Late-Life Factors Associated with Healthy Aging in Older Men

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OBJECTIVES: To identify potentially modifiable late-life biological, lifestyle, and sociodemographic factors associated with overall and healthy survival to age 85.

DESIGN: Prospective longitudinal cohort study with 21 years of follow-up (1991–2012).

SETTING: Hawaii Lifespan Study.

PARTICIPANTS: American men of Japanese ancestry (mean age 75.7, range 71–82) without baseline major clinical morbidity and functional impairments (N = 1,292).

MEASUREMENTS: Overall survival and healthy survival (free from six major chronic diseases and without physical or cognitive impairment) to age 85. Factors were measured at late-life baseline examinations (1991–1993).

RESULTS: Of 1,292 participants, 1,000 (77%) survived to 85 (34% healthy) and 309 (24%) to 95 (<1% healthy). Late-life factors associated with survival and healthy survival included biological (body mass index, ankle–brachial index, cognitive score, blood pressure, inflammatory markers), lifestyle (smoking, alcohol use, physical activity), and sociodemographic factors (education, marital status). Cumulative late-life baseline risk factor models demonstrated that age-standardized (at 70) probability of survival to 95 ranged from 27% (no factors) to 7% (≥5 factors); probability of survival to 100 ranged from 4% (no factors) to 0.1% (≥5 factors). Age-standardized (at 70) probability of healthy survival to 90 ranged from 4% (no factors) to 0.01% (≥5 factors). There were nine healthy survivors at 95 and one healthy survivor at 100.

CONCLUSION: Several potentially modifiable risk factors in men in late life (mean age 75.7) were associated with markedly greater probability of subsequent healthy survival and longevity. **J Am Geriatr Soc 62:880–888, 2014.**

Key words: healthy aging; risk factors; longevity; longitudinal cohort study; late-life

Healthy aging is an important goal for older adults, clinicians, and society.[1] Identifying potentially modifiable factors to improve the probability of healthy aging may enhance length and quality of life and reduce healthcare costs.[2] Although several paradigms of healthy aging have been proposed, including compression of morbidity,[3] effective aging,[4] and healthspan,[5] the paradigm that has most captured the imagination of clinicians and lay public alike is Rowe and Kahn's[6] concept of successful aging. It had a transformational effect on the field of gerontology that still reverberates today in the scientific literature and the popular consciousness.[7] The Rowe and Kahn model[8] set a high bar for "success" in its conceptualization of healthy aging—surviving into old age without major diseases or disability—but one that is consistent with much of the general public's notion of a "vibrant old age."

Midlife studies of healthy aging have consistently identified smoking, overweight and obesity, physical activity, alcohol use, and marital status as important (and potentially modifiable) factors for healthy aging.[9–11] Guidelines for risk factors in midlife may not be optimal in old age, including those for body mass index (BMI) and body weight,[12] cholesterol,[13] blood pressure,[14] and blood sugar.[15] Optimal alcohol intake levels for older adults are controversial.[16] It is likely that smoking continues to cause harm in late life, and cessation may affect outcomes regardless of how late in life it occurs, but more research is needed.[17]

Prior studies have examined late-life risk factors associated with survival, summarized in a recent review,[18–22] but data are limited on survival free of major clinical diseases with maintenance of high cognitive and physical function.[23,24] Data are particularly limited on late-life factors associated with healthy survival beyond age 85, an

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DOI: 10.1111/jgs.12796

0002-8614/14/$15.00

increasingly important outcome because nonagenarians and centenarians are the most rapidly growing segment of the oldest-old population.[25] Longer survival suggests greater likelihood of spending down retirement savings and facing mounting healthcare and long-term care costs.[26] According to retirement planners, married couples have a 25% chance at age 65 that one will survive to beyond 95 years.[27] Few objective data exist to assess risk for physical and cognitive impairment at these very old ages, with even fewer data on modifying this risk. With more elderly adults surviving into their 90s and beyond, such data are important for financial, healthcare, and long-term care planning.

A phenotype of healthy aging consistent with common paradigms (no major clinical diseases with good physical and cognitive function)[9] was previously operationalized, and avoidance of nine common, modifiable midlife risk factors was associated with a likelihood of healthy survival that was up to six times as great as that of subjects with six or more of the risk factors. Based on this, it was hypothesized there are potentially modifiable risk factors present in late life associated with extended health span, and that some factors would be more important in late life than in midlife, whereas other factors important in midlife might be less important in late life. Therefore, the current study had three principal aims: Identify late-life predictors of healthy survival into very old ages. Compare late-life and midlife predictors, particularly regarding modifiable risk factors. Assess the odds of achieving further healthy years.

METHODS

Study Population and Procedures

The Honolulu Heart Program began in 1965 as a population-based prospective study of cardiovascular diseases with 8,006 American men of Japanese ancestry (AJA) (recruited from World War II service records of 9,877 men with valid contact information) born between 1900 and 1919 and living on the island of Oahu.[28]

For the current study, 3,734 subjects (80% of original Honolulu Heart Program cohort survivors) were examined at the late-life baseline examination in 1991 to 1993. Men with prevalent major chronic diseases, functional impairment, or cognitive impairment (n = 2,442) were excluded (to focus on development of unhealthy survival in those who were healthy (true incidence study)), as were those aged 83 and older at the late-life baseline examination (to permit at least 3 years of longitudinal survival follow-up from the late-life baseline), leaving an analytical sample of 1,292 men born between 1909 and 1919 followed for mortality and healthy survival status for up to 21 years (1991–2012).

