Exceptional Longevity in Men

Modifiable Factors Associated With Survival and Function to Age 90 Years

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Background: Prospective data on nongenetic determinants of exceptional longevity are limited, and information on long-lived men and their functional status is particularly sparse. We examined modifiable factors associated with a life span of 90 or more years and late-life function in men.

Methods: In this prospective cohort study of 2357 healthy men (mean age, 72 years) within the Physicians' Health Study (1981-2006), biological and lifestyle factors and comorbid conditions were assessed by self-report with baseline and annual questionnaires. Mortality and incidence of major diseases were confirmed by medical record review. Late-life function was assessed 16 years after baseline by the Medical Outcomes Study 36-Item Short-Form Health Survey.

Results: A total of 970 men (41%) survived to at least age 90 years. Smoking was associated with increased risk of mortality before age 90 years (hazard ratio [HR]; 2.10; 95% confidence interval [CI], 1.75-2.51), and similar associations were observed with diabetes (HR, 1.86; 95% CI, 1.52-2.26), obesity (HR, 1.44; 95% CI, 1.10-1.90), and hypertension (HR, 1.28; 95% CI, 1.15-1.43). Regular exercise was associated with a nearly 30% lower mortality risk (HR, 0.72; 95% CI, 0.62-0.83). The probability of a 90-year life span at age 70 years was 54% in the absence of smoking, diabetes, obesity, hypertension, or sedentary lifestyle. It ranged from 36% to 22% with 2 adverse factors and was negligible (4%) with 5. Compared with nonsurvivors, men with exceptional longevity had a healthier lifestyle (67% vs 53% had ≤1 adverse factor), had a lower incidence of chronic diseases, and were 3 to 5 years older at disease onset. They had better late-life physical function (mean ± SD score [maximum 100], 73 ± 23 vs 62 ± 30; $P < .001$) and mental well-being (mean score, 84 ± 14 vs 81 ± 17; $P = .03$). More than 68% (vs 45%) rated their late-life health as excellent or very good, and less than 8% (vs 22%) reported fair or poor health ($P < .001$ for trend). Regular exercise was associated with significantly better—and smoking and overweight with significantly worse—late-life physical function. Smoking also was associated with a significant decrement in mental function.

Conclusion: Modifiable healthy behaviors during early elderly years, including smoking abstinence, weight management, blood pressure control, and regular exercise, are associated not only with enhanced life span in men but also with good health and function during older age.

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EXCEPT FOR RARE REPORTS about long-lived men such as Sardinia's "Methuselahs,"[1] studies of exceptional longevity are dominated by data on women. It is unclear why relatively few men live to a very advanced age.

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Data from twin studies suggest that genetic determinants account for about 25% of the variation in life span,[2] leaving perhaps 75% affected by potentially modifiable factors. However, modifiable factors that might interact with genetic influences to promote exceptional longevity have not been clearly identified. Prospective studies of mortality risks in elderly populations typically have had short observational periods of 5 to 10 years,[3,4] with some exceptions,[5,6] and have focused on survival within average life spans of 75 to 85 years.[6-8] Studies of nonagenarians and centenarians, on the other hand, generally have been retrospective or cross-sectional analyses of relatively small numbers of survivors, including few men.[9,10] In addition, prevalence of disease and disability in these oldest populations is typically high,[11,12] and it is unclear what factors earlier in life might potentiate not only a very long life but also good health and function at an advanced age.

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Therefore, we used prospective data on more than 2350 men in the Physicians' Health Study (PHS) who had the potential to live to or beyond age 90 years during a 25-year follow-up to address 2 principal questions. First, what potentially modifiable factors are associated with survival to an exceptional age in men (defined by us as ≥90 years)? Second, do men with exceptional longevity have reduced incidence of age-associated diseases? We also assessed functional status in late life to determine if modifiable factors associated with longevity were also associated with good health and function at an advanced age.

