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Contemporary Prevalence of Gout and Hyperuricemia in the United States and Decadal Trends: The National Health and Nutrition Examination Survey 2007-2016

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Abstract

Objectives: To estimate the contemporary prevalences of gout and hyperuricemia and their decadal trends in the US, as well as the prevalence of urate-lowering therapy (ULT) use among gout patients, using data from the latest and prior nationally-representative samples of US men and women (National Health and Nutrition Examination Survey [NHANES] 2007–2016).

Methods: Using data from 5,467 participants from NHANES 2015–2016, we estimated the latest prevalence of gout and hyperuricemia. During the NHANES, all participants were asked about a history of health professional-diagnosed gout and medication use. Hyperuricemia was defined as a serum urate level >7.0 mg/dL in men and >5.7 mg/dL in women. We examined decadal trends in these estimates using data from the NHANES 2007–2016 and ULT usage trends using the NHANES 2007–14 (the latest data available to date).

Results: The prevalence of gout was 3.9% (9.2 million) among US adults in 2015–2016 (5.2% [5.9 million] and 2.7% [3.3 million] among men and women, respectively). Mean serum urate levels were 6.0 mg/dL among men and 4.8 mg/dL among women, with hyperuricemia prevalences of 20.2% and 20.0%, respectively. The prevalences of gout and hyperuricemia remained stable over the past decade (P for trend >0.05). The prevalence of ULT use among patients with gout was 33% during 2007–2014 and remained stable over time (P for trend >0.05).

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Keywords

Gout; Hyperuricemia; Epidemiology; NHANES

INTRODUCTION

Gout is an inflammatory arthritis that is triggered by the crystallization of monosodium urate inside the joints and is preceded by hyperuricemia. Gout flares lead to substantial morbidity by causing severe pain, reduced quality of life (1), decreased physical function (1,2), increased healthcare costs (3), and lost economic productivity (3). Furthermore, gout is strongly associated with the metabolic syndrome (4), and may contribute to myocardial infarction (5,6), type 2 diabetes mellitus (7), chronic kidney disease (CKD) (8), and premature mortality (5,9,10).

The prevalence of gout and hyperuricemia in the United States (US) more than doubled between the 1960s and the 1990s and continued to increase steadily afterwards until at least 2007–2008, according to the National Health and Nutrition Examination Survey (NHANES) (11). It remains unknown whether these trends have continued over the past decade. To address this issue, we examined the latest prevalence of gout and hyperuricemia (NHANES 2015–2016) and their decadal trends using the NHANES 2007–2016. We also determined the latest national prevalence of urate-lowering therapy (ULT) use, as well as purported factors associated with achievement of a therapeutic target serum urate level in gout patients (NHANES 2007–2014).

METHODS

Study Population.

The NHANES is a cross-sectional survey designed to assess the health and nutritional status of adults and children in the US. The survey utilizes a complex, multistage probability design to provide a nationally-representative sample of the non-institutionalized US civilian population, and is unique in that it combines interviews and physical examinations with various laboratory data measurements (http://www.cdc.gov/nchs/nhanes/about_nhanes.htm). In this analysis, we used the five most recent NHANES cycles that asked about the presence of gout, spanning 2007 to 2016 (i.e., NHANES 2007–2016). After a home interview, participants were invited to attend examination sessions where blood and urine specimens were obtained. There were 29,201 participants (14,161 men and 15,040 women) aged 20 years and older for whom interview, physical examination, and laboratory data were available across the NHANES 2007–2016. In the current study, we analyzed individuals for whom complete information was available for gout status (n=29,169 in the NHANES 2007–16) and serum urate (n=26,355 in the NHANES 2007–2016). Data on prescription medication use, including ULT, were collected but not yet available for the last NHANES

survey cycle; therefore, we analyzed the 13,516 participants for whom these data were available in the NHANES 2007–14.

Assessment of Gout, Urate-Lowering Therapy Usage.

During the home interviews in the NHANES, all subjects were asked, "Has a doctor or other health professional ever told you that you had gout?" Additionally, current prescription medication usage was assessed by asking "In the past 30 days, have you used or taken medication for which a prescription is needed?" excluding prescription vitamins or minerals. ULT was defined as one of the following medications either alone or in combination: allopurinol, febuxostat, or probenecid.

Serum Urate Measurement and Definitions of Hyperuricemia.

