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## Depression, Obesity, and Metabolic Syndrome: Prevalence and Risks of Comorbidity in a Population-Based Study of Mexican Americans

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### Abstract

**Introduction**—We examine the prevalence of depression and obesity, and metabolic syndrome, in a population-based cohort of Mexican Americans living on the US/Mexico border.

**Methods**—We analyzed extensive clinical and laboratory data from 1798 Mexican Americans aged 35 to 64 years. Depression was measured using the Center for Epidemiological Studies – Depression (CES-D) scale. Weighted data were analyzed to establish prevalence of obesity, metabolic syndrome and Depression. Univariate and multivariate weighted regression models were used to test potential associations between these disorders.

**Results**—Using weighted prevalence methods, we found high rates of obesity (51%) metabolic syndrome (46%) and depression (29%). The most consistent risk for depression was associated with female gender. Metabolic syndrome was not associated with depression; however we found significant increased risk for two subcomponents, Low HDL and increased waist circumference. Severe obesity was significantly associated with both mild and severe depression.

**Conclusions**—In this large population-based sample of Mexican-Americans, we observed significant associations between obesity related biomarkers and depression that may be targets for public health interventions.

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The prevalence of obesity in the US has reached epidemic proportions affecting over 30% of the adult population over the age of 18<sup>1,2</sup>. Worldwide, obesity has a tremendous economic burden<sup>3,4</sup> with roughly \$147 billion dollars in costs attributed to obesity and related health conditions annually<sup>5</sup>. In addition to the economic burden to society, there is extensive evidence linking obesity to poor physical outcomes in particular cardiovascular disease, hypertension, stroke, obstructive sleep apnea, and type-2 diabetes<sup>3</sup>. Obesity is also a contributor to metabolic syndrome<sup>6</sup> which is a clustering of major cardiovascular risk factors that include a constellation of atherogenic dyslipidemias, elevated blood pressure,

increased waist circumference and elevated glucose<sup>7</sup>. In terms of mental health, obesity and metabolic syndrome have been associated with poorer outcomes particularly in regards to depression<sup>3, 8–10</sup>

The significant but modest association between obesity and depression has been replicated in many studies<sup>9, 11</sup>. A meta-analysis of cross sectional community studies revealed an odds ratio of 1.18 (95% CI 1.01–1.37)<sup>11</sup> and a meta-analysis of longitudinal studies estimated the odds ratio to be 1.58 (95% CI 1.33–1.87). The mechanisms for the co-occurrence of these disorders is complex with proposed biological components such as adipose induced inflammation<sup>12, 13</sup>, Hypothalamic-Pituitary- Adrenal (HPA) alterations<sup>14</sup> and psychosocial factors such as stigma and low self esteem<sup>15</sup> all identified as potential contributors.

Hispanics now comprise the largest ethnic-minority group residing in the United States accounting for 15% of the population and over 46 million people<sup>16</sup>, with depression as the most common mental illness in this ethnic group<sup>17–19</sup>. Existing studies suggest that obesity and depression are highly prevalent among Hispanic populations<sup>20, 21, 22</sup>. Within Latino/Hispanic populations, Mexican-Americans (MA), who number over 31 million, are the largest single subgroup and the fastest growing ethnic group in the U.S. with a 54% increase between 2000 and 2010<sup>16</sup>. Alarming, recent reports of MA populations estimate the prevalence of obesity to be between 50%–70%<sup>1, 23, 24</sup>. With the increased prevalence of obesity, it is not surprising that obesity related sequelae such as cardiovascular disease<sup>25–27</sup> diabetes<sup>28–30</sup> and metabolic syndrome have also been shown to be significantly more prevalent in MA populations<sup>31</sup>. Given that depression has been associated separately with obesity<sup>9</sup> and metabolic syndrome<sup>10</sup>, examining the link between depression and obesity and metabolic syndrome in Mexican-Americans may have significant public health implications and provide a potential target for intervention.

