Assessing the Roles of Demographic, Social, Economic, Environmental, Health-Related, and Political Factors on Risk of Osteoporosis Diagnosis among Older Adults

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Abstract

Purpose: The study provides a comprehensive assessment of how determinants of health across demographic, psychological, mobility-related, health, environmental, and economic domains are associated with the diagnosis of osteoporosis and tests three hypotheses, including: 1) a diverse set of variables across domains will predict osteoporosis, 2) chronic inflammation as a result of stress (represented by high-sensitivity C-reactive protein) will not be associated with osteoporosis, and 3) the model developed will have high accuracy in predicting osteoporosis.

Methods: Logistic regression and Cox proportional hazards models of osteoporosis diagnosis were estimated using data from 14,792 and 13,169 participants (depending on model) in the 2012–2016 waves of the Health and Retirement Study, including the Biomarker Study, the Contextual Data Resource, and validated measures of childhood socio-economic status. Predictive accuracy was assessed using k-Nearest Neighbors Discriminant Analysis.

Results: Demographic, environmental, and health-related factors were associated with osteoporosis diagnosis, and predictive accuracy of the models was good. High-sensitivity C-reactive protein was not associated with osteoporosis diagnosis.

Conclusion: Social determinants identified indicate access to health care, inequalities in the greater social environment (e.g., access to resources), and overall health (i.e., underlying medical conditions) are key components for developing osteoporosis and indicate underlying health inequities in this sample. There is a need to further address the interplay between primary health care and social determinants of health.

Mini Abstract

Chronic stress from social/environmental pressures has been proposed to affect bone health through increased inflammation. We demonstrate that inflammation from prolonged stress does not cause changes to bone health through inflammation but instead impacts access to health care, social inequalities, and overall health, which in turn impact bone health.

Keywords

social determinants of health; bone health; biomarkers; longitudinal analysis; aging

Importance of Understanding Osteoporosis Determinants

Osteoporosis leads to more than 2 million factures in the United States each year [1], and older women (50+) are particularly susceptible. These fractures lead to morbidity, mortality, and increased health care spending [1]. The annual cost related to fractures in the United States was estimated at 57 billion dollars for 2018 and is forecasted to rise to 95 billion dollars by the year 2040 [2]. These costs may be further increased by individuals impacted by accelerated aging. Therefore, it is important from economic and quality of life perspectives to identify and quantify the risk factors that affect osteoporosis in order to implement preventative measures and reduce the risk of developing disease.

Accelerated aging is associated with the development of advanced age-related diseases [3], such as cardiovascular disease (CVD) [4]. Aging and accelerated aging are linked to increased inflammation, which leads to the development of advanced age-related disease and/or mobility limitations in a process known as "inflammaging" [5]. More specifically, increased inflammation as measured through high sensitivity C-reactive protein (hs-CRP) has been linked to increased risk for CVD and osteoporosis [6], although findings have been mixed on the nature of this latter relationship, as others have reported increased hs-CRP as protective of bone mineral density [BMD; 7]. Our study investigates determinants across six domains (demographic, psychological, mobility-related, health, environmental, and economic) that are associated with increased inflammation and/or the development of osteoporosis, using a conceptual model derived from the social epidemiological literature (Fig. 1). Our approach is relatively unique, incorporating a wide range of contexts to examine bone health.

The underlying premise behind this conceptual model is that various social and environmental factors can lead to biological changes in the body that then have cascading consequences. For example, social position and social inequality are posited to promote chronic stress exposure [8]. Similarly, social adversity is hypothesized to influence health and disease through social and physical environments, behaviors, and psychosocial stress and cognitive processes [4]. These mechanisms may then provoke a biological response that eventually leads to health problems or disease [4]. Barr [8] describes how the experience of stress from a variety of sources causes a hypothalamic-pituitary-adrenal (HPA) axis response. This reaction can lead to both acute and chronic stress responses in the body, the combination of which is considered allostatic load. A rise in allostatic load then can lead

to a chronic increase in stress hormones, which precipitate physiologic injury, such as an increase in inflammatory biomarkers [8].

The final step in the conceptual figure is the link to osteoporosis diagnosis. Riancho and Brennan-Olsen [10] conceptualize osteoporotic fracture risk as an outcome of lifestyle, risk factors, and the aforementioned inflammatory state that arises from the chronic stress response. Thus, theoretically we might expect to see direct effects of some exposure mechanisms on risk of osteoporosis, along with indirect effects operating through inflammatory processes, the consequences of which can be measured through inflammatory biomarkers. However, recent empirical research draws into question the existence of a true causal link between inflammatory biomarkers and osteoporosis, as opposed to a confounding relationship [11–13].

In the osteoporosis literature, there is a lack of research examining associations between mobility measures, long-term exposure to pollutants, childhood socioeconomic status, and allostatic load. Here, we endeavor to estimate the role of six domains (demographic, psychological, mobility-related, health, environmental, and economic) in the development of osteoporosis, along with more commonly investigated risk factors. We hypothesize that: 1. A wide variety of variables across all domains will be predictive of osteoporosis diagnosis; 2. Net of the factors tested in Hypothesis 1, and consistent with recent research, chronic inflammation (as a result of prolonged stress), as measured by hs-CRP, will not be associated with increased risk of osteoporosis diagnosis; and 3. After accounting for variables across all domains, the model will have a strong capacity to predict osteoporosis diagnosis.

Data and Methods

Data

The data come from the 2012–2016 waves of the Health and Retirement Study (HRS) (the years for which osteoporosis diagnosis is available). We combine data from the RAND Longitudinal File[1] with additional variables from the Core Interviews (including the osteoporosis indicator) and data from the sensitive health Biomarker studies, the restricted Contextual Data Resource (CDR), and validated measures of childhood socio-economic status [14]. The RAND HRS Longitudinal file is data derived from all waves of the HRS. It contains cleaned and processed variables, that are largely harmonized across waves, from the Core and Exit Interviews of the HRS. RAND-developed variables cover demographics, health insurance, family structure, health, mobility, economic, and other factors [15, 16]. In each wave half of the sample has biomarker data collected for the Biomarker Study. For example, one half had biomarker data collected in 2012 and the other half in 2014; 2012–2016 Biomarker Study data are used. Finally, we include data from the CDR to provide contextual information. We use data from the Decennial Census and American Community Survey data files [17], the EPA-derived pollution files [18, 19], and the Uniform Crime Report files [20]. The sample includes all respondents between the ages of 50 and 90 for

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[1]The RAND HRS Longitudinal File is an easy-to-use dataset based on the HRS core data. This file was developed at RAND with funding from the National Institute on Aging and the Social Security Administration.

whom data are available (N = 14,792 [model without hs-CRP] and 13,169 [model with hs-CRP]). The research in this paper was determined to be exempt by the University of La Verne Institutional Review Board.

