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ORIGINAL ARTICLE

Cardiometabolic risk factors in treatment-seeking youth versus population youth with obesity

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Summary

Background

Although obesity affects approximately one in five youths, only a fraction is treated in pediatric weight management clinics. Characteristics distinguishing youth with obesity who seek weight management treatment from those who do not are largely unknown. Yet identification of specific health characteristics which differentiate treatment-seeking from non-treatment seeking youth with obesity may shed light on underlying motivations for pursuing treatment.

Objectives

Compare the cardiometabolic profiles of an obesity treatment-seeking sample of youth to a population-based sample of youth with obesity, while controlling for body mass index (BMI).

Methods

This cross-sectional study included participants, ages 12–17 years, with obesity from the Pediatric Obesity and Weight Evaluation Registry (POWER) and National Health and Nutrition Examination Survey, representing the treatment-seeking and population samples, respectively. Mean differences were calculated for systolic and diastolic blood pressure percentiles, total cholesterol, low-density and high-density lipoprotein-cholesterol, triglycerides, fasting glucose, glycated hemoglobin and alanine aminotransferase, while adjusting for age, sex, race/ethnicity, insurance status, and multiple of the 95th BMI percentile.

Results

The POWER and National Health and Nutrition Examination Survey cohorts included 1,823 and 617 participants, respectively. The POWER cohort had higher systolic blood pressure percentile (mean difference 17.4, 95% confidence interval [14.6, 20.1], $p < 0.001$), diastolic blood pressure percentile (21.8 [19, 24.5], $p < 0.001$), triglycerides (42.3 [28, 56.5], $p < 0.001$) and alanine aminotransferase (7.5 [5.1, 9.8], $p < 0.001$) and lower fasting glucose (-6.9 [-8.2, -5.6], $p < 0.001$) and high-density lipoprotein-cholesterol (-2.3 [-3.8, -0.9], $p < 0.002$). There were no differences in total cholesterol or low-density lipoprotein-cholesterol or clinical differences in glycated hemoglobin.

Conclusion

For a given BMI, obesity treatment-seeking youth are more adversely affected by cardiometabolic risk factors than the general population of youth with obesity. This suggests that treatment-seeking youth may represent a distinct group that is at particularly high risk for the development of future cardiometabolic disease.

Keywords: Cardiometabolic risk factor, population, treatment seeking.

Introduction

Youth with obesity who fail to improve their body mass index (BMI) via primary care clinic interventions should be referred to comprehensive multidisciplinary weight management programs (1). These multidisciplinary programs provide intensive lifestyle modification therapy and, when indicated, more aggressive treatments such as pharmacotherapy and bariatric surgery to improve weight status and obesity-related comorbidities (1,2). Although approximately one in five youths in the USA is afflicted with obesity (3), only a small fraction are treated in such multidisciplinary programs. Identification of specific health characteristics which differentiate youth with obesity who seek weight management treatment programs versus those who do not may shed light on underlying motivations for patients to seek such treatment. Furthermore, identification of the differential health characteristics of treatment-seeking youth may have implications for access to such care and should inform the types of interventions provided by these multidisciplinary programs.

To date, only small studies have examined differences between population samples and treatment-seeking samples of youth with obesity, and most of these have focused on rates of mental illness. Although most of these studies suggest that treatment-seeking youth with obesity have higher rates of mental health disorders compared with population samples of youth with obesity (4–6), it is not known if these differences extend to cardiometabolic risk factors and other obesity-related comorbidities. Accordingly, the aim of this study was to compare the cardiometabolic risk factor profiles between two large, contemporary cohorts of youth with obesity: a treatment-seeking sample derived from the Pediatric Obesity Weight Evaluation Registry (POWER) (7) and a population sample derived from the National Health and Nutrition Examination Survey (NHANES). Owing to the fact that comorbidities such as hypertension, impaired glucose tolerance and dyslipidemia are largely driven by degree of adiposity, it was hypothesized that treatment-seeking and population samples of youth with obesity would have similarly high rates of cardiometabolic derangements when accounting for BMI.

