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Differences in the Prevalence of Nocturnal Polyuria in the U.S. by Definition: Results from the Epidemiology of Nocturnal Polyuria Study

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Study Need and Importance: Nocturnal polyuria (NP), defined as excessive production of urine during sleep, is one of the main causes of nocturia. The EpiNP (Epidemiology of Nocturnal Polyuria) Study was a population-representative study of men and women aged 30 years or older to assess the prevalence of NP in the United States. This article presents bladder diary data parameters by NP definition (using nocturnal polyuria index >33% and rate of nocturnal urine production >90 ml/hour), by NP groups, including idiopathic NP (without underlying causes), NP associated with overactive bladder (NPOAB), bladder outlet obstruction (NPBOO; men) and comorbidities (NPCom), and by sex.

What We Found: A total of 10,190 participants completed a baseline survey of lower urinary tract symptoms, comorbidities and burden. A total of 1,763 participants who completed the survey (49.3% of those invited) also completed 3-day bladder diaries. Measures of urine production (maximum nighttime volume, total volume, nocturnal urine production) were higher in both men and women with idiopathic NP and NPCom using both NP definitions versus other NP groups. The median number of nighttime urinations was greatest for NPOAB and NPBOO in men, and NPOAB and NPCom in women. For both NP definitions, bother associated with nighttime voiding differed by NP subgroup but was highest in NPBOO for men and NPOAB for women.

Limitations: As this was a U.S.-based study, these findings may not be generalizable to other countries. However, the sampling methods support the assumption that the findings are representative of U.S. adults aged 30 and older.

Interpretation for Patient Care: Study findings may provide clues to nocturia treatment in emphasizing factors influencing urine production in comparison to factors influencing bladder capacity. As NP is prevalent in both sexes with clinically relevant nocturia, providers should address the causative, potentially serious underlying medical and urological pathophysiological conditions which contribute to NP.

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Differences in the Prevalence of Nocturnal Polyuria in the U.S. by Definition: Results from the Epidemiology of Nocturnal Polyuria Study

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Purpose: Prevalence data on nocturnal polyuria (NP), nocturia caused by overproduction of urine during sleep, is primarily limited to men and varies by NP definition. This U.S.-representative epidemiological study of men and women ≥30 years old assessed the prevalence of NP.

Materials and Methods: Consenting participants completed the baseline EpiNP (Epidemiology of Nocturnal Polyuria) survey (eg Lower Urinary Tract Symptoms Tool, comorbidities). All reporting ≥2 voids/night and a target of 100 random respondents reporting 0 or 1 void/night were asked to complete 3-day bladder diaries. NP was defined as nocturnal polyuria index (NPI) >0.33 (NPI33) and nocturnal urine production >90 ml/hour (NUP90). Extrapolated prevalence was stratified by sex and subgroups: idiopathic (without underlying causes), associated with overactive bladder (NPOAB), bladder outlet obstruction (NPBOO; men) and comorbidities. Voided volumes and timing, including first uninterrupted sleep period, were assessed by subgroup.

Abbreviations and Acronyms

EpiNP = Epidemiology of Nocturnal Polyuria
FUSP = first uninterrupted sleep period
ICS = International Continence Society
LUTS = lower urinary tract symptoms
MVV = maximum voided volume
NI = nocturia index
NP = nocturnal polyuria
NPBOO = nocturnal polyuria associated with bladder outlet obstruction
NPCom = nocturnal polyuria associated with comorbidities
NPI = nocturnal polyuria index
NPI33 = nocturnal polyuria index >33%
NPOAB = nocturnal polyuria associated with overactive bladder
NUP = nocturnal urine production
NUP90 = nocturnal urine production >90 ml/hour

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Editor's Note: This article is the fourth of 5 published in this issue for which Category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 226 and 227.

Results: A total of 10,190 individuals completed the baseline survey; mean age (range) was 54.4 (30–95). A total of 3,938 individuals were invited to complete the diary; 1,763 (49.3%) completed 3-day bladder diaries. Urine production (maximum nighttime volume, total volume, nocturnal urine production, nocturia index) was higher in both men and women with idiopathic NP and comorbidities. The median number of nighttime voids was greatest for NPBOO in men and NPOAB in women. Bother associated with nighttime voiding differed by NP subgroup but was highest in NPBOO for men (NPI33: 69.6%; NUP90: 71.1%) and NPOAB for women (NPI33: 67.5%; NUP90: 66.0%).

Conclusions: This population-based NP prevalence study including men and women characterizes NP subgroups and provides insights into nocturia treatment by emphasizing factors influencing urine production versus factors influencing bladder capacity.

Key Words: epidemiology, nocturia, polyuria, cross-sectional studies, prevalence

Nocturnal polyuria (NP) is defined by the International Continence Society (ICS) as "excessive production of urine during the main sleep period"[1,2] and is one of the main causes of nocturia. Various conditions have been associated with NP, such as overactive bladder,[3,4] bladder outlet obstruction and comorbidities such as hypertension, heart disease, diabetes and sleep apnea.[1,5–7] However, NP may occur in the absence of these conditions ("idiopathic NP"); when associated with a disturbance in the diurnal rhythm in the antidiuretic hormone system, the condition is referred to as the NP syndrome.[8–10]

The ICS recognized that "excessive production of urine" is not clearly defined. Various definitions of NP, including nocturnal urine production based on body weight greater than 10 ml/kg and nocturia index (NI) greater than 1.5 (nocturnal urine volume/maximum voided volume [MVV]) have been proposed,[11,12] although the most commonly used definitions are nocturnal polyuria index (NPI) >33% (NPI33; nocturnal urine volume >33% of the 24-hour total urine volume) and rate of nocturnal urine production (NUP) >90 ml/hour (NUP90).[13,14] Importantly, a consensus definition of NP has not yet been agreed upon.[1]

Only 1 large high-quality study has examined the prevalence of NP, which varied significantly according to the definition used.[15] The longitudinal, community-based Krimpen Study estimated NP prevalence among men in the Netherlands aged 50–78 years using NPI33 and NUP90. Approximately 80% with nocturia had NP when using NPI33, and only 15% when using NUP90 (calculated from 1:00 a.m. to 6:00 a.m./5 hours, the period that 90% of the men were in bed with the intention to sleep). A recent study conducted in 1,400 women found that prevalence of NP differed considerably, from 21.5%–77%, depending upon NP definition.[16]

As such, a large cross-sectional, population-representative study of both men and women (Epidemiology of Nocturnal Polyuria [EpiNP] Study) was conducted to assess the prevalence of NP in the U.S.; adjusted overall NP prevalence using NPI33 was 31.5% (men) and 38.5% (women), and was 23.8% (men) and 18.1% (women) using NUP90.[17] The main objective of this analysis was to compare bladder diary data parameters by NP definition (NPI33 and NUP90) to further evaluate the characteristics of NP definitions and examine potential sex-based differences.

