Prevalence of cardiometabolic diseases in underweight: a nationwide cross-sectional study

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Abstract

This study aimed to estimate the nationwide prevalence of cardiometabolic diseases (CMDs) among adults with underweight in the US general population. Using data from the National Health and Nutrition Examination Survey (1999-2020), we estimated the age-standardized prevalence of dyslipidemia, hypertension, diabetes, chronic kidney disease, cardiovascular disease, and the presence of 0 or at least 2 CMDs. Multivariable Poisson regressions were used to compare CMD prevalence between subgroups, adjusting for age, sex, and race/ethnicity. Among the 855 adults with underweight included, the weighted mean age was 40.8 years, with 68.1% being women and 70.4% non-Hispanic White. The estimated prevalence rates were 23.4% for dyslipidemia (95% CI, 19.4%-27.5%), 15.6% for hypertension (95% CI, 13.3%-17.8%), 2.5% for diabetes (95% CI, 1.5%-3.5%), 7.9% for chronic kidney disease (95% CI, 6.9%-8.8%), and 6.1% for cardiovascular disease (95% CI, 4.3%-7.9%). The prevalence of having 0 and at least 2 CMDs was 50.6% (95% CI, 44.1%-57.0%) and 12.3% (95% CI, 8.1%-16.4%), respectively. Non-Hispanic Black adults had significantly higher prevalence of diabetes (adjusted prevalence ratio, 3.35; 95% CI, 1.35-8.30) compared to non-Hispanic White adults. In conclusion, approximately half of the underweight adults had at least one CMD, and 12.3% had at least two CMDs. Prevention and management of CMDs in underweight adults are critical yet neglected public health challenges.

Keywords: underweight, cardiometabolic diseases, NHANES, prevalence, body mass index

Abbreviations: body mass index (BMI); cardiometabolic diseases (CMDs); cardiorespiratory fitness (CRF); false discovery rate (FDR); confidence intervals (CIs); Healthy Eating Index-2015 (HEI-2015); National Health and Nutrition Examination Survey (NHANES); prevalence ratios (PRs)

INTRODUCTION

Cardiometabolic diseases (CMDs) are a group of common but often preventable diseases encompassing cardiovascular disease and metabolic disorders, which are a major public health concern worldwide.[1] Existing studies have focused on quantifying burden of CMDs in general populations or people with obesity.[2, 3] Data regarding the burden of CMDs specifically among people with underweight are scarce. However, underweight has been associated with increased risk of cardiovascular disease and mortality, according to repeatedly reported J- or U-shaped associations of body mass index (BMI) with cardiovascular disease and mortality in both general and diseased populations.[4-7] In the United States, ~1.6% of adults aged 20 years or older were underweight in 2017-2018, equivalent to ~4 million individuals.[8] However, the nationwide prevalence of CMDs among US adults with underweight is unclear.

Using nationally representative data from the National Health and Nutrition Examination Survey (NHANES) in 1999-2020, we sought to estimate the prevalence of a range of CMDs among US adults with underweight.

METHODS

Data source and study design

NHANES is a continuous, multistage, nationally representative survey of the non-institutionalized civilian resident US population. The survey has been conducted periodically in 2-year cycles since 1999, collecting data through in-home interviews and study visits at mobile examination centers. However, the NHANES program suspended field operations in March 2020 due to the pandemic of coronavirus disease 2019. Therefore, data collected from 2019 to March 2020 were combined with the data from the 2017-2018 cycle to form a nationally representative sample. This study included 10 cycles between 1999-2000 and 2017-2020. The overall response rate ranged from 51% to 84% for the interview component and from 46.9% to 80% for the examination component. Participants aged 20 years or older

were included. Pregnant women were excluded.

The National Center for Health Statistics Research Ethics Review Board approved NHANES. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Shanghai Jiao Tong University School of Medicine Public Health and Nursing Research Ethics Review Committee (ethics number: SJUPN-202102-B). Written informed consent was obtained from all participants.

Underweight and covariates

Height and weight were collected by trained health technicians. BMI was computed by dividing an individual's weight in kilograms by their height in meters squared. BMI <18.5 kg/m^2 defined underweight and the inclusion criterion of this study. Self-reported information on age, sex, race/ethnicity, education, and medical conditions was collected during the household interview. Race/ethnicity was self-reported according to fixed-category questions. Alcohol consumption, leisure-time physical activity, sleep duration, smoking status, and dietary intake were self-reported. Diet quality was assessed by Healthy Eating Index-2015 (HEI-2015).[9]

Definition of CMDs

CMDs included dyslipidemia, hypertension, prediabetes, diabetes, chronic kidney disease, and cardiovascular disease. Dyslipidemia was defined as having a total cholesterol level ≥240 mg/dL or a high-density lipoprotein cholesterol level <40 mg/dL for men or <50 mg/dL for women or self-reported current use of lipid-lowering drugs.[10] Hypertension was defined as having blood pressure ≥130/80 mm Hg or self-reported current use of anti-hypertensive drugs. Blood pressure was based on the average of all available measurements. Diabetes was defined as having a self-reported diagnosis of diabetes by a physician or other health professional, a fasting plasma glucose level ≥126 mg/dL or a hemoglobin A1c level ≥6.5%.

