Exercise Capacity and All-Cause Mortality in African American and Caucasian Men With Type 2 Diabetes

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OBJECTIVE — The purpose of this study was to assess the association between exercise capacity and mortality in African Americans and Caucasians with type 2 diabetes and to explore racial differences regarding this relationship.

RESEARCH DESIGN AND METHODS — African American (n = 1,703; aged 60 ± 10 years) and Caucasian (n = 1,445; aged 62 ± 10 years) men with type 2 diabetes completed a maximal exercise test between 1986 and 2007 at the Veterans Affairs Medical Centers in Washington, DC, and Palo Alto, California. Three fitness categories were established (low-, moderate-, and high-fit) based on peak METs achieved. Subjects were followed for all-cause mortality for 7.3 ± 4.7 years.

RESULTS — The adjusted mortality risk was 23% higher in African Americans than in Caucasians (hazard ratio 1.23 [95% CI 1.1–1.4]). A graded reduction in mortality risk was noted with increased exercise capacity for both races. There was a significant interaction between race and METs ($P < 0.001$) and among race and fitness categories ($P < 0.001$). The association was stronger for Caucasians. Each 1-MET increase in exercise capacity yielded a 19% lower risk for Caucasians and 14% for African Americans ($P < 0.001$). Similarly, the risk was 43% lower (0.57 [0.44–0.73]) for moderate-fit and 67% lower (0.33 [0.22–0.48]) for high-fit Caucasians. The comparable reductions in African Americans were 34% (0.66 [0.55–0.80]) and 46% (0.54 [0.39–0.73]), respectively.

CONCLUSIONS — Exercise capacity is a strong predictor of all-cause mortality in African American and Caucasian men with type 2 diabetes. The exercise capacity-related reduction in mortality appears to be stronger and more graded for Caucasians than for African Americans.

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Poor exercise capacity is a well-established independent predictor of cardiovascular and overall mortality among healthy subjects and patients with diabetes and/or cardiovascular disease (CVD) (1–5), whereas increased physical activity and higher cardiorespiratory fitness confer health benefits in proportion to the level of fitness (1,2,6), independent of BMI (3,4). Increases in physical activity patterns have thus emerged as an integral part of the prevention and management of type 2 diabetes (5–7).

African Americans have a two- to sixfold higher risk for developing diabetes (8) and approximately double the diabetes death rate (9) compared with Caucasians. Socioeconomic and quality of health care differences have been cited as possible reasons for this apparent racial disparity (10–12). When access to health care is comparable, significantly lower overall mortality rates were reported among a National population of African American veterans versus Caucasians with diabetes (10).

An intriguing finding is that African American diabetic subjects exhibit significantly lower exercise capacity than do Caucasian diabetic subjects (13). The relationship between exercise capacity and mortality risk in African American diabetic subjects has not been reported previously, and possible racial differences regarding this relationship have not been explored.

The Veterans Health Administration in the U.S. Department of Veterans Affairs Health Care System ensures equal access to high-quality health care independent of a patient's financial status (14). In addition, the Veterans Affairs Medical Center (VAMC) electronic health information database is well suited to determine mortality accurately (15), thus providing an opportunity to assess the association between exercise capacity and mortality under comparable medical care.

In the present study, we assessed the relationship between exercise capacity and all-cause mortality in diabetic subjects and possible racial differences regarding this relationship.

RESEARCH DESIGN AND METHODS

— Between July 1986 and 30 November 2007, a symptom-limited exercise tolerance test (ETT) was administered to veterans with type 2 diabetes at the VAMC in Washington, DC, and Palo Alto, California, either as part of routine evaluations or to assess exercise-induced ischemia. This information along with the individual's medical history has been electronically stored.

From this database we excluded women and those with any of the following: *1*) history of an implanted pacemaker, *2*) left bundle branch block, *3*) unstable symptom, and *4*) impaired chronotropic response. After these exclusions, the participant group comprised 1,703 African Americans and 1,445 Caucasians. The

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Table 1—*Demographic and clinical characteristics for African Americans and Caucasians with type 2 diabetes*