METHODS

Study Design

This epidemiological study was conducted in 2 parts: a web-based EpiNP survey and an at-home bladder diary. The study received Institutional Review Board approval from Ethical & Independent Review Services (Independence, Missouri; E&I Study No. 19089-01; Clinical Trial Registration No. NCT04125186). All participants provided electronic informed consent prior to participation.

EpiNP Survey

The web-based EpiNP survey (administered in U.S. English and U.S. Spanish) had a target recruitment of 10,000 men and women ≥30 years old who were representative of the U.S. general population based on age strata, sex and race. Respondents were recruited from an online panel (YouGov, Palo Alto, California). Inclusion criteria were age ≥30 years, provision of informed consent and ability to use the Internet. Those currently pregnant or ≤12 months postpartum, or who had surgery in the last 6 months, a urinary tract infection, atypical circadian patterns (eg working nighttime shifts) or recent participation in a YouGov survey were excluded. Outcome measures included the Lower Urinary Tract Symptoms (LUTS) Tool[18] and lifestyle and sociodemographic questions. Men completed the International Prostate Symptom Score.[19] Detailed methods for the EpiNP survey and weighting are described elsewhere.[17]

Bladder Diary

Following survey completion, all who reported ≥2 voids per night on the LUTS Tool were prompted with an additional consent to complete a 3-day web-based bladder diary in which the time, volume and urgency of each void were recorded.[20] Additionally, a randomly selected subset of approximately 100 participants reporting 0 or 1 void per night were asked to participate in the 3-day bladder diary to confirm their self-report. To complete the diary, participants were mailed a packet containing bladder diary directions, at-home and portable urine collection containers, and unique links to access the online bladder diary.[17]

Statistical Analyses

EpiNP Baseline Survey. All statistical analyses were performed using SAS/STAT®, version 9.4. Sample matching was used to construct population-representative samples of respondents weighting all data as appropriate. The sampling frame was constructed by stratified sampling of adults aged ≥30 years from the 2017 American Community Survey 1-year sample.[21]

EpiNP Bladder Diary Derivations of Volumes Voided. Frequency and voided volumes were calculated per ICS guidelines.[1,8] A 24-hour period was defined as 30 minutes after waking each day to 30 minutes after waking the next day. Each nocturnal period was defined as the time interval between 5 minutes after going to bed with the intention to sleep to the time of rising the next day.[1] All 3 diary days were utilized in analysis.

First uninterrupted sleep period (FUSP) was calculated as the time from 5 minutes after going to bed to sleep to the first nocturnal void. Nocturnal voided volume was calculated as the sum of volumes associated with nocturnal voids per 24-hour period (including the first morning void within 30 minutes after waking). If participants voided greater than 30 minutes before bedtime, the nocturnal urine production was prorated hourly according to van Mastrigt and Eijskoot.[22] Average nocturnal voided volume was calculated as the sum of nocturnal voided volumes from each 24-hour period, divided by the number of completed 24-hour periods. Average daily (24-hour period) voided volume was similarly calculated.

NI was calculated as the nocturnal voided volume divided by the MVV. MVV was defined as the maximum volume of a single void, during daytime or nighttime hours, across all days recorded in the bladder diary.[23]

Definitions of NP. The prevalence of NP was calculated using 2 definitions of NP: NPI33,[24] defined as average nocturnal voided volume/average 24-hour voided volume >0.33, and NUP90,[13,15] defined as average nocturnal urine production/average sleep duration, >90 ml/hour.

Respondents who did not meet NPI33 or NUP90 criteria were classified as "No NP." For all others, the following subgroups were identified: NP with symptoms suggestive of overactive bladder (NPOAB) defined as the presence of urinary urgency, urgency with the fear of leaking or urge incontinence; NP with symptoms suggestive of bladder outlet obstruction (NPBOO) defined as total International Prostate Symptom Score ≥13;[25,26] NP associated with comorbidities (NPCom) defined as self-reported diabetes, hypertension, heart disease or sleep apnea; and idiopathic NP defined when NPI33 or NUP90 criteria were met but criteria for other subgroups were not. It is assumed but not verified (as endogenous arginine vasopressin was not measured) that a subset of respondents with idiopathic NP had NP syndrome.

NP Prevalence. Estimates for overall prevalence by sex and NP subgroup were calculated for all participants with 3 days of completed bladder diaries.[17]

Demographic and Bladder Diary Data

Descriptive analyses were used to evaluate the demographic and bladder diary data by NP subgroups, definitions and sex. For continuous variables, mean, standard deviation and range were calculated; for categorical variables, frequency and percentage were calculated.

RESULTS

EpiNP Survey

A total of 10,190 individuals (4,893 men and 5,297 women) participated in the survey (see Figure) and closely matched the targeted recruitment scheme. The population weighted demographic and clinical characteristics are presented in the supplementary Table (https://www.jurology.com). The majority were White (75%), followed by Black/African American (12%) and Asian (6%); 15% were Hispanic or Latino.

