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Original Research Article

Impact of 8 lifestyle factors on mortality and life expectancy among United States veterans: The Million Veteran Program

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A B S T R A C T

Background: Lifestyle medicine has been proposed as a way to address the root causes of chronic disease and their associated health care costs.
Objective: This study aimed to estimate mortality risk and longevity associated with individual lifestyle factors and comprehensive lifestyle therapy.
Methods: Age- and sex-specific mortality rates were calculated on the basis of 719,147 veterans aged 40–99 y enrolled in the Veteran Affairs Million Veteran Program (2011–2019). Hazard ratios and estimated increase in life expectancy were examined among a subgroup of 276,132 veterans with complete data on 8 lifestyle factors at baseline. The 8 lifestyle factors included never smoking, physical activity, no excessive alcohol consumption, restorative sleep, nutrition, stress management, social connections, and no opioid use disorder.
Results: On the basis of 1.12 million person-years of follow-up, 34,247 deaths were recorded. Among veterans who adopted 1, 2, 3, 4, 5, 6, 7, and 8 lifestyle factors, the adjusted hazard ratios for mortality were 0.74 (0.60–0.90), 0.60 (95% CI: 0.49, 0.73), 0.50 (95% CI: 0.41, 0.61), 0.43 (95% CI: 0.35, 0.52), 0.35 (95% CI: 0.29, 0.43), 0.27 (95% CI: 0.22, 0.33), 0.21 (95% CI: 0.17, 0.26), and 0.13 (95% CI: 0.10, 0.16), respectively, as compared with veterans with no adopted lifestyle factors. The estimated life expectancy at age 40 y was 23.0, 26.5, 28.8, 30.8, 32.7, 35.1, 38.3, 41.3, and 47.0 y among males and 27.0, 28.8, 33.1, 38.0, 39.2, 41.4, 43.8, 46.3, and 47.5 y for females who adopted 0, 1, 2, 3, 4, 5, 6, 7, and 8 lifestyle factors, respectively. The difference in life expectancy at age 40 y was 24.0 y for male veterans and 20.5 y for female veterans when comparing adoption of 8–9 lifestyle factors.
Conclusions: A combination of 8 lifestyle factors is associated with a significantly lower risk of premature mortality and an estimated prolonged life expectancy.

Keywords: lifestyle, preventive medicine, life expectancy, mortality, longevity

Introduction

Noncommunicable chronic diseases are associated with >80% of all health care dollars and are the leading cause of morbidity and mortality in the United States [1]. Estimated years of life lost because of the chronic diseases range from 7.5 to 20 y, depending on calculation methods used and characteristics of the study population [2–4]. These chronic conditions are common and costly. More importantly, they are also largely preventable. Previous studies estimate that ~90% of diabetes, 80% of coronary artery disease, 70% of cardiovascular mortality,

Abbreviations: CI, confidence interval; CMS, Centers for Medicaid & Medicare Services; CVD, cardiovascular disease; EHRs, electronic health records; GAD-2, Generalized Anxiety Disorder 2; HR, hazard ratio; hPDI, healthful plant-based diet index; METs, metabolic equivalents; MVP, Million Veteran Program; NDI, National Death Index; PAF, population-attributable fraction; PHQ-2, Patient Health Questionnaire 2; VA, Veterans Affairs; VHA, Veterans Health Administration.

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and 50% of cancer mortality can be attributed to nonadherence to living a healthy lifestyle [5–8]. Thus, promoting a healthier lifestyle has been proposed as a method for primary prevention of chronic disease and mortality as well as healthy aging and longevity.

Beyond traditional lifestyle factors, such as healthy eating, regular physical activity, and not smoking, recent studies highlight the importance of stress management, avoidance of risky substances, and having social connections for the prevention of chronic diseases [9–13]. Lack of restorative sleep and depression has also been associated with increased incidence of multiple chronic diseases, including cardiovascular disease (CVD), cancer, diabetes, and total mortality [9–11]. In addition, the effects of loneliness and social isolation have been studied in association with well-established risk factors for mortality in a recent meta-analysis [12]. The concept of lifestyle medicine uses evidence-based lifestyle interventions such as adopting a whole-food, plant-predominant eating pattern, regular physical activity, restorative sleep, stress management, avoidance of risky substances, and positive social connections as a low-risk approach for the treatment and potential reversal of chronic diseases [13]. As lifestyle medicine treats the underlying causes of disease rather than its symptoms, it provides a potential avenue for altering the course of spiraling health care costs incurred in part as a result of prescription medications and surgical procedures.

Although research on individual low-risk lifestyle factors have been associated with a lower risk of chronic diseases and mortality, to date, to our knowledge, no study has evaluated all factors combined in relation to life expectancy. Such research requires the collection of comprehensive information on lifestyle factors along with a sufficient follow-up period to observe cases of mortality. The Department of Veterans Affairs (VA) Million Veteran Program (MVP) provides a unique opportunity to estimate how a combination of all proposed modifiable low-risk lifestyle factors affect the risk of mortality and life expectancy among United States veterans. We hypothesize that both individual and combined low-risk lifestyle factors are associated with a lower risk of total mortality. In addition, we will translate this lower risk of mortality into an estimation of additional life expectancy attributable to adopting comprehensive lifestyle features.