The measurement of serum urate in the NHANES 2007–2016 is described elsewhere (4,12), including details of quality-control procedures (13). Values are reported in milligrams per deciliter (mg/dL) and can be converted to micromoles per liter (μ mol/L) by multiplying by 59.48. Our primary definition of hyperuricemia was a serum urate level >7.0 mg/dL among men and a serum urate level >5.7 mg/dL among women. We also employed alternative definitions of hyperuricemia regardless of sex (i.e., serum urate level >6.0 mg/dL, which is the usual target level in gout care (14,15), as well as >7.0 mg/dL, which is above the super-saturation point) (14,16).

Statistical Analysis.

All statistical analyses were performed using survey commands of Stata to account for the clusters and strata of the complex study design of the NHANES, as well as to incorporate sample weights (Version 15.1, Stata Corporation, College Station, Texas). These procedures generated estimates for the total civilian, non-institutionalized population of the US. The prevalence (%) of gout and hyperuricemia, mean serum urate level, and ULT usage (%) among gout patients were first calculated in the entire US adult population and then stratified by sex, age, and racial/Hispanic origin (specifically non-Hispanic white, non-Hispanic black, Hispanic, and other groups). To examine decadal trends, we employed logistic regression using the midpoint from each two-year continuous NHANES survey cycle spanning 2007 to 2016 as a categorical independent variable, with gout and hyperuricemia prevalence modeled as a function of thereof (17). Population estimates (in millions) were calculated using totals from the American Community Survey or Current Population Survey as per the NHANES analytic guidelines (18). Logistic regression models were used to examine the purported factors associated with ULT usage among gout patients, adjusting for sex and age. Linear and logistic regression models were used to evaluate the association of various purported factors with mean serum urate levels and whether patients with gout receiving ULT reached a serum urate level <6.0 mg/dL (the typical therapeutic target in gout care) (15), respectively. For all measures, we calculated 95% confidence intervals (CIs). All reported P values are two-sided.

RESULTS

Prevalence of gout in the US, 2015–2016.

The mean age of the NHANES 2015–2016 sample was 47.9 years, 48.1% of the participants were male, and 63.8% were non-Hispanic whites The prevalence of gout was 3.9% among US adults, which corresponds to an estimated 9.2 million adults with gout in 2015–2016 (Table 1). The prevalence was 5.2% (5.9 million) among men and 2.7% (3.3 million) among women. The prevalence of gout increased with age, with the lowest gout prevalence (0.7% or 0.6 million) in individuals aged 20 to 39 years and the highest (8.7% or 1.0 million) in individuals aged 80 years or older (Table 1). The prevalence of gout among Medicare-eligible individuals (aged 65 years or older) was 8.6%, which corresponds to an estimated 4.0 million US adults with gout.

Prevalence of hyperuricemia and mean serum urate levels in the US, 2015–2016.

Using our primary definition, the prevalence of hyperuricemia among men was 20.2% (22.8 million) and 20.0% (24.4 million) among women according to the same sex-specific serum urate levels (Table 2). The prevalence of serum urate >7.0 mg/dL regardless of sex was 11.9% overall (27.9 million), 20.2% among men, and 4.2% among women. The prevalence of serum urate levels >6.0 mg/dL was 32.3% overall (75.8 million), 49.5% among men (55.8 million), and 16.4% among women (20.0 million). The overall mean serum urate level was 5.39 mg/dL (95% CI, 5.34 to 5.45), with mean serum urate levels of 6.04 mg/dL and 4.79 mg/dL among men and women, respectively. The prevalence of hyperuricemia increased with age, with the highest prevalence (27.8% or 3.1 million) among individuals aged 80 years or older (Table 2). Among those aged 65 years or older, the prevalence of hyperuricemia was 27.2%, which corresponds to 12.6 million older adults with hyperuricemia.

Decadal trends in the prevalence of gout and hyperuricemia in the US (2007–2016).

The prevalence of gout among US adults was stable over the past decade (P value for trend = 0.69), including when stratified by sex and race/ethnicity (P values for trend > 0.2) (Table 3). Similarly, the prevalence of hyperuricemia was stable over the past decade when stratified by sex (P values for trend > 0.2) (Supplemental Table 1). The prevalence of hyperuricemia decreased among non-Hispanic blacks from 25.7% in 2007–08 to 22.6% in 2015–16 (P value for trend = 0.04), but remained stable among other racial/ethnic groups (Supplemental Table 1). The prevalence of both gout and hyperuricemia among adults aged 80 years or older decreased over this time period also (P values for trend < 0.05) (Table 3 and Supplemental Table 1).