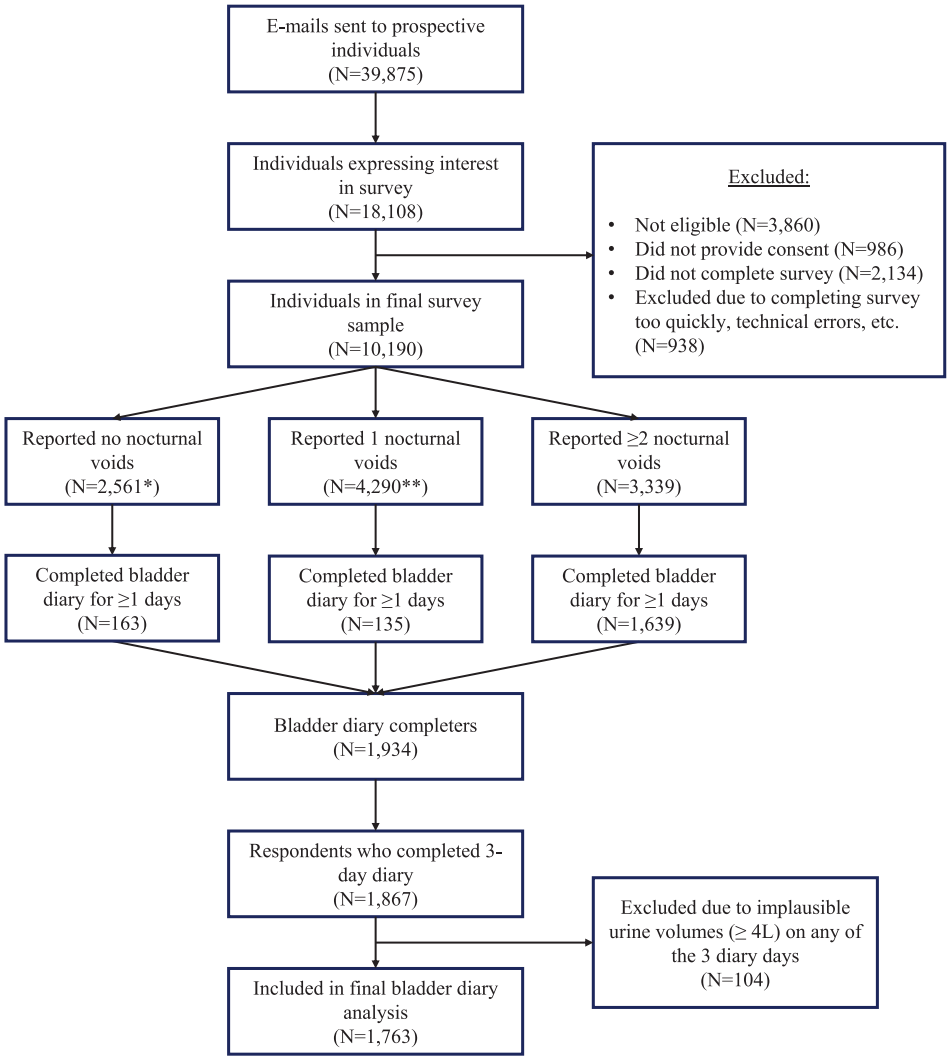
EpiNP Bladder Diary

Among the EpiNP survey respondents, 3,938 (38.6%) were invited to complete the bladder diary; 1,934 (49.1%) completed at least 1 diary day; 1,763 (44.8%) completed all 3 days and were included in this bladder diary analysis (718 men and 1,045 women; see Figure). The sociodemographic characteristics of 3-day bladder diary completers are reported in Table 1. Characteristics of nonresponders to the bladder diary invitation were similar to those who completed at least 1 bladder diary day, and characteristics of bladder diary completers were similar to the overall EpiNP survey completers, indicating that the bladder diary completer sample is representative of the overall sample (see supplementary Table, https://www.jurology.com).

Bladder Diary Data

The overall extrapolated NP prevalence estimates have been previously published.[17] Demographic and bladder diary data by NP definition, subgroup and sex are found in Tables 2 and 3. The median age was lowest for men and women with idiopathic NP (men: NPI33: 52.0; NUP90: 50.0; women: NPI33: 49.5; NUP90: 54.0) when compared to other NP groups. Men and women with idiopathic NP and no NP (by either definition) were less likely to be obese.

Measures of urine production (eg maximum nighttime volume, total volume, NUP, NI) were generally higher for both sexes with idiopathic NP and NPCom using NUP90 when compared to NPI33 (Tables 2 and 3). For both NP definitions, the median number of nighttime urinations was greatest for NPOAB (NPI33 and NUP90: 3.0) and NPBOO (NPI33 and NUP90: 3.3) in men, and NPOAB (NPI33: 3.0, NUP90: 3.3) and NPCom (NPI33 and NUP90: 2.8) in women. Median FUSP was greater for all NP groups/sexes when using NPI33 and shortest among NPOAB for both sexes and NPBOO among men. Interestingly, the average NI was



* 327 individuals were randomized for potential participation in the bladder diary portion of the study

** 287 individuals were randomized for potential participation in the bladder diary portion of the study

Figure. Selection of EpiNP Study sample.

highest in both sexes with NPOAB (all ≥2.1) and men with NPBOO.

Bother ≥"somewhat" associated with nocturia was reported between 26.1% and 71.1% of respondents and tended to be higher in women. Bother differed by NP subgroup (highest in NPBOO for men [NPI33: 69.6%; NUP90: 71.1%] and NPOAB for women [NPI33: 67.5%; NUP90: 66.0%]) and was relatively similar regardless of NP definition.

LUTS

Reported LUTS among individuals experiencing symptoms at least "sometimes," by sex and NP subgroup using NPI33 are presented in Table 4 (similar results were found using NUP90; data not shown). Frequent urination was prevalent among all subgroups in both sexes, affecting most individuals with NPOAB (men: 58.3%; women: 74.7%), most men with NPBOO (86.3%) and most individuals with no NP (men: 57.8%; women: 59.9%). Terminal dribble was common, particularly among women with NPOAB (66.1%), men with NPBOO (84.6%) and individuals with no NP (men: 59.6%; women: 50.0%). Urinary urgency was common in NPOAB (men: 58.3%; women: 74.7%), men with NPBOO (62.1%) and women with no NP (52.9%). Stress incontinence (laughing, sneezing, coughing) was prevalent in women (range: 12.2% in idiopathic NP to 57.0% in NPOAB).

