Appendix Table 2. Interactions Between Aerobic Capacity and BMI Among Men Aged 18 y in Relation to Subsequent Risk for Type 2 Diabetes Mellitus*

Variable	Aerobic Capacity (Tertiles)						HR (95% CI) for Aerobic Capacity Within Strata of BMI	
	High		Medium		Low		Medium Aerobic Capacity	Low Aerobic Capacity
	Cases, *n/N*	HR (95% CI)	Cases, *n/N*	HR (95% CI)	Cases, *n/N*	HR (95% CI)		
BMI								
Normal	3388/505 332	1.00	6969/483 883	1.21 (1.15–1.26); P <0.001	15 561/425 559	1.89 (1.81–1.97); P <0.001	1.21 (1.15–1.26); P <0.001	1.89 (1.81–1.97); P <0.001
Overweight or obese	138/9400	2.63 (2.21–3.11); P <0.001	635/23 393	3.60 (3.30–3.93); P <0.001	7317/86 858	5.46 (5.22–5.71); P <0.001	1.16 (1.09–1.23); P <0.001	2.08 (1.73–2.43); P <0.001
HR (95% CI) for BMI within strata of aerobic capacity	–	2.63 (2.21–3.11); P <0.001	–	2.99 (2.74–3.24); P <0.001	–	2.89 (2.80–2.98); P <0.001	–	–
Interaction on additive scale: RERI (95% CI)	–	–	–	0.77 (0.25–1.29); P = 0.004	–	1.95 (1.48–2.41); P <0.001	–	–
Interaction on multiplicative scale: ratio of HRs (95% CIs)	–	–	–	1.14 (0.92–1.35); P = 0.21	–	1.10 (0.91–1.29); P = 0.30	–	–

BMI = body mass index; HR = hazard ratio; RERI = relative excess risk due to interaction.
* HRs are adjusted for year of the military conscription examination, muscle strength, family history of diabetes, education, and neighborhood socioeconomic status.

Appendix Table 3. Interactions Between Muscle Strength and BMI Among Men Aged 18 y in Relation to Subsequent Risk for Type 2 Diabetes Mellitus*

Variable	Muscle Strength (Tertiles)						HR (95% CI) for Medium Muscle Strength Within Strata of BMI	HR (95% CI) for Low Muscle Strength Within Strata of BMI
	High		Medium		Low			
	Cases, *n/N*	HR (95% CI)	Cases, *n/N*	HR (95% CI)	Cases, *n/N*	HR (95% CI)		
BMI								
Normal	7092/500 917	1.00	9661/490 314	1.28 (1.24 to 1.32); P <0.001	9168/423 543	1.65 (1.60 to 1.71); P <0.001	1.28 (1.24 to 1.32); P <0.001	1.65 (1.60 to 1.71); P <0.001
Overweight or obese	278/7313	2.88 (2.55 to 3.25); P <0.001	1090/21 588	3.35 (3.14 to 3.58); P <0.001	6722/90 750	4.92 (4.74 to 5.10); P <0.001	1.16 (1.01 to 1.32; P = 0.038	1.71 (1.50 to 1.92); P <0.001
HR (95% CI) for BMI within strata of muscle strength	–	2.88 (2.55 to 3.25); P <0.001	–	2.62 (2.45 to 2.78); P <0.001	–	2.97 (2.87 to 3.07); P <0.001	–	–
Interaction on additive scale: RERI (95% CI)	–	–	–	0.19 (-0.20 to 0.59); P = 0.34	–	1.39 (1.02 to 1.75); P <0.001	–	–
Interaction on multiplicative scale: ratio of HRs (95% CIs)	–	–	–	0.91 (0.79 to 1.03); P = 0.155	–	1.03 (0.90 to 1.16); P = 0.62	–	–

BMI = body mass index; HR = hazard ratio; RERI = relative excess risk due to interaction.
* HRs are adjusted for year of the military conscription examination, aerobic capacity, family history of diabetes, education, and neighborhood socioeconomic status.