Prevalence and associations of current urate-lowering therapy use among gout patients in the US from 2007–2014.

The prevalence of current ULT use among gout patients was 35.5% (3.3 million) in the NHANES 2013–2014 (43.0% [2.9 million] among men and 15.5% [0.40 million] among women) (Table 4). Across the NHANES 2007–2014, the overall prevalence of ULT use among patients with gout was 32.8% and this remained similar over time (Supplementary

Table 2). Allopurinol comprised 95.3% (95% CI, 92.2% to 98.4%) of all ULT usage. Among gout patients, male sex, obesity, and CKD stage 3 were all independently associated with 2–3 times higher odds of receiving ULT (adjusted odds ratios [ORs] 2.99 [95% CI, 2.05 to 4.34]; 2.00 [95% CI, 1.12 to 3.59], and 2.07 [95% CI, 1.11 to 3.84], respectively) (Table 5).

Prevalence and associations of achieving a serum urate level <6.0 mg/dL among gout patients in the US from 2007–2014.

The prevalence of gout patients with a therapeutic target serum urate level (<6.0 mg/dL) was 37.7% (95% CI, 34.0% to 41.6%) in 2007–2014 (31.6% [95% CI, 27.1% to 36.4%] among men and 51.8% [95% CI, 43.3% to 60.2%] among women). The mean serum urate levels were 5.78 mg/dL (95% CI, 5.52 to 6.04) among ULT users and 6.92 mg/dL (95% CI, 6.74 to 7.09) among non-ULT users in 2007–2014 (for which data on ULT were available). After adjusting for age, sex, race/ethnicity, education, body mass index, hypertension, glomerular filtration rate, thiazide diuretic use, and alcohol use, gout patients taking ULT had a mean serum urate level 1.40 mg/dL (95% CI, 1.13 to 1.67) lower than those not on ULT (Supplemental Table 3). As such, gout patients receiving ULT had more than six times higher odds of having a therapeutic serum urate level target of < 6.0 mg/dL compared to those not receiving ULT (adjusted OR 6.21; 95% CI, 3.93 to 9.81) (Table 6 and Supplemental Table 4). By contrast, male sex, obesity, CKD stage 3, and thiazide diuretic use were associated with a 50% lower odds for reaching a serum urate level <6.0 mg/dL (adjusted ORs 0.25 [95% CI, 0.13 to 0.47], 0.41 [95% CI, 0.24 to 0.70], and 0.50 [95% CI, 0.27 to 0.89], respectively) (Table 6).

DISCUSSION

Using the latest, nationally-representative sample of US men and women, we found that the prevalences of gout and hyperuricemia remain substantial, although they appeared to have plateaued over the past decade. Specifically, the prevalence of self-reported health professional or physician-diagnosed gout in the US in 2015-16 was 3.9% (9.2 million adults), which is the same as in 2007–2008 (3.9% or 8.3 million adults) (11). For hyperuricemia, approximately 47.1 million adults in the US met the sex-specific criteria for hyperuricemia in 2015–2016, corresponding to a prevalence of 20.1%, whereas the prevalence of hyperuricemia defined as a serum urate level of >7.0 mg/dL regardless of sex was 11.9% (27.9 million US adults). These prevalence estimates are also similar to those in the NHANES 2007-2008 (11). These data indicate that although the prevalences of gout and hyperuricemia have plateaued over the latest decade, their frequency and burden remain substantial with ongoing population growth. Given that men have a significantly higher prevalence of a serum urate level above super-saturation point (>7.0 mg/dL) than women, their prevalence of gout is relatively lower than expected compared to women, possibly supporting the notion that hyperuricemia may be more strongly associated with gout in women than in men.

The current stability of gout and hyperuricemia prevalences overall may be related to the plateauing trends of CKD and hypertension in the US over a similar time period (19,20), given their strong associations with gout and hyperuricemia (8,21). The prevalence of

obesity among US adults had similarly levelled off between 2005 and 2014 (17); however, the latest extended analysis from 2007 to 2016 found another rising trend of obesity (22). The realization of the impact of this obesity trend on the overall burden of gout and hyperuricemia could be lagging or insufficient, similar to the aforementioned trends in hypertension and CKD to date (19,20), which are also strongly influenced by obesity (23,24). The observed reduction in the prevalences of gout and hyperuricemia among adults aged 80 years or older from 2007 to 2016 in our study appeared to mirror the fall in the prevalence of CKD among this subgroup (20). To that end, further extended analyses should elucidate the potential impact of the rising obesity trend and other risk factor changes over time on gout and hyperuricemia.