DISCUSSION

This study is the first population-based prevalence study of NP inclusive of men and women aged 30 years and older. Overall, NP is highly prevalent in the U.S. for both men and women. However,

Table 1. *Participant demographic and clinical characteristics: bladder diary analysis sample with 3-day data*

Characteristic	Total	Men	Women
No. pts (%)	1,763	718 (40.7)	1,045 (59.3)
Age:			
Mean yrs (SD)	56.5 (13.9)	57.0 (13.4)	56.1 (14.2)
Median (range)	58 (30.0—95.0)	59 (30.0—88.0)	57 (30.0—95.0)
No. race (%):			
White	1,313 (74.5)	545 (75.9)	768 (73.5)
Black or African American	262 (14.9)	99 (13.8)	163 (15.6)
American Indian or Alaska Native	7 (0.4)	1 (0.1)	6 (0.6)
Asian	67 (3.8)	28 (3.9)	39 (3.7)
Other	113 (6.4)	45 (6.3)	68 (6.5)
Missing	1 (0.1)	0 (0.0)	1 (0.1)
No. ethnicity (%):			
Hispanic or Latino	229 (13.0)	98 (13.6)	131 (12.6)
Missing	3 (0.2)	1 (0.1)	2 (0.2)
No. education (%):			
Elementary/primary school	7 (0.4)	2 (0.3)	5 (0.5)
Secondary/high school	254 (14.4)	88 (12.3)	166 (15.8)
Some college	498 (28.2)	190 (26.5)	308 (29.5)
College degree	626 (35.5)	266 (37.0)	360 (34.4)
Postgraduate degree	371 (21.0)	168 (23.4)	203 (19.4)
Other	7 (0.4)	4 (0.6)	3 (0.3)
Body mass index:			
Mean (SD)	30.1 (7.5) in 1,749 pts	29.7 (6.5) in 717 pts	30.4 (8.1) in 1,032 pts
Median (range)	29 (8.7—71.7)	28 (8.7—66.6)	29 (14.4—71.7)
No. comorbid conditions (%):*			
None	376 (21.3)	154 (21.4)	222 (21.2)
Arthritis	612 (34.7)	205 (28.6)	407 (38.8)
Anxiety	453 (25.7)	124 (17.3)	329 (31.5)
Depression	473 (26.8)	160 (22.3)	313 (30.0)
Heart disease	140 (7.9)	67 (9.3)	73 (7.0)
High blood pressure	780 (44.2)	368 (51.3)	412 (39.3)
Mobility limitations	250 (14.2)	92 (12.8)	158 (15.1)
Neurological conditions	89 (5.0)	35 (4.9)	54 (5.2)
Sleep apnea	197 (11.2)	122 (17.0)	75 (7.2)
Sleep difficulties	302 (17.1)	97 (13.5)	205 (19.6)
Other sleep disorder	54 (3.1)	27 (3.8)	27 (2.6)
Waist circumference:			
Mean inches (SD)	40.2 (7.8) in 1,751 pts	41.6 (6.9) in 713 pts	39.3 (8.2) in 1,038 pts
No. ≥102 cm/40.2 inches (%) in men†		370 (51.5)	
No. ≥88 cm/34.6 inches (%) in women†			748 (71.6)
Neck circumference:			
Mean inches (SD)	15.1 (2.5) in 1,749 pts	16.6 (1.9) in 712 pts	14.1 (2.4) in 1,037 pts
No. ≥42.5 cm/16.73 inches (%) in men†		329 (45.8)	
No. ≥36.5 cm/14.02 inches (%) in women†			403 (38.6)

* Responses are not mutually exclusive.
† Threshold cut point as a marker of obesity.

prevalence varied considerably depending upon NP definition used. As expected, prevalence was consistently higher when using NPI33 compared to NUP90.[15] Importantly, observed differences in NP prevalence were much higher among women than men. The difference among men was not as prevalent as observed in the Krimpen Study, possibly due to the wider age range included (≥30 years versus 50—78 years in the Krimpen Study), as age is known to affect NPI,[24] and differences in the denominator for NUP used between studies. The NUP90 definition yielded individuals with higher mean urinary volumes, including maximum daytime, nighttime and 24-hour volume, and FUSP measures when compared to the NPI33.

Key insight of the characteristics of men and women with a lesser tendency toward nocturia was gleaned from comparing respondents with no NP. In both sexes, irrespective of NP definition, those without NP had nocturia around twice per night on average in comparison with those with NP whose nocturia severity was closer to 3 times per night. "No NP" respondents had less nocturia than NP respondents due to much lower nocturnal urine production. These findings may provide clues to nocturia treatment in emphasizing factors influencing urine production in comparison to factors influencing bladder capacity. As NP is prevalent in both sexes with clinically relevant nocturia, providers should address the causative, potentially serious underlying medical and urological pathophysiological conditions which contribute to this highly prevalent and often bothersome lower urinary tract symptom.

Table 2. *Demographic and bladder diary data by NP subgroups, NP definition and sex (3-day summary) in 718 men*