Herein we examine the prevalence of depression and obesity, and metabolic syndrome, in a randomly selected population-based cohort of 1,798 Mexican Americans living on the US/Mexico border as part of a larger Cameron County Hispanic Cohort: (CCHC)<sup>24</sup>. Within the whole cohort (n= 2583), we have observed the prevalence of obesity (48.5%)<sup>24</sup>, and metabolic syndrome (43%)<sup>27, 31</sup> occurring at epidemic proportions and linked with a host of other health conditions.

## Study population

These participants were recruited between the years 2004–2010, as part of the CCHC<sup>24</sup>. Subjects were selected with stratified two-stage random sampling based on the 2000 census tract data in the city of Brownsville, Texas, situated on the US–Mexico border. This cohort is predominantly Mexican-American (>98%). Willing participants completed a comprehensive questionnaire regarding basic demographic information, medical history, medication use, and social and family history as described previously<sup>24</sup>. Our sample is predominantly female n = 1181 (66%) with a mean age of 44.3 (±15.40) that does not differ between genders.

Depression was measured using the Center for Epidemiological Studies –Depression (CES-D) a 20-item scale developed for epidemiologic studies of depressive symptoms in the general population with a cutoff score of 16 being suggestive of depression<sup>32</sup>. Consistent with prior studies<sup>33</sup>, we further classified individuals as mildly depressed if their CES-D score was 16–26, and severely depressed if their score was ≥27. As described previously<sup>24</sup>, body mass index (BMI) for each subject was calculated based on measured height and weight with their shoes removed by using a portable electronic scale and recorded to the nearest 0.2 kg and height measured to the nearest 0.2 cm by using a stadiometer. We categorized BMI scores as obese (≥30 kg/m<sup>2</sup>) and later subdivided the obese subjects as mildly obese (30–39 kg/m<sup>2</sup>) and severely obese (BMI ≥40 kg/m<sup>2</sup>). Metabolic syndrome was defined using the American Heart Association definition<sup>7</sup>, which requires the presence of at least three of the following: elevated waist circumference, ≥102 cm or 40 inches for men or ≥88 cm or 35 inches for women; elevated triglycerides ≥150 mg/dl; reduced High density lipoprotein (HDL) cholesterol <40 mg/dl for men or, 50 mg/dl for women; elevated blood pressure ≥130/85 mm Hg or use of medication for hypertension; and elevated fasting glucose ≥100 mg/dl. Blood samples were taken and aliquots immediately stored at –70°C for a range of clinical and experimental assays. Blood glucose measurement was performed on site and stored specimens were sent in batches to a CLIA approved clinical laboratory for clinical chemistries. All participants provided written informed consent and this study has been approved by the Institutional Review Board of the University of Texas Health Science Center at Houston.

## Statistical analysis

From the original cohort of 2,583 subjects, 1,798 had complete data and were included in this study. These 1,798 subjects did not differ from the original cohort in terms of age and gender status. To correct the imbalance of the sampling ratios of genders and age groups, and to adjust the sample to population scale, we incorporated age and gender adjusted sampling weights into our analysis as fully described previously<sup>24</sup>. In addition to the sampling weights adjustments, in the analysis we took into account the potential clustering (correlated data) among subjects within the same household and subjects within the same census blocks. All analyses were performed using SAS version 9.1 (SAS Institute, Inc, Cary, North Carolina) and Stata 10 SE (StataCorp LP, College Station, Texas), with adjustments in the respective statistical packages for sampling design. For descriptive purposes, demographic and clinical characteristics were analyzed using chi-square and F-tests for categorical and continuous variables across the depression strata. Data are presented as weighted means (SE) for continuous variables and as frequencies and unweighted and weighted percentages for categorical variables. Univariate analysis with weighted logistic regression was performed in order to examine obesity, cholesterol and metabolic syndrome and demographic characteristics and estimate the odds ratios depression compared to non-depressed subjects. The variables that had a statistically significant effect at <0.05 level in the univariate analyses were examined in multivariable logistic regression model. Given that prior work has noted gender differences in regards to metabolic outcomes<sup>31, 34</sup>, and depression<sup>35</sup> we explored the potential effects of these variables separately for males and females. In addition, we focused on cases with more severe clinical presentation as this may

reduce heterogeneity and has been a useful strategy in biomarker research<sup>36–38</sup>. We therefore used a similar analytic strategy to further explore severe obesity and severe depression as our phenotypes.