Methods

Sample

This cross-sectional study compared two large contemporary cohorts of adolescents with obesity: an obesity treatment-seeking sample and a population-based sample. The treatment-seeking cohort was obtained from the POWER. POWER, established in 2013, is an ongoing national registry of patients ≤18 years of age with obesity (age-specific and sex-specific BMI ≥95th percentile) who are seeking care in 1 of 27 multicomponent pediatric weight management clinics/programs from 20 states in the USA (ClinicalTrials.gov NCT02121132). The purpose of POWER is to identify the characteristics of patients and clinics/programs in order to identify variables that predict favorable outcomes. Program inclusion criteria include those that provide multicomponent pediatric weight management treatment for youth with obesity and that agree to collect the required data elements including patient height, weight, age, race and ethnicity. Each program was responsible for obtaining IRB approval. More information on the establishment of POWER is available elsewhere (7). POWER data for this study were collected from May 2014 through April 2016. All POWER sites endorsed this study. The population-based cohort of youth with obesity was obtained from NHANES 2009–2010, 2011–2012 and 2013–2014 data cycles to utilize available data that best matched the duration when POWER data was collected while increasing the sample size. NHANES is a continuous annual survey of the US population's health that was started in 1999 and releases data to the public in 2-year intervals (8). NHANES includes subject interviews, physical examinations and fasting laboratory evaluations.

From both samples, POWER and NHANES, participants were included if they were between 12 and 17 years of age, had obesity (age-specific and sex-specific BMI ≥95th percentile), and had at least one of the following outcomes measured: systolic blood pressure, diastolic blood pressure, total cholesterol (TC), LDL-cholesterol (LDL-c), HDL-cholesterol (HDL-c), triglycerides (TG), non-HDL-cholesterol (non-HDL-c), fasting glucose (FG), fasting insulin, and hemoglobin A1c (HbA1c). Participants missing all outcomes were excluded (43 from POWER and 11 from NHANES), as were those with glucose and/or HbA1c values consistent with diabetes.

Measures and definitions

Self-reported age, race and ethnicity were collected from both POWER and NHANES, and for this study race and ethnicity were combined into one category. Height, weight and blood pressure were measured at the baseline visits to the weight management programs/clinics for the POWER cohort and by trained personnel in the NHANES cohort. Fasting lipid panel, FG, fasting insulin, HBA1c and

ALT were collected at baseline or within 6 months prior to the baseline visits for the POWER sample and according to standard protocols for the NHANES sample. See Table 1 for definitions of cut-points for classes I, II and III obesity (9), elevated blood pressure (10), dyslipidemia (11), prediabetes, homeostasis model assessment-insulin resistance (HOMA-IR), and abnormal ALT (12).

Statistical analysis

To account for the complex, multilevel sampling structure of NHANES, sampling weights were provided for each individual with the data (8). Given the structure of POWER, there are no provided sampling weights, so equal sample weight was assumed for each subject. Sampling weights were normalized to sum to 1 within each study, and then normalized in the combined POWER/NHANES dataset by the proportion of data coming from each study. Descriptive characteristics of the POWER and NHANES cohorts were calculated with weighted mean (weighted SD) or weighted % to account for the weighted structure of the data. All analyses were conducted in R v3.3.1. (13). The survey package in R was used to take into account the weighted structure of the data for analyses for all linear and logistic regressions.

Table 1 Definitions of normal and abnormal measures of cardiometabolic variables

Cardiometabolic variable	Cutoffs
Obesity	Class I BMI ≥100% of 95th percentile Class II BMI ≥120% of 95th percentile Class III BMI ≥140% of 95th percentile
Blood pressure	Normal if SBP and DBP < 90th percentile Pre-HTN if SBP or DBP ≥90th and < 95th percentile HTN if SBP or DBP ≥95th percentile
Glucose	Non-diabetic if HbA1c <5.7% and fasting glucose <100 mg/dL Pre-diabetic if HbA1c 5.7–6.4% or fasting glucose 100–125 mg/dL Diabetic if HbA1c ≥6.5% or fasting glucose ≥126 mg/dL
LDL-c	Normal if LDL-c < 110 mg/dL Borderline High if LDL-c 110–130 mg/dL High if LDL-c ≥ 130 mg/dL
Triglycerides	Normal if triglycerides <90 mg/dL Borderline high if triglycerides 90–129 High if triglycerides ≥130 mg/dL
HDL-c	Normal if HDL-c > 45 mg/dL Borderline Low if HDL-c 40–45 mg/dL Low if HDL-c ≤ 40 mg/dL
ALT	Normal ALT <25 U/L (males); <22 U/L (female patients) Moderately elevated ALT 25–40 (male patients); 22–40 (female patients) Severely elevated if ALT ≥40 (male and female patients)

BMI, body mass index; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; HDL-c, HDL-cholesterol; LDL-c, LDL-cholesterol; SBP, systolic blood pressure.