Our findings appear in contrast to recent reports from other countries that found increasing trends in gout during the overlapping period. The nationally-representative New Zealand Health Survey found that the overall prevalence of self-reported physician-diagnosed gout among those aged 15 years or older nearly doubled from 1.6% in 2011–2012 to 2.9% in 2015–2016 (P < 0.001), with a concomitant increase in the prevalence of obesity over the same period (25,26). Similarly, a Canadian study using administrative health claims found an increasing prevalence trend from 2.4% in 2000 to 3.8% in 2012 among the overall population (27); moreover, a United Kingdom (UK) general practice population-based study also found an increasing trend from 2.03% in 2007 to 2.49% in 2012 (28). Finally, an analysis of Korean health insurance claims data showed that the prevalence of gout more than doubled from 0.35% in 2007 to 0.76% in 2015 (29). Despite the rising prevalence rates in these countries, it is notable that the latest estimates from these countries are still lower than the most recent estimate for the US, likely reflecting the obesity epidemic observed in the US as well as differences in diet and lifestyle factors.

The frequency of ULT use among gout patients remained largely unchanged between 2007–2014 in the US, with approximately one-third of gout patients reporting ULT use. Our ULT use prevalence was largely in line with previous estimates from other countries, including Canada (approximately 22%) (27), the UK (30% to 38%) (28,30,31), Western Sweden (42%) (32), and New Zealand (41%) (33). These prevalences should depend on the rate of ULT initiation as well as continuation. To that end, a recent meta-analysis recently estimated adherence to ULT in the US to be 40% (95% CI, 33% to 47%) (34), with earlier studies reporting adherence rates as low as 10% (35). Barriers to the appropriate treatment of gout include provider knowledge gaps surrounding treatments and clinical guidelines as well as insufficient patient education, including about the cause of gout and the 'curable' nature of the condition (36). It remains to be seen whether this will worsen with the new gout care guidelines published by the American College of Physicians, which does not endorse a ULT approach for treat-to-target serum urate level (37), unlike rheumatology guidelines (14,15).

The effect of ULT was apparent even in this national cross-sectional study, with 59% of ULT users and 31% non-users reaching the target serum urate level of <6.0 mg/dL. Conversely, we found that male sex, obesity, CKD, and thiazide diuretic use were inversely associated with reaching the therapeutic serum urate level. Given the well-established role of serum urate levels for gout flares, these data suggest a potential need for more aggressive therapy among these sub-groups. Furthermore, intervening on modifiable risk factors for

hyperuricemia, such as obesity and diuretic use, would improve chances of achieving a therapeutic serum urate level. To that end, losartan and calcium channel blockers were found to be associated with a lower risk of developing gout among people with hypertension, whereas diuretics, β-blockers, angiotensin converting enzyme inhibitors, and non-losartan angiotensin-II receptor blockers were associated with an increased risk of gout (38).

Strengths and limitations of our study deserve comment. Given the nationally-representative sample of US men and women in our study, our findings are generalizable to the US population. We also employed sex-specific definitions of hyperuricemia to allow comparisons based on laboratory definitions used in previous studies (11,39). Nevertheless, our secondary definitions addressed the urate saturation point as well as the usual therapeutic target serum urate level. While serum urate level data in our study are objective lab-based measures, gout was ascertained as self-reported, health professional-diagnosed gout. Thus, gout prevalence in this study is likely inflated, similar to prevalence estimates for other conditions from the NHANES. Depending on the diagnostic criteria and study population of previous studies, the concordance rate of self-reported cases of gout ranged from 44% to 100% % (40–43). Nevertheless, the 'true' prevalence of gout would still be substantial even if it were half of what we observed. Furthermore, the trend data on gout in our study were internally consistent with those on serum urate level data, the precursor of gout. In addition, our assessment of ULT penetration was based on prior 30-day use. Given that patients are frequently non-compliant with ULT, and/or may discontinue ULT for extended periods, these data may underestimate the overall history of ULT use among the subjects. Furthermore, although we did not find a significant change in the trends of gout or hyperuricemia prevalence from 2007 to 2016, another limitation is that ten years may not be long enough to detect what might actually be a significant trend(s) over a longer period. The previous study by Zhu et al., for example, examined trends in gout and hyperuricemia prevalence from 1988 to 2008, and identified a significant increase in the prevalences of both over this time (11). Similarly, data on ULT usage were only available for the NHANES 2007-2014 but not for the most recent NHANES 2015-2016 cycle, which is another limitation. Consequently, further extended analyses should be conducted to assess trends in gout and hyperuricemia over a longer time period when these data come available.