Fasting plasma glucose was measured among those who were fasted for 8 to <24 hours. Plasma glucose data between 2005-2006 and 2017-2020 were calibrated according to the recommended equation from NHANES.[11] Among participants without being diagnosed with diabetes before, a hemoglobin A1c level of 5.7-6.4% or a fasting plasma glucose level of 100-125 mg/dL defined prediabetes. Chronic kidney disease was defined as having a urine albumin to creatinine ratio ≥30 mg/g or an estimated glomerular filtration rate <60 mL/min/1.73 m^2.[12] Urine and serum creatinine levels were calibrated.[13] Estimated glomerular filtration rate was computed according to the Chronic Kidney Disease Epidemiology Collaboration equation.[14] Cardiovascular disease was a composite endpoint of self-reported congestive heart failure, coronary heart disease, heart attack, and stroke. Two or more CMDs commonly co-occur within an individual.[2] Therefore, having 0 and at least 2 of the following diseases were studied: dyslipidemia, hypertension, diabetes, chronic kidney disease, and cardiovascular disease.

Statistical analysis

The characteristics of the study participants were described using weighted percentages or weighted mean (SE). The prevalence of CMDs alone and in combination was estimated in the total sample and by age (20-39, 40-59, and ≥60 years), sex (men and women), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other), and education (less than high school, high school graduate, some college, and college graduate or higher). Estimates were age standardized to the 1999-2020 NHANES nonpregnant adult population with underweight. Multivariable Poisson regressions were used to estimate the prevalence ratios (PRs) for comparing the prevalence of CMDs between subgroups, adjusting for age, sex, and race/ethnicity. Subgroup differences in the PRs of CMDs were obtained from weighted Poisson regression models. *P* values were adjusted using false discovery rate (FDR) corrections.

Post-hoc analyses were conducted to help interpret the prevalence of CMDs in adults with underweight. First, the prevalence of CMDs in the general population was compared by weight category (underweight, normal weight, overweight, and obese) using multivariable Poisson regressions, adjusting for age, sex, and race/ethnicity. Using underweight as the reference, PRs and 95% confidence intervals (CIs) were derived for other weight categories. Second, the prevalence of CMDs among adults with underweight was estimated by different lifestyle factors: non-excessive drinking (≥4-5 drinks/day, or ≤14 drinks/week for men or ≤7 drinks/week for women; yes/no),[15] meeting physical activity guidelines (≥150 minutes per week of moderate-intensity or ≥75 minutes per week of vigorous-intensity leisure-time activity; yes/no), meeting recommended sleep duration (sleep duration of 7-9 hours per day; yes/no), smoking status (self-reported and grouped into 3 categories; current, former, and never), and low Healthy Eating Index-2015 score (<50 or ≥50). Subgroup differences were compared using the F tests.

Appropriate sampling weights and design variables were considered to account for the stratified, multistage probability cluster sampling method. Complete case analysis was implemented for primary analysis unless missing data for specific analysis exceeded 10% according to the NHANES analytical guidelines.[16] When missing data exceeded 10%, the original sampling weights of the respondent sample were adjusted using a weight factor that accounted for the differences between respondents and nonrespondents, based on the Lohr's method.[17] A post-hoc analysis revealed sex and racial/ethnic differences between individuals with missing data and those without; age and education attainment did not differ between the two groups (**eTable 1**). Participants were therefore classified into 8 subgroups defined by sex (men and women) and race/ethnicity (non-Hispanic black, non-Hispanic white, Hispanic, and other).[18] The weight factor for each subgroup was calculated as the sum of the weights for all eligible individuals (including those with missing data) divided by the sum of the weights for those with complete data. The adjusted sampling weight for each respondent in a subgroup was then multiplied by the subgroup weight factor. A sensitivity analysis using

multiple imputations was also conducted to assess the robustness of the prevalence estimates in the presence of missing data ≥10%. We employed PROC MI procedure in SAS (v 9.4) and used the fully conditional specification method.[19] The following covariates were included: age, sex, race/ethnicity, education level, estimated glomerular filtration rate, urine albumin-to-creatinine ratio, and chronic kidney disease status. All missing values were assumed to be missing at random. All analyses were conducted using SAS statistical software, version 9.4 (SAS Institute Inc.).