## Results

Using weighted prevalence methods, half of our total sample (52%) was obese. We further classified 44% of the sample as mildly obese and 7% as severely obese with BMI  $\geq 40$ . We also found 46% of these subjects met criteria for metabolic syndrome. For depression, 29% of the sample had CES-D scores in the clinically significant range  $\geq 16$  with 15% classified as mildly depressed (CES-D scores 16–26), and 14% severely depressed (CES-D scores  $\geq 27$ ) (See Table 1).

Comparing our measures in the sample by gender also found significantly higher mean CESD depression scores in females ( $F_{1, 1052} = 27.61, p < 0.0001$ ). We also found a significantly higher percentage of females with depression (34.4%) ( $F_{1, 1052} = 13.21, p = 0.0003$ ) using a weighted analysis. There was no statistically significant difference of mean BMI or percentage metabolic syndrome between females and males, however more males had elevated triglycerides (51.2%) ( $F_{1, 1052} = 9.12, p = 0.0026$ ), more males had elevated glucose (50.9%) ( $F_{1, 1052} = 8.87, p = 0.003$ ), and more females had low HDL (60%) ( $F_{1, 1052} = 19.8, p < 0.0001$ ), and increased waist circumference (78.5%) ( $F_{1, 1052} = 25.76, p < 0.0001$ ) (see Table 1).

Using separate weighted univariate logistic regression we examined the broad CES-D cutoff for Depression (CESD score  $\geq 16$ ) for age, gender, obesity, cholesterol, metabolic syndrome and its subcomponents. We found that higher risk for depression was associated with female gender (OR=2.28; 95% CI 1.46–3.56) as seen in Table 2. When we examined the subcomponents of metabolic syndrome separately, low HDL (OR=1.64; 95% CI 1.34–2.01) and increased waist circumference (OR=1.63; 95% CI 1.05–2.53) had significantly higher odds ratios for depression (Table 2) and these remained significant when adjusting for age (Table 2 Model 2). In a Multivariate analyses including age, gender, low HDL, and waist circumference, only the higher odds ratio for depression by female gender (OR=2.03; 95% CI 1.34–3.10) remained significant (Table 2, Model 3). No significant statistical interaction between the variables was found.

Using a similar strategy in multivariate multivariable weighted logistic regression we explored potential associations between our extreme phenotypes including moderate (CESD score  $16 < 27$ ) and severe depression (CESD score  $\geq 27$ ) as well as mild obesity (BMI score  $30 < 40$ ) and severe obesity (BMI score  $\geq 40$ ). In these analyses we found significant associations for female gender as a predictor of mild (OR = 1.79; 95% CI 1.17–2.73) and severe depression (OR = 3.09; 95% CI 1.29–7.36) which remained significant when controlling for age (as seen in Table 3, Models 1 and 2). In these analyses severe obesity was also a significant predictor of mild (OR = 2.31; 95% CI 1.34–4.01) and severe depression (OR = 2.68; 95% CI 1.47–4.89) (as seen in Table 3, Models 1 and 2). Although metabolic syndrome was not a predictor of depression, when we examined the subcomponents of metabolic syndrome separately, low HDL (OR = 1.61; 95% CI 1.08–2.38) and increased

waist circumference (OR = 1.68; 95% CI 1.10–2.56) had significantly elevated odd's ratios for mild depression and these same factors remained unchanged when adjusting for age (Table 3). We then including these risk factors in a multivariate model however we excluded increased waist circumference as 99% of our severely obese subjects also had elevated waist circumference. This strategy revealed female gender (OR = 2.89; 95% CI 1.46–5.74), being severely obese (OR = 2.31; 95% CI 1.26–4.25), and having low HDL (OR = 1.50; 95% CI 1.00–2.26), were all significantly associated with increased risk for severe depression (see Table 3).

