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Depressive symptoms are associated with worsened severity of the metabolic syndrome in African American women independent of lifestyle factors: A consideration of mechanistic links from the Jackson heart study

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Abstract

Background—Depression and the metabolic syndrome (MetS) are both risk factors for cardiovascular disease and type 2 diabetes mellitus. Prior studies in predominantly White populations demonstrated that individuals with depressive symptoms at baseline are more likely to develop future MetS. We tested the hypothesis that depressive symptoms would contribute to a more pronounced increase in MetS severity among African Americans in the Jackson Heart Study (JHS).

Methods—We used repeated-measures modeling among 1743 JHS participants during Visits 1–3 over 8 years of follow-up to evaluate relations between depressive symptom score (Center for

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Conflict of interest

None.

Contributors

Matthew J. Gurka participated in the design, analysis and writing up of the research. Abhishek Vishnu participated in the design and analysis of the research. Olivia I. Okereke participated in the interpretation of the results and writing up of the research. Solomon Musani participated in the design and analysis of the research. Mario Sims participated in the design, analysis and interpretation of the research. Mark D. DeBoer participated in the design, analysis, interpretation and write-up of the research and had primary responsibility for the final content. All authors approved of the final manuscript as submitted and agree to be accountable for all aspects of the work.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.psyneuen.2016.02.030>.

Epidemiologic Survey-Depression (CES-D)) at baseline and a sex- and race/ethnicity-specific MetS severity Z-score at each visit.

Results—20.3% of participants had a CES-D score ≥ 16 , consistent with clinically-relevant depressive symptoms. Higher depressive-symptom scores were associated with higher MetS severity in women but not men ($p = 0.005$ vs. $p = 0.490$). There was no difference by depressive symptom score with rate of change in MetS severity over time. Both depressive-symptom score and MetS severity Z-score were associated with lower levels of physical activity and higher levels of C-reactive protein; however, addition of these to the regression model did not attenuate the association between depressive symptoms and MetS severity.

Conclusion—African American women but not men in the JHS exhibit relationships between baseline depressive symptoms and MetS severity over an 8-year period. These data may have implications for targeting of MetS-associated lifestyle changes among individuals with depressive symptoms.

Keywords

Depression; Metabolic syndrome; Risk

1. Introduction

Depression and the metabolic syndrome (MetS) are both precursors to type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) and have been linked bidirectionally to each other (Dunbar et al., 2008; Joynt et al., 2003; Mezuk et al., 2008; Rikknen et al., 2007; Sims et al., 2015; Skilton et al., 2007). In a large *meta*-analysis comprised almost exclusively of white participants, individuals classified as having depression at baseline had an odds ratio (OR) of 1.52 for developing later MetS, while those classified as having MetS at baseline had an OR of developing depression of 1.49 (Pan et al., 2012). While still unclear, these connections have been postulated to relate to shared lifestyle practices, systemic inflammation and activation of stress hormone pathways (Berk et al., 2013; Dunbar et al., 2008; Raison et al., 2006; Rikknen et al., 2007). Given risk conveyed for T2DM and CVD, the inter-related nature of depression and MetS raises significant issues for the screening and intervention for both disorders.

Nevertheless, the relationship is unclear between depression and MetS among African Americans for whom both depression and MetS are under-recognized. Physicians surveyed regarding patients with depressive symptoms were less likely to recognize or treat these symptoms among African Americans than among white patients (Breslau et al., 2005; Gallo et al., 2005), while other studies have revealed that African Americans exhibit depressive symptoms for a longer period of time (Breslau et al., 2005).

African Americans are also less likely to be classified as having MetS (Park et al., 2003; Walker et al., 2012), despite having more T2DM (Cowie et al., 2010), and more death from CVD (Mensah et al., 2005). This appears to result from a bias in the criteria traditionally used to categorize MetS (DeBoer, 2011; Sumner and Cowie, 2008). Using criteria such as those from the Adult Treatment Panel-III (ATP-III) (Grundy et al., 2005), MetS is

categorized by an individual having abnormal values in at least three of the five components of MetS (high values of waist circumference [WC], blood pressure [BP], triglycerides and fasting glucose and low HDL-cholesterol). However, the cut-off values for these components are based on population norms and may not be accurate among all sub-groups. For example, African Americans in general have lower triglyceride levels and are therefore less likely to have elevations above the cut-off, contributing to a falsely lower estimation of MetS prevalence (Sumner and Cowie, 2008). These criteria carry a further limitation by virtue of being binary—limiting the ability to assess whether depression confers worsening over time in the processes underlying MetS—potentially leading to a more severely abnormal metabolic state. Because of the differences in how MetS is manifested among African Americans and because of the limits of binary MetS criteria, we recently formulated a sex- and race/ethnicity-specific MetS severity score, which is a Z-score that can be used to assess how severely MetS is manifested in an individual and to follow changes in MetS severity over time (Gurka et al., 2012, 2014; Vishnu et al., 2015). This score has been linked to risk for future CVD and T2DM over time (DeBoer et al., 2015a, 2015b).