RESULTS

A total of 855 participants with underweight were analyzed. Specific sample size for each outcome varied (**Figure 1**). The weighted mean age was 40.8 years (SE, 0.6), 68.1% were women, and 70.4% were non-Hispanic White (**Table 1**). Missing data were found for dyslipidemia (n = 79 [9.2%]), hypertension (n = 39 [4.6%]), chronic kidney disease (n = 86 [10.0%]), and cardiovascular disease (n = 5 [0.6%]). For stratification variables, missing data were found only for education (n = 2 [0.2%]).

The estimated prevalence of each CMDs among adults with underweight was 23.4% (95% CI, 19.4% to 27.5%) for dyslipidemia, 15.6% (95% CI, 13.3% to 17.8%) for hypertension, 21.2% (95% CI, 16.6% to 25.8%) for prediabetes, 2.5% (95% CI, 1.5% to 3.5%) for diabetes, 7.9% (95% CI, 6.9% to 8.8%) for chronic kidney disease, and 6.1% (95% CI, 4.3% to 7.9%) for cardiovascular disease (**Table 2**). The estimated prevalence of having 0 and at least 2 CMDs was 50.6% (95% CI, 44.1% to 57.0%) and 12.3% (95% CI, 8.1% to 16.4%), respectively. Regarding the subgroup results, the prevalence of all CMDs was significantly higher in older adults aged at least 60 years than young adults aged 20-39 years, except for dyslipidemia (PR 1.81 (1.04-3.16), FDR-adjusted *P*=0.08) (**Table 3**). No sex difference in the prevalence of CMDs was identified. Racial/ethnic difference in the prevalence of CMDs was only found for diabetes. Non-Hispanic Black adults had a significantly higher prevalence of diabetes (PR 3.35 [95% CI, 1.35-8.30], FDR-adjusted *P* =0.045) than non-Hispanic White adults. The

prevalence of having 0 CMDs was significantly lower in older and middle-aged adults than young adults. The prevalence of having at least 2 CMDs was significantly higher in older and middle-aged adults than young adults. No significant difference in the prevalence of composite CMDs outcomes by sex, race or education level was identified.

Post-hoc analyses showed that adults with underweight had the highest prevalence of chronic kidney disease among all weight categories (all $P < 0.01$). No significant difference in the prevalence of cardiovascular disease was found across weight categories (all $P > 0.05$) (**eTable 2**). Among adults with underweight, the prevalence of all CMDs was significantly lower in those who met the physical activity guideline recommendation than those who did not meet. The prevalence of all CMDs, except for diabetes, was significantly lower in never smokers than former or current smokers (**eTable 3**). Adults with healthier lifestyle behaviors (e.g., non-excessive drinking, meeting physical activity guidelines, never smoking, and not low diet quality) had a significantly higher prevalence of having 0CMDs than that in their counterparts (all $P < 0.05$). No significant difference in the prevalence of all CMDs, except for cardiovascular disease, was found between those who met the recommended sleep duration and those who did not.

The prevalence of chronic kidney disease among adults with underweight using different missing data handling methods was similar. Compared with complete case analysis, only small differences in the point estimates were found using adjusted weights (≤0.3%) and multiple imputations (≤1.4%) (**eTable 4**).

DISCUSSION

Among adults with underweight in the United States, only 50.6% had absence of CMDs and 12.3% lived with at least 2 CMDs. Diabetes and hypertension disproportionately affected non-Hispanic Blacks. The prevalence of CMDs was higher in older than younger adults, but did not vary by education level. No sex difference was observed.

Adults with underweight are commonly perceived as having a low burden of CMDs, but our results did not support this. In our study, only half of adults with underweight had no CMDs. Of all the CMDs examined, the prevalence of dyslipidemia was the highest achieving ~23%, followed by hypertension of ~16%, while the prevalence of diabetes was relatively low. Published studies that reported the prevalence of CMDs often merged the underweight adults into the normal-weight group,[20, 21] and rarely estimated the prevalence of CMDs in underweight separately.[22, 23] Only one study conducted specifically among US adults with underweight was identified based solely on self-reported data, reporting a prevalence of cardiovascular disease of 7.3% in 2013, similar to the estimate from our study.[24] The high prevalence of CMDs in the underweight population implies that being underweight does not necessarily mean being cardiometabolically healthy.[23] A cross-sectional study found that nearly 20% of the underweight population were classified as metabolically abnormal, defined as having 2 or more criteria of metabolic syndrome.[25] Ectopic fat deposition in the liver and pancreas may confer a large role on the development of CMDs in the underweight population.[26]

Similar to the findings from overweight and obese populations, multimorbidity of CMDs was also common in underweight based on our study. Unhealthy lifestyle behaviors are well-established risk factors for CMDs. Evidence has shown that unhealthy lifestyle behaviors may even cause more severe health problems in non-obese individuals, including those who were underweight, than obese adults.[27] In our study, the prevalence of CMDs was highly prevalent among underweight adults with unhealthy lifestyle behaviors. Of all the lifestyle factors except for sleep duration, compared with underweight adults with a healthier lifestyle, those with a less healthier lifestyle had a 6%-16% higher prevalence of having at least 2 CMDs. Despite the differential influences of each lifestyle factor, the findings suggest that targeting multiple unhealthy lifestyle behaviors may be needed for the prevention and management of CMDs among adults with underweight.