In conclusion, these findings from a nationally-representative sample of US adults indicate that the prevalences of gout and hyperuricemia remain substantial. These data also suggest that while the absolute numbers of patients with these conditions has risen with the population, their prevalences have plateaued over the past decade, likely due to the stabilization of risk factor conditions for gout and hyperuricemia. Our findings also indicate that approximately one-third of gout patients are taking ULT and only just over one-third of gout patients are at the rheumatology guideline target serum urate level for disease control (14,15). Male sex, obesity, CKD, and thiazide diuretic use were risk factors for failing to reach a therapeutic serum urate level at the US general population level, suggesting the potential need for a more aggressive approach among these groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Prevalence of Gout and Number of Affected Adults in the US, NHANES 2015-2016*

	Prevalence, % (95% CI)	Prevalence, % (95% CI) US Adults with Gout (in millions)
All	3.9 (3.3, 4.7)	9.18
Sex		
Male	5.2 (4.4, 6.2)	5.86
Female	2.7 (2.0, 3.8)	3.33
Age		
20–39	0.7~(0.3, 1.5)	0.56
40-59	3.4 (2.2, 5.3)	2.89
60-79	8.8 (7.2, 10.7)	4.77
80	8.7 (5.8, 12.7)	0.97
Race/ethnicity		
Non-Hispanic White	4.0 (3.1, 5.3)	6.13
Non-Hispanic Black	4.8 (3.8, 6.0)	1.31
Hispanic	2.0 (1.4, 2.9)	0.73
Other	5.2 (3.4, 7.9)	0.99

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Table 2.

Prevalence of hyperuricemia † , number of US adults with hyperuricemia, and mean serum urate levels, NHANES 2015–2016 *

	Prevalence of hyperuricemia, % (95% CI) [†]	No. of US adults with hyperuricemia, millions †	Prevalence of hyperuricemia >7.0 mg/dL, % (95% CI)	No. of US adults with hyperuricemia >7.0 mg/dL, millions	Serum urate level, mean (95% CI) mg/dL
Total population	20.1 (17.8, 22.4)	47.13	11.9 (10.2, 13.9)	27.9	5.39 (5.34 to 5.45)
Sex					
Male	20.2 (16.6, 24.3)	22.76	20.2 (16.6, 24.3)	22.8	6.04 (5.95 to 6.13)
Female	20.0 (17.8, 22.4)	24.37	4.2 (3.3, 5.3)	5.1	4.79 (4.73 to 4.86)
Age					
20–39	16.6 (13.6, 20.1)	14.07	11.3 (9.1, 14.1)	9.62	5.33 (5.23 to 5.42)
40–59	18.7 (15.1, 22.9)	15.71	11.3 (8.4, 14.9)	9.48	5.32 (5.20 to 5.43)
60–79	26.1 (22.7, 29.8)	14.20	13.5 (11.0, 16.6)	7.37	5.58 (5.46 to 5.70)
80	27.8 (21.0, 35.8)	3.10	13.2 (9.1, 19.0)	1.48	5.54 (5.34 to 5.74)
Race/ethnicity					
Non-Hispanic White	21.4 (18.1, 25.1)	32.59	12.7 (10.3, 15.6)	19.36	5.43 (5.34 to 5.51)
Non-Hispanic Black	22.6 (20.9, 24.3)	6.15	12.9 (11.4, 14.6)	3.51	5.42 (5.36 to 5.47)
Hispanic	14.9 (12.6, 17.5)	5.33	9.1 (7.3, 11.2)	3.25	5.23 (5.15 to 5.32)
Other	17.0 (13.8, 20.7)	3.23	10.1 (8.2, 12.4)	1.92	5.40 (5.30 to 5.50)

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CI = 95% confidence interval.

 \dot{f} Hyperuricemia was defined as a serum urate level of >7.0mg/dL in males, and >5.7mg/dL in females

Table 3.