Variables

The dependent variable is osteoporosis diagnosis, which is a binary variable taking a value of 1 if the respondent reports being told by a doctor that they have osteoporosis and 0 otherwise. The independent variables were identified based on theory and prior research and then narrowed down using a combination of Spearman correlations and change-in estimate variable selection methods [21]. The change-in estimate method evaluates the change in the main predictor variable's coefficient, and variables that impact it by 10% or more (which are confounders) are retained in the model. This approach has been shown to be excellent at identifying confounders [21], which were an important part of our modeling process. The variables selected from this routine are discussed, below.

Demographic and socioeconomic variables include age (continuous), sex (binary male/ female), race and ethnicity (1-White, 2-Black, 3- Some other race/ethnicity, the latter of which could not be disaggregated due to sample size), household income (continuous), and mother's education level (continuous; in years). These come from the RAND Longitudinal file, with the exception of race and ethnicity, which also incorporates the HRS Restricted Race data. In addition, the Cox proportional hazards model incorporates marital status (measured as: married/cohabiting, separated/divorced, widowed, never married), and education (measured as: less than high school, GED, high school graduate, some college, and college or more). The Cox model also contains two variables specific to the respondent's childhood: the number of household adults [measured as lived with both parents (biological) = 0, lived with both parents (one biological) = .1, had both parents but did not live together = .2, did not have both parents = .3; , 14], and maternal investment [measured effort, teaching, and attention by mother; , 14], which represents the quality of the respondent's relationship with their mother [14].

To understand which potential health-related factors could be predictors for osteoporosis, health behaviors and health condition variables were obtained from the RAND Longitudinal data and Biomarker study data. For mental health, we use the respondent's score on the Center for Epidemiological Studies Depression Scale that measures depressive symptoms (continuous) and a question asking if the respondent has psychological problems (0- No, 1- Yes). For health behaviors, the respondent's alcohol consumption was measured through the number of alcoholic drinks a respondent consumed on a given day. Respondents were also asked about current or previous health problems measured categorically: heart problems (0- No, 1- Yes) and arthritis (0-No, 1-Yes). Health characteristics include the respondent's weight (recorded in kilograms) and several measures that collectively represent a measure of allostatic load. Allostatic load is measuring using an index created by the authors, and partially based on McCrory et al. [22], that ranges from 0–8. A value of 1 is assigned when the respondent has a value greater than the 75th percentile for each of the following variables: systolic blood pressure, diastolic blood pressure, pulse, total cholesterol, hs-CRP, A1c, Cystatin C; or has waist circumference greater than 35 inches for women or 40 inches

for men. We then sum across each of these to get the index score. To measure access to health care, we include whether the respondent is covered by Medicare (0- No, 1- Yes). Finally, to evaluate overall health, a measure of the number of times respondents spent the night in the hospital over the prior two years is used. Cox models also incorporate a measure of self-reported health (measured continuously, ranging from excellent to poor) and a categorical measure of diabetes created by the authors (0= no diabetes, 1=diabetes with medication, 2=diabetes with no medication).

Mobility and measures of activity were obtained from the RAND Longitudinal dataset. Most of these variables are measured continuously as indices. The Activities of Daily Living Index summarizes the respondent's difficulty with performing daily tasks such as bathing, eating, dressing, walking across a room, and getting in or out of bed. The Instrumental Activities of Daily Living Index summarizes the respondent's difficulty with using a telephone, taking medication, and handling money. The Change in Gross Motor Skills Index is the change in the respondent's difficulty with walking one block, walking across the room, climbing one flight of stairs, and bathing. The following mobility variables are measured categorically: the respondent's difficulty with sitting for two hours (0- No, 1- Yes) and difficulty getting up from a chair (0- No, 1- Yes). Cox models also include the Mobility Index (index of difficulty walking one block, walking several blocks, walking across a room, climbing one flight of stairs, and climbing several flights of stairs) and the Large Muscle Index (index of difficulty sitting for two hours, getting up from a chair, stooping or kneeling and crouching, and pushing or pulling a large object).

Environmental factors span measures of demographic, air pollution, and crime data for the respondent's area in which they lived at the time of data collection. The first measure is the percent of non-Hispanic Black/African American residents living in the respondent's county; this comes from the US Decennial Census and American Community Survey component of the CDR. The percent of non-Hispanic White residents living in the respondent's county is also included. The following measures come from HRS-CDR Pollution: Mean O_3 (ozone) for April, Mean O_3 for November, and Mean PM 2.5 for March. The Cox model also includes Mean O_3 for the second (April-June) and third (July-September) quarters, Mean PM 2.5 for February, and the annual count of rapes by county, which comes from the HRS-CDR Uniform Crime Report data.

To look at inflammation's relationship to osteoporosis, some models include measures of hs-CRP; hs-CRP is measured in two ways: high-low hs-CRP and high-medium-low hs-CRP. High hs-CRP is defined as hs-CRP greater than 3 mg/dl [e.g., 23]. In the tri-level version of hs-CRP, low hs-CRP is less than 1 mg/dl and medium hs-CRP is between 1 mg/dl and 3 mg/dl [24]. Values of hs-CRP greater than 10 mg/dl are dropped, as they indicate probable underlying medical conditions [25].

Analytic Strategy

Two statistical approaches were employed to examine the six variable domains' associations with osteoporosis. Because osteoporosis diagnosis is a binary outcome variable, we estimate logistic regression models, which provide odds ratios for a positive osteoporosis diagnosis for each predictor variable. The logit was evaluated with McFadden's Pseudo R^2. To

examine age-dependency of a positive osteoporosis diagnosis, we also estimate Cox proportional hazards models. Cox regression is a semi-parametric survival analysis that estimates the hazard of a positive osteoporosis diagnosis for each covariate. Age at survey, irrespective of age at which osteoporosis was diagnosed, is the time scale variable. As these are longitudinal panel data, we include a variable to denote wave. The Cox model calculates the cumulative hazard for receiving a positive osteoporosis diagnosis at a specific age (time t) as shown in Equation 1:

$$h(t) \ = \ h(t_0)\exp(b_1 X_1 + b_2 X_2 + \ldots b_p X_p)$$

(1)

In this equation $h(t)$ is the expected hazard at a certain age and $h(t_0)$ is the baseline at birth (when all covariates are zero). The proportionality assumption of the Cox model that assumes the covariates' effect on survival (i.e., living without osteoporosis) is constant over time was evaluated using a test of the Schoenfeld residuals. Both the logit and Cox models were examined for multicollinearity via the variance inflation factor (VIF). Kaplan-Meier survival plots were also produced and log-rank tests examined sex differences within osteoporosis diagnosis status.