Methods

Study population

MVP is a nationally representative, prospective cohort study of veterans designed to examine genetic and nongenetic determinants of chronic diseases. MVP combines data from self-reported surveys (the MVP Baseline and Lifestyle Surveys), electronic health records (EHRs), and biospecimen samples collected at baseline. Details of the research design can be found elsewhere [14,15]. Briefly, active users of the Veterans Health Administration (VHA) are eligible for MVP enrollment. Recruitment and enrollment began in 2011 primarily through mail invitations with the goal of enrolling ≥1 million veterans. All participants signed informed consent and the VA Central Institutional Review Board approved the MVP protocol. The MVP Baseline Survey is included as part of initial mailed invitational materials; therefore, participants may complete the MVP Baseline Survey before or after enrollment in MVP. Once a Veteran enrolls in MVP, the MVP Lifestyle Survey is available for completion and is mailed typically within 2–4 wk after enrollment.

As of 2020, MVP had 819,417 participants. Inclusion criteria for this study consisted of MVP participants who responded to both the MVP Baseline and Lifestyle Surveys. Those under the age of 40 y old or missing data on lifestyle factors, (biological) sex, or death records were excluded from this study. In detail, of the 819,417 MVP enrollees, 379,852 participants completed both the MVP Baseline and MVP Lifestyle Surveys. Information collected from these surveys include data on age, sex, race, education, body weight, height, and low-risk lifestyle factors at baseline. Additional information on health conditions, comorbidities, and medication use were obtained through the VHA EHR. We defined baseline in this study as the time a participant completed the MVP Lifestyle Survey, and we defined the end of study follow-up as 31 December 2019 or death, whichever came first.

Of the 379,852 participants with completed MVP Lifestyle Surveys, we excluded responders after 2019 (n = 30,541), participants with missing records of sex (n = 8), participants aged <40 y (n = 12,685), and those with implausible death records (n = 671). We also excluded MVP participants with missing data on any of the low-risk lifestyle factors (n = 59,815), which yielded a final population of 276,132 participants for this research study (Supplemental Figure 1).

Assessment of the low-risk lifestyle factors

The concept of preventive lifestyle medicine proposes 6 clusters of low-risk lifestyle factors [13,16]: nutrition, physical activity, stress management, restorative sleep, avoidance of risky substances, and social connections. Within MVP, there is comprehensive information on 3 risky substances, including smoking, opioid use, and alcohol use such that avoidance of each risky substance was evaluated as an independent low-risk lifestyle factor in this study. In total, we included 8 low-risk lifestyle factors: adhering to a whole-food, plant-predominant eating pattern, having regular consistent physical activity, managing negative stress, not smoking, having restorative sleep, no excessive alcohol consumption, no opioid use disorder, and having positive social connections. The assessment of each low-risk lifestyle factor cluster is described in detail within "eMethods" in the online-only Data Supplement. In brief, healthy eating habits, also called "food medicine," suggest following a whole-food, plant-predominant eating pattern. In MVP, this was assessed using the healthful plant-based diet index (hPDI) [17–19]. Physical activity was assessed using the metabolic equivalent (METs) value that was assigned on the basis of the intensity of physical activities and the frequency of leisure time activities [20]. Stress management was assessed by the 4-item Patient Health Questionnaire for anxiety and depression [21], which included 2 questions for Generalized Anxiety Disorder 2 (GAD-2) and 2 questions for Patient Health Questionnaire 2 score (PHQ-2) [21]. Anxiety and depression were used as proxies to estimate stress management within this study. Restorative sleep was estimated by hours of usual sleep each day [22]. Social connections were estimated using the Medical Outcomes Survey for Social Support [23], whereas smoking status was determined using an algorithm developed for VHA EHRs [24]. Excessive alcohol consumption was assessed by self-reported greatest number of drinks of alcohol in a typical month [25] and opioid use disorder was identified using VHA EHR [26,27].

The number of low-risk lifestyle factors was developed using 8 subscores with each scored as 1 (healthy) or 0 (unhealthy). The number of low-risk lifestyle factors ranged from 0 to 8.

Below is the scoring method of each subscore:

- Nutrition: "1" = upper 40% of hPDI; "0" = lower 60% of hPDI [17,18]
- Physical activity: "1" = leisure time activity ≥7.5 MET-h/wk; "0" leisure time activity <7.5 MET-h/week [20]

- Managing stress: "1" = GAD-2 <3 and PHQ-2 <3; "0" = GAD-2 ≥3 or PHQ-2 ≥3 [21]
- Restorative sleep: "1" = sleep duration of 7–9 h per d, otherwise "0" [22]
- Social connections: "1" = positive social interaction score ≥50; "0" = positive social interaction score <50 [23]
- Avoidance of risky substances, particularly smoking: "1" = never smokers; "0" = ever smokers [24]
- Avoidance of risky substances, particularly excessive alcohol consumption: "1" = never drinking or typically no more than 4 drinks in a day; "0" = 5 or more drinks in a day in a typical month (4 for females) [25]
- Avoidance of risky substances, particularly opioid use disorder: "1" = no opioid use disorder; "0" = opioid use disorder [26,27]

Outcome ascertainment

The outcome of this research was all-cause mortality and life expectancy. Deaths were identified through combined information from the VA Corporate Data Warehouse, Centers for Medicaid & Medicare Services (CMS) database, and National Death Index (NDI) database [28, 29]. The life expectancy of MVP participants was estimated by multilifetable methods using the sex- and age-specific mortality rates [30–32].