Decadal Trend of Gout Prevalence in the US, NHANES 2007–2016 *

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	NHANES 2007–2008	NHANES 2009–2010	NHANES 2009-2010 NHANES 2011-2012 NHANES 2013-2014 NHANES 2015-2016	NHANES 2013-2014	NHANES 2015-2016	
Total population	3.9 (3.3, 4.5)	3.7 (3.0, 4.6)	3.6 (2.8, 4.7)	4.0 (3.2, 5.1)	3.9 (3.2, 4.7)	0.69
Sex						
Male	5.9 (4.8, 7.2)	5.3 (3.9, 7.1)	4.7 (3.9, 5.8)	6.0 (4.9, 7.4)	5.2 (4.4, 6.2)	0.75
Female	2.0 (1.6, 2.5)	2.3 (1.8, 2.9)	2.6 (1.8, 4.0)	2.2 (1.4, 3.3)	2.7 (2.0, 3.8)	0.23
Age						
20–39	$0.8\ (0.5,\ 1.4)$	1.0 (0.4, 2.4)	0.7 (0.3, 1.6)	0.8 (0.4, 1.4)	0.7 (0.3, 1.4)	0.50
40–59	3.5 (2.6, 4.6)	2.9 (2.2, 3.9)	3.4 (2.0, 5.7)	4.1 (2.7, 6.1)	3.4 (2.3, 5.1)	0.60
60–79	8.5 (6.6, 10.9)	8.3 (7.0, 9.9)	7.6 (5.4, 10.6)	8.6 (6.9, 10.5)	8.8 (7.3, 10.6)	0.75
80	12.6 (10.3, 15.3)	12.2 (8.9, 16.6)	10.3 (6.9, 15.1)	7.5 (5.2, 10.9)	8.7 (6.0, 12.4)	0.01
Race/ethnicity						
Non-Hispanic White	4.0 (3.4, 4.8)	4.3 (3.4, 5.4)	4.2 (3.0, 5.8)	4.6 (3.6, 6.0)	4.0(3.1, 5.3)	0.84
Non-Hispanic Black	5.0(3.6, 6.8)	4.4 (3.2, 6.0)	4.4 (3.7, 5.2)	4.6 (3.4, 6.1)	4.8 (3.8, 6.0)	0.93
Hispanic	1.7 (1.2, 2.4)	0.9 (0.5, 1.5)	1.2 (0.7, 2.0)	1.8 (1.3, 2.6)	2.0 (1.4, 2.9)	0.09
Other	4.5 (1.9, 10.2)	2.6(1.4, 4.9)	2.3 (1.5, 3.4)	2.4 (1.5, 3.7)	5.2 (3.4, 7.9)	0.54

Prevalence of Current Urate-Lowering Therapy (ULT) Use among Gout Patients in the US, NHANES 2013-2014*

	Prevalence, % (95% CI)	Prevalence, % (95% CI) Gout Patients on urate-lowering therapy (in millions)
Π	35.5 (25.9, 46.4)	3.28
Sex		
Female	15.5 (9.3, 24.7)	0.40
Male	43.0 (31.5, 55.3)	2.86
Age		
20–39	42.9 (13.2, 78.9)	0.27
40–59	33.1 (15.4, 57.3)	1.15
60–79	37.3 (27.6, 48.2)	1.62
80	31.1 (13.8, 55.9)	0.26
Race/ethnicity		
Non-Hispanic White	35.0 (24.2, 47.6)	2.47
Non-Hispanic Black	26.5 (17.6, 37.9)	0.32
Hispanic	57.7 (38.7, 74.7)	0.35
Other	43.4 (17.3, 73.8)	0.18

Table 5.

Current Urate-Lowering Therapy (ULT) † Use and Associations Among Gout Patients in the US, NHANES 2007–2014 *