Examining significant factors separately by gender revealed that severe obesity (OR = 2.79; 95% CI 1.40–5.54), and increased waist circumference (OR = 2.11; 95% CI 1.11–4.01), were statistically significant for females as predictors of severe depression, and severe obesity (OR = 2.91; 95% CI 1.53–5.52), and Low HDL (OR = 1.60; 95% CI 1.02–2.49), were significant as predictors for mild depression in females. For males no single variable significantly predicted mild or severe depression.

## Discussion

In this large randomly selected population-based sample of Mexican-Americans, we observed an alarmingly high prevalence of depression (29 %) and putative risk factors, of obesity (51%), and metabolic syndrome (45%). These prevalence rates are all greater than national estimates of depression (9%)<sup>39</sup>, obesity (33%)<sup>1</sup> and metabolic syndrome (22%)<sup>40</sup> suggesting a particular vulnerability in our cohort.

Our most consistent finding that females were observed to have higher levels of depression regardless of the cutoff used, is in line with a large body of depression literature<sup>35, 41, 42</sup>. The explanation for increased depression in women seems to be multi-factorial with puberty and associated sex hormone changes<sup>43</sup> as well as stress-reactivity, thyroid hormones, pre-existing anxiety, response styles and stress associated with gender roles as possible contributing factors<sup>35</sup>.

As noted by prior studies obesity and increased waist circumference were also noted as risk factors for depression<sup>44–47</sup>. In our cohort these anthropomorphic findings were especially noteworthy when we examined severe depression and were largely driven by severely obese females. Our findings mirror other studies that note women<sup>11, 20, 48</sup> with severe obesity<sup>20, 48</sup> are at particularly high risk for depression. Although not significant in our sample, the relationship between metabolic syndrome and depression has been reported to be stronger in women<sup>49, 50</sup>.

Given the common co-occurrence of obesity and depression, a causal relationship between these disorders can be difficult to untangle<sup>11, 51</sup>. In a study of the temporal relationship between obesity and depression, depressed subjects who were not obese at baseline were not more likely to become obese than were non-depressed subjects, however obese subjects without baseline depression, were twice as likely to develop depression during the 5-year period compared to non-obese subjects<sup>46</sup> suggesting obesity precedes depressive symptoms. However recent meta-analytic studies examining longitudinal studies find the relationship

between obesity and depression to be bidirectional<sup>52</sup>. For example eight studies found obesity at baseline increased the risk of onset of depression at follow-up (OR=1.55; 95% CI 1.22–1.98) and nine studies found depression increased the odds for developing obesity (OR= 1.58; 95% CI, 1.33–1.87)<sup>52</sup>. One putative mechanism for the relationship between obesity and depression is the secretion by adipocytes of adipocytokines such as (Interleukin (IL)-1b, IL-6, IL-8, IL-10, TNF-a, TGF-b,) resulting in a state of chronic low level inflammation in obese subjects<sup>12</sup>. These pro-inflammatory cytokines cross the blood brain barrier and can directly influence brain physiology which may contribute directly to the development of depressive symptoms<sup>12, 1353</sup>. Conversely, the HPA axis activation seen in depression marked by increased cortisol<sup>54</sup> may induce abdominal obesity<sup>55</sup>. Additionally we recently reported significant but negative genetic correlations between BMI and cortical and subcortical regions suggesting the same genetic factors that increase BMI could lead to decreases in brain anatomy<sup>56</sup>.

Although Metabolic syndrome was not a significant predictor of depression in our sample two subcomponents of metabolic syndrome Low HDL and increased waist circumference were. Low HDL is known for its associated cardiovascular risk<sup>57, 58</sup> and it has also been linked with depression<sup>59, 60</sup>. Of interest low HDL's purported cardiovascular risk effects are believed to be due to a loss of the anti-inflammatory and antioxidative properties of HDL-C<sup>58, 61</sup>. This mechanism is consistent with the hypothesis linking increased inflammatory markers to depression<sup>12, 53, 62</sup>, and may account our findings associating depression with low HDL.