Assessment of covariates

Information on covariates, including age, sex, BMI, race, ethnicity, socioeconomic status, current marriage status, and education level, was collected through self-reported surveys at baseline. Race on the MVP Baseline Survey included "White," "Black/African American," "American Indian/Alaska Native," "Pacific Islander," "Chinese," "Japanese," "Asian Indian," "Other Asian," "Filipino," and "other." Participants were asked "Are you Spanish, Hispanic, or Latino?" with following choices: "No, not Spanish, Hispanic, Latino," " Yes, Mexican, Mexican American, Chicano," "Yes, Puerto Rican," "Yes, Cuban," and "Yes, other Spanish, Hispanic, Latino." For covariate adjustment, we classified participants by a combination of their responses to race and ethnicity questions as either non-Hispanic White, non-Hispanic Black, Hispanic, or other.

Statistical analysis

The mortality rates (per 1000 person-years) were calculated using a Poisson regression model, and the rates were adjusted for sex and age. The Cox proportional hazards model was used to estimate hazard ratios (HRs) with their 95% confidence intervals (CIs) of all-cause mortality according to the number of low-risk lifestyle factors and individual low-risk factors. The multivariable model was adjusted for age, sex, race/ethnicity, education level, income, marriage status, and BMI. In addition, we conducted stratified analyses to test the robustness of our findings by examining the association between the number of low-risk lifestyle factors and mortality in subgroups defined by age, sex, race/ethnicity, education level, income level, marriage status, BMI, and self-reported diagnosis of diabetes, CVD, or cancer at baseline.

We calculated the hypothetical population-attributable fraction (PAF), an estimation of the percentage of mortality in the study population that theoretically would not have occurred during the follow-up period if all veterans had been in the low-risk category, assuming that the observed associations represented causal effects. For these analyses, we used a single binary categorical variable (with all 8 low-risk factors) and compared participants in the low-risk category with the rest of the population (without all 8 low-risk factors or with any high-risk factor) to calculate the HRs. We combined these HRs with the prevalence of the low-risk category to estimate the population-attributable risk.

In a sensitivity analysis, we further adjusted for history of hypertension, hypercholesterolemia, diabetes, cancer, and CVD at baseline. To test the robustness of our findings and limit the potential for reverse causality, in a second sensitivity analysis, we examined the association between the number of low-risk lifestyle factors and the mortality among the relative healthy population after further excluding participants with diabetes, heart disease, stroke, and cancer at baseline. In the third sensitivity analysis, we quantified the association between the number of low-risk lifestyle factors and the mortality after excluding deaths or participants with <1-y follow-up. In the fourth sensitivity analysis, we kept all missing values in any of the low-risk lifestyle factors at baseline and imputed missing values by applying a multiple imputation approach. All data analyses were performed using SAS software version 9.4 (SAS Institute) at a 2-tailed α value of 0.05.

Because the basic life expectancies at different ages are distinct for males and females, all estimations of life expectancy were calculated separately for male veterans and female veterans. We applied a multilifetable method to estimate the life expectancy of participants with different numbers of low-risk lifestyle factors (henceforth "exposure groups"), which included the following 3 pieces of information [2,30–32]:

1. All-cause mortality rates by sex and age;
2. Prevalence of exposure groups by sex and age;
3. Sex-specific HRs for all-cause in each exposure group compared with the reference exposure group.

A detailed description of life expectancy estimation is presented in "eMethods" in the online-only Data Supplement.

Results

In total, the study population included 276,132 participants with 256,816 (93%) male veterans and 19,316 (7%) female veterans. At baseline, participants with a higher number of low-risk lifestyle factors were more likely to be currently married, have a higher level of education and family income, less likely to be obese, and less likely to be Black (Table 1).

With a total of 1.12 million person-years of follow-up, 34,247 deaths were recorded (male veterans 32,350; female veterans 897). The age- and sex-adjusted mortality rate of veterans with zero low-risk lifestyle factors was 70.2 (95% CI: 57.9, 85.2) per 1000 person-years. The trend in the mortality risk was continuously decreasing and graded with the increasing number of adopted low-risk lifestyle factors. Among veterans with 8 low-risk lifestyle factors, the age- and sex-adjusted mortality rate was 6.8 (95% CI: 5.8, 8.0) per 1000 person-years (Table 2).

