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Profiles of sociodemographic, behavioral, clinical and psychosocial characteristics among primary care patients with comorbid obesity and depression

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ABSTRACT

The objective of this study is to characterize profiles of obese depressed participants using baseline data collected from October 2014 through December 2016 for an ongoing randomized controlled trial (n = 409) in Bay Area, California, USA. Four comorbidity severity categories were defined by interaction of the binary levels of body mass index (BMI) and depression Symptom Checklist 20 (SCL20) scores. Sociodemographic, behavioral, clinical and psychosocial characteristics were measured. Mean (SD) age was 51 (12.1) years, BMI 36.7 (6.4) kg/m^2, and SCL20 1.5 (0.5). Participants in the 4 comorbidity severity categories had similar sociodemographic characteristics, but differed significantly in the other characteristics. Two statistically significant canonical dimensions were identified. Participants with BMI ≥ 35 and SCL20 ≥ 1.5 differed significantly from those with BMI < 35 and SCL20 < 1.5 on dimension 1, which primarily featured high physical health (e.g., central obesity, high blood pressure and impaired sleep) and mental health comorbidities (e.g., post-traumatic stress and anxiety), poor health-related quality of life (in general and problems specifically with obesity, anxiety, depression, and usual daily activities), and an avoidance problem-solving style. Participants with BMI < 35 and SCL20 ≥ 1.5 differed significantly from those with BMI ≥ 35 and SCL20 < 1.5 on dimension 2, which primarily included fewer Hispanics, less central obesity, and more leisure-time physical activity, but greater anxiety and post-traumatic stress and poorer obesity- or mental health-related quality of life. In conclusion, patients with comorbid obesity and depression of varying severity have different profiles of behavioral, clinical and psychosocial characteristics. This insight may inform analysis of treatment heterogeneity and development of targeted intervention strategies.

Trial registration: ClinicalTrials.gov #NCT02246413

1. Introduction

Obesity and depression are serious health concerns in the United States (U.S.), both showing steadily increasing prevalence in the past decade (Flegal et al., 2016; Pratt and Brody, 2014). More than two-thirds of U.S. adults have obesity based on a body mass index (BMI) ≥ 30 kg/m^2 (Flegal et al., 2016). Over 15.7 million (6.6%) have experienced at least 1 major depressive episode in a 12-month period

Abbreviations: SCL20, Depression Symptom Checklist 20; EHR, Electronic health record; PCPs, Primary care providers; MET, Metabolic equivalent of task; SPSI-R:S, Social Problem-Solving Inventory—Revised: Short Form; PHQ, Patient Health Questionnaire; GAD7, Generalized Anxiety Disorder Scale; MINI, Mini-International Neuropsychiatric Interview; PTSD, Posttraumatic stress disorder; EQ-5D-5 L, European Quality of Life-5 Dimension-5 Levels; SF-8, Short Form-8 Health Survey

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(SAMHSA, 2015), with a life time prevalence of 18.6% (Gonzalez et al., 2010). Additionally, mounting epidemiologic evidence has shown a temporally reciprocal, positive relationship between these 2 conditions; namely, people with obesity are more likely to develop new-onset depression, and vice versa (Blaine, 2008; Luppino et al., 2010; Markowitz et al., 2008; Wiltink et al., 2013). Comorbid obesity and depression exact even greater morbidity and disability than either condition alone. They share major health sequelae, such as diabetes and cardiovascular disease, and have synergistic adverse effects on treatment adherence and response and quality of life (Katon, 2011; Ladwig et al., 2006; Werrij et al., 2006). Evidence-based behavioral therapies are recommended treatment options for obesity and depression based on studies that focused on each condition separately (American Psychiatric Association, 2010; Jensen et al., 2014). However, randomized controlled trials (RCTs) of similar approaches have shown mixed results when applied to treat comorbid depression and obesity (Linde et al., 2011; Ludman et al., 2010; Pagoto et al., 2013).

Obesity and depression are complex disorders, with heterogeneous etiology and clinical manifestations. So far, effects observed in RCTs of behavioral treatments for each condition have been modest and variable. Expected heterogeneity among individuals with both conditions is poorly understood, but likely important for population characterization and for treatment development. Yet, few studies to date have exclusively focused on patients with comorbid obesity and depression. Evidence is lacking on individual characteristics, or their combinations (profiles), that may differentiate patients with varying severity levels of the comorbidity. Addressing this gap will provide insights into the nature and extent of heterogeneity within a growing population afflicted with 2 major public health problems. The knowledge gained would improve the understanding of treatment heterogeneity, and inform the development and testing of targeted treatments.

In this study, we leveraged rigorously assessed baseline data from a large ongoing RCT of an integrated behavior therapy for obese depressed adult patients in primary care (Ma et al., 2015). The main objective was to examine whether patients with obesity and depression had different profiles of sociodemographic, behavioral, clinical, and psychosocial characteristics according to the severity levels of their comorbidity.

2. Methods

2.1. Study design

This cross-sectional study used baseline data collected from October 2014 through December 2016 for a 2-arm RCT, titled “Research Aimed at Improving Both Mood and Weight (RAINBOW).” The RAINBOW trial aims to compare an integrated behavioral intervention with usual care for adult patients with comorbid obesity and depression seen in primary care. The Institutional Review Board for the health system where recruitment occurred approved the trial; all enrolled participants provided written informed consent. The full RAINBOW trial protocol was previously published (Ma et al., 2015). The current study examined only baseline data.

