

Smoking and Bladder Symptoms in Women

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OBJECTIVE: To estimate the relation of smoking status and smoking intensity with bladder symptoms.

METHODS: Questionnaires were mailed to 3,000 women (aged 18–79 years) randomly identified from the Finnish Population Register. Case definitions for stress urinary incontinence (SUI), urgency, and urgency urinary incontinence (UUI) were “often” or “always” based on

reported occurrence (never, rarely, often, always). Case definitions for urinary frequency were based on reporting of longest voiding interval as less than 2 hours and for nocturia reporting of at least two voids per night. Potential confounders included comorbidities, medications, sociodemographic, lifestyle, and reproductive factors.

RESULTS: Responses totaled 2,002 (67.0%). Frequency was reported by 7.1%, nocturia 12.6%, SUI 11.2%, urgency 9.7%, and UUI 3.1%. In the multivariable analyses, smoking was associated with urgency (odds ratio [OR] 2.7, 95% confidence interval [CI] 1.7–4.2 for current and OR 1.8, CI 1.2–2.9 for former compared with never smokers) and frequency (OR 3.0, CI 1.8–5.0 for current and OR 1.7, CI 1.0–3.1 for former smokers) but not with nocturia and SUI. Adjusted prevalence differences between never and current smokers were 6.0% (3.0–9.1%) for urgency and 6.0% (3.3–8.7%) for frequency. Similarly, current heavy (compared with light) smoking was associated with additional risk of urgency (OR 2.1, CI 1.1–3.9) and frequency (OR 2.2, CI 1.2–4.3).

CONCLUSION: Urgency and frequency are approximately three times more common among current than never smokers. Parallel associations for urgency and frequency with smoking intensity suggest a dose–response relationship. Nocturia and SUI are not associated with smoking. These results suggest an additional rationale for smoking cessation in women seeking medical attention for bladder symptoms and highlight the diversity between such symptoms.

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Earlier studies have suggested that bladder symptoms (urinary frequency, nocturia, urinary incontinence [UI], and urinary urgency) are the most common and most bothersome urinary symptoms in women.¹ They are associated with increased risk of comorbidities and quality-of-life impairment.² Because bladder symptoms are more common in the older individuals, the prevalence of these symptoms will likely increase as the population ages.³

Additional tables are available in the Appendix online at <http://links.lww.com/AOG/A250>.

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Despite increasing public awareness of smoking as a major source of morbidity and mortality and health policy changes to reduce smoking rates, the number of smokers worldwide has increased.⁴ Now nearly 250 million women in the world are daily smokers with 22% of women in high-resource countries and 9% of women in low- and middle-resource countries.⁴ Although smoking increases illness burden for many conditions, the relation between smoking and lower urinary tract symptoms remains unclear.^{2,5} Earlier studies have been inconsistent, perhaps as a result of failing to distinguish among UI types or by analyzing all urinary symptoms as a single cluster. Because various bladder symptoms probably have different etiologies,⁵⁻⁷ combining them may have obscured important associations.

We estimated the effect of smoking status and intensity on frequency, nocturia, stress urinary incontinence (SUI), urgency, and urge urinary incontinence (UUI) in a population-based cohort of women aged 18–79 years.

MATERIALS AND METHODS

The Finnish National Nocturia and Overactive Bladder Study aims to estimate the prevalence, natural history, effect, and risk factors for urinary symptoms at the population level. Detailed study procedures have been published.⁸⁻¹⁰ Briefly, in 2003–2004, questionnaires were mailed to 3,000 women randomly identified from the Finnish Population Register. Stratification by age was used in subject selection with oversampling of younger age groups to ensure an adequate number of individuals with bladder symptoms in each age band. The questionnaires elicited information on smoking and bladder symptoms. Furthermore, information on numerous conditions and medications as well as sociodemographic, anthropometric, lifestyle, and reproductive factors was assessed. Exemption from ethical review was granted by the ethics committee of the Pirkanmaa Hospital District (Tampere, Finland) as is permitted in Finland. Strengthening the Reporting of Observational Studies in Epidemiology recommendations were followed.¹¹

In the primary analyses, subjects were classified as never, former, or current smokers by questionnaire: “Have you ever smoked?” (yes or no) and “Do you still smoke?” (yes or no). In the secondary analyses, current smokers were classified by smoking intensity: “How many cigarettes do you smoke per day?” (scale: 1–10 cigarettes per day, 11–20 cigarettes per day, and more than 20 cigarettes per day). Information on bladder symptoms was collected using the Danish Prostatic Symptom Score,¹² with an additional

nocturia question from the American Urological Association Symptom Index¹³ (Table 1 in the Appendix, available online at <http://links.lww.com/AOG/A250>). Women reporting SUI, urgency, and UUI to occur often or always were defined as having the disorder. Frequency was defined as the longest interval between each urination reported as less than 2 hours and nocturia as at least two voids per night (Table 1 in the Appendix, <http://links.lww.com/AOG/A250>). Earlier findings support the use of these cutoff points.^{8,9}

In the analyses, unconditional logistic regression was used separately for each bladder symptom with presence of the bladder symptom as the outcome. All confidence intervals (CIs) were likelihood-based.¹⁴ Analyses were performed with SPSS 16.0.1. Confidence Interval Analysis 2.0.0 software was used for calculating age-standardized prevalence rates with age standardization based on the population structure of Finland in 2004.