METHODS

STUDY POPULATION

Participants were enrolled in the PHS, a cohort of 22 071 US male physicians assembled in 1981 to 1984 as a randomized trial of aspirin and beta carotene in the primary prevention of cardiovascular disease and cancer.[13] Men were generally healthy at randomization, without a history of cancer (excluding nonmelanoma skin cancer), myocardial infarction, transient cerebral ischemia or stroke, or other serious diseases. A detailed description of the PHS has been previously published.[13] Each participant provided written consent, and the PHS was approved by the institutional review board of Brigham and Women's Hospital, Boston, Massachusetts.

Participants in the present study were born on or before December 31, 1915, and had the potential to survive to age 90 years during follow-up ending March 31, 2006. We defined survival to age 90 as "exceptional longevity" because it far exceeded the 46- to 52-year estimated life expectancy for a man born in the United States in 1900 to 1915.[14] Furthermore, men reaching age 90 years would have lived 10 to 15 years longer than the predicted remaining life expectancy for men in their birth cohort surviving to age 65 to 70 years.[14]

EXPOSURE INFORMATION

Baseline Data

Participants gave self-reported information on demographic and health variables, including birth date, height, weight, systolic and diastolic blood pressures, history or treatment of hypertension (systolic/diastolic blood pressure ≥140/≥90 mm Hg), total cholesterol level, history or treatment of high cholesterol level (≥240 mg/dL [to covert to millimoles per liter, multiply by 0.0259]), history of diabetes or angina, smoking status (never, former, or current), frequency of alcohol consumption (rarely/never, 1-3 drinks per month, 1-6 drinks per week, or ≥1 drink per day), and frequency of vigorous exercise sufficient to cause sweat (rarely/never, <1 time per week, 1-6 times per week, or ≥1 times per day). Body mass index was calculated as weight in kilograms divided by height in meters squared.

Follow-up Data

Twice during the first year and annually thereafter, participants were sent questionnaires asking about changes in health or lifestyle habits, occurrence of chronic diseases or risks, and end points of interest. Nonrespondents were contacted by telephone. The percentage of participants with complete questionnaire data was greater than 96%.[15]

OUTCOMES

Mortality

Survival to age 90 years was the primary outcome of this study. Deaths were confirmed by the PHS end points committee of physicians after review of medical records, autopsy reports, and death certificates. The follow-up rare for mortality in the PHS approximates 99%.[15]

Disease

Secondary outcomes were major age-related diseases: cancer (excluding nonmelanoma skin cancer); coronary heart disease (myocardial infarction, coronary artery bypass graft, or percutaneous coronary angioplasty); and stroke. These outcomes were confirmed through medical record review by the PHS end points committee according to previously described procedures.[16] We also examined occurrence of heart failure, chronic obstructive pulmonary disease, peripheral vascular disease, Parkinson disease, and arthritis. Only the first event in each disease category was considered for analysis.

Function

We assessed functional status by the physical function and mental health subscales of the Medical Outcomes Study 36-Item Short-Form 36 Health Survey (SF-36)[17] included in the 16-year follow-up questionnaire (1998-1999). Each subscale is scored separately from 0 (lowest level of functioning) to 100 (highest level). For this study we also scored separately 2 questions from the mental health items relating to depression. We used the SF-36 question on self-rated health as a general measure of health-related quality of life. We assessed social contact by questions relating to frequency of contact with a close confidant.

STATISTICAL ANALYSES

We compared survivors to age 90 years with nonsurvivors in baseline characteristics, follow-up data, and incidence of outcomes using χ^2 tests for categorical variables and paired *t* tests or nonparametric tests, as appropriate, for continuous variables. We used Cox proportional hazards models to calculate the hazard ratio (HR) and 95% confidence interval (CI) for mortality before age 90 years according to baseline factors. Person-time was calculated from PHS enrollment to the minimum date of age 90 years, last contact, or death. All participants had the potential to reach age 90 years. We adjusted for baseline age (continuous) in an initial model and included adjustment for the following additional baseline factors in a multivariable model: body mass index; smoking status; alcohol intake; exercise frequency; history of hypertension, diabetes, high cholesterol level, or angina; and randomized treatment assignments (aspirin or beta carotene). Models including quadratic and cubic adjustments for baseline age did not improve model fit. Tests for linear trend across categorical variables were performed by entering the variable as a single ordinal term in the models. The assumption of proportional hazards was assessed by Schoenfeld residuals and was satisfied.

