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ORIGINAL ARTICLE

Cardiovascular disease, bone fracture, and all-cause mortality risks among postmenopausal women by arthritis and veteran status: A multistate Markov transition analysis

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Abstract Arthritis, a chronic inflammatory condition linked to cardiovascular disease (CVD) and bone fracture, is more frequent among military veterans and postmenopausal women. This study examined correlates of arthritis and relationships of arthritis with risks of developing CVD, bone fractures, and mortality among postmenopausal veteran and non-veteran women. We analyzed longitudinal data on 135,790 (3,436 veteran and 132,354 non-veteran) postmenopausal women from the Women's Health Initiative who were followed-up for an average of 16 years between enrollment (1993–1998) and February 17, 2024. Regression and multistate Markov modeling were applied to meet study objectives. The prevalence of arthritis at enrollment (1993–1998) did not differ by veteran status in a fully adjusted logistic model. Variable selection yielded 5 key predictors of prevalent arthritis among veterans and 15 key predictors among non-veterans. In fully-adjusted Cox models, prevalent arthritis was associated with CVD (hazard ratio [HR] = 1.08, 95% confidence interval [CI]: 1.05, 1.10) and all-cause mortality (HR = 1.03, 95% CI: 1.01, 1.05) risks among non-veterans only, but was not associated with bone fracture risk irrespective

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of veteran status. Transition probabilities between health and CVD and between bone fracture and death were higher among women with *vs.* without arthritis. The latter transition was more strongly related to arthritis among non-veteran *vs.* veteran women. In conclusion, among postmenopausal women, prevalent arthritis was associated with greater probabilities of transitioning from a healthy state to CVD and from bone fracture to death, with worse prognosis after bone fracture among those who did not serve in the military.

Keywords Arthritis · Bone fracture · Cardiovascular disease · Menopause · Multistate · Veteran

Introduction

Arthritis, which includes rheumatoid arthritis (RA) and osteoarthritis (OA), is a chronic inflammatory condition characterized by pain symptoms and functional limitations [1]. RA is a progressive autoimmune disease that causes joint inflammation, resulting in painful deformity and immobility, especially in the fingers, wrists, feet, and ankles [2]. Conversely, OA is predominantly characterized by pain and stiffness in the hip, knee, and thumb joints, primarily due to bone and cartilage degeneration [3]. In the US, the burden of arthritis is substantial among older adults, women, and veterans. Centers for Disease Control and Prevention data indicate that 21.2% of US adults, or 53.2 million people, had physician-diagnosed arthritis between 2019 and 2021, resulting in functional limitations among 44% of affected individuals, with arthritis being more prevalent in women (20.9%) *vs.* men (16.3%), and in veterans (24.2%) *vs.* non-veterans (18.5%) [4–6]. As such, women veterans can be considered a high-risk population for arthritis, RA, and OA. Pain symptoms associated with arthritis can hinder physical activity, which may lead to greater risks of obesity, type 2 diabetes, hypertension, sleep disorders, cardiovascular disease (CVD), and premature death [4–7].

Arthritis becomes more common in women postmenopause, as sex hormones, especially estrogens, are critically important in maintaining cartilage homeostasis [8]. Postmenopausal loss of estrogens can lead to joint damage through increased levels of reactive oxygen species and pro-inflammatory cytokines [9]. Chronic inflammation that is common to RA and OA may also increase bone fracture risk [10]. To date, no epidemiological studies have investigated the prevalence, risk/protective factors, and health consequences of arthritis among postmenopausal women by veteran status. A better understanding of the risk and protective factors for arthritis and its associated health consequences by veteran status could inform the development of tailored preventive strategies for postmenopausal women.

The main objectives of this study were to: (1) examine correlates of prevalent arthritis among postmenopausal women by veteran status; (2) examine the prospective association between prevalent arthritis and risks of CVD, bone fractures, and all-cause mortality in postmenopausal women by veteran status; and (3) estimate transition probabilities from a healthy state to death through CVD and/or bone fracture using multistate Markov models, stratified by arthritis and veteran status. We hypothesized that the prevalence of arthritis would be higher among veteran *vs.* non-veteran postmenopausal women. We

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also hypothesized that correlates of prevalent arthritis and the association of prevalent arthritis with future risks of CVD, bone fracture, and all-cause mortality among postmenopausal women varied by veteran status. Finally, we hypothesized that the probability of transition from a healthy state to death through intermediate health outcomes, namely CVD or bone fracture, would be higher among postmenopausal women with prevalent arthritis *vs.* postmenopausal women without prevalent arthritis, and that these estimates would vary among veteran *vs.* non-veteran postmenopausal women.

Methods

Women's Health Initiative The Women's Health Initiative (WHI) is a longitudinal study aimed at reducing heart disease, breast, colorectal, and osteoporosis in postmenopausal women [11–16]. The study enrolled a multiethnic sample of postmenopausal women aged 50 to 79 years between 1993 and 1998 at 40 clinical centers in 24 US states and the District of Columbia. The WHI clinical trials (WHI-CT) examined menopausal hormone therapy, calcium and vitamin D supplementation, and a low-fat diet, while the WHI Observational Study (WHI-OS) focused on postmenopausal morbidity and mortality risks. After the main WHI studies were completed, 76.9% participants took part in the Extension Study 1 (2005–2010) and 86.9% in the Extension Study 2 (2010–2015) [17–21]. Data were collected through self-administered questionnaires, in-person/telephone interviews, and clinical assessments. WHI-CT and WHI-OS participants completed similar assessments at their enrollment (1993–1998) visit. More details regarding the WHI study are provided elsewhere [22–27].

Design and participants The study population was restricted to WHI-CT and WHI-OS participants with no missing data on veteran and arthritis statuses as well as selected demographic, socioeconomic, lifestyle, and health characteristics at enrollment (1993–1998) and who were followed up between enrollment (1993–1998) and February 17, 2024.

Measures

Veteran status Veteran status was defined as a dichotomous (Yes/No) variable based on a WHI participant's response to a self-reported questionnaire item ["Have you served in the US armed forces on active duty for a period of 180 days or more?"] at enrollment (1993–1998). WHI participants responding positively were classified as veterans (N = 3,719) and those responding negatively were classified as non-veterans (N = 141,802), whereas those with missing data on veteran status (N = 16,258) were excluded from the analytic sample, as described elsewhere [16, 28–34]. We examined veteran status among WHI participants as the exposure of interest, i.e., as a correlate of prevalent arthritis and as a stratifying variable, i.e., when examining correlates of prevalent arthritis and the association of prevalent arthritis with future CVD, bone fracture, and all-cause mortality risks.

Prevalent arthritis We relied on self-reported data collected using Form 30 (Medical History) at enrollment (1993–1998). Specifically, we used the ARTHRIT item ("Did your doctor ever say that you had arthritis?"), which classifies participants as having ever been diagnosed with arthritis (N = 76,192), having never been diagnosed with arthritis (N = 84,168), or having missing data on this item (N = 1,341). Among those classified as having ever been diagnosed with arthritis, the follow-up RHEUMAT item ("What type of arthritis do you have?") was used to classify arthritis as RA among those answering 'Rheumatoid Arthritis' (N = 7,872) and as OA among those answering 'Other/Don't Know' (N = 64,551). Prevalent arthritis was defined as self-reported RA or OA at enrollment (1993–1998). Because of limited sample size, RA and OA groups were distinguished for descriptive purposes only. Further details regarding the definition of arthritis in the WHI study are provided in Online Resource 1.