2.2. Participants

Participant recruitment occurred in the family and internal medicine departments of multiple medical centers within a large community-based multispecialty group practice in the Silicon Valley, California. English-speaking patients ≥ 18 years of age who did not have exclusionary medical (e.g., diabetes or cardiovascular disease) or psychiatric comorbidities (e.g., psychotic or bipolar disorders) completed a multistep screening process. First, patients whose electronic health record (EHR) documented BMI ≥ 30 kg/m^2 (≥ 27 if Asian), with or without indications of depression (e.g., prior diagnosis or antidepressant prescriptions), were pre-identified for approval of study contact by their primary care providers (PCPs). All PCP-approved patients received recruitment invitations by email or mail (if no email address in EHR). A bifurcated screening strategy was then used for efficiency. Study staff proactively called to screen patients with prior depression based on EHR. Because of their expected lower eligibility rates, patients *without* prior depression were incentivized with raffles to self-screen using the 9-item Patient Health Questionnaire (PHQ9) (Kroenke et al., 2001), and study staff called only those who self-screened eligible. Finally, all participants must have completed an in-person baseline measurement visit and passed final EHR review and approval by the study physician to be randomized.

2.3. Dependent variables

BMI (kg/m^2) was calculated based on height and weight measured by trained study coordinators at baseline. As per standardized protocol (Measures from the PhenX Toolkit, 2011), duplicate measurements were taken in light indoor clothes and no shoes using calibrated equipment, and rounded to the nearest 0.1 cm for height and the nearest 0.1 kg for weight. Depression severity was measured using the Symptom Checklist 20 items (SCL20) (Derogatis et al., 1974; Glass et al., 1978; Goldberg et al., 1976). To elucidate different profiles, we divided these 2 baseline measures according to commonly used cut-points, and then combined them to create 4 comorbidity severity categories. We used BMI ≥ 35 kg/m^2 (Class II obesity) as the cut-point for high severity obesity and SCL20 ≥ 1.5 as the cut-point for high severity depressive symptoms.(Linde et al., 2011) These cut-points were appropriate also based on the study sample means. The 4 comorbidity severity categories included the lowest severity (BMI < 35 and SCL20 < 1.5), depression-dominant intermediate severity (BMI < 35 and SCL20 ≥ 1.5), obesity-dominant intermediate severity (BMI ≥ 35 and SCL20 < 1.5), and the highest severity (BMI ≥ 35 and SCL20 ≥ 1.5).

2.4. Independent variables

2.4.1. Sociodemographic characteristics

Participants self-reported their age, sex, race, ethnicity, education, family annual income, marital status and household size.

2.4.2. Behavioral characteristics

These included measures of diet, physical activity, sleep quality, and problem solving orientation and skills. Trained study coordinators administered a single 24-h diet recall to each participant by phone using the multiple pass method (Conway et al., 2004; Conway et al., 2003) through the Windows-based Nutrition Data System for Research (NDSR, Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN, USA). These data were used to compute each participant's Dietary Approaches to Stop Hypertension (DASH) concordance index as a measure of overall diet quality (Mellen et al., 2008). The study coordinators also administered in person the Stanford 7-day Physical Activity Recall, which provided data on leisure time physical activity in metabolic equivalent of task (MET) minutes per week (Blair et al., 1985). Participants self-administered the PROMIS sleep disturbance and sleep impairment scales, 8 items each (Yu et al., 2011), and the 25-item Social Problem-Solving Inventory—Revised: Short Form (SPSI-R:S). The latter includes 5 subscales for positive problem orientation (PPO), negative problem orientation (NPO), rational problem solving (RPS), impulsive/careless style (ICS), and avoidance style (AS) (D'Zurilla et al., 1998).

2.4.3. Clinical characteristics

These included waist circumference, blood pressure (BP), binge eating disorder, anxiety, and posttraumatic stress disorder. The study coordinators obtained duplicate measurements of waist circumference using a nonstretchable tape placed in a horizontal plane around the

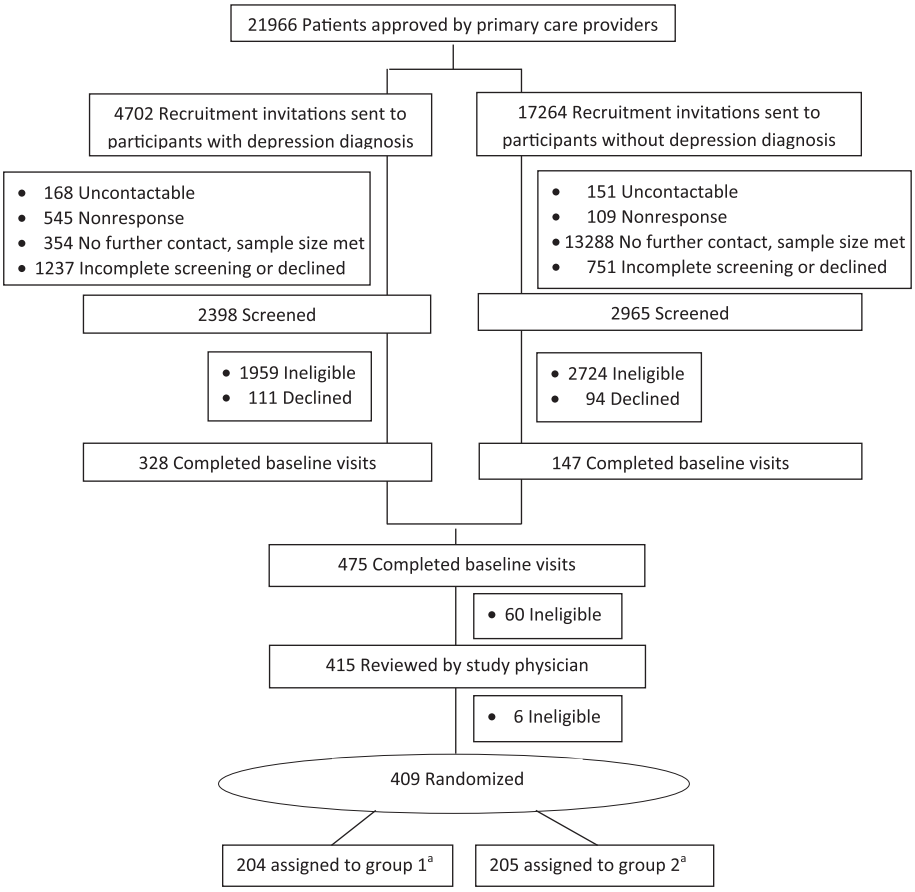

Fig. 1. Participant flow of the Research Aimed at Improving Both Mood and Weight (RAINBOW) trial in Bay Area, California, USA, 2014–2016. [a]Treatment assignments remain masked given that the trial is still ongoing at the time of this study, which uses only baseline data.

abdomen at the level of the right iliac crest according to standardized protocol (Measures from the PhenX Toolkit, 2011). They followed the American Heart Association standards for resting BP measurements (Pickering et al., 2005). Participants self-administered the eating disorder module of the Patient Health Questionnaire (PHQ-ED) (Spitzer et al., 1999), the Generalized Anxiety Disorder Scale (GAD7) (Spitzer et al., 2006), and the Panic Disorder module of the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998), and the 17-item posttraumatic stress disorder (PTSD) checklist – Civilian Version (Weathers et al., 1993).