When examined individually, each of the 8 lifestyle factors was significantly associated with the risk of total mortality; after adjustment of age, sex, race/ethnicity, education, income, marriage status, and BMI, the multiadjusted HR of mortality was 0.95 (95% CI: 0.93, 0.97) for those who with positive social connections, 0.82 (95% CI: 0.80, 0.84) for those having restorative sleep, 0.79 (95% CI: 0.77, 0.80) for those adopting a whole-food, predominantly plant-based eating pattern, 0.81 (95% CI: 0.79, 0.83) for those with no excessive alcohol consumption, 0.71 (95% CI: 0.69, 0.72) for those able to manage stress without anxiety/depression, 0.70 (95% CI: 0.68, 0.71) for never smokers, 0.62 (95% CI: 0.58, 0.66) for those with no opioid use disorder, and 0.54 (95% CI: 0.53, 0.56) for those with physical activity of ≥7.5 METs-h/wk, compared with their counterparts without the low-

TABLE 1
Baseline characteristics according to number of low-risk lifestyle factors

	Number of low-risk lifestyle factors									All
	0	1	2	3	4	5	6	7	8	
N	559	5301	17,892	39,405	64,412	73,306	50,673	20,501	4083	276,132
Percentage	0.2	2.0	6.5	14.3	23.3	26.5	18.4	7.4	1.5	
Age (y) (mean)	58.0	60.1	62.0	64.3	66.4	68.0	68.4	67.4	66.1	66.5
Male veterans (%)	94.8	93.8	92.8	92.9	93.7	93.5	92.8	90.5	87.5	93.0
BMI (≥30 kg/m^2) (%)	42.0	43.8	46.4	45.4	43.2	39.5	34.5	28.0	19.5	39.7
Non-Hispanic White (%)	65.8	71.4	72.7	75.7	80.4	83.3	85.5	86.3	87.0	81.3
Non-Hispanic Black (%)	22.5	17.6	16.6	14.2	11.0	8.9	7.2	6.1	4.7	10.2
Hispanic (%)	8.4	7.7	7.6	7.1	5.9	5.5	5.2	5.2	5.8	5.9
Currently married (%)	18.6	30.0	37.4	43.9	51.9	59.7	64.7	68.0	70.6	55.2
Educational level (%)										
High school	26.7	28.4	27.1	26.3	24.3	20.9	15.5	10.0	5.5	21.0
Some college	34.3	32.0	31.1	29.9	28.7	26.8	23.6	19.5	14.5	26.8
College or above	21.3	23.2	27.1	30.2	35.2	42.5	52.3	63.2	74.0	41.4
Missing	17.7	16.4	14.7	13.6	11.8	9.8	8.6	7.3	6.0	10.8
Family annual income (%)										
<30k	54.7	42.8	39.2	34.4	29.3	24.1	19.0	14.7	12.6	26.4
30k–60k	17.5	24.3	26.5	27.9	29.8	30.6	29.5	26.6	21.5	29.0
>60k	5.7	10.7	13.6	17.2	21.5	26.4	33.2	41.0	48.2	25.4
Missing	22.0	22.1	20.7	20.4	19.4	18.8	18.3	17.7	17.7	19.2
Low-risk lifestyle factors (%)										
Upper 40% of hPDI	0.0	3.8	13.9	21.0	28.2	40.1	60.9	80.2	100.0	39.8
Activity ≥7.5 METs-h/wk	0.0	1.2	3.8	6.9	11.1	19.1	37.0	68.7	100.0	22.3
Never smoking	0.0	0.8	5.5	10.7	16.1	25.9	45.2	69.2	100.0	27.4
No frequent binge drinking	0.0	6.5	24.3	39.1	53.7	74.2	87.2	95.3	100.0	64.1
Sleep 7–9 h/d	0.0	4.0	15.4	30.9	51.9	71.2	83.9	92.3	100.0	60.2
No opioid use disorder	0.0	71.8	88.0	95.2	98.1	99.3	99.8	99.9	100.0	97.1
Neither anxiety nor depression	0.0	4.5	25.1	53.8	77.9	90.8	96.6	98.8	100.0	78.2
Positive social interaction score ≥50	0.0	7.3	24.1	42.5	63.1	79.2	89.3	95.5	100.0	68.5
Baseline prevalence (%)										
Diabetes	24.8	27.0	29.0	29.4	28.3	26.7	24.0	18.6	13.0	26.2
Cardiovascular diseases	22.0	24.5	25.9	26.0	25.6	24.2	21.9	18.1	13.1	23.8
Cancers	20.3	21.4	24.4	26.8	30.2	32.3	33.4	33.4	33.1	30.6

Abbreviations: hPDI, healthy Plant-diet Index; MET, metabolic equivalent.

risk lifestyle factor, respectively (Table 2). When further considering the population proportion, the PAF of not following all 8 low-risk lifestyle factors was 64.4% (58.4%–69.5%), with top 3 PAFs being physical inactivity, ever smoking, and an eating pattern not consistent with whole-foods or primarily plant-based (Table 2).

Adopting a combination of the individual low-risk lifestyle factors showed an increasing protective effect on the mortality risk: per low-risk lifestyle factor increment was associated 19% less risk of mortality (HR = 0.814, 95% CI: 0.808, 0.821, *P* trend < 0.001), which was 0.815 (95% CI: 0.809, 0.822) in male veterans and 0.79 (95% CI: 0.75, 0.83) in female veterans. Compared with adopting zero low-risk lifestyle factors, a combination of 8 individual low-risk lifestyle factors was associated with an HR of 0.13 (95% CI: 0.10–0.16) for all-cause mortality (Table 2), which was consistent in male veterans (HR= 0.125, 95% CI: 0.097, 0.161) and female veterans (HR = 0.14, 95% CI: 0.04, 0.50) (Figure 1A).

