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Publication Date

2021-04-28

DOI

10.1007/s40257-021-00600-z

Peer reviewed

American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-021-00600-z

ORIGINAL RESEARCH ARTICLE

Psoriasis Severity and Cardiometabolic Risk Factors in a Representative US National Study

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Accepted: 19 March 2021

Abstract

Background Psoriasis is associated with metabolic syndrome; however, the relationship of psoriasis severity with individual cardiometabolic risk factors is not clear. There is a reporting gap between the cardiometabolic risks among patients with psoriasis and what has been reported in the literature using US samples.

Objectives The objective of this study was to examine the disease burden of psoriasis and assess the associations of psoriasis severity and cardiometabolic risk factors in a nationally representative sample.

Methods We conducted a cross-sectional study using the weighted pooled data from the National Ambulatory Medical Care Survey (NAMCS) 2007 through 2016. The NAMCS data were collected from US office-based physicians. Each physician was randomly assigned a specific week to report a sample of their cases. Patients were categorized as severe psoriasis if they were prescribed at least one systemic therapy. We used logistic regression models adjusting for potential confounders to estimate the associations of psoriasis severity with individual cardiometabolic factors.

Results There were about 3.3 million office-based psoriasis visits per year with a mean age of 50 years, a female-to-male ratio of 1:1, and severe disease in 23%. We observed greater values of blood pressure, lipid profiles, and higher body mass index among patients with psoriasis, compared with patients without psoriasis. A higher proportion of the psoriasis patient group were overweight and obese (73.6% vs 62.9% in the non-psoriasis patient group). Compared to mild case groups, severe case groups tended to have a higher proportion of overweight/obese with a body mass index $\geq$ 25 kg/m^2 (77% vs 73%). Obesity was weakly associated with psoriasis severity (adjusted odds ratio = 1.37, 95% confidence interval 0.98–1.91 for mild disease and adjusted odds ratio = 1.42, 95% confidence interval 0.80–2.52 for severe cases).

Conclusions Cardiometabolic factors are related health issues in psoriasis, and obesity is associated with greater psoriasis severity.

Key Points

Obesity and metabolic syndrome are critical health problems in the USA and even more serious issues among patients with psoriasis.

The psoriasis population was more likely to have elevated blood pressure, dyslipidemia, and higher body mass index than the non-psoriasis population.

Obesity is associated with greater psoriasis severity.

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Published online: 28 April 2021

1 Introduction

Psoriasis is a chronic inflammatory skin disorder and involves multiple organ systems [1], which may complicate the treatment course and induce further morbidity and mortality. Although rates of comorbidities such as obesity, dyslipidemia, and metabolic syndrome are increased in patients with psoriasis relative to the general public [2–6], the relationship between psoriasis severity and each cardiometabolic factor specifically was seldom studied [7].

The US prevalence of psoriasis has increased [8]; 2009–10 estimates put the prevalence among adults at about 3.2% [9, 10]. Among patients with psoriasis, about a quarter were severe cases, defined as > 10% body surface area involvement [11], and 10–15% were treated with biologics [12, 13]. In a claims-based study, the most prevalent cardiometabolic comorbidities among patients with psoriasis were hyperlipidemia, hypertension, diabetes mellitus, and obesity [12]. However, most published studies used medical codes rather than laboratory values to identify comorbidities. A UK study demonstrated a dose-dependent relationship between psoriasis severity and the metabolic syndrome (adjusted odds ratio [aOR] = 1.22 for mild, aOR = 1.56 for moderate, and aOR = 1.98 for severe disease), using body mass index (BMI) [> 30 kg/m^2] to measure obesity [7]. A meta-analysis observed a positive association between psoriasis and obesity by BMI (odds ratio [OR] = 1.73) and by abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women, OR = 1.76) [5]. Another meta-analysis reported a dose–response relationship of obesity comparing patients with mild and severe psoriasis with non-psoriasis controls (OR = 1.46 in mild cases and OR = 2.23 in severe cases) [14]. However, the only US-based study included in both analyses was a hospital-based study in 2002 [15], and the high prevalence of obesity in the USA would suggest the need for additional studies. Although the association of obesity and psoriasis was confirmed in two US nationally representative datasets [16], the relationship of disease severity and obesity was not evaluated.

In the most recent, large-scale US prevalence study of psoriasis and metabolic syndrome from the National Health and Nutrition Examination Survey (NHANES; 2003–6), psoriasis was positively associated with the metabolic syndrome (aOR = 1.96) [17]. According to the joint American Academy of Dermatology-National Psoriasis Foundation guideline of caring for patients with psoriasis with comorbidities, dermatologists should be more active with regard to referring patients to other healthcare providers, such as intern medicine specialists or dietitians, to improve patients' health and prevent future comorbidities and mortality [18]. There is a need for an updated understanding of the associations of each cardiometabolic parameter and psoriasis severity using nationally representative data.

In this study, we used data from the National Ambulatory Medical Care Survey (NAMCS) to assess the burden of psoriasis in the USA and the association of psoriasis severity with individual cardiometabolic parameters, including BMI, systolic and diastolic blood pressure (SBP/DBP), mean arterial pressure, fasting sugar level, glycohemoglobin (HbA1c), total cholesterol level, triglyceride (TG) level, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Although it had been reported that cardiometabolic comorbidities are prevalent among the psoriasis population from studies using a large database in Europe and a meta-analysis and the severity of psoriasis was associated with a higher cardiovascular risk assessed by scoring systems from hospital-based studies [19, 20], we hypothesized that obesity and metabolic syndrome are truly nonignorable and persistent issues among patients with psoriasis in the USA and cardiometabolic factors are related to the severity of psoriasis.