To illustrate the estimated probability of 90-year survival according to specific baseline risks and their additive effects, we used a logistic regression model with the same covariates and adjustments as in the multivariable proportional hazards model. In secondary analyses, we examined possible effect modification by birth cohort on survival to age 90 years through strati-

Table 1. Baseline Characteristics of 2357 Men Who Did or Did Not Survive to Age 90 Years[a]

Characteristic	Survivors (n = 970)	Nonsurvivors (n = 1387)	P Value
Biological			
Age, y	72.9 (4.5)	71.7 (3.8)	<.001
Height, cm	175.9 (6.9)	176.5 (7.0)	.006
Weight, kg	75.7 (9.2)	77.0 (9.9)	.001
BMI	24.4 (2.4)	24.7 (2.8)	.08
BMI category, %			
<25.0	61.7	58.5	.02
25.0-29.9	36.3	37.1	
≥30.0	2.0	4.3	
Systolic blood pressure, mm Hg	133.5 (13.0)	135.0 (13.7)	.005
Diastolic blood pressure, mm Hg	79.6 (7.5)	80.8 (7.4)	<.001
Hypertension, %	41.6	49.1	<.001
Total cholesterol, mg/dL[b]	215.4 (44.8)	214.5 (48.8)	.71
Hypercholesterolemia, %	13.9	13.8	.96
Diabetes, %	3.7	8.6	<.001
Angina, %	4.1	6.1	.04
Congestive heart failure, %	0.6	0.4	.37
COPD, %	3.5	4.3	.32
Peripheral vascular disease, %	1.7	3.8	.002
Parkinson disease, %	0.1	0.7	.05
Arthritis, %	6.1	1.9	<.001
Geographic region, %			
Northeast	32.7	29.8	.62
Midwest	18.8	19.7	
South or Southwest	25.7	28.2	
Mountain or Pacific	22.6	21.6	
Other	0.3	0.8	
Health habits			
Cigarette smoking, %			
Never	50.0	38.6	<.001
Past	44.5	48.7	
Current	5.5	12.7	
Alcohol intake, %			
Rarely/never	18.2	18.1	.22
1-3 drinks/mo	10.0	8.3	
1-6 drinks/wk	36.8	34.8	
≥1 drinks/d	35.0	38.8	
Exercise frequency, %			
Rarely/never	18.4	24.8	.001
1-4 times per mo	24.3	24.8	
2-4 times per wk	36.4	31.4	
≥5 times per wk	20.8	19.0	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease.

SI conversion factor: To convert cholesterol to millimoles per liter, multiply by 0.0259.

[a] Data are given as mean (SD) unless otherwise indicated.

[b] Mean total cholesterol levels are for 431 survivors and 548 nonsurvivors.

fied analyses (birth years 1898-1907 and 1908-1915). We also examined the impact of modifiable baseline behavioral factors (weight, smoking, alcohol consumption, and exercise) on functional status in later life using ordinary least squares regression, adjusting for the same baseline covariates, as well as for prevalent diseases potentially affecting function.

All analyses were performed using SAS software version 9.1 (SAS Institute Inc, Cary, North Carolina). All *P* values were 2-tailed, and *P*<.05 was considered statistically significant.

RESULTS

Of 2357 men with the potential to reach age 90 years during the 25-year follow-up study, 970 (41%) survived to or beyond age 90 years and 1387 did not (median follow-up: survivors, 17.9 years to age 90 years; nonsurvivors, 11.7 years). Mean ages at death were 83 years (nonsurvivors) and 93 years (518 survivors [53%] who died during continued observation) (*P*<.001).

Table 1 gives the baseline characteristics of the population. The mean age was 72 years (range, 66-84 years), with survivors being slightly older. Survivors were less likely to be obese or have smoking history and were more likely to exercise than nonsurvivors. They had slightly lower blood pressures, and fewer had hypertension, diabetes, and angina. Prevalence of chronic disease was low in this population, and survivors and nonsurvivors showed little difference.