Demographic, socioeconomic, lifestyle, and health characteristics As described in the Online Resource 2, we examined several characteristics collected at enrollment (1993–1998) as correlates of prevalent arthritis and as potential confounders for hypothesized relationships between arthritis, CVD, bone fracture, and all-cause mortality risks, among veteran and non-veteran women.

Cardiovascular disease risk Incidence of fatal and non-fatal CVD from enrollment (1993–1998)

was evaluated up to February 17, 2024, by obtaining binary outcome and time-to-event data from Form 33 (Medical History Update). Using adjudicated outcomes, incident coronary heart disease (CHD) was defined as fatal and non-fatal myocardial infarction, angina, or coronary revascularization (i.e. angioplasty or coronary artery bypass surgery). Furthermore, incident CVD was defined as incident CHD, stroke, transient ischemic attack, congestive heart failure, or carotid artery surgery. Finally, cardiovascular mortality was defined as deaths from CHD, stroke, congestive heart failure, and other CVDs as coded in the WHI documentation. CVD risk was defined in terms of the first occurrence of a fatal or non-fatal CVD event during the follow-up period. Further details regarding the definition of CVD risk in the WHI study are described elsewhere [35–37].

Bone fracture risk WHI participants reported clinical fractures on medical update forms, collected every 6 months from WHI-CT women and every 12 months from WHI-OS women [38]. Incidence of self-reported bone fractures at different anatomical sites (upper arm, lower arm, elbow, spine, tailbone, hip, upper leg, lower leg, foot) from enrollment (1993—1998) up to February 17, 2024, were evaluated by obtaining binary outcome and time-to-event data. Bone fracture risk was defined in terms of the first occurrence of a bone fracture event during the follow-up period. Further details regarding the definition of bone fracture risk in the WHI study are provided in Online Resource 3.

All-cause mortality risk Semi-annual or annual follow-up telephone calls were performed with the objective of death ascertainment. Trained staff members contacted participants' family, friends, and medical care providers, and the National Death Index and obituaries were also used as sources of mortality data. Nevertheless, ~ 1–2% of participants were deemed lost to follow-up [22–24, 39]. The underlying cause of death was used to estimate cause-specific mortality rates, with cardiovascular-specific and cancer-specific deaths being centrally adjudicated [39]. WHI participants in the final analytic sample were followed from enrollment (1993–1998) up to February 17, 2024, to evaluate the risk of mortality from any cause.

Statistical analysis All statistical analyses were conducted with SAS version 9.4 (SAS Institute, Cary, NC) and Stata version 18 (StataCorp, College Station, TX). The conceptual framework for these analyses is shown in Fig. 1. Veteran and non-veteran women in the final analytic sample were first compared on demographic, socioeconomic, lifestyle, and health characteristics at enrollment (1993–1998). Pearson's Chi-square test and independent samples t-test were carried out to assess bivariate relationships. Their non-parametric counterparts were also used as needed. Second, logistic regression models were constructed to estimate odds ratios (OR) and 95% confidence intervals (CI) for associations of veteran status with prevalent arthritis, before and after sequential adjustment for demographic, socioeconomic, lifestyle and health characteristics. Third, logistic regression with forward, backward, and stepwise variable selection – HPLOGISTIC procedure – as well as the least absolute shrinkage and selection operator (LASSO) method – HPGENSELECT procedure – with defaults of LASSORHO = 0.8 and LASSOSTEPS = 20, were applied to select the regression model that optimizes the value of the Schwarz Bayes criterion. Final logistic regression models were constructed to identify key risk/protective characteristics

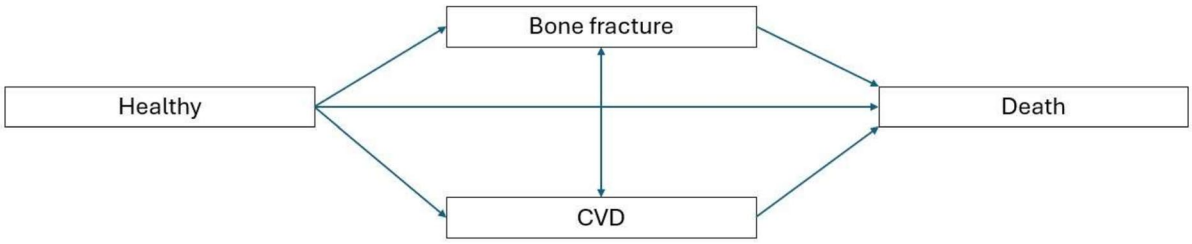

Fig. 1 Conceptual framework – women's health initiative

correlated with arthritis, overall, and by veteran status. Fourth, incidence rates (per 1,000 person-years) with their 95% confidence intervals (CI) were calculated and Kaplan–Meier curves were constructed for CVD, bone fracture, and all-cause mortality risks by arthritis and veteran statuses over a maximum follow-up time of ~ 30 years. We also fit Cox proportional hazards models to estimate hazard ratios (HR) with their 95% CI. Specifically, we examined associations of arthritis with CVD, bone fracture, and all-cause mortality risks by veteran status, before and after adjustment for demographic, socioeconomic, lifestyle, and health characteristics. We verified proportional hazards assumptions using exposure-by-time interactions within fully adjusted Cox regression models as well as by examining Schoenfeld residuals. Finally, we applied multistate Markov modeling using Stata commands (*streg* and *stmerlin*) to estimate transition probabilities between a healthy state and death through CVD and bone fracture by arthritis and veteran statuses. A multistate Markov model is a stochastic process that, in this study, provides insights into how postmenopausal women transition between distinct health-related states over time, allowing for the evaluation of covariate effects on each transition [40]. While semiparametric techniques, such as the Cox proportional hazards model, are commonly used, parametric models within multistate Markov frameworks have been shown to offer advantages in prediction, extrapolation, and quantification [40]. We accounted for multiple testing using familywise Bonferroni correction. After examining patterns of missingness, we implemented complete subject analyses, whereby two-tailed statistical tests were assessed at an α level of 0.05.

Results

Of 161,808 postmenopausal women enrolled in the WHI, 144,524 had no missing data on veteran or arthritis statuses, and the final analytic sample consisted of 135,790 women (3,436 veteran and 132,354 non-veteran) with no missing data on demographic, socioeconomic, lifestyle, and health characteristics. Furthermore, 1,847 veterans (185 RA, 1,647 OA, 15 unknown) and 62,713 non-veterans (6,640 RA, 55,498 OA, 575 unknown) had prevalent arthritis at enrollment (1993–1998). Accordingly, the prevalence of arthritis was estimated at 47.5%, 53.8%, and 47.4%, among the overall, veteran, and non-veteran groups of postmenopausal women, respectively (Fig. 2).

As shown in Table 1, veteran and non-veteran postmenopausal women significantly differed on several background characteristics evaluated at enrollment (1993–1998). Veterans were generally older, more frequently of white race and non-Hispanic ethnicity, unmarried, not working/retired/disabled, and more likely to report histories of smoking and/or alcohol consumption than their non-veteran counterparts. Although veterans had higher average 2015 Healthy Eating Index (HEI-2015) and physical activity scores and lower depressive symptoms scores, they also had more comorbidities and were more likely to report a history of bone fracture than their non-veteran counterparts.