The institutional review board of Kuakini Medical Center approved all examinations. Written informed consent was obtained at each examination.

Risk Factor Measures

The late-life baseline physical examination measured height, weight, grip strength, timed 10-foot walk, seated blood pressure, forced expiratory volume in 1 second, ankle–brachial index (ABI), cognitive function (Cognitive Abilities Screening Instrument (CASI)),[29] and depressive symptoms (11-item Center for Epidemiologic Studies Depression Scale).[30] Fasting blood samples were examined for total cholesterol, triglycerides, high-density lipoprotein cholesterol, fibrinogen, white blood cell (WBC) count, hemoglobin, insulin, and glucose. Current and past smoking history, alcohol consumption, physical activity, social and demographic characteristics were collected according to self-report.

Continuous variables were dichotomized (high/low) using conventional cut points or median values. Published risk cut points from national expert panels or mortality and morbidity studies included waist–hip ratio (>0.99),[31] forced expiratory volume in 1 second (<2.1 L),[32] diastolic blood pressure (DBP; >90 mmHg),[33] ABI (<0.9),[34] city blocks walked per day (<12),[35] triglycerides (≥150 mg/dL),[33] high-density lipoprotein cholesterol (<40 mg/dL),[33] fasting glucose (≥126 mg/dL),[36] fasting insulin (≥20 μU/mL),[37] fibrinogen (>3.51 g/L),[38] WBC (>6,000/mm^3),[39] CASI scores (intermediate (74.0–81.9) vs high (≥82.0)),[29] and depressive symptoms (11-item Center for Epidemiologic Studies Depression Scale score ≥9).[30]

Factors without published cut points were dichotomized at median levels, including handgrip strength (≤33 kg), gait speed (≤0.75 m/s), and physical activity index (≤30.4). Several variables had U-shaped relationships with survival and were divided based on mortality distribution and previous literature: BMI (≥25.0, 19.0–24.9, <19.0 kg/m^2);[40] systolic blood pressure (SBP) (<120, 120–160, >160 mmHg);[33] and hemoglobin (<13, 13–15, >15 g/dL).[41]

Additional variable definitions included education (≥12 vs <12 years),[9] self-rated health (fair or poor vs good or excellent),[42] smoking (never, past, current), and alcohol intake (standardized into ounces of alcohol per month: never drinker (0 ounces/month); mild intake (>0–15 ounces/month, ≤1 drink per day); moderate to heavy intake (>15 ounces/month, >1 drink per day)).[43]

Outcome Measures

Chronic disease and survival data were obtained through comprehensive surveillance of hospital discharges, death certificates, autopsies, and repeat examinations[44] through 2012.

To identify factors associated with nonsurvival and unhealthy survival, subjects were assigned to one of three survival phenotypes: nonsurvivors, unhealthy survivors, and healthy survivors. Nonsurvivors were men who died before age 85 (mean age at death 81.3, range 73.9–84.9). Unhealthy survivors were classified according to a phenotype that operationalized Rowe and Kahn's popular criteria:[9] men who survived to age 85 with one or more of six major, age-related chronic diseases (coronary heart disease, stroke, cancer (excluding nonmelanoma skin cancer), chronic obstructive pulmonary disease, Parkinson's disease, and treated diabetes mellitus), physical impairment, or cognitive impairment. Healthy survivors were men who survived to age 85 free of these chronic diseases and physical and cognitive impairment.[9]

Physical impairment was defined as difficulty walking half a mile.[9] Cognitive impairment was defined as CASI score of less than 74.[45] Chronic disease, physical impairment, and cognitive impairment were determined at each examination from 1991 to 1993 through 2012.

Statistical Analysis

Three analyses were performed to examine the relationship between risk factors at late-life baseline (age mid-70s) and healthy, unhealthy, and nonsurvival.

First, general linear models were used to compare mean late-life baseline (herein referred to as baseline) risk factors according to survival phenotype, adjusted for age at baseline. This provided a raw estimate of the differences between risk factors between survival phenotypes.

Second, separate logistic regression models were used to examine associations between baseline risk factors and likelihood of nonsurvival versus overall survival and unhealthy survival versus healthy survival. Because of the large number of variables considered in the analyses, stepwise logistic regression was used to select the subset of variables for the final model by including only variables with *P*-values smaller than the preselected significance level ($P < .10$). Each variable meeting the preselected significance level was added individually until no additional variables met this preselected significance level. Sensitivity analyses were performed including all participants through age 84 at baseline and excluding the first 3 years of follow-up, and the results did not change significantly (data not shown). All *P*-values were two-tailed. $P \leq .05$ was considered significant in regression analyses.