The HRS uses a complex survey sampling design, so we estimate our models using appropriate survey sampling methodology (sample stratum, sample PSU, and weights), instituting the *svy* commands in Stata 16.0 and the survey package [26] in R [27]. Missing data is addressed using listwise deletion for those variables with small amounts of missing data. Finally, we use k-Nearest Neighbors Discriminant Analysis (k-NNDA, k=3), which is a nonparametric machine learning algorithm that sorts observations into clusters utilizing neighboring data values and using Mahalanobis distances derived from the pooled covariance matrix. k-NNDA assessed the prediction accuracies of the independent variables selected in the logit and Cox models using cross-validation [28] in SAS 9.4.

Results

The original sample prior to application of statistical modeling, less missing strata and zero weights, was 18,900 (Supplementary Information Table 1). Survey-weighted descriptive statistics for the analytic sample are shown in Table 1. Approximately 8% of the sample reported an osteoporosis diagnosis. About 38% of the sample has moderate hs-CRP levels, while 26% has high hs-CRP levels. More than 80% of the sample identifies as White, with 10% identifying as Black/African American, and 6% identifying as some other race/ethnicity. The survey-weighted descriptive statistics for the Kaplan-Meier plots and log-rank tests can be found in Supplementary InformationTable 1.

Results for the logit models are shown in Table 2. Model 1 (without hs-CRP as a predictor) has a McFadden's pseudo R^2 value of 0.19, indicating a very good model fit [29]. Examining demographic and economic factors first, the results show that female respondents have a much higher odds ratio for reporting an osteoporosis diagnosis. By contrast, individuals identifying as Black/African American have a much lower odds ratio for reporting an osteoporosis diagnosis compared to those reporting a White race/ethnicity.

All other demographic variables and the only economic variable (total household income) are confounders.

Turning next to mental/physical health/health behaviors/medical coverage, having a higher score on the CESD (indicative of worse depressive symptoms) and reporting psychological problems are associated with higher odds of an osteoporosis diagnosis. Further, if the respondent reported having arthritis they also have significantly increased odds of reporting an osteoporosis diagnosis. Higher weight in kilograms and higher allostatic load are associated with a lower odds ratio for reporting an osteoporosis diagnosis; the significance of allostatic load is probably driven by the inclusion of waist circumference in the index. Conversely, a greater number of hospital stays in the prior two years is associated with a higher odds ratio for reporting an osteoporosis diagnosis, as is Medicare coverage compared to no Medicare coverage. All other health/health behavior variables are confounders.

Focusing on the mobility variables, a higher score on the ADL index (indicating greater difficulty with ADLs) is associated with a higher odds ratio for reporting an osteoporosis diagnosis, while a higher IADL score yields a lower odds ratio for reporting an osteoporosis diagnosis. Difficulty getting up from a chair on one's own increases odds of reporting an osteoporosis diagnosis. The remaining mobility variables are confounders.

We also examine contextual variables related to where the respondent lived. A higher level of ozone exposure in April is associated with increased risk of reporting an osteoporosis diagnosis. Other contextual variables, including mean ozone for November, mean PM 2.5 for March, percent non-Hispanic Black in the respondent's county, and percent non-Hispanic White in the respondent's county are confounders. The k-NNDA accuracy of the same independent variables is 77.31%.

Models 2 and 3 present results with binary hs-CRP and tri-level hs-CRP as predictors. The hs-CRP variables are not significant predictors of osteoporosis in either model, contrary to some expectations in the literature, but in support of recent research and our second hypothesis. The k-NNDA accuracies are 77.06% and 76.93%, respectively.

Results for the Cox models are shown in Table 3. In Model 4, without CRP as a predictor, females have a higher hazard ratio than males, consistent with the logit models. Identifying as a member of a race/ethnicity other than White or Black/African American is associated with a higher hazard ratio of reporting osteoporosis diagnosis. For education, compared to having less than a high school education, those with more education have an increased hazard of reporting an osteoporosis diagnosis. In terms of family background variables, having a good quality relationship with one's mother is associated with a reduced hazard ratio for an osteoporosis diagnosis. Compared to being married or cohabiting, widowed respondents have a lower hazard of reporting an osteoporosis diagnosis. Family structure during childhood (number of adults in the household) is a confounder of osteoporosis diagnosis.

For health-related variables, worse self-reported health is associated with a greater hazard of reporting an osteoporosis diagnosis, as is a higher CESD score, the latter of which is consistent with the logit model results. Respondents who reported a diabetes diagnosis and

taking medication for their diabetes have a lower hazard ratio for osteoporosis diagnosis than those without a diabetes diagnosis. Consistent with the logit models, arthritis displays an increased hazard of reporting an osteoporosis diagnosis. Other health- and mobility-related variables, including number of alcoholic drinks, the mobility index, the large muscle index, and ADLs are confounders of osteoporosis.

Finally, for the variables describing the context in which the respondent lived, similar to the logit model results, ozone exposure for the second quarter (April-June) generates a higher hazard ratio for reporting an osteoporosis diagnosis, while PM 2.5 for February is associated with a lower hazard. Other variables related to the context in which the respondent lived, including mean ozone for the third quarter (July-September), and the annual count of rapes at the county level are confounders. The prediction accuracy from k-NNDA is slightly lower than the logit models: 74.33%.

Models 5 and 6 present results with binary and tri-level hs-CRP as predictors. hs-CRP is not a significant predictor of reporting an osteoporosis diagnosis in either model. However, controlling for CRP does modestly attenuate the results for a few variables. The VIF for all models was less than 10. k-NNDA accuracy is 74.09% and 74.12%, respectively.

The Kaplan-Meier survivorship plots (Figs. 2 & 3) show that in the sample of respondents without osteoporosis, females live longer after about the age of 60 (Fig. 2). Alternatively, in the sample with osteoporosis, males live dramatically longer than females, starting at around age 55 (Fig. 3). In comparison to one another, the sample with osteoporosis displays increased survivorship over the sample without osteoporosis, starting at age 55 in both sexes (Figs. 2 & 3). Log rank tests indicate these trends between the sexes are significant (Fig. 2: χ = 80.6596, p-value = <0.0001; Fig. 3: χ^2 = 305.9969, p-value = <0.0001).