Table 2 presents results of logistic regression models for veteran status as a predictor of prevalent arthritis, before and after sequentially controlling for demographic, lifestyle, and health characteristics at enrollment (1993–1998). Although the unadjusted model indicated increased odds of prevalent arthritis among veteran *vs.* non-veteran (OR = 1.29, 95% CI: 1.21, 1.38) postmenopausal women, the relationship became statistically non-significant in a fully-adjusted model (OR = 1.04, 95% CI: 0.97, 1.12).

Multivariable logistic regression models whereby all selected demographic, socioeconomic, lifestyle, and health characteristics were added to models for correlates of prevalent arthritis are displayed before and after stratifying by veteran status in Table 3. Among veteran and non-veteran women alike, age, body mass index (BMI), history of bone fracture, number of comorbidities, worse self-rated health, depressive symptoms, and having a current healthcare provider were significant predictors of prevalent arthritis. Furthermore, WHI component, region of residence, race, ethnicity, education, occupation, household income, neighborhood socioeconomic status, smoking status, alcohol consumption, HEI-2015 and physical activity scores were related to prevalent arthritis only among non-veterans. Using forward, backward, stepwise, and LASSO variable selection strategies (Online Resource 4, Table S.1.), key risk/protective characteristics were identified (Online Resource 4, Table S.2.), and these characteristics were dichotomized as needed for use as covariates within multistate Markov models. In the overall study

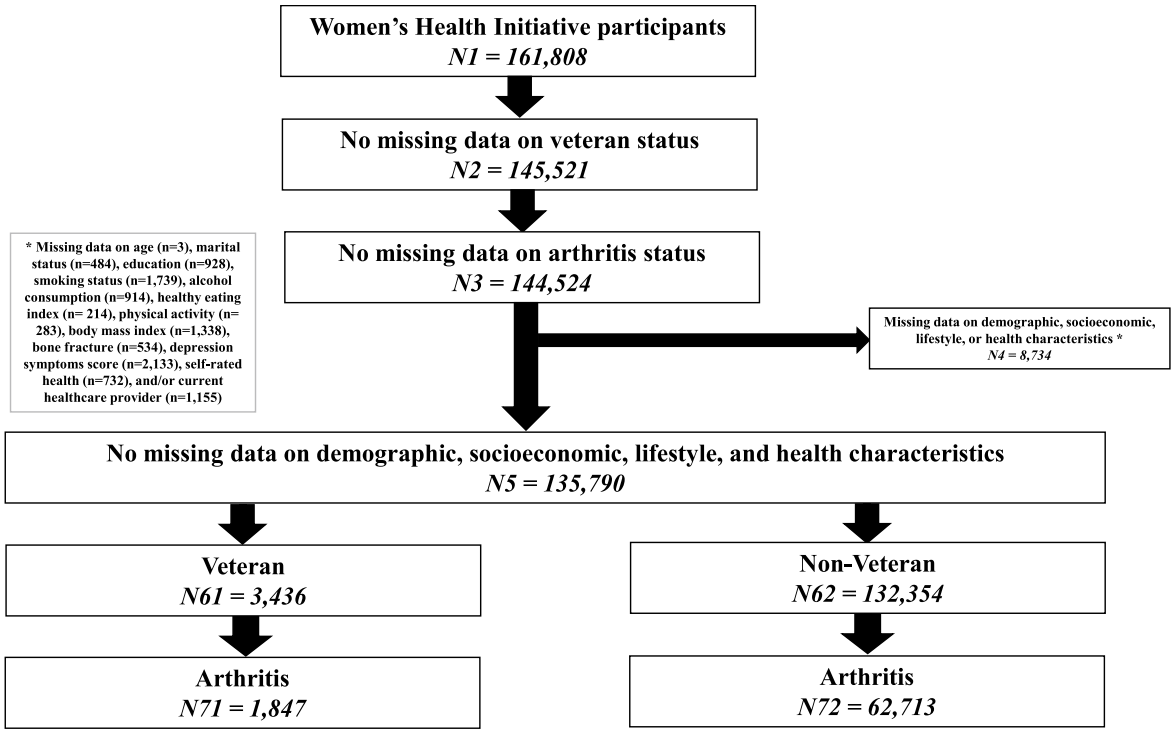

Fig. 2 Study flowchart – women's health initiative

population and among non-veteran women, these key correlates of arthritis were WHI component (WHI-CT *vs.* WHI-OS), region of residence (Midwest, Northeast, South, West), age (years), race (White *vs.* other groups), occupation (Not working/Retired/Disabled *vs.* other groups), household income (≥ $100,000 *vs.* other groups), smoking status (never smoker, past smoker, current smoker), BMI (kg/m^2), history of bone fracture (Yes *vs.* No), number of comorbid conditions (≥ 1 *vs.* 0), self-rated health (Fair/Poor *vs.* Excellent/Very Good/Good), current healthcare provider (Yes *vs.* No), as well as HEI-2015, physical activity, and depressive symptoms scores. Among veteran women, key correlates of arthritis were age (years), BMI (kg/m^2), number of comorbidities (≥ 1 *vs.* 0), self-rated health (Fair/Poor *vs.* Excellent/Very Good/Good), and depressive symptoms score.

In the final analytic sample, a total of 29,751 CVD, 10,425 bone fracture, and 50,577 all-cause death events occurred between enrollment (1993–1998) and February 17, 2024, over mean (± standard deviation) follow-up times of 16.4 (± 8.9), 16.8 (± 8.8), and 17.8 (± 8.4) years, respectively. As shown in Online Resource 4 Table S.3., incidence rates (95% CI) among study-eligible women were estimated at 13.4 (13.2, 13.5), 4.6 (4.4, 4.7), and 21.0 (20.8, 21.2) per 1,000 person-years for CVD, bone fractures, and all-cause mortality, respectively, with higher rates among veteran *vs.* non-veteran women and among those with *vs.* without prevalent arthritis at enrollment (1993—1998) (Online Resource 4, Fig. S.1.).

Prevalent arthritis was associated with CVD and all-cause mortality risks in unadjusted models involving veteran women (*CVD:* HR = 1.47, 95% CI: 1.29, 1.67; *all-cause mortality:* HR = 1.53, 95% CI: 1.39, 1.69) and with CVD, bone fracture, and mortality risks in unadjusted models involving non-veteran women (*CVD:* HR = 1.65, 95% CI: 1.61, 1.69; *bone fractures:* HR = 1.20, 95% CI: 1.16, 1.25; *all-cause mortality:* HR = 1.54, 95% CI: 1.51, 1.56). In fully-adjusted models, these relationships were attenuated and became non-significant among veteran women. Among non-veteran women, only relationships involving CVD (HR = 1.08, 95%

Table 1 Demographic, socioeconomic, lifestyle and health characteristics of study participants by veteran status (n = 135,790)