Third, separate survival curves examined age-standardized (at age 70) years of overall survival and healthy survival by number of risk factors present using follow-up data through 2012. As in a previous study of midlife risk factors,[9] the objective was to estimate the probability of overall or healthy survival based on total number of risk factors using an easily understood risk score based on simply adding the number of risk factors. Cumulative effects of multiple risk factors were assessed using a survival risk score. The risk factors used in the survival risk score were selected from the variables significant in the stepwise logistic regression models of nonsurvival versus survival, whereas the risk factors used in the healthy survival risk score were selected from the variables significant in the stepwise logistic regression models of unhealthy versus healthy survival. Dummy variables were created to correspond to number of risk factors in the survival risk score (0–4 and ≥5) and the healthy survival risk score. Analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC).

RESULTS

Of the 1,292 men included in this study, 292 (23%) died before age 85 (nonsurvivors); 556 (43%) survived to 85 with disease or disability (unhealthy survivors); and 444 (34%) survived to 85 free of major chronic disease, physical disability, and cognitive impairment (healthy survivors). Of this study sample, 983 (76.1%) died before 95, 300 (23.2%) were unhealthy survivors, and only nine (<1%) were healthy survivors at 95.

Table 1 displays age-adjusted baseline late-life characteristics of the three survival phenotypes (healthy survivors, unhealthy survivors, nonsurvivors) for age 85. Sociodemographically, fewer healthy survivors were unmarried. Biologically, healthy survivors had faster 10-foot walk time, greater handgrip strength, and lower DBP than unhealthy survivors and nonsurvivors. Although all men were cognitively intact at baseline (CASI score ≥74), healthy survivors had higher CASI scores than the other groups. Fewer healthy survivors had depressive symptoms and fair or poor self-rated health. Healthy survivors also had lower fasting glucose, fasting insulin, fibrinogen, and WBC count. Healthy survivors smoked less or were nonsmokers, drank less alcohol, had more physical activity, and walked more.

Table 2 shows age-adjusted odds ratios from initial logistic regression analyses for factors that were significantly ($P < .05$) associated with nonsurvival versus survival or unhealthy versus healthy survival. Sociodemographically, unmarried men were less likely to survive, and of those who survived, less education was associated with greater odds of poor health. Biologically, U-shaped mortality relationships necessitated three-level variables for BMI, SBP, and hemoglobin. Lower BMI, SBP, and hemoglobin were associated with nonsurvival, whereas higher BMI and SBP were associated with unhealthy survival. Consistently high odds ratios for nonsurvival and unhealthy survival were associated with slow 10-foot walk times, high SBP and DBP, low-normal cognitive function on CASI examination, low ABI, fair or poor self-rated health, high fasting insulin, high fibrinogen, and high-normal WBC count (≥6,000 cells/mm^3). Poor outcomes were observed for current smoking and walking fewer blocks per day.

Table 3 shows variables significant in age-adjusted logistic regression analyses that were included in stepwise logistic regression analyses. Blood pressure and high fibrinogen were significantly associated with greater likelihood of nonsurvival and unhealthy survival. Several variables selected for the nonsurvival outcome analyses differed from the unhealthy survival outcome analyses. Low BMI was associated with nonsurvival versus survival, whereas high BMI was associated with unhealthy versus healthy survival. Unmarried status, current and past smoking, high alcohol intake and low physical activity index were associated with nonsurvival versus survival but were not significant for the unhealthy survival outcome. Low education, low-normal CASI, low ankle–brachial index and high WBC count were associated with unhealthy versus healthy survival but were not significant in the nonsurvival outcome model.

Figure 1 displays the years of further survival according to number of risk factors present, age-standardized at 70 years. There is clear separation in years of survival based on number of late-life risk factors present, with survival up to and beyond age 100 more common in men with no risk factors. In men with no risk factors at late-life baseline (standardized to age 70), 58% survived to age 90, compared with 32% of men with five or more risk factors. In men with no late-life risk factors, 27% survived to age 95, compared with 7% of men with five or more risk factors. In men with no late-life risk factors, 4% survived to age 100, compared with 0.1% of men with five or more risk factors.

Table 1. Baseline Late-Life Characteristics According to Survival (to Age 85) Phenotype Standardized to Age 76