Subgroup differences by demographic variables and socioeconomic status in the prevalence of CMDs were not as widely present in the underweight population as previously reported in general adult populations,[28, 29] suggesting that the entire underweight group was at risk of developing CMDs. This distinction suggests possibilities of different etiologies and risk factor profiles for CMDs between adults with underweight and those with overweight/obesity, which require future investigations to elucidate. Nonetheless, the disproportionate burden of diabetes in non-Hispanic Black adults with underweight was in line with the racial/ethnic disparities in diabetes well-described in general adult populations.[30, 31] Racial/ethnic disparities in the prevalence of CMDs found in previous studies were largely due to racial/ethnic disparities in the prevalence of overweight and obesity, social risk factors, and lifestyle behaviors.[32, 33] The NHANES data did not allow accurate classification of diabetes type, but it is possible that type 1 diabetes accounted for a substantial proportion. To understand pathophysiological mechanisms leading to CMDs in underweight, it is critical to understand the causes of underweight itself. Unlike underweight mainly resulting from inadequate nutrition in many low- and middle-income countries, underweight in the US may be multifactorial, including malnutrition, chronic diseases, and a personal choice due to body image dissatisfaction, among others.[34] Effective prevention and management of CMDs are not possible without correctly understanding the underlying causes of underweight.

Although the underlying contributors to the high prevalence of CMDs in underweight populations are poorly understood, improving cardiometabolic health among underweight people is clearly an urgent public health need. Published data on characterizing distributions of lifestyle risk factors in underweight are scarce. Our study found that underweight people who had a healthier lifestyle, including non-excessive drinking, more physical activity, never smoking, and higher-quality diet, had a lower prevalence of various CMDs. These findings suggest that improving lifestyle may be critical to improving cardiometabolic health in people with underweight as in people with overweight or obesity.[35] Furthermore, evidence has shown that underweight individuals tended to have lower cardiorespiratory fitness (CRF)

compared to those with normal weight.[36, 37] Lower CRF is known to be associated with higher risks of CMDs and mortality.[38, 39] CRF can possibly be improved through reducing alcohol intake, eating healthy diet, and increasing physical activity especially resistance training,[39-43] but these data may not be equally applicable to underweight people. Whether such lifestyle modifications would result in a similar improvement in CRF specifically in people with underweight requires further investigation.

Strengths and limitations

To our knowledge, this is the first study to comprehensively characterize the landscape of CMDs in underweight, using both self-reported and laboratory data from a large nationally representative sample. However, this study has several limitations. First, misdiagnosis of CMDs was possible due to the use of self-reported data and one-time laboratory measurements. Second, this was a cross-sectional study, thus the causal relationship between underweight and CMDs cannot be inferred. Third, because of the small sample size, several subgroup estimates had a relative standard error greater than 30% and thus should be interpreted with caution. Fourth, missing data may have caused bias in some estimates, but we used both multiple imputations and weight adjustment approach to address missing data. Results from these two approaches were similar.

Conclusions

Contrary to the commonly assumed low burden of CMDs in the underweight population, nearly half of adults with underweight had at least 1 CMDs, and nearly one eighth had at least 2 CMDs. Screening of CMDs in underweight population may be considered. More resources should be allocated to prevention and management of CMDs in this understudied group.

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Author Contribution: Drs Zhou and Zhong had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Chen, Zhou, Zhong.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Chen, Zhong.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Chen, Zhong.

Administrative, technical, or material support: Zhou, Zhong.

Ethical approval: The National Center for Health Statistics Research Ethics Review Board approved NHANES. All participants signed informed consent. Shanghai Jiao Tong University School of Medicine Public Health and Nursing Research Ethics Review Committee approved this study, approval number [SJUPN-202102-B].

Data availability: The data that support the findings of this study are openly available at https://www.cdc.gov/nchs/nhanes/.

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Table 1. Characteristics for adults with underweight[a]

Characteristics	**No. of Participants**	**Weighted %**
Total	855	100.0
Age group, y		
20-39	407	54.7
40-59	209	27.8
≥ 60	239	17.5
Sex		
Men	334	31.9
Women	521	68.1
Race/ethnicity[b]		
Non-Hispanic White	412	70.4
Non-Hispanic Black	209	11.7
Hispanic	92	6.8
Other	142	11.1
Education level[c]		
Less than high school	228	20.4
High school graduate	197	24.7
Some college	242	28.6
College graduate or higher	186	26.3

[a] Underweight was defined as having body mass index <18.5 kg/m^2.