Results

The POWER cohort included 1,823 subjects and the NHANES cohort included 617. Demographics, BMI classifications and cardiometabolic variables are presented in Table 2. There was an equal distribution of sex, although the POWER sample had a lower proportion of white and privately insured participants. The POWER sample had more participants with classes II and III obesity, prehypertension, hypertension, prediabetes, high LDL-c, high TG, low HDL-c and elevated ALT.

When comparing the mean differences of discrete values between POWER and NHANES (Table 3) while adjusting for age, sex, race/ethnicity, insurance status and multiple of the 95th BMI percentile, the POWER sample overall and for each of the three obesity classes had clinically and statistically higher systolic blood pressure, diastolic blood pressure and ALT and lower FG. Also, the POWER sample overall had higher TG and lower HDL-c. The POWER and NHANES samples overall and in each of the obesity classes showed no consistent differences in TC, LDL-c, fasting insulin and HOMA-IR, or clinical differences in HbA1c.

The odds of meeting criteria for hypertension was 8.72 times higher ($p < 0.001$) for those in POWER compared with NHANES. The odds of having high triglycerides, low HDL-c or high ALT were each approximately twice as high for the POWER participants compared with the NHANES participants. The odds of having high LDL-c or prediabetes was not statistically different between groups (Table 4).

Discussion

In comparing the cardiometabolic profiles between a treatment-seeking sample of youth with obesity and a population sample of youth with obesity, only TC, LDL-c, HbA1c, insulin and HOMA-IR were similar between these two samples, even when adjusting for BMI and demographics. The treatment-seeking youth with obesity had higher TG, lower HDL-c, higher blood pressure and higher ALT compared with the population sample of youth with obesity. Paradoxically, treatment-seeking youth had *lower* FG. These differences remained consistent, for the most part, when youth were separated into different categories of degree of obesity.

Table 2 Summary of demographics and cardiometabolic risk factors for POWER and NHANES cohorts overall

Co-variate	POWER	NHANES
N	1,823	617
Female	55.5%	50.2%
15–17 Years old	41.1%	49.2%
Race/Ethnicity		
Black/African American	20.6%	16.4%
Hispanic/Latino	26.4%	24.4%
Other/Multiracial	10.9%	7.4%
White	42.2%	51.8%
Insurance Type		
None	0.8%	0.1%
Private only	31.2%	47.3%
Public only	57.3%	41.8%
Private+Public	0.0%	2.9%
Unknown insurance	10.5%	0.0%
Missing	0.2%	7.9%
Any insurance coverage	88.5%	92.1%
Missing	10.7%	0.2%
BMI classification		
Class 1 obesity	27.4%	62.9%
Class 2 obesity	35.7%	24.6%
Class 3 obesity	36.9%	12.5%
Cardiometabolic variables		
Non-hypertensive	66.6%	91.5%
Pre-hypertension	11.5%	5.6%
Hypertension	20.0%	1.8%
Missing	1.9%	1.1%
Prediabetes	13.2%	10.3%
Missing	61.7%	70.3%
Normal LDL	32.0%	30.6%
Borderline high LDL	5.9%	7.1%
High LDL	4.4%	2.0%
Missing	57.8%	60.3%
Normal triglycerides	14.8%	23.6%
Borderline high triglycerides	12.0%	7.8%
High triglycerides	16.3%	8.4%
Missing	56.9%	60.3%
Normal HDL-c	14.4%	17.1%
Borderline low HDL-c	9.9%	12.7%
Low HDL-c	18.5%	12.4%
Missing	57.2%	57.8%
Normal ALT	24.7%	58.8%
Moderate ALT elevation	24.1%	21.5%
Severe ALT elevation	14.0%	9.5%
Missing	37.2%	10.2%

Values presented are weighted %. HDL-c, HDL-cholesterol; LDL, low-density lipoprotein.