Our goal in the current study was to assess the relationship between depressive symptoms and MetS severity over time among participants of the Jackson Heart Study (JHS), a cohort of African Americans in the Jackson, MS metropolitan area. Specifically, we hypothesized that African Americans with a higher degree of depressive symptoms would have a higher MetS severity at baseline and a more significant worsening of MetS severity over 8 years of follow-up. We further explored whether both depressive symptoms and MetS had links to lifestyle, inflammation and cortisol—all factors that can be noted in both processes.

2. Methods

2.1. Cohort

JHS is the largest longitudinal, single-site study of cardiovascular risk in African Americans. The cohort consists of 5301 participants age 21–95 years (Taylor et al., 2005). We utilized data from JHS Visit 1 (2000–2004), Visit 2 (2005–2008) and Visit 3 (2009–2013). During Visit 1, baseline information was gathered by certified interviewers in both home settings and during the clinic visit. These questionnaires focused on data regarding income, education, and lifestyle factors, including tobacco smoking, ethanol consumption, dietary patterns and the amount of physical activity (Taylor et al., 2005).

2.1.1. Depressive symptoms measures—During Visit 1, participants were given a take-home questionnaire with the Center for Epidemiologic Studies Depression (CES-D) scale (Radloff, 1977). This consists of 20 items for which the participant rates the frequency (on a 0–3-point scale) of depressive symptoms, with questions further divided into 4 sub-scales depressed affect (items 3, 6, 14, 17, and 18), positive affect (items 4, 8, 12, and 16), somatic/retarded activity (items 1, 2, 7, 11, and 20) and interpersonal (items 15 and 19). The scores are summed for a total score. Depression has been typically classified based on a total score ≥ 16 (Radloff, 1977). In recognizing that depression manifests as a range of symptoms, from none to sub-threshold/subclinical to clinical, the majority of our analysis utilized this score as a continuous measure as performed previously (Ragland et al., 2005).

2.1.2. Clinical and laboratory measures—At each visit, participants had MetS components measured using standardized protocols (Taylor et al., 2008, 2005). WC assessed by 2 separate measurements at the level of the umbilicus, parallel to the floor using non-dispensable measuring tape. Sitting BP was measured twice at 5-minute intervals and averaged. Fasting blood samples of glucose and lipids were measured at the Central Laboratory of the University of Minnesota. Serum cortisol drawn at random time of day was measured by chemiluminescent immunoassay performed with the Siemens Advia Centaur (Siemens). Serum high sensitivity C-reactive protein (hsCRP) was measured by the latex particle immunoturbidimetric assay (from ITA and from Roche Diagnostics, Indianapolis, IN).

Nutrient information was assessed via four separate 24-hour dietary recalls (2 weekdays and 2 weekend days) scheduled approximately 1 month apart and administered by registered dietitians using University of Minnesota Nutrition Data System for Research software (version 4.04, 2001, Nutrition Coordinating Center, University of Minnesota, Minneapolis) (Carithers et al., 2009).

Physical activity was assessed via the JHS Physical Activity Cohort (JPAC) survey, which was administered by trained interviewers (Dubbett et al., 2005). The JPAC determines activity scores based on the frequency of activities for four domains of PA: 1. Active living (walking and biking for leisure and transportation and watching television), 2. Work (sitting, standing, walking, lifting heavy loads, and sweating from exertion at work; work activity was analyzed only for participants who reported either working or doing volunteer work in the past year), 3. Home life (care giving, preparing and cleaning up from meals, routine and major house cleaning, gardening/yard work, and heavy outdoor and household labor), and 4. Sport (participation in up to 3 recreational activities, and scores take into account the frequency, duration, and intensity of each of the activities reported). For each of these an index score (0–5) was generated, and a total score was computed as the sum of the index scores. Total scores were significantly correlated with 24-hour accelerometer counts ($\rho = 0.24$), and with three days of pedometer counts obtained about four months following the survey ($\rho = 0.32$) (Smitherman et al., 2009).

Lifestyle variables were broken down into categories of “poor health,” “intermediate health,” and “ideal health” according to definitions determined by American Heart Association (AHA) guidelines (Supplementary Table 1) (Lloyd-Jones et al., 2010).

2.1.3. MetS classification and Z-score—Traditional MetS was defined using the ATP-III criteria for adults (Grundy et al., 2005); participants had to meet 3 of the following 5 criteria: concentration of triglycerides ≥ 1.69 mmol/L (150 mg/dL), HDL-C <1.04 mmol/L (40 mg/dL) for men and <1.3 mmol/L (50 mg/dL) for women, WC ≥ 102 cm for males and ≥ 88 cm for females, glucose concentration ≥ 5.55 mmol/L (100 mg/dL), and systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg (Grundy et al., 2005).

