Published in final edited form as:

J Psychosom Res. 2010 December 1; 69(6): 549–554. doi:10.1016/j.jpsychores.2010.04.018.

A Moderator-Mediator Analysis of Coronary Heart Disease Mortality

Robert D. Keeley, MD, MSPH and Margaret Driscoll, MSM

Denver Health Medical Center, Denver, CO

Department of Family Medicine, University of Colorado Health Sciences Center, Aurora, CO

Abstract

Objective—To better understand how risk factors for Coronary Heart Disease (CHD) mortality may interact.

Methods—We conducted a moderator-mediator analysis of a representative national sample of 5,027 and 2,902 community-dwelling women and men in the first National Health and Nutrition Examination Survey free of CHD in 1982. The outcome was 10-year CHD mortality.

Results—267 subjects experienced CHD mortality. In the complete sample, gender moderated the effect of depressive symptoms, and among women race-ethnicity moderated the effect of nonleisure activity on CHD mortality, defining 3 subgroups for further analysis: men, white women, and black/ other women. Among men, baseline differences from median age (55 to 64 years), systolic blood pressure (129 to 158 mmHg), or self-rated general health (“good” to “poor”) were associated with equivalent increases in 10-year CHD mortality from 2.3% to 5.3% (Area-under-the-curve effect size (ES)=.53). These factors appeared to mediate the effect of education on CHD mortality. *Severe depression* in men was associated with higher 10-year CHD mortality than less or no depression, 10.0% versus 2.5% (ES =.55). Among white women, increasing baseline age (from median 51 to 65 years) was also associated with 10-year mortality (1.2% to 13.4%, ES =.56), as was higher blood pressure (from median 125 to 151 mm Hg) or worse self-rated health (from median “very good” to “fair”) to a lesser extent (1.2% to 3.5%, ES =.51).

Conclusion—Moderators (gender, race-ethnicity) defined possible pathways to CHD mortality characterized by varying factors and interactions between factors, highlighting potential utility for targeted interventions among community-dwelling persons.

Keywords

CHD-related mortality; depression; moderator-mediator analysis

© 2010 Elsevier Inc. All rights reserved.

Address correspondence and requests for reprints to: Robert D. Keeley, MD, MSPH, Department of Family Medicine, University of Colorado-Denver Health Sciences Center and Denver Health, Wellington Webb Primary Care Center, 301 W. 6th Ave, Denver, CO 80204; (303) 602-8080 [phone]; (303) 602-8176 [fax]; or Robert.Keeley@ucdenver.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Elucidating how risk factors interact over time may facilitate targeting and tailoring interventions to improve outcomes. For instance, while depressive symptoms have been associated with poor cardiovascular outcomes (1–6), Ferketich et al. noted they may be associated with higher risk for men than women (7). Among women, an interaction between race and increasing body mass index may lead to higher mortality for whites than blacks (8). To better understand how risk factors interact, we conducted a moderator-mediator analysis (9,10) of coronary heart disease (CHD) related mortality in a sample of U.S. adults.

Based upon previous studies, we hypothesized that gender and race-ethnicity are moderators, and non-leisure activity a possible mediator, of CHD mortality. Specifically, we hypothesized that: 1. depressive symptoms would be differentially associated with increased CHD mortality in men relative to women; 2. higher BMI would also be associated with CHD mortality more among white than black women (7,8,11); and 3. effects of depressive symptoms on CHD mortality would appear to be mediated by non-leisure activity (12).

METHODS

Sample and Study Design

The First National Health and Nutrition Survey (NHANES I) is a multistage, stratified, national probability sample of non-institutionalized persons aged 1 to 74 years conducted between 1971 and 1974 (13,14) that has been analyzed in many longitudinal studies of mortality (7,15). Of this original cohort, 14,407 adults were included in the 1982 NHANES I Epidemiologic Follow-up Survey. Participants completing 1982 Center for Epidemiologic Studies Depression scale (CES-D) data were eligible (5,947 women and 3,560 men), and were followed through 1992. Those reporting a history of a heart condition, heart attack, or angina (920 women and 658 men) were excluded, leaving 5,027 women and 2,902 men for analysis.