	Total (n = 135,790) N (%)	Veteran (n = 3,436) N (%)	Non-Veteran (n = 132,354) N (%)
WHI component:		P = 0.12	
CT	54,006 (39.77)	1322 (38.47)	52,684 (39.81)
OS	81,784 (60.23)	2114 (61.53)	79,670 (60.19)
Region of residence:		P < 0.0001	
Midwest	30,301 (22.31)	543 (15.80)	29,758 (22.48)
Northeast	34,435 (25.36)	922 (26.83)	33,513 (25.32)
South	30,523 (22.48)	616 (17.93)	29,907 (22.60)
West	40,531 (29.85)	1355 (39.44)	39,176 (29.60)
Age (years):		P < 0.0001	
Mean ± SD	63.29 ± 7.19	67.05 ± 7.94	63.19 ± 7.15
		P < 0.0001	
50–59	44,271 (32.60)	729 (21.22)	43,542 (32.90)
60–69	61,497 (45.29)	1003 (29.19)	60,494 (45.71)
70–79 +	30,022 (22.11)	1704 (49.59)	28,318 (21.40)
Race:		P < 0.0001	
American Indian/Alaska Native	427 (0.31)	6 (0.17)	421 (0.32)
Asian	3678 (2.71)	35 (1.02)	3643 (2.75)
Native Hawaiian/Other Pacific Islanders	125 (0.09)	4 (0.12)	121 (0.09)
Black	11,331 (8.34)	227 (6.61)	11,104 (8.39)
White	116,158 (85.54)	3068 (89.29)	113,090 (85.45)
More than one race	1628 (1.20)	50 (1.46)	1578 (1.19)
Unknown/Not reported	2443 (1.80)	46 (1.34)	2397 (1.81)
Ethnicity:		P < 0.0001	
Hispanic	128,920 (94.94)	3321 (96.65)	125,599 (94.90)
Non-Hispanic	5701 (4.20)	92 (2.68)	5609 (4.24)
Unknown/Not reported	1169 (0.86)	23 (0.67)	1146 (0.87)
Marital status:		P < 0.0001	
Married/Partnered	84,843 (62.48)	1691 (49.21)	83,152 (62.83)
Single	5981 (4.40)	354 (10.30)	5627 (4.25)
Divorced	21,728 (16.00)	621 (18.07)	21,107 (15.95)
Widowed	23,238 (17.11)	770 (22.41)	22,468 (16.98)
Education:		P < 0.0001	
Less than high school	6657 (4.90)	51 (1.48)	6606 (4.99)
High school	23,130 (17.03)	348 (10.13)	22,782 (17.21)
Some college	51,426 (37.87)	1415 (41.18)	50,011 (37.79)
Completed college or higher level	54,577 (40.19)	1622 (47.21)	52,955 (40.01)
Occupation:		P < 0.0001	
Managerial/professional	24,875 (18.32)	467 (13.59)	24,408 (18.44)
Technical/sales/administrative	40,552 (29.86)	891 (25.93)	39,661 (29.97)
Service/labor	12,355 (9.10)	257 (7.48)	12,098 (9.14)
Homemaker	21,647 (15.94)	543 (15.80)	21,104 (15.95)
Other	8777 (6.46)	220 (6.40)	8557 (6.47)
Not working/Retired/Disabled	25,263 (18.60)	1011 (29.42)	24,252 (18.32)
Unknown/Not reported	2321 (1.71)	47 (1.37)	2274 (1.72)

Table 1 (continued)

	Total ($n = 135,790$) N (%)	Veteran ($n = 3,436$) N (%)	Non-Veteran ($n = 132,354$) N (%)
Household income:		P < 0.0001	
< $20,000	20,383 (15.01)	567 (16.50)	19,816 (14.97)
$20,000-$49,999	56,835 (41.86)	1620 (47.15)	55,215 (41.72)
$50,000-$99,999	37,423 (27.56)	857 (24.94)	36,566 (27.63)
≥ $100,000	12,619 (9.29)	220 (6.40)	12,399 (9.37)
Unknown/Not reported	8530 (6.28)	172 (5.01)	8358 (6.31)
Neighborhood socioeconomic status:		P = 0.26	
1st tertile	45,587 (33.57)	1187 (34.55)	44,400 (33.55)
2nd tertile	35,010 (25.78)	909 (26.46)	34,101 (25.76)
3rd tertile	41,184 (30.33)	999 (29.07)	40,185 (30.36)
Missing	14,009 (10.32)	341 (9.92)	13,668 (10.33)
Smoking status:		P < 0.0001	
Never Smoker	69,098 (50.89)	1536 (44.70)	67,562 (51.05)
Past Smoker	57,396 (42.27)	1602 (46.62)	55,794 (42.16)
Current Smoker	9296 (6.85)	298 (8.67)	8998 (6.80)
Alcohol consumption:		P < 0.0001	
Non-Drinker	14,637 (10.78)	226 (6.58)	14,411 (10.89)
Former Drinker	25,285 (18.62)	707 (20.58)	24,578 (18.57)
< 1 drink/week	44,769 (32.97)	1153 (33.56)	43,616 (32.95)
≥ 1 drink/week	51,099 (37.63)	1350 (39.29)	49,749 (37.59)
Healthy Eating Index – 2015:		P < 0.0001	
Mean ± SD	65.27 ± 10.40	66.06 ± 10.33	65.26 ± 10.41
Physical activity [Metabolic equivalent-hours/week]:		P = 0.002	
Mean ± SD	12.53 ± 13.75	13.26 ± 14.19	12.51 ± 13.74
BMI(kg/m^2):		P = 0.36	
Mean ± SD	27.92 ± 5.96	27.83 ± 5.81	27.92 ± 5.96
		P = 0.14	
< 25	48,441 (35.67)	1206 (35.10)	47,235 (35.69)
25- < 30	46,930 (34.56)	1241 (36.12)	45,689 (34.52)
≥ 30	40,419 (29.77)	989 (28.78)	39,430 (29.79)
Obesity (BMI ≥ 30 kg/m2):		P = 0.20	
Yes	40,419 (29.77)	989 (28.78)	39,430 (29.79)
No	95,371 (70.23)	2447 (71.22)	92,924 (70.21)
Bone fracture:		P < 0.0001	
Yes	52,626 (38.76)	1531 (44.56)	51,095 (38.60)
No	83,164 (61.24)	1905 (55.44)	81,259 (61.40)
Comorbid conditions:		P < 0.0001	
Mean ± SD	0.88 ± 0.98	1.04 ± 1.06	0.88 ± 0.98
		P < 0.0001	
0	57,731 (42.51)	1244 (36.20)	56,487 (42.68)
1–2	69,156 (50.93)	1858 (54.07)	67,298 (50.85)
≥ 3	8903 (6.56)	334 (9.72)	8569 (6.47)
Self-rated health:		P = 0.62	

Table 1 (continued)

	Total ($n=135,790$) N (%)	Veteran ($n=3,436$) N (%)	Non-Veteran ($n=132,354$) N (%)
Excellent/Very Good/Good	123,858 (91.21)	3126 (90.98)	120,732 (91.22)
Fair/Poor	11,932 (8.79)	310 (9.02)	11,622 (8.78)
Depressive symptoms:		P = 0.007	
Mean ± SD	1.51 ± 2.11	1.42 ± 2.03	1.51 ± 2.12
		P = 0.08	
≤ 0.06	65,253 (48.05)	1701 (49.51)	63,552 (48.02)
> 0.06	70,537 (51.95)	1735 (50.49)	68,802 (51.98)
Current healthcare provider:		P = 0.21	
Yes	127,687 (94.03)	3248 (94.53)	124,439 (94.02)
No	8103 (5.97)	188 (5.47)	7915 (5.98)

Abbreviations: BMI Body Mass Index, *CT* Clinical Trials, *OS* Observational Study, *SD* Standard deviation, *WHI* Women's Health Initiative

CI: 1.05, 1.10) and all-cause mortality (HR = 1.03, 95% CI: 1.01, 1.05) risks remained significant after adjustment for background characteristics (Table 4).