MetS severity Z-score was calculated using formulas published elsewhere (Gurka et al., 2012, 2014). Briefly, these scores were formed using confirmatory factor analysis of the 5 traditional components of MetS (as above) to determine the weighted contribution of each of

these components to a latent MetS “factor” on a sex-and race/ethnicity-specific basis. Confirmatory factor analysis was performed on data from the National Health and Nutrition Examination Survey (NHANES) for adults age 20–64 years (Gurka et al., 2014) divided into six sub-groups based on sex and the following self-identified race/ethnicities: non-Hispanic white, non-Hispanic black and Hispanic. For each of these six population sub-groups, loading coefficients for the 5 MetS components were determined toward a single MetS factor. The loading coefficients were then used to generate equations to calculate a standardized MetS severity score for each sub-group (<http://mets.health-outcomes-policy.ufl.edu/calculator/>). These MetS severity scores are Z-scores (with 99.75% of values ranging from –3 to 3) of relative MetS severity on a sex- and race/ethnicity-specific basis, with higher scores indicating worse MetS severity.

2.1.4. Statistics—Exclusion criteria were: presence of diabetes at baseline (n = 1213), absence of CESD data (n = 1609), and incomplete MetS data at either Visits 1 or Visit 3 (n = 736) (Supplementary Fig. 1). At Visit 2 a lower proportion of participants were fasting, which excluded some participants from calculation of MetS severity scores. Visit 2 scores when available were still used in the longitudinal analysis described below. All analyses were performed using SAS Version 9.4 (Cary, NC) with statistical significance set to $p = 0.05$. All participant characteristics were summarized as means $\pm$ standard deviations (continuous variables) or frequencies and percentages (categorical variables), both for the entire analysis sample and by depressive symptom category (CES-D ≥ 16 vs. CES-D < 16), with statistical comparisons between these two depression groups performed by *t*-tests or chi-square tests, respectively.

Our analyses proceeded according to the following steps:

1. Primary analysis for relationship between depressive symptoms and MetS. The primary analysis involved modeling MetS severity over the three time points via a Gaussian repeated measures model that assumed an unstructured correlation among the potential three observations per individual. The Kenward-Roger estimate of the denominator degrees of freedom was used in making inferences (Kenward and Roger, 1997). The requirement of ignorably missing data was most likely met because the majority of missing fasting lab data at Visit 2 was due to procedural reasons rather than because these missing participants had worse (or better) outcomes. Specifically, the initial mean model of MetS severity at each of the three visits included baseline CES-D score (continuous), and the interaction of CES-D score with the visit variable. This was done to examine a) whether there was an association between depressive symptoms and MetS severity at baseline and b) whether the trajectory of MetS severity differed across the three visits for those with higher CES-D scores. Other initial covariates were included due to their potential to confound this association of interest: baseline age, education level, household income, and health insurance status. Given our the sex-specific nature of the MetS severity score (Gurka et al., 2014) and previous literature that identified sex differences in somatic manifestations of

depression (Pan et al., 2012), we included interactions between sex and CES-D as well as the visit variable to assess sex as a potential modifier of any relationship between baseline depression and MetS severity over time. For both males and females, we assessed model-generated mean MetS severity scores for a CES-D score of 16 (the standard cut-off to categorize the presence of clinically-representative depressive symptoms), as well as 8 and 24 to represent scores above and below this cut-off.

2. Consideration of factors that might be mediators of any potential link between depressive symptoms and MetS. Lifestyle factors were assumed to be potential mediators, in that depressive symptoms could impact one's lifestyle, which in turn could lead to worsened MetS. Thus, certain lifestyle factors (smoking, nutrition, physical activity) were examined more closely before being included in the aforementioned model. Unfortunately, a comprehensive mediation analysis was not possible due to the fact this set of data was only collected in entirety at Visit 1. However, we proceeded with an informal examination of these baseline factors independent of inclusion of traditional confounders described in the first step of the analysis above. For smoking, nutrition, and physical activity, AHA categories (Lloyd-Jones et al., 2010) (Supplementary Table 1) were used; in addition, for nutrition, total daily caloric intake was examined. We did not evaluate ethanol consumption because of the relative paucity of heavy drinking in the sample. We similarly evaluated for whether hsCRP and cortisol as measures of inflammation and stress, respectively, were associated with MetS severity across the three visits and/or depressive symptom score at baseline. These items were then added to the model described in Step 1 above, and parameter estimates related to CES-D in particular were compared between the two models. Major differences between these estimates ($> 10\%$) to indicate at a minimum these variables act as confounders of the relationships of interest.
3. Consideration of potential relationships of sub-scales of CES-D with MetS. Finally, we evaluated whether the depressed affect, positive affect, somatic/retarded activity or interpersonal sub-scales were individually related to MetS, using the baseline model (step 1 above) with any retained potential mediators found in (2).