2.4.4. Psychosocial characteristics

These included health-related quality of life, obesity-related psychosocial problems, and disability, all by self-report. The European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) has 5 dimensions (mobility, self-care, usual activities, pain and discomfort, and depression and anxiety) scored on 5 levels (no, slight, moderate, severe, or extreme problems) (Badia et al., 1998). The Short Form-8 Health Survey (SF-8) is an 8-item version of the SF-36 that measures overall health-related quality of life (Ware et al., 2001). The 8-item Obesity-Related Problem Scale measures the impact of obesity on psychosocial functioning (Karlsson et al., 2003). The Sheehan Disability Scale measures the extent to which people's symptoms impair work/school, social, and family life and the number of days when the symptoms cause them to miss and/or be unproductive at work/school (Sheehan and Sheehan, 2008).

2.5. Statistical analysis

Percentages and means (standard deviations [SD]) were used to describe the baseline characteristics. We used Fisher's least significant difference method, which has two steps. First, we performed bivariate analyses using analysis of variance (ANOVA) (for continuous variables) and Chi-square tests (for categorical variables) to compare the sociodemographic, behavioral, clinical, and psychosocial characteristics across the 4 comorbidity severity categories. Second, variables with P values < 0.05 were then further assessed for pairwise comparisons using Student's t-tests for continuous variables and Chi-square tests for categorical variables.

Canonical discriminant analysis was used to derive linear combinations of the independent variables (i.e., characteristic profiles) that might significantly differentiate the 4 comorbidity severity categories. Canonical discriminant analysis is a multivariate dimension-reduction technique that derives a linear combination of explanatory variables that has the highest possible multiple correlation with the groups of a classification variable. The dimension defined by the linear combination is the first canonical dimension. This maximum multiple correlation is called the first canonical correlation. The coefficients of the linear combination are the canonical coefficients. The second canonical dimension is obtained by finding the linear combination with the next highest possible multiple correlation with the groups that is uncorrelated with the first canonical dimension. The process of extracting canonical dimensions can be repeated until the number of canonical dimensions equals the number of original variables or the number of groups minus one, whichever is smaller. In this study, canonical discriminant analysis was used to identify dimensions representing linear combinations of baseline characteristics that had statistically significant multiple correlations with the 4 comorbidity severity categories. It included only the baseline characteristics with P values < 0.05 from bivariate analyses. The categorical variables are coded as dummy variables in the canonical discriminant analysis. Standardized canonical coefficients measured the strength and direction of correlation of each dimension with the characteristics. Participant scores on each dimension were calculated as a sum of the products of canonical coefficients

Table 1
Sociodemographic, behavioral, clinical and psychosocial characteristics as well as Canonical multivariate dimension scores among participants, overall and by comorbid obesity and depression severity category, in Bay Area, California, USA, 2014-2016[a].