Observed transitions (Online Resource 4, Fig. S.2.), estimated survival probabilities of being in each of the four states (healthy, CVD, bone fracture, all-cause death) (Fig. 3), and estimated transition probabilities out of CVD and bone fracture (Online Resource 4, Fig S.3.) were displayed graphically. After evaluating differences in beta coefficients, Akaike's and Bayesian Information Criteria between distinct multistate Markov modeling strategies (Online Resource 4, Table S.4.), Weibull models were selected to examine arthritis status (*Model I*) and the interaction effects of arthritis-by-veteran status (*Model II*) in relation to the six transitions between the four states, adjusting for key correlates of arthritis as previously described. As shown in Table 5 and Figs. S.4-S.5. in Online Resource 4, estimated probabilities of experiencing transitions 1 (healthy to CVD) and 6 (bone fracture

Table 2 Difference in the prevalence of arthritis between veteran and non-veteran women in the Women's Health Initiative, controlling for demographic, socioeconomic, lifestyle, and health characteristics at enrollment (1993—1998) (n = 135,790)[a]

	OR	95% CI	P
Model 0: Unadjusted	1.29	1.21, 1.38	< 0.0001
Model 1: Demographic	1.05	0.98, 1.13	0.18
Model 2: Demographic + Socioeconomic	1.07	0.99, 1.15	0.05
Model 3: Demographic + Socioeconomic + Lifestyle	1.07	0.99, 1.14	0.07
Model 4: Demographic + Socioeconomic + Lifestyle + Health	1.04	0.97, 1.12	0.25

Abbreviations: CI Confidence Interval, *OR* Odds Ratio. [a] Demographic characteristics include WHI component (WHI-CT, WHI-OS), region of residence [Midwest, Northeast, South, West], age [in years], race [American Indian/Alaska Native, Asian, Native Hawaiian/Other Pacific Islanders, Black, White, More than one race, Unknown/Not reported], ethnicity [Hispanic, non-Hispanic, Unknown/Not reported], marital status [Married/Partnered, Single, Divorced, Widowed]. Socioeconomic characteristics include education [less than high school, high school, some college, completed college or higher level], occupation [managerial/professional, technical/sales/administrative, service/labor, homemaker, other, not working/Retired/Disabled, unknown/not reported], household income [< $20,000, $20,000-$49,999, $50,000-$99,999, ≥ $100,000, unknown/not reported], and neighborhood socioeconomic status (tertiles). Lifestyle characteristics include smoking status [Never Smoker, Past Smoker, Current Smoker], alcohol consumption [Non-Drinker, Former Drinker, < 1 drink/week, ≥ 1 drink/week], the 2015 Healthy Eating Index (HEI-2015), and physical activity [Metabolic equivalent-hours/week]. Health characteristics include body mass index (kg/m^2), history of bone fracture (Yes, No), number of comorbid conditions (0, 1–2, 3 +), depressive symptoms score, self-rated health [Excellent/Very Good/Good, Fair/Poor]), and current healthcare provider (Yes, No)

Table 3 Multivariable logistic regression models for demographic, socioeconomic, lifestyle, and health characteristics as correlates of prevalent arthritis among Women's Health Initiative participants, before and after stratifying by veteran status ($n = 135,790$)

	Total ($n = 135,790$) OR (95% CI)	Veteran ($n = 3,436$) OR (95% CI)	Non-Veteran ($n = 132,354$) OR (95% CI)
WHI component:			
CT	0.90 (0.88, 0.92)	0.90 (0.78, 1.06)	0.90 (0.88, 0.92)
OS	Ref	Ref	Ref
Region of residence:			
Midwest	1.11 (1.08, 1.15)	0.98 (0.79, 1.22)	1.11 (1.08, 1.16)
Northeast	1.10 (1.07, 1.14)	0.95 (0.79, 1.14)	1.11 (1.07, 1.14)
South	1.15 (1.11, 1.19)	0.98 (0.80, 1.21)	1.16 (1.12, 1.19)
West	Ref	Ref	Ref
Age (years):	1.05 (1.05, 1.05)	1.04 (1.03, 1.05)	1.05 (1.05, 1.05)
Race:			
American Indian/Alaska Native	1.26 (1.03, 1.55)	0.43 (0.06, 2.87)	1.28 (1.04, 1.58)
Asian	0.76 (0.70, 0.83)	1.18 (0.55, 2.49)	0.76 (0.70, 0.82)
Native Hawaiian/Other Pacific Islanders	0.45 (0.29, 0.67)	–	0.47 (0.30, 0.70)
Black	1.02 (0.98, 1.07)	1.13 (0.84, 1.53)	1.02 (0.97, 1.06)
White	Ref	Ref	Ref
More than one race	1.07 (0.97, 1.19)	0.48 (0.26, 0.91)	1.09 (0.99, 1.22)
Unknown/Not reported	0.96 (0.87, 1.06)	0.95 (0.46, 1.98)	0.96 (0.87, 1.07)
Ethnicity:			
Hispanic	0.87 (0.81, 0.93)	1.05 (0.64, 1.68)	0.87 (0.81, 0.93)
Non-Hispanic	Ref	Ref	Ref
Unknown/Not reported	0.88 (0.77, 1.01)	1.28 (0.45, 3.62)	0.87 (0.76, 1.01)
Marital status:			
Married/Partnered	Ref	Ref	Ref
Single	0.98 (0.93, 1.04)	1.05 (0.81, 1.35)	0.98 (0.92, 1.04)
Divorced	0.96 (0.93, 0.99)	0.91 (0.74, 1.13)	0.96 (0.93, 0.99)
Widowed	0.97 (0.94, 1.00)	1.04 (0.86, 1.27)	0.97 (0.94, 1.00)
Education:			
Less than high school	1.11 (1.04, 1.17)	1.09 (0.58, 2.03)	1.11 (1.04, 1.18)
High school	1.05 (1.01, 1.09)	0.94 (0.71, 1.23)	1.06 (1.02, 1.09)
Some college	1.05 (1.02, 1.08)	1.04 (0.87, 1.24)	1.05 (1.02, 1.08)
Completed college or higher level	Ref	Ref	Ref
Occupation:			
Managerial/professional	0.87 (0.83, 0.90)	0.78 (0.60, 1.00)	0.87 (0.83, 0.90)
Technical/sales/administrative	0.93 (0.90, 0.97)	0.97 (0.78, 1.19)	0.93 (0.90, 0.97)
Service/labor	1.03 (0.98, 1.08)	1.15 (0.84, 1.57)	1.02 (0.97, 1.08)
Homemaker	1.02 (0.98, 1.06)	1.07 (0.84, 1.35)	1.02 (0.98, 1.06)
Other	0.95 (0.90, 1.00)	0.99 (0.72, 1.35)	0.95 (0.90, 1.00)
Not working/Retired/Disabled	Ref	Ref	Ref
Unknown/Not reported	0.85 (0.77, 0.93)	1.09 (0.59, 2.03)	0.84 (0.77, 0.92)
Household income:			
< $20,000	1.21 (1.15, 1.28)	1.17 (0.80, 1.72)	1.21 (1.14, 1.29)
$20,000-$49,999	1.11 (1.06, 1.16)	1.07 (0.77, 1.47)	1.11 (1.06, 1.16)
$50,000-$99,999	1.05 (1.00, 1.09)	1.10 (0.80, 1.51)	1.05 (1.00, 1.09)
≥ $100,000	Ref	Ref	Ref

Table 3 (continued)