In the general pediatric population and even in the context of obesity, high LDL-c is rare and is usually related to familial hypercholesterolemia; thus, the lack of difference in LDL-c between the treatment-seeking sample and the population sample of youth with obesity is not surprising. However, because the aetiology of high TG and low HDL-c *is* often related to adiposity, comparable levels of TG and HDL-c between the treatment-seeking and population cohorts were expected when adjusting for BMI. The unexpectedly identified differences may be related to a referral bias in that the American Academy of Pediatrics recommends screening for dyslipidemia in children with obesity (1) and abnormal results may have served as a prompt for referral to a pediatric weight management program.

The prevalence of hypertension in the general population of youth is approximately 2–4% (14). Yet, in this study of youth with obesity, the population cohort prevalence was only 1.8% and substantially more in the treatment-seeking sample at 20%. While obesity is associated with elevated blood pressure, the Bogalusa Heart Study, a large longitudinal study of cardiovascular disease risk factors in youth, found that the correlation between BMI and blood pressure was only 0.3 (15). Thus, other unmeasured variables are likely contributing to the high blood pressure in the treatment-seeking group or perhaps these patients represent a different phenotype of children with obesity who have particularly adverse metabolic profiles including high blood pressure (16). Additionally, there may be more "white coat hypertension" in the treatment-seeking group compared with the population-based sample or there may be more technical difficulties related to measuring blood pressure in the clinical setting (such as cuff-size) which may not be present in the more standardized, research setting. Finally, the higher prevalence of hypertension in the treatment-seeking cohort may also be related to referral bias as, similar to dyslipidemia screening, the American Academy of Pediatrics recommends universal screening for elevated blood pressure (17).

Regarding the diabetes risk lab tests, no discernible or clinically meaningful differences in HbA1c, insulin, HOMA-IR or diagnosis of prediabetes (impaired FG or borderline HbA1c) between groups were identified, as hypothesized. In contrast to these findings, lower FG levels in the treatment-seeking sample of children were observed. The explanation for this finding is unclear and cannot be determined from this study. Speculatively, this finding could be related to differences in Tanner stage between cohorts, which is known to influence insulin and glucose metabolism (18). Moreover, this finding could be spurious as large population-based studies are conflicted as to whether using FG or HbA1c is the most appropriate metric for determining prediabetes/diabetes risk and prevalence (19). Finally, the differences in FG levels may be related to differences in the laboratory analysis methods between the two cohorts. While the NHANES laboratory methods are standardized, the POWER methods are not.

Table 3 Mean difference between POWER and NHANES adjusted for sex, age, race/ethnicity (African American, Asian/Other, Latino/Hispanic and White), insurance status (Private or Private+Public, Public or None, Missing or Unknown) and multiple of the 95th BMI percentile for all subjects and each obesity class