Characteristic	Overall Sample, N = 1,292	Healthy Survival, n = 444 (34%)	Unhealthy Survival, n = 556 (43%)	Nonsurvival, n = 292 (23%)	*P*-Value
	Mean ± Standard Deviation				
Sociodemographic					
Age at baseline	75.7 ± 2.8	77.0 ± 3.1	75.2 ± 2.5	74.9 ± 2.4	<.001
Years of education	10.9 ± 3.1	11.3 ± 3.2	10.6 ± 3.0	10.6 ± 2.9	.004
Unmarried, %	16.4 ± 37.0	12.7 ± 35.1	14.9 ± 34.7	24.9 ± 42.2	<.001
Anthropometric and physiologic					
Body mass index, kg/m^2	23.7 ± 2.9	23.4 ± 2.8	24.0 ± 2.7	23.4 ± 3.1	.97
Waist–hip ratio	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	.02
Forced expiratory volume in 1 second, L	2.2 ± 0.5	2.2 ± 0.4	2.2 ± 0.4	2.1 ± 0.5	<.001
10-foot walk time, seconds	3.6 ± 1.0	3.5 ± 0.9	3.6 ± 1.0	3.8 ± 1.1	<.001
Grip strength, kg	32.4 ± 5.8	33.0 ± 5.2	32.5 ± 5.6	31.4 ± 5.9	<.001
Seated systolic blood pressure, mmHg	148.9 ± 21.7	147.0 ± 20.0	149.5 ± 21.4	150.5 ± 24.3	.04
Seated diastolic blood pressure mmHg	81.6 ± 10.4	80.7 ± 9.4	81.7 ± 10.2	82.8 ± 11.9	.01
Hypertension, %[a]	73.0 ± 44.4	72.2 ± 44.4	73.7 ± 44.2	72.8 ± 45.0	.88
Cognitive Abilities Screening Instrument score (range 0–100)	88.3 ± 5.9	90.0 ± 5.3	87.3 ± 6.0	87.4 ± 5.7	<.001
Ankle-brachial index	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	<.001
11-item Center for Epidemiologic Studies Depression Scale score[b]	3.4 ± 3.3	2.9 ± 3.0	3.5 ± 3.5	3.9 ± 3.4	<.001
Fair or poor self-rated health (%)	23.6 ± 42.5	18.5 ± 39.8	24.5 ± 42.6	30.1 ± 45.6	<.001
Hematological and biochemical					
Total cholesterol, mg/dL	194.8 ± 31.1	194.8 ± 32.0	195.6 ± 30.1	193.0 ± 31.6	.46
Triglycerides, mg/dL	148.8 ± 93.3	143.3 ± 80.1	152.6 ± 89.1	150.1 ± 116.7	.36
High-density lipoprotein cholesterol, mg/dL	51.7 ± 12.8	52.7 ± 12.7	50.6 ± 12.1	52.3 ± 13.9	.71
Fasting glucose, mg/dL	106.8 ± 15.7	104.8 ± 11.4	107.7 ± 16.9	108.0 ± 18.4	.01
Fasting insulin, μU/mL	13.9 ± 8.1	12.8 ± 7.0	14.2 ± 7.4	15.0 ± 10.3	<.001
Fibrinogen, mg/dL	299.3 ± 57.2	288.4 ± 50.3	301.8 ± 58.0	311.4 ± 62.3	<.001
White blood cell count, 1,000 cells/μL	6.1 ± 2.0	5.7 ± 2.6	6.1 ± 1.6	6.5 ± 1.8	<.001
Hemoglobin, g/dL	15.1 ± 1.2	15.1 ± 1.1	15.2 ± 1.1	15.1 ± 1.4	.42
Health habits					
Current smoker, %	7.3 ± 26.1	3.8 ± 19.3	7.0 ± 25.5	13.5 ± 34.2	<.001
Past smoker, %	54.9 ± 49.8	53.8 ± 50.0	53.1 ± 49.7	60.1 ± 49.0	.11
Never smoked, %	37.8 ± 48.5	42.4 ± 49.6	39.9 ± 48.7	26.4 ± 43.8	<.001
Smoking, pack-years	23.2 ± 30.7	17.6 ± 25.5	23.1 ± 31.0	32.6 ± 35.3	<.001
Alcohol consumption, ounces/month	19.0 ± 41.4	15.2 ± 26.3	17.4 ± 42.2	28.0 ± 55.3	<.001
Physical Activity Index[c]	31.5 ± 4.6	31.9 ± 4.7	31.6 ± 4.6	30.9 ± 4.4	.005
City blocks walked per day	16.2 ± 17.8	17.8 ± 17.6	16.1 ± 17.5	14.1 ± 18.5	.01

Aged 71–82 at baseline; men aged 83 and older at baseline were excluded.

[a]Blood pressure of 140/90 or higher or antihypertensive medication use.

[b]Scores ≥9 meet criteria for presence of depressive symptoms.

[c]Metabolic work performed in a typical 24-hour day measured at late-life baseline.

Figure 2 displays the years of healthy survival according to number of risk factors present, age-standardized at 70 years. There is clear separation in years of healthy survival based on number of late-life risk factors present. Healthy survival to age 85 was 13 times as common in men with no risk factors at late-life baseline (standardized to age 70, 26%) as in men with five or more risk factors (2%). In men with no risk factors at late-life baseline, 4% remained healthy at age 90, compared with 0.01% of men with five or more risk factors at late-life baseline. Only nine men met operationalized Rowe and Kahn[9] healthy survival criteria at age 95 (0.2%), and only one (0.002%) met healthy survival criteria at age 100.