	Idiopathic NP		NPOAB		NPBOO		NPCom		No NP	
Men	NPI33 (29 pts)	NUP90 (12 pts)	NPI33 (36 pts)	NUP90 (23 pts)	NPI33 (227 pts)	NUP90 (173 pts)	NPI33 (37 pts)	NUP90 (27 pts)	NPI33 (389 pts)	NUP90 (483 pts)
Median yrs age (IQR: 25%–75%)	52.0 (39.0–62.0)	50.0 (35.0–62.5)	63.5 (54.5–71.5)	62.0 (54.0–68.0)	61.0 (53.0–69.0)	61.0 (55.0–68.0)	64.0 (56.0–71.0)	63.0 (49.0–67.0)	56.0 (44.0–64.0)	57.0 (44.0–65.0)
No. body mass index ≥30 kg/m^2 (%)	9 (31.0)	3 (25.0)	17 (47.2)	11 (47.8)	111 (48.9)	90 (52.0)	16 (43.2)	12 (44.4)	134 (34.4)	171 (35.4)
Median waist circumference (IQR: 25%–75%)	39.0 (36.0–45.0)	41.0 (35.3–44.8)	42.0 (37.8–47.6)	42.0 (37.5–48.0)	42.3 (38.0–47.0) in 224 pts	43.0 (39.0–48.0) in 171 pts	42.0 (39.0–45.0)	42.0 (38.5–46.0)	40.0 (36.0–44.0) in 387 pts	40.0 (36.0–44.0) in 480 pts
Median hrs slept (IQR: 25%–75%)	8.4 (8.1–9.3)	8.3 (7.2–9.2)	8.3 (7.7–9.5)	7.6 (7.0–9.0)	8.5 (7.8–9.4)	8.0 (7.4–9.0)	9.1 (7.8–9.7)	8.0 (7.4–9.0)	7.8 (7.0–8.4)	8.1 (7.3–8.9)
Median ml/hr NUP (IQR: 25%–75%)	79.6 (49.8–85.5)	120.4 (106.4–147.87)	79.4 (60.8–127.7)	117.7 (106.9–151.1)	92.4 (68.4–121.9)	114.0 (98.8–133.6)	89.4 (60.6–119.8)	119.8 (106.0–138.9)	55.2 (37.8–81.5)	55.0 (38.4–69.6)
Median nighttime voids (IQR: 25%–75%)	2.3 (1.3–3.0)	2.5 (2.0–3.0)	3.0 (2.5–4.0)	3.0 (2.7–4.0)	3.3 (2.7–4.0)	3.3 (2.3–4.0)	2.3 (2.0–3.0)	2.3 (2.0–3.3)	2.0 (1.3–2.7)	2.0 (1.3–3.0)
Median max daytime vol (IQR: 25%–75%)	266.7 (216.7–358.3)	416.7 (336.7–558.3)	263.3 (209.2–320.8)	350.0 (291.7–416.7)	266.7 (200.0–350.0)	333.3 (277.3–403.3)	325.0 (266.7–400.0)	425.0 (316.7–533.3)	313.3 (233.3–391.7)	266.2 (200.0–350.0)
Median max nighttime vol (IQR: 25%–75%)	346.7 (300.0–483.3)	583.3 (450.0–708.3)	331.7 (283.3–470.8)	450.0 (383.3–566.7)	350.0 (266.7–450.0)	408.3 (341.7–541.7)	453.0 (358.3–550.0)	550.0 (453.0–700.0)	293.3 (216.7–400.0)	273.3 (206.7–358.3)
Median 24-hr vol (IQR: 25%–75%)	1,575.0 (1,305.0–1,950.0)	2,707.5 (2,188.3–3,141.7)	1,723.3 (1,186.7–2,370.0)	2,691.7 (2,256.7–2,958.3)	1,841.7 (1,436.0–2,433.3)	2,471.3 (2,159.3–2,958.3)	2,011.7 (1,475.0–2,538.3)	2,660.3 (2,201.7–3,225.0)	1,753.3 (1,286.7–2,412.3)	1,480.0 (1,183.3–1,868.3)
Median hrs:mins FUSP (IQR: 25%–75%)	3:50 (2:48–5:20)	3:46 (2:11–4:08)	2:40 (2:02–3:11)	2:17 (1:30–3:07)	2:34 (1:55–3:46)	2:30 (1:39–3:43)	3:38 (2:29–5:07)	3:22 (2:23–4:40)	4:10 (2:51–6:05)	3:58 (2:38–5:55)
Median FUSP vol (IQR: 25%–75%)	300.0 (241.7–366.7)	395.8 (343.3–625.0)	250.0 (200.0–358.3)	383.3 (275.0–433.3)	258.3 (183.3–383.3)	321.7 (241.7–450.0)	408.3 (283.3–495.0)	475.0 (366.7–575.0)	250.0 (175.4–362.5)	233.3 (166.7–325.0) in 482 pts
Median NI (IQR: 25%–75%)	1.6 (1.2–2.2)	1.7 (1.5–2.5)	2.2 (1.7–2.8)	2.2 (1.9–3.1)	2.3 (1.9–2.8)	2.3 (1.8–2.8)	1.8 (1.6–2.1)	1.7 (1.5–2.5)	1.3 (1.0–1.7)	1.5 (1.0–1.9)
No. NI ≥1.5 (%)	17 (58.6)	9 (75.0)	34 (94.4)	22 (95.7)	208 (91.6)	150 (86.7)	29 (78.4)	20 (74.1)	143 (36.8)	230 (47.6)
No. nocturia bother ≥somewhat (%)	11 (37.9)	4 (33.3)	14 (38.9)	6 (26.1)	158 (69.6)	123 (71.1)	16 (43.2)	12 (44.4)	206 (53.0)	260 (53.8)

NPI33 is the most commonly used NP definition,[14] traditionally being used among aged 65+ years, with lower thresholds proposed for younger than 65 years, such as NPI20 for younger individuals and 20%–33% for middle-aged adults.[1,27,28] However, these age categories and NPI thresholds have not been validated[1] and were not used in this study. The use of these lower NPI thresholds for individuals aged <65 years would have resulted in even higher prevalence estimates of NP than reported, given that the study sample included adults aged 30+ years.

While NUP90 was used as a definition for NP, this measure was developed in men and the rate of NUP in women is not well understood. However, in the present study average NUP/hour was relatively similar across men and women. The Krimpen Study calculated NUP90 based on a standard 5 hours of sleep, while our study calculated NUP90 based on actual hours slept (prorated per van Mastrigt and Eijskoot[22] description if the last void was greater than 30 minutes before bed), which varied from individual to individual. The average sleep duration for both men and women in this study was approximately 8 hours (range of medians across NP definitions and subgroups, men: 7.6 to 9.1; women: 8.1 to 8.7).

Additional definitions of NP have been proposed in the literature, including the use of the NI >1.5.[12] Baines et al compared various definitions of NP and found that the NI >1.5 was associated with a relatively high sensitivity and specificity compared to other measures, and suggested that NI >1.5 may be more appropriate in women.[16] Our study found that average NI exceeded the 1.5 threshold for both sexes for all NP subgroups (defined using NUP90 and NPI33), and either met or nearly met the 1.5 threshold for the No NP group in men and women. These findings indicate the relative differences between NP definitions and highlight the importance of using 1 generally accepted measure for future research.

