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Original Research

Relationship between body mass index and cardiometabolic health in a multi-ethnic population: A project baseline health study

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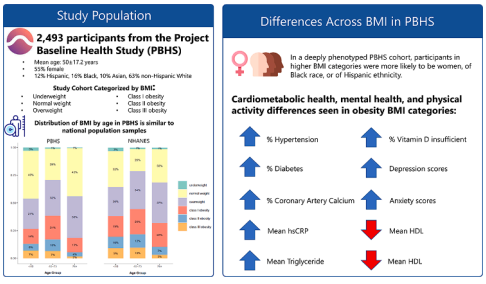
HIGHLIGHTS

- Obesity is a known cardiovascular risk factor, and the prevalence of obesity continues to rise.
- Using a multiethnic and deeply phenotyped population in the Project Baseline Health Study, we identified multiple associations of cardiometabolic and mental health characteristics with body mass index (BMI).
- The distribution of BMI by age group in the Project Baseline Health Study was comparable to that of the National Health and Nutrition Examination Survey (NHANES), suggesting generalizability of the study population.
- Cardiometabolic, mental health, and physical activity differences do exist across categories of BMI within the Project Baseline Health Study.
- Given that obesity is a strong cardiovascular risk factor, the Project Baseline Health Study provides a unique opportunity to better understand novel associations with obesity that can lead to targeted preventative efforts.

GRAPHICAL ABSTRACT



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ABSTRACT

Objective: Obesity is associated with a higher risk of cardiovascular disease. Understanding the associations between comprehensive health parameters and body mass index (BMI) may lead to targeted prevention efforts.
Methods: Project Baseline Health Study (PBHS) participants were divided into six BMI categories: underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), class I obesity (30–34.9 kg/m^2), class II obesity (35–39.9 kg/m^2), and class III obesity (BMI ≥40 kg/m^2). Demographic, cardiometabolic, mental health, and physical health parameters were compared across BMI categories, and multivariable logistic regression models were fit to evaluate associations.
Results: A total of 2,493 PBHS participants were evaluated. The mean age was 50±17.2 years; 55 % were female, 12 % Hispanic, 16 % Black, and 10 % Asian. The average BMI was 28.4 kg/m^2±6.9. The distribution of BMI by age group was comparable to the 2017–2018 National Health and Nutrition Examination Survey (NHANES) dataset. The obesity categories had higher proportions of participants with CAC scores >0, hypertension, diabetes, lower HDL-C, lower vitamin D, higher triglycerides, higher hsCRP, lower mean step counts, higher mean PHQ-9 scores, and higher mean GAD-7 scores.
Conclusion: We identified associations of cardiometabolic and mental health characteristics with BMI, thereby providing a deeper understanding of cardiovascular health across BMI.

1. Introduction

The prevalence of obesity continues to rise across the United States (U.S.) in both adult and pediatric populations[1]. Currently, an estimated 2 in 5 U.S. adults are classified as having obesity (body mass index [BMI] >30 kg/m^2), and an estimated 150 billion dollars are spent annually due to obesity-related healthcare costs[1–3]. These costs are expected to increase with time, which places a high financial burden on the U.S. healthcare system.

Importantly, obesity is an independent risk factor for cardiovascular disease (CVD) and upstream cardiometabolic consequences (e.g. type 2 diabetes mellitus [DM] and hypertension [HTN]). Recently, the decline in CVD mortality has slowed down, correlating with the rising obesity epidemic[4]. Studies have shown obesity to be associated with certain malignancies in a weight-dependent fashion[5,6]. Additionally, the COVID-19 pandemic highlighted that obesity increased the risk of a broad set of non-cardiometabolic, non-cancer health outcomes, including in-hospital death, mechanical ventilation, venous thromboembolism, and dialysis[7]. Thus, obesity is a major public health crisis with significant morbidity and mortality and is expected to lower the overall life expectancy for Americans[8]. While many studies have evaluated a small set of clinical parameters in less granular BMI categories, and often in non-diverse participants, there is a need to understand a broad set of clinical, laboratory, and mental health drivers associated with obesity to understand these complex relationships and begin to determine multidisciplinary, optimal interventions.

The Project Baseline Health Study (PBHS) is an ongoing, prospective, longitudinal study designed to better understand patterns of disease and health outcomes in a contemporary context where large amounts of data, including from a digital health device, can be aggregated, with a focus on a diverse population across race, sex, age, and comorbidities. In this study, leveraging this unique cohort we sought to evaluate cardiometabolic, mental health, and physical activity characteristics across BMI categories.