Outcome	POWER mean (SD)	NHANES mean (SD)	Adjusted mean difference (POWER-NHANES) (95% CI)	*P*-value
All subjects				
Systolic BP (mm Hg)	118.9 (12.1)	111.1 (10.2)	6.5 (5.5, 7.6)	<0.001
Systolic BP percentile	67.8 (26.5)	46.9 (26.4)	17.3 (14.5, 20)	<0.001
Diastolic BP (mm Hg)	69.1 (9.9)	57.7 (13.9)	10.1 (8.8, 11.4)	<0.001
Diastolic BP percentile	60 (25.1)	34.6 (26.8)	21.9 (19.1, 24.7)	<0.001
HbA1c (%)	5.4 (0.4)	5.3 (0.3)	0.1 (0, 0.1)	0.038
Fasting glucose (mg/dL)	89.3 (8.8)	95.7 (7.1)	−6.9 (−8.2, −5.6)	<0.001
Fasting insulin (uU/mL)	26 (23)	24.9 (13.4)	−2.3 (−5.1, 0.6)	0.117
HOMA-IR	5.8 (5.2)	5.9 (3.4)	−0.9 (−1.6, −0.2)	0.014
Total cholesterol (mg/dL)	159.4 (35.6)	155.6 (28.3)	3.6 (−1.1, 8.2)	0.131
LDL-c (mg/dL)	92.5 (29.8)	90.9 (24.7)	0.8 (−3.3, 4.9)	0.707
Triglycerides (mg/dL)	131.9 (81.3)	95.6 (59.2)	33.6 (22.9, 44.3)	<0.001
HDL-c (mg/dL)	42 (10.5)	45.7 (9.6)	−2.4 (−3.9, −0.9)	0.002
Non-HDL-c (mg/dL)	117.3 (36.1)	109.9 (28)	5.9 (1.3, 10.4)	0.012
ALT (U/L)	33.4 (29)	24.2 (19.1)	7.8 (5.5, 10.1)	<0.001
Class 1 obesity				
Systolic BP (mm Hg)	115.7 (11.8)	109.7 (9.8)	6.7 (5.2, 8.3)	<0.001
Systolic BP percentile	62.4 (27.5)	43.5 (26.3)	18.9 (14.8, 23)	<0.001
Diastolic BP (mm Hg)	66.9 (9.6)	56.9 (13.8)	10.4 (8.4, 12.3)	<0.001
Diastolic BP percentile	54.9 (25)	32.6 (26.1)	21.9 (17.9, 26)	<0.001
HbA1c (%)	5.3 (0.3)	5.3 (0.3)	0.1 (0, 0.2)	0.062
Fasting glucose (mg/dL)	88.6 (8.5)	94.6 (7)	−6.2 (−8.1, −4.3)	<0.001
Fasting insulin (uU/mL)	20.9 (22.4)	19.7 (8.3)	0.2 (−4.2, 4.5)	0.939
HOMA-IR	4.7 (5.2)	4.6 (2.1)	−0.2 (−1.2, 0.8)	0.710
Total cholesterol (mg/dL)	158.7 (34.8)	153.9 (27.5)	4.4 (−2.2, 11)	0.190
LDL-c (mg/dL)	91.1 (29.9)	87.6 (23.9)	3.5 (−2.5, 9.6)	0.255
Triglycerides (mg/dL)	133.5 (85.6)	97.3 (62.4)	32.3 (15.7, 48.8)	<0.001
HDL-c (mg/dL)	43 (10.2)	46.5 (9.6)	−2.8 (−4.9, −0.7)	0.010
Non-HDL-c (mg/dL)	115.5 (35.9)	107.4 (27.8)	6.9 (0.3, 13.6)	0.041
ALT (U/L)	28.7 (20.1)	22.8 (20.8)	5.7 (2.1, 9.3)	0.002
Class 2 obesity				
Systolic BP (mm Hg)	117.5 (10.5)	111.4 (10.5)	6.6 (4.8, 8.5)	<0.001
Systolic BP percentile	65.5 (25.8)	47.4 (25.2)	17.8 (13, 22.6)	<0.001
Diastolic BP (mm Hg)	68.2 (9.3)	57.6 (13.4)	10.7 (8.4, 13.1)	<0.001
Diastolic BP percentile	58.4 (24.7)	33.9 (26.4)	24.5 (19.5, 29.5)	<0.001
HbA1c (%)	5.4 (0.4)	5.3 (0.3)	0.1 (0, 0.2)	0.014
Fasting glucose (mg/dL)	89.3 (8.1)	98.2 (7.6)	−8.2 (−10.7, −5.8)	<0.001
Fasting insulin (uU/mL)	23.2 (15.9)	31.7 (15.8)	−7.5 (−12.5, −2.5)	0.004
HOMA-IR	5.1 (3.7)	7.8 (4.3)	−2.3 (−3.7, −1)	<0.001
Total cholesterol (mg/dL)	163.7 (39.1)	159.1 (30.9)	3.8 (−4.9, 12.5)	0.396
LDL-c (mg/dL)	94.8 (32)	96.5 (26.7)	−1.9 (−9.2, 5.4)	0.607
Triglycerides (mg/dL)	133 (88.6)	88.7 (42.1)	42 (27.8, 56.3)	<0.001
HDL-c (mg/dL)	42.6 (10)	45.2 (10.2)	−2.8 (−5.6, 0)	0.053
Non-HDL-c (mg/dL)	120.7 (40)	113.9 (29.9)	6.2 (−2.2, 14.7)	0.149
ALT (U/L)	34 (29.3)	26.1 (16)	8.4 (5.1, 11.7)	<0.001
Class 3 obesity				
Systolic BP (mm Hg)	122.6 (12.7)	116.1 (10)	5.8 (3.6, 8.1)	<0.001
Systolic BP percentile	74.1 (25.2)	59.4 (25.4)	11.3 (5.2, 17.5)	<0.001
Diastolic BP (mm Hg)	71.5 (10.3)	61.3 (14.8)	9.2 (5.8, 12.6)	<0.001
Diastolic BP percentile	65.3 (24.4)	44.3 (28.2)	18 (11.2, 24.8)	<0.001
HbA1c (%)	5.4 (0.4)	5.5 (0.3)	−0.1 (−0.2, 0)	0.123
Fasting glucose (mg/dL)	90 (9.6)	96 (5.6)	−7.5 (−10, −4.9)	<0.001