	Total ($n = 135,790$) OR (95% CI)	Veteran ($n = 3,436$) OR (95% CI)	Non-Veteran ($n = 132,354$) OR (95% CI)
Unknown/Not reported	1.06 (1.00, 1.13)	0.98 (0.64, 1.52)	1.07 (1.00, 1.13)
Neighborhood socioeconomic status:			
1st tertile	1.05 (1.02, 1.09)	1.03 (0.85, 1.24)	1.05 (1.02, 1.09)
2nd tertile	1.03 (0.99, 1.06)	0.94 (0.78, 1.14)	1.03 (1.00, 1.06)
3rd tertile	Ref	Ref	Ref
Unknown/Not reported	1.08 (1.04, 1.13)	1.16 (0.89, 1.52)	1.08 (1.04, 1.13)
Smoking status:			
Never Smoker	Ref	Ref	Ref
Past Smoker	1.07 (1.04, 1.09)	1.14 (0.98, 1.33)	1.07 (1.04, 1.09)
Current Smoker	0.99 (0.95, 1.04)	0.80 (0.61, 1.06)	0.99 (0.95, 1.05)
Alcohol consumption:			
Non-Drinker	Ref	Ref	Ref
Former Drinker	1.14 (1.09, 1.19)	1.15 (0.83, 1.59)	1.14 (1.09, 1.19)
< 1 drink/week	1.05 (1.01, 1.09)	1.15 (0.84, 1.57)	1.05 (1.01, 1.09)
≥ 1 drink/week	1.03 (0.99, 1.08)	1.09 (0.79, 1.49)	1.03 (0.99, 1.08)
Healthy Eating Index – 2015:	1.00 (1.00, 1.00)	0.99 (0.99, 1.00)	1.00 (1.00, 1.00)
Physical activity [Metabolic equivalent-hours/week]	0.99 (0.99, 0.99)	1.00 (0.99, 1.01)	0.99 (0.99, 0.99)
BMI(kg/m^2):	1.04 (1.03, 1.04)	1.04 (1.01, 1.06)	1.04 (1.03, 1.04)
Obesity (BMI ≥ 30 kg/m2):			
Yes	1.04 (0.99, 1.08)	1.19 (0.92, 1.53)	1.04 (0.99, 1.08)
No	Ref	Ref	Ref
Bone fracture:			
Yes	1.27 (1.24, 1.30)	1.22 (1.06, 1.42)	1.27 (1.24, 1.30)
No	Ref	Ref	Ref
Comorbid conditions:			
0	Ref	Ref	Ref
1–2	1.33 (1.29, 1.36)	1.37 (1.17, 1.60)	1.33 (1.29, 1.36)
≥ 3	1.93 (1.84, 2.04)	1.83 (1.38, 2.42)	1.94 (1.84, 2.05)
Self-rated health:			
Excellent/Very Good/Good	Ref	Ref	Ref
Fair/Poor	1.97 (1.88, 2.06)	2.00 (1.50, 2.67)	1.97 (1.88, 2.06)
Depressive symptoms:	1.05 (1.04, 1.06)	1.06 (1.02, 1.10)	1.05 (1.04, 1.06)
Current healthcare provider:			
Yes	1.66 (1.57, 1.74)	1.47 (1.07, 2.02)	1.66 (1.58, 1.75)
No	Ref	Ref	Ref

Abbreviations: BMI Body Mass Index, *CI* Confidence Interval, *CT* Clinical Trials, *OR* Odds Ratio, *OS* Observational Study, *WHI* Women's Health Initiative

to death) were significantly higher among women with *vs.* without arthritis, with difference in survival between non-arthritis and arthritis groups shown in the last panel of Fig. S.4. and S.5. for each of these transitions, simulating 15 years of follow-up across observed baseline ages. Similarly, the relationship between arthritis status and experiencing transition 6 (bone fracture to death) was stronger among non-veteran *vs.* veteran women, as indicated by a significant interaction effect between veteran and arthritis statuses in a model that adjusted for previously described correlates of arthritis (Table 5).

Table 4 Associations of arthritis with future risks of cardiovascular disease, bone fracture, and all-cause mortality by veteran status in the Women's Health Initiative, controlling for demographic, socioeconomic, lifestyle, and health characteristics at enrollment (1993—1998) (n = 135,790)[a]

	HR (95% CI)		
	Total (n = 135,790)	Veteran (n = 3,436)	Non-Veteran (n = 132,354)
Cardiovascular disease:			
Model 0: Unadjusted	1.65 (1.61, 1.69)	1.47 (1.29, 1.67)	1.65 (1.61, 1.69)
Model 1: Demographic	1.28 (1.25, 1.31)	1.17 (1.03, 1.33)	1.28 (1.26, 1.32)
Model 2: Demographic + Socioeconomic	1.25 (1.22, 1.28)	1.16 (1.03, 1.33)	1.25 (1.22, 1.28)
Model 3: Demographic + Socioeconomic + Lifestyle	1.23 (1.20, 1.26)	1.15 (1.01, 1.31)	1.23 (1.20, 1.26)
Model 4: Demographic + Socioeconomic + Lifestyle + Health	1.08 (1.05, 1.10)	0.99 (0.87, 1.13)	1.08 (1.05, 1.10)
Bone fracture:			
Model 0: Unadjusted	1.20 (1.16, 1.25)	1.08 (0.88, 1.33)	1.20 (1.16, 1.25)
Model 1: Demographic	1.06 (1.02, 1.10)	0.96 (0.78, 1.19)	1.06 (1.02, 1.11)
Model 2: Demographic + Socioeconomic	1.06 (1.02, 1.10)	0.96 (0.77, 1.18)	1.06 (1.02, 1.11)
Model 3: Demographic + Socioeconomic + Lifestyle	1.06 (1.02, 1.09)	0.96 (0.77, 1.18)	1.06 (1.02, 1.10)
Model 4: Demographic + Socioeconomic + Lifestyle + Health	1.03 (0.98, 1.07)	0.96 (0.77, 1.18)	1.03 (0.99, 1.07)
All-Cause Mortality:			
Model 0: Unadjusted	1.54 (1.51, 1.57)	1.53 (1.39, 1.69)	1.54 (1.51, 1.56)
Model 1: Demographic	1.17 (1.15, 1.19)	1.16 (1.05, 1.28)	1.17 (1.15, 1.19)
Model 2: Demographic + Socioeconomic	1.14 (1.13, 1.17)	1.16 (1.05, 1.28)	1.15 (1.13, 1.17)
Model 3: Demographic + Socioeconomic + Lifestyle	1.14 (1.12, 1.16)	1.15 (1.04, 1.27)	1.13 (1.11, 1.16)
Model 4: Demographic + Socioeconomic + Lifestyle + Health	1.03 (1.02, 1.05)	1.06 (0.95, 1.17)	1.03 (1.01, 1.05)