	Total	African American	Caucasian	*P**
n	3,148	1,703	1,445	—
Age (years)	61 ± 10	60 ± 10	62 ± 10	<0.001
BMI (kg/m^2)	30 ± 5.6	30 ± 5.5	30 ± 5.7	0.27
Resting heart rate (beats/min)	76 ± 14	76 ± 14	76 ± 14	0.82
Resting systolic blood pressure (mmHg)	135 ± 21	136 ± 22	134 ± 21	0.1
Resting diastolic blood pressure (mmHg)	80 ± 12	81 ± 12	78 ± 12	<0.001
CVD (%)	49.7	51.7	47.3	<0.001
Smoking (%)	42	35.1	50.2	<0.001
Hypertension (%)	73.6	75.6	71.3	0.007
Family history of coronary heart disease	14.8	12.3	18.8	<0.001
Dyslipidemia (%)	26.9	34.6	17.9	<0.001
β-Blockers (%)	18.3	13.1	24.4	<0.001
Calcium channel blockers (%)	21.4	20.6	22.4	0.23
ACE inhibitors (%)	37.5	34.6	40.9	<0.001
Diuretics (%)	15.7	18.6	12.3	<0.001
Aspirin (%)	5.9	5.9	5.8	0.511
Statins (%)	14.6	9.4	20.7	<0.001
Insulin (%)	30.7	33.7	22.8	<0.001
Oral glycemic agents (%)	34.2	33.2	36.8	0.13
Exercise data*				
Peak heart rate (beats/min)	135 ± 25	138 ± 25	131 ± 25	<0.001
Peak systolic blood pressure (mmHg)	183 ± 32	188 ± 33	176 ± 31	<0.001
Peak diastolic blood pressure (mmHg)	86 ± 16	89 ± 16	82 ± 15	<0.001
Peak METs (3.5 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$)	6.4 ± 2.3	6.3 ± 2.0	6.5 ± 2.6	0.001

Data are means ± SD. **P* values represent comparisons between African Americans and Caucasians.

study was approved by the institutional review board at each institution, and all subjects gave written informed consent before undergoing ETT.

All demographic, clinical, and medication information was obtained from the individual's computerized medical records just before ETT. Each individual was asked to verify the computerized information, including history of chronic disease, current medications, and smoking habits. Body weight and height were assessed by a standardized scale and recorded before the test. BMI was calculated as weight in kilograms divided by the square of height in meters. Demographic data are included in Table 1.

Dates of death were verified from the Veterans Affairs Beneficiary Identification and Record Locator System File. This system is used to determine benefits to survivors of veterans, and it has been shown to be complete and accurate (95%) (16). Vital status was determined as of 28 February 2008.

Exercise testing was performed using the Bruce protocol at the VAMC in Washington, DC, and by an individualized ramp protocol as described elsewhere (17) at the VAMC in Palo Alto, California. Peak exercise capacity (METs) was estimated using standardized equations based on peak speed and grade for the ramp protocol (17) and on peak exercise time for the Bruce protocol (18). Subjects were encouraged to exercise until volitional fatigue in the absence of symptoms or other indications for stopping (19). The use of handrails was discouraged but allowed when necessary for balance and safety. Age-predicted peak exercise heart rate was determined on the basis of a population-specific equation (20). Medications were not altered before testing.

Three fitness categories were established on the basis of the MET level achieved. Those who achieved a peak MET level ≤5 METs (lowest 25%) of the METs achieved by the cohort comprised the low fitness category (low-fit; n = 934); those whose MET level was >75% (≥8 METs) comprised the highest fitness category (high-fit; n = 762). Those remaining (5.1–7.9 MET level) comprised the moderate fitness category (moderate-fit; n = 1,452).

Statistical analysis

Follow-up time is presented as mean ± SD and median of years. Mortality rate was calculated as the ratio of events by the number of persons or by the person-years of observation. Continuous variables are presented as mean values ± SD and categorical variables as relative frequencies (percentage). Associations between categorical variables were tested using χ^2 analysis. One-way ANOVA was applied to determine age and BMI differences between races and fitness categories. Because of racial differences in age, ANCOVA was used to assess whether racial difference existed in exercise test variables, using age as a covariate. Age and BMI were used as covariates when comparisons among fitness categories were made. Post hoc procedures were performed (Bonferroni) for multiple comparisons. Equality of variances between groups was tested by Levene's test.