2. Methods

2.1. Study populations

The study design for the PBHS study has been previously published[9]. The PBHS study is a multi-site collaboration to map health and disease transitions through deep phenotyping, creating a unique dataset encompassing a wide spectrum of phenotypic measures to allow for observational discovery. This study was approved by two Institutional Review Boards (IRBs), and all participants were appropriately consented for use of biospecimens and data. This study was performed in accordance with the Declaration of Helsinki. PBHS participants were recruited through IRB-approved advertisements, clinical referrals, and community recruitment activities. Recruitment occurred at four different study locations: Stanford University (Palo Alto, California), Duke University (Durham, North Carolina and Kannapolis, North Carolina sites), and the California Healthy Lifestyles Institute (CHLI, Los Angeles, California). Participants were then directed to visit the Project Baseline Health Study website (www.projectbaseline.com) or to connect with a call center to learn about the study and/or enroll in the registry. Selected registrants were then selected to participate in the cohort study based on demographics and disease risk patterns while others remained on a waitlist for other opportunities to engage in clinical research. The study population was selected to include a broad range of participants across the health spectrum, including those with no known risk factors or disease, those at varying levels of disease risk, and those already with a disease diagnosis. All selected participants completed an extensive 2-day enrollment protocol, which included demographics, medical history intake, vitals, cardiac imaging (coronary calcium computed tomography [CT], echocardiography, stress echocardiography), mental health surveys, and laboratory data to build a deeply phenotyped population. Heart rate (HR), step count, and other health parameters were collected by a proprietary digital health device worn on the wrist for >10 h daily. Enrollment and data collection for the PBHS study began in 2017, and participants were followed for at least 4 years. The current study was a cross-sectional analysis.

The distribution of BMI across age groups were compared with the 2017–2018 release of the National Health and Nutrition Examination Survey (NHANES) dataset. NHANES is a program of studies designed to assess the health and nutritional status of adults and children across the U.S. The data are obtained from a combination of interviews and physical assessments. The NHANES interview includes demographic, socioeconomic, dietary, and health-related questions. The examination portion includes medical, dental, physiological, and laboratory test information and is publicly available.

2.2. Statistical analysis

For this study, we used enrollment data from all PBHS participants. Participants were divided into six BMI categories based on national standards: underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), class I obesity (30–34.9 kg/m^2), class II obesity (35–39.9 kg/m^2), and class III obesity (BMI ≥40 kg/m^2)[10]. Data on comorbidities, including prior myocardial infarction (MI), prior stroke, HTN, DM, or any type of cancer, and medication (aspirin and statin) were obtained through patient-reported surveys. Laboratory and coronary artery calcium (CAC) scoring data were obtained at the individual sites and read centrally by a core lab at one institution. CAC >0 was stratified further into three

non–age-adjusted risk groups: CAC 1–100, CAC 101–400, and CAC >400. Vitals, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), height, and weight were obtained at the baseline visit. For mental health examination, we evaluated scores based on the Patient Health Questionnaire-9 (PHQ-9) (Table S1). PHQ-9 scores of 0–4 suggest no depression, 5–9 mild depression, 10–14 moderate depression, 15–19 moderately severe depression, and 20–27 severe depression[11]. Additionally, we evaluated scores based on the Generalized Anxiety Disorder-7 (GAD-7) questionnaire (Table S2). Cumulative GAD-7 scores of 5, 10, and 15 are cut-off points for mild, moderate, and severe anxiety, respectively[12]. Physical activity was assessed using step counts from the digital health devices worn by participants. The average step count for Americans is approximately 4000 steps in a day, and ≤4000 steps per day was considered sedentary.

Baseline demographic, vitals, medical history, laboratory, and cardiac imaging characteristics of patients were compared across the six BMI groups. For univariate analyses, the Jonckheere-Terpstra test was used to assess the monotonic trend in continuous variables across BMI groups and Pearson's chi-squared test was used for categorical characteristics (medical history, imaging). Multivariable logistic regression analyses adjusted for age, sex, ethnicity, race, smoking, and study sites were used to assess associations between BMI groups and unique clinical variables analyzed as binary outcomes (mean PHQ-9 score >5, suggestive of at least mild depression, vs. PHQ-9 score ≤5; mean GAD-7 score >10, suggestive of at least moderate anxiety, vs. GAD-7 score ≤10; mean step count >4000, average American daily step count, vs. ≤4000; high-sensitivity C-reactive protein [hs-CRP] levels ≥2 mg/L, suggestive of high cardiovascular risk; and CAC >0, suggestive of coronary plaque). All statistical analyses were conducted using R version 3.6.3. All 95 % confidence intervals (CIs) and *p*-values were based on 2-sided hypothesis tests, where a nominal $P < 0.05$ was considered statistically significant.

3. Results

A total of 2493 participants were included in this study. Participants were recruited from four different site locations: Stanford University (n = 1009), Duke University (Durham, North Carolina [n = 482], Kannapolis, North Carolina [n = 516]), and CHLI (n = 486). Overall, the mean age at enrollment was 50.0 ± 17.2 years; the study population was 55 % female, 63 % non-Hispanic White, 13 % Hispanic (all races), 16 % non-Hispanic Black, and 10 % non-Hispanic Asian. Approximately 21 % of the study population had a history of HTN; 12 % had a history of DM; 2 % had a history of prior stroke; 2 % had a history of prior MI; and 8 % had a history of any cancer. Furthermore, approximately 38 % of the study population had CAC >0; 10 % were on aspirin therapy; and 12 % were on statin therapy.

The average BMI across the study population was 28.4 ± 6.87 kg/m^2. A similar distribution of BMI categories was observed across age groups in the 2017–2018 release of nationally representative estimates from NHANES (Fig. 1**).** The overall baseline and cardiometabolic characteristics of the study population by BMI category can be found in Tables 1 and 2, respectively.