Continues

Table 3. *Continued*

Outcome	POWER mean (SD)	NHANES mean (SD)	Adjusted mean difference (POWER-NHANES) (95% CI)	*P*-value
Fasting insulin (uU/mL)	33.6 (27.7)	32.6 (15.3)	−0.4 (−9.3, 8.4)	0.923
HOMA-IR	7.4 (6.1)	7.7 (3.5)	−0.6 (−2.5, 1.4)	0.576
Total cholesterol (mg/dL)	155.8 (31.9)	156.8 (26)	−0.9 (−11.1, 9.4)	0.871
LDL-c (mg/dL)	91.4 (27.1)	94.1 (21.7)	−2.6 (−11, 5.8)	0.541
Triglycerides (mg/dL)	129.2 (68.6)	101.5 (70.1)	21.6 (−3.8, 46.9)	0.097
HDL-c (mg/dL)	40.5 (11.1)	42.7 (7.7)	−1 (−4.3, 2.3)	0.556
Non-HDL-c (mg/dL)	115.5 (31.4)	114.1 (24.2)	0.4 (−8.7, 9.5)	0.937
ALT (U/L)	36.5 (33.6)	27 (16.1)	9 (4.4, 13.6)	<0.001

BMI, body mass index; BP, blood pressure; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment-insulin resistance; HDL-c, HDL-cholesterol; LDL-c, LDL-cholesterol; NHANES, National Health and Nutrition Examination Survey; POWER, Pediatric Obesity and Weight Evaluation Registry.

Table 4 Odds ratios between NHANES and POWER adjusted for sex, race/ethnicity (African American, Asian/Other, Latino/Hispanic and White), insurance status (Private or Private+Public, Public or None, Missing or Unknown) and multiple of the 95th BMI percentile for all subjects and each obesity class

Outcome	POWER (%)	NHANES (%)	Adjusted odds ratio (95% CI)	*P*-value
All subjects				
Hypertension criteria met	20.4	2.2	8.60 (4.66, 15.86)	<0.001
Prediabetes	34.4	40.0	0.78 (0.53, 1.14)	0.202
High LDL	10.4	5.5	1.71 (0.90, 3.23)	0.101
High triglycerides	38.0	20.3	2.17 (1.44, 3.26)	<0.001
Low HDL	43.3	25.5	1.76 (1.23, 2.52)	0.002
High ALT	22.3	9.6	2.56 (1.76, 3.72)	<0.001
Class 1 obesity				
Hypertension criteria met	13.8	1.4	12.16 (4.31, 34.31)	<0.001
Prediabetes	27.7	30.3	0.81 (0.45, 1.47)	0.494
High LDL	10.5	4.5	2.21 (0.82, 5.97)	0.117
High triglycerides	38.2	22.2	2.09 (1.20, 3.62)	0.009
Low HDL	38.6	22.4	1.94 (1.17, 3.24)	0.011
High ALT	15.7	7.5	2.06 (1.13, 3.74)	0.018
Class 2 obesity				
Hypertension criteria met	16.0	2.1	9.99 (2.95, 33.83)	<0.001
Prediabetes	32.4	49.6	0.75 (0.37, 1.51)	0.415
High LDL	10.8	9.7	0.84 (0.32, 2.25)	0.734
High triglycerides	34.9	14.1	3.06 (1.45, 6.47)	0.004
Low HDL	40.3	26.0	1.86 (0.99, 3.48)	0.055
High ALT	21.7	12.6	2.38 (1.31, 4.31)	0.005
Class 3 obesity				
Hypertension criteria met	29.4	5.8	5.02 (1.90, 13.31)	0.001
Prediabetes	41.8	56.2	0.56 (0.25, 1.23)	0.150
High LDL	9.8	2.3	4.09 (0.73, 23.03)	0.111
High triglycerides	40.9	23.6	1.76 (0.71, 4.39)	0.227
Low HDL	50.6	38.0	1.42 (0.62, 3.22)	0.406
High ALT	27.9	13.0	2.72 (1.25, 5.93)	0.012

CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NHANES, National Health and Nutrition Examination Survey; POWER, Pediatric Obesity and Weight Evaluation Registry.