The relative risk for mortality was calculated for each fitness category. Kaplan-Meier survival curves were generated for the three fitness categories. Cox proportional hazard models were used to determine the variables that were significantly associated with mortality among fitness categories. The analyses were adjusted for age, BMI, history of CVD, cardiovascular medications (ACE inhibitors, β-blockers, calcium channel blocker, diuretics, and statins) and risk factors (hypertension, dyslipidemia, and smoking). Racial differences regarding the effect of exercise capacity on mortality risk were tested using a dummy variable that combined the exercise data with race. $P < 0.05$ using two-sided tests was considered statistically significant. All statistical analyses were performed using SPSS software (version 15.0; SPSS, Chicago, IL).

RESULTS — The mean ± SD follow-up period was 7.3 ± 5 years (median 6.4) and 23,137 person-years. There were 823 deaths (26.1%), resulting in an average annual mortality of 3.56%. Of those

who died, 509 (29.9%) were African Americans and 314 (21.7%) were Caucasians.

Approximately 79% of subjects achieved a peak heart rate of ≥85% of the age-predicted value. Approximately 44% of those who did not achieve this level were receiving β-blockers.

Participants' characteristics and exercise data are presented in Table 1. African Americans were younger than Caucasians ($P < 0.001$). After controlling for age, African Americans had higher resting diastolic blood pressure and were more likely to have CVD, hypertension, and dyslipidemia and to be treated with diuretics and insulin. Caucasians were more likely to smoke, have a family history of coronary heart disease, and be treated with β-blockers, ACE inhibitors, statins, and oral glycemic agents. After adjustment for age and resting diastolic blood pressure, the peak exercise systolic and diastolic blood pressure and heart rate were significantly higher in African Americans versus Caucasians, whereas peak MET level was higher in Caucasians.

Adjusted mortality for age, CVD, risk factors, resting diastolic blood pressure, cardiovascular medication, insulin and oral glycemic agents, and METs revealed that all-cause mortality was 23% higher (hazard ratio [HR] 1.23 [95% CI [1.02–1.47]; $P = 0.02$) in African Americans than in Caucasians. This relationship was consistent within moderate-fit (1.31 [1.04–1.64]) and high-fit categories (2.31 [1.44–3.70]) with no significant racial differences in mortality rates within the low-fit category (1.16 [0.94–1.44]).

African Americans who died were significantly older (64 ± 10 vs. 59 ± 9 years; $P < 0.001$) and had higher resting systolic blood pressure (143 ± 23 vs. 133 ± 21 mmHg; $P < 0.001$) compared with those still alive. They also had lower BMI (28.7 ± 5.4 vs. 30.7 ± 5.5; $P < 0.001$) and were more likely to smoke and have a higher prevalence of CVD.

Similarly, Caucasians who died were older (66 ± 9 vs. 61 ± 9 years; $P < 0.001$) and had higher resting systolic blood pressure (139 ± 23 vs. 133 ± 20 mmHg; $P < 0.001$) than those alive. In addition, they had significantly lower BMI (28.4 ± 4.8 vs. 30.9 ± 5.8; $P < 0.001$) and diastolic blood pressure (77 ± 12 vs. 79 ± 11 mmHg; $P < 0.001$) and were more likely to have CVD.

Comparisons among fitness categories revealed that age was significantly lower ($P < 0.001$) for the high-fit versus moderate-fit and low-fit categories (56 ± 9.2, 61 ± 10, and 65 ± 9 years, respectively). Similar findings were observed for both races. BMI was lower ($P < 0.05$) in the high-fit compared with the moderate-fit and low-fit categories (30.3 ± 5.9 vs. 30.6 ± 5.6 vs. 29.5 ± 5.1 for low-, moderate-, and high-fit, respectively). Thus, age and BMI were used as covariates when differences in resting and exercise heart rate, blood pressure, and MET levels among the fitness categories were assessed.

Exercise capacity and other clinical predictors of total mortality for the entire group and for each race are presented in Table 2. Survival analysis revealed a 16% reduction in mortality risk for every 1-MET increase in exercise capacity in the entire cohort ($P < 0.001$), 14% in African Americans ($P < 0.001$), and 19% in Caucasians ($P < 0.001$).

There were 394 (42.2%) deaths in the low-fit, 339 (23.3%) in the moderate-fit, and 90 (11.8%) in the high-fit category (Fig. 1). Among African Americans, there were 230 (46.4%) deaths in the low-fit, 224 (26.7%) in the moderate-fit, and 55 (14.9%) in the high-fit category. In Caucasians, there were 164 (37.4%) deaths in the low-fit category, 115 (18.8%) in the moderate-fit, and 35 (8.9%) in the high-fit category.