Table 2 gives age- and multivariable-adjusted HRs for mortality before age 90 years for potentially modifiable baseline factors. Current smoking was associated with a 2-fold increased risk of mortality (HR, 2.10; 95% CI, 1.75-2.51). Diabetes, obesity, and hypertension were associated with increased risks of 86%, 44%, and 28%, respectively. In contrast, vigorous exercise was associated with approximately 20% to 30% decreased mortality risk before age 90 years (*P* value for trend, .003). Alcohol intake and high cholesterol level showed no mortality effects.

Incidence of cancer and cardiovascular disease, as well as associated risk factors, was lower among survivors compared with nonsurvivors and occurred at a 3- to 5-year older age. Similar patterns were apparent for other age-associated diseases (**Table 3**).

In age-stratified analyses, mean age at death was 9 years older for survivors to age 90 years who later died during the study period, compared with nonsurvivors, in both birth cohorts (1898-1907 and 1908-1915). Patterns of factors associated with 90-year survival were similar in the 2 cohorts, and there was no effect modification by birth year (*P* value for interaction for all covariates, >.11). Increased risks of mortality before age 90 years were associated with smoking (103%-201%), diabetes (61%-92%), obesity (36%-44%), and hypertension (28%-38%). Regular exercise was associated with a 30% decreased mortality risk before age 90 years in both groups. There was no influence of birth cohort on incidence or age at onset of disease outcomes.

Compared with having no adverse baseline factors (smoking, diabetes, obesity, hypertension, or sedentary lifestyle), the age-adjusted odds of survival to age 90 years with 1, 2, 3, or 4 or more adverse factors was reduced by 33%, 49%, 75%, and 88%, respectively (*P* value for trend, <.001). Survivors had significantly fewer adverse factors at baseline compared with nonsurvivors, including a significantly greater number with none (**Table 4**).

The **Figure** illustrates the association between specific factors at age 70 years and the probability that a man would live to age 90 years. If he did not smoke and had normal blood pressure and weight (BMI <25), no diabetes, and a moderate exercise habit (2-4 times per week),

Table 2. Age- and Multivariable-Adjusted Hazard Ratios for Mortality Before Age 90 Years for Potentially Modifiable Factors

Variable	Hazard Ratio (95% Confidence Interval) Age Adjusted[a]	Multivariable Adjusted[b]
Biological		
BMI		
<25.0	1 [Reference]	1 [Reference]
25.0-29.9	1.03 (0.92-1.15)	0.97 (0.86-1.08)
≥30.0	1.70 (1.31-2.21)	1.44 (1.10-1.90)
P value for trend	.02	.40
Hypertension	1.30 (1.17-1.44)	1.28 (1.15-1.43)
Diabetes	1.88 (1.56-2.27)	1.86 (1.52-2.26)
Hypercholesterolemia	0.93 (0.79-1.08)	0.92 (0.79-1.08)
Angina	1.27 (1.02-1.59)	1.09 (0.86-1.40)
Health habits		
Cigarette smoking		
Never	1 [Reference]	1 [Reference]
Past	1.26 (1.12-1.41)	1.30 (1.16-1.47)
Current	2.09 (1.76-2.49)	2.10 (1.75-2.51)
P value for trend	<.001	<.001
Alcohol intake[c]		
Rarely/never	1 [Reference]	1 [Reference]
1-3 drinks/mo	0.87 (0.69-1.08)	0.89 (0.71-1.11)
1-6 drinks/wk	0.92 (0.79-1.08)	0.95 (0.81-1.11)
≥1 drinks/d	1.04 (0.89-1.21)	0.99 (0.84-1.16)
P value for trend	.39	.90
Exercise frequency[d]		
Rarely/never	1 [Reference]	1 [Reference]
1-4 times/mo	0.77 (0.66-0.89)	0.78 (0.67-0.91)
2-4 times/wk	0.69 (0.60-0.79)	0.72 (0.62-0.83)
≥5 times/wk	0.73 (0.62-0.86)	0.81 (0.69-0.96)
P value for trend	<.001	.003