Information on self-reported physician-diagnosed comorbidity (33 conditions) (Box 1 in the Appendix, <http://links.lww.com/AOG/A250>), regular use of prescribed medication (28 groups according to the Anatomical Therapeutic Chemical classification system, which divides drugs into different groups according to the organ or system that they act, their therapeutic and chemical characteristics, or both¹⁵) (Table 2 in the Appendix, <http://links.lww.com/AOG/A250>), sociodemographic factors (marital status, education, employment, urbanity), body mass index (BMI [calculated as weight (kg)]/[height (m)²]; less than 25, 25.0–30; 30 or greater), coffee (cups per day) and alcohol (grams per day) consumption, and female reproductive factors (parity, postpartum period, menopause, menopausal hormone therapy, hysterectomy) were treated as potential confounders.^{10,16} The vast majority of information on variables was collected by questions modified from earlier studies conducted by the Finnish National Public Health Institute. Furthermore, pregnancy information was based on the questionnaire and the Finnish Population Register, which also provided information on parity and urbanity. Age, BMI, coffee consumption, parity, and alcohol were used as continuous variables. Confounder scores were used to provide summary information about multiple potential confounders. It was used in the multivariate analysis to control for confounding by adjustment.¹⁷ Confounder scores were calculated based on comorbidity and medication among subjects responding on all symptoms. Age-adjusted odds ratios (ORs) with CIs then were calculated for each comorbidity and medication. All factors associated with a symptom were used to construct the confounder score formulas (where OR_{rf} is the OR for a risk factor):



$$CS = \sum_{i=1}^n (OR_{rf} - 1)_n \text{ AND only if } P < .05 \text{ for } OR_{rf}$$

where CS indicates confounder score.

Separately for each symptom, analyses were performed for smoking status and smoking intensity (Tables 3 and 4 in the Appendix, <http://links.lww.com/AOG/A250>). First, ORs were calculated for each symptom with adjustment for age (age-adjusted). Second, multivariable analyses with adjustment for confounders were performed (multivariable). Information on age, confounder scores, body mass index, coffee consumption, and alcohol consumption was available, respectively, for 100%, 100%, 97%, 95%, and 77% of women (basic analysis population). Moreover, information on each sociodemographic factor was available for more than 99% of women. Hence, information on every factor was well reported (except alcohol consumption, which was not significantly associated with either symptom). All factors associated ($P < .05$) with each symptom in the age-adjusted analyses were entered into the multivariable models as potential confounders. Finally, backward (stepwise) elimination techniques were used in logistic regression analysis to select variables for the final model of each symptom. At each step, the covariate that caused the smallest change in the exposure effect estimate (compared with the full model estimate) on deletion was removed (multivariable). The process was stopped when deletion of any of the remaining variables caused a relative change of more than 10% in the ORs for smoking.

In analysis for prevalence difference, binomial regression with identity link was used with adjustment for age group and pertinent confounder score. Analyses were performed with Stata 8.

RESULTS

Of the 3,000 women approached for the study, 2,002 (67.0%) participated; 11 were unavailable and 114 were excluded because of pregnancy, puerperium, or urinary tract infection (Fig. 1). Of the participants, 1,790 (94.8%) answered all bladder symptom and smoking status questions (basic analysis population for age-adjusted smoking status analyses). Of the women, 24.1% (95% CI 22.1–26.2) were former and 23.2% (21.2–25.1) current smokers. For more characteristics, including symptom prevalence estimates, see Table 1 and Figure 2.