	Gout Patients on ULT, %	Unadjusted OR (95% CI)	Age- and sex-adjusted OR (95% CI)	Fully-adjusted OR (95% CI)**
Age				
20–39	24.5 (11.2, 45.6)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
40–59	25.5 (17.7, 35.3)	$1.05\ (0.39,2.85)$	1.19(0.44, 3.19)	1.31 (0.45, 3.81)
60-79	38.6 (31.6, 46.2)	$1.94\ (0.69, 5.46)$	2.20 (0.78, 6.22)	2.11 (0.65, 6.89)
80	34.3 (25.7, 44.0)	1.60(0.61, 4.23)	2.04 (0.77, 5.36)	1.73 (0.52, 5.80)
Sex				
Female	19.3 (14.9, 24.5)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Male	38.8 (33.0, 45.0)	2.66 (1.90, 3.72)	2.79 (2.03, 3.84)	2.99 (2.05, 4.34)
Race/ethnicity				
Non-Hispanic White	33.6 (27.7, 40.2)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Non-Hispanic Black	28.3 (22.7, 34.5)	0.78 (0.50, 1.21)	$0.87\ (0.54,1.40)$	$0.84\ (0.53,1.34)$
Hispanic	31.6 (20.5, 45.2)	0.91 (0.49, 1.69)	$0.94\ (0.48,1.83)$	$0.92\ (0.45,1.90)$
Other	32.1 (19.8, 47.7)	0.93 (0.46, 1.89)	$0.93\ (0.43,\ 2.01)$	1.10 (0.51, 2.38)
Education				
Some high school	32.4 (24.4, 41.6)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
High school or GED	42.5 (32.9, 52.7)	1.54(0.90, 2.63)	1.49~(0.86, 2.56)	1.49(0.87, 2.53)
Some college	23.3 (16.0, 32.6)	0.63 (0.34, 1.19)	0.66 (0.33, 1.30)	0.66 (0.34, 1.29)
College graduate	34.9 (25.5, 45.6)	1.12 (0.58, 2.14)	0.97 (0.51, 1.84)	$0.95\ (0.50,1.83)$
Body mass index				
$24.9 \mathrm{kg/m^2}$	23.9 (15.0, 35.9)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
25.0 kg/m^2 to 29.9kg/m^2	33.7 (27.2, 40.7)	1.61 (0.84, 3.08)	1.60(0.83, 3.09)	$1.63\ (0.86,\ 3.08)$
30.0kg/m^2	34.5 (28.3, 41.2)	1.67 (0.92, 3.06)	1.94 (1.04, 3.62)	2.00 (1.12, 3.59)
Hypertension				
No	30.6 (21.0, 42.2)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Yes	33.7 (28.5, 39.3)	1.15 (0.67, 1.99)	1.11 (0.66, 1.87)	1.09 (0.62, 1.91)
Glomerular filtration rate (GFR)				
GFR 90mL/min	24.8 (16.2, 36.1)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
GFR 60 to 89mL/min	33.7 (27.1, 41.0)	$1.54\ (0.85, 2.79)$	$1.29\ (0.69,\ 2.41)$	1.30 (0.71, 2.38)

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	Gout Patients on ULT, %	Unadjusted OR (95% CI)	Gout Patients on ULT, % Unadjusted OR (95% CI) Age- and sex-adjusted OR (95% CI) Fully-adjusted OR (95% CI)**	Fully-adjusted OR (95% CI)**
GFR 30 to 59mL/min	41.9 (34.9, 49.3)	2.18 (1.28, 3.71)	1.96 (1.05, 3.66)	2.07 (1.11, 3.84)
GFR < 30mL/min	29.9 (14.1, 52.6)	1.29 (0.37, 4.50)	1.41(0.41, 4.83)	$1.51 \ (0.45, 5.06)$
Alcohol Use				
No	30.0 (21.5, 40.2)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Yes	33.7 (27.7, 40.2)	1.18 (0.67, 2.08)	0.76~(0.41, 1.39)	$0.90\ (0.48,1.68)$
Chiazide diuretic				
No	33.9 (28.4, 39.9)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Yes	28.4 (19.8, 38.9)	0.78 (0.46, 1.31)	0.77 (0.46, 1.29)	$0.68\ (0.39,1.18)$

eights. 95% CI = 95% confidence interval. GED = General Educational Development

** For all the other covariates in the table

 $\overset{f}{\prec}_{A n y}$ one of allopurinol, febuxostat or probenecid either alone or in combination

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Factors associated with serum urate < 6.0 mg/dL among patients with Gout in the US, NHANES 2007–2014^{*}