Outcome – 10-year CHD Mortality

Was ascertained with the National Death Index and through tracing of vital status via proxy interview. ICD-9 codes 410 to 414 defined CHD-related deaths (13).

Possible Independent Variables

Based upon theory and literature review, we selected 9 *domains* with a total of 39 possible risk factors for CHD mortality: 1. *Socio-demographic*: age, gender (16), race-ethnicity (white, black, other), marital status, poverty index, rural-urban area, education (16–18); 2. *Health-related behaviors*: alcohol and tobacco use, leisure and non-leisure time activity (19,20); 3. *Morbidity*: diabetes, hypertension; 4. *Pain*: neck-back, joint, leg; (19,21) 5. *Self-rated health states*: depressive symptoms (continuous and dichotomized) (22,23), anxiety, general health (24,25); 6. *Laboratory*: serum cholesterol, hemoglobin, sedimentation rate, albumin, uric acid, iron and binding capacity, and urinary albumin and glucose (26–29); 7. *Medications*: aspirin, diuretic, any blood pressure medication; 8. *Anthropomorphic*: systolic and diastolic blood pressure, height and weight, body mass index (continuous and categorized) (15); 9. *Dietary*: Vitamin A, C, and coffee/ tea intake.

Moderator-mediator analysis (30–35)

We organized possible risk factors by time and then by domain, then selected factors with a univariate association with CHD mortality (Spearman $R \geq .10$ and $P < .01$). For subsequent *overlapping*, *proxy*, *moderator* and *mediator* analyses, CHD mortality was the dependent variable; the two risk factors of interest and their interaction were independent factors. If

both main effects or the interaction were significant for correlated factors (Spearman $R \geq .20$, $P < .01$) we considered the factors *overlapping* (same time slot) or *mediated/mediating* (across time), versus *proxy* or *moderating/moderated* for uncorrelated factors. *Overlapping* preceded *proxy* analyses within, and then across domains, leaving independent risk factors in each time slot. *Proxy* risk factors noted within-domain were set aside from across-domain analyses. When a moderator was noted, the dataset was split by subgroups defined by the moderator, and the above exploratory process repeated within each subgroup (30).

Data Management

Descriptive statistics were generated with PROCs SURVEYFREQ and SURVEYMEANS, and logistic regression analyses with SURVEYLOGISTIC in SAS version 9.1 (SAS, Carey, IN). We accepted a two-tailed $P < .01$ as significant during the moderator-mediator analysis, and $P < .05$ for the final multivariate logistic regression models and for area-under-the-curve clinical effect sizes (ES) (36,37). All analyses were weighted and nested with independent variables centered (38).

RESULTS

Characteristics of the Participants (Table 1)

Over 10 years of follow-up, 267 (3.4%) of 7929 participants experienced CHD mortality (138 women and 129 men).

Risk Factors for CHD Mortality-Complete Sample

Age, systolic blood pressure, self-rated health, and cholesterol were associated with CHD mortality. Gender apparently moderated the effect of depressive symptoms (interaction $est = .03$, $P = .003$) or of severe depression (CES-D score ≥ 23 (39), interaction $est = .60$, $P < .0001$) (Table 2-**Model 1**). Relative to having severe depression, men with less or no depression experienced lower CHD mortality (2.5% versus 10.0% (weighted percent)), while their female counterparts had somewhat higher mortality (2.4% versus .9%) (40). The ES for severe depression was higher for men ($ES = .54$ (95% CI .52, .56, small)) than for women ($ES = .49$ (95% CI .48, .51, null)).

Male Subgroup

Age, blood pressure, severe depression, self-rated health, and educational attainment were associated with CHD mortality. No within-domain analyses surfaced. In across-domain analyses, age, blood pressure, and self-rated health overlapped (Table 2-**Model 2**) (30,41). Adjustment for non-leisure activity (12,42) did not substantially decrease the OR for severe depression ($OR = 3.1$ (95% CI 1.1, 8.5) without, and $OR = 2.9$ (95% CI 1.1, 8.1) with activity).

The overlapping variable appeared to completely mediate the effect of education (overlapping variable $est = 1.01$, $P < .000$; educational years $est = -.03$, $P = .64$; interaction $est = -.005$, $P = .86$, $n = 2835$, $c\text{-statistic} = .85$). Higher educational attainment correlated with younger baseline age (Spearman $R = -.38$), lower blood pressure ($R = -.21$), and better self-rated health ($R = -.36$). No further moderators emerged.