2 Methods

2.1 Study Design and Population

The NAMCS has been conducted by the US National Center for Health Statistics annually since 1989. The survey is designed to provide an objective estimation of the ambulatory medical care visits to US office-based physicians. The NAMCS data were collected from physicians, increasing the accuracy and precision compared with patient-based surveys. Physicians were grouped into sampling strata according to their specialties, doctor type, practice type, and metropolitan statistical area location. Subsamples were further randomly assigned to the 52 weeks in the specific year, e.g., each physician was randomly assigned a specific week to report a sample of their cases. Physicians were suggested to keep a daily patient list during the assigned reporting week. Visits were selected from the list by using a random start and a predetermined sampling interval, to obtain a systematic random sample of visits. The sampling procedures were designed based on the physician's estimated visits and the number of working days for the week, therefore approximately 30 records would be completed during the assigned reporting week. We conducted a cross-sectional study of NAMCS data from 1 January, 2007 through 31 December, 2016 (dataset available from CDC: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/dataset_documentation/namcs/stata). There were 508,000 unweighted observations (visits collected during the study period) representing an estimated 977 million visits per year.

2.2 Ascertainment of Psoriasis and Severity of Psoriasis

Psoriasis and treatment were defined by diagnostic codes (Table 1 of the Electronic Supplementary Material [ESM]). The control group reflects the population who had used outpatient healthcare services in the USA and did not have a psoriasis diagnosis at that specific visit. The control group may have had other chronic diseases. Our aim in this paper focused on cardiometabolic factors in psoriasis, therefore we did not perform a subgroup analysis by diagnosis. Medications in NAMCS were classified by the Multum Lexicon Plus system [21]. Systemic treatments for psoriasis were categorized into (1) phototherapy; (2) older systemic therapies, including methotrexate, cyclosporine, and acitretin; and (3) biologics, including adalimumab, etanercept, infliximab, ustekinumab, and secukinumab. We used therapy modalities as a proxy to define the severity of the disease as previously described [22]: patients with a diagnosis of psoriasis were categorized as severe cases if they were prescribed at least one systemic therapy; otherwise they were considered to have mild disease.

2.3 Biomarkers of Cardiometabolic Disorders

We analyzed demographic factors and cardiometabolic parameters, including BMI, SBP, DBP, mean arterial pressure, fasting sugar level, HbA1c, total cholesterol level, TG, LDL-C, and HDL-C. Body mass index categories were based on World Health Organization criteria: (1) underweight, BMI < 18.5 kg/m^2; (2) normal, 18.5 kg/m^2 $\leq$ BMI < 25 kg/m^2; (3) overweight, 25 kg/m^2 $\leq$ BMI < 30 kg/m^2; (4) obese class I, 30 kg/m^2 $\leq$ BMI < 35 kg/m^2; (5) obese class II, 35 kg/m^2 $\leq$ BMI < 40 kg/m^2; (6) obese class III, BMI ≥ 40 kg/m^2. Because NAMCS lacks information on waist circumference, we used criteria modified from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guideline as a proxy of the metabolic syndrome, assuming people who meet two or more of the following conditions have metabolic syndrome: (1) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg; (2) TG ≥ 150 mg/dL; (3) HDL-C < 40 mg/dL in male subjects or HDL-C < 50 mg/dL in female subjects; or (4) fasting glucose level ≥ 100 mg/dL.

2.4 Statistical Analysis

To obtain a representative national estimate, we weighted the sampled visit by the inverse of the selection probabilities, which also accounted for survey nonresponse, geographic region, and metropolitan statistical area location. Sampling errors were determined using STATA (Version 15.0).

To compare demographic distributions, Chi-square tests were used for categorical variables and *t* tests were used for continuous variables. We used logistic regression models to estimate the association between psoriasis and cardiometabolic factors, adjusting for potential confounders, such as sex, age, region of residency, race/ethnicity, and smoking, to obtain ORs and their corresponding 95% confidence intervals. The decision on variables for adjustment was based on the literature [1, 3, 7]. Sex, age, region of residency, race/ethnicity, and smoking were the covariates included in the final model for the logistic regression analysis of metabolic syndrome and BMI. For each element of metabolic syndrome, estimates were adjusted for sex, age, BMI, and all other parameters in the metabolic syndrome, to independently determine the effect of each parameter on disease severity, according to the methods described in the literature [7]. For SBP, DPB, HbA1c, total cholesterol, and LDL-C, adjustments were on sex and age. Because of potential biases caused by missing data, we used multiple imputation for missing values, assuming that missing is at random [23]. The number of imputed datasets created in the multiple imputation model was five, with BMI, SBP, DBP, total cholesterol level, LDL-C, HDL-C, TG, HbA1C, fasting sugar level, and tobacco use included in the analyses. The summary of the imputed dataset was shown in Table 2 of the ESM. For imputed data analyses, effect estimates for all cardiometabolic parameters were adjusted for sex, age, region of residency, race/ethnicity, and smoking, while factors under the umbrella of metabolic syndrome, including SBP/DBP, TG, HDL-C, and fasting sugar level, were also adjusted for BMI and all other cardiometabolic parameters within the criteria of metabolic syndrome.

3 Results

There were an estimated 3.3 million office visits with the diagnosis of psoriasis annually. The mean age of patients with psoriasis was 50 years, with a female-to-male ratio of nearly 1:1 (Table 1). Compared to non-psoriatic controls, a higher proportion of patients with psoriasis was middle-aged (40.8% vs 29.7%, $p < 0.0001$), non-Hispanic White (79.9% vs 70.8%, $p < 0.0001$), and living in the Midwest (27.2% vs 19.7%, $p = 0.001$). Body mass index was higher in psoriasis patients across the 10 years of observation (Fig. 1 of the ESM), with differences in the 10-year-average (29.9 kg/m^2 vs 27.7 kg/m^2). Metabolic syndrome was more common in psoriasis visits than in non-psoriasis visits (8.5% vs 6.2%). Although not statistically significant, we observed trends toward greater total cholesterol, LDL-C, and TG levels among patients with psoriasis compared with patients without psoriasis (Fig. 2 of the ESM).