Characteristic within domain	All (n = 409)	Lowest severity (n = 107)	Depression-dominant intermediate severity (n = 102)	Obesity-dominant intermediate severity (n = 96)	Highest severity (n = 104)	P value
Sociodemographic domain						
Clinic site						0.31
Los Altos	76	16	22	21	17	
Mountain view	123	32	26	29	36	
Palo Alto	166	45	49	35	37	
Sunnyvale	44	14	5	11	14	
Age, year	51.0 ± 12.1	52.4 ± 11.9	50.1 ± 12.6	51.6 ± 10.9	49.7 ± 12.6	0.34
Female, %	70.2 (287/409)	64.5 (69/107)	68.6 (70/102)	74.0 (71/96)	74.0 (77/104)	0.37
Race/ethnicity, %		1,2	1	2	2	0.02
Non-Hispanic white	70.7 (289/409)	69.2 (74/107)	71.6 (73/102)	77.1 (74/96)	65.4 (68/104)	
Non-Hispanic black	1.5 (6/409)	0.9 (1/107)	0 (0/102)	3.1 (3/96)	1.9 (2/104)	
Asian/Pacific islander	9.8 (40/409)	13.1 (14/107)	15.7 (16/102)	4.2 (4/96)	5.8 (6/104)	
Hispanic	13.7 (56/409)	14.0 (15/107)	7.8 (8/102)	13.5 (13/96)	19.2 (20/104)	
Other race	4.4 (18/409)	2.8 (3/107)	4.9 (5/102)	2.1 (2/96)	7.7 (8/104)	
Education, %						0.16
High school/GED or less	6.8 (28/409)	6.5 (7/107)	3.9 (4/102)	7.3 (6/96)	9.6 (10/104)	
Some college	24.0 (98/409)	25.2 (27/107)	24.5 (25/102)	24.0 (23/96)	22.1 (23/104)	
College graduate	36.7 (150/409)	35.5 (38/107)	28.4 (29/102)	37.5 (36/96)	45.2 (47/104)	
Post college	32.5 (133/409)	32.7 (35/107)	43.1 (44/102)	31.3 (30/96)	23.1 (24/104)	
Income, %, n = 365						0.81
< $35,000	8.5 (31/365)	7.1 (7/98)	8 (7/88)	7 (6/86)	11.8 (11/93)	
$35,000– < $55,000	6.6 (24/365)	6.1 (6/98)	8 (7/88)	7 (6/86)	5.4 (5/93)	
$55,000– < $75,000	10.4 (38/365)	11.2 (11/98)	10.2 (9/88)	7 (6/86)	12.9 (12/93)	
$75,000– < $100,000	11.8 (43/365)	8.2 (8/98)	11.4 (10/88)	16.3 (14/86)	11.8 (11/93)	
$100,000– < $125,000	12.1 (44/365)	10.2 (10/98)	12.5 (11/88)	8.1 (7/86)	17.2 (16/93)	
$125,000– < $150,000	8.2 (30/365)	9.2 (9/98)	8 (7/88)	9.3 (8/86)	6.5 (6/93)	
≥$150,000	42.5 (155/365)	48 (47/98)	42 (37/88)	45.3 (39/86)	34.4 (32/93)	
Marital status, %, n = 406		1	1	1,2	2	0.03
Married/living with a partner	60.6 (246/406)	69.2 (74/107)	62.7 (64/102)	61.3 (57/93)	49.0 (51/104)	
Single/separated/divorced/widowed	39.4 (160/406)	30.8 (33/107)	37.3 (38/102)	38.7 (36/93)	51.0 (53/104)	
Household size, %, n = 400						0.87
< 2	19.0 (76/400)	17.3 (18/104)	16.3 (16/98)	20.8 (20/96)	21.6 (22/102)	
= 2	36.0 (144/400)	37.5 (39/104)	36.7 (36/98)	38.5 (37/96)	31.4 (32/102)	
3 +	45.0 (180/400)	45.2 (47/104)	46.9 (46/98)	40.6 (39/96)	47.1 (48/102)	
Behavioral domain						
DASH score[b], n = 406	2.3 ± 1.3	2.4 ± 1.3	2.3 ± 1.2	2.2 ± 1.3	2.2 ± 1.3	0.36
Leisure-time physical activity, MET mins/week[c]	713.2 ± 870	842.8 ± 816[1]	904.9 ± 1189[1]	563.0 ± 662[2]	530.5 ± 642[2]	0.002
PROMIS sleep disturbance raw score[d]	22.6 ± 3.2	22.2 ± 3.3	23.0 ± 3.5	22.2 ± 3.1	22.8 ± 2.6	0.15
PROMIS sleep impairment raw score[e]	22.1 ± 5.9	19.8 ± 5.3[1]	23.9 ± 6.1[2]	20.7 ± 5.3[1]	24.0 ± 5.8[2]	< 0.001
SPSI-R:S raw score, n = 399[f]	11.9 ± 2.6	12.4 ± 2.5[1]	11.4 ± 2.7[2]	12.2 ± 2.2[1,3]	11.6 ± 2.8[2,3]	0.009
PPO raw score, n = 405[f]	9.7 ± 4.3	10.2 ± 4.3	9.2 ± 4.1	9.8 ± 4.5	9.8 ± 4.4	0.45
NPO raw score, n = 408[f]	8.5 ± 3.6	7.8 ± 3.4[1]	9.6 ± 3.7[2]	7.2 ± 3.2[1]	9.5 ± 3.6[2]	< 0.001
RPS raw score, n = 404[f]	9.5 ± 4.3	9.6 ± 4.6	9.7 ± 4.2	9.1 ± 4.3	9.4 ± 4.2	0.79
ICS raw score, n = 407[f]	4.4 ± 3.5	4.4 ± 3.7	4.7 ± 3.6	4.0 ± 2.9	4.4 ± 3.6	0.62
AS raw score, n = 407[f]	6.9 ± 4.6	5.5 ± 3.5[1]	8.0 ± 5.1[2]	6.6 ± 3.9[1,3]	7.4 ± 5.1[2,3]	< 0.001
Clinical domain						
Waist circumference, cm	115.7 ± 13.6	108.6 ± 8.3[1]	108.1 ± 7.6[1]	123.4 ± 13.2[2]	123.3 ± 14.9[2]	< 0.001
SBP, mmHg, n = 408	120.2 ± 12.0	118.6 ± 12.6[1]	118.3 ± 11.4[1]	121.9 ± 12.9[2]	122.0 ± 10.6[2]	0.03
DBP, mmHg, n = 408	79.3 ± 9.1	78.0 ± 9.7[1]	78.2 ± 8.4[1]	81.0 ± 9.5[2]	80.0 ± 8.3[1,2]	0.05
Binge eating disorder, %	40.8 (167/409)	35.5 (38/107)	34.3 (35/102)	43.8 (42/96)	50.0 (52/104)	0.07
Generalized anxiety disorder scale-7 score[g], n = 407	8.4 ± 5.1	6.5 ± 4.6[1]	11.0 ± 4.9[2]	6.1 ± 4.0[1]	9.7 ± 4.9[3]	< 0.001
Panic disorder, %, n = 399						0.13
No panic disorder	87.2 (348/399)	86.8 (92/106)	84.7 (83/98)	94.7 (89/94)	83.1 (84/101)	
Panic disorder lifetime	7.8 (31/399)	6.6 (7/106)	10.2 (10/98)	2.1 (2/94)	11.9 (12/101)	
Limited symptom attacks lifetime	1.0 (4/399)	2.8 (3/106)	1.0 (1/98)	0 (0/94)	0 (0/101)	
Panic disorder current	4.0 (16/399)	3.8 (4/106)	4.1 (4/98)	3.2 (3/94)	5.0 (5/101)	
Post-traumatic stress disorder severity score, n = 404[h]	39.0 ± 12.5	32.9 ± 10.1[1]	45.9 ± 12.4[2]	33.4 ± 8.7[1]	43.4 ± 12.8[2]	< 0.001
Psychosocial domain						
EQ-5D-5L: mobility, %, n = 408		1,2	1	2,3	3	0.009
No problems	63.7 (260/408)	71 (76/107)	74.5 (76/102)	56.3 (54/96)	52.4 (54/103)	
Slight problems	27.5 (112/408)	22.4 (24/107)	18.6 (19/102)	35.4 (35/96)	33.0 (34/103)	
Moderate problems	7.8 (32/408)	3.7 (4/107)	6.9 (7/102)	7.3 (7/96)	13.6 (14/103)	
Severe problems	0.5 (2/408)	0.9 (1/107)	0 (0/102)	0 (0/96)	1.0 (1/103)	
Extreme problems	0.5 (2/408)	1.9 (2/107)	0 (0/102)	0 (0/96)	0 (0/103)	
EQ-5D-5L: self-care, %, n = 407						0.08
No problems	89.4 (364/407)	97.2 (103/106)	88.2 (90/102)	89.6 (86/96)	82.5 (85/103)	