Elevated ALT, which has its limitations in that it under estimates liver pathology in youth (12,20), is nonetheless a clinically relevant marker of nonalcoholic fatty liver disease (NAFLD). Youth with obesity and severe obesity often present with NAFLD (38–65%) at higher prevalence rates than in the general population (13%) as defined by

liver biopsy (21,22). Thus, while treatment-seeking youth had consistently higher ALT than the population-based sample, both samples likely have much higher prevalence rates of NAFLD than was suggested by their ALT.

Although this treatment-seeking cohort of youth with obesity had an overall worse cardiometabolic profile compared with the population-based sample of youth with obesity, the profiles of these treatment seekers are similar to other treatment-seeking cohorts from around the world. For example, a large survey of 26,008 children (mean age 12.6 years, 56% girls, mean BMI 29.4 kg/m^2) with overweight (BMI $>$ 90th percentile) or obesity ($>$97th percentile) who were treated in any of 98 weight management treatment centers from Germany, Austria and Switzerland examined the cardiometabolic status in these patients (23). Among the subgroup of patients with BMI $>$ 99.5 percentile, the hypertension prevalence was nearly 45%, low HDL-c prevalence was 15% and high triglyceride prevalence was 17%.

The hypothesis for this study was that treatment-seeking youth with obesity and youth with obesity from the general population would have similarly poor cardiometabolic profiles when adjusting for BMI. This finding would have served as a "call to action" for more availability of weight management programs given the enormous number of youth with obesity who are not receiving obesity treatment. However, overall, the results were not consistent with this hypothesis. The reasons for the presence of differences in cardiometabolic profiles between treatment-seeking and population obesity are unclear but could be related to any number of unmeasured confounding variables. One of these variables, which may be especially relevant, is mental illness. Rates of mental illness are known to be higher among treatment-seeking youth with obesity compared with the general population of youth with obesity (4–6), and mental illness also has adverse effects on cardiometabolic health (24). Future studies should include measurements of mental illness as a potential moderator of the association between treatment-seeking status and poor cardiometabolic health.

Strengths of this study include the large sample size, nationally representative nature of both cohorts and generalizability of findings due to the racial/ethnic and gender distributions of the cohorts. Limitations of this study include methods of data collection were not uniform across the pediatric weight management clinics/programs used in the treatment-seeking sample and the amount of missing data. Also, confounding variables such as diet, physical activity, pubertal status, emotional stress/mental illness and direct measures of adiposity (particularly visceral adiposity) were not available for measurement. All of these factors, each to a variable degree, may be associated with cardiovascular disease risk factors and with obesity status. As stated earlier, referral bias may also account for some of the differences in cardiometabolic profiles between the treatment-seeking and population cohorts of youth with obesity. Specifically, it may be that those with comorbidities are more likely to be seen in weight management clinics. This bias would be exacerbated if weight management clinics require the presence of comorbidities as a prerequisite for referral. However, a survey of the programs included in POWER identified that 56% of the programs required potential patients to have a BMI $>$ 85th percentile before enrolling and 36% of the programs required potential patients to have a BMI $>$95th percentile. Only 8% required the additional presence of a comorbid condition (7). Indeed, the American Academy of Pediatrics recommends that patients with obesity should be referred to multidisciplinary weight management programs when there is no weight loss achieved with less structured weight management interventions. The comorbidity status alone is not an indication for referral (1). Finally, the sample sizes of youth with classes II and III obesity in the treatment-seeking cohort were much larger than the population cohort which may have affected the outcomes.

Conclusion

In general, the prevalence of cardiometabolic risk factors increases with the degree of obesity in children and adolescents (25). However, this study demonstrated that for a given BMI, obesity treatment-seeking youth are more adversely affected by these risk factors than the general population of youth with obesity. This suggests that youth who are receiving care in multicomponent pediatric weight management clinics/programs may represent a distinct group that is at particularly high risk for the development of future cardiometabolic disease. Identification of factors contributing to the more adverse cardiometabolic profiles may provide insight into effective treatments.

Conflict of interest statement

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Author Contributions

CF, JR, ASK, SK and AG conceptualized and designed the study, wrote the initial draft and reviewed and revised the manuscript. AMK and KR completed statistical analyses and reviewed and revised the manuscript. All authors had final approval of the submitted and published versions.

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