DISCUSSION

Elderly adults, healthcare providers, and policy-makers share a common stake in optimizing odds of good health at older ages, so evidence-based information on potentially modifiable risk factors is needed. Although only 29.7% of individuals aged 65 to 74 report a disability, 49.6% of individuals aged 75 and older report one or more disabilities.[46]

Table 2. Age-Adjusted Likelihood of Selected Baseline Risk Factors According to Survival Status at Age 85

Baseline Risk Factor	Nonsurvival (n = 292) vs Survival (n = 1,000)	Unhealthy (n = 556) vs Healthy (n = 444) Survival
	Odds Ratio (95% Confidence Interval) *P*-Value	
Sociodemographic		
Education <12 years	1.03 (0.79–1.34) .84	1.69 (1.29–2.20) <.001
Unmarried in late life	2.11 (1.51–2.94) <.001	1.16 (0.80–1.68) .45
Anthropometric and physiologic		
Body mass index, kg/m^2 (reference 19.0–24.9)		
<19.0	2.79 (1.59–4.87) <.001	0.64 (0.31–1.31) .22
≥25.0	1.02 (0.76–1.36) .91	1.69 (1.26–2.28) <.001
Waist–hip ratio >0.99	1.20 (0.83–1.73) .33	1.49 (1.01–2.21) .04
Forced expiratory volume in 1 second <2.1 L	1.67 (1.26–2.21) <.001	1.12 (0.85–1.48) .43
Walk speed ≤0.75 m/s[a]	1.40 (1.07–1.83) .01	1.27 (0.97–1.66) .08
Grip strength <33 kg	1.29 (0.99–1.70) .06	1.08 (0.83–1.42) .56
Systolic blood pressure, mmHg (reference 120–160)		
<120	1.68 (1.01–2.78) .04	1.02 (0.59–1.78) .94
>160	1.38 (1.02–1.85) .04	1.57 (1.16–2.13) .004
Seated diastolic blood pressure >90 mmHg	1.50 (1.08–2.08) .01	1.86 (1.29–2.69) .001
Hypertension	0.98 (0.73–1.32) .91	1.13 (0.84–1.51) .43
Cognitive Abilities Screening Instrument score 74–81.9	1.39 (0.97–1.98) .07	2.75 (1.87–4.05) <.001
Ankle–brachial index <0.9	2.12 (1.30–3.45) .003	2.31 (1.26–4.25) .007
Center for Epidemiologic Studies Depression 11-item Scale score ≥9	1.50 (0.93–2.44) .10	1.54 (0.90–2.63) .12
Fair or poor self-rated health	1.54 (1.13–2.09) .007	1.41 (1.02–1.96) .04
Hematological and biochemical		
Triglycerides ≥150 mg/dL	0.90 (0.68–1.18) .44	1.16 (0.89–1.53) .27
High-density lipoprotein cholesterol <40 mg/dL	1.06 (0.75–1.52) .73	1.37 (0.95–1.96) .09
Glucose ≥126 mg/dL	1.30 (0.79–2.13) .30	2.49 (1.38–4.46) .002
Insulin ≥20 μU/mL	1.34 (0.95–1.88) .09	1.54 (1.06–2.25) .02
Fibrinogen >351 mg/dL	2.00 (1.43–2.80) <.001	2.09 (1.38–3.17) <.001
White blood cell count >6,000 cells/μL	1.69 (1.29–2.22) <.001	1.56 (1.18–2.05) .002
Hemoglobin, g/dL (reference 13–15)		
<13	2.25 (1.18–4.32) .01	0.85 (0.40–1.81) .68
>15	1.19 (0.89–1.58) .24	1.21 (0.92–1.59) .17
Health habits		
Smoker (reference never)		
Past	1.76 (1.29–2.39) <.001	1.03 (0.78–1.35) .83
Current	3.75 (2.29–6.12) <.001	1.99 (1.06–3.75) .03
Alcohol use, ounces/month (reference 1–15)		
Never	0.80 (0.57–1.12) .19	1.10 (0.81–1.50) .54
>15	1.54 (1.10–2.15) .01	1.04 (0.73–1.47) .83
Physical Activity Index ≤30.4	1.42 (1.08–1.86) .01	0.98 (0.75–1.28) .88
Blocks walked per day <12	1.45 (1.10–1.91) .008	1.25 (0.95–1.64) .11

[a]Walk speed determined on timed 10-foot (3-m) walk at usual pace.

Although interventional studies are required to find definitive evidence, this prospective, observational cohort study identified several potentially modifiable late-life factors associated with subsequent healthy survival, suggesting that, even in old age, it may not be too late to affect future health.

The findings that emerged may share some similarities but also have important differences from prior studies of midlife. Hypertension in mid- and late life was a risk factor for nonsurvival and unhealthy survival, but the adverse effects of high triglycerides and high glucose, although robust in midlife,[9] are not as apparent in late life. High BMI in midlife[9] was associated with nonsurvival and unhealthy survival, whereas in late life, low BMI was associated with nonsurvival and high BMI with unhealthy survival. Current smoking had an important role in midlife[9] and late life. Thus, the current study provides additional evidence for clinicians to continue to encourage smoking cessation, regardless of age. Although physical activity in midlife did not appear to be protective,[9] low physical activity in late life was associated with greater mortality. In midlife,[9] drinking more than three alcoholic drinks per day was associated with nonsurvival and unhealthy survival, whereas in late life, drinking more than one drink per day (15 ounces/month) was associated with nonsurvival, suggesting that alcohol limits should be lower in late life.