(continued on next page)

Table 1 *(continued)*

Characteristic within domain	All (n = 409)	Lowest severity (n = 107)	Depression-dominant intermediate severity (n = 102)	Obesity-dominant intermediate severity (n = 96)	Highest severity (n = 104)	P value
Slight problems	7.9 (32/407)	1.9 (2/106)	7.8(8/102)	8.3 (8/96)	13.6 (14/103)	
Moderate problems	2.5 (10/407)	0 (0/106)	3.9 (4/102)	2.1 (2/96)	3.9 (4/103)	
Severe problems	0 (0/407)	0 (0/106)	0 (0/102)	0 (0/96)	0 (0/103)	
Extreme problems	0.2 (1/407)	0.9 (1/106)	0 (0/102)	0 (0/96)	0 (0/103)	
EQ-5D-5L: usual activities, %		1	2	3	4	< 0.001
No problems	49.1 (201/409)	67.3 (72/107)	52.9 (54/102)	47.9 (46/96)	27.9 (29/104)	
Slight problems	35.0 (143/409)	23.4 (25/107)	25.5 (26/102)	43.8 (42/96)	48.1 (50/104)	
Moderate problems	13.7 (56/409)	7.5 (8/107)	18.6 (19/102)	8.3 (8/96)	20.2 (21/104)	
Severe problems	1.7 (7/409)	0 (0/107)	2.9 (3/102)	0 (0/96)	3.8 (4/104)	
Extreme problems	0.5 (2/409)	1.9 (2/107)	0 (0/102)	0 (0/96)	0 (0/104)	
EQ-5D-5L: pain/discomfort, %		1	1,2,3	2	3	0.005
No problems	21.8 (89/409)	32.7 (35/107)	21.6 (22/102)	18.8 (18/96)	13.5 (14/104)	
Slight problems	46.2 (190/409)	42.1 (45/107)	48 (49/102)	53.1 (52/96)	42.3 (44/104)	
Moderate problems	28.1 (114/409)	23.4 (25/107)	23.5 (24/102)	28.1 (26/96)	37.5 (39/104)	
Severe problems	3.7 (15/409)	1.9 (2/107)	5.9 (6/102)	0 (0/96)	6.7 (7/104)	
Extreme problems	0.2 (1/409)	0 (0/107)	1.0 (1/102)	0 (0/96)	0 (0/104)	
EQ-5D-5L: anxiety/depression, %		1	2	1	2	< 0.001
No problems	8.3 (35/409)	15.0 (16/107)	2.9 (3/102)	13.5 (14/96)	1.9 (2/104)	
Slight problems	42.5 (174/409)	59.8 (64/107)	30.4 (31/102)	54.2 (52/96)	26.0 (27/104)	
Moderate problems	40.3 (164/409)	22.4 (24/107)	50 (51/102)	30.2 (28/96)	58.7 (61/104)	
Severe problems	6.8 (28/409)	1.9 (2/107)	13.7 (14/102)	1.0 (1/96)	10.6 (11/104)	
Extreme problems	2.0 (8/409)	0.9 (1/107)	2.9 (3/102)	1.0 (1/96)	2.9 (3/104)	
Obesity-related problem raw score[i], n = 408	2.0 ± 0.7	1.7 ± 0.8[1]	2.2 ± 0.6[2]	1.9 ± 0.7[3]	2.3 ± 0.7[2]	< 0.001
Sheehan disability score[j], n = 403	12.0 ± 6.8	8.6 ± 6.2[1]	15.0 ± 6.9[2]	9.6 ± 5.9[1]	14.5 ± 5.7[2]	< 0.001
SF-8 physical component score[k], n = 408	45.2 ± 8.6	47.5 ± 7.7[1]	46.4 ± 8.3[1,2]	44.7 ± 8.3[2]	42.3 ± 9.1[3]	< 0.001
SF-8 mental component score[k], n = 408	37.5 ± 9.5	42.2 ± 8.1[1]	32.9 ± 8.9[2]	41.4 ± 8.9[1]	33.5 ± 8.2[2]	< 0.001
Canonical multivariate dimension scores						
Dimension 1, n = 391	0 ± 1.32	−1.24 ± 0.95[1]	0.08 ± 1.03[2]	−0.03 ± 1.00[2]	1.16 ± 1.02[3]	< 0.001
Dimension 2, n = 391	0 ± 1.23	−0.06 ± 0.76[1]	1.11 ± 0.93 [2]	−0.95 ± 1.11[3]	−0.16 ± 1.18[1]	< 0.001

Abbreviations: AS, Avoidance Style; BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; EQ-5D-5L, European Quality of Life-5 dimensions-5 levels; ICS, impulsivity/carelessness style; MET, metabolic equivalent task; NPO, negative problem orientation; PPO, positive problem orientation; PROMIS, Patient-Reported Outcomes Measurement Information System; RPS, rational problem solving; SBP, systolic blood pressure; SCL20, Symptom Checklist-20; SF-8, Short Form 8 Health Survey; SPSI-R:S, Social Problem Solving Inventory -Revised: Short Form.

[1,2,3] and [4] Different superscripts denote statistically significant differences.

[a] 4 comorbidity severity categories: lowest severity (BMI < 35 and SCL20 < 1.5), depression-dominant intermediate severity (BMI < 35 and SCL20 ≥ 1.5), obesity-dominant intermediate severity (BMI ≥ 35 and SCL20 < 1.5), and highest severity (BMI ≥ 35 and SCL20 ≥ 1.5). Plus-minus values are means ± SD; total n = 409 unless noted otherwise.