To assess total mortality risk associated with exercise capacity, we compared the moderate- and high-fit categories with the low-fit (Cox proportional hazard) category. The adjusted relative risks of these comparisons are presented in Table 3. The risk of mortality was 37% lower for those with an exercise capacity between 5.1 and 7.9 METs ($P < 0.001$) and 67% lower for those who achieved ≥8 METs ($P < 0.001$). The findings did not change substantially when participants who died within the first year of follow-up were excluded.

To assess racial differences in mortality risk, we probed for interaction between race and fitness. A significant interaction was noted between race and METs ($P < 0.001$) and among race and fitness categories ($P < 0.001$). Thus, we examined mortality rates among fitness categories for each race (Table 3). The low-fit category was used as the referent.

In African Americans, the relative risk was 34% lower for those achieving 5.1–7.9 METs ($P < 0.001$) and 46% lower for those achieving ≥8 METs ($P < 0.001$). In Caucasians, the relative risk was 43% lower ($P < 0.001$) for those achieving 5.1–7.9 METs and 67% lower ($P < 0.001$) for those achieving ≥8 METs.

Finally, we addressed the effects of exercise capacity on mortality risk when expressed as a percentage of age-predicted values, calculated on the basis of an equation derived from a large cohort of veterans referred for exercise testing (2). These analyses resulted in no significant differences relative to the findings when exercise capacity was expressed as an absolute value.

Table 2—*HRs (95% CI) for all-cause mortality according to exercise capacity*

	HR (95% CI)	*P*
All (n = 3,148)		
Peak exercise capacity (for each 1-MET increment)	0.79 (0.76–0.82)	<0.001
Adjusted for age and BMI	0.82 (0.79–0.86)	<0.001
Adjusted for age, BMI, cardiovascular risk factors, CVD, and cardiovascular medications	0.84 (0.81–0.87)	<0.001
African Americans (n = 1,703)		
Peak exercise capacity (for each 1-MET increment)	0.80 (0.76–0.84)	<0.001
Adjusted for age and BMI	0.85 (0.93–0.96)	<0.001
Adjusted age, BMI, cardiovascular risk factors, CVD, and cardiovascular medications†	0.86 (0.82–0.90)	<0.001
Caucasians (n = 1,445)		
Peak exercise capacity (for each 1-MET increment)	0.77 (0.73–0.82)	<0.001
Adjusted for age and BMI	0.81 (0.76–0.85)	<0.001
Adjusted age, BMI, cardiovascular risk factors, CVD, and cardiovascular medications†	0.81 (0.77–0.86)	<0.001

*Cardiovascular risk factors include hypertension, dyslipidemia, and smoking. †Cardiovascular medications include ACE inhibitors, β-blockers, calcium channel blockers, diuretics, insulin, aspirin, and statins.

CONCLUSIONS — The findings of the current study support a strong inverse and graded association between exercise capacity and risk for all-cause mortality in