Estimated life expectancy at age 40 y for veterans who adopted zero low-risk lifestyle factors was 23.0 y for male veterans (e.g., on average, living to 63.0) and 27.0 y for female veterans (e.g., on average, living to 67.0). In contrast, for those who adopted all 8 low-risk lifestyle factors, we projected a life expectancy at age 40 y of 47.0 y for male veterans (on average living to 87.0) and 47.5 y for female veterans (on average living to 87.5). Equivalently, male veterans who adopted 8 low-risk lifestyle factors could gain 24.0 y of life expectancy at age 40 y, on average, and female veterans could gain 20.5 y of life expectancy at age 40 y compared with those adopting zero low-risk lifestyle factors at age 40 (Figure 1B).

Although estimated gain in life expectancy was attenuated with aging, at the age of 50, male veterans could still gain 21.3 y of additional life expectancy and female veterans could gain 18.9 y by adopting all 8 lifestyle factors rather than none. Similarly, at age 60, adopting 8 lifestyle factors compared with none was associated with 18.0 additional years of life for female veterans and 16.5 y of life expectancy for male veterans (Figure 1C).

To test the robustness of our estimations, we conducted several sensitivity analyses. Multivariate-adjusted HR (age, sex, race/ethnicity, education, income, marriage status, and BMI) associated with per increment of individual low-risk lifestyle factors was 0.826 (95% CI: 0.819, 0.832) after further adjustment of chronic conditions, 0.82 (95% CI: 0.81, 0.83) in the 1-y lag analysis, 0.80 (95% CI: 0.79, 0.81) after excluding baseline prevalent cancers, diabetes, and CVD, and 0.834 (95% CI: 0.832, 0.835) after applying multiple imputations (Table 3).

Significant associations between adherence to low-risk lifestyle factors and lower risk of mortality were found in all subgroups with a relatively stronger protective effect among younger, White veterans without baseline obesity, diabetes, or CVDs compared with their counterparts, respectively (all *P*s for interaction < 0.001) (Figure 2). Because social determinants of health are often highly correlated, stratification factors were combined and we observed a similar

TABLE 2
Hazard ratio of mortality according to number of low-risk lifestyle factors ($N = 260,351$)

	No. of veterans	No. of deaths	Mortality rate (/1000 PYs, 95% CI)	Age- and sex-adjusted HRs (95% CI)	Multiadjusted HRs (95% CI)	PAF (%, 95% CI)
Number of low-risk lifestyle factors						
0	559	103	70.2 (57.9, 85.2)	1.0 (ref.)	1.0 (ref.)	
1	5301	794	48.6 (45.4, 52.1)	0.70 (0.57, 0.86)	0.74 (0.60, 0.90)	
2	17,892	2542	38.2 (36.8, 39.8)	0.55 (0.45, 0.66)	0.60 (0.49, 0.73)	
3	39,405	5515	31.2 (30.3, 32.0)	0.44 (0.37, 0.54)	0.50 (0.41, 0.61)	
4	64,412	8979	25.7 (25.2, 26.3)	0.36 (0.30, 0.44)	0.43 (0.35, 0.52)	
5	73,306	9437	20.6 (20.1, 21.0)	0.29 (0.24, 0.35)	0.35 (0.29, 0.43)	
6	50,673	5208	15.5 (15.0, 15.9)	0.22 (0.18, 0.26)	0.27 (0.22, 0.33)	
7	20,501	1510	11.7 (11.1, 12.3)	0.16 (0.13, 0.20)	0.21 (0.17, 0.26)	
8	4083	159	6.8 (5.8, 8.0)	0.09 (0.07, 0.12)	0.13 (0.10, 0.16)	64.4 (58.4, 69.5)
P for trend				<0.0001	<0.0001	
HR per score (1 unit)				0.785 (0.779, 0.791)	0.814 (0.808, 0.821)	
Percentage of individual low-risk factors and HRs						
Upper 40% of hPDI (40%)				0.77 (0.75, 0.79)	0.79 (0.77, 0.80)	13.8 (13.4, 14.5)
Physical active ≥7.5 METs-h/wk (22%)				0.50 (0.49, 0.52)	0.54 (0.53, 0.56)	39.9 (38.9, 41.8)
Never smoking (27%)				0.65 (0.64, 0.67)	0.70 (0.68, 0.71)	23.8 (23.4, 24.7)
No frequent binge drinking (64%)				0.75 (0.74, 0.77)	0.81 (0.79, 0.83)	7.8 (7.3, 8.7)
Sleep 7–9 h/d (60%)				0.78 (0.76, 0.79)	0.82 (0.80, 0.84)	8.1 (7.5, 9.1)
No opioid use disorder (97%)				0.53 (0.50, 0.57)	0.62 (0.58, 0.66)	1.8 (1.7, 2.1)
Neither anxiety nor depression (78%)				0.66 (0.64, 0.68)	0.71 (0.69, 0.72)	8.2 (8.0, 8.6)
Positive social interaction score >50 (68%)				0.85 (0.83, 0.87)	0.95 (0.93, 0.97)	1.7 (1.3, 2.3)

The mortality rates (per 1000 person-years) were calculated using a Poisson regression model and are sex- and age-adjusted rates. The HRs were calculated using a Cox proportional hazards regression model and adjusted by age, sex, BMI (kg/m^2: <25, 25–29.9, ≥30), race and ethnicity (non-Hispanic White, non-Hispanic Black/Africa American, Hispanic, others), marriage status (currently married, not married, or missing), educational level (high school or less, some years of college, college or above, or missing), and family income levels (<30k, 30–60k, >60k, or missing).
Abbreviations: CI, confident interval; hPDI, healthy Plant-diet Index; HR, hazard ratio (of mortality); MET, metabolic equivalent; PAF, population-attributable fraction (of not following the low-risk factors); PY, person-year.

protective pattern for the mortality risk when stratified by a number of social determinants of health (Supplemental Figure 2).