[b] Race/ethnicity was self-reported. The "other" group included other non-Hispanic races or multiple races.

[c] Two participants refused to report or did not know their education level.

Table 2. Prevalence of cardiometabolic diseases among adults with underweight[a]

Characteristics	Dyslipidemia[b]		Hypertension[c]		Prediabetes[d]		Diabetes[e]	
	No.	Prevalence, % (95% CI)[i]	No.	Prevalence, % (95% CI)[i]	No.	Prevalence, % (95% CI)[i]	No.	Prevalence, % (95% CI)[i]
Total	776	23.4 (19.4 to 27.5)	816	15.6 (13.3 to 17.8)	366	21.2 (16.6 to 25.8)	366	2.5 (1.5 to 3.5)
Age group, y								
20-39	376	19.4 (14.4 to 24.5)	385	10.2 (6.2 to 14.3)	182	10.6 (5.4 to 15.7)	182	0.4 (-0.2 to 0.9)[l]
40-59	183	23.4 (15.2 to 31.7)	202	33.6 (24.3 to 42.9)	87	27.1 (17.5 to 36.6)	87	2.5 (0.3 to 4.7)[l]
≥ 60	217	36.3 (27.0 to 45.6)	229	69.3 (62.2 to 76.3)	97	46.8 (31.7 to 62.0)	97	8.7 (4.0 to 13.5)
Sex								
Men	292	17.9 (12.4 to 23.5)	324	32.4 (26.5 to 38.4)	142	30.5 (21.0 to 40.1)	142	3.2 (1.2 to 5.3)[l]
Women	484	25.9 (20.6 to 31.2)	492	24.3 (19.9 to 28.6)	224	17.1 (12.0 to 22.3)	224	2.0 (0.8 to 3.1)
Race/ethnicity[j]								
Non-Hispanic White	377	24.6 (19.3 to 29.9)	396	25.5 (20.7 to 30.3)	171	19.8 (13.8 to 25.8)	171	1.6 (0.5 to 2.6)[l]
Non-Hispanic Black	181	23.9 (17.1 to 30.7)	199	39.7 (33.5 to 45.9)	74	23.3 (13.6 to 33.1)	74	4.9 (1.6 to 8.1)[l]

Hispanic	83	16.1 (8.7 to 23.6)	85	21.8 (14.4 to 29.1)	40	29.2 (15.5 to 42.9)	40	3.7 (-0.4 to 7.5)[l]
Other	135	20.1 (11.6 to 28.6)	136	25.5 (18.0 to 33.0)	81	25.1 (13.8 to 36.3)	81	4.1 (0.8 to 7.5)[l]
Education level[k]								
Less than high school	205	27.7 (19.2 to 36.3)	222	34.2 (25.3 to 43.2)	104	24.4 (15.3 to 33.5)	104	3.4 (1.1 to 6.0)[l]
High school graduate	178	27.0 (18.3 to 35.6)	184	34.6 (24.5 to 44.6)	75	29.7 (19.4 to 40.0)	75	2.8 (0.3 to 5.3)[l]
Some college	218	22.9 (16.1 to 29.6)	228	22.8 (17.4 to 28.1)	103	20.6 (12.1 to 29.2)	103	2.7 (0.9 to 4.5)[l]
College graduate or higher	174	17.6 (9.1 to 26.2)	180	18.8 (12.8 to 24.8)	83	13.2 (4.8 to 21.6)[l]	83	0.8 (-0.8 to 2.4)[l]

Table 2 (continued). Prevalence of cardiometabolic diseases among adults with underweight[a]

	Chronic kidney disease[f]		**Cardiovascular disease[g]**		**Having 0 CMDs[h]**		**Having at least 2 CMDs[h]**	
Characteristics	**No.**	**Prevalence, % (95% CI)[i]**	**No.**	**Prevalence, % (95% CI)[i]**	**No.**	**Prevalence, % (95% CI)[i]**	**No.**	**Prevalence, % (95% CI)[i]**
Total	769	7.9 (6.9 to 8.8)	850	6.1 (4.3 to 7.9)	352	50.6 (44.1 to 57.0)	353	12.3 (8.1 to 16.4)
Age group, y								
20-39	374	10.1 (8.5 to	407	1.5 (1.4 to	173	65.4 (56.7 to	17	8.8 (2.3 to