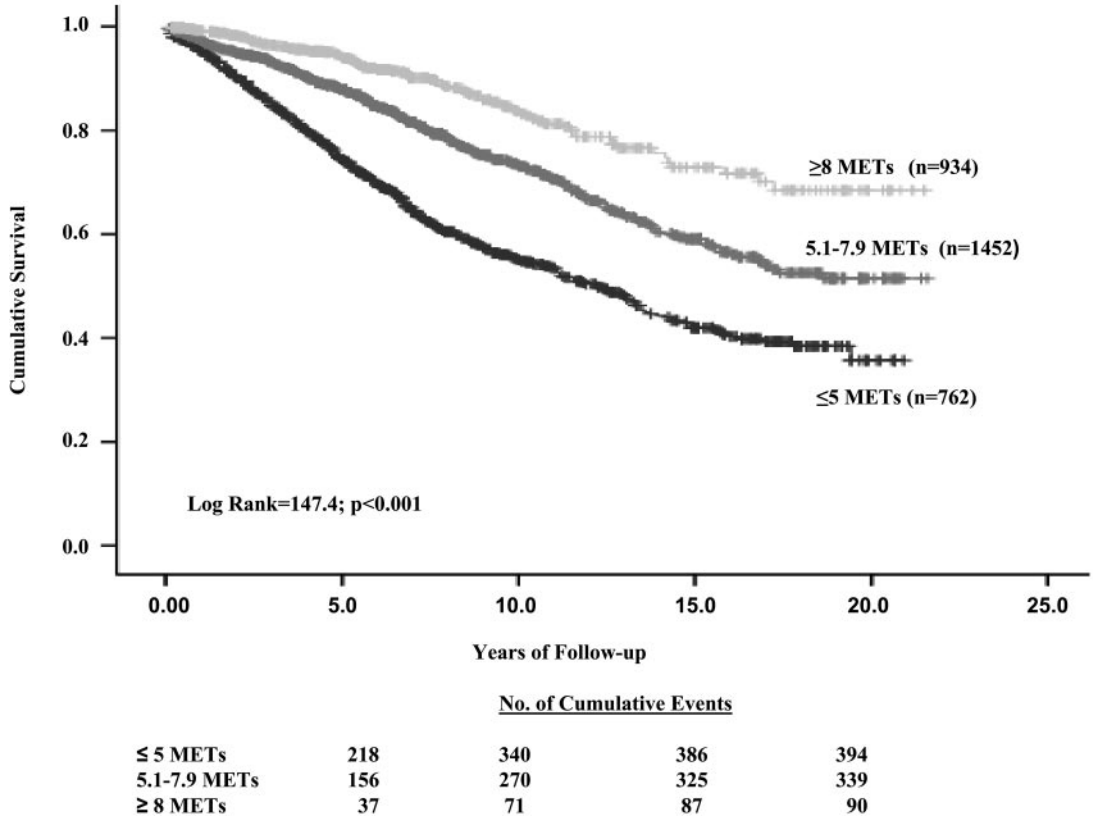

Figure 1—*Cumulative survival for the entire cohort according to fitness categories.*

middle-aged and older African American and Caucasian male Veterans with type 2 diabetes. After adjustment for age, BMI, cardiovascular risk factors, and cardiac medications, total mortality risk was progressively lower as exercise capacity increased beyond 5 METs (Table 3). Our findings support previous reports of an inverse relationship between aerobic fitness and total mortality in both healthy and diseased populations (1–5). They also confirm a previous report in predominantly male Caucasian diabetic subjects that the largest proportional reduction in risk occurs between the least fit and the moderate fit categories (4).

The current study is unique because it is the first to provide information on the association between exercise capacity and mortality risk in African American men with type 2 diabetes and to compare these

Table 3—*Relative risk for all-cause mortality according to fitness categories*

	Low fit	Moderate fit	High fit	*P**
MET level achieved	≤5 METs	5.1–7.9 METs	≥8 METs	
Entire cohort (n = 3,148)				
Age-adjusted	Referent	0.62 (0.53–0.71)	0.41 (0.32–0.52)	<0.001
Multi-adjusted†	Referent	0.63 (0.55–0.73)	0.41 (0.33–0.53)	<0.001
Excluding deaths that occurred during the first year of follow-up	Referent	0.63 (0.53–0.73)	0.43 (0.14–0.55)	<0.001
African-Americans (n = 1,703)				
Age-adjusted	Referent	0.65 (0.54–0.78)	0.54 (0.39–0.73)	<0.001
Multi-adjusted†	Referent	0.66 (0.55–0.80)	0.54 (0.39–0.73)	<0.001
Excluding deaths that occurred during the first year of follow-up	Referent	0.65 (0.53–0.79)	0.56 (0.40–0.77)	<0.001
Caucasians (n = 1,445)				
Age-adjusted	Referent	0.55 (0.43–0.70)	0.32 (0.22–0.47)	<0.001
Multi-adjusted†	Referent	0.57 (0.44–0.73)	0.33 (0.22–0.48)	<0.001
Excluding deaths that occurred during the first year of follow-up	Referent	0.57 (0.43–0.72)	0.34 (0.23–0.51)	<0.001

Data are HRs (95% CI). **P* values are for both the moderate-fit and high-fit categories compared with the low-fit category (referent) and for linear trend. †Adjusted for age, BMI, ACE inhibitors, β-blockers, calcium channel blockers, diuretics, statins, hypertension, dyslipidemia, and smoking.

relationships with those in a similar group of Caucasians. In this regard, it is important to emphasize that a strong, inverse, and dose-response reduction in the mortality risk for both African Americans and Caucasians was observed. Equally important is the finding of racial disparities in this relationship. More specifically, we noted that the exercise-related reduction in mortality may be stronger and more graded for Caucasians than for African Americans. For example, the adjusted mortality risk reduction per each 1-MET increase in exercise capacity was significantly greater for Caucasians (19%) than for African Americans (14%). Furthermore, comparisons between fitness categories revealed significant and clinically relevant differences in the mortality risk reduction between races. Compared with those in the low-fit category (≤5 METs), the mortality risk reduction for those achieving 5.1–7.9 METs was 43% for Caucasians and 34% for African Americans. In the high-fit category (≥8 METs), the risk was lowered by 67% (an additional 24% reduction) in Caucasians and only by 46% (an additional 12% reduction) in African Americans (Table 3).