[b] DASH scores were calculated based on combining 9 nutrient targets (i.e., total fat, saturated fat, protein, cholesterol, fiber, magnesium, calcium, sodium, and potassium) according to a previously publish algorithm (Mellen et al., 2008). The intermediate target of each nutrient was half-way between the DASH target and population mean (based on the National Health and Nutrition Examination Surveys 2007–2008, latest data available at the inception of this study). For a nutrient, participants reaching the DASH target were assigned 1 point, those reaching the intermediate target were assigned a half-point, and those not meeting the intermediate target were given 0 point. The DASH score was the sum of points for all 9 nutrients.

[c] MET minutes/week were calculated as leisure time moderate activity minutes × 4 + hard activity minutes × 6 + very hard activity minutes × 10 from the Stanford 7-Day Physical Activity Recall.

[d] (Raw sum × number of items on the short form) / number of items answered. Each of the 8 questions ranges from 1 not at all to 5 very much. The higher the score the greater sleep disturbance.

[e] (Raw sum × number of items on the short form) / number of items answered. Each of the 8 questions ranges from 1 not at all to 5 very much. The higher the score the greater sleep impairment.

[f] SPSI-R:S score = (PPO raw score/5) + (20- NPO raw score)/5 + (RPS raw score/5) + (20- ICS raw score)/5 + (20- AS raw score)/5; the higher the score the more productive overall problem-solving orientation and skills. Subscales (PPO, NPO, RPS, ICS, and AS) are raw scores without reversal.

[g] GAD7 scores were calculated by assigning 0, 1, 2, and 3 points to the response categories of "not at all," "several days," "more than half the days," and "nearly every day," respectively, and summing the points of the 7 questions. Scores of 5, 10, and 15 are cutoff points for mild, moderate, and severe anxiety, respectively.

[h] Sum of 17-item scores based on the responses ranging from 1 not at all to 5 extremely. Levels of post-traumatic stress scores are low (17–33), moderate (34–43), and high (44–85).

[i] Average of 8 questions with a range of 0–3. The higher the score the more obesity-related psychosocial problems.

[j] Sum of 3 items measuring global functional impairment with a range from 0 (unimpaired) to 30 (highly impaired).

[k] Physical and mental component scores of the SF8 measure self-reported overall physical and mental functioning. These summary scales have been normalized in the U.S. population (value = 50). The higher the score the better health-related quality of life.

and the participant's individual values for the characteristics. These scores were then compared among the 4 comorbidity severity categories using ANOVA. All analyses were conducted in SAS version 9.4 (SAS Institute Inc., Cary, North Carolina). Statistical significance was defined as $P < 0.05$ (2-sided).

3. Results

3.1. Baseline characteristics

As shown in Fig. 1, 21,966 patients (4702 with and 17,264 without prior depression as per EHR) were sent recruitment invitations. A majority of patients without prior depression (13,288) received no further attempts if they had not self-screened when the target enrollment was met, whereas this was the case for only 354 patients with prior depression as a result of proactive staff screening of this higher risk group.

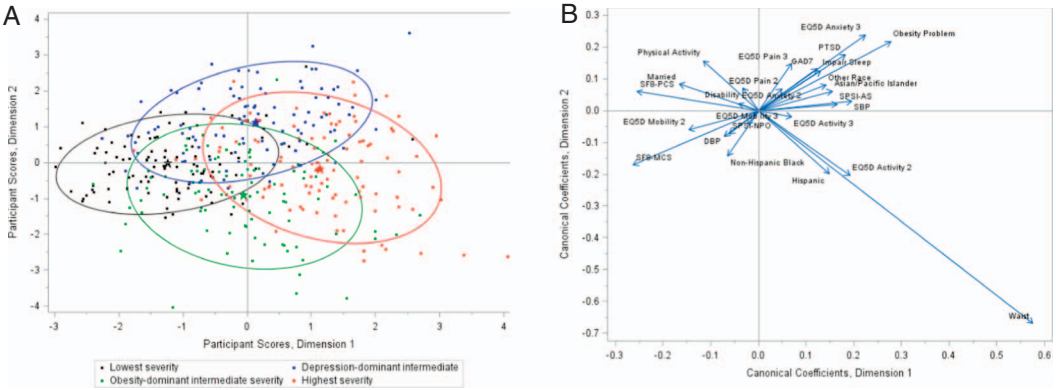

Fig. 2. Canonical discriminant analysis results of baseline characteristics for participants in Bay Area, California, USA, 2014–2016. A. Distribution of participants' dimension scores according to the 4 comorbidity severity categories. Each dot represents an individual participant. Individual dots (participants) of one color belong to the ellipse of the same color denoting each comorbidity severity category: black, lowest severity; blue, depression-dominant intermediate severity; green, obesity-dominant intermediate severity; and red, highest severity. Each ellipse indicates an 80% confidence ellipse for the mean of each severity category marked by a star in the center of the ellipse. B. Correlation coefficients of individual characteristics in the 2 canonical dimensions. Abbreviations: AS, Avoidance Style; BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; EQ-5D-5L, European Quality of Life-5 dimensions-5 levels; ICS, impulsivity/carelessness style; Married, marital status, married/living with another person; MET, metabolic equivalent task; NPO, negative problem orientation; PPO, positive problem orientation; PROMIS, Patient-Reported Outcomes Measurement Information System; RPS, rational problem solving; SBP, systolic blood pressure; SCL20, Symptom Checklist-20; SF-8, Short Form 8 Health Survey; SPSI-R:S, Social Problem Solving Inventory -Revised: Short Form. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

A total of 5363 patients (2398 with and 2965 without prior depression) completed screening, 475 (328 and 147) screened eligible and completed baseline visits, and 409 (285 and 124) proved fully eligible and were randomized. These participants were middle aged (mean 51 [SD 12.1] years), primarily women (70.2%), non-Hispanic White (70.7%), and college educated (69.2%) (Table 1). Most (62.8%) reported annual family income at or above $100,000. Their mean BMI was 36.7 (SD 6.4) kg/m^2 and mean SCL20 score was 1.5 (0.5).