In the age-adjusted analyses, all bladder symptoms (except nocturia, which bordered on significance) were associated with smoking (data not shown). In the multivariable analyses (never smokers

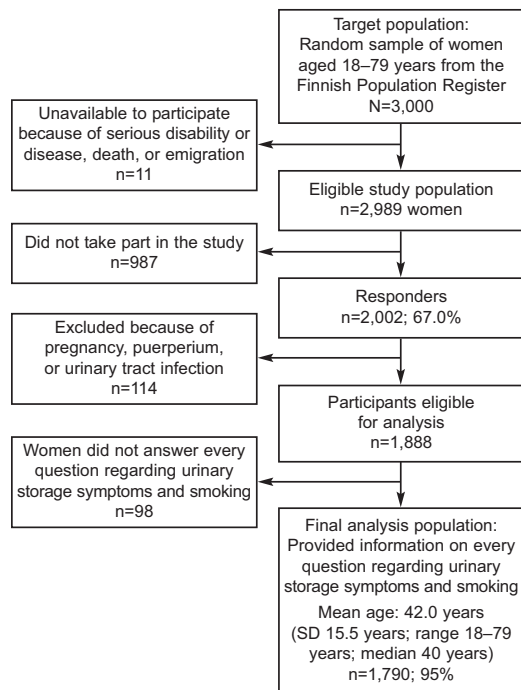


Fig. 1. Study flow chart showing the final population of women included in the analysis. SD, standard deviation.

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as reference), current smoking was associated with urgency (OR 2.7, CI 1.7–4.2) and frequency (OR 3.0, CI 1.8–5.0) but not with nocturia (OR 1.1, CI 0.7–1.8) or SUI (OR 0.8, CI 0.5–1.3) or UUI (OR 1.5, CI 0.6–3.8). Consistent but weaker associations with urgency and frequency were also found for former smoking (Table 2). Absolute prevalence differences between never and current smokers were 6.0% (3.0–9.1%) for urgency and 6.0% (3.3–8.7%) for frequency (adjusted for age group and pertinent confounder score).

Similarly, in the smoking intensity analyses (light smoking as reference), heavy smoking was associated with urgency (OR 2.1, CI 1.1–3.9) and frequency (OR 2.2, CI 1.2–4.3) but not with nocturia (OR 1.4, CI 0.6–2.9), SUI (OR 1.3, CI 0.6–2.8), or UUI (OR 1.7, CI 0.3–8.5) (Table 3).

DISCUSSION

In our large, population-representative study of women with a wide range of ages, current and former smoking were associated with urgency and frequency but not with nocturia or SUI. In a similar fashion, heavy smoking was associated with urgency and frequency but not with the other symptoms. These results suggest an additional rationale for smoking cessation in women seeking medical attention for



Table 1. Age Distribution, Smoking, Prevalence of Bladder Symptoms, and Demographic Characteristics Among the 1,790 Women Included

Characteristic	Crude	Age-Standardized*	
		Prevalence	95% CI
Age groups (y)			
18–29	451 (25.2)		
30–39	443 (24.7)		
40–49	393 (22.0)		
50–59	199 (11.1)		
60–69	209 (11.7)		
70–79	95 (5.3)		
Smoking status ^{††}			
Never	874 (48.8)	52.7	50.4–55.0
Former	457 (25.5)	24.1	22.1–26.2
Current	459 (25.6)	23.2	21.2–25.1
Smoking intensity (cigarettes/d) ^{†§}			
Light smoking (1–10)	255 (57.2)	56.8	50.5–63.0
Heavy smoking (more than 10)	191 (42.8)	43.2	35.8–48.2
Bladder symptoms			
Frequency	113 (6.3)	7.1	5.7–8.4
Nocturia	176 (9.8)	12.6	10.8–14.4
Stress urinary incontinence	171 (9.6)	11.2	9.5–12.8
Urgency	153 (8.6)	9.7	8.2–11.3
Urgency urinary incontinence	41 (2.3)	3.1	2.1–4.1
Education			
Basic level	411 (23.2)	28.3	25.4–31.3
Vocational school	554 (31.2)	30.9	28.1–33.7
College	441 (24.8)	23.0	20.7–25.3
University	369 (20.8)	17.7	15.8–19.6
Employment			
Student	250 (14.1)	10.8	9.5–12.2
Employed	1,073 (60.6)	55.9	52.3–59.5
Unemployed	129 (7.3)	7.1	5.7–8.4
Retired	320 (18.1)	26.2	23.2–29.3
Marital status			
Never married	352 (19.7)	16.9	15.0–18.7
Married or living together	1,205 (67.5)	66.7	62.6–70.8
Divorced or separated	138 (7.7)	8.2	6.7–9.6
Widowed	89 (5.0)	8.3	6.5–10.0

CI, confidence interval.

Data are n (%) unless otherwise specified.

* Age standardization was performed using the age structure of Finland (beginning of 2004).

[†] No differences were found in smoking status or smoking intensity between women responding at different mailing rounds.

^{††} We also assessed snuff consumption. Because only one woman (0.1%) reported current use and 24 (1.4%) reported former use, we did not include it in further analyses. Snuff use was not associated with any bladder symptom.