Discussion

Accelerated aging was examined for osteoporosis outcomes, using social determinants of health. We find support for all three hypotheses. We investigated the role of inflammation in influencing osteoporosis, showing that hs-CRP does not play a role in increasing the odds/hazards ratios of diagnosis with osteoporosis net of demographic, health-related, and other factors. Instead, logit models point to sex, psychological and physical health, Medicare coverage, and ozone exposure as potential contributors to being diagnosed with osteoporosis at any age. Cox models, which elicit age-dependent information, also point to race/ethnicity and respondent education as predictors of osteoporosis. Thus, determinants across several domains are important predictors of osteoporosis diagnosis. The predictive accuracy of the final models is good.

The prevalence of osteoporosis in our analytic sample from the HRS is 7.8%, which is low in comparison to other studies focused on the United States [e.g., 30, 31], irrespective of demographics. Limiting the HRS sample to people who identify as Non-Hispanic White, the most commonly reported sub-group, results in a prevalence of 9.64%, which aligns well with the nationally representative NHANES 2017–2018 (33: 12%) and NHANES 2005–2006 (34: 10%) samples, years that closely pre-date and post-date our sample. The

HRS sample reported here is nationally representative not only for people identifying as Non-Hispanic White, but also for a broad range of racial and ethnic groups, which provides greater insight into social determinants influencing risk of osteoporosis diagnosis in the American population. It is further insightful for other populations by providing a framework of how various risk factor domains affect bone health.

Consistent with prior literature, sex is important to explaining osteoporosis diagnosis; women lose BMD at a higher rate and earlier age compared to men and have a four times higher risk of developing osteoporosis compared to men [32]. While our Kaplan-Meier plots show that males in our sample living with osteoporosis survive longer than females living with it (the opposite of the pattern for those without osteoporosis), the sample with osteoporosis is predominately female (88.33%), as younger males with fatal medical conditions or who reached the end of their lifespan likely already exited the sample due to death, leaving more robust males remaining. Likewise, females are older in the sample with osteoporosis as younger individuals were removed from the sample via death or dropout. This provides a unique opportunity to examine survivorship in males living to older ages and provides novel insight into what risk factors affect their probability of developing osteoporosis.

Aligned with our current findings, prior research indicates that osteoporosis is less common among Black/African Americans as compared to individuals who identify as White, Hispanic, or Asian American [33]; one study found the highest risk to be among Asian Americans [33]. Moreover, access to preventative measures and treatment of osteoporosis differs by race/ethnicity [34], which is likely reflected in the significant coefficients in both the logit and Cox models. Further, the literature indicates higher education levels are protective over bone density [35], but our results demonstrate the opposite pattern: those with at least a GED have a higher risk of osteoporosis diagnosis than those without a high school education. Not surprisingly, evidence for the relationship between BMD and education level is not strong. Other work has noted this trend and suggested understanding it requires a cohort study examining changes in SES (including education) over time [35]. Our study does this to some extent with household income and educational attainment, still yielding similar results.

In terms of childhood socioeconomic environment and the life course, one predictor (maternal investment) is significant in the Cox model, indicating an age-dependency component. Childhood socioeconomic advantage (defined as educational level of male and female heads of household, welfare status, and childhood financial status) displays varied results in the literature; it is positively associated with lumbar spine BMD, but not femoral [36]. When adult attainment was added to a model with childhood advantage, childhood advantage's significance was reduced [36]. In this study, the Cox model has a highly significant p-value for the measure of maternal investment when evaluated with adult education level in the same model, which is a strong result in a longitudinal sample and demonstrates childhood and adulthood SES are important factors for osteoporosis risk. Specifically for childhood environment, increased maternal investment is protective.

Somewhat surprisingly, widowed respondents in our sample have a lower hazard of reporting an osteoporosis diagnosis in the Cox model after accounting for age and other important characteristics, although their unadjusted level of osteoporosis diagnosis is higher. However, a descriptive analysis of widowed respondents (Supplementary Information Table 2) indicates that despite them being much older on average and having slightly worse health, they are advantaged in ways that may offset their risk factors after accounting for age, including higher levels of positive social support, better self-rated health, and greater social engagement.

Turning to health, worse self-reported health is associated with a higher hazard of an osteoporosis diagnosis and taking diabetic medication as a diabetes patient is protective over bone health in the Cox model. In a previous study, researchers found that a high self-reported frailty score was associated with low calcaneal BMD among a community dwelling elder population [37]. For mental health, a higher CESD score and psychological problems are associated with higher risk of reporting an osteoporosis diagnosis in our sample, which is consistent with other research [38]. A greater number of hospital stays means higher odds of osteoporosis diagnosis in our sample, likely due to comorbidities with osteoporosis and stays due to osteoporotic fracture, which are costly both clinically and economically [1, 2].

In our sample, respondents with Medicare coverage have a higher risk for osteoporosis diagnosis compared to respondents not covered by Medicare. King and Fiorentino [39] found that cuts to Medicare Part B in 2007 impeded access to DXA scans. In 2011, the Patient Protection and Affordable Care Act (ACA) removed some barriers to getting DXA scans [1], making them more accessible. The change in Medicare likely introduced heterogeneity in the dataset, and subsequently our analysis, for respondents falling under the different provisions. Further complicating matters for osteoporosis patients with Medicare, among Medicare beneficiaries who suffered from frailty fractures, little attention has been given to osteoporosis after fractures take place, and treatment is even lower in select subpopulations with an overall low level of care [40].

For mobility, difficulty on the Activities of Daily Living Index and getting up from a chair are associated with an increased risk for osteoporosis, though difficulties on the Instrumental Activities of Daily Living Index are associated with reduced risk. Individuals with osteoporosis have difficulty with mobility [41], as it affects the bony microstructure and weakens the cancellous bone. It is therefore expected that we issues with mobility would be detected in our sample of patients living with osteoporosis, and that there may be heterogeneous relationships.

The impact by the physical environment, i.e., air pollution, is minimal with only mean ozone for April (and the second quarter) yielding an increased odds ratio for reporting an osteoporosis diagnosis. By contrast, in the Cox model, greater PM 2.5 exposure in February is associated with a lower hazard of reporting an osteoporosis diagnosis. Research indicates that ozone [42], among other types of air pollution, is detrimental to bone health, probably due to decreased vitamin D uptake, which may be the mechanism for increased risk of osteoporosis from pollution exposure. Air pollution may also limit the amount of time individuals spend outside, thus increasing risk of vitamin D deficiency in a second way [42].

The results of PM 2.5 are not surprising given the mixed nature of other studies' findings [43]. Further, the temporal component is February, a month where few people are spending time outside to have exposure to PM 2.5. Therefore, this information, combined with the larger, but still significant *p*-value, suggests this finding may be spurious.