Discussion

On the basis of data of 34,247 deaths accrued during >1 million person-years follow-up of veterans, we found that the reduced risk for mortality was associated with 8 individual low-risk lifestyle factors. We estimated that comprehensive adherence to all 8 low-risk lifestyle factors could prolong life expectancy at age 40 y by 24.0 y for male veterans and 20.5 y for female veterans, compared with those who adopted zero low-risk lifestyle factors.

Our estimations of individual lifestyle factors and mortality risk were consistent with previous findings. An average of 5 y of life expectancy lost was estimated among veteran smokers compared with veterans who never smoked [33]. This was consistent with the findings among the general population [34]. Mortality risk and related loss of life expectancy associated with substance-use disorders and mental disorders were equal or stronger in comparison with heavy smoking [35]. Traditionally, well-established lifestyle factors associated with increased life expectancy include not smoking, being physical active, eating healthy, with or without moderate alcohol drinking, and maintaining a normal BMI, which, in combination, was associated with a range of 3.4–17.9 y of additional life expectancy, as reported in Japan [36], the United Kingdom [37,38], Canada [39], Denmark [40], Norway [40], Germany [40,41], United State [2], the Netherland [42], and Singapore [43]. Current analysis of 8 low-risk lifestyle factors together increased the estimation of gained life expectancy to >20 y. Compared with previous estimations of lifestyle and life expectancy, current analysis among veterans further included having restorative sleep, managing stress, having social connections, and not having opioid use disorder, as well as no excessive alcohol consumption. These lifestyle factors were included in the evidence-based guidelines on lifestyle medicine recommended by 40 subject matter experts at the Lifestyle Medicine Research Summit [15,16]. Those newly included factors were strongly associated with increased mortality, especially opioid use disorder. This highlights the importance of controlling such unhealthy behaviors at the individual level to potentially improve veteran lifespan. Although, from a population perspective, only a small number of veterans in MVP reported having opioid use disorder, the major PAFs were still traditional lifestyles factors such as physical activity, nutrition, and not smoking.

A unique merit of our work is the adoption of the Concept of Preventive Medicine in estimation of life expectancy for the first time. This was possible because of the large MVP cohort with comprehensive data collection among veterans from diverse socioeconomic and racial/ethnic backgrounds [14,15]. Another strength was the consistent findings of different sensitivity analysis that supported the robustness of our estimations. Several limitations of the present research warrant consideration. First, our estimation is based on observational data. Although we have carefully controlled for confounding factors, our results do not imply causal effects. Future work is warranted to replicate our findings and to confirm the causal relationship. Second, our cohort included only veterans. Despite having a study population with diversity of race and socioeconomic status, our specific findings might not be generalizable to the general population. Our predominantly male population is an additional study limitation because it restricted the statistical power to conduct sensitivity analysis of age-specific HRs among females. However, when considering the large sample size, we still included >18,000 females which is a sample size comparable to study populations of lifestyle and life expectancy studies in other countries [37,40–42]. Lastly, the overall population and mortality cases

