International Journal of Preventive Medicine

Editorial Open Access

Race and Ethnic Differences in Additive and Multiplicative Effects of Depression and Anxiety on Cardiovascular Risk

Shervin Assari[1,2,3]

[1]Department of Psychiatry, School of Medicine, University of Michigan, Ann Arbor, MI, USA, [2]Center for Research on Ethnicity, Culture, and Health, University of Michigan School of Public Health, Ann Arbor, MI, USA, [3]Department of Health Behavior and Health Education, University of Michigan School of Public Health, Ann Arbor, MI, USA

Correspondence to:
Dr. Shervin Assari, Department of Psychiatry, School of Medicine, University of Michigan, 4250 Plymouth Rd, Ann Arbor, MI 48105, USA.
E-mail: assari@umich.edu

How to cite this article: Assari S. Race and ethnic differences in additive and multiplicative effects of depression and anxiety on cardiovascular risk. Int J Prev Med 2016;7:22.

Starting from the obvious, we all know that depression increases the risk of obesity[1] cardiovascular conditions,[2] other chronic medical conditions,[3] and dying from suicide.[4] Assuming that associations in health are universal and one size fits all, medical and public health literature has historically ignored the potential group differences in paths and mechanisms that cause health and illness, and also consequences of having a health condition.[5] Thus, much is still to be learned about potential variations in the associations across demographic and socio-economic groups.

The same is true for additive and multiplicative effects of anxiety and depression on cardiovascular health. Although we know that anxiety and depressive disorders are both bad for our health, we still need to learn more about how our group membership changes our vulnerability to additive and multiplicative effects of these risk factors!

There are some growing evidence regarding the contextual effects of race, ethnicity, gender, and place in shaping separate effects of risk and protective factors on health.[6] These contextual factors are also able to change additive and multiplicative effects of risk and protective factors even when their separate effects are similar.[7-14] Race, ethnicity, gender, and their intersections modify the separate[15] and combined[16] effects of anxiety and depressive disorders on obesity,[15-17] cardiovascular diseases (CVDs)[6,17-19] and well-being.[7] The International Journal of Preventive Medicine[10-12] and a few other journals[13,14,20,21] are making an immense contribution to this field by publishing the results of empirical evidence suggesting how race, ethnicity, and gender operate as moderators.

Cooper *et al*.,[22] Lewis *et al*.,[6,18] Capistrant *et al*.,[23] Assari *et al*.,[17,19,24] and Hicken *et al*.,[25] have particularly reported Black-White differences in the effect of depression on coronary artery disease (CAD) and CAD risk factors such as obesity. Cooper *et al*. investigated racial and ethnic differences in the cross-sectional association between comorbid posttraumatic stress disorder (PTSD) and CAD among patients with depression. Applying logistic regressions to a mega data set (n = 24,719 medical records) from the Department of Veterans Affairs authors found very intriguing results: Among individuals with depression, comorbid PTSD is linked to lower odds of CAD for Whites while the association between comorbid PTSD and CAD is reverse for Blacks.[22] The results are very important given the tendency of depression and PTSD to co-occur,[26-31] and the disproportionately high rate of CVD among Blacks.[22]

In 2011, Lewis *et al*. examined the association between depressive symptoms and overall mortality from CVD, CAD, and stroke in a sample of 6158 community-dwelling older adults. Authors used Cox proportional hazards models to time-to-event over a 9–12-year follow-up. In race-stratified models adjusted for age and sex, high depressive symptoms predicted CVD mortality among Blacks (hazard ratio [HR], 1.95) but not Whites. The study also showed a significant race by depressive symptoms interaction (P = 0.03). Similar findings were observed for CAD and stroke mortality. Authors concluded that elevated depressive symptoms are associated with multiple indicators of CVD mortality in older Blacks, but not Whites.[6]

In a prospective study in 2013, Capistrant *et al*. compared Blacks and Whites for the longitudinal association

between depressive symptoms and CVD mortality. They analyzed data from the Health and Retirement Study with 2638 Black and 15,132 White nationally representative community-dwelling elders (a nationally representative sample of U.S. adults aged ≥50). After an average follow-up of 9.2 years, the associations between elevated depressive symptoms and mortality from stroke, CAD, or total CVD were assessed using Cox proportional hazards models to estimate adjusted HRs. The hazard associated with elevated depressive symptoms did not differ significantly by race ($P > 0.15$), suggesting that race does not modify the effect of depression as a CVD mortality risk factor.[23]

Assari and Sonnega also used data from the HRS and showed that the longitudinal association between high depressive symptoms and incident heart disease over 20 years may differ for Blacks and Whites.[24] In another study, Assari used the National Survey of American Life (NSAL) data and showed that Blacks and Whites have differential patterns of comorbidity between anxiety, depression, and medical conditions like heart disease. In this study, heart disease and atherosclerosis were associated with 12-month genaral anxiety disorder (GAD) among Caribbean Blacks, but not African Americans or non-Hispanic Whites. Hypertension was associated with 12-month major depressive disorder (MDD) among African Americans, and heart disease was associated with 12-month MDD among Caribbean Blacks. None of the CVDs were associated with 12-month MDD among non-Hispanic Whites. The study suggested that mental health associates of CVDs depend on race and ethnicity.[19]

In 2015, Assari and Caldwell used data of 1170 Black adolescents (810 African Americans and 360 Caribbean blacks) and measured obesity based on the cut-off points based on the body mass index (BMI) appropriate for age and gender and also 12-month MDD using the Composite International Diagnostic Interview (CIDI). Although there was no association between obesity and MDD in the pooled sample of Black adolescents, there was a significant interaction between ethnicity and obesity on MDD. When authors tested the association across intersections of ethnicity and gender, a positive association was found among Caribbean Black females but not Caribbean Black males, African American males, or African American females.[17]