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a]Adjusted for age at baseline (N = 2357 unless otherwise specified).
[b]Adjusted for age, BMI, smoking status, alcohol intake, exercise frequency, hypertension, diabetes, hypercholesterolemia, angina, and treatment assignment (all at baseline) (for multivariable-adjusted hazard ratio, n = 2280).
[c]For age-adjusted hazard ratio, n = 2315.
[d]For age-adjusted hazard ratio, n = 2316.

Table 3. Incidence[a] and Age[b] at Occurrence of Risk Factors and Diseases During Follow-up[c]

Risk Factor/Disease	Survivors (n = 970)	Nonsurvivors (n = 1387)	*P* Value
Hypertension			
Incidence	34.6	38.0	. . .
Age	79.0 (6.2)	75.3 (5.1)	<.001
Diabetes			
Incidence	3.6	5.5	. . .
Age	80.4 (5.6)	78.6 (4.5)	.04
Hypercholesterolemia			
Incidence	12.4	11.0	. . .
Age	82.0 (5.4)	78.0 (5.2)	<.001
Angina			
Incidence	12.5	14.8	. . .
Age	80.4 (5.5)	76.7 (4.6)	<.001
Cancer			
Incidence	13.7	36.6	. . .
Age	81.9 (5.0)	78.8 (5.1)	<.001
Coronary heart disease[d]			
Incidence	10.2	18.6	. . .
Age	80.3 (6.2)	77.3 (6.1)	<.001
Stroke			
Incidence	6.3	15.4	<.001
Age	83.8 (4.4)	79.2 (5.5)	<.001
Congestive heart failure			
Incidence	6.7	9.1	. . .
Age	83.6 (6.9)	80.4 (5.6)	<.001
COPD[d]			
Incidence	15.4	19.0	. . .
Age	77.0 (11.9)	73.3 (12.9)	<.001
Peripheral vascular disease			
Incidence	6.7	10.0	. . .
Age	79.6 (8.5)	74.1 (8.6)	<.001
Parkinson disease			
Incidence	2.8	4.9	. . .
Age	85.9 (3.9)	78.2 (8.2)	<.001
Arthritis			
Incidence	14.4	10.3	. . .
Age	76.0 (12.6)	74.7 (8.4)	.17

Abbreviations: COPD, chronic obstructive pulmonary disease; ellipses, missing *P* value.
[a]Incidence rates (per 1000 person-years) (percentage) are calculated according to number of cases occurring in population at risk during median follow-up periods of 17.9 years for survivors (until age 90 years) and 11.7 years for nonsurvivors.
[b]Mean (SD), y.
[c]Until death in nonsurvivors or age 90 years in survivors.
[d]Myocardial infarction, coronary artery bypass graft, or coronary revascularization.

his probability of living an additional 20 years was 54%. If he had a sedentary lifestyle, however, his probability was only 44%. If also hypertensive, obese, or a smoker, his probability of achieving a 90-year life span was reduced to 36%, 26%, and 22%, respectively. With 3 adverse factors (eg, sedentary lifestyle, obesity, and diabetes), his probability was only 14%, and it was negligible (4%) with 5 factors.

A sample of 686 men, mean age 86 years (range, 83-89 years), provided functional assessment approximately 16 years after baseline (506 survivors and 185 nonsurvivors). Survivors scored significantly higher in physical function and mental health, and they reported less depression than nonsurvivors (**Table 5**). They had better self-rated health (*P* value for trend, <.001), and more than 68% considered their health to be "very good" or "excellent" compared with less than 45% among nonsurvivors. A small group of survivors aged 90 to 101 years at assessment (n = 110) reported similar self-rated health, with 67% considering it to be "very good" or "excellent." Survivors and nonsurvivors did not differ in social contact. Survivors had lower incidence and later age at onset of age-related diseases compared with nonsurvivors, similar to the pattern of the total study population (Table 3).