It is noteworthy that in our previous work in >15,600 veterans with multiple risk factors (1), a close scrutiny of the database revealed that racial disparities were evident only in diabetic subjects. The mechanism(s) responsible for the racial disparity in the association of exercise capacity and mortality risk in diabetic men are not readily evident and are beyond the scope of this study. Nevertheless, because obesity has been identified as a risk factor for impaired exercise capacity (21) and is more common among African Americans (22), we examined possible racial differences in the prevalence of obesity as one likely explanation. However, the prevalences of overweight for both African Americans and Caucasians were 49.8 and 49.0% versus 50.7% for obese, respectively ($P = 0.35$). We also noted no significant racial differences in waist circumference in 182 diabetic subjects with available waist circumference data ($P = 0.116$).

Another possible mechanism may be racial differences in vascular reactivity. Endothelium-dependent vasodilatation is significantly impaired in healthy African American adults (23) and diabetic subjects (24) compared with that in the corresponding groups of Caucasians. In the current study, impaired vascular reactivity may have been more prevalent or more severe in African Americans than in Caucasians.

It is also possible that the racial differences on the impact of exercise capacity on mortality risk may be due to racial differences on adherence to medical therapy or socioeconomic factors that we were not able to account for in this study. We also probed for racial differences between the two sites regarding fitness but found no interactions. Finally, genetic differences between the two races cannot be discounted.

Another notable aspect of our study relates to the socioeconomic strata of our cohort. Most information on the association between exercise capacity and total mortality in diabetic subjects has been derived from predominantly middle to upper socioeconomic status Caucasians (3–5). Socioeconomic factors for such individuals may be more favorable and allow for a more optimal management of their diabetes. Thus, the reported benefits of exercise in such populations may be exaggerated compared with that in individuals in relatively low socioeconomic strata. Our cohort consists of Caucasian and African American veterans who mostly represent relatively lower socioeconomic strata. Thus, our findings support the notion that higher exercise capacity is associated with lower all-cause mortality in men with type 2 diabetes, independent of socioeconomic status.

Finally, the equal access to high-quality health care provided by the Veterans Health Administration in the U.S. Department of Veterans Affairs Health Care System, independent of a patient's financial status, strengthens the contention that increased exercise capacity provides protection against premature mortality in diabetic men.

Our study has some limitations. The inverse association between cardiorespiratory fitness and mortality does not prove cause and effect relationships. Although similar reciprocal relationships have been demonstrated between fitness and CVD mortality, we only had information on all-cause mortality and did not have data on cardiovascular mortality. However, using all-cause mortality as an end point in clinical investigations is viewed as objective, unbiased, and accurate, whereas use of cardiovascular mortality has been criticized as highly inaccurate (25). The onset of diabetes and other chronic diseases, severity and duration of therapy, and status of physical activity could not be evaluated because of incomplete records. This problem may explain part of the racial disparity noted. Finally, our findings are based on men only and cannot be extrapolated to women.

In summary, our findings support the concept that exercise capacity is a strong predictor of all-cause mortality in African American and Caucasian men with type 2 diabetes. The reduction is graded and more pronounced in Caucasians than in African Americans. It is important to emphasize that the inherent limitations of any epidemiological study do not permit definitive statements and that the finding regarding racial differences should be confirmed by future studies. Despite these limitations, our findings raise the intriguing possibility that racial differences in fitness-related health benefits may exist and that research on racial disparities should be pursued.

Our findings extend the public health message regarding the health benefits of cardiorespiratory fitness to men with diabetes and support the concept that exercise capacity should be given as much attention by clinicians as other major risk factors and that health care professionals should encourage diabetic subjects to initiate and maintain a physically active lifestyle consisting of moderate-intensity activities.

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