3.1. Demographic and clinical parameters stratified by BMI categories

When stratified by clinically relevant BMI categories, a total of 40 participants were classified in the underweight category (BMI <18.5 kg/m^2), 859 participants in the normal weight category (BMI 18.5–24.9 kg/m^2), 771 participants in the overweight category (BMI 25–29.9 kg/m^2), 454 participants in the class I obesity category (BMI 30–34.9 kg/m^2), 212 participants in the class II obesity category (BMI 35–39.9 kg/m^2), and 157 participants in the class III obesity category (BMI ≥40 kg/m^2) (Table 1). A higher proportion of women was observed in the underweight (80 %), class II obesity (65 %), and class III obesity (70 %) categories. Over one-third of study participants with class II and III obesity self-identified as Black compared with <8 % of participants with normal weight. Additionally, Hispanic ethnicity was overrepresented in the higher BMI categories, whereas Asian participants were more represented in the underweight and normal BMI categories.

Cardiometabolic risk factors were significantly different across BMI categories. Blood pressure and HR increased in a graded fashion across BMI categories, with the highest mean blood pressure (129±14.9/80

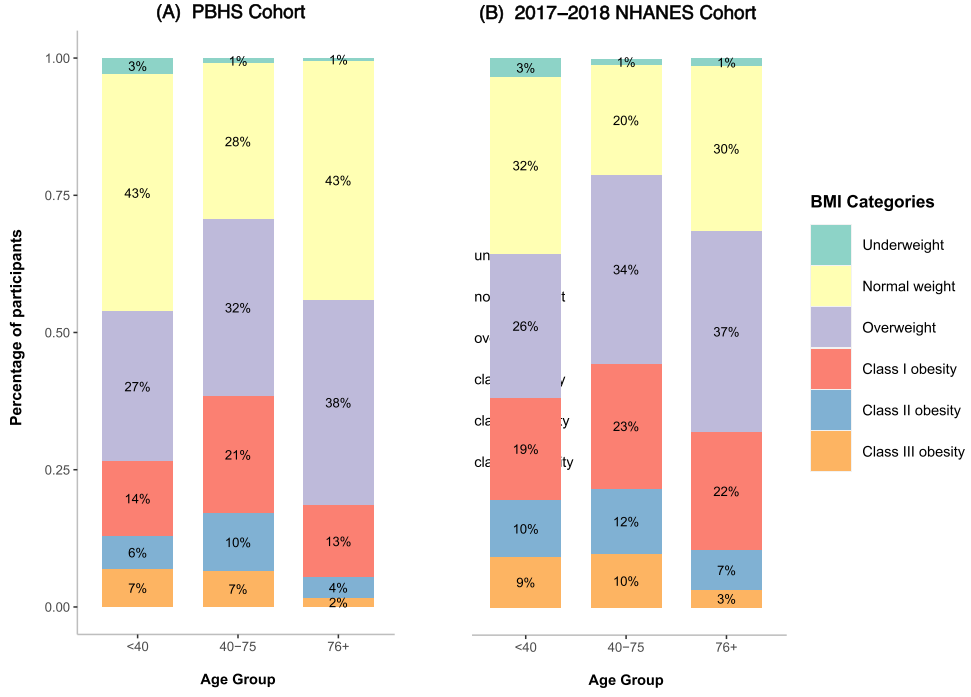

Fig. 1. Panel A represents the percentage of participants across color-coded BMI categories (y axis) by age (x axis) in the PBHS cohort. Panel B represents the percentage of participants across color-coded BMI categories (y axis) by age (x axis) in the 2017–2018 NHANES cohort. BMI, body mass index; NHANES, National Health and Nutrition Examination Survey; PBHS, Project Baseline Health Study.

Table 1
Baseline characteristics.