Modifiable behaviors associated with survival to exceptional age also showed a significant impact on function. Smoking or overweight was associated with substantially worse physical function score (up to 10.3 and 8.9 points lower, respectively) (**Table 6**). Moderate vigorous exercise, in contrast, was associated with significantly better physical function (up to 10.6 points higher score). Smoking also was associated with a significant dec-

Table 4. Prevalence[a] of Adverse Modifiable Factors[b] at Baseline Among Men Who Did or Did Not Survive to Age 90 Years

Adverse Factors, No.	Survivors (n = 970)	Nonsurvivors (n = 1387)	*P* Value
0	24.1	14.8	
1	42.5	38.4	
2	27.8	33.0	<.001
3	5.3	12.5	
≥4	0.3	1.4	

[a] Data are given as percentage of men in group.
[b] Factors at baseline significant in multivariable proportional hazards model predicting mortality before age 90 (smoking, diabetes, obesity, hypertension, and lack of exercise).

rement in mental health score of up to 7 points (model not shown).

COMMENT

In this 25-year prospective study of 2357 men, potentially modifiable biological and behavioral factors were associated with exceptional longevity of 90 or more years. Smoking, diabetes, obesity, and hypertension significantly reduced the likelihood of a 90-year life span, while regular vigorous exercise substantially improved it. Birth cohort did not influence these associations. Furthermore, men with a life span of 90 or more years also had better physical function, mental well-being, and self-perceived health in late life compared with men who died at a younger age. Adverse factors associated with reduced longevity—smoking, obesity, and sedentary lifestyle—also were significantly associated with poorer functional status in elderly years.

Men living to age 90 years or older had a lower incidence and older age at onset of cancer, coronary heart disease, stroke, and other diseases than did men dying at a younger age. These prospective findings support observations from cross-sectional and retrospective studies of nonagenarians and centenarians hypothesizing that exceptional longevity is achieved by escaping or delaying disease processes responsible for high morbidity and mortality.[10] However, our results also extend these studies by demonstrating the strong association between nongenetic, highly modifiable biological and behavioral factors and exceptional life span that includes both reduced or delayed disease as well as good functional status at an advanced age.

Longitudinal studies of elderly cohorts have documented the unfavorable mortality risks of smoking,[5] diabetes,[18] obesity,[19] hypertension,[20] and physical inactivity,[21] although prospective data on their risk to survival beyond 85 years have been limited.[6] Our study provides evidence of the continued mortality risks of these factors at an even older age and shows the detrimental and long-term impact of smoking, obesity, and inactivity on late-life function and well-being. This is particularly noteworthy with regard to obesity, given the controversy about its health consequences and mortality risk in elderly individuals and the increasing prevalence of overweight and obesity in older US adults.[22]

The substantial association between regular vigorous exercise and exceptional longevity extends the available literature on survival benefits of exercise in very old individuals. While the mortality advantage of exercise in younger adults is well-established, including seminal studies in large cohorts of men,[21] fewer studies have examined its impact on survival beyond age 75 years.[8,23] Our results strongly support continued mortality benefits for men in this older age group and furthermore demonstrate a significant positive association between regular vigorous exercise in elderly years and good late-life physical function. Our findings are in contrast to 2 recent reports finding no association between physical activity at midlife and subsequent survival to age 85 years in men,[6,7] but those populations were relatively sedentary. Of note, the men in our study were all generally healthy at baseline, and there was no difference in prevalent disease between survivors and nonsurvivors who did not exercise. Thus, it is unlikely that our findings on exercise resulted from survivors being more likely to exercise because they were healthier at baseline than nonsurvivors.

Prospective data on the association between alcohol use and longevity of 90 or more years are limited. However, longitudinal studies of elderly populations of younger ages have reported reduced mortality with light to moderate alcohol consumption compared with abstinence,[24] as well as increased mortality with high consumption.[6,24] No association between mortality and moderate alcohol intake in men older than age 74 years also has been reported.[25] In our study of generally healthy men (mean age, 72 years at baseline), alcohol was not related to survival to age 90 or to functional status in late life.