Neither the logit nor the Cox models show a significant predictive relationship between hs-CRP and osteoporosis diagnosis. While it was long established that hs-CRP was linked to bone remodeling via interleukin 6 (IL-6) [44], and associated with osteoclastogenesis, osteoclastic activity, and reduced osteoclastic apoptosis [45], recent research shows this relationship is flawed [12] and hs-CRP is likely a confounder and not a causal predictor [13]. hs-CRP inhibits osteoblast and osteoclast differentiation [12], causing effects that cancel one another out. More specifically, Mendelian randomization of genetic data finds no causal relationship between hs-CRP and BMD [11].

The main limitation of the study is the measurement of the outcome variable. Osteoporosis diagnosis is an important condition to explore, but diagnosis can only occur through interaction with the health care system. Thus, individuals without access to health care may not know they have osteoporosis. As mentioned earlier, screening and treatment rates for osteoporosis are low, even among those with a prior fracture. Thus, our outcome measure likely underestimates the true proportion of the HRS with osteoporosis. Studying objectively measured BMD may provide additional insights with regard to the role of variables across the six domains studied for osteoporosis risk, but these data are not available in most longitudinal surveys in the United States. Similarly, our self-reported health variable may not have captured undiagnosed medical conditions, which would bias our estimates of the relationship between self-reported health and osteoporosis and underestimate the impact of poor self-rated health on osteoporosis diagnoses. In other words, our estimate of the odds of poor self-rated health as a risk factor for developing osteoporosis is a minimum value. Further, our race/ethnicity variable lacked the resolution to divide it into more meaningful categories due to sample size. Finally, some of the predictor variables are measured in less precise ways than is ideal. For example, the arthritis variable does not distinguish between osteoarthritis and rheumatoid arthritis, and the measure of diabetes does not distinguish between Type 1 and Type 2. Nonetheless, this study offers one of the first comprehensive examinations of the role of a wide range of social determinants for osteoporosis diagnosis among older adults.

This study utilized a social epidemiological approach to examine the social determinants that potentially cause accelerated aging and may be associated with osteoporosis. A variety of predictors were identified that indicate access to health care, inequalities in the greater social environment (e.g., access to resources), and overall health (i.e., underlying medical conditions) are the most important factors for receiving an osteoporosis diagnosis and indicate underlying health inequities in this sample. Our analysis supports the need to address the interplay between primary health care and social determinants of health together.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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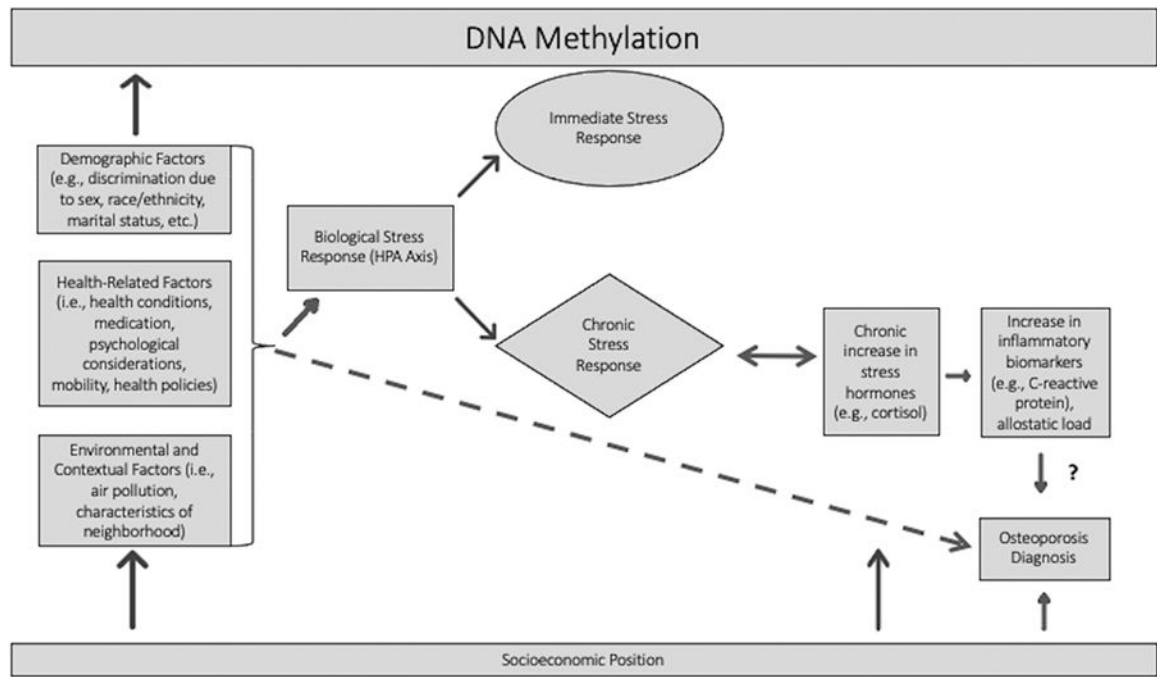
Fig. 1.
Conceptual Model derived from Barr [8], Gough and Godde [9], Kubzansky [4], and Riancho and Brennan-Olsen [10]
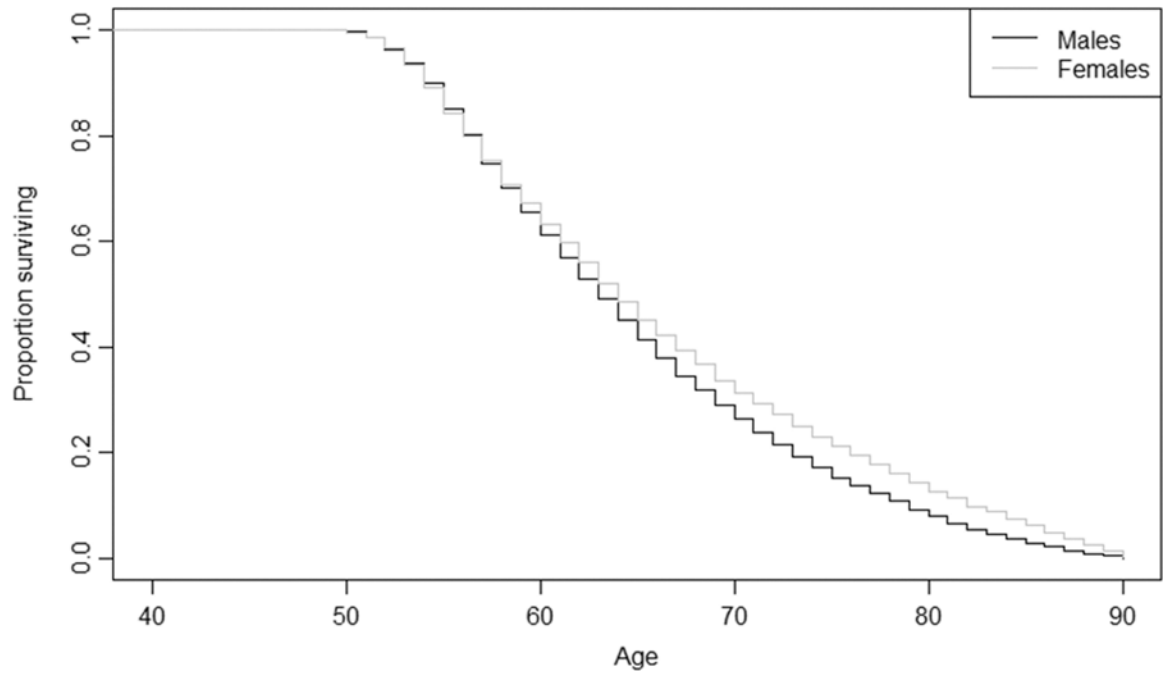
Fig. 2.
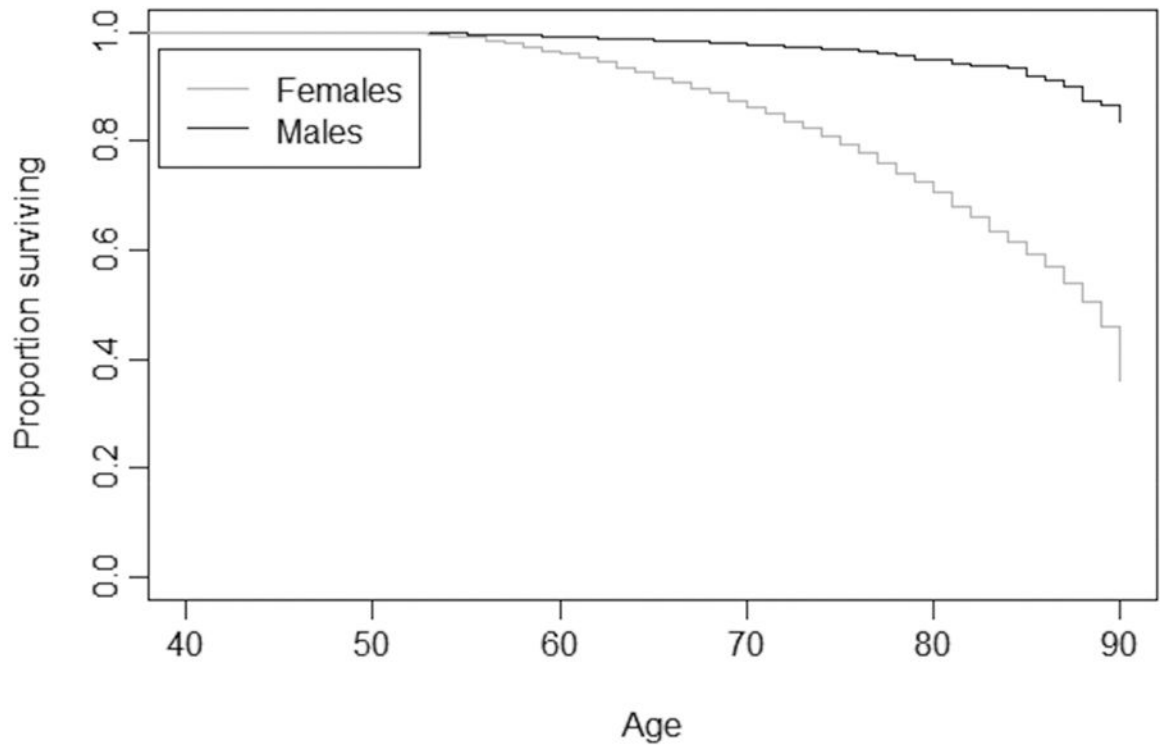Kaplan-Meier Survivorship Plot for Sex Differences in Respondents without Osteoporosis