Approximately 762,000 visits by patients with psoriasis (23%) were by patients with severe psoriasis. Among them, biologics were the most frequently (56%) used treatments

Table 1 Demographic distribution of samples from the National Ambulatory Medical Care Survey, 2007–2016

	Psoriasis (*n*/year = 3,270,590; SE = 194,657)	Without psoriasis (*n*/year = 973,914,383; SE = 22,331,823)	Overall (*n*/year = 977,184,973)
Sex, *n*/year (%)			
Female	1,651,537 (50.5)	569,386,069 (58.5)	571,037,605 (58.4)
Male	1,619,053 (49.5)	404,528,314 (41.5)	406,147,368 (41.6)
Age, years			
Mean (SE)	50.2 (0.90)	45.9 (0.24)	45.9 (0.23)
Age groups, years, *n*/year (%)			
Under 15	176,185 (5.4)	153,512,588 (15.8)	153,688,774 (15.7)
15–24	204,956 (6.3)	74,627,041 (7.7)	74,831,997 (7.7)
25–44	746,248 (22.8)	192,581,949 (19.8)	193,328,196 (19.8)
45–64	1,334,920 (40.8)	289,320,834 (29.7)	290,655,754 (29.8)
65–74	475,351 (14.5)	136,462,447 (14.0)	136,937,798 (14.0)
75 and over	332,930 (10.2)	127,409,523 (13.1)	127,742,453 (13.1)
Race/ethnicity, *n*/year (%)			
Non-Hispanic White	2,612,647 (79.9)	689,790,438 (70.8)	692,403,085 (70.9)
Non-Hispanic Black	236,213 (7.2)	102,322,487 (10.5)	102,558,700 (10.5)
Hispanic	327,068 (10.0)	129,807,794 (13.3)	130,134,862 (13.3)
Non-Hispanic other[a]	94,662 (2.9)	51,993,664 (5.3)	52,088,326 (5.3)
Geographic regions, *n*/year (%)[b]			
Northeast	581,247 (17.8)	191,250,705 (19.6)	191,831,952 (19.6)
Midwest	888,170 (27.2)	191,951,128 (19.7)	192,839,298 (19.7)
South	1,104,383 (33.8)	367,474,501 (37.7)	368,578,884 (37.7)
West	696,791 (21.3)	223,238,048 (22.9)	223,934,839 (22.9)
Height, cm			
Mean (SE)	168.4 (1.04)	158.4 (0.25)	158.4 (0.25)
Weight, kg			
Mean (SE)	84.5 (1.94)	71.8 (0.26)	71.9 (0.26)
BMI, kg/m^2			
Mean (SE)	29.9 (0.65)	27.7 (0.06)	27.7 (0.06)
BMI category, *n*/year (%)[c]			
Underweight	36,995 (3.3)	44,474,537 (9.1)	44,511,532 (9.1)
Normal range	261,970 (23.1)	136,307,571 (28.0)	136,569,541 (28.0)
Overweight	330,843 (29.2)	143,499,458 (29.5)	143,830,301 (29.5)
Obese class I	202,674 (17.9)	88,563,782 (18.2)	88,766,456 (18.2)
Obese class II	175,543 (15.5)	41,771,662 (8.6)	41,947,205 (8.6)
Obese class III	123,981 (11.0)	32,518,639 (6.7)	32,642,620 (7.7)
SBP			
Mean, mmHg (SE)	127 (1.0)	124 (0.1)	124 (0.1)
SBP ≥ 120 mmHg, *n*/year (%)	1,032,332 (73.2)	385,553,010 (62.2)	386,585,342 (62.2)
DBP			
Mean, mmHg (SE)	77 (0.6)	75 (0.1)	75 (0.1)
DBP ≥ 80 mmHg, *n*/year (%)	680,711 (48.3)	227,296,532 (36.7)	227,977,242 (36.7)
MAP			
Mean, mmHg (SE)	94 (0.6)	91 (0.1)	91 (0.1)
MAP ≥ 100 mmHg, *n*/year (%)	368,698 (26.2)	134,915,452 (21.8)	135,284,150 (21.8)
Fasting sugar level			
Mean, mg/dL (SE)	111 (5.5)	111 (0.5)	111 (0.5)
≥ 100 mg/dL, *n*/year (%)	110,699 (51.4)	34,491,121 (46.1)	34,601,819 (46.1)

Table 1 (continued)

	Psoriasis (*n*/year = 3,270,590; SE = 194,657)	Without psoriasis (*n*/year = 973,914,383; SE = 22,331,823)	Overall (*n*/year = 977,184,973)
HbA1c			
Mean, % (SE)	6.6 (0.31)	6.5 (0.05)	6.6 (0.05)
HbA1c ≥ 6.5%, *n*/year (%)	37,049 (44.1)	11,965,810 (37.5)	12,002,859 (37.5)
Total cholesterol			
Mean, mg/dL (SE)	196 (7.9)	181 (0.5)	181 (0.5)
≥ 200 mg/dL, *n*/year (%)	95,166 (42.6)	24,116,790 (30.3)	24,211,956 (30.4)
LDL-C			
Mean, mg/dL (SE)	112 (7.8)	103 (0.4)	103 (0.4)
LDL-C ≥ 70 mg/dL, *n*/year (%)	173,570 (85.6)	64,040,397 (83.5)	64,213,967 (83.5)
HDL-C			
Mean, mg/dL (SE)	48 (2.7)	53 (0.2)	53 (0.2)
Female subjects < 50 mg/dL, *n*/year (%)	43,131 (45.2)	16,141,664 (37.3)	16,184,795 (37.3)
Male subjects < 40 mg/dL, *n*/year (%)	44,813 (37.1)	11,276,284 (32.7)	11,321,097 (32.7)
TG			
Mean, mg/dL (SE)	165 (17.4)	138 (0.9)	138 (0.9)
TG ≥ 150 mg/dL, *n*/year (%)	89,880 (40.9)	24,596,727 (31.9)	24,686,607 (31.9)
Metabolic syndrome proxy, *n*/year (%)[d]			
Yes	121,932 (8.5)	38,473,802 (6.2)	38,595,735 (6.2)
No	1,314,498 (91.5)	587,136,651 (93.9)	588,451,150 (93.8)
Alcohol dependence, *n*/year (%)			
Yes	6,989 (0.7)	2,273,606 (0.8)	2,280,596 (0.8)
No	973,906 (99.3)	278,522,376 (99.2)	279,496,282 (99.2)
Tobacco use, *n*/year (%)			
Current	443,026 (20.6)	91,456,912 (12.7)	91,899,938 (12.4)
Never or not current	1,710,360 (79.4)	626,214,822 (87.3)	627,925,182 (87.2)
Past medical history, *n*/year (%)			
Diabetes mellitus	309,397 (9.5)	117,960,629 (12.1)	118,270,027 (12.1)
Hypertension	762,591 (23.3)	267,766,591 (27.5)	268,529,182 (27.5)
Hyperlipidemia	408,962 (12.5)	165,460,521 (17.0)	165,869,483 (17.0)
Obesity	227,099 (6.9)	71,737,546 (7.4)	71,964,645 (7.4)
CAD, IHD, or MI	111,511 (3.4)	45,504,275 (4.7)	45,615,786 (4.7)