3.2. Bivariate analyses

Participants in the 4 comorbidity severity categories had similar sociodemographic characteristics, but they differed significantly on behavioral, clinical and psychosocial characteristics (Table 1). Regardless of depression severity based on SCL20, participants with greater obesity (BMI ≥ 35) had less leisure-time physical activity, larger waist circumference, and higher systolic and diastolic BP than those with less obesity (BMI < 35). Regardless of obesity severity, participants with more vs. less severe depression (SCL20 ≥ 1.5 vs. < 1.5) reported less productive problem solving as indicated by worse SPSI-P:S total scores as well as higher scores on its negative problem orientation and avoidance style subscales. They also reported greater anxiety on the GAD7, higher post-traumatic stress, and poorer mental health-related quality of life on both the EQ-5D-5L and the SF8. Additionally, they had more obesity-related psychosocial problems, more impaired sleep, and greater disability. Furthermore, with increasing levels of the comorbidity severity, an increasingly higher percentage of participants reported more problems with mobility, usual daily activities, pain or discomfort based on the EQ-5D-5L as well as poorer physical health on the SF8. Between the 2 intermediate severity categories, the depression-dominant type had a higher percentage of Asians and a lower percentage of Hispanics than the obesity-dominant type.

3.3. Multivariate analysis

Canonical discriminant analysis identified 2 orthogonal dimensions representing statistically significant combinations of sociodemographic, behavioral, clinical and psychosocial characteristics. The canonical variates of dimension 1 and 2 explained 43% and 35%, respectively, of the total variance of the 4 comorbidity severity categories. Participants in the highest (BMI ≥ 35 and SCL20 ≥ 1.5) and lowest (BMI < 35 and SCL20 < 1.5) comorbidity severity categories had the most extreme mean scores (1.16 vs. -1.24, $P < 0.001$) on the canonical dimension 1. Participants in the depression-dominant (BMI < 35 and SCL20 ≥ 1.5) and obesity-dominant (BMI ≥ 35 and SCL20 < 1.5) intermediate severity categories had the highest and lowest mean scores (1.11 vs. -0.95, $P < 0.001$), respectively, on the canonical dimension 2 (Table 1 and Fig. 2A). According to characteristics with the highest positive or negative correlation coefficients (Table 2 and Fig. 2B), the canonical dimension 1 featured a profile of high physical health (e.g., central or abdominal obesity as indicated by high waist circumference, high BP, and impaired sleep) and mental health comorbidities (e.g., PTSD and anxiety), poor physical and mental health-related quality of life (in general and problems specifically with obesity, anxiety, depression, and usual daily activities), and an avoidance problem-solving style. The canonical dimension 2 combined some of the same characteristics, though with coefficients of different strength or direction compared to the dimension 1, as well as additional characteristics. Dimension 2 primarily featured fewer Hispanics, less central or abdominal obesity, and more leisure-time physical activity, but more anxiety and post-traumatic stress and poorer obesity- or mental health-related quality of life (problems specifically with obesity, anxiety, depression, pain, and discomfort).

4. Discussion

Using rigorously assessed baseline data from a well-characterized RCT sample, this study showed important behavioral, clinical, and psychosocial heterogeneities according to comorbidity severity within a sociodemographically homogeneous group of obese depressed adult patients in primary care. The results showed that compared with participants with comorbid obesity and depression of the lowest severity, those with the highest severity featured a profile of significantly higher burden of physical and mental health comorbidities, poorer generic and condition-specific quality of life, and an avoidance problem-solving style. Even among participants with intermediate comorbidity severity, the profiles varied for the depression-dominant vs. the obesity-dominant type where the former included fewer Hispanics, less central obesity, and more physical activity, but greater mental health comorbidities and related impairments in quality of life.

The past 25 years have witnessed a growth of the literature on the relationship between obesity and depression. The first generation of studies focused on the cross-sectional prevalence of one disease

Table 2
Standardized coefficients from canonical discriminant analysis for individual sociodemographic, behavioral, clinical, psychosocial characteristics of participants in Bay Area, California, USA, 2014–2016 (n = 392)[a].

Characteristic	Dimension 1[b]	Dimension 2[c]
Sociodemographic		
Race/ethnicity (reference = Non-Hispanic white)		
Non-Hispanic black	− 0.06	− 0.14
Asian/Pacific islander	0.15	0.06
Hispanic	0.15	− 0.20
Other race	0.14	0.08
Marital status (reference = single/separated/divorced/widowed)		
Married/living with another person	− 0.17	0.08
Behavioral		
Leisure-time physical activity	− 0.12	0.16
PROMIS sleep impairment raw score	0.13	0.13
SPSI-R:S NPO raw score	− 0.06	− 0.07
SPSI-R:S AS raw score	0.16	0.02
Clinical		
Waist circumference	0.58	− 0.67
SBP	0.19	− 0.03
DBP	− 0.07	− 0.08
Generalized anxiety disorder scale-7 score	0.12	0.13
Post-traumatic stress disorder severity score	0.18	0.18
Psychosocial		
EQ-5D-5 L: mobility (reference = no problems)		
Slight problems	− 0.15	− 0.06
Moderate/severe/extreme problems	− 0.02	− 0.04
EQ-5D-5 L: usual activities (reference = no problems)		
Slight problems	0.19	− 0.20
Moderate/severe/extreme problems	0.07	− 0.02
EQ-5D-5 L: pain/discomfort (reference = no problems)		
Slight problems	0.05	0.07
Moderate/severe/extreme problems	0.07	0.15
EQ-5D-5 L: anxiety/depression (reference = No problems)		
Slight problems	− 0.04	0.02
Moderate/severe/extreme problems	0.22	0.24
Obesity-related problem raw score	0.28	0.22
Sheehan disability score	− 0.03	0.07
SF8 physical component score	− 0.25	0.06
SF8 mental component score	− 0.26	− 0.17

Abbreviations: AS, avoidance style; DBP, diastolic blood pressure; EQ-5D-5L, European Quality of Life-5 dimensions-5 levels; NPO, negative problem orientation; PROMIS, Patient-Reported Outcomes Measurement Information System; SBP, systolic blood pressure; SF-8, Short Form 8 Health Survey; SPSI-R:S, Social Problem Solving Inventory -Revised: Short Form.