Fig. 3.
Kaplan-Meier Survivorship Plot for Sex Differences in Respondents with Osteoporosis

TABLE 1

Descriptive Statistics for Analytic Sample without and with hs-CRP

Variable	Without hs-CRP		With hs-CRP	
	Mean (SE)/ Proportion	N	Mean (SD)/ Proportion	N
Osteoporosis- Yes	0.078	14,792	0.078	13,169
Osteoporosis- No	0.922	14,792	0.922	13,169
Sex- Female	0.512	14,792	0.508	13,169
Age	65.673 (0.261)	14,792	65.705 (0.272)	13,169
Race/Ethnicity				
Black/African American	0.096	14,792	0.088	13,169
Another Race/Ethnicity	0.063	14.729	0.063	13,169
Respondent's Mother's Education Level	10.688 (0.091)	14,792	10.715 (0.088)	13,169
Total Household Income	92040.81 (2711.999)	14,792	94702.72 (2881.841)	13,169
Center for Epidemiological Studies Depression Scale	1.267 (0.025)	14,792	1.213 (0.024)	13,169
Psychological Problems- Yes	0.193	14,792	0.189	13,169
# of Alcoholic Drinks	0.954 (0.024)	14,792	0.965 (0.024)	13,169
Heart Problems- Yes	0.227	14,792	0.221	13,169
Arthritis- Yes	0.570	14.792	0.562	13,169
Weight in Kilograms	83.64 (0.238)	14,792	82.806 (0.231)	13,169
Allostatic Load	2.168 (0.021)	14,792	2.122 (0.022)	13,169
Number of times respondent spent night in the hospital	0.388 (0.012)	14,792	0.359 (0.011)	13,169
Covered by Medicare- Yes	0.507	14,792	0.502	13,169
Activities of Daily Living Index	0.236 (0.008)	14,792	0.211 (0.008)	13,169
Instrumental Activities of Daily Living Index	0.095 (0.005)	14,792	0.088 (0.004)	13,169
Change in Gross Motor Skills Index	0.075 (0.007)	14,792	0.069 (0.008)	13,169
Difficulty Sitting for Two Hours- Yes	0.183	14,792	0.174	13,169
Difficulty Getting Up from a Chair- Yes	0.353	14,792	0.339	13,169
Mean Ozone for April	46.086 (0.160)	14,792	46.115 (0.162)	13,169
Mean Ozone for November	31.518 (0.144)	14,792	31.536 (0.145)	13,169
Mean PM 2.5 for March	8.693 (0.070)	14,792	8.690 (0.071)	13,169
Proportion Non-Hispanic Black	0.119	14,729	0.118	13,169
Proportion Non-Hispanic White	0.683	14,729	0.687	13,169
Wave 11	0.371	14,792	0.374	13,169
Wave 12	0.371	14,792	0.320	13,169
Wave 13	0.313	14,792	0.305	13,169
High sensitivity C-reactive protein (mg/dl)				
Moderate: greater than 1–3			0.377	13,169
High: greater than 3			0.257	13,169