The lack of an association between history of hypercholesterolemia and exceptional longevity in this study is consistent with data from other[8] but not all[7] prospective studies examining survival to or beyond age 80 years. Although maintaining favorable lipid profiles may have positive health benefits even in elderly years, the effect on mortality in old age is controversial.[26] We did not have lipoprotein fractions to compare with findings from observational studies suggesting that exceptional longevity may be associated with lipoprotein particle size, independent of lipid levels.[27]

A number of investigations have estimated singular effects of modifiable metabolic and behavioral factors on changes in average but not exceptional life expectancy.[21,28] Smoking, diabetes, obesity, and hypertension each are predicted to reduce life expectancy by 1 to 5 years, while higher physical activity may add up to 5 years. A composite lifestyle of healthy behaviors has been suggested to potentially increase life expectancy by 10 years.[29] Our study demonstrates the significant and progressive reduction in the probability of an exceptional 90-year life span by the accumulation of adverse modifiable factors. Interestingly, men with exceptional longevity had healthy behaviors and few adverse factors and lived on average 10 years longer than men with less favorable characteristics.

Although the impact of certain midlife mortality risks in elderly years is controversial,[30] our study suggests that

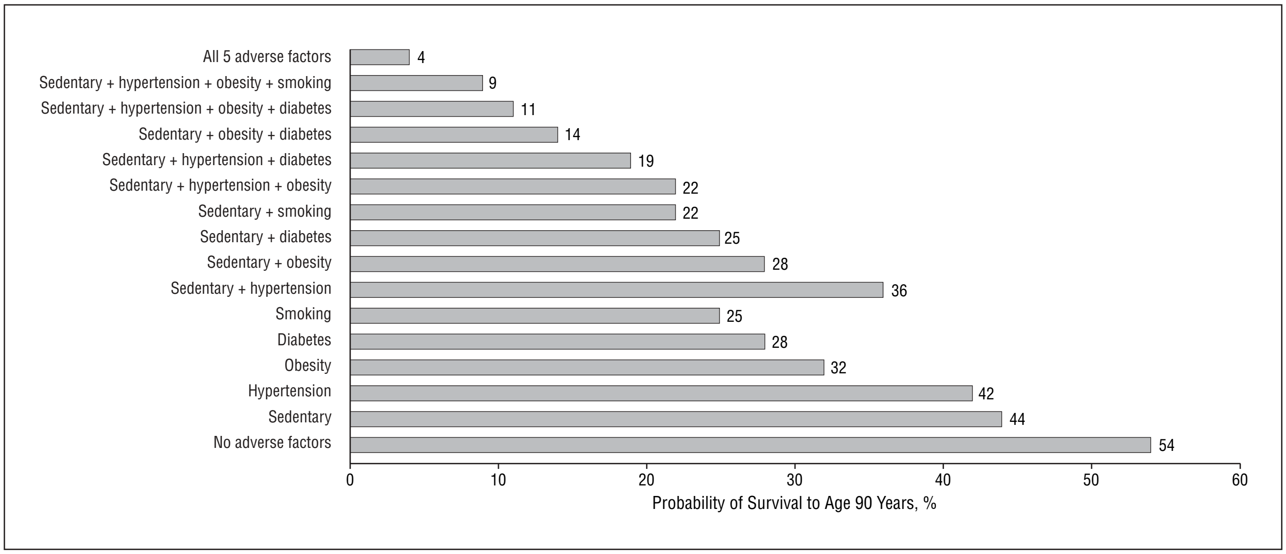

Figure. Probability of an additional 20-year survival to age 90 years for a 70-year-old man, according to the presence of 0 to 5 modifiable adverse factors at baseline, including smoking, diabetes, obesity, hypertension, and sedentary lifestyle, or their common clustering.