The ramifications of obesity are major public health issues in America. Lifestyle changes such a healthy diet and increased physical activity are the accepted interventions for addressing obesity<sup>63</sup>, and are reported to have beneficial effects in decreasing depressive symptoms<sup>64</sup>. However promoting a healthy diet and increased physical activity is difficult<sup>65</sup> and will require a concerted effort across multiple domains. These will include altering environmental factors that promote unhealthy food, improved healthcare approaches, government policies, and improved access to environments for physical activity<sup>6663</sup>. The cohort described above with increased obesity, metabolic syndrome, and depression may be particularly vulnerable as they are of lower SES, and few have medical coverage<sup>24</sup> and thus unmet medical needs<sup>27</sup>. Given that there is considerable evidence of inadequate mental health care needs in Mexican Americans<sup>67, 68</sup> addressing these issues may be daunting requiring a comprehensive, adaptable community oriented design<sup>69</sup>.

This study is cross sectional in nature therefore cannot address the issues of causality or directionality. This cohort also consisted primarily of women, was of lower SES and the majority (70%) preferred to respond in Spanish which raises issues of acculturation, and gender that were not the primary focus of this study. Although depression was not the primary focus of this study, the CES-D is a well accepted measure of depressive symptoms in a population<sup>32, 70</sup>, however it does not follow strict DSM criteria, cannot establish chronicity and number of episodes and does not account for confounding or co-morbid psychiatric conditions. Despite these limitations the breadth and sample size of this study allow for exploration based on gender, and multiple risk factors such as severe depression



and marked obesity that provide further insight as to the relationship between physical and mental disorders.

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**Table 1**

Demographic and Clinical Variables by Gender represented by weighted means and their SE for continuous variables and Unweighted frequencies with unweighted and weighted percentages for categorical variables.

	Female n=1181	Male n=617	Total (%) n=1798
Age	44.30 (0.74)	41.52 (1.23)	43.33 (0.69)
BMI	30.84 (0.36)	31.09 (0.32)	30.93 (0.26)
CESD score	14.01 (0.67) ***	8.75 (0.76)	12.18 (0.52)
Obese: BMI 30	630 (53.3%)	300 (48.6%)	930 (51.7%)
Weighted %	(49.3%)	(54.4%)	(51.1%)
Subcategories			
BMI 30–39	519 (43.9%)	258 (41.8%)	777 (43.2%)
Weighted %	(40.7%)	(49.5%)	(43.7%)
BMI 40	111 (9.4%)	42 (6.8%)	153 (8.5%)
Weighted %	(8.7%)	(4.9%)	(7.3%)
Metabolic Syndrome	552 (46.7%)	260 (42.1%)	812 (45.2%)
Weighted %	(46.9%)	(42.8%)	(45.5%)
Sub components			
Hypertension	260 (22.0%)	155 (25.1%)	415 (23.1%)
Weighted %	(21.3%)	(27.1%)	(23.3%)
Elevated Triglycerides	418 (35.3%)	311 (50.4%)	729(40.5%)
Weighted %	(37.9%)	(51.2%) **	(42.5%)
Elevated Glucose	486 (41.1%)	314 (51.0%)	800 (44.4%)
Weighted %	(38.9%)	(50.9%) **	(43.1%)
Low HDL	708(60.0%)	251(41.0%)	959 (53.3%)
Weighted %	(60.6%) **	(41.7%)	(54.1%)
Waist Circumference	957 (81.0%)	340(55.1%)	1297(72.1%)
Weighted %	(78.5%) ***	(57.8%)	(71.4%)
Depression	418 (35.4%)	116(18.8%)	534(29.7%)
Weighted %	(34.4%) ***	(18.8%)	(28.9%)
Subcategories			
Mild	218 (18.5%)	80 (13.0%)	298 (16.6%)
Weighted %	(16.7%)	(11.6%)	(14.9%)
Severe	200 (16.9%)	36 (5.8%)	236 (13.1%)
Weighted %	(17.7%)	(7.11%)	(14.0%)