	Overall (N = 2493)	Underweight(BMI <18.5 kg/m^2) (N = 40)	Normal (BMI 18.5–24.9 kg/m^2) (N = 859)	Overweight(BMI 25–29.9 kg/m^2) (N = 771)	Class I Obesity (BMI 30–34.9 kg/m^2) (N = 454)	Class II Obesity (BMI 35–39.9 kg/m^2) (N = 212)	Class III Obesity (BMI ≥40 kg/m^2) (N = 157)	P-value*
BMI, mean (SD)	28.4 (6.87)	17.6 (1.02)	22.5 (1.71)	27.3 (1.44)	32.3 (1.46)	37.3 (1.37)	46.0 (5.29)	<0.001
Weight, mean (SD)	81.8 (21.4)	49.0 (5.39)	64.7 (9.36)	79.7 (9.78)	93.4 (11.5)	105.0 (12.2)	130.0 (20.6)	<0.001
Height (cm), mean (SD)	170.0 (9.65)	167.0 (7.56)	169.0 (9.47)	171.0 (9.60)	170.0 (10.2)	167.0 (9.38)	168.0 (9.06)	0.4
Age, mean (SD)	50.0 (17.2)	42.4 (18.1)	48.1 (18.8)	52.0 (17.1)	52.1 (15.5)	50.7 (14.4)	46.0 (14.3)	0.002
Age category (yrs), N (%)								
<40	828 (33.2 %)	24 (60.0 %)	359 (41.8 %)	225 (29.2 %)	113 (24.9 %)	50 (23.6 %)	57 (36.3 %)	<0.001
40–75	1481 (59.4 %)	15 (37.5 %)	420 (48.9 %)	477 (61.9 %)	317 (69.8 %)	155 (73.1 %)	97 (61.8 %)	
76+	184 (7.4 %)	1 (2.5 %)	80 (9.3 %)	69 (8.9 %)	24 (5.3 %)	7 (3.3 %)	3 (1.9 %)	
Sex, N (%)								
Male	1123 (45.0 %)	8 (20.0 %)	346 (40.3 %)	424 (55.0 %)	223 (49.1 %)	75 (35.4 %)	47 (29.9 %)	<0.001
Female	1370 (55.0 %)	32 (80.0 %)	513 (59.7 %)	347 (45.0 %)	231 (50.9 %)	137 (64.6 %)	110 (70.1 %)	
Ethnicity, N (%)								
Non-Hispanic	2195 (88.0 %)	36 (90.0 %)	770 (89.6 %)	690 (89.5 %)	385 (84.8 %)	182 (85.8 %)	132 (84.1 %)	0.031
Hispanic	291 (11.7 %)	4 (10.0 %)	88 (10.2 %)	76 (9.9 %)	69 (15.2 %)	29 (13.7 %)	25 (15.9 %)	
Race, N (%)								
White	1575 (63.2 %)	27 (67.5 %)	568 (66.1 %)	514 (66.7 %)	287 (63.2 %)	105 (49.5 %)	74 (47.1 %)	<0.001
Black or African American	398 (16.0 %)	4 (10.0 %)	67 (7.8 %)	103 (13.4 %)	93 (20.5 %)	74 (34.9 %)	57 (36.3 %)	
Asian	260 (10.4 %)	7 (17.5 %)	133 (15.5 %)	91 (11.8 %)	19 (4.2 %)	6 (2.8 %)	4 (2.5 %)	
American Indian or Alaska Native	31 (1.2 %)	0 (0 %)	9 (1.0 %)	6 (0.8 %)	6 (1.3 %)	6 (2.8 %)	4 (2.5 %)	
Native Hawaiian or Other Pacific Islander	27 (1.1 %)	1 (2.5 %)	10 (1.2 %)	3 (0.4 %)	7 (1.5 %)	2 (0.9 %)	4 (2.5 %)	
Other Race	202 (8.1 %)	1 (2.5 %)	72 (8.4 %)	54 (7.0 %)	42 (9.3 %)	19 (9.0 %)	14 (8.9 %)	
Enrollment site, N (%)								
Stanford	1009 (40.5 %)	21 (52.5 %)	425 (49.5 %)	325 (42.2 %)	144 (31.7 %)	48 (22.6 %)	46 (29.3 %)	<0.001
Durham	482 (19.3 %)	6 (15.0 %)	125 (14.6 %)	126 (16.3 %)	118 (26.0 %)	66 (31.1 %)	41 (26.1 %)	
CHLI	486 (19.5 %)	11 (27.5 %)	210 (24.4 %)	160 (20.8 %)	69 (15.2 %)	21 (9.9 %)	15 (9.6 %)	
Kannapolis	516 (20.7 %)	2 (5.0 %)	99 (11.5 %)	160 (20.8 %)	123 (27.1 %)	77 (36.3 %)	55 (35.0 %)	
Vitals								
SBP (mmHg), Mean (SD)	123.0 (16.0)	113.0 (13.9)	118.0 (15.8)	124.0 (15.4)	128.0 (15.4)	130.0 (14.6)	129.0 (14.9)	<0.001
DBP (mmHg), Mean (SD)	75.8 (9.9)	70.3 (9.5)	72.5 (8.8)	75.7 (9.6)	79.2 (10.1)	81.1 (9.4)	79.5 (9.8)	<0.001
Pulse (bpm), Mean (SD)	67.4 (11.6)	70.4 (10.6)	64.8 (10.6)	66.2 (11.2)	68.9 (12.3)	71.7 (10.9)	76.6 (10.8)	<0.001
Medical history								
Prior heart attack, N (%)	49 (2.0 %)	0 (0 %)	11 (1.3 %)	12 (1.6 %)	15 (3.3 %)	7 (3.3 %)	4 (2.5 %)	0.1
Prior stroke, N (%)	39 (1.6 %)	0 (0 %)	11 (1.3 %)	13 (1.7 %)	9 (2.0 %)	1 (0.5 %)	5 (3.2 %)	0.3
Diabetes, N (%)	288 (11.6 %)	0 (0 %)	36 (4.2 %)	68 (8.8 %)	77 (17.0 %)	54 (25.5 %)	53 (33.8 %)	<0.001
Hypertension, N (%)	517 (20.7 %)	3 (7.5 %)	76 (8.8 %)	134 (17.4 %)	150 (33.0 %)	89 (42.0 %)	65 (41.4 %)	<0.001
Any cancer, N (%)	200 (8.0 %)	3 (7.5 %)	70 (8.1 %)	69 (8.9 %)	32 (7.0 %)	18 (8.5 %)	8 (5.1 %)	0.6
Mental health scores								
PHQ-9 score, mean (SD)	5.3 (4.20)	4.5 (1.73)	4.9 (3.73)	5.1 (3.80)	5.5 (4.18)	5.8 (4.75)	8.1 (6.50)	0.001
PHQ-9 ≥ 5, N (%)	740 (29.7 %)	11 (27.5 %)	251 (29.2 %)	217 (28.1 %)	137 (30.2 %)	61 (28.8 %)	63 (40.1 %)	0.041