Female subgroups

After identifying the independent within-time risk factors, the across-time analyses revealed that race-ethnicity apparently moderated the effect of leisure-time activity on CHD mortality, and the interaction remained significant after adjustment for age and BMI (43) (interaction white vs black $est = .36$, $P = .006$, $c\text{-statistic} = .89$) (Table 2-**Model 3**).

A decrease in leisure-time activity among whites was associated with an increase in CHD mortality from .8% with “much” to 1.4% with “moderate”, to 4.4% with “little to none” activity. Among blacks, CHD mortality was 1.6% with “much”, 3.7% with “moderate”, and 2.9% with “little to none” activity. The complex interaction precluded dichotomization and ES calculation.

Among white women, systolic blood pressure and self-rated health overlapped, and age was independent (Table 2-**Model 4**). No apparent mediators were uncovered. Among 665 black and 46 “other” race-ethnicity women there were 22 CHD-related deaths, halting further subgroup analyses.

DISCUSSION

The findings suggest that: a) gender was associated with two different pathways to CHD mortality; and b) for women, race-ethnicity was associated with two additional pathways to mortality (ie, gender and race are moderators). This is the first study to our knowledge to suggest that gender moderated the effect of depression on CHD mortality, with severe depression exerting a larger clinical effect in men relative to women.

While our hypothesis that race would moderate the effect of BMI on CHD mortality was not affirmed, race did appear to moderate a factor related to BMI, leisure-time activity level (44). Decreasing leisure-time activity was associated with greater CHD mortality for white, but not black, women. Our finding that, among men, non-leisure activity did not account for the association between depression and CHD differed from results of a study of subjects with heart disease (12), possibly due to substantial differences in the subject populations. Mediation analyses suggested the protective effect of educational attainment among men may be explained through baseline associations with lower age, higher self-rated health, and lower blood pressure (18,43). Education has been associated with healthful behaviors, e.g. hypertension treatment (18,45).

Study limitations are those common to datasets such as NHANES, including self-reported health states, and ascertainment of CHD mortality through death certificates. Strengths include carefully standardized methods, long follow-up, a large number of events, and mortality as end point (28). Setting the alpha at $P=.01$ during the moderator-mediator analysis limited the risk of Type I error due to multiple comparisons. Confirmatory moderator analyses in other datasets would be adequately powered to limit type II error, e.g. 80% power to detect the small moderating effect size of gender on depression with two-tailed alpha at $P=.05$. Maximizing power to detect moderators and mediators occurs with increasing the n , minority representation, and prevalences of risk factors and CHD events (46). External validity may be compromised by changes in the prevalence, recognition, and treatment of hypertension, depression, and hyperlipidemia since NHANES I.

CONCLUSIONS

Moderators (gender, race-ethnicity) defined possible pathways to CHD mortality characterized by varying factors and interactions between factors, thereby enhancing understanding of for whom specific risk factors may be most relevant. The proposed mediators and risk factors emerging from our study can be further tested in community-based trials that: a) increase educational attainment for men; b) screen for and treat severe depression among men age 36 to 74 years; and c) treat potentially modifiable causes of poor self-rated health for males and for white females, to potentially improve CHD mortality. Moderator-mediator analyses of datasets such as NHANES III with additional possible risk factors and greater representation of racial and ethnic subgroups are needed.

Acknowledgments

None reported.

Funding/Support: Funded in part by a grant from the National Institute of Mental Health (K23 MH082997) to Robert Keeley.