[a] Results based on 388 participants who had complete data for all the characteristics used in the Canonical discriminant analysis.

[b] Dimension 1: Canonical function F(78, 1074) = 5.78, $P < 0.0001$; R^2 of the canonical correlation = 0.43.

[c] Dimension 2: Canonical function F(50, 720) = 3.95, $P < 0.0001$; R^2 of the canonical correlation = 0.35.

(depression) between individuals with and without the other disease (obesity), and revealed a significant positive association between the 2 conditions.(de Wit et al., 2010; Onyike et al., 2003; Roberts et al., 2000) Prospective observational studies emerging later have documented a temporally bidirectional relationship whereby people with obesity are more likely to develop new-onset depression, and vice versa (Blaine, 2008; Roberts et al., 2003; Roberts et al., 2000). Investigating variability in disease severity and the associated clinical and individual factors among persons with both obesity and depression is crucial for the purpose of understanding and treating all segments of this growing comorbid population. For instance, we (Ma and Xiao, 2009) and others (Onyike et al., 2003; Preiss et al., 2013) have found that within an obese sample, depression was more prevalent in severely obese adults (BMI ≥ 40) compared to their mildly obese counterparts (BMI 30–35 kg/m^2). Moreover, this relationship appears to be stronger and more consistent in women than in men. Among obese women, a higher likelihood of depression is associated with younger age (< 65 years), higher education (high school education or higher), other medical comorbidities (e.g., asthma, diabetes, arthritis, and cardiovascular diseases), and poorer self-rated health status. The current study extends the available observational literature on comorbid obesity and depression by focusing specifically on important characteristics across multiple domains among patients affected by both of these complex and seemingly intractable diseases.

Our findings provide support for the contention that evaluating the severity of both obesity and depression and their behavioral, clinical and psychosocial heterogeneity may be necessary to develop better targeted interventions for patients with the comorbidity. In this study, the 2 identified dimensions explained a high percentage (78%) of the variance of the 4 comorbidity severity categories. Dimension 1 significantly differentiated the highest and lowest comorbidity severity categories, while dimension 2 significantly differentiated the 2 intermediate severity categories. Compared with the lowest severity category, the highest severity category featured a combination of higher physical (e.g., high BP and impaired sleep) and mental health comorbidities (e.g., PTSD and anxiety), poorer quality of life, and an avoidance problem-solving style. Compared with the obesity-dominant intermediate category, the depression-dominant intermediate category also had greater mental health comorbidities and related impairments in quality of life (e.g., problem specifically with anxiety, depression, pain, and discomfort). This could have high scientific and clinical significance especially given the disappointing results from prior trials of cognitive behavioral therapies for treating this comorbidity (Linde et al., 2011; Ludman et al., 2010; Pagoto et al., 2013). For example, perhaps patients with high comorbidity severity or with the depression-dominant type could benefit from additional targeted interventions that may augment cognitive behavioral techniques with mindfulness-based stress reduction to address anxiety, post-traumatic stress, and avoidance problem-solving style. Patients with high comorbidity severity may also benefit from specifically targeted interventions to address medical comorbidities such as hypertension and sleep disorders, such as review of treatment options for these comorbidities with their PCP, and if indicated, referral to a specialist for further evaluation and treatment (e.g., possible overnight polysomnography study to rule out obstructive sleep apnea). The frequently comorbid condition of pain with depression and obesity could also be specifically targeted either by considering alternative antidepressant medication options with the PCP such as duloxetine or a tricyclic anti-depressant, and if indicated, referral to a Pain Specialist if pain remains inadequately controlled with interventions by the PCP.

These findings should be interpreted with consideration of several study limitations. First, the cross-sectional nature of this study precludes any inference regarding causal relationships between the comorbidity severity and the characteristics. Second, the generalizability of findings may be limited due to the rigorous enrollment process for a 2-year RCT. To promote the generalizability of the sample, we deliberately recruited from not just patients with indications of depression in their EHR but also a general sample of obese adults. It is important to note that 147 of 2965 (5%) patients without prior indications of depression screened eligible. Of the 409 randomized participants, 124 (30.3%) were from this apparently not depressed recruitment pool based on EHR alone, including 32.7%, 26.5%, 42.7% and 21.2% in the lowest, depression-dominant intermediate, obesity-dominant intermediate and highest severity categories, respectively (P = 0.005). Sensitivity analysis including prior depression indicator variable did not change the canonical discriminant analysis results (data not shown). Nevertheless, participants in our study sample may not represent obese and depressed populations of different sociodemographic segments or in different health care settings. The observed profiles among the 4 obesity and depression severity categories warrant

replication in diverse populations with these comorbidities. In particular, population-specific studies in minority groups such as Asians, Hispanics, and African Americans are warranted because the relationships between obesity and depression and the characteristic profiles may vary.

In conclusion, rates of obesity and depression continue to rise and present clinical management challenges. There is an urgent need to better understand the constellation of clinical and personal factors that predispose people to varying severity of these frequent comorbid conditions. This study suggests that certain profiles featuring a clustering of behavioral, clinical and psychosocial factors depending on the comorbidity severity may be especially important. The findings help improve the understanding of heterogeneity in this complex comorbid population, and may provide a basis for elucidating treatment heterogeneity. Importantly, this information could then inform targeting of intervention strategies to enhance treatment potency and efficiency.

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Conflict of interest

The authors declare that they have no financial, research, organizational, or other interests to disclose that are relevant to the execution of this research or this publication.

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