(*continued on next page*)

Table 1 (*continued*)

	Overall (*N* = 2493)	Underweight(BMI <18.5 kg/m^2) (*N* = 40)	Normal (BMI 18.5–24.9 kg/m^2) (*N* = 859)	Overweight(BMI 25–29.9 kg/m^2) (*N* = 771)	Class I Obesity (BMI 30–34.9 kg/m^2) (*N* = 454)	Class II Obesity (BMI 35–39.9 kg/m^2) (*N* = 212)	Class III Obesity (BMI ≥40 kg/m^2) (*N* = 157)	*P*-value*
GAD-7 score, mean (SD)	3.2 (4.14)	4.2 (4.69)	3.0 (3.92)	2.9 (3.88)	3.4 (4.27)	3.6 (4.34)	4.8 (5.19)	0.006
GAD-7 Score ≥10, N (%)	226 (9.1 %)	6 (15.0 %)	65 (7.6 %)	55 (7.1 %)	47 (10.4 %)	23 (10.8 %)	30 (19.1 %)	<0.001
Daily step count, mean (SD)	6690 (3160)	7740 (3730)	7080 (3040)	7120 (3210)	6180 (3040)	5520 (3010)	5100 (2880)	<0.001

*Overall Project Baseline Health Study cohort (data release 4/28/2021). World Health Organization body mass index classes: underweight, <18.5 kg/m^2; normal weight, 18.5–24.9 kg/m^2; overweight, 25.0–29.9 kg/m^2; class I obesity, 30.0–34.9 kg/m^2; class II obesity, 35.0–39.9 kg/m^2; and class III, obesity ≥40.0 kg/m^2. *P*-values were calculated using the Jonckheere-Terpstra trend test and Pearson's chi-squared test. BMI, body mass index; CHLI, California Health & Longevity Institute; DPB, diastolic blood pressure; GAD-7, General Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9; SBP, systolic blood pressure.

Table 2
Cardiometabolic and laboratory parameters.

	Overall (*N* = 2493)	Underweight (BMI <18.5 kg/m^2) (*N* = 40)	Normal (BMI 18.5–24.9 kg/m^2) (*N* = 859)	Overweight (BMI 25–29.9 kg/m^2) (*N* = 771)	Class I Obesity (BMI 30–34.9 kg/m^2) (*N* = 454)	Class II Obesity (BMI 35–39.9 kg/m^2) (*N* = 212)	Class III Obesity (BMI ≥40 kg/m^2) (*N* = 157)	*P*-value*
Total cholesterol (mg/dl), mean (SD)	184.0 (39.4)	179.0 (39.7)	186.0 (39.3)	185.0 (39.0)	184.0 (41.5)	185.0 (37.2)	178.0 (37.9)	0.4
LDL (mg/dL), mean (SD)	99.5 (33.7)	90.0 (26.2)	97.5 (32.7)	100 (33.3)	101 (37.3)	103 (32.3)	100 (33.3)	0.002
HDL (mg/dL), mean (SD)	63.5 (22.7)	81.6 (27.4)	70.5 (23.2)	60.9 (19.7)	55.7 (21.7)	53.6 (22.1)	51.8 (21.3)	<0.001
Triglycerides, mean (SD)	135.0 (101)	94.8 (52.5)	101.0 (61.1)	140.0 (107)	168.0 (108)	177.0 (150)	149.0 (83.8)	<0.001
hsCRP (mg/L), mean (SD)	2.9 (5.9)	0.8 (0.8)	1.4 (2.7)	2.2 (6.1)	3.6(5.4)	5.8 (6.7)	9.4 (11.0)	<0.001
hsCRP ≥2 (mg/L), N (%)	836 (33.5 %)	4 (10.0 %)	118 (13.7 %)	203 (26.3 %)	229 (50.4 %)	149 (70.3 %)	133 (84.7 %)	<0.001
Vitamin D (ng/ml), mean (SD)	29.6 (13.1)	30.1 (11.9)	32.9 (13.6)	30.3 (12.4)	27.3 (12.0)	23.7 (11.7)	22.3 (12.1)	<0.001
Vitamin *D* < 30 (ng/ml), N (%)	1293 (51.9 %)	20 (50.0 %)	356 (41.4 %)	382 (49.5 %)	275 (60.6 %)	146 (68.9 %)	114 (72.6 %)	<0.001
Any CAC score, N (%)								
0	1440 (57.8 %)	32 (80.0 %)	590 (68.7 %)	427 (55.4 %)	225 (49.6 %)	93 (43.9 %)	73 (46.5 %)	<0.001
>0	944 (37.9 %)	7 (17.5 %)	234 (27.2 %)	314 (40.7 %)	213 (46.9 %)	103 (48.6 %)	73 (46.5 %)	
CAC score groups, N (%)								
0	1443 (57.9 %)	32 (80.0 %)	591 (68.8 %)	428 (55.5 %)	226 (49.8 %)	93 (43.9 %)	73 (46.5 %)	<0.001
1–100	523 (21.0 %)	6 (15.0 %)	138 (16.1 %)	156 (20.2 %)	112 (24.7 %)	62 (29.2 %)	49 (31.2 %)	
101–400	219 (8.8 %)	1 (2.5 %)	48 (5.6 %)	80 (10.4 %)	49 (10.8 %)	28 (13.2 %)	13 (8.3 %)	
>400	199 (8.0 %)	0 (0.0 %)	47 (5.5 %)	77 (10.0 %)	51 (11.2 %)	13 (6.1 %)	11 (7.0 %)	
Aspirin, N (%)	237 (9.5 %)	1 (2.5 %)	44 (5.1 %)	97 (12.6 %)	63 (13.9 %)	19 (9.0 %)	13 (8.3 %)	<0.001
Statin, N (%)	298 (12.0 %)	1 (2.5 %)	53 (6.2 %)	106 (13.7 %)	79 (17.4 %)	33 (15.6 %)	26 (16.6 %)	<0.001