As this was a U.S.-based study, NP prevalence estimates may not be generalizable to other countries. However, the sampling methods used support the assumption that the findings are representative of U.S. adults aged 30 years and older. All comorbid medical conditions and responses to inclusion/exclusion criteria were self-reported by participants, and thus may have inaccuracies. Despite the large baseline sample size, the sample sizes of some age- and gender-stratified subgroups of NP requiring a 3-day bladder diary were low, decreasing the associated precision of those prevalence estimates. Further, this study is limited in that liquid intake volumes were not collected. Future research should seek to determine normal

Table 3. *Demographic and bladder diary data by NP subgroups, NP definition and sex (3-day summary) in 1,045 women*

	Idiopathic NP		NPOAB		NPCom		No NP	
Women	NPI33 (82 pts)	NUP90 (32 pts)	NPI33 (363 pts)	NUP90 (203 pts)	NPI33 (54 pts)	NUP90 (36 pts)	NPI33 (546 pts)	NUP90 (774 pts)
Median yrs age (IQR: 25%—75%)	49.5 (38.0—63.0)	54.0 (39.5—59.5)	61.0 (51.0—70.0)	60.0 (50.0—68.0)	55.0 (43.0—67.0)	57.5 (48.0—67.0)	55.0 (42.0—64.0)	56.0 (43.0—66.0)
No. body mass index $\geq$30 kg/m^2 (%)	27 (32.9)	11 (34.4)	174 (47.9)	105 (51.7)	28 (51.9)	22 (61.1)	235 (43.0)	326 (42.1)
Median inches waist circumference (IQR: 25%—75%)	37.0 (32.0—40.0) in 81 pts	36.0 (31.0—42.0)	40.0 (35.0—45.0)	40.0 (35.0—46.0) in 202 pts	42.0 (36.0—46.0) in 53 pts	41.0 (37.0—47.5) in 35 pts	38.5 (33.0—43.5) in 541 pts	38.5 (33.3—43.5) in 769 pts
Median hrs slept (IQR: 25%—75%)	8.6 (7.9—9.2)	8.4 (7.3—9.2)	8.7 (7.9—9.4)	8.1 (7.3—9.0)	8.7 (7.6—9.2)	8.2 (7.4—9.0)	8.0 (7.1—8.8)	8.3 (7.6—9.2)
Median ml/hr NUP (IQR: 25%—75%)	70.5 (58.0—86.5)	112.8 (101.2—130.0)	84.6 (59.1—114.8)	118.2 (101.1—143.8)	91.3 (66.4—125.9)	122.6 (95.6—137.8)	50.8 (33.0—70.6)	53.7 (37.3—69.7)
Median nighttime voids (IQR: 25%—75%)	2.7 (2.0—3.0)	2.7 (1.7—3.3)	3.0 (2.3—3.7)	3.3 (2.3—4.0)	2.8 (2.3—3.7)	2.8 (2.3—3.7)	2.0 (1.3—2.7)	2.3 (1.7—3.0)
Median max daytime vol (IQR: 25%—75%)	246.7 (200.0—341.7)	427.5 (300.0—533.3)	265.0 (200.0—335.0)	335.0 (273.3—433.3)	300.0 (225.0—350.0)	362.5 (283.3—441.7)	300.0 (226.0—400.0)	259.2 (200.0—341.7)
Median max nighttime vol (IQR: 25%—75%)	353.3 (266.7—483.3)	533.3 (416.7—708.3)	350.0 (266.7—466.7)	450.0 (361.7—566.7)	387.5 (271.7—550.0)	518.3 (425.0—572.7)	275.0 (200.0—358.3)	275.0 (208.3—336.7)
Median 24-hr vol (IQR: 25%—75%)	1,441.7 (1,058.3 —1,908.3)	2,498.3 (2,037.5—3,087.5)	1,716.7 (1,258.3—2,216.7)	2,455.0 (1,991.7—2,910.0)	1,891.7 (1,239.3—2,410.0)	2,439.2 (2,104.2—2,883.3)	1,685.8 (1,219.7—2,250.0)	1,442.5 (1,108.3—1,873.3)
Median hrs:mins FUSP (IQR: 25%—75%)	3:34 (2:20—5:30)	3:06 (1:42—4:22	2:45 (1:52—3:55)	2:30 (1:42—3:23)	2:50 (1:58—3:59)	2:21 (1:42—3:26)	4:07 (2:37—5:53)	3:53 (2:30—5:40)
Median FUSP vol (IQR: 25%—75%)	266.7 (175.0—366.7)	354.2 (263.3—591.7)	266.7 (170.0—366.7)	336.7 (258.3—488.3)	270.8 (216.7—400.0)	320.8 (265.0—465.0)	225.0 (159.2—325.0)	216.7 (150.0—300.0)
Median NI (IQR: 25%—75%)	1.7 (1.4—2.1)	1.6 (1.3—2.3)	2.1 (1.7—2.5)	2.2 (1.8—2.6)	1.9 (1.6—2.5)	2.1 (1.6—2.5)	1.3 (1.0—1.7)	1.5 (1.0—1.9)
No. NI $\geq$1.5 (%)	56 (68.3)	19 (59.4)	313 (86.2)	176 (86.7)	44 (81.5)	31 (86.1)	181 (33.2)	368 (47.5)
No. nocturia bother $\geq$somewhat (%)	41 (50.0)	15 (46.9)	245 (67.5)	134 (66.0)	26 (48.1)	17 (47.2)	361 (66.1)	507 (65.5)

Table 4. *Prevalence of LUTS ≥sometimes by NP subgroup (based on NPI33 definition)*