3. Results

3.1. Participant characteristics

We evaluated data from 1743 participants in examining the relationship between baseline depression and future change in MetS severity. Compared to excluded participants ($N = 3558$), those evaluated in the analysis had similar sex distribution, insurance status and nutrition quality, but were younger, had lower CRP, higher model's income, higher education status and poor health due to smoking and physical activity. Characteristics of participants included in the analysis are shown by baseline depressive symptom status (CES-

$D < 0.05$ or $p < 0.05$) in Table 1. Compared to those without clinically-relevant depressive symptoms, those with depressive symptoms were slightly younger and more likely to be in lower income and education groups. Those with depressive symptoms also had poorer nutrition as assessed by AHA recommendations, higher overall daily caloric intake, less PA, as well as higher levels of cortisol. Using simple univariate comparisons, there were no significant differences at baseline between those with and without depressive symptoms overall in the burden of MetS as assessed using either the prevalence of ATP-III MetS or MetS Z-scores. Individuals with depressive symptoms at baseline had higher MetS severity Z-scores at visit 2 and had a higher prevalence of ATP-III MetS at visits 2 and 3 (Table 1).

3.1.1. Prospective relationship between baseline depressive symptoms and change in MetS

—We next evaluated for potential relations between the degree of depressive symptoms and MetS severity without respect to potential mediators (analysis 1 in the Methods). Table 2 displays the primary repeated-measures model with the outcome being MetS severity score and the predictors being CES-D and other standard sociodemographic adjustments; Fig. 1 displays model-derived MetS Z-scores by CES-D score. Contrary to our hypothesis, in neither sex did individuals with higher depressive symptom score exhibit a greater rate of change in MetS severity over time. Females but not males had higher overall MetS severity Z-scores with increasing depressive symptoms score that were exhibited at baseline. There was also a visit-by-sex interaction with respect to MetS severity score in that females, but not males, exhibited worsening MetS severity between visits 2 and 3. Additionally, the prevalence of ATP-III MetS increased similarly among both groups by baseline CES-D score (data not shown).

3.1.2. Analysis of potential mediators

—We next considered potential mediators of the relationship between depressive symptoms and MetS by evaluating lifestyle and serum factors potentially associated with both MetS and depressive symptoms (analysis 2 from above). Table 3 provides repeated measures models of MetS severity related to AHA risk classifications of smoking, nutrition and physical activity. In addition, simple comparisons of baseline mean CES-D scores between these classifications via *t*-tests are presented. Among these lifestyle factors, smoking, low physical activity, and higher daily caloric intake were related to higher depressive symptoms scores. Only low physical activity and higher daily caloric intake were also related to higher MetS severity. However, since the interaction between smoking and visit with respect to MetS severity over time was close to significant ($p = 0.124$), as well as the fact that those included in this analysis had significantly different rates of smoking (results not shown), we also continued to examine smoking. We further assessed the potential that hsCRP and cortisol could be possible mediators. hsCRP (natural log scale) was associated with both CES-D score ($r = 0.075$, $p = 0.002$) and MetS severity ($r = 0.310$, $p < 0.001$), while cortisol was not associated with either CES-D ($r = -0.033$, $p = 0.169$) or MetS severity ($r = -0.022$, $p = 0.357$).

We subsequently added baseline physical activity, smoking status, caloric intake, and hsCRP (at each of the three visits) as covariates in the previous regression model (Table 4). Addition of the factors did not change the strength of relationship between CES-D and MetS severity

in females (in both cases β estimate 0.008, $p < 0.01$) or the rate of change of MetS severity between visits.

3.1.3. Subscales of depressive symptoms—We next considered subscales of CES-D to evaluate whether MetS severity was related to any particular domain of depressive symptoms (analysis 3 from the Methods). In considering the main regression model and its final covariates among women given the sex-depressive-symptoms interaction term), only the Somatic/Retarded Activity subscale was significantly associated (Table 5). This subscale consists of questions related to being bothered by unusual concerns, not having appetite, feeling as though everything required more effort, having restless sleep and not being able to get going. Subscales related to depressed affect, positive affect and interpersonal relationships were not related to MetS severity. A similar analysis among men showed no association between any of the CES-D subscales and MetS severity (results not shown).

4. Discussion

Depressive symptoms remains a significant public health concern in part because of its risks related to CVD, (Joynt et al., 2003; O'Brien et al., 2015) and T2DM (Mezuk et al., 2008) and in part because it may be under-recognized, particularly among African Americans (Gallo et al., 2005). In this cohort of African American participants of the Jackson Heart Study, we found that women (but not men) with an increasing degree of depressive symptoms at baseline had higher MetS severity over the course of follow-up. This characteristic of the depression-MetS relationship being stronger in women is consistent with a *meta*-analysis of cohorts with almost exclusively white individuals (Pan et al., 2012). Our study was unique in assessing for differences in the rate of change in MetS severity as a function of baseline depressive symptoms. Our original hypothesis was that individuals with a higher degree of depressive symptoms at baseline would exhibit a more rapid worsening of the severity of MetS over time. Instead, we found that while women with more depressive symptoms (compared to those with fewer symptoms) had higher MetS severity, they experienced a similar rate of metabolic deterioration over time. This suggests a potential model in which the increase in risk of future ATP-III MetS among individuals with depressive symptoms at baseline may be driven not by a higher rate of MetS progression, but by higher baseline MetS severity (though still before ATP-III MetS diagnosis) and continued progression of MetS severity over time. In the clinical care of individuals with depressive symptoms, this may raise a need to encourage lifestyle modification that may reduce the rate of MetS progression and avoid future metabolic and disease sequelae.