BMI body mass index, *CAD* coronary artery disease, *DBP* diastolic blood pressure, *HbA1c* hemoglobin A1c, *HDL-C* high-density lipoprotein-cholesterol, *IHD* ischemic heart disease, *LDL-C* low-density lipoprotein-cholesterol, *MAP* mean arterial pressure, *MI* myocardial infarction, *SBP* systolic blood pressure, *SE* standard error, *TG* triglyceride

[a]Non-Hispanic other includes Asian, multiple races, and native Hawaiian/other Pacific Islander

[b]Geographic regions: (1) Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont; (2) Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin; (3) South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia; (4) West: Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming, Alaska, Hawaii

[c]BMI category: (1) underweight, BMI < 18.5 kg/m^2; (2) normal range, 18.5 kg/m^2 ≤ BMI < 25 kg/m^2; (3) overweight, 25 kg/m^2 ≤ BMI < 30 kg/m^2; (4) obese class I, 30 kg/m^2 ≤ BMI < 35 kg/m^2; (5) obese class II, 35 kg/m^2 ≤ BMI < 40 kg/m^2; (6) obese class III, BMI ≥ 40 kg/m^2

[d]Metabolic syndrome proxy: two or more conditions in (1) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, (2) TG ≥ 150 mg/dL, (3) HDL-C < 40 mg/dL in male subjects, or HDL-C < 50 mg/dL in female subjects, or (4) fasting glucose level ≥ 100 mg/dL

(Table 3 of the ESM). Demographic factors, such as the estimated mean age and the distribution of sex and race, were not different between severe and mild cases (Table 2). There were more people who received healthcare for severe psoriasis living in the Midwest (36% vs 24%). Compared with mild case groups, severe case groups tended to have a higher proportion of patients who were middle-aged (53% vs 37%), overweight and obese (77% vs 73%), with higher

Table 2 Demographic distribution of psoriatic samples from the National Ambulatory Medical Care Survey, 2007–2016

	Mild cases (*n*/year = 2,508,091; SE = 160,383)	Severe cases (*n*/year = 762,499; SE = 70,827)	*P*-value
Sex, *n*/year (%)			0.2
Female	1,300,222 (51.8)	351,315 (46.1)	
Male	1,207,869 (48.2)	411,184 (53.9)	
Age, years			
Mean (SE)	49.9 (1.12)	51.5 (1.09)	0.3
Age groups, years, *n*/year (%)			0.0001*
Under 15	168,213 (6.7)	176,185 (1.1)	<0.0001*
15–24	182,349 (7.3)	204,956 (3.0)	0.009
25–44	558,120 (22.3)	746,248 (24.7)	0.5
45–64	932,878 (37.2)	1,334,920 (52.7)	<0.0001*
65–74	377,790 (15.1)	475,351 (12.8)	0.5
75 and over	288,741 (11.5)	332,930 (5.8)	0.067
Race/ethnicity, *n*/year (%)			0.8
Non-Hispanic White	1,992,238 (79.4)	620,409 (81.4)	0.6
Non-Hispanic Black	190,012 (7.6)	46,201 (6.1)	0.5
Hispanic	248,334 (9.9)	78,734 (10.3)	0.9
Non-Hispanic other[a]	77,507 (3.1)	17,155 (2.3)	0.4
Geographic regions, *n*/year (%)[b]			0.012*
Northeast	474,954 (18.9)	106,293 (13.9)	0.1
Midwest	611,075 (24.4)	277,094 (36.3)	0.007*
South	896,097 (35.7)	208,285 (27.3)	0.052
West	525,964 (21.0)	170,826 (22.4)	0.7
Height, cm			
Mean (SE)	167.8 (1.23)	170.9 (1.36)	0.077
Weight, kg			
Mean (SE)	83.1 (2.40)	89.9 (2.62)	0.060
BMI, kg/m^2			
Mean (SE)	30.0 (0.06)	29.5 (0.65)	0.7
BMI category, *n*/year (%)[c]			0.3
Underweight	35,140 (3.9)	1856 (0.8)	0.051
Normal range	211,325 (23.3)	50,645 (22.5)	0.9
Overweight	261,632 (28.8)	69,211 (30.8)	0.8
Obese class I	140,584 (15.5)	62,090 (27.6)	0.073
Obese class II	149,146 (16.4)	26,397 (11.8)	0.6
Obese class III	109,510 (12.1)	14,471 (6.4)	0.2
SBP			
Mean, mmHg (SE)	126 (1.2)	128 (1.7)	0.3
SBP ≥ 130 mmHg, *n*/year (%)	425,696 (38.5)	141,392 (46.3)	0.3
DBP			
Mean, mmHg (SE)	76 (0.8)	80 (1.0)	0.012*
DBP ≥ 85 mmHg, *n*/year (%)	189,908 (17.2)	75,741 (24.9)	0.2
MAP			
Mean, mmHg (SE)	93 (0.8)	96 (1.1)	0.045*
MAP ≥ 100 mmHg, *n*/year (%)	263,824 (23.9)	104,874 (34.5)	0.1
Fasting sugar level			
Mean, mg/dL (SE)	105 (4.7)	132 (13.9)	0.060
≥ 100 mg/dL, *n*/year (%)	74,932 (45.1)	35,767 (72.6)	0.1
HbA1c			