	Men (718 pts)					Women (1,045 pts)			
Symptom (%)	Idiopathic NP (29 pts)	NPOAB (36 pts)	NPBOO (227 pts)	NPCom (37 pts)	No NP (389 pts)	Idiopathic NP (82 pts)	NPOAB (363 pts)	NPCom (54 pts)	No NP (546 pts)
No. frequent urination (%)	11 (37.9)	21 (58.3)	196 (86.3)	12 (32.4)	225 (57.8)	21 (25.6)	271 (74.7)	28 (51.9)	327 (59.9)
No. daytime urination ≥9 (%)	2 (6.9)	5 (13.9)	49 (21.6)	1 (2.7)	77 (19.8)	10 (12.2)	99 (27.3)	9 (16.7)	165 (30.2)
No. nocturia ≥2 (%)	21 (72.4)	32 (88.9)	221 (97.4)	28 (75.7)	297 (76.3)	62 (75.6)	341 (93.9)	50 (92.6)	430 (78.8)
No. feeling bladder not empty (%)	1 (3.4)	10 (27.8)	141 (62.1)	4 (10.8)	144 (37.0)	11 (13.4)	181 (49.9)	12 (22.2)	230 (42.1)
No. terminal dribble (%)	8 (27.6)	17 (47.2)	192 (84.6)	12 (32.4)	232 (59.6)	22 (26.8)	240 (66.1)	25 (46.3)	273 (50.0)
No. urgency (%)	0 (0.0)	21 (58.3)	141 (62.1)	0 (0.0)	160 (41.1)	0 (0.0)	271 (74.7)	0 (0.0)	289 (52.9)
No. hesitancy (%)	5 (17.2)	4 (11.1)	106 (46.7)	1 (2.7)	124 (31.9)	9 (11.0)	87 (24.0)	8 (14.8)	114 (20.9)
No. intermittency (%)	1 (3.4)	1 (2.8)	116 (51.1)	1 (2.7)	114 (29.3)	5 (6.1)	94 (25.9)	11 (20.4)	130 (23.8)
No. straining (%)	0 (0.0)	0 (0.0)	47 (20.7)	0 (0.0)	47 (12.1)	1 (1.2)	47 (12.9)	4 (7.4)	68 (12.5)
No. weak stream (%)	0 (0.0)	4 (11.1)	132 (58.1)	3 (8.1)	121 (31.1)	4 (4.9)	94 (25.9)	7 (13.0)	102 (18.7)
No. split stream (%)	1 (3.4)	1 (2.8)	85 (37.4)	3 (8.1)	93 (23.9)	3 (3.7)	71 (19.6)	4 (7.4)	87 (15.9)
No. urgency with fear of leaking (%)	0 (0.0)	4 (11.1)	95 (41.9)	0 (0.0)	105 (27.0)	0 (0.0)	258 (71.1)	0 (0.0)	231 (42.3)
No. bladder pain (%)	0 (0.0)	0 (0.0)	33 (14.5)	0 (0.0)	29 (7.5)	3 (3.7)	61 (16.8)	1 (1.9)	71 (13.0)
No. dysuria (%)	0 (0.0)	0 (0.0)	23 (10.1)	0 (0.0)	17 (4.4)	1 (1.2)	29 (8.0)	3 (5.6)	21 (3.8)
No. incontinence (%):									
Post-micturition	6 (20.7)	11 (30.6)	106 (46.7)	4 (10.8)	132 (33.9)	6 (7.3)	133 (36.6)	4 (7.4)	150 (27.5)
UUI	0 (0.0)	6 (16.7)	85 (37.4)	0 (0.0)	72 (18.5)	0 (0.0)	227 (62.5)	0 (0.0)	203 (37.2)
SUI (sneezing, coughing etc)	0 (0.0)	0 (0.0)	16 (7.0)	0 (0.0)	15 (3.9)	10 (12.2)	207 (57.0)	12 (22.2)	209 (38.3)
SUI (physical activities)	0 (0.0)	0 (0.0)	21 (9.3)	0 (0.0)	19 (4.9)	0 (0.0)	70 (19.3)	0 (0.0)	65 (11.9)
Nocturnal enuresis	0 (0.0)	0 (0.0)	15 (6.6)	0 (0.0)	17 (4.4)	2 (2.4)	130 (35.8)	5 (9.3)	125 (22.9)
Leak during sexual activity	0 (0.0)	0 (0.0)	6 (2.6)	0 (0.0)	19 (4.9)	2 (2.4)	32 (8.8)	0 (0.0)	37 (6.8)
Leak for no reason	0 (0.0)	0 (0.0)	2 2 (9.7)	1 (2.7)	26 (6.7)	0 (0.0)	86 (23.7)	0 (0.0)	87 (15.9)

SUI, stress urinary incontinence. *UUI*, urgency urinary incontinence.
Denominator for percent is based on the full unweighted population of those with 3 complete days of bladder diary data.

ranges of urine production in both adult sexes by age and weight, and using standard definitions of NP.

CONCLUSIONS

This first population-based study of NP prevalence among both men and women found NP is common in the U.S. Prevalence estimates were higher for all categories of NP using the NPI33 definition compared to NUP90 for both sexes, but the difference was considerably more pronounced among women, indicating a potential area of unmet need and future research. In the absence of an international consensus on the definition used to calculate NP, both measures should be reported in future studies to indicate the variability in NP identification associated with NUP90 and NPI33.

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REFERENCES

1. Hashim H, Blanker MH, Drake MJ et al: International Continence Society (ICS) report on the terminology for nocturia and nocturnal lower urinary tract function. Neurourol Urodyn 2019; **38:** 499.
2. D'Ancona C, Haylen B, Oelke M et al: The International Continence Society (ICS) report on the terminology for adult male lower urinary tract and pelvic floor symptoms and dysfunction. Neurourol Urodyn 2019; **38:** 433.
3. Abrams P, Cardozo L, Fall M et al: The standardisation of terminology of lower urinary tract function: report from the Standardisation Subcommittee of the International Continence Society. Neurourol Urodyn 2002; **21:** 167.
4. Schmidbauer J, Temml C, Schatzl G et al: Risk factors for urinary incontinence in both sexes. Analysis of a health screening project. Eur Urol 2001; **39:** 565.
5. Asplund R: Nocturia in relation to sleep, somatic diseases and medical treatment in the elderly. BJU Int 2002; **90:** 533.
6. Cornu JN, Abrams P, Chapple CR et al: A contemporary assessment of nocturia: definition, epidemiology, pathophysiology, and management—a systematic review and meta-analysis. Eur Urol 2012; **62:** 877.
7. Yoshimura K, Terada N, Matsui Y et al: Prevalence of and risk factors for nocturia: analysis of a health screening program. Int J Urol 2004; **11:** 282.
8. Weiss JP: Nocturia: focus on etiology and consequences. Rev Urol 2012; **14:** 48.
9. Chang SC, Lin AT, Chen KK et al: Multifactorial nature of male nocturia. Urology 2006; **67:** 541.
10. Asplund R: The nocturnal polyuria syndrome (NPS). Gen Pharmacol 1995; **26:** 1203.
11. Homma Y, Yamaguchi O, Kageyama S et al: Nocturia in the adult: classification on the basis of largest voided volume and nocturnal urine production. J Urol 2000; **163:** 777.
12. Burton C, Weiss JP, Parsons M et al: Reference values for the nocturnal bladder capacity index. Neurourol Urodyn 2011; **30:** 52.
13. Blanker MH, Bernsen RM, Bosch JL et al: Relation between nocturnal voiding frequency and nocturnal urine production in older men:a population-based study. Urology 2002; **60:** 612.
14. Hofmeester I, Kollen BJ, Steffens MG et al: Impact of the International Continence Society (ICS) report on the standardisation of terminology in nocturia on the quality of reports on nocturia and nocturnal polyuria: a systematic review. BJU Int 2015; **115:** 520.
15. van Doorn B, Blanker MH, Kok ET et al: Prevalence, incidence, and resolution of nocturnal polyuria in a longitudinal community-based study in older men: the Krimpen Study. Eur Urol 2013; **63:** 542.
16. Baines G, Da Silva AS, Cardozo L et al: Defining nocturnal polyuria in women. Neurourol Urodyn 2021; **40:** 265.
17. Weiss JP, Bosch JLHR, Chapple CR et al: The Prevalence of Nocturnal Polyuria in the United States: Results from the Epidemiology of Nocturnal Polyuria Study. Eur Urol Focus 2022; doi: 10.1016/j.euf.2021.12.016.
18. Coyne KS, Barsdorf AI, Thompson C et al: Moving towards a comprehensive assessment of lower urinary tract symptoms (LUTS). Neurourol Urodyn 2012; **31:** 448.
19. Barry MJ, Fowler FJ Jr, O'Leary MP et al: The American Urological Association Symptom Index for benign prostatic hyperplasia. J Urol 1992; **148:** 1549.
20. Dmochowski RR, Sanders SW, Appell RA et al: Bladder-health diaries: an assessment of 3-day vs 7-day entries. BJU Int 2005; **96:** 1049.
21. U.S. Census Bureau: 2017 American Community Survey Single-Year Estimates, 2018. Available at https://www.census.gov/newsroom/press-kits/2018/acs-1year.html.
22. van Mastrigt R and Eijskoot F: Analysis of voided urine volumes measured using a small electronic pocket balance. Scand J Urol Nephrol 1996; **30:** 257.
23. Weiss JP, Blaivas JG, Stember DS et al: Nocturia in adults: etiology and classification. Neurourol Urodyn 1998; **17:** 467.
24. Van Kerrebroeck P, Abrams P, Chaikin D et al: The standardization of terminology in nocturia: report from the standardization subcommittee of the International Continence Society. BJU Int, suppl., 2002; **90:** 11.
25. Axcrona K, Aaltomaa S, Da Silva CM et al: Androgen deprivation therapy for volume reduction, lower urinary tract symptom relief and quality of life improvement in patients with prostate cancer: degarelix vs goserelin plus bicalutamide. BJU Int 2012; **110:** 1721.
26. Roehrborn CG, Siami P, Barkin J et al: The effects of dutasteride, tamsulosin and combination therapy on lower urinary tract symptoms in men with benign prostatic hyperplasia and prostatic enlargement: 2-year results from the CombAT study. J Urol 2008; **179:** 616.
27. van Haarst EP and Bosch JR: A cutoff value based on analysis of a reference population decreases overestimation of the prevalence of nocturnal polyuria. J Urol 2012; **188:** 869.
28. Zumrutbas AE, Bozkurt AI, Alkis O et al: The prevalence of nocturia and nocturnal polyuria: can new cutoff values be suggested according to age and sex? Int Neurourol J 2016; **20:** 304.

EDITORIAL COMMENT

Nocturnal polyuria (NP) is widely implicated as the most common overall cause of nocturia in adults, but current understanding of NP epidemiology is largely derived from prior cohorts of older men. The EpiNP (Epidemiology of Nocturnal Polyuria) Study is the first population-based prevalence study of NP to enroll both sexes and was also designed as representative of the U.S. general population based on race and age. This article details bladder diary outcomes from EpiNP respondents, allowing for further characterization of nocturia across key NP subgroups, thus providing valuable clinical context to these data.

Comparing all NP subgroups, the greatest nocturia severity was identified among respondents with concurrent symptoms of overactive bladder (OAB) or bladder outlet obstruction (BOO). This finding underscores the shortcomings of traditional lower urinary tract pharmacotherapies for nocturia, which are more often of statistical than clinical significance,[1] while also highlighting the importance of emerging data to suggest that nocturia patients with OAB or BOO (with or without NP) may benefit from interventions targeting nocturnal urine production.[2] Additionally, this study affirms that NP can often present in both sexes in the absence of OAB or BOO, either attributable to concurrent urine volume-promoting medical comorbidities or idiopathic. Effective identification of these distinct NP subgroups is highly relevant to the clinical management of nocturia, given that they follow a treatment algorithm markedly different from OAB/BOO.[3] The present data also reveal greater variability in the prevalence of NP in women versus men across different definitions of NP, emphasizing the urgent need for more research on the appropriateness of current terminology and management standards for nocturia in women.

Notwithstanding the direct commercial interests of the sponsoring/funding organizations in antidiuretic replacement therapy, this is a methodologically sound survey which amassed an unparalleled volume of voiding diary data, most importantly with purposeful inclusion of groups traditionally underrepresented in research on this pervasive condition.

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REFERENCES

1. Monaghan TF, Weiss JP, Everaert K et al: Pharmacologic management of nocturnal polyuria: a contemporary assessment of efficacy, safety, and progress toward individualized treatment. Ther Adv Urol 2021; **13:** 1756287220988438.
2. Epstein MR, Monaghan T and Weiss JP: Etiology of nocturia response in men with diminished bladder capacity. Neurourol Urodyn 2019; **38:** 215.
3. Everaert K, Herve F, Bosch R et al: International Continence Society consensus on the diagnosis and treatment of nocturia. Neurourol Urodyn 2019; **38:** 478.