In a study Hicken *et al*., examined the association between obesity and depression in non-Hispanic White, non-Hispanic Black, and Mexican American women among 3,666 women aged 20 years and older participated in the 2005–2008 National Health and Nutrition Examination Surveys. The association between obesity and depression varied significantly, however, by race/ethnicity. The obesity-depression associations for Black women were different from the positive association found for White women. Among White women, obesity was associated with the significantly greater likelihood of depression compared to normal weight. Among Black women, although not statistically significant, results suggested an inverse association between obesity and depression.[25]

In 2009, Lewis *et al*. studied aortic and coronary calcification by electron beam tomography and depressive symptoms using the Center for Epidemiologic Studies Depression Scale among 508 women (38% African American, 62% white). They showed that depression was associated with a greater amount of aortic calcification (beta = 0.03, $P = 0.01$), and there was a significant race × depressive symptoms interaction (beta = 0.07, $P = 0.006$). Race-specific multivariable models documented a significant association between depressive symptoms and aortic calcification only among African Americans, but not Whites.[18]

Johnson-Lawrence *et al*. used data from 1,277 African American, 629 Caribbean Black, and 371 non-Hispanic White men from the NSAL and examined associations between race/ethnicity and experiencing one or more chronic physical health conditions in logistic regression models stratified by age and 12-month mood/anxiety disorder status. They also showed that Black-White differences in health are evident among men. Among men aged 45 + years with mood/anxiety disorders, African Americans had greater odds of chronic physical health conditions than Whites.[32]

Watkins *et al*. used NSAL adult data and showed that lifetime MDD was associated with at least one chronic medical condition among African Americans and Caribbean Blacks, but not non-Hispanic Whites. For Caribbean Blacks, stronger associations were found between MDD and general anxiety disorder with one or more chronic medical conditions compared to African Americans and non-Hispanic whites.[33]

Thus, a growing evidence suggests that social groups based on race, ethnicity, and gender differ in separate, combined, and interactive effects of depressive and anxiety disorders on various aspects of health including well-being, suicide, CVDs, and medical conditions.[9,10,16] Confounding, random variation, bias, measurement error, competing risk factors, power, or differential distribution of exposure or outcome may also cause effect modifications.[34] Kamangar has discussed the above methodological circumstances.[34] Inconsistencies may also be due to other methodological factors. For instance, the study by Cooper *et al*. has been performed in clinical setting while the studies by Assari and Sonnega,[24] Lewis

et al.,[6] and Capistrant *et al*.,[23] are all community-based. Inconsistencies between community- and clinic-based studies have been frequently shown.[35,36] This is partly because compared to clinical studies, population-based studies tend to have lower statistical power -at least in part -due to a lower prevalence of severe forms of outcomes in the general population.[37]

It is still necessary to study why the links between physical and mental health vary based on contextual factors such as race, ethnicity, and gender.[15,16,38-40] Context-specific additive and multiplicative effects of anxiety and depression may be due to the differential distribution of comorbidity between anxiety and depressive disorders based on these factors. Even if separate distributions of anxiety and depressive disorders are identical, their joint distribution may depend on race or ethnicity.[41]

A major part of the literature reviewed above supports the differential effect hypothesis.[42,43] Based on this hypothesis, racial and ethnic groups have different susceptibility to the effects of risk and protective factors, which at least partially explains racial and ethnic health disparities. This mechanism is different from the differential exposure hypothesis which attributes health disparities to higher levels of exposure to risk factors among racial and ethnic minority groups.

Among Black older adults, possibly due to the presence of multi-morbidity,[44] any additional disorder may result in a disproportionately larger morbidity compared to Whites. Thus, among minority groups, multiple conditions may compete to gain limited personal and professional care such as time and money.[45]

In addition, if depressed, Blacks less frequently receive evidence-based treatment of depression,[46,47] which may increase the risk of poor outcomes, including CAD. It has already been shown that depression vastly differs between Blacks and Whites in various terms including, but not limited to socio-economics, presentations, comorbidities, and clinical outcomes.[48,49] Compared to Whites, diagnosis and treatment of depression in Blacks more frequently happen in primary care settings, where depression treatment is less evidence-based.[49] The low quality of depression treatment may add to the burden of high stigma, low trust, adherence, and acceptability of pharmaceutical interventions among Blacks with depression.[50,51]

In any study that compares Blacks and Whites with depressive or anxiety disorders, Blacks may receive a lower quality treatment than Whites. Researchers may explore if the differential quality of treatment explains Black-White differences in outcomes associated with multiple psychiatric disorders. As the associations between depression, anxiety, and comorbid medical conditions are reciprocal,[45,52] researchers may be cautious about collider stratification. We believe that the study by Cooper *et al*. may be biased due to collider stratification.[53,54]

Based on multiple studies in different disciplines,[6,10,15,16,22] race- and ethnic–specific paths are rules rather than exceptions and deserve more scholarly attention. Future research should compare reciprocal effects of depression, anxiety, and chronic medical conditions.[52] The results of cross-sectional studies require longitudinal replication, as well. As vulnerability to risk and protective factors may differ across racial and ethnic groups, it is always fruitful to conceptualize race and ethnicity as moderators.[6,10,15,16,22]

Future studies should explore the underlying causes of such variation. Studying mental and chronic physical health problems together may help identify mechanisms that underlie racial disparities among Blacks and other racial and ethnic minority groups. Instead of the one-size fits all approach, researchers may compare racial and ethnic groups for vulnerability to determinants of health.

Received: 27 Aug 14 **Accepted:** 03 Apr 15
Published: 13 Jan 16

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	DOI: 10.4103/2008-7802.173931