The mechanistic links between depressive symptoms and MetS have been a source of speculation, with potential shared relationships between lifestyle factors and physiologic processes related to stress hormones and systemic inflammation (Capuron et al., 2008; Dunbar et al., 2008; Katon et al., 2010; Räikkönen et al., 2007). In this cohort, we did not find relationships between smoking, drinking or nutrition with MetS severity. While certain lifestyle factors (physical activity, caloric intake) were linked to both a greater degree of depressive symptoms and higher MetS severity, adjusting for them did not alter the relationship between depressive symptoms and MetS. This suggests that the relationship between depressive symptoms and MetS may go beyond lifestyle factors. Nevertheless,

because of the diversity of lifestyle factors related to MetS (as well as difficulty in accurately measuring lifestyle factors in most epidemiologic research), as well as our inability to perform a formal mediation analysis given the timing of the data collected in JHS, the possibility remains that there could be a combination of poor lifestyle behaviors in the setting of depression that together contribute to MetS. Future studies are needed to formally assess the possible mediating relationships of these lifestyle factors with depressive symptoms and MetS, as well as obesity and CVD risk in general.

Systemic inflammation has been postulated to be in the causative pathway between MetS and depressive symptoms for several reasons. MetS has long been known to be associated with low levels of inflammation, at least in part due to adipocyte dysfunction and macrophage infiltration of visceral adipose tissue (DeBoer, 2013). Administration of the cytokine interferon alpha as a cancer treatment has been noted to induce depressive symptoms (Musselman et al., 2001). Depression has also been noted to be associated with higher levels of hsCRP and IL-6 (Berk et al., 2013; Danner et al., 2003; Raison et al., 2006). One group of researchers found that inclusion of hsCRP in the regression model caused a 10% reduction in the β coefficient of the association between MetS and depressive symptom score (Capuron et al., 2008). While we found that hsCRP levels exhibited linear relationships between both MetS severity and depressive symptoms, we did not note any attenuation in the relationship between MetS and depressive symptoms when hsCRP was included in the model. Other researchers have suggested that stress pathway activation including cortisol could be in the bi-directional causative pathway between MetS and depression (Björntorp and Rosmond, 2000; Dunbar et al., 2008). Cortisol as measured in this study, (i.e., not at a consistent time of day) were associated with depressive symptoms but not with MetS severity. Further evaluation using more rigorous assessments of the hypothalamic-pituitary-adrenal axis is warranted. An additional limitation regarding the potential mediators is that we did not have measures at each visit for all of these variables. Changes in these factors over time could have revealed a role in the worsening of MetS.

The reason that these findings are observed in African American women and not men is unclear. Prior surveys have noted that women are more likely to experience somatic symptoms with depression (Silverstein and Levin, 2014). In considering sub-scales of the CES-D, we found that worsened MetS severity was only linked to the somatic/retarded activity scale, corresponding to these symptoms and marked by low energy, poor sleep and low appetite. Notably, some of these characteristics (low sleep (Hall et al., 2008), potential for lower physical activity) correspond both to our data among those with higher MetS and to proposed mechanisms that may underlie these relationships (Pan et al., 2012; Strine et al., 2008). These characteristics may compensate beyond the low appetite item, which was not apparent overall in this cohort, as evidenced by the higher caloric intake among participants with depressive symptoms.

The relations between MetS and depression carry particular importance among African American individuals, who have higher rates of T2DM (Cowie et al., 2010) and death from CVD (Mensah et al., 2005)—diseases linked to depression. While African Americans have similar (Breslau et al., 2005; Kessler et al., 2005) or slightly lower (González et al., 2010; Wang et al., 2000; Williams et al., 2007) rates of depression over their lifetime (compared to

whites), they are less likely to have their depression diagnosed (Gallo et al., 2005) or treated by physicians (Gallo et al., 2005; Kessler et al., 2005), and have longer duration of symptoms (Breslau et al., 2005). Among participants of the Jackson Heart Study, we found a prevalence of 20.3% of clinically relevant depressive symptoms (i.e., CES-D 16) at baseline. This compares to a range of other estimates of depression from 21% in a community sample of African Americans with a mean age of 57 years using the short 11-item version of the CES-D (Miller et al., 2004) down to 11% of middle-aged respondents to a nationally-representative survey, diagnosed with major depressive disorder by DSM-III criteria (Wang et al., 2000). Because individuals with depression may be less likely to comply with other disease treatments (Dunbar et al., 2008), improved recognition and treatment of depression in African Americans may help to facilitate health improvements that span beyond depression alone.