Table 2 (continued)

	Mild cases (*n*/year = 2,508,091; SE = 160,383)	Severe cases (*n*/year = 762,499; SE = 70,827)	*P*-value
Mean, % (SE)	6.8 (0.38)	6.1 (0.30)	0.1
HbA1c ≥ 6.5%, *n*/year (%)	32,254 (53.3)	4794 (20.4)	0.1
Total cholesterol			
Mean, mg/dL (SE)	203 (7.0)	155 (22.4)	0.043*
≥ 200 mg/dL, *n*/year (%)	86,506 (45.7)	8660 (25.4)	0.3
LDL-C			
Mean, mg/dL (SE)	117 (8.0)	86 (18.0)	0.1
LDL-C ≥ 100 mg/dL, *n*/year (%)	102,340 (59.3)	5732 (19.0)	0.028*
HDL-C			
Mean, mg/dL (SE)	49 (2.8)	42 (5.6)	0.2
Female < 50 mg/dL, *n*/year (%)	36,077 (43.0)	7054 (62.0)	0.4
Male < 40 mg/dL, *n*/year (%)	32,783 (32.1)	12,030 (64.3)	0.3
TG			
Mean, mg/dL (SE)	172 (19.5)	124 (24.6)	0.1
TG ≥ 150 mg/dL, *n*/year (%)	85,241 (45.6)	4640 (14.0)	0.029*
Metabolic syndrome proxy, *n*/year (%)[d]			0.3
Yes	104,947 (9.4)	16,985 (5.4)	
No	1,014,703 (90.6)	299,795 (94.6)	
Alcohol dependence, *n*/year (%)			0.3
Yes	6426 (0.8)	563 (0.3)	
No	752,071 (99.2)	221,836 (99.7)	
Tobacco use, *n*/year (%)			0.2
Current	314,648 (19.3)	128,378 (24.5)	
Never or not current	1,315,292 (80.7)	395,068 (75.5)	
Past medical history, *n*/year (%)			
Diabetes mellitus	213,661 (8.5)	95,737 (12.6)	0.1
Hypertension	556,494 (22.2)	206,097 (27.0)	0.2
Hyperlipidemia	338,999 (13.5)	69,963 (9.2)	0.1
Obesity	164,629 (6.6)	62,470 (8.2)	0.5
CAD, IHD, or MI	105,649 (4.2)	5862 (0.8)	0.015*

BMI body mass index, *CAD* coronary artery disease, *DBP* diastolic blood pressure, *HbA1c* hemoglobin A1c, *HDL-C* high-density lipoprotein-cholesterol, *IHD* ischemic heart disease, *LDL-C* low-density lipoprotein-cholesterol, *MAP* mean arterial pressure, *MI* myocardial infarction, *SBP* systolic blood pressure, *SE* standard error, *TG* triglyceride, *$p < 0.05$, statistically significant

[a]Non-Hispanic other includes Asian, multiple races, and native Hawaiian/other Pacific Islander

[b]Geographic regions: (1) Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont; (2) Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin; (3) South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia; (4) West: Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming, Alaska, Hawaii

[c]BMI category: (1) underweight, BMI < 18.5 kg/m^2; (2) normal range, 18.5 kg/m^2 ≤ BMI < 25 kg/m^2; (3) overweight, 25 kg/m^2 ≤ BMI < 30 kg/m^2; (4) obese class I, 30 kg/m^2 ≤ BMI < 35 kg/m^2; (5) obese class II, 35 kg/m^2 ≤ BMI < 40 kg/m^2; (6) obese class III, BMI ≥ 40 kg/m^2

[d]Metabolic syndrome proxy: two or more conditions in (1) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, (2) TG ≥ 150 mg/dL, (3) HDL-C < 40 mg/dL in male subjects, or HDL-C < 50 mg/dL in female subjects, or (4) fasting glucose level ≥ 100 mg/dL

DBP, mean arterial pressure, and fasting sugar levels, but lower point estimates of HbA1c and lipid profiles.

In crude estimates for non-psoriasis as the controls, both severe cases and mild cases were more often overweight or obese (Table 3). A correlation was observed for obesity severity and psoriasis in mild cases but not in severe cases. However, after controlling for possible confounders, the adjusted OR was close to the null, with increases only seen in obese class III in the mild group vs non-psoriasis controls (aOR = 2.38). When we dichotomized BMI at a cut-off point

Table 3 cOR and aOR from logistic regression models comparing mild cases and severe cases to non-psoriatic controls, samples from the National Ambulatory Medical Care Survey, 2007–16