Abbreviations: CI Confidence Interval, *HR* Hazard Ratio, *WHI-CT* Women's Health Initiative Clinical Trials, *WHI-OS* Women's Health Initiative Observational Study; [a] Demographic characteristics include WHI component (WHI-CT, WHI-OS), region of residence [Midwest, Northeast, South, West], age [in years], race [American Indian/Alaska Native, Asian, Native Hawaiian/Other Pacific Islanders, Black, White, More than one race, Unknown/Not reported], ethnicity [Hispanic, non-Hispanic, Unknown/Not reported], marital status [Married/Partnered, Single, Divorced, Widowed]. Socioeconomic characteristics include education [less than high school, high school, some college, completed college or higher level], occupation [managerial/professional, technical/sales/administrative, service/labor, homemaker, other, not working/Retired/Disabled, unknown/not reported], household income [< $20,000, $20,000-$49,999, $50,000-$99,999, ≥ $100,000, unknown/not reported], and neighborhood socioeconomic status (tertiles). Lifestyle characteristics include smoking status [Never Smoker, Past Smoker, Current Smoker], alcohol consumption [Non-Drinker, Former Drinker, < 1 drink/week, ≥ 1 drink/week], the 2015 Healthy Eating Index (HEI-2015), and physical activity [Metabolic equivalent-hours/week]. Health characteristics include body mass index (kg/m^2), history of bone fracture (Yes, No), number of comorbid conditions (0, 1–2, 3 +), depressive symptoms score, self-rated health [Excellent/Very Good/Good, Fair/Poor]), and current healthcare provider (Yes, No)

Discussion

Women currently constitute the fastest growing segment among military veterans in the US, and this trend has been attributed to improved opportunities for women within the military [29, 41]. In this longitudinal study, we analyzed data on 135,790 WHI participants and estimated prevalence rates of arthritis at 47.5%, 53.8%, and 47.4%, among the overall, veteran, and non-veteran groups of postmenopausal women. Given that the burden of arthritis increases with age, it is plausible that ~ 50% of postmenopausal women, 50 to 79 years of age, would be diagnosed with arthritis, with prevalence rates considerably higher than those of adults (21.2%), women (20.9%) and veterans (24.2%) in the US [4–6]. The study used logistic regression, Cox regression and multistate Markov modeling to analyze these data. Consistent with previous studies [1], the unadjusted model showed increased odds of prevalent arthritis among veteran

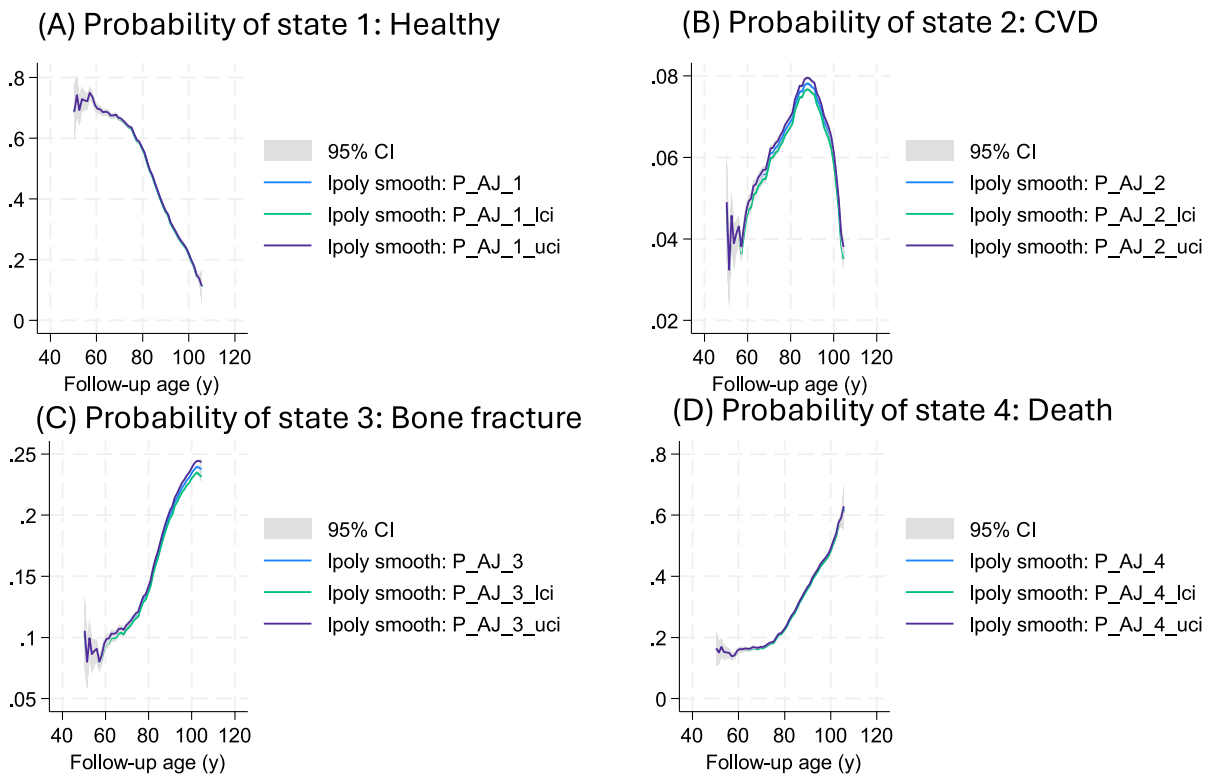

Fig. 3 Multistate survival probability – probability of being in each of four states (healthy [state 1], cardiovascular disease [state 2], bone fracture [state 3], death [state 4]) over time – women's health initiative

women, but this relationship between veteran and arthritis statuses at baseline became non-significant in a fully-adjusted model. A total of 15 characteristics were identified as key correlates of arthritis among non-veteran women, compared to 5 characteristics among veteran women. Beyond age, key correlates of arthritis were primarily health-related among veterans. Prevalent arthritis was unrelated to bone fracture risk among veteran and non-veteran women but was related to CVD and all-cause mortality risks in fully-adjusted models involving non-veteran women. Six transitions between the four states (Transition 1 (healthy to CVD), Transition 2 (healthy to bone fracture), Transition 3 (healthy to death), Transition 4 (bone fracture to CVD), Transition 5 (CVD to death), Transition 6 (bone fracture to death)) were identified. Significant differences in transition probabilities over time were observed according to arthritis status for transitions between the healthy state and CVD, and between bone fracture and death. The significant arthritis-by-veteran status interaction effect for transitioning between bone fracture and death suggests that veteran women may exhibit resilience against poor prognosis after a bone fracture possibly because of a phenomenon referred to as the "healthy soldier effect" [42] – lower morbidity and mortality risks among active duty and retired military personnel compared to the general population – or because of better lifestyle, including diet and physical activity, among veteran *vs.* non-veteran postmenopausal women potentially counteracting the adverse health consequences of arthritis.

Our findings indicate that veteran and non-veteran women differed by demographic, socioeconomic, lifestyle, and health characteristics. After adjusting for these characteristics, veteran status was not related to prevalent arthritis. Previous studies have established that veterans differ from their non-veteran counterparts with regard of health trajectories over the lifespan, in part because there are a multitude of background characteristics that can influence entering the military and also because stressful exposures associated

Table 5 Multistate Markov modeling for arthritis with and without interaction effects by veteran status as a predictor of transitions between a healthy state and all-cause death through cardiovascular disease and bone fracture in the Women's Health Initiative, controlling for demographic, socioeconomic, lifestyle, and health characteristics at enrollment (1993—1998) ($n = 135{,}790$)[a]