[§] Of the current smokers, 97.5% provided information for smoking intensity. Two smoking-intensity groups (11–20 cigarettes/d and more than 20 cigarettes/d) were combined (more than 10 cigarettes/d; heavy smoking) as a result of very low prevalence of smoking more than 20 cigarettes per day (4.8% of the current smokers).

^{||} Information on education, employment, and marital status was available for 1,775 (99.2%), 1,772 (99.0%), and 1,784 (99.7%) women, respectively.

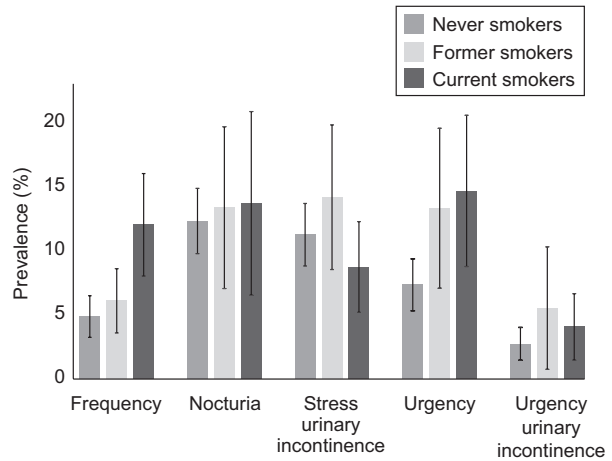


Fig. 2. Age-standardized prevalence of bladder symptoms among never, former, and current smokers. Error bars represent 95% confidence intervals.

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urinary storage symptoms and highlight the diversity between such symptoms. In analyses without adjustment for confounding, other significant associations for smoking with bladder symptoms were also found, highlighting the importance of appropriate analysis.

Despite substantial research interest in bladder symptoms, few studies have assessed the effect of smoking on these conditions. Earlier studies have focused on the association of smoking with UI (without distinguishing among subtypes) in women and

Table 2. Primary Analysis of the Study: Odds Ratios of Smoking Status for Bladder Symptoms in Multivariable Analyses*

	Smoking Status			P for Trend
	Never Smoker	Former Smoker	Current Smoker	
Frequency	1.0	1.7 (1.0–3.1)	3.0 (1.8–5.0)	<.001
Nocturia	1.0	1.0 (0.6–1.5)	1.1 (0.7–1.8)	.6
SUI	1.0	1.4 (0.9–2.1)	0.8 (0.5–1.3)	.6
Urgency	1.0	1.8 (1.2–2.9)	2.7 (1.7–4.2)	<.001
UUI	1.0	1.8 (0.8–4.3)	1.5 (0.6–3.8)	.4

SUI, stress urinary incontinence; UUI, urgency urinary incontinence.

Data are odds ratio or odds ratio (95% confidence interval) unless otherwise specified.

* Adjusted for identified confounders (frequency: frequency confounder score, coffee consumption, menopausal status, employment, and education; nocturia: age, nocturia confounder score, body mass index, parity, postpartum period, menopausal status, employment, and education; SUI: SUI confounder score, body mass index, parity, menopausal status, employment, and education; urgency: urgency confounder score, body mass index, menopausal status, and employment; UUI: age, UUI confounder score, coffee consumption, and parity [Table 3 in the Appendix, available online at <http://links.lww.com/AOG/A250>]).



Table 3. Secondary Analysis of the Study: Odds Ratios of Smoking Intensity for Bladder Symptoms in Multivariable Analyses*

	Smoking Intensity		P for Trend
	Light Smoking (1–10 Cigarettes/d)	Heavy Smoking (More than 10 Cigarettes/d)	
Frequency	1.0	2.2 (1.2–4.3)	.02
Nocturia	1.0	1.4 (0.6–2.9)	.4
SUI	1.0	1.3 (0.6–2.8)	.6
Urgency	1.0	2.1 (1.1–3.9)	.02
UUI	1.0	1.7 (0.3–8.5)	.5

SUI, stress urinary incontinence; UUI, urgency urinary incontinence. Data are odds ratio or odds ratio (95% confidence interval) unless otherwise specified.

* Also adjusted for identified confounders (frequency: frequency confounder score and education; nocturia: nocturia confounder score, and body mass index; SUI: age, SUI confounder score, and parity; urgency: urgency confounder score, and education; UUI: age, UUI confounder score, and body mass index [Table 4 in the Appendix, available online at <http://links.lww.com/AOG/A250>]).

composite lower urinary tract symptom scores (suggestive of benign prostatic hyperplasia) in men.^{2,5} Given the differing risk factors for SUI compared with UUI^{7,18} and for the various lower urinary tract symptoms symptoms,⁵ failure to accurately classify UI to separate individual symptoms may have masked associations, biased the results, or both. Importantly, no smoking cessation trials have assessed the effect on lower urinary tract symptoms of stopping tobacco use