		11.7)		1.5)		74.1)	7	15.4)[l]	
40-59	185	19.6 (18.4 to 20.7)	208	8.6 (7.2 to 10.1)	85	37.6 (24.0 to 51.2)	82	28.4 (15.0 to 41.9)	
≥ 60	210	41.0 (38.3 to 43.8)	235	17.0 (13.8 to 20.2)	94	18.7 (8.0 to 29.3)	94	55.0 (41.1 to 69.0)	
Sex									
Men	285	14.7 (13.9 to 15.5)	330	4.4 (4.0 to 4.8)	136	44.8 (34.4 to 55.3)	135	17.5 (11.2 to 23.8)	
Women	484	19.6 (18.1 to 21.1)	520	7.0 (6.0 to 8.0)	216	51.7 (43.7 to 59.7)	218	24.4 (17.0 to 31.9)	
Race/ethnicity[j]									
Non-Hispanic White	371	18.0 (16.6 to 19.5)	410	6.0 (5.0 to 6.9)	169	48.7 (40.4 to 57.0)	166	23.0 (15.8 to 30.2)	
Non-Hispanic Black	175	24.6 (23.5 to 25.8)	208	7.5 (6.8 to 8.1)	67	40.2 (28.4 to 51.9)	69	25.9 (16.9 to 34.8)	
Hispanic	85	14.5 (13.9 to 15.1)	91	8.6 (8.2 to 8.9)	36	47.5 (31.7 to 63.3)	39	14.6 (7.6 to 21.7)	
Other	138	13.6 (13.4 to 13.8)	141	4.4 (4.3 to 4.5)	80	60.5 (48.7 to 72.2)	79	19.7 (11.1 to 28.3)	
Education level[k]									
Less than high	199	24.8 (19.9 to	225	10.1 (9.3 to	98	40.9 (26.6 to	97	20.9 (12.9 to	

school		29.8)		10.9)		55.1)		28.9)
High school graduate	177	20.8 (18.8 to 22.9)	196	8.1 (5.6 to 10.6)	73	40.8 (28.0 to 53.6)	74	34.5 (18.1 to 50.9)
Some college	219	15.1 (14.1 to 16.2)	241	6.6 (6.1 to 7.1)	98	50.8 (38.7 to 62.9)	102	21.9 (13.1 to 30.6)
College graduate or higher	173	13.6 (12.7 to 14.5)	186	0.9 (0.7 to 1.1)	82	62.8 (50.1 to 75.5)	79	13.0 (5.0 to 21.0)

Abbreviation: CI, confidence interval; CMDs, cardiometabolic diseases.

[a] Underweight was defined as body mass index <18.5 kg/m^2.

[b] Dyslipidemia was defined as having a total cholesterol level ≥240 mg/dL or a high-density lipoprotein cholesterol level <40 mg/dL for men or <50 mg/dL for women or self-reported current use of lipid-lowering drugs.

[c] Hypertension had blood pressure ≥130/80 mm Hg or self-reported current use of anti-hypertensive drugs.

[d] Prediabetes had a hemoglobin A1c level of 5.7-6.4% or a fasting plasma glucose level of 100-125 mg/dL among people without self-reported diabetes.

[e] Diabetes was defined as having a self-reported diagnosis of diabetes by a physician or other health professional, a fasting plasma glucose level ≥126 mg/dL or a hemoglobin A1c level ≥6.5%.

[f] Chronic kidney disease was defined as having a urine albumin to creatinine ratio ≥30 mg/g or an estimated glomerular filtration rate <60 mL/min/1.73 m^2.

[g] Cardiovascular disease was a composite endpoint of self-reported congestive heart failure, coronary heart disease, heart attack, and stroke.

[h] CMDs included dyslipidemia, hypertension, diabetes, chronic kidney disease, and cardiovascular disease.

[i] Estimates by age group were unadjusted. Other estimates were age standardized to the 1999-2020 National Health and Nutrition Examination Survey non-pregnant adult population with underweight, using the age groups 20 to 39 years, 40 to 59 years, and 60 years or older.

[j] Race/ethnicity was self-reported. The "other" group included other non-Hispanic races or multiple races.

[k] Participants refused to report or did not know their education level for the analysis of dyslipidemia (n =1), hypertension (n =2). prediabetes (n =1), diabetes (n =1), chronic kidney disease (n =1), cardiovascular disease (n =2), having 0 CMDs (n =1), and having at least 2 CMDs (n =1).

[l] Relative standard error ≥30%.