	Mild		Severe		Mild		Severe	
	cOR (95% CI)	*P*-value	cOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Metabolic syndrome proxy[b]	1.58 (1.02–2.44)	0.041*	0.86 (0.29–2.61)	0.8	1.96 (1.25–3.07)	0.003*	0.45 (0.15–1.32)	0.1
SBP ≥ 130 mmHg or DBP ≥ 85 mmHg	1.08 (0.75–1.54)	0.7	1.44 (0.89–2.32)	0.1	0.51 (0.23–1.12)	0.1	0.93 (0.08–10.87)	1.0
Fasting sugar level ≥ 100 mg/dL	0.96 (0.48–1.92)	0.9	3.11 (0.77–12.58)	0.1	1.60 (0.66–3.88)	0.3	0.91 (0.08–10.97)	0.9
HDL-C, female subjects < 50 mg/dL or male subjects < 40 mg/dL	1.08 (0.56–2.07)	0.8	3.19 (0.62–16.40)	0.2	0.51 (0.19–1.38)	0.2	1.41 (0.12–16.56)	0.8
TG ≥ 150 mg/dL	1.79 (0.94–3.41)	0.077	0.35 (0.08–1.51)	0.2	1.20 (0.51–2.82)	0.7	0.16 (0.03–1.05)	0.06
BMI category[a]								
Underweight or normal range	Ref		Ref		Ref		Ref	
Overweight	1.34 (0.90–2.00)	0.2	1.66 (0.72–3.84)	0.2	1.13 (0.72–1.77)	0.6	1.36 (0.54–3.44)	0.5
Obese class I	1.16 (0.75–1.82)	0.5	2.41 (1.00–5.80)	0.049*	1.10 (0.67–1.79)	0.7	1.89 (0.74–4.83)	0.2
Obese class II	2.62 (1.02–6.70)	0.045*	2.18 (0.73–6.44)	0.2	1.50 (0.81–2.77)	0.2	1.41 (0.45–4.39)	0.6
Obese class III	2.47 (1.43–4.26)	0.001*	1.53 (0.50–4.67)	0.6	2.38 (1.32–4.29)	0.004*	1.41 (0.40–5.96)	0.6
BMI > 30 kg/m^2	1.56 (1.03–2.39)	0.038*	1.68 (1.03–2.76)	0.039*	1.37 (0.98–1.91)	0.063	1.42 (0.80–2.52)	0.2
SBP ≥ 130 mmHg	1.06 (0.75–1.50)	0.7	1.46 (0.89–2.38)	0.1	1.02 (0.65–1.60)	0.9	1.39 (0.82–2.37)	0.2
DBP ≥ 85 mmHg	1.12 (0.76–1.63)	0.6	1.78 (1.04–3.05)	0.035*	1.06 (0.72–1.58)	0.8	1.70 (0.99–2.91)	0.05
Fasting sugar level ≥ 100 mg/dL	0.96 (0.48–1.92)	0.9	3.11 (0.77–12.58)	0.1	1.06 (0.54–2.08)	0.9	2.93 (0.70–12.2)	0.1
HDL-C, female subjects < 50 mg/dL or male subjects < 40 mg/dL	1.08 (0.56–2.07)	0.8	3.19 (0.62–16.40)	0.2	1.07 (0.55–2.08)	0.8	3.25 (0.62–17.11)	0.2
TG ≥ 150 mg/dL	1.79 (0.94–3.41)	0.077	0.35 (0.08–1.51)	0.2	1.82 (0.96–3.43)	0.066	0.34 (0.07–1.57)	0.2
HbA1c ≥ 6.5%	1.91 (0.78–4.65)	0.2	0.43 (0.06–2.95)	0.4	2.09 (0.86–5.09)	0.1	0.44 (0.06–3.13)	0.4
Total cholesterol ≥ 200 mg/dL	1.94 (1.00–3.74)	0.05*	0.78 (0.18–3.37)	0.7	2.07 (1.05–4.09)	0.036*	0.86 (0.21–3.52)	0.8
LDL-C ≥ 100 mg/dL	1.43 (0.70–2.94)	0.3	0.23 (0.05–1.18)	0.08	1.36 (0.65–2.85)	0.4	0.22 (0.04–1.12)	0.07

aOR adjusted odds ratio, *BMI* body mass index, *CI* confidence interval, *DBP* diastolic blood pressure, *HbA1c* hemoglobin A1c, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein-cholesterol, *Ref* reference, *SBP* systolic blood pressure, *TG* triglyceride, *$p < 0.05$, statistically significant

Logistic regression models: (1) metabolic syndrome proxy and BMI category, controlling for sex, age, race/ethnicity, geographic regions, and tobacco use; (2) parameters under metabolic syndrome, controlling for sex, age, BMI, and all other parameters within metabolic syndrome; (3) all cardiometabolic parameters except for metabolic syndrome proxy and BMI categories, controlling for sex and age

[a]BMI category: (1) underweight, BMI < 18.5 kg/m^2; (2) normal range, 18.5 kg/m^2 ≤ BMI < 25 kg/m^2; (3) overweight, 25 kg/m^2 ≤ BMI < 30 kg/m^2; (4) obese class I, 30 kg/m^2 ≤ BMI < 35 kg/m^2; (5) obese class II, 35 kg/m^2 ≤ BMI < 40 kg/m^2; (6) obese class III, BMI ≥ 40 kg/m^2

[b]Metabolic syndrome proxy: two or more conditions in (1) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, (2) TG ≥ 150 mg/dL, (3) HDL-C < 40 mg/dL in male subjects, or HDL-C < 50 mg/dL in female subjects, or (4) fasting glucose level ≥ 100 mg/dL

of 30 kg/m^2 consistent with other studies to define obesity, there was only a weak trend for disease severity and obesity. We observed a positive association between the metabolic syndrome, defined as meeting two or more conditions of the NCEP ATP III guideline in this study, and mild psoriasis (aOR = 1.96). Because the effect estimates of metabolic syndrome were 1.58 (cOR) and 1.96 (aOR) for mild disease and 0.86 (cOR) and 0.45 (aOR) for severe disease, the direction of bias was toward the null. Among factors within the metabolic syndrome, there was no single cardiometabolic factor independently associated with disease severity in adjusted analyses.

The results from the multiple imputation suggested a dose-dependent relationship between obesity and psoriasis

severity. Compared with non-psoriasis controls, both severe case groups and mild case groups had higher proportions of the metabolic syndrome. When controlling for potential confounders and all other parameters within metabolic syndrome, TG was independently related to mild psoriasis, but not severe psoriasis. Albeit not significant, DBP, fasting glucose, HDL-C, total cholesterol, and LDL-C seem to be positively related to psoriasis severity (Table 4).

4 Discussion

In this large national representative sample of US adults, we found that obesity and metabolic syndrome are critical issues in the general population and more serious among patients with psoriasis. Although NAMCS data cannot directly estimate psoriasis prevalence, these surveys, conducted across 10 years, provide updated statistics of comorbid conditions across severity subgroups among all patients with psoriasis.