Table 5. Functional Health Status and Self-rated Health in Late Life in Men Who Did or Did Not Survive to Age 90 Years or Older

Functional Health Status/Self-rated Health	Survivors (n = 506)	Nonsurvivors (n = 185)	*P* Value
Age at assessment, mean (SD), y	86.2 (1.9)	85.3 (1.5)	<.001
Physical function[a]	73.4 (23.0)	62.0 (30.0)	<.001
Mental well-being[b]	84.4 (13.8)	81.2 (17.4)	.03
Depression[c]	91.2 (14.9)	87.4 (17.4)	.008
Social contact[d]	81.6 (31.1)	80.0 (33.4)	.81
Self-rated health, %			
Excellent	25.5	15.7	
Very good	42.7	29.2	
Good	24.1	33.0	<.001
Fair	6.7	17.3	
Poor	1.0	4.9	

[a] Mean (SD) composite score of 10 questions regarding limitation in self-care; mobility; walking; stair climbing; lifting or carrying groceries; participating in moderate activities; and participating in vigorous activities. Higher score indicates better function.

[b] Mean (SD) composite score of 5 questions regarding mood. Higher score indicates better function.

[c] Mean (SD) composite score of 2 questions regarding mental well-being. Higher score indicates less depression.

[d] Mean (SD) composite score of 2 questions regarding availability of a close confidante and frequency of contact. Higher score indicates more contact.

Table 6. Relative Impact of Modifiable Factors on Functional Status in Late Life[a,b]

Factor	Mean Difference (95% Confidence Interval) in Physical Function[c]
BMI	
≥25	−5.7 (−8.9 to −1.2)
<25	1 [Reference]
Smoking status	
Past or current	−6.41 (−10.3 to −2.6)
Never	1 [Reference]
Alcohol consumption, d/wk	
Daily	1.51 (−3.4 to 6.4)
1-6	2.29 (−2.6 to 7.1)
<1	1 [Reference]
Exercise, times/wk	
≥5	1.93 (−3.4 to 7.3)
2-4	6.41 (2.3 to 10.6)
≤1	1 [Reference]

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

[a] Factors assessed in late midlife (mean age, 69.6 years) in 790 men who provided subsequent functional assessment at a mean age of 86 years.

[b] Values are least squares estimates adjusted for baseline age and comorbidity (hypertension, diabetes, angina, congestive heart failure, chronic obstructive pulmonary disease, arthritis, Parkinson disease, and peripheral vascular disease).

[c] Composite score of 10 questions regarding limitation in self-care; mobility; walking; stair climbing; lifting or carrying groceries; participating in moderate activities; and participating in vigorous activities. The scale ranged from 0 to 100, with the higher score indicating better function (mean scores: survivors to age ≥90 y, 73.4; nonsurvivors, 62.0).

many remain important, at least among men. Not only were smoking, diabetes, obesity, hypertension, and physical inactivity negatively associated with exceptional longevity, but smoking, obesity, and inactivity were also strongly associated with poorer function at advanced age. Thus, our results suggest that healthy lifestyle and risk management should be continued in elderly years to reduce mortality and disability.

This study has a number of strengths, including prospective design, large sample size, substantial data on risk factors, completeness in ascertainment and number of outcome events, and long follow-up.

This study also has several potential limitations. Information on biological and behavioral factors was self-reported, and inaccurate measurements and random misclassification were possible, which could underestimate associations. Restricting the population to initially healthy, mostly white, male physicians affects the generalizability of results, although it reduces confounding by disease, education, socioeconomic status, and presumed access to health care. Furthermore, restriction to male subjects was an important advantage because existing data on exceptional longevity have come principally from women. Although we adjusted for many factors potentially associated with longevity, our analyses did not include a number of other variables that also may influence life span. Finally, this study did not capture the effect of possible changes in all risk factors and in functional status over the follow-up period.

In summary, these prospective data from 2357 men suggest that modifiable biological and lifestyle factors, assessed at a mean age of 72 years, are associated with exceptional longevity of 90 or more years and with high functional status in late life. If confirmed in other studies, this would suggest that encouraging favorable lifestyle behaviors, including smoking abstinence, weight management, blood pressure control, and exercise, may not only enhance life expectancy but may also reduce morbidity and functional decline in elderly years.

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