Inflammatory factors, including fibrinogen and WBC count, appear to have increasingly important roles in late life. High levels of each predicted greater mortality risk, possibly reflecting dysregulation of the immune system and the inflammatory state that accompanies aging.[47] Subclinical diseases in late life, including subclinical cardiovascular

Table 3. Stepwise Logistic Regression Model of Risk of Death (Nonsurvival) or Unhealthy Survival (Usual Survival) at Age 85

Risk Factor	Nonsurvival (n = 292) vs Survival (n = 1,000)[a]	Unhealthy (n = 556) vs Healthy (n = 444) Survival
	Odds Ratio (95% Confidence Interval) *P*-Value	
Sociodemographic		
Education <12 years	Not included	1.45 (1.08–1.95) .01
Unmarried at examination 4	1.51 (1.01–2.26) .04	Not included
Anthropometric and physiological		
Body mass index, kg/m^2		
<19 vs ≥19	2.25 (1.12–4.51) .02	Not included
≥25 vs <25	Not included	1.65 (1.20–2.27) .002
Waist–hip ratio >0.99	Not included	Not selected
Forced expiratory volume in 1 second <2.1	1.32 (0.97–1.80) .08	Not included
Grip strength <33 kg	Not selected	Not included
Walk speed ≤0.75 m/s	Not selected	Not selected
Systolic blood pressure, mmHg		
<120	Not selected	Not included
120–160	1.00 (reference)	Not included
>160	Not selected	Not included
>160 vs ≤160	Not included	1.49 (1.07–2.07) .02
Diastolic blood pressure >90 mmHg	1.53 (1.06–2.21) .02	Not selected
Cognitive Abilities Screening Instrument score 74–81.9	Not selected	2.48 (1.59–3.85) <.001
ABI <0.9	Not selected	2.12 (1.08–4.16) .03
11-item Center for Epidemiologic Studies Depression Scale ≥9	Not selected	Not included
Fair or poor self-rated health	Not selected	1.36 (0.95–1.93) .09
Hematological and biochemical		
High-density lipoprotein cholesterol <40 mg/dL	Not included	Not selected
Glucose ≥126 mg/dL	Not included	Not selected
Insulin ≥20 μU/mL	Not selected	Not selected
Fibrinogen >351 mg/dL	1.59 (1.09–2.32) .02	1.98 (1.26–3.10) .003
White blood cell count >6,000 cells/μL	1.30 (0.95–1.77) .10	1.39 (1.03–1.87) .03
Hemoglobin <13 vs ≥13 g/dL	Not selected	Not included
Health habits		
Past smoker vs never	1.46 (1.04–2.04) .03	Not included
Current smoker vs never	2.32 (1.30–4.15) .005	Not selected
Alcohol >15 vs ≤15 ounces/month	1.52 (1.10–2.09) .01	Not included
Physical Activity Index ≤30.4	1.41 (1.04–1.91) .02	Not included
Blocks walked per day <12	1.32 (0.98–1.79) .07	Not selected

[a]N = sample size for final logistic regression models (final model n = 1,138 for mortality model; n = 914 for healthy survival model because of missing data). Variables not selected by the nonsurvival versus survival model included grip strength, walk speed, systolic blood pressure, Cognitive Abilities Screening Instrument score, ankle–brachial index (ABI), depressive symptoms, fair or poor self-rated health, fasting insulin level, and hemoglobin level. Variables not selected by the unhealthy survival versus healthy survival model included waist-hip ratio, walk speed, diastolic blood pressure, current smoking, city blocks walked, high-density lipoprotein cholesterol, glucose level, and fasting insulin level. Age was forced into the models (data not shown). Not included indicates not selected for model because of nonsignificance ($P > .05$) on univariate analyses.

disease (lower ABI) and early cognitive impairment (lower CASI score), were associated with higher risk of unhealthy survival, supporting a role for continued risk factor modification and research on more effective means of secondary prevention. The Cardiovascular Health Study (CHS), which assessed white men and women aged 65 and older who maintained cognitive function and activity of daily living independence (rather than ability to walk half a mile) and avoided major chronic diseases, with an average 8 years of follow-up,[24] supported these findings. Factors associated with healthy survival included younger age, regular physical activity, and lower rates of subclinical cardiovascular disease and related risk factors (ABI, carotid intimal thickness, electrocardiographic abnormality, diabetes mellitus, smoking, and C-reactive protein).

Most importantly, a clear dose-response relationship was found between number of risk factors and age-standardized probability of overall and healthy survival, with a 13 times as great probability of living another 10 years in good health and up to a 40 times as great probability of living another 25 years, by avoiding particular late-life risk factors. Healthy survival to age 85 was 13 times as common in men with no risk factors at late-life baseline (standardized to age 70, 26%) as in men with five or more risk factors (2%), and overall survival to age 100 was 40 times as common in men with no late-life risk factors (4%) as in men who had five or more risk factors (0.1%).