This study had several limitations. We only had data regarding depressive symptoms at baseline and were thus unable to track for changes in depressive symptoms over time. We also lacked data regarding depressive symptoms on a large portion of JHS, potentially biasing the analytic sample. Specifically, participants who filled out the depressive symptoms questionnaire were younger with higher income and education status, potentially leading to an under-representation of individuals with clinically-relevant depression. The actual prevalence of depression in JHS may thus be higher than reported here. It is unclear whether this potential under-representation of depressed individuals would have altered the sex and MetS relationships that we found. We also limited our analysis to those individuals with MetS variables at Visit 3 to allow for the examination of changes over time; however, this approach also leads to a potentially biased sample of participants that continued in the cohort over approximately 8 years. We were unable to perform a formal mediation analysis and instead only were able to examine for associations between potential mediators and MetS and depressive symptoms—and whether inclusion of potential mediators attenuated the relationship between depressive symptoms. Finally, we lacked data on treatments for depression, which may have both altered the response of some participants to the survey and can themselves be associated with unhealthy weight gain (McIntyre et al., 2010). However, the study also had several strengths, including assessment of depression, lifestyle factors, and MetS-related variables. Other strengths include the use of a well-characterized sample of African Americans and the ability to measure changes in MetS severity in this study.

5. Conclusion

Increased attention the inter-relationships between MetS and depressive symptoms among African American women is needed, given the importance of both depression and MetS as risk factors for CVD and given that individuals with depression may be less likely to comply with treatment in the setting of disease (Dunbar et al., 2008). Screening for depression among patients with MetS may be warranted, with increased efforts toward treatment of depression and MetS toward improved CVD risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Model-Estimated Mean MetS Z-score over Time by Baseline Depression Score (CES-D) and Sex. Data shown are from the model described in Table 3. CES-D score was significantly linked to MetS severity score in women but not men ($p < 0.05$) and between Visits 2 and 3 there was a significantly higher rise in MetS severity over time in women but not men ($p < 0.01$).

Table 1

Characteristics of analytic cohort by status of baseline depressive symptoms.

Characteristic	Overall	Without clinically relevant depressive symptoms (CES-D < 16)	Clinically relevant depressive symptoms (CES-D ≥ 16)	p-value ^b
n	1743 ^a	1390	353	–
Female, n (%)	1119 (64.2%)	861 (61.9%)	258 (73.1%)	< 0.001
Baseline lifestyle/SES characteristics, n (%)				
Income Level				< 0.001
Poor	157 (10.4%)	88 (7.3%)	69 (22.7%)	
Lower-Middle	299 (19.8%)	222 (18.4%)	77 (25.3%)	
Upper-Middle	472 (31.3%)	377 (31.3%)	95 (31.2%)	
Affluent	582 (38.5%)	519 (43.0%)	63 (20.7%)	
Education				< 0.001
HS or Less	468 (26.9%)	338 (24.4%)	130 (36.8%)	
Less than College	519 (29.8%)	381 (27.4%)	138 (39.1%)	
College or higher	754 (43.3%)	669 (48.2%)	85 (24.1%)	
Health Insurance	1523 (87.6%)	1244 (89.6%)	279 (79.7%)	< 0.001
AHA health indicator for ^c :				
Smoking				0.002
Current smoker	181 (10.5%)	123 (9.0%)	58 (16.6%)	
Former smoker (quit <12 mo ago)	16 (0.9%)	12 (0.9%)	4 (1.2%)	
Never smoker (quit >12 ago)	1520 (88.5%)	1233 (90.1%)	287 (82.2%)	
Nutrition ^c				0.069
0–1 healthy food components daily	1123 (64.4%)	877 (63.1%)	246 (69.7%)	
2–3 healthy food components daily	603 (34.6%)	499 (35.9%)	104 (29.5%)	
4 healthy food components daily	17 (1.0%)	14 (1.1%)	3 (0.8%)	
Physical activity ^d				< 0.001
Inactive	715 (41.0%)	538 (38.7%)	177 (50.1%)	
Moderately active	612 (35.1%)	494 (35.6%)	118 (33.4%)	
Active	415 (23.8%)	357 (25.7%)	58 (16.4%)	
Alcohol drinking ^e				0.132
None	921 (52.8%)	749 (53.9%)	172 (48.7%)	
Moderate ^e	759 (43.6%)	595 (42.8%)	164 (46.5%)	
Heavy ^e	63 (3.6%)	46 (3.3%)	17 (4.8%)	
Calories per Day				0.006
<1500 kcals	519 (30.4%)	428 (31.4%)	91 (26.4%)	
1500–1999 kcals	382 (22.4%)	306 (22.5%)	76 (22.0%)	
2000–2499 kcals	309 (18.1%)	257 (18.9%)	52 (15.1%)	
2500 kcals	498 (29.2%)	372 (27.3%)	126 (36.5%)	
Baseline Participant Clinical Data, Mean (SD)				
Age (years)	52.5 (12.0)	52.8 (11.8)	51.3 (12.6)	0.032

Characteristic	Overall	Without clinically relevant depressive symptoms (CES-D < 16)	Clinically relevant depressive symptoms (CES-D ≥ 16)	p-value ^b
BMI (kg/m ²)	31.2 (6.8)	31.0 (6.8)	31.7 (7.1)	0.081
Waist Circumference (cm)	98.1 (15.5)	97.8 (15.3)	99.4 (16.0)	0.087
SBP (mmHg)	124.2 (16.6)	124.2 (16.5)	123.9 (17.1)	0.755
DBP (mmHg)	79.5 (10.2)	79.5 (10.2)	79.6 (10.3)	0.873
Triglycerides (mg/dL)	98.3 (56.2)	97.6 (56.3)	101.1 (55.6)	0.297
HDL (mg/dL)	52.4 (14.6)	52.5 (14.6)	51.9 (14.6)	0.556
Glucose (mg/dL)	89.9 (8.7)	90.1 (8.7)	89.4 (8.7)	0.162
Cortisol	9.4 (3.9)	9.5 (4.0)	8.9 (3.6)	0.015
hsCRP (mg/L)	0.5 (0.7)	0.4 (0.7)	0.5 (0.6)	0.077
ATP-III MetS Status (n (%))				
Visit 1	493 (28.3%)	382 (27.5%)	111 (31.4%)	0.140
Visit 2	429 (26.4%)	327 (25.1%)	102 (31.6%)	0.018
Visit 3	635 (36.4%)	489 (35.2%)	146 (41.4%)	0.031
MetS Z-Score (Mean (SD))				
Visit 1	-0.10 (0.70)	-0.12 (0.69)	-0.04 (0.72)	0.061
Visit 2	0.08 (0.80)	0.05 (0.75)	0.22 (0.82)	0.003
Visit 3	0.13 (0.84)	0.10 (0.84)	0.20 (0.84)	0.074
Visit 1 CES-D Component Score (Mean (SD))				
Depressed affect (Range: 0–15)	1.85 (2.59)	0.95 (1.38)	5.40 (3.16)	< 0.001
Positive affect (Range: 0–12)	3.46 (3.26)	2.85 (3.03)	5.84 (3.08)	< 0.001
Somatic and retarded activity (Range: 0–15)	2.67 (2.44)	1.92 (1.78)	5.62 (2.45)	< 0.001
Interpersonal (Range: 0–6)	0.51 (0.92)	0.30 (0.65)	1.34 (1.29)	< 0.001

^aEffective sample size may be less for certain variables due to missing values.

^bChi-square test for categorical variables; t-test for continuous variables.

^cSee Supplementary Table 1 for definitions of AHA categories.

^dModerately active: 1–149 min/wk moderate intensity exercise or 1–74 min/wk vigorous intensity; active: 150 min/wk of moderately intense activity or 75 min/wk of vigorous activity.

^eModerate drinking: Males > 0–2 drinks/day, Females > 0 to 1 drinks/day. Heavy drinking: Males > 2 drinks/day, Females > 1 drinks/day.

Table 2

Mixed Model of Baseline Depressive Symptom Score on Change in MetS Z-score.

Model covariate	β Estimate (SE)	p-value
Intercept	-0.656 (0.103)	<0.001
Baseline age	0.010 (0.002)	<0.001
Baseline insurance	-0.154 (0.057)	0.007
Education		
High school degree or less	0.044 (0.051)	0.383
Some college	0.062 (0.045)	0.161
College degree or higher	–	–
Baseline income level		
Poor	0.095 (0.071)	0.181
Lower-middle class	0.068 (0.054)	0.208
Upper-middle class	-0.010 (0.044)	0.816
Affluent	–	–
Males (difference from females, Visit 1)	0.158 (0.062)	0.011
Visit 2 (increment from Visit 1) *		
Females	0.213 (0.019)	<0.001
Males	0.212 (0.026)	<0.001
Visit 3 (increment from Visit 1) *		
Females	0.260 (0.019)	<0.001
Males	0.169 (0.026)	<0.001
CES-D Score (one-point increment) **		
Females	0.008 (0.003)	0.005
Males	-0.003 (0.004)	0.490

* Significant sex $\times$ visit interaction ($p = 0.005$).** Significant sex $\times$ CES-D score interaction ($p = 0.028$).

Table 3

Univariate Associations between Health Behaviors and Metabolic Syndrome Z-score over Time^a.

	Mixed Model of MetS Z-score Across All Three Visits [*]			Visit 1 CES-D Score Comparisons ^{**}	
	Mean MetS Z-Score at:			Mean	t-test p-value
	Visit 1	Visit 2	Visit 3		
Poor health due to smoking status					
Poor: current smoker	-0.107	0.158	0.199	13.07	
Intermediate/ideal: previous or never smoker	-0.105	0.098	0.110	9.96	
Poor health due to physical activity					
Poor: 0 min of MVPA	-0.070	0.159	0.165	10.76	
Intermediate/Ideal: > 0 min of MVPA	-0.204	-0.050	-0.002	8.87	
Poor health due to nutrition					
Poor: 0–1 healthy food Components	-0.102	0.110	0.127	10.32	
Intermediate/ideal: 2–5 healthy Food components	-0.128	-0.035	-0.010	8.76	
Calories per day					
<2500	-0.092	0.099	0.115	9.84	
2500	-0.129	0.132	0.150	11.38	

Abbreviations; CES-D = Center for Epidemiologic Survey-Depression; MVPA = moderate or vigorous physical activity. P values <0.05 are in bold.

^a Data shown are for specific behaviors (smoking, nutrition, physical activity) broken down into AHA categories (further described in Supplementary Table 1). For each of these categories, mean MetS Z-scores are provided for each visit. P values are provided in assessing for the difference in these mean MetS scores (between behavior categories) and for whether this relationship varied between JHS visits. In the final 2 columns on the right, mean CES-D scores at visit 1 are shown by behavior category, with p values for difference in CES-D between categories.

^{*} Including all four categories in one model as well as covariates included in Table 2 model resulted in only Physical Activity being significant (main factor p = 0.0079, interaction with visit p = 0.5091).

^{**} Including all four poor health indicators in one linear model (as well as covariates in Table 2 model) resulted in Physical Activity (p = 0.040) and Smoking (p < 0.001) being significantly associated with CES-D score at Visit 1.

Table 4

Mixed Model of Baseline Depressive Symptom Score on Change in MetS Z-score Adjusting for Lifestyle Factors and hsCRP^a.

Model Covariate	β Estimate (SE)	p-value
Intercept	-0.718 (0.110)	<0.001
Baseline age	0.010 (0.002)	<0.001
Baseline insurance	-0.158 (0.057)	0.006
Education		
High school degree or less	0.048 (0.052)	0.353
Some college	0.057 (0.045)	0.209
College degree or higher	–	–
Baseline income level		
Poor	0.088 (0.072)	0.221
Lower-middle class	0.066 (0.055)	0.233
Upper-middle Class	-0.014 (0.045)	0.753
Affluent	–	–
Poor health due to:		
Physical activity (0 min of MVPA)	0.090 (0.042)	0.033
Smoking (current smoker)	-0.021 (0.056)	0.706
Caloric Intake > 2500 kcals	0.010 (0.041)	0.809
hsCRP	0.065 (0.011)	<0.001
Males (Difference from females, Visit 1)	0.197 (0.063)	0.002
Visit 2 (increment from Visit 1) *		
Females	0.212 (0.020)	<0.001
Males	0.208 (0.026)	<0.001
Visit 3 (increment from Visit 1) *		
Females	0.253 (0.020)	<0.001
Males	0.161 (0.026)	<0.001
CES-D Score (one-point increment) **		
Females	0.008 (0.003)	0.011
Males	-0.006 (0.004)	0.212

^aEstimates shown are β estimates for MetS severity Z-score (dependent variable) associated with the baseline and subsequent variables shown.

* Significant sex $\times$ visit interaction ($p = 0.006$).

** Significant sex $\times$ CES-D score interaction ($p = 0.012$).

Table 5

Mixed Model of Baseline Depressive Symptom Factors and their Association with MetS Severity in Women.

Model covariate	β Estimate (SE)	p-value
Intercept	-0.923 (0.135)	<0.001
Baseline age	0.014 (0.002)	<0.001
Baseline insurance	-0.186 (0.072)	0.010
Education		
High school degree or less	0.106 (0.065)	0.101
Some college	0.046 (0.057)	0.415
College degree or higher	–	–
Baseline income level		
Poor	0.151 (0.083)	0.069
Lower-middle class	0.108 (0.067)	0.107
Upper-middle class	0.012 (0.056)	0.832
Affluent	–	–
Poor health due to:		
Physical activity (0 min of MVPA)	0.073 (0.054)	0.178
Smoking (current smoker)	-0.059 (0.073)	0.421
Caloric intake > 2500 kcals	0.005 (0.054)	0.921
hsCRP	0.063 (0.012)	<0.001
Visit 2 (increment from Visit 1)	0.213 (0.019)	<0.001
Visit 3 (increment from Visit 1)	0.253 (0.020)	<0.001
CES-D Factor Score (one-point increment)		
Depressed affect (blues, depressed, lonely, cry, sad)	0.006 (0.011)	0.588
Positive affect (good, hopeful, happy, enjoy)	0.000 (0.007)	0.956
Somatic and retarded activity (bothered, appetite, effort, sleep, get going)	0.023 (0.012)	0.047
Interpersonal (unfriendly, dislike)	-0.003 (0.027)	0.897