Bibliography

1. Aromaa A, Raitasalo R, Reunanen A, Impivaara O, Heliovaara M, Knekt P, Lehtinen V, Joukamaa M, Maatela J. Depression and cardiovascular diseases. *Acta Psychiatr Scand Suppl* 1994;377:77–82. [PubMed: 8053372]
2. Penninx BW, Beekman AT, Honig A, Deeg DJ, Schoevers RA, van Eijk JT, van Tilburg W. Depression and cardiac mortality: results from a community-based longitudinal study. *Arch Gen Psychiatry* 2001 Mar;58(3):221–227. [PubMed: 11231827]
3. Ahto M, Isoaho R, Puolijoki H, Vahlberg T, Kivela SL. Stronger symptoms of depression predict high coronary heart disease mortality in older men and women. *Int J Geriatr Psychiatry* 2007 Aug;22(8):757–763. [PubMed: 17133654]
4. Wassertheil-Smoller S, Shumaker S, Ockene J, Talavera GA, Greenland P, Cochrane B, Robbins J, Aragaki A, Dunbar-Jacob J. Depression and cardiovascular sequelae in postmenopausal women. The Women's Health Initiative (WHI). *Arch Intern Med* 2004 Feb 9;164(3):289–298. [PubMed: 14769624]
5. Penninx BW, Beekman AT, Honig A, al E. Depression and cardiac mortality: results from a community-based longitudinal study. *Arch Gen Psychiatry* 2001;58:221–227. [PubMed: 11231827]
6. Dickens C, McGowan L, Percival C, Tomenson B, Cotter L, Heagerty A, Creed F. New onset depression following myocardial infarction predicts cardiac mortality. *Psychosom Med* 2008 May;70(4):450–455. [PubMed: 18434496]
7. Ferketich AK, Schwartzbaum JA, Frid DJ, Moeschberger ML. Depression as an antecedent to heart disease among women and men in the NHANES I study. National Health and Nutrition Examination Survey. *Arch Intern Med* 2000 May 8;160(9):1261–1268. [PubMed: 10809028]
8. Abell JE, Egan BM, Wilson PW, Lipsitz S, Woolson RF, Lackland DT. Age and race impact the association between BMI and CVD mortality in women. *Public Health Rep* 2007 Jul–Aug;122(4):507–512. [PubMed: 17639654]
9. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986 Dec;51(6):1173–1182. [PubMed: 3806354]
10. Ware JH. The limitations of risk factors as prognostic tools. *N Engl J Med* 2006 Dec 21;355(25):2615–2617. [PubMed: 17182986]
11. Mendes de Leon CF, Krumholz HM, Vaccarino V, Williams CS, Glass TA, Berkman LF, Kas SV. A population-based perspective of changes in health-related quality of life after myocardial infarction in older men and women. *J Clin Epidemiol* 1998 Jul;51(7):609–616. [PubMed: 9674668]
12. Whooley MA, de Jonge P, Vittinghoff E, Otte C, Moos R, Carney RM, Ali S, Dowray S, Na B, Feldman MD, Schiller NB, Browner WS. Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease. *JAMA* 2008 Nov 26;300(20):2379–2388. [PubMed: 19033588]
13. Cox CS, Mussolino ME, Rothwell ST, Lane MA, Golden CD, Madans JH, Feldman JJ. Plan and operation of the NHANES I Epidemiologic Followup Study, 1992. *Vital Health Stat* 1 1997 Dec; (35):1–231. [PubMed: 9564279]
14. Miller HW. Plan and operation of the health and nutrition examination survey. United states--1971–1973. *Vital Health Stat* 1 1973 Feb;1–46. (10a).
15. Fang J, Wylie-Rosett J, Alderman MH. Exercise and cardiovascular outcomes by hypertensive status: NHANES I epidemiological follow-up study, 1971–1992. *Am J Hypertens* 2005 Jun;18(6):751–758. [PubMed: 15925731]