9	Gout Patients with serum urate < 6.0mg/dL, %	Unadjusted OR (95% CI)	Age- and sex-adjusted OR (95% CI)	Fully-adjusted OR (95% CI)**
Urate-lowering therapy $^{ eq}$				
No	30.6 (26.4, 35.2)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Yes	59.0 (50.7, 66.8)	3.26 (2.25, 4.72)	4.50 (2.91, 6.96)	6.21 (3.93, 9.81)
Age				
20–39	22.9 (10.2, 43.9)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
40–59	42.9 (33.4, 52.9)	2.52 (0.85, 7.48)	2.32 (0.79, 6.84)	2.65 (0.73, 9.65)
6019	39.7 (31.7, 48.3)	2.21 (0.92, 5.31)	2.06 (0.87, 4.88)	2.63 (0.89, 7.76)
80	42.5 (33.4, 52.2)	2.49 (0.87, 7.16)	2.12 (0.74, 6.06)	3.52 (0.86, 14.47)
Sex				
Female	52.3 (42.7, 61.8)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Male	34.5 (29.2, 40.1)	0.48 (0.30, 0.78)	$0.49\ (0.30,0.80)$	0.25 (0.13, 0.47)
Race/ethnicity				
Non-Hispanic White	41.7 (36.5, 47.2)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Non-Hispanic Black	34.6 (27.9, 42.0)	0.74 (0.53, 1.04)	0.66 (0.46, 0.95)	0.82 (0.55, 1.22)
Hispanic	36.1 (26.0, 47.7)	0.79 (0.47, 1.34)	$0.89\ (0.50,1.55)$	1.20 (0.55, 2.64)
Other	22.9 (13.3, 36.5)	0.41 (0.21, 0.83)	$0.45\ (0.21,\ 0.98)$	0.26 (0.12, 0.56)
Education				
Some high school	37.9 (32.3, 43.8)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
High school or GED	37.9 (27.7, 49.3)	1.00 (0.57, 1.74)	1.05 (0.59, 1.88)	$0.80\ (0.41,1.58)$
Some college	35.8 (28.5, 43.9)	0.91 (0.60, 1.40)	0.90 (0.60, 1.34)	0.93 (0.52, 1.68)
College graduate	47.6 (37.6, 57.7)	1.49 (0.92, 2.40)	1.73 (1.07, 2.82)	1.97 (1.08, 3.57)
Body mass index				
24.9kg/m ²	49.3 (37.9, 60.8)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
25.0 kg/m^2 to 29.9kg/m^2	44.8 (34.9, 55.1)	0.83 (0.41, 1.70)	0.85 (0.42, 1.70)	0.70 (0.36, 1.38)
30.0kg/m ²	35.0 (29.7, 40.6)	0.55 (0.32, 0.97)	$0.52\ (0.30,\ 0.92)$	0.40 (0.22, 0.71)
Hypertension				
No	46.3 (37.4, 55.4)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Yes	37.6 (32.4, 43.1)	0.70 (0.46, 1.07)	0.65(0.43, 0.99)	0.81 (0.54, 1.21)

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	Gout Patients with serum urate < 6.0mg/dL, % Unadjusted OR (95% CI) Age- and sex-adjusted OR (95% CI) Fully-adjusted OR (95% CI)**	Unadjusted OR (95% CI)	Age- and sex-adjusted OR (95% CI)	Fully-adjusted OR (95% CI)**
Glomerular filtration rate (GFR)				
GFR 90mL/min	48.4(39.0, 58.0)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
GFR 60 to 89mL/min	38.4 (31.6, 45.7)	0.66 (0.39, 1.13)	0.63 (0.36, 1.09)	$0.45\ (0.24,0.85)$
GFR 30 to 59mL/min	34.4 (24.2, 46.2)	$0.56\ (0.29,1.06)$	0.43 (0.22, 0.84)	$0.24 \ (0.11, \ 0.53)$
GFR < 30mL/min	24.7 (12.1, 43.9)	0.35 (0.12, 0.98)	$0.22\ (0.07,0.70)$	$0.11 \ (0.03, 0.51)$
Alcohol Use				
No	46.7 (38.6, 55.1)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Yes	38.0 (32.7, 43.5)	0.70 (0.47, 1.04)	0.91 (0.58, 1.42)	0.69 (0.43, 1.12)
Thiazide diuretic				
No	42.8 (37.5, 48.3)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Yes	27.1 (18.8, 37.5)	$0.50\ (0.29,\ 0.86)$	$0.44\ (0.25,0.78)$	$0.50\ (0.27,\ 0.89)$

CI = 95% confidence interval.

** For all the other covariates in the table

 $\overset{f}{\mathcal{A}}$ Any one of all opurinol, febuxostat or probenecid alone or in combination