The strengths of the current study are several. One, it is the only known study to operationalize the Rowe and Kahn paradigm of healthy aging from late life, reflecting age-associated diseases and disabilities with follow-up into the nonagenarian and centenarian years. Two, in addition to the 21-year follow-up, this study also provides a comprehensive examination of 26 risk factors, some not

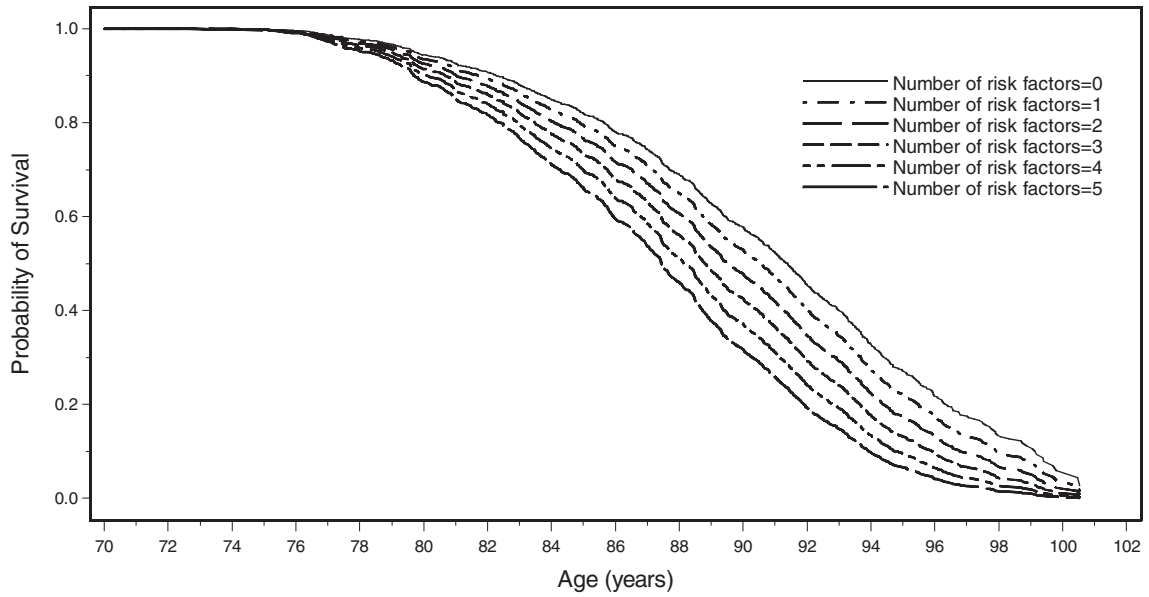

Figure 1. Age-standardized (at 70) probability of survival according to number of risk factors present at baseline. The probabilities of survival were estimated assuming that all six groups start at age 70 in the graph. All participants were Japanese-American men followed from late-life baseline (1991–1993) to 2012. Survival risk score indicates the number of risk factors (unmarried, body mass index <19 kg/m^2, forced expiratory volume in 1 second <2.1, diastolic blood pressure >90 mmHg, past smoker, current smoker, alcohol use >15 ounces/month, low physical activity index, fewer than 12 city blocks walked per day, fibrinogen >351 mg/dL, white blood cell count >6,000 cells/μL.