Table 3. Subgroup differences in the prevalence of cardiometabolic diseases among adults with underweight[a]

Characteristics	Prevalence ratio (95% CI)[b]							
	Dyslipidemia[c]	**FDR-adjusted *P* value[k]**	**Hypertension**	**FDR-adjusted *P* value[k]**	**Prediabetes[e]**	**FDR-adjusted *P* value[k]**	**Diabetes[f]**	**FDR-adjusted *P* value[k]**
Age group, y								
20-39	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
40-59	1.15 (0.66-1.98)	0.63	3.27 (1.65-6.48)	0.001	2.76 (1.41-5.42)	0.009	8.32 (2.12-32.55)	0.009
≥ 60	1.81 (1.04-3.16)	0.08	6.69 (3.67-12.20)	<.001	4.47 (2.46-8.13)	<.001	25.49 (6.07-106.92)	<.001
Sex								
Men	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
Women	1.44 (0.89-2.32)	0.14	0.78 (0.57-1.07)	0.13	0.55 (0.32-0.96)	0.049	0.72 (0.31-1.64)	0.47
Race/ethnicity[j]								
Non-Hispanic White	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
Non-Hispanic Black	1.04 (0.68-1.60)	0.86	1.43 (1.03-1.98)	0.12	0.97 (0.43-2.19)	0.95	3.35 (1.35-8.30)	0.045
Hispanic	0.65 (0.27-	0.86	0.75 (0.39-1.45)	0.60	1.49 (0.78-	0.72	3.04 (0.63-14.57)	0.21

Other	0.85 (0.47-1.58)	0.86	0.95 (0.58-1.55)	0.83	1.15 (0.61-2.83)	0.95	2.92 (1.18-7.22)	0.045
Education level									
Less than high school	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
High school graduate	0.93 (0.49-1.75)	0.82	1.09 (0.67-1.79)	0.73	1.38 (0.65-2.92)	0.62	0.91 (0.20-4.06)	0.96
Some college	0.79 (0.44-1.43)	0.66	0.70 (0.43-1.15)	0.24	0.89 (0.45-1.78)	0.75	1.09 (0.30-3.96)	0.96
College graduate or higher	0.58 (0.34-0.99)	0.15	0.64 (0.37-1.10)	0.24	0.59 (0.25-1.40)	0.62	0.40 (0.13-1.23)	0.36

Table 3 (continued). Subgroup differences in the prevalence of cardiometabolic diseases among adults with underweight[a]

	Prevalence ratio (95% CI)[b]							
Characteristics	**Chronic kidney disease[g]**	**FDR-adjusted *P* value[k]**	**Cardiovascular disease[h]**	**FDR-adjusted *P* value[k]**	**Having 0 CMDs[i]**	**FDR-adjusted *P* value[k]**	**Having at least 2 CMDs[i]**	**FDR-adjusted *P* value[k]**
Age group, y								
20-39	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
40-59	1.87 (0.93-3.78)	0.08	6.86 (1.82-25.81)	0.005	0.58 (0.37-0.89)	0.02	3.06 (1.47-6.35)	0.007
≥ 60	3.99 (2.20-7.23)	<.001	12.97 (4.12-40.83)	<.001	0.29 (0.16-0.51)	<.001	6.20 (3.44-11.19)	<.001
Sex								
Men	1.00		1.00		1.00		1.00 (reference)	

	(reference)		(reference)		(reference)			
Women	1.39 (0.78-2.47)	0.27	1.73 (0.82-3.64)	0.15	1.16 (0.88-1.52)	0. 30	1.44 (0.91-2.29)	0.14
Race/ethnicity[j]								
Non-Hispanic White	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
Non-Hispanic Black	1.49 (0.86-2.57)	0.48	1.26 (0.49-3.20)	0.63	0.86 (0.63-1.18)	0.54	1.26 (0.76-2.09)	0.56
Hispanic	0.79 (0.32-1.96)	0.61	1.68 (0.49-3.20)	0.63	0.99 (0.63-1.56)	0.97	0.53 (0.31-0.91)	0.09
Other	0.78 (0.39-1.57)	0.61	0.67 (0.21-2.12)	0.63	1.26 (1.00-1.58)	0.18	0.89 (0.55-1.46)	0.66
Education level								
Less than high school	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
High school graduate	0.83 (0.40-1.72)	0.62	0.87 (0.33-1.90)	0.62	1.00 (0.58-1.71)	1.00	1.57 (0.83-2.98)	0.36
Some college	0.58 (0.30-1.09)	0.15	0.60 (0.19-1.93)	0.59	1.23 (0.77-1.96)	0.60	0.99 (0.50-1.98)	0.98
College graduate or higher	0.56 (0.28-1.10)	0.15	0.14 (0.02-0.89)	0.12	1.49 (0.91-2.43)	0.39	0.62 (0.29-1.33)	0.36

Abbreviation: CI, confidence interval; CMDs, cardiometabolic diseases.

[a] Underweight was defined as body mass index <18.5 kg/m^2.

[b] Prevalence ratio was estimated using Poisson regressions, adjusting for age, sex, and race/ethnicity when appropriate.