TABLE 2

Logistic regression models of osteoporosis diagnosis

McFadden Pseudo R^2: 0.19

Variable	Model 1: No hs-CRP (N=14,792)		Model 2: With binary hs-CRP (N=13,169)		Model 3: With tri-level hs-CRP (N=13,169)	
	Odds Ratio (95% CI)	p	Odds Ratio (95% CI)	p	Odds Ratio (95% CI)	p
Sex- Female	5.8885 (4.5990, 7.5395)	<0.001	6.3028 (4.888, 8.1272)	<0.001	6.2714 (4.8608, 8.0914)	<0.001
Age	1.0062 (0.9943, 1.0183)	0.3158	1.0049 (0.9931, 1.0168)	0.4270	1.0048 (0.993, 1.0167)	0.4344
Race/Ethnicity						
Black/African American	0.6151 (0.4598, 0.8230)	0.0027	0.6272 (0.4546, 0.8653)	0.0081	0.6279 (0.4548, 0.867)	0.0086
Another Race/Ethnicity	0.8758 (0.6268, 1.2238)	0.4432	0.9099 (0.6568, 1.2605)	0.5743	0.9095 (0.6565, 1.26)	0.5731
Respondent's Mother's Education Level	0.9992 (0.9802, 1.0186)	0.9356	0.9993 (0.9785, 1.0206)	0.9492	0.9995 (0.9788, 1.0207)	0.9649
Total Household Income	0.9999 (0.9999, 1.0000)	0.3672	0.9999 (0.9999, 1.0000)	0.2713	0.9999 (0.9999, 1.0000)	0.2780
Center for Epidemiological Studies Depression Scale	1.0485 (1.0124, 1.0859)	0.0126	1.0518 (1.0101, 1.0953)	0.0208	1.0519 (1.0103, 1.0952)	0.0206
Psychological Problems- Yes	1.31159 (1.0894, 1.5894)	0.0079	1.3508 (1.1056, 1.6504)	0.0064	1.3517 (1.107, 1.6506)	0.0062
# of Alcoholic Drinks	0.9614 (0.8938, 1.0342)	0.2994	0.9242 (0.8574, 0.9961)	0.0484	0.9245 (0.8575, 0.9967)	0.0502
Heart Problems- Yes	1.062 (0.8708, 1.2953)	0.5569	1.0576 (0.8611, 1.299)	0.5973	1.0575 (0.8611, 1.2986)	0.5979
Arthritis- Yes	2.1600 (1.7527, 2.6619)	<0.001	2.1054 (1.7047, 2.6002)	<0.001	2.1041 (1.7044, 2.5976)	<0.001
Weight in Kilograms	0.9821 (0.9772, 0.9869)	<0.001	0.9809 (0.9752, 0.9866)	<0.001	0.9806 (0.9749, 0.9865)	<0.001
Allostatic Load	0.8810 (0.8331, 0.9317)	<0.001	0.8901 (0.8372, 0.9464)	<0.001	0.8883 (0.835, 0.945)	<0.001
Number of Times Respondent Spent Night in the Hospital	1.0954 (1.0384, 1.1555)	0.0022	1.1173 (1.0512, 1.1876)	<0.001	1.1173 (1.0513, 1.1874)	0.0013
Covered by Medicare- Yes	1.4085 (1.0336, 1.9193)	0.0381	1.4104 (1.0503, 1.894)	0.0297	1.4128 (1.0527, 1.8961)	0.0289
Activities of Daily Living Index	1.2080 (1.1092, 1.3157)	<0.001	1.2027 (1.0855, 1.3326)	<0.001	1.2036 (1.0868, 1.3329)	0.0014
Instrumental Activities of Daily Living Index	0.7910 (0.6577, 0.9512)	0.0185	0.7495 (0.6122, 0.9177)	0.0092	0.7504 (0.6133, 0.9183)	0.0094
Change in Gross Motor Skills Index	0.9988 (0.9094, 1.0969)	0.9799	1.0118 (0.9065, 1.1294)	0.8351	1.0115 (0.9061, 1.1292)	0.8397
Difficulty Sitting for Two Hours- Yes	1.0690 (0.8860, 1.2897)	0.4918	1.0729 (1.0499, 1.0963)	0.5284	1.0707 (0.8628, 1.3285)	0.5404
Difficulty Getting Up from a Chair- Yes	1.3320 (1.1168, 1.5887)	0.0033	1.3640 (1.1219, 1.6583)	<0.001	1.3626 (1.1213, 1.6558)	0.0043
Mean 03 for April	1.0312 (1.0086, 1.0543)	0.0108	1.0355 (1.0121, 1.0594)	0.0056	1.0354 (1.0121, 1.0594)	0.0058
Mean 03 for November	1.0059 (0.9857, 1.0265)	0.5718	1.0022 (0.9838, 1.021)	0.8168	1.0023 (0.9839, 1.0211)	0.8082
Mean PM2.5 for March	0.9858 (0.9515, 1.0212)	0.4330	0.9828 (0.9466, 1.0204)	0.3721	0.9834 (0.9473, 1.0208)	0.3871
Percent Non-Hispanic Black in County	1.1124 (0.5620, 2.2016)	0.7619	0.8575 (0.4434, 1.6584)	0.6513	0.8550 (0.4421, 1.6536)	0.6453
Percent Non-Hispanic White in County	1.0742 (0.8195, 1.4081)	0.6081	1.0856 (0.8338, 1.4133)	0.5467	1.0842 (0.8331, 1.4110)	0.5521

Variable	Model 1: No hs-CRP (N=14,792)		Model 2: With binary hs-CRP (N=13,169)		Model 3: With tri-level hs-CRP (N=13,169)	
	Odds Ratio (95% CI)	p	Odds Ratio (95% CI)	p	Odds Ratio (95% CI)	p
Wave	0.5449 (0.4985, 0.5957)	<0.001	0.5531 (0.4997, 0.6122)	<0.001	0.5537 (0.5006, 0.6125)	<0.001
High-Sensitivity C-reactive Protein (mg/dl) - Greater than 3			0.9056 (0.7161, 1.1453)	0.4147		
High-Sensitivity C-reactive Protein (mg/dl)						
Greater than 1 – 3					1.0549 (0.8996, 1.2370)	0.5157
Greater than 3					0.9357 (0.7239, 1.2097)	0.6163