*Overall Project Baseline Health Study cohort (data release 4/28/2021). World Health Organization body mass index classes: underweight, <18.5 kg/m^2; normal weight, 18.5–24.9 kg/m^2; overweight, 25.0–29.9 kg/m^2; class I obesity, 30.0–34.9 kg/m^2; class II obesity, 35.0–39.9 kg/m^2; and class III, obesity ≥40.0 kg/m^2. *P*-values were calculated using the Jonckheere-Terpstra trend test and Pearson's chi-squared test. CAC, coronary artery calcium; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

±9.6 mmHg) and the highest mean HR (77±10.8 bpm) in the class III obesity category. The mean total cholesterol levels and the mean LDL-C levels were similar across BMI categories, whereas the mean HDL-C levels decreased across increasing BMI categories and the mean triglyceride levels increased with increasing BMI categories. The mean hsCRP levels were higher in the higher BMI categories compared with the normal weight category. Additionally, this inverse relationship was observed with mean vitamin D levels.

The prevalence of HTN and DM was higher across increasing BMI categories, but the proportions of participants with a history of MI, stroke, and cancer were similar across all BMI categories.

A higher proportion of participants in the obesity categories were on statin therapy (17 %, 16 %, and 17 % for class I, class II, and class III obesity, respectively) compared with participants in the normal weight category (6 %). Additionally, the proportion of aspirin use was higher in the obesity categories (14 %, 9 %, and 8 % for class I, class II, and class III obesity, respectively) compared with the normal weight category (5 %).

3.2. Coronary artery calcium scores across BMI categories

Nearly half of participants with class I, class II, and class III obesity had CAC detected. In the BMI categories of obesity, a higher proportion of participants had a CAC score of 1–100 (low) compared with scores of 101–400 (moderate risk) or >400 (high risk). The greatest proportion of participants with CAC >400 were in the class I obesity BMI category (11.2 %).

3.3. Mental health and physical activity parameters across BMI categories

The overall mean PHQ-9 score for the study population was 5.3 ± 4.2, above the threshold for depression (PHQ-9 score of 5). The class III obesity category had the highest mean PHQ-9 score compared with the other BMI categories (8.1 ± 6.5 vs 4.9 ± 3.7 for the normal weight category). The overall mean GAD-7 score for the study population was 3.1 ± 4.1 (minimal GAD-7 score for anxiety being 5). The highest mean GAD-7 score among the BMI categories was in the class III obesity group (4.8 ± 5.2) compared with the normal weight group (3.0 ± 3.9).

The mean daily step count for the entire population was 6690±3160. The mean step count decreased with increasing BMI category (class I obesity [6180±3040], class II obesity [5520±3010], and class II obesity [5100±2880]).

3.4. Multivariable models for BMI categories

Five multivariable logistic regression models were fitted using the following cardiometabolic markers of risk as the binary response variables: 1) CAC >0 (Yes/No), 2) hsCRP >3 mg/L, 3) PHQ-9 score >5 (signals mild depression), 4) GAD-7 score >10 (signals moderate anxiety), and 5) physical parameters, such as a mean step count >4000 (average step count for Americans) to determine associations with BMI category (Table 3). In these multivariable models, an inverse relationship was found between a mean step count ≥4000 in the overweight category (OR 0.80, 95 % CI 0.58–0.99, $p = 0.04$) and the class III obesity category (OR 0.69, 95 % CI 0.50–0.95, $p = 0.02$) compared with the normal weight category. PHQ-9 ≥ 5 and hsCRP >3 mg/L were positively associated with the overweight category (OR 1.4, 95 % CI 1.0–1.9, $p = 0.04$) and (OR 1.8, 95 % CI 1.3–2.6, $p = 0.001$), respectively. However, no significant associations were found between CAC >0, hsCRP >3 mg/L, PHQ-9 ≥ 5, and GAD-7 ≥ 10 among the obesity BMI categories compared with the normal weight category.

Additionally, a positive association was observed between CAC >0 (OR 2.8, 95 % CI 1.9–4.3, $p < 0.001$), hsCRP >3 mg/L (OR 37.8, 95 % CI 17.2–82.9, $p < 0.001$), PHQ-9 ≥ 5 (OR 2.4, 95 % CI 1.5–4.0, $p < 0.001$), and GAD-7 ≥ 10 (OR 1.7, 95 % CI 1.0–2.8, $p = 0.03$) with the underweight BMI category compared with the normal weight category.