[c] Dyslipidemia was defined as having a total cholesterol level ≥240 mg/dL or a high-density lipoprotein cholesterol level <40 mg/dL for men or <50 mg/dL for women or self-reported current use of lipid-lowering drugs.

[d] Hypertension had blood pressure ≥130/80 mm Hg or self-reported current use of anti-hypertensive drugs.

[e] Prediabetes had a hemoglobin A1c level of 5.7-6.4% or a fasting plasma glucose level of 100-125 mg/dL among people without self-reported diabetes.

[f] Diabetes was defined as having a self-reported diagnosis of diabetes by a physician or other health professional, a fasting plasma glucose level ≥126 mg/dL or a hemoglobin A1c level ≥6.5%.

[g] Chronic kidney disease was defined as having a urine albumin to creatinine ratio ≥30 mg/g or an estimated glomerular filtration rate <60 mL/min/1.73 m^2.

[h] Cardiovascular disease was a composite endpoint of self-reported congestive heart failure, coronary heart disease, heart attack, and stroke.

[i] CMDs included dyslipidemia, hypertension, diabetes, chronic kidney disease, and cardiovascular disease.

[j] Race/ethnicity was self-reported. The "other" group included other non-Hispanic races or multiple races.

[k] *P* values were adjusted using false discovery rate method to control the type I error for multiple comparisons in subgroup differences.

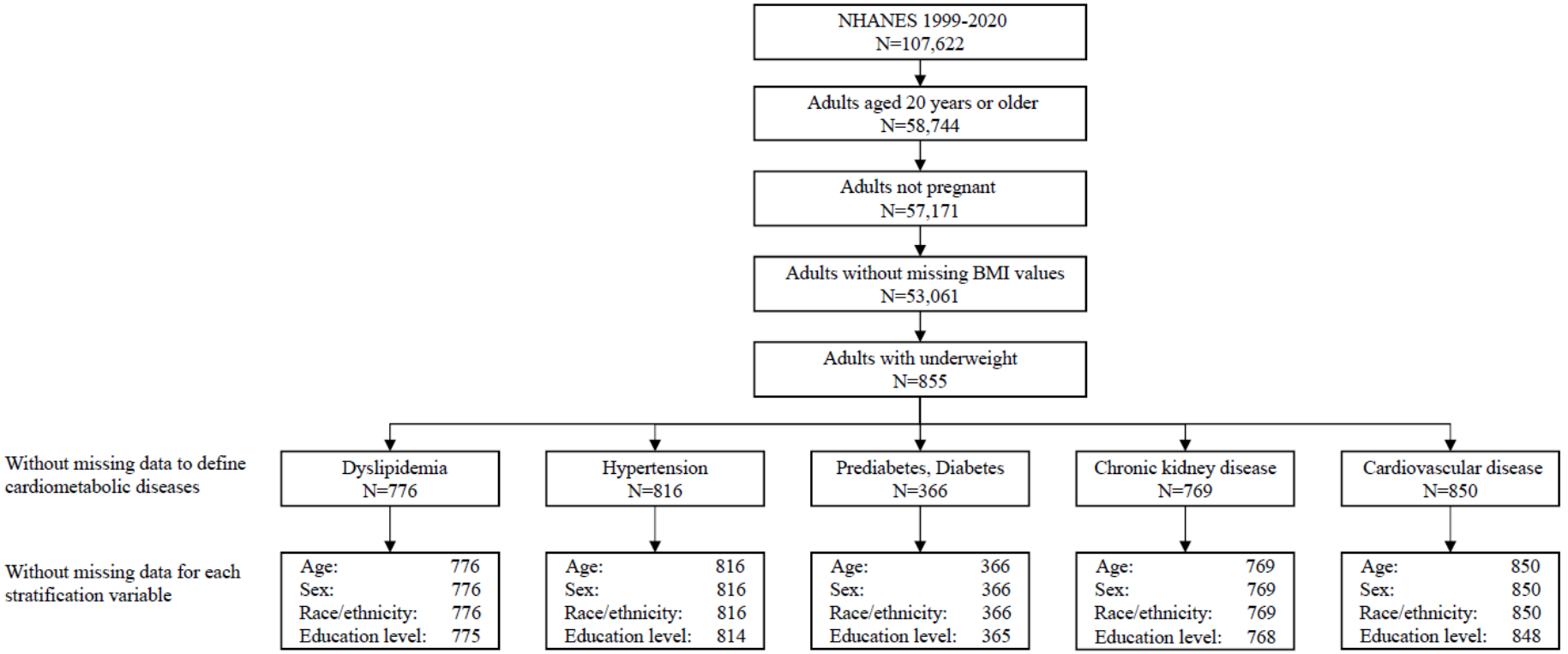

Figure 1. flow chart of the study sample.