Table 4 Samples with multiple imputation

	Mild		Severe		Mild		Severe	
	cOR (95% CI)	*P*-value	cOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Metabolic syndrome proxy[b]	1.53 (1.04–2.24)	0.032*	1.54 (0.99–2.37)	0.053	1.51 (1.02–2.23)	0.039*	1.52 (0.99–2.34)	0.054
SBP ≥ 130 mmHg or DBP ≥ 85 mmHg	1.29 (1.01–1.64)	0.042*	1.27 (0.79–2.06)	0.3	1.03 (0.75–1.40)	0.9	0.98 (0.57–1.68)	0.9
Fasting sugar level ≥ 100 mg/dL	1.14 (0.84–1.55)	0.4	1.25 (0.87–1.81)	0.2	0.94 (0.70–1.27)	0.7	1.07 (0.73–1.57)	0.7
HDL-C, female subjects < 50 mg/dL or male subjects < 40 mg/dL	1.30 (0.95–1.78)	0.09	1.33 (0.57–3.13)	0.4	1.08 (0.74–1.56)	0.7	1.25 (0.45–3.45)	0.6
TG ≥ 150 mg/dL	1.69 (1.14–2.51)	0.013*	1.56 (0.89–2.73)	0.1	1.54 (1.02–2.31)	0.039*	1.40 (0.70–2.80)	0.3
BMI category[a]								
Underweight or normal range	Ref		Ref		Ref		Ref	
Overweight	1.30 (0.83–2.02)	0.2	1.38 (0.89–2.15)	0.2	1.21 (0.76–1.92)	0.4	1.22 (0.76–1.94)	0.4
Obese class I	1.35 (0.93–1.95)	0.1	1.79 (0.88–3.65)	0.1	1.24 (0.84–1.84)	0.3	1.56 (0.74–3.27)	0.2
Obese class II	2.29 (1.25–4.18)	0.01*	2.29 (1.20–4.38)	0.014*	2.10 (0.13–3.91)	0.023*	1.98 (1.01–3.89)	0.046*
Obese class III	2.38 (1.46–3.89)	0.002*	2.13 (1.14–3.98)	0.018*	2.21 (1.31–3.72)	0.006*	1.87 (0.98–3.58)	0.059
BMI > 30 kg/m^2	1.59 (1.17–2.17)	0.006*	1.72 (1.11–2.66)	0.019*	1.50 (1.10–2.06)	0.015*	1.57 (1.00–2.48)	0.05
SBP ≥ 130 mmHg	1.24 (0.96–1.60)	0.1	1.28 (0.83–1.96)	0.2	1.10 (0.81–1.49)	0.5	1.09 (0.67–1.75)	0.7
DBP ≥ 85 mmHg	1.33 (1.00–1.77)	0.047*	1.50 (0.89-2.52)	0.1	1.26 (0.95-1.69)	0.1	1.41 (0.83-2.37)	0.2
Fasting sugar level ≥ 100 mg/dL	1.14 (0.84–1.55)	0.4	1.25 (0.87–1.81)	0.2	1.13 (0.83–1.54)	0.4	1.24 (0.86–1.79)	0.3
HDL-C, female subjects < 50 mg/dL or male subjects < 40 mg/dL	1.30 (0.95–1.78)	0.09	1.33 (0.57–3.13)	0.4	1.43 (1.02–1.99)	0.037*	1.56 (0.62–3.96)	0.3
TG ≥ 150 mg/dL	1.69 (1.14–2.51)	0.013*	1.56 (0.89–2.73)	0.1	1.75 (1.18–2.60)	0.01*	1.63 (0.93–2.84)	0.08
HbA1c ≥ 6.5%	0.90 (0.67–1.23)	0.5	0.90 (0.65–1.24)	0.5	0.91 (0.67–1.24)	0.5	0.91 (0.66–1.26)	0.6
Total cholesterol ≥ 200 mg/dL	1.27 (0.98–1.91)	0.06	1.43 (0.86–2.37)	0.1	1.42 (1.01–1.99)	0.044*	1.51 (0.91–2.51)	0.1
LDL-C ≥ 100 mg/dL	1.15 (0.86–1.56)	0.3	1.19 (0.74–1.92)	0.4	1.19 (0.88–1.62)	0.2	1.25 (0.78–2.01)	0.3

cOR and aOR from logistic regression models comparing mild cases and severe cases to non-psoriatic controls, the National Ambulatory Medical Care Survey, 2007–2016

aOR adjusted odds ratio, *BMI* body mass index, *CI* confidence interval, *DBP* diastolic blood pressure, *HbA1c* hemoglobin A1c, *HDL-C* high-density lipoprotein-cholesterol, *LDL-C* low-density lipoprotein cholesterol, *Ref* reference, *SBP* systolic blood pressure, *TG* triglyceride, *p < 0.05, statistically significant

Logistic regression models: (1) all cardiometabolic parameters, controlling for sex, age, race/ethnicity, geographic regions, and tobacco use; (2) parameters under metabolic syndrome, controlling for sex, age, race/ethnicity, geographic regions, BMI, and all other variables within metabolic syndrome

[a]BMI category: (1) underweight, BMI < 18.5 kg/m^2; (2) normal range, 18.5 kg/m^2 ≤ BMI < 25 kg/m^2; (3) overweight, 25 kg/m^2 ≤ BMI < 30 kg/m^2; (4) obese class I, 30 kg/m^2 ≤ BMI < 35 kg/m^2; (5) obese class II, 35 kg/m^2 ≤ BMI < 40 kg/m^2; (6) obese class III, BMI ≥ 40 kg/m^2

[b]Metabolic syndrome proxy: two or more conditions in (1) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, (2) TG ≥ 150 mg/dL, (3) HDL-C < 40 mg/dL in male subjects, or HDL-C < 50 mg/dL in female subjects, or (4) fasting glucose level ≥ 100 mg/dL

The distribution of demographic factors and BMI among our patients with psoriasis were compatible with the recent National Psoriasis Foundation report [11], suggesting the representativeness of our estimates.

According to NHANES (2003–6), the average BMI was 30.3 kg/m^2 in patients with psoriasis and 28.1 kg/m^2 in patients without psoriasis [17], which were close to our estimates. Obesity is prevalent among US patients with psoriasis—from 14.2% in claim-based data, with obesity defined by diagnosis, [12] to 62.9% in NHANES, with obesity defined by abdominal obesity, [17]—with a greater prevalence than seen among all US adults (29.5%) [15–17, 24]. Genetic studies suggest a possible causal relationship of higher BMI and a higher risk of psoriasis [25]. Obesity should be addressed in psoriasis practice as well as for the general US population.