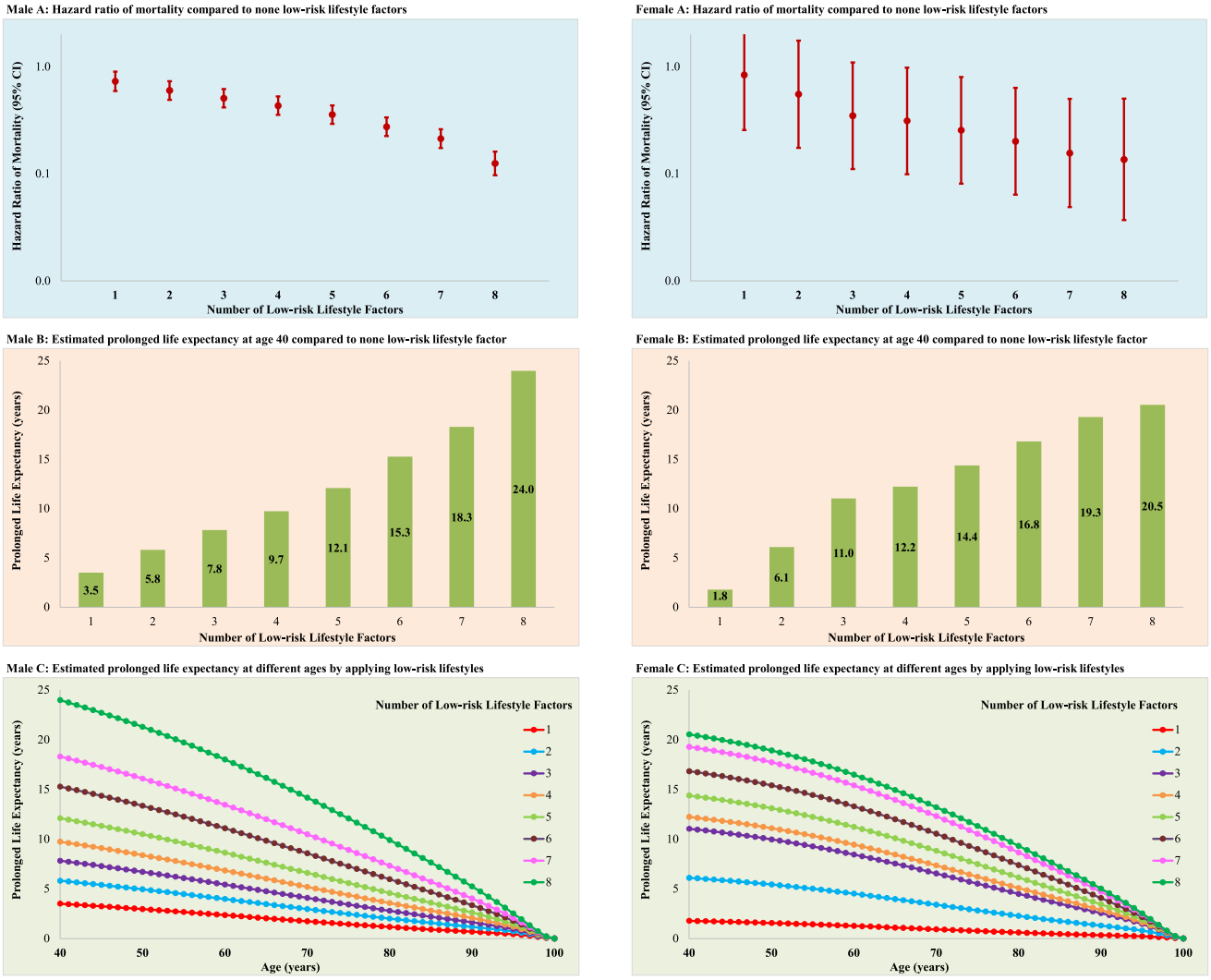

FIGURE 1. Life expectancy at age 40 y according to number of low-risk lifestyle factors.

TABLE 3
Sensitivity analyses of association between number of low-risk lifestyle factors and risk of mortality[1]

	Sensitivity 1	Sensitivity 2	Sensitivity 3	Sensitivity 4
	Further adjusted chronic conditions	Excluded participants with <1-y follow-up	Excluded cancers, diabetes, and CVD at baseline	Imputation for missing lifestyle factors at baseline[2]
No. of veterans	276,132	259,949	154,036	335,947
No. of deaths	34,247	28,982	14,175	45,045
Number of low-risk lifestyle factors				
0	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
1	0.74 (0.60, 0.90)	0.73 (0.58, 0.91)	0.79 (0.60, 1.02)	0.70 (0.68, 0.72)
2	0.60 (0.50, 0.74)	0.58 (0.47, 0.72)	0.58 (0.45, 0.75)	0.57 (0.55, 0.59)
3	0.51 (0.42, 0.62)	0.49 (0.39, 0.60)	0.47 (0.36, 0.60)	0.49 (0.47, 0.50)
4	0.45 (0.37, 0.54)	0.42 (0.34, 0.52)	0.40 (0.31, 0.51)	0.43 (0.41, 0.44)
5	0.37 (0.31, 0.45)	0.35 (0.28, 0.44)	0.33 (0.25, 0.42)	0.36 (0.35, 0.37)
6	0.29 (0.24, 0.35)	0.27 (0.22, 0.34)	0.24 (0.18, 0.31)	0.28 (0.27, 0.29)
7	0.23 (0.19, 0.28)	0.21 (0.17, 0.26)	0.19 (0.14, 0.24)	0.23 (0.22, 0.23)
8	0.14 (0.11, 0.18)	0.13 (0.10, 0.17)	0.11 (0.08, 0.16)	0.14 (0.13, 0.14)
P for trend	<0.0001	<0.0001	<0.0001	<0.0001
HR per score	0.826 (0.819, 0.832)	0.82 (0.81, 0.83)	0.80 (0.79, 0.81)	0.834 (0.832, 0.835)

Abbreviation: CVD, cardiovascular disease.

[1] The HRs were calculated using a Cox proportional hazards regression model and adjusted by age, sex, BMI (kg/m^2: <25, 25–29.9, ≥30), race and ethnicity (non-Hispanic White, non-Hispanic Black/Africa American, Hispanic, others), marriage status (currently married, not married, or missing), educational level (high school or less, some years of college, college or above, or missing), and family income levels (<30k, 30–60k, >60k, or missing).

[2] Imputation for the missing low-risk lifestyle factors applying a multiple imputation approach (number of imputations = 25).