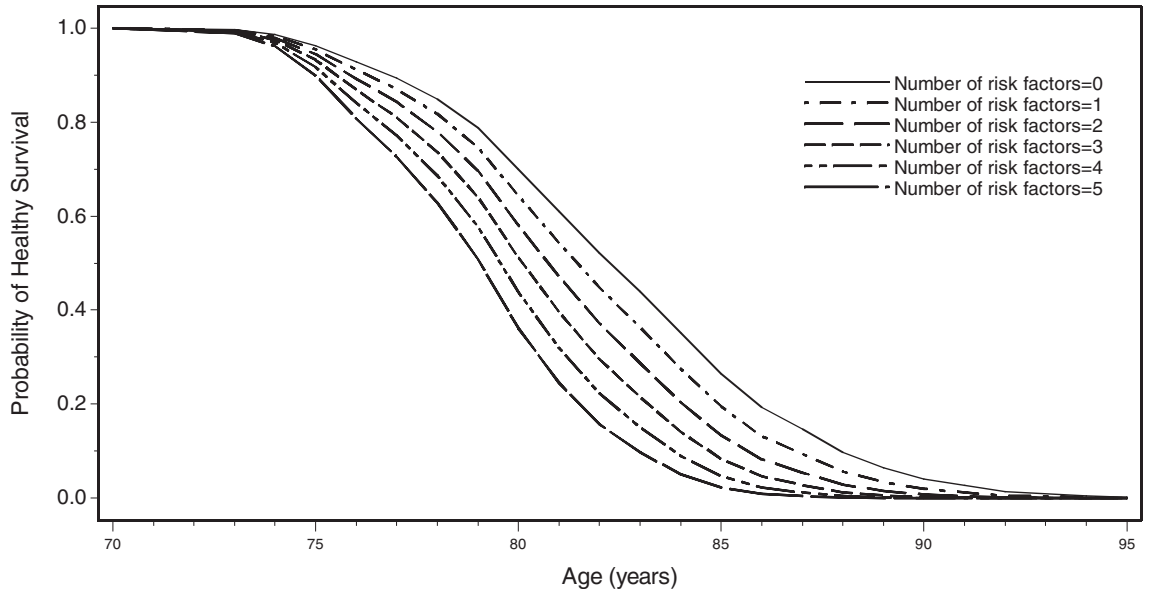

Figure 2. Age-standardized (at 70) probability of healthy survival (free of chronic disease, cognitive impairment, and disability) according to number of risk factors present at baseline. The probabilities of healthy survival were estimated assuming that all six groups start at age 70 in the graph. All participants were Japanese-American men followed from late-life baseline (1991–1993) to 2012. Of those alive at age 85, exceptional survival was defined as absence of six major chronic diseases and absence of physical and cognitive disability. Survival risk score indicates number of risk factors (education <12 years, body mass index ≥25 kg/m^2, systolic blood pressure >160, Cognitive Abilities Screening Instrument score 74–81.9, ankle–brachial index <0.9, poor self-rated health, fibrinogen >351 mg/dL, white blood cell count >6,000 cells/μL).

previously studied in late-life healthy aging. This longitudinal study design, in which men entered the study in midlife in 1965 and were all born between 1909 and 1919, minimized bias due to age at entry and birth cohort. Although it is not an interventional study, and thus causation cannot be established, several interesting findings emerged that may have implications for patient care, research, and public health.

There are several limitations to this study. The study population comprised Japanese-American men, and generalizability to other populations may be limited because of genetic, sociocultural, cohort, or other effects. It is likely

that the sample had greater longevity than other populations, because 50% of the cohort who were healthy at late-life baseline and 25% of the original 1965 cohort recruited in midlife (45–68) survived to age 90. These findings may also not be generalizable to women, who were not included in this cohort.

Several implications of these data for older adults are worth noting. Although survival and healthy survival appear markedly better for those who avoid late-life risk factors, the limits of aging "successfully" according to the Rowe and Kahn criteria were apparent. By the nonagenarian years, even for those who avoided all major risk factors, only 4% were still "healthy" at age 90, and only one person remained healthy until 100. Although the Rowe and Kahn criteria set a high bar for health, so do many aging baby boomers. Nevertheless, despite frequent stories in the media about extraordinarily healthy and active centenarians, the probability of most us becoming centenarians is low,[48] and the likelihood of being healthy according to common standards is even lower.[49] In the current study, even if a participant was a healthy septuagenarian and avoided major risk factors, the probability of healthy survival to 100 was only 0.002% (1/444).

On an encouraging note, for those who wish to maximize their longevity, perhaps in somewhat less-robust health, there may be much they can do. For healthy, active, septuagenarian men with no major risk factors, a substantial number in the current study lived into their 90s and 100s (58% to 90, 27% to 95, 4% to 100). Although the study did not assess women, they generally outnumber men 4:1 by the centenarian years,[50] so there is reason to believe that their odds of longevity are even better. Healthy septuagenarians who avoid common late-life risk factors would be well advised to plan ahead to mitigate financial, health, and long-term care challenges, which are likely to accompany such longevity.

CONCLUSION

Even in late life, risk and protective factors, some modifiable, were found to be associated with likelihood of overall and healthy survival. Future research is needed to determine whether modification of these risk factors in late life will enhance overall and healthy survival. This study suggests that there may be much that can be done to improve the probability of healthy aging and longevity—even at older ages.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the participants of the Honolulu Heart Program, Honolulu-Asia Aging Study, and Hawaii Lifespan Study for their 48 years of commitment to this research.

Portions of this study were presented at the annual meeting of the American Geriatrics Society, Washington, DC, May 2008, and at the Gerontological Society of America annual meeting, New Orleans, Louisiana, November 2010.

Conflict of Interest: Drs. Bell, Masaki, Curb, Willcox, Willcox, and Poon received grant funding from NIH.

This research was supported by the John A. Hartford Center of Excellence in Geriatrics, Department of Geriatric Medicine, John A. Burns School of Medicine, University of Hawaii; the Kuakini Medical Center; and the National Institutes of Health (NIH) (Contract N01-AG-4–2149, Grants 5 U01 AG019349–05, 5R01AG027060–06 (Kuakini Hawaii Lifespan Study), 5R01AG038707–02 (Kuakini Hawaii Healthspan Study), and 1R13AG041931 from the National Institute on Aging and Contract N01-HC-05102 from the National Heart, Lung, and Blood Institute).

Author Contributions: Study concept and design, acquisition of data: B.J. Willcox, Chen, Masaki, He, Curb, Grove, Donlon. Analysis and interpretation of data: Bell, Chen, Masaki, Yee, He, Grove, B.J. Willcox, Poon, C. Willcox. Preparation of manuscript: Bell, Masaki, Chen, He, B.J. Willcox. Critical revision of manuscript: Bell, Chen, Masaki, Yee, He, Grove, Donlon, Curb, B.J. Willcox, Poon, C. Willcox.

Sponsor's Role: The investigators retained full independence in the conduct of this research, and the funding organizations had no role in design or conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

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