	HR	95% CI	P
Transition 1:			
Model I:			
Arthritis status	1.11	1.08, 1.14	< 0.0001
Model II:			
Arthritis status	1.11	1.08, 1.14	< 0.0001
Veteran status	1.04	0.93, 1.16	0.43
Arthritis status x Veteran status	0.93	0.81, 1.07	0.32
Transition 2:			
Model I:			
Arthritis status	1.02	0.98, 1.07	0.27
Model II:			
Arthritis status	1.03	0.98, 1.07	0.23
Veteran status	1.19	1.00, 1.40	0.04
Arthritis status x Veteran status	0.93	0.74, 1.17	0.54
Transition 3:			
Model I:			
Arthritis status	1.02	0.99, 1.05	0.07
Model II:			
Arthritis status	1.02	0.99, 1.05	0.08
Veteran status	1.02	0.91, 1.14	0.74
Arthritis status x Veteran status	1.04	0.89, 1.20	0.64
Transition 4:			
Model I:			
Arthritis status	1.06	0.93, 1.21	0.34
Model II:			
Arthritis status	1.07	0.94, 1.22	0.33
Veteran status	1.28	0.79, 2.06	0.31
Arthritis status x Veteran status	0.93	0.50, 1.71	0.81
Transition 5:			
Model I:			
Arthritis status	0.97	0.93, 1.02	0.22
Model II:			
Arthritis status	0.97	0.93, 1.01	0.18
Veteran status	1.01	0.84, 1.21	0.91
Arthritis status x Veteran status	1.10	0.88, 1.39	0.39
Transition 6:			
Model I:			
Arthritis status	1.08	1.01, 1.15	0.03
Model II:			
Arthritis status	1.09	1.02, 1.16	0.01
Veteran status	1.10	0.87, 1.39	0.41
Arthritis status x Veteran status	0.73	0.52, 0.99	0.05

Abbreviations: BMI Body mass index, *CI* Confidence Interval, *HEI-2015* 2015 Healthy Eating Index, *HR* Hazard Ratio, *WHI-CT* Women's Health Initiative Clinical Trials, *WHI-OS* Women's Health Initiative Observational Study, *Note:* Transition 1 (healthy → cardiovascular disease), Transition 2 (healthy → bone fracture), Transition 3 (healthy → death), Transition 4 (bone fracture → cardiovascular disease), Transition 5 (cardiovascular disease → death), Transition 6 (bone fracture → death). [a] All models were adjusted for WHI component (WHI-CT *vs.* WHI-OS), region of residence (Midwest, Northeast, South, West), age (years), race (White *vs.* other groups), occupation (Not working/Retired/Disabled vs. other groups), household income (≥ $100,000 *vs.* other groups), smoking status (never smoker, past smoker, current smoker), BMI (kg/m^2), history of bone fracture (Yes *vs.* No), number of comorbid conditions (≥ 1 *vs.* 0), self-rated health (Fair/Poor *vs.* Excellent/Very Good/Good), current healthcare provider (Yes *vs.* No), as well as HEI-2015, physical activity, and depressive symptoms scores

with military service are known to lead to deleterious health outcomes, as described elsewhere [28, 30, 32]. The burden of arthritis is rising in the US, particularly among military veterans [1]. Based on analyses of the Musculoskeletal Disorders Cohort (MSD) which consists of 5,237,763 patients receiving Veterans Health Administration healthcare services with diagnosed arthritis, joint, back, and neck disorders, the most common MSD diagnoses were non-traumatic joint disorder (27%), back disorder (25%), and OA (21%) [43]. A higher prevalence of arthritis reported, in the literature, among veterans *vs.* non-veterans may have been masked in the WHI because only postmenopausal women were included, a group with a high burden of arthritis resulting in a ceiling effect. Using data from the 2017–2021 CDC Behavioral Risk Factor Surveillance System, the prevalence of diagnosed arthritis was estimated among veterans and non-veteran men and women [1]. For men 18–44 years of age, veterans had twice the prevalence of arthritis as compared to non-veterans, whereas for men aged 45–64 years, being a veteran was associated with 30% higher arthritis prevalence [1]. Women veterans aged 18–44 years had 60% higher arthritis prevalence, while women veterans aged 45–64 years had 20% higher arthritis prevalence, than their non-veteran counterparts [1].

We also observed a positive relationship of prevalent arthritis with increased risks of CVD and all-cause mortality as well as transitions involving these two states consistent with studies generally focused on arthritis [4–7], RA [37, 39] and OA [7], although these studies were not specifically focused on postmenopausal women or on disparities by veteran status. A study of postmenopausal women from the WHI examined the relationships of arthritis with bone fracture, and after ~ 7.80 years of follow-up, a total of 24,137 fractures had occurred, with age-adjusted fracture rates being highest among the RA group, intermediate in the OA group, and lowest in the non-arthritic group [44]. Unlike that study, we did not identify a strong relationship between prevalent arthritis and bone fracture risk, especially after controlling for background characteristics. This counter-intuitive finding may be explained by adjustment for a history of bone fractures which may have attenuated the hypothesized relationship.

The distinct patterns among veteran and non-veteran groups of postmenopausal women in the transition probabilities from bone fracture to all-cause death according to arthritis status is consistent with the idea that these two groups may differ from each other in terms of behaviors (alcohol consumption [33], physical activity [34], sedentary time [34], depressive symptoms [15], sleep [15, 16]), symptoms (fatigue [15], pain [15], vasomotor symptoms [45]), as well as morbidity (diabetes [16], CVD [16], bone density and fracture [30], physical function [15], cognitive function [32], successful, effective, and optimal aging [29]), and mortality [31, 33, 46] outcomes, as reported in previous analyses of WHI data. Furthermore, it is plausible that a better health profile among veterans may be protective against transitions observed among non-veterans, although it is also plausible that veterans have other vulnerabilities that may outweigh the impact of arthritis on these transitions, especially with respect to prognosis after bone fracture.

A strength of this study is the comprehensive assessment among all WHI participants at enrollment, enabling the evaluation of a wide range of risk/protective characteristics as correlates of prevalent arthritis as well as adjustment for confounders of hypothesized relationships. In addition, the WHI study findings can be generalized to postmenopausal women residing in diverse geographical areas within the US. However, this study also has several limitations. First, a subset of the WHI population was used for performing these secondary analyses potentially leading to selection bias. Second, information bias is likely since data collected at enrollment and later follow-up times were mostly self-reported, although other data sources consisted of direct measurement, adjudication with medical records, or the National Death Index. Third, residual confounding remains a concern for this observational study. Fourth, the role of chance in analyses stratified by veteran status cannot be ruled out, given that the number of veteran women was considerably less than that of non-veteran women. Sample size limitations also precluded our ability to distinguish risk/protective characteristics and outcomes associated with RA and OA. Finally, WHI participants were volunteers at clinical centers who met eligibility criteria for the WHI-CTs or the WHI-OS, restricting our ability to generalize study findings to younger females of diverse racial/ethnic background.

In conclusion, among postmenopausal women, prevalent arthritis was associated with greater probabilities of transitioning from a healthy state to CVD and from bone fracture to death, with worse prognosis

after bone fracture among those who did not serve in the military. Larger studies are needed that can disentangle the respective roles of RA and OA in different CVD and bone fracture subtypes as well as all-cause mortality risks among veteran and non-veteran postmenopausal women.

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Author contributions Conception and design: HAB, MAB, JW, RB, JT. Analysis and interpretation of the data: HAB, MAB. Drafting of the article: HAB, MAB. Critical revision of the article for important intellectual content: All authors. Final approval of the article: All authors. Provision of study materials or patients: JWW. Statistical expertise: HAB, MAB, JW. Obtaining of funding: Not applicable. Administrative, technical, or logistic support: HAB, JT. Collection and assembly of data: HAB, MAB, JWW.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request and approval from the Women's Health Initiative.

Declarations

Conflicts of interest The authors declare no conflicts of interest.

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