Table 3
Multivariable analyses via logistic regression.

Outcomes	BMI group (ref=normal)	OR	95 % CI	*P*-value*
CAC >0	Underweight	2.8	(1.8, 4.3)	<0.001
	Overweight	1.2	(0.9, 1.6)	0.2
	Class I obesity	1.0	(0.6, 1.7)	0.9
	Class II obesity	1.0	(0.6, 1.8)	0.9
	Class III obesity	1.0	(0.7, 1.4)	0.9
hsCRP ≥2 mg/L	Underweight	30.1	(17.7, 51.1)	<0.001
	Overweight	1.9	(1.4, 2.8)	<0.001
	Class I obesity	0.7	(0.4, 1.3)	0.2
	Class II obesity	1.6	(0.8, 3.0)	0.2
	Class III obesity	0.9	(0.7, 1.4)	0.8
PHQ-9 ≥5	Underweight	2.5	(1.5, 4.1)	<0.001
	Overweight	1.5	(1.0, 2.0)	0.02
	Class I obesity	1.2	(0.7, 2.1)	0.5
	Class II obesity	1.2	(0.7, 2.2)	0.5
	Class III obesity	1.0	(0.7, 1.5)	0.9
GAD-7 ≥10	Underweight	1.7	(1.0, 2.8)	0.04
	Overweight	1.3	(0.9, 1.9)	0.09
	Class I obesity	1.6	(0.9, 2.9)	0.1
	Class II obesity	0.8	(0.4, 1.5)	0.5
	Class III obesity	1.4	(0.9, 2.1)	0.1
Mean step count ≥4000	Underweight	0.3	(0.2, 0.5)	<0.001
	Overweight	0.7	(0.6, 1.0)	0.02
	Class I obesity	0.9	(0.6, 1.5)	0.7
	Class II obesity	1.5	(0.9, 2.4)	0.1
	Class III obesity	0.7	(0.5, 1.0)	0.03

*All models were adjusted for enrollment age, sex, ethnicity, race, current smoking status, and enrollment site. The rationale for cut-offs for the above outcomes is as follows: a CAC score >0 suggests some coronary plaque; an hsCRP level of 3 or higher suggests a high risk for cardiovascular events; a mean PHQ-9 score of 5 or higher suggests depression; a mean GAD-7 score of 10 or higher suggests general anxiety disorder; and a mean step count of 4000 is the average step count for Americans. CAC, coronary artery calcium; CI, confidence interval; GAD-7, General Anxiety Disorder-7; hsCRP, high-sensitivity C-reactive protein; OR, odds ratio; PHQ-9, Patient Health Questionnaire-9.

4. Discussion

Using baseline data from the prospective, longitudinal PBHS study, we identified multiple clinical, laboratory, imaging, and digital health parameters that differ across BMI categories. Our results show that female and historically marginalized racial/ethnic groups were more likely to be overrepresented in the higher BMI categories. Additionally, a higher proportion of participants with HTN and DM were observed in the obesity categories, although the distributions of prior MI, stroke, and cancer were similar. Participants in the obesity BMI categories had lower HDL-C levels and higher triglyceride levels. Additionally, higher mean hsCRP levels were observed in a graded fashion across the obesity categories, and nearly half of participants in the obesity categories had some CAC, one of the strongest markers of future cardiovascular risk. Furthermore, mean step counts were lower at higher BMI categories and mean mental health survey scores, suggestive of depression/anxiety, were higher with higher BMIs. Overall, these results highlight the broad cardiometabolic and non-cardiometabolic health parameters across BMI categories.

This current study shows similar demographic patterns of obesity when compared with previous large population studies. For instance, a study using NHANES data that characterized trends in obesity prevalence among 44,324 participants between 2007 and 2008 and 2015–2016 found that the prevalence of obesity was significantly higher in females compared with males[13]. Similarly, our results show that in both class II and class III obesity categories, females made up over 60 % of the study population. Furthermore, our observations of higher obesity rates in Black study participants are similar to the Centers for Disease Control and Prevention (CDC) data showing a particularly higher prevalence of obesity in African Americans compared with other races[14]. Moreover, Asians were overrepresented in the lower BMI categories, a finding that is consistent with U.S. population data[14]. Several factors could contribute to race-based differences in the prevalence of obesity, including cultural differences in body image[15], socioeconomic standards[16], and adiposity measures that are calibrated for different racial groups[17,18]. Thus, given the similarities to other patient cohorts stratified by BMI both in terms of clinical demographics and laboratory data, our results suggest that the PBHS study can serve as a representative data source.

Our findings on the relationship between comorbidities and obesity are consistent with established obesity trends[19–23]. The proportion of participants with HTN was higher in the obesity categories than in the normal weight category. The mechanism of how HTN and obesity are linked appears to be multifactorial, involving a combination of environmental factors, sympathetic nervous system, renin-angiotensin system, sodium retention, or other metabolic pathways less studied[19,20]. Overall, the proportion of participants with a prior diagnosis of HTN was approximately 21 %, which is lower than the national prevalence[24]. However, this could be due to the lower mean age of the study

population and self-reporting of the diagnosis. Additionally, as expected, the diagnosis of DM was more prevalent among patients with obesity compared with those with normal weight. Multifactorial etiologies for this link exist, ranging from environmental factors to insulin resistance, or beta cell dysfunction of the pancreas[23]. Despite both HTN and DM being risk factors for CVD, we did not observe a higher prevalence of a history of MI or stroke in these categories. However, approximately 38 % of the study population had CAC >0. Furthermore, we did not observe a higher prevalence of a cancer diagnosis in the obesity categories as previously reported[5,6].