We summarized the results from related articles in the literature, including systemic reviews and meta-analyses, studies from NHANES, and large population-based studies from the UK (THIN, the Health Improvement Network; GPRD, General Practice Research Database). The comparisons between our observations and the findings in the literature regarding (a) metabolic syndrome, (b) parameters within metabolic syndromes, and (c) other cardiometabolic factors are presented in Table 4 of the ESM [1, 5–7, 14, 17, 22, 26–30].

According to the NCEP ATP III guideline, individuals meeting three or more of the criteria were defined as having metabolic syndrome. Because of a lack of waist circumference data in NAMCS, we substituted a metabolic syndrome proxy with two or more of the NCEP ATP III criteria. The substantial missing values in our observations might lead to an underestimation in metabolic syndrome in psoriasis. The prevalence of metabolic syndrome in psoriasis was 40% from NHANES (2003–6) [17] and 25% in US adults from NHANES (1999–2006) [31]. We did observe a weakly higher proportion of metabolic syndrome among the psoriasis population than the non-psoriasis population, which was comparable to the conclusion of a recent systemic review [32]. In our study, a positive association between metabolic syndrome and psoriasis was observed in mild disease, as compared to non-psoriasis controls. However, we did not observe a similar association in the severe psoriasis group. Missing data bias could be one of the explanations, as supported by our imputed data analysis.

In analyzing each component within metabolic syndrome in NAMCS, there seemed to be a trend for a positive association between disease severity and SBP, DBP, fasting glucose level, BMI, and HDL-C, which was consistent with the analysis on past medical history (hypertension, diabetes, and obesity). Interestingly, hyperlipidemia and a history of cardiovascular diseases (coronary artery disease, ischemic heart disease, and myocardial infraction) were not positively related to disease severity. Although a recent study demonstrated that lipid criteria might be less sensitive for myocardial burden in psoriasis, the severity of psoriasis and its relationship to cardiovascular stress was not addressed [33].

Other studies have reported a positive association between diabetes and psoriasis, including evidence of a dose–response relationship [6, 29]. In our dataset, mean fasting glucose level and mean HbA1c were not different between psoriasis and non-psoriasis populations, but there was an association between prediabetes or diabetes and psoriasis severity.

The inconsistency between our findings and the results from other studies was mainly from the heterogeneity in definitions of variables, including the metabolic syndromes (World Health Organization criteria or NCEP ATP III criteria), the cardiometabolic parameters (by diagnostic codes or by laboratory results), obesity (by BMI as the substitute for abdominal obesity in NCEP ATP III criteria), disease severity (by body surface area or by medications), and the missing data bias in our study. Furthermore, study designs, uncontrolled confounders, and generalizability among the studies could also explain the discrepancy. It is possible that the past medical histories were under-reported, which only captured 7% of the psoriasis population with obesity, whereas in our analysis defining obesity by BMI criteria, about 44% of them were obese. This discrimination demonstrated the impacts of information bias.

In our analysis, smoking and alcohol abuse are more prevalent health issues in psoriasis with obesity than in non-psoriasis with obesity (28.4% and 2% vs 15.3% and < 1%, respectively). Only 6% of the psoriasis patient group with obesity received weight-reduced education. Although one can speculate that diet and lifestyle change may improve BMI and further lower the risk of cardiovascular events, recent studies suggested central obesity is a sensitive factor for cardiovascular burden [33, 34]. Carefully conducted large-scale studies are needed to estimate the true effect size of lifestyle modification on obesity and cardiovascular morbidities in psoriasis.

The cross-sectional study design limits causal inference. We identified severe cases by medication, which might not capture all severe cases but may reflect access to healthcare. Patients receiving phototherapy could have been included as severe [22]; however, the number receiving phototherapy is small. The lack of objective measurements to validate outcome classifications, such as body surface area or Psoriasis Area and Severity Index scores, may lead to misclassification, with biases possible in either direction. Although information on central obesity was missing, we assumed our proxy could capture the metabolic syndrome. This assumption was expected to have limited impact because 62.9% of

the study population was overweight or obese, and, according to the Centers for Disease Control and Prevention, abdominal obesity in the USA in 2015–2016 was 69% in female individuals and 48% in male individuals [35].

5 Conclusions

The US population is at high risk of abnormalities in cardiometabolic parameters and related cardiovascular comorbidities, and the risk is even greater in patients with psoriasis. In the USA, obesity was associated with psoriasis severity. The implementation of interdisciplinary teamwork from different specialties in caring for patients with psoriasis has been suggested and may benefit the psoriasis population [18]. Further interventional studies for a healthy lifestyle or weight control are needed to confirm the effects on psoriasis severity.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40257-021-00600-z.

Declarations

Funding This project is a part of I-Chun Lin's field study. I-Chun Lin received a summer research fellowship from the Department of Epidemiology at the University of California, Los Angeles.

Conflicts of Interest/Competing Interests Steven R. Feldman has received research, speaking, and/or consulting support from Galderma, Amgen, Almirall, Alvotech, Leo Pharma, BMS, Boehringer Ingelheim, Mylan, Celgene, Pfizer, Ortho Dermatology, Abbvie, Samsung, Janssen, Lilly, Menlo, Merck, Novartis, Regeneron, Sanofi, Novan, Qurient, National Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate, and National Psoriasis Foundation. I-Chun Lin, Julia Heck, and Liwei Chen have no conflicts of interest that are directly relevant to the content of this article.

Ethics approval The NAMCS dataset is publicly available and contains de-identified data, therefore no institutional review board approval is required.

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and material The NAMCS dataset is available from the Centers for Disease Control and Prevention at https://ftp.cdc.gov/pub/Health_Statistics/NCHS/dataset_documentation/namcs/stata.

Code availability Not applicable.

Authors' contributions SRF contributed to the study concept. ICL was responsible for the study design, statistical analysis, and manuscript drafting. SRF and JEH supervised the project. ICL, JEH, and SRF interpreted the data. ICL, JEH, LC, and SRF provided feedback on the manuscript, approved the final manuscript for submission, and are accountable for the accuracy and integrity of the manuscript.

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