16. Mainous AG 3rd, King DE, Garr DR, Pearson WS. Race, rural residence, and control of diabetes and hypertension. *Ann Fam Med* 2004 Nov–Dec;2(6):563–568. [PubMed: 15576542]
17. Zajacova A. Education, gender, and mortality: does schooling have the same effect on mortality for men and women in the US? *Soc Sci Med* 2006 Oct;63(8):2176–2190. [PubMed: 16781036]
18. Fiscella K, Franks P. Should years of schooling be used to guide treatment of coronary risk factors? *Ann Fam Med* 2004 Sep–Oct;2(5):469–473. [PubMed: 15506583]
19. Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a prognostic index for 4-year mortality in older adults. *Jama* 2006 Feb 15;295(7):801–808. [PubMed: 16478903]
20. Wessel TR, Arant CB, Olson MB, Johnson BD, Reis SE, Sharaf BL, Shaw LJ, Handberg E, Sopko G, Kelsey SF, Pepine CJ, Merz NB. Relationship of physical fitness vs body mass index with coronary artery disease and cardiovascular events in women. *Jama* 2004 Sep 8;292(10):1179–1187. [PubMed: 15353530]
21. May M, Lawlor DA, Brindle P, Patel R, Ebrahim S. Cardiovascular disease risk assessment in older women - can we improve on Framingham?: British Women's Heart and Health prospective cohort study. *Heart*. 2006 Mar 17;
22. Sheehan TJ, Fifield J, Reisine S, Tennen H. The measurement structure of the Center for Epidemiologic Studies Depression Scale. *J Pers Assess* 1995 Jun;64(3):507–521. [PubMed: 7760258]
23. Watson D, Tellegen A. Toward a consensual structure of mood. *Psychol Bull* 1985 Sep;98(2):219–235. [PubMed: 3901060]
24. DeSalvo KB, Bloser N, Reynolds K, He J, Muntner P. Mortality prediction with a single general self-rated health question. A meta-analysis. *J Gen Intern Med* 2006 Mar;21(3):267–275. [PubMed: 16336622]
25. Chen YT, Miller PD, Barrett-Connor E, Weiss TW, Sajjan SG, Siris ES. An approach for identifying postmenopausal women age 50–64 years at increased short-term risk for osteoporotic fracture. *Osteoporos Int* 2007 Sep;18(9):1287–1296. [PubMed: 17464525]
26. Timmer JR, Ottervanger JP, Hoorntje JC, De Boer MJ, Suryapranata H, Van't Hof AW, Zijlstra F. Prognostic value of erythrocyte sedimentation rate in ST segment elevation myocardial infarction: interaction with hyperglycaemia. *J Intern Med* 2005 May;257(5):423–429. [PubMed: 15836658]
27. Natali A, L'Abbate A, Ferrannini E. Erythrocyte sedimentation rate, coronary atherosclerosis, and cardiac mortality. *Eur Heart J* 2003 Apr;24(7):639–648. [PubMed: 12657222]
28. Fang J, Alderman MH. Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971–1992. National Health and Nutrition Examination Survey. *Jama* 2000 May 10;283(18):2404–2410. [PubMed: 10815083]
29. Arant CB, Wessel TR, Olson MB, Bairey Merz CN, Sopko G, Rogers WJ, Sharaf BL, Reis SE, Smith KM, Johnson BD, Handberg E, Mankad S, Pepine CJ. Hemoglobin level is an independent predictor for adverse cardiovascular outcomes in women undergoing evaluation for chest pain: results from the National Heart, Lung, and Blood Institute Women's Ischemia Syndrome Evaluation Study. *J Am Coll Cardiol* 2004 Jun 2;43(11):2009–2014. [PubMed: 15172405]
30. Kraemer, HC.; Lowe, KK.; Kupfer, DJ. *To Your Health: How to Understand what Research Tells us About Risk*. Oxford: Oxford University Press; 2005.
31. Essex MJ, Kraemer HC, Armstrong JM, Boyce WT, Goldsmith HH, Klein MH, Woodward H, Kupfer DJ. Exploring risk factors for the emergence of children's mental health problems. *Arch Gen Psychiatry* 2006 Nov;63(11):1246–1256. [PubMed: 17088505]
32. Boyce WT, Essex MJ, Alkon A, Goldsmith HH, Kraemer HC, Kupfer DJ. Early father involvement moderates biobehavioral susceptibility to mental health problems in middle childhood. *J Am Acad Child Adolesc Psychiatry* 2006 Dec;45(12):1510–1520. [PubMed: 17135997]
33. Kraemer HC, Frank E, Kupfer DJ. Moderators of treatment outcomes: clinical, research, and policy importance. *Jama* 2006 Sep 13;296(10):1286–1289. [PubMed: 16968853]
34. Kraemer HC, Stice E, Kazdin A, Offord D, Kupfer D. How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *Am J Psychiatry* 2001 Jun;158(6):848–856. [PubMed: 11384888]

35. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and Moderators of Treatment Effects in Randomized Clinical Trials. *Arch Gen Psychiatry* 2002;59(10):877–883. [PubMed: 12365874]
36. Kraemer HC, Kupfer DJ. Size of treatment effects and their importance to clinical research and practice. *Biol Psychiatry* 2006 Jun 1;59(11):990–996. [PubMed: 16368078]
37. Kraemer HC. A simple effect size indicator for two-group comparisons? A comment on r equivalent. *Psychol Methods* 2005 Dec;10(4):413–419. [PubMed: 16392996]
38. Kraemer HC, Blasey CM. Centring in regression analyses: a strategy to prevent errors in statistical inference. *Int J Methods Psychiatr Res* 2004;13(3):141–151. [PubMed: 15297898]
39. Kirmayer LJ, Robbins JM, Dworkind M, Yaffe MJ. Somatization and the recognition of depression and anxiety in primary care. *Am J Psychiatry* 1993 May;150:734–741. [PubMed: 8480818]
40. Whisman MA, McClelland GH. Designing, testing, and interpreting interactions and moderator effects in family research. *J Fam Psychol* 2005 Mar;19(1):111–120. [PubMed: 15796657]
41. Wang TJ, Gona P, Larson MG, Tofler GH, Levy D, Newton-Cheh C, Jacques PF, Rifai N, Selhub J, Robins SJ, Benjamin EJ, D'Agostino RB, Vasan RS. Multiple biomarkers for the prediction of first major cardiovascular events and death. *N Engl J Med* 2006 Dec 21;355(25):2631–2639. [PubMed: 17182988]
42. Arrieta A, Russell LB. Effects of leisure and non-leisure physical activity on mortality in U.S. adults over two decades. *Ann Epidemiol* 2008 Dec;18(12):889–895. [PubMed: 19041587]
43. Everson-Rose SA, House JS, Mero RP. Depressive symptoms and mortality risk in a national sample: confounding effects of health status. *Psychosom Med* 2004 Nov–Dec;66(6):823–830. [PubMed: 15564345]
44. Barengo NC, Hu G, Lakka TA, Pekkarinen H, Nissinen A, Tuomilehto J. Low physical activity as a predictor for total and cardiovascular disease mortality in middle-aged men and women in Finland. *Eur Heart J* 2004 Dec;25(24):2204–2211. [PubMed: 15589637]
45. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, Magid DJ. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med* 2006 Sep 25;166(17):1836–1841. [PubMed: 17000939]
46. Aguinis H, Beaty JC, Boik RJ, Pierce CA. Effect size and power in assessing moderating effects of categorical variables using multiple regression: a 30-year review. *J Appl Psychol* 2005 Jan;90(1): 94–107. [PubMed: 15641892]

Table 1Baseline characteristics of the NHEFS participants by gender^a

Characteristics	% or Mean (SD [*])	
	Women (n = 5027)	Men (n=2902)
Age (years)	53.7 (13.9)	55.9 (14.4)
Black	10.8	10.7
Education (years)	11.5 (2.9)	11.5 (3.6)
Married	66.4	82.7
Separated, widowed, divorced	29.0	12.5
Never married	4.6	4.8
Diabetes	5.2	5.7
Hypertension	32.9	30.2
Current smoking	27.6	31.1
Self-rated general health	2.4 (1.1) (Very Good to Good)	2.4 (1.1) (Very Good to Good)
Systolic blood pressure	126.3 (19.6)	131.5 (18.5)
Non-leisure activity level	2.2 (.7) (Moderately active)	2.0 (.7) (Moderately active)
% of poverty line	262.8 (166.0)	297.2 (179.2)
Body mass index	26.1 (5.4)	26.5 (3.9)
Alcoholic drinks/ week (#)	1.3 (2.3)	2.4 (3.1)
Depressive symptom score (0–60) (CES-D score)	8.8 (8.6)	6.8 (7.1)
Probable major depression (CES-D≥16)	17.5	9.8
Severe depression (CES- D≥23)	7.2	4.1