The PBHS cohort enables the assessment of additional markers of cardiometabolic risk, such as CAC, hsCRP, and vitamin D. We found that CAC was prevalent in the higher obesity classes, with scores mostly between 1 and 100. In a similarly sized cohort of 2359 participants (mean age 53 years, 50 % female, and 47 % Hispanic/Latino), 28 % had a CAC score of 1–99, which is similar to our results[25]. Furthermore, obesity was associated with the presence of coronary plaque. In another larger study of 36,509 individuals, a multivariate regression model showed a higher odds of CAC >0 in the groups with overweight (OR 1.1, 95 % CI 1.1–1.2) and obesity (OR 1.5, 95 % CI 1.4–1.6)[26]. Additionally, compared with normal BMI, individuals with obesity had a higher risk of cardiovascular disease and all-cause mortality[26]. In our multivariate logistic regression model, CAC >0 was associated most strongly with the underweight BMI category and not with the overweight or obesity categories. This could be a result of overall low numbers across BMI categories and residual unmeasured confounders in the underweight category, such as chronic inflammatory disease and malnutrition. However, based on linear trends across BMI categories, our results show a general increase in the proportion of CAC scores between 1 and 100 and 101–400 in the higher BMI categories.

In addition to the prevalence of CAC, linear trends show higher mean hsCRP values with higher BMI categories. However, our multivariable logistic regression model for elevated hsCRP showed a positive association with the underweight category and overweight category, but not for the obesity categories, although this could again be a result of low numbers and confounding from chronic inflammatory diseases that were not accounted for in the multivariable model. Further research is certainly warranted on the interplay between hsCRP and obesity as elevated hsCRP is an independent predictor of cardiovascular risk and abdominal obesity[27–29].

Low vitamin D levels have been linked to cardiometabolic disease and obesity in previous studies[30]. We found lower mean values in the obesity categories compared with the normal weight and underweight categories. This finding further supports the residual cardiometabolic risk that participants with obesity may have. Certainly, further research is needed on long-term cardiovascular outcomes in individuals with obesity and low vitamin D.

In addition to cardiometabolic risk factors, we assessed mental health measures, including PHQ-9 scores to assess for depression and GAD-7 scores to assess for anxiety. Based on mean GAD-7 scores, significant anxiety did not seem as prevalent as depression across BMI categories. For instance, among the underweight and obesity categories, the mean PHQ-9 score was >5, which is the lowest threshold for depression. However, across BMI, the mean GAD-7 score did not cross the threshold of 10 for significant anxiety. Of note, our findings show lower mean step counts at higher BMI categories compared with lower BMI categories, supporting the presence of less physical activity in individuals with obesity. Since the PBHS study is ongoing with longitudinal measures, including step count and serial PHQ-9 survey assessments, future research will be able to assess temporal associations and interactions between obesity, step counts, and onset of depressive symptoms.

4.1. Limitations

There are limitations to the study that are important to note. First, this was a cross-sectional analysis with limitations specific to that type of study design. As such, cause-and-effect with obesity cannot be disentangled. Second, much of the comorbidity data and medication data were patient-reported and subject to bias or error. Third, study follow-up is ongoing and we have insufficient data for outcomes; however, the scope of this study was to define the characteristics of participants at different BMI categories within the unique PBHS cohort. Fourth, only four sites recruited participants; however, efforts were made to increase diversity at each of the individual sites and a comparison with NHANES data shows overall similarity to national estimates of obesity.

5. Conclusion

In conclusion, we identified important differences in cardiometabolic, mental health, and physical activity by BMI categories within the PBHS cohort. The findings are consistent with prior studies showing the adverse effect of obesity on risk factors. Our work adds novelty of a deeply phenotyped modern cohort with detailed imaging, laboratory, and wearable device data for future studies. Additionally, the high burden of cardiometabolic risk factors and depression in participants with overweight and obesity further supports the importance of early weight management, especially in light of clinical trial data showing the benefit of therapeutics targeting obesity[31–40].

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CRediT authorship contribution statement

Nishant P. Shah: Conceptualization, Methodology, Writing – review & editing. **Rong Lu:** Conceptualization, Writing – review & editing, Formal analysis, Investigation, Data curation. **Francois Haddad:** Writing – review & editing. **Scarlet Shore:** Writing – review & editing. **Terry Schaack:** Writing – review & editing. **Jessica Mega:** Conceptualization, Writing – review & editing, Supervision. **Neha J. Pagidipati:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Latha Palaniappan:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Kenneth Mahaffey:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Svati H. Shah:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Fatima Rodriguez:** Conceptualization, Methodology, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Data availability

The deidentified PBHS data corresponding to this study are available upon request for the purpose of examining its reproducibility. Requests are subject to approval by PBHS governance.

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Supplementary materials

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