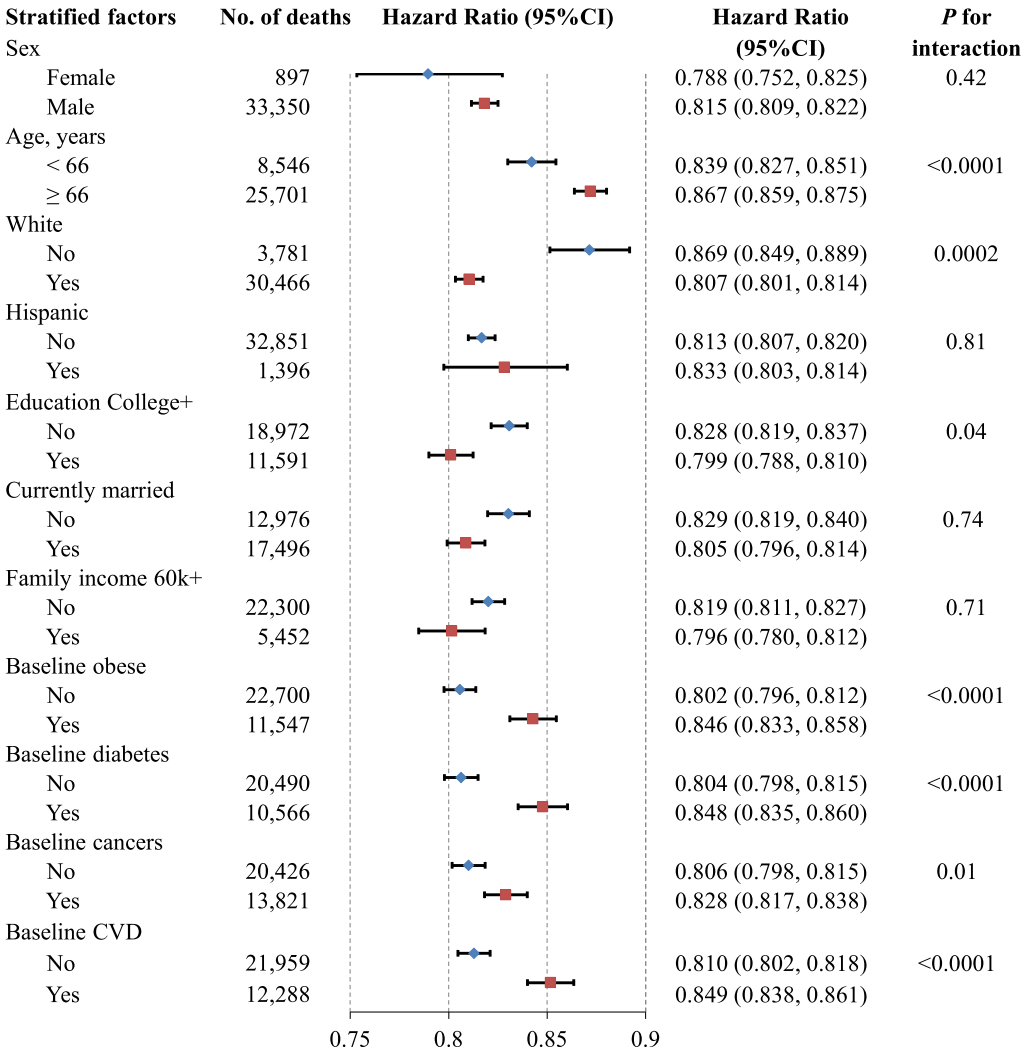

FIGURE 2. Stratified analysis of the hazard ratio of mortality associated with per number of low-risk lifestyle factors (a corrected alpha level of 0.0015 was used applying a desired alpha level of 0.05 with a total of 33 comparisons, applying the Bonferroni correction to account for multiple comparisons).

were relatively small among the group who adhered to all 8 low-risk lifestyle factors. However, the continuous and graded prolonged life expectancy associated with increasing number of low-risk lifestyle factors suggests that any improvement in lifestyle toward adopting low-risk factors would result in certain benefit, and the more intensive, the better.

In conclusion, findings from this investigation of MVP participants showed that all low-risk lifestyle factors were associated with a lower risk of premature mortality and the combination of low-risk lifestyle factors demonstrated a continuous and graded effect. Adherence to all 8 low-risk lifestyle factors was associated with an estimation of >20 y of prolonged life expectancy at age 40. Our estimation of graded prolonged lifestyle expectancy associated with increasing intensive low-risk lifestyle changes provides scientific support to promote lifestyle medicine as a means for individuals to directly influence their own health.

Author contributions

The authors' responsibilities were as follows – XTN, SBW, SH, YS, LD, JMG, KC, PWFW: designed the cohort, collected the data, and managed the project; YL, DDW, FBH, WCW: designed the research; XTN, YL, DDW: conducted the research; YL: analyzed data; XTN, YL: wrote the paper; YL: had primary responsibility for final content; and all authors: read and approved the final manuscript.

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Ethical approval

The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the VA Central Institutional Review Board, Washington, DC (protocol: MVP000, date of approval: 2010). Written informed consent form was obtained from all subjects/patients.

Data availability

Data cannot be shared publicly because of VA policies regarding data privacy and security. Data contain potentially identifying and sensitive patient information. All relevant summary level data are included in the manuscript. For investigators with appropriate authorizations within the Department of Veterans Affairs, requests for data access can be made.

Conflict of interest

The authors report no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2023.10.032.

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