* SD=Standard Deviation

^aValues are percentages, unless otherwise indicated

Table 2

Logistic Regression Models*

Multiple Logistic Regression	Estimate	Odds Ratio (95% CI)	P-Value
Model 1 Moderator interaction – men and women n=7785 ^a (256 CHD-related deaths)			
Intercept	−4.80		<.0001
Age	1.65		<.0001
Body mass index	.29		.001
Non-leisure activity level	−.012		.89
Severe depression (CES-D ≥23)	.12		.47
Male	.72		<.0001
Severe depression × male	.61		.0003
			c-statistic=.86
Model 2 Final model – men n=2853 ^b (126 CHD-related deaths)			
Intercept	−3.59		<.0001
Male overlap ^d	1.66	5.3 (95% CI 3.7, 7.6) AUC=.55 (small ES)	<.0001
Severe depression (CES-D ≥23)	1.19	3.3 (95% CI 1.2, 8.3) AUC=.55 (small ES)	.018
			c-statistic=.85
Model 3 Moderator interaction – women n=4935 ^e (134 CHD-related deaths)			
Intercept	−10.65		<.0001
Age	1.72		<.0001
Body mass index	.15		.22
Leisure-time activity level	−.48		.0007
Black	−.43		.067
Other race-ethnicity (reference white)	5.42		<.0001
Leisure-time activity*black	.36		.006
Leisure-time activity*other race-ethnicity	.66		<.0001
			c-statistic=.89
Model 4 Final model–white women n=4203 ^f (111 CHD deaths)			
Intercept	−5.56		<.0001
Age (median=51, SD=13.9)	1.63	5.1 (95% CI 3.7, 7.1) (AUC=.56, small ES)	<.0001
Blood Pressure-self-rated health overlap ^b	.39	1.5 (95% CI 1.2, 2.1) (AUC=.51, very small ES)	.003

Multiple Logistic Regression	Estimate	Odds Ratio (95% CI)	P-Value
			c-statistic=.90

Gender was not correlated with depressive symptoms (Spearman $R=-.06$).

Adjustment for age and functional impairment (non-leisure activity level and body mass index) (25) did not substantially alter the results of the moderator model

[^] Total subjects in the sample is 7929. n= 144 omitted due to missing data.

^a age (median 55 years, SD 14.4), systolic blood pressure (median 129 mmHg, SD 18.5), and self-rated general health (median 2 (very good), SD 1.1) form an overlapping variable. Self-rated health has anchors excellent, very good, good, fair or poor.

Increasing self-rated general health scores (range 1–5) represent worse self-rating.

Male overlap (centered) $= [(-3.77 + (1.33 * \text{age}) + (.52 * \text{SBP}) + (.28 * \text{Self-rated health}) - (.29 * \text{age} * \text{SBP})) + 3.59] / 1.66$.

An increase in SBP from median 129 to 188 mm Hg, or in age from median 55 to 73 years, while maintaining other overlapping factors at the median level, increases the overlap by 1 SD, and was associated with an increase in 10-year CHD mortality from 2.3% to 12.1%. Maximal decrease in Self-rated health from median “good” to “poor” was associated a 0.5 SD increase in the overlap variable, and with increased mortality from 2.3% to 5.3%.

[‡] total males in complete sample is 2902. N=49 omitted from analysis due to missing data.

Race-ethnicity (black versus white and other race-ethnicity) and leisure-time activity level were not correlated (Spearman $R=.07$).

Adjustment for age and body mass index did not substantially alter the results of the moderator model.

[¶] Total number of females in complete sample is 5027. n=92 omitted from analysis due to missing data

^b Systolic blood pressure (median 125 mm Hg, SD 20.4) and self-rated general health (median 2 (very good), SD 1.1) form an overlapping variable. Female overlap (centered) $= [(-4.39 + (.65 * \text{self-rated health}) + (.81 * \text{blood pressure}) - (.19 * \text{self-rated health} * \text{blood pressure})) + 4.42] / 1.03$

An increase in systolic blood pressure from median 125 to 150.9 mm Hg, or a decrease in self-rated health from median “very good” to “fair”, would increase the overlap by 1 SD, with associated change in mortality from 1.2% to 3.5%.

[§] Total number of females in subgroup is 4293. n=90 omitted from analysis due to missing data.

^{*} Ordinal variables centered at the median. Odds ratios and AUC effect sizes are calculated per 1 SD increase from median value.