TABLE 3

Cox proportional hazards model results with osteoporosis diagnosis as the outcome variable and age-at-wave the time scale

Variable	Model 1: No hs-CRP (N=11,206)		Model 2: With binary hs-CRP (N=10,024)		Model 3: With tri-level hs-CRP (N=10,024)	
	Hazard Ratio (95% CI)	p	Hazard Ratio (95% CI)	p	Hazard Ratio (95% CI)	p
Sex - Female	7.4335 (5.8046, 9.5196)	<0.0001	8.2340 (6.2223, 10.9121)	<0.0001	8.2400 (6.2174, 10.9206)	<0.0001
Race/Ethnicity						
Black/African American	0.7781 (0.5479, 1.1051)	0.1612	0.7975 (0.5519, 1.1523)	0.2282	0.7969 (0.5517, 1.1511)	0.2263
Another Race/Ethnicity	1.4309 (1.0529, 1.9446)	0.0221	1.4351 (1.0609, 1.9411)	0.0191	1.4343 (1.0606, 1.9397)	0.0192
Education Level						
GED	1.9150 (1.2773, 2.8709)	0.0017	1.8493 (1.2136, 2.8179)	0.0042	1.8452 (1.2107, 2.8123)	0.0044
High School Grad	1.3288 (1.0429, 1.6931)	0.0214	1.2389 (0.9604, 1.5981)	0.0992	1.2375 (0.9575, 1.5995)	0.1034
Some College	1.6164 (1.2679, 2.0607)	0.0001	1.4960 (1.1716, 1.9102)	0.0012	1.4947 (1.1687, 1.9115)	0.0014
College and Above	1.6601 (1.2948, 2.1285)	<0.0001	1.5325 (1.1911, 1.9718)	0.0009	1.5297 (1.1864, 1.9725)	0.0010
Marital status						
Separated/Divorced	0.9853 (0.8058, 1.2048)	0.8850	0.9604 (0.7624, 1.2098)	0.7318	0.9610 (0.7621, 1.2118)	0.7365
Widowed	0.4929 (0.4297, 0.5654)	<0.0001	0.4710 (0.4054, 0.5471)	<0.0001	0.4710 (0.4056, 0.5470)	<0.0001
Never Married	0.7715 (0.5001, 1.1902)	0.2409	0.7592 (0.4919, 1.1717)	0.2135	0.7592 (0.4920, 1.1715)	0.2132
Family Structure: Number of Household Adults during Childhood	1.7114 (0.9776, 2.9959)	0.0600	1.6540 (0.9299, 2.9419)	0.0868	1.6558 (0.9319, 2.9422)	<0.0001
Maternal Investment	0.6876 (0.5830, 0.8110)	<0.0001	0.7031 (0.5943, 0.8319)	<0.0001	0.7029 (0.5940, 0.8318)	<0.0001
Self-Reported Health	1.1055 (1.0237, 1.1938)	0.0105	1.0916 (0.9996, 1.1920)	0.0512	1.0917 (0.9997, 1.1921)	0.0511
Center for Epidemiological Studies Depression Scale	1.0813 (1.0467, 1.1171)	<0.0001	1.0881 (1.0489, 1.1287)	<0.0001	1.0877 (1.0484, 1.1286)	<0.0001
Diabetes						
Yes and take medication	0.6147 (0.4830, 0.7823)	<0.0001	0.5913 (0.4542, 0.7696)	<0.0001	0.5916 (0.4548, 0.7694)	<0.0001
Yes and do not take medication	1.0074 (0.7842, 1.2942)	0.9541	1.0897 (0.8180, 1.4516)	0.5571	1.0885 (0.8147, 1.4542)	0.5664
Arthritis: Yes	1.3219 (1.0769, 1.6227)	0.0076	1.3177 (1.0724, 1.6191)	0.0086	1.3177 (1.0726, 1.6188)	0.0086
# of Alcoholic Drinks	1.0340 (0.9389, 1.1386)	0.4963	1.0290 (0.9306, 1.1379)	0.5779	1.0291 (0.9309, 1.1377)	0.5759
Mobility Index	0.9538 (0.8925, 1.0193)	0.1634	0.9549 (0.8901, 1.0243)	0.1969	0.9549 (0.8902, 1.0244)	0.1973
Large Muscle Index	1.0635 (0.9930, 1.1391)	0.0783	1.0672 (0.9923, 1.1476)	0.0801	1.0676 (0.9927, 1.1481)	0.0780
Activities of Daily Living Index	0.9993 (0.9099, 1.0974)	0.9881	0.9614 (0.8604, 1.0742)	0.4864	0.9612 (0.8604, 1.0737)	0.4838
Mean O3 for Second Quarter (April-June)	1.0344 (1.0133, 1.0559)	0.0013	1.0381 (1.0170, 1.0597)	0.0004	1.0381 (1.0172, 1.0595)	0.0003

Variable	Model 1: No hs-CRP (N=11,206)		Model 2: With binary hs-CRP (N=10,024)		Model 3: With tri-level hs-CRP (N=10,024)	
	Hazard Ratio (95% CI)	p	Hazard Ratio (95% CI)	p	Hazard Ratio (95% CI)	p
Mean O3 for Third Quarter (July - September)	0.9890 (0.9736, 1.0046)	0.1673	0.9868 (0.9712, 1.0026)	0.1009	0.9869 (0.9715, 1.0025)	0.1010
Mean PM 2.5 February	0.9731 (0.9477, 0.9992)	0.0429	0.9716 (0.9475, 0.9963)	0.0249	0.9715 (0.9473, 0.9964)	0.0249
Annual Count of Rapes by County	1.0001 (0.9999, 1.0002)	0.1365	1.0001 (0.9999, 1.0002)	0.0689	1.0001 (0.9999, 1.0003)	0.0686
Wave	0.5591 (0.0539, 0.6204)	<0.0001	0.5618 (0.5440, 0.5802)	<0.0001	0.5617 (0.4980, 0.6335)	<0.0001
High-Sensitivity C-reactive Protein (mg/dl) - Greater than 1–3			0.8814 (0.7187, 1.0808)	0.2130		
High-Sensitivity C-reactive Protein (mg/dl)						
Greater than 1 – 3					0.9818 (0.8409, 1.1462)	0.8156
Greater than 3					0.8727 (0.6936, 1.0980)	0.2451