\* 0.05,

\*\* 0.01,

\*\*\* 0.001,

**Table 2**Weighted Odds Ratios <sup>a</sup> and 95%CI for Depression and Selected Risk Factors

Risk Factors	Unadjusted OR (95% CI)	Model 2 Adjusted for age (95% CI)	Model 3 <sup>b</sup> (95% CI)
Age	1.01 (0.99–1.02)		1.00 (0.99–1.02)
Female	<b>2.28 (1.46–3.56)</b>	<b>2.26 (1.46–3.49)</b>	<b>2.03 (1.34–3.10)</b>
Obesity	1.02 (0.73–1.44)		
Cholesterol	1.00 (0.99–1.01)		
Metabolic Syndrome	1.22 (0.87–1.73)		
<i>Metabolic Syndrome Components</i>			
Hypertension	0.98 (0.68, 1.43)		
Triglycerides	0.89 (0.62, 1.26)		
Elevated Glucose	1.01 (0.72, 1.41)		
Low HDL	<b>1.64 (1.34–2.01)</b>	<b>1.61 (1.11–2.33)</b>	1.39 (0.96–1.02)
Waist Circumference	<b>1.63 (1.05–2.53)</b>	<b>1.60 (1.03–2.49)</b>	

<sup>a</sup> reference category compared to Non-depressed<sup>b</sup> HDL, Waist Circumference, Gender and Age in the model

**Table 3**Weighted Odds Ratios <sup>a</sup> and 95%CI for Depression and Selected Risk Factors

<b>Risk Factors</b>	<b>Unadjusted OR (95% CI)</b>	<b>Model 2 Adjusted for age (95% CI)</b>	<b>Adjusted OR <sup>b</sup> (95% CI)</b>
<b>Age</b>			
Mild depression	1.01 (0.99–1.02)		1.01 (0.99–1.02)
Severe depression	1.01 (0.99–1.02)		1.01 (0.99–1.02)
<b>Female</b>			
Mild depression	<b>1.79 (1.17–2.73)</b>	<b>1.76 (1.17–2.67)</b>	1.42 (0.90–2.24)
Severe depression	<b>3.09 (1.29–7.36)</b>	<b>3.06 (1.31–7.15)</b>	<b>2.89 (1.46–5.74)</b>
<b>Severe Obesity (BMI&gt;=40)</b>			
Mild depression	<b>2.31 (1.34–4.01)</b>	<b>2.29 (1.33–3.96)</b>	<b>1.96 (1.13–3.41)</b>
Severe depression	<b>2.68 (1.47–4.89)</b>	<b>2.66 (1.47–4.81)</b>	<b>2.31 (1.26–4.25)</b>
<b>Cholesterol</b>			
Mild depression	1.00 (0.99–1.002)		
Severe depression	1.00 (0.99–1.004)		
<b>Metabolic Syndrome</b>			
Mild depression	1.14 (0.79–1.66)		
Severe depression	1.33 (0.79–2.25)		
<i>Metabolic Syndrome Components</i>			
<b>Hypertension</b>			
Mild depression	1.15 (0.76–1.76)		
Severe depression	0.82 (0.49–1.39)		
<b>Triglycerides</b>			
Mild depression	0.70 (0.48–1.02)		
Severe depression	1.12 (0.68–1.86)	1.09 (0.60–1.98)	1.25 (0.56–2.80)
<b>Elevated Glucose</b>			
Mild depression	1.01 (0.70–1.45)		
Severe depression	1.00 (0.61–1.66)		
<b>Low HDL</b>			
Mild depression	<b>1.61 (1.08–2.38)</b>	<b>1.61 (1.08–2.39)</b>	<b>1.50 (1.00–2.26)</b>
Severe depression	1.61 (0.91–2.86)	1.61 (0.91–2.87)	1.29 (0.72–2.29)
<b>Waist Circumference</b>			
Mild depression	<b>1.68 (1.10–2.56)</b>	<b>1.65 (1.06–2.56)</b>	
Severe depression	1.58 (0.78–3.21)	1.55 (0.78–3.10)	

<sup>a</sup> reference category compared to Non-depressed<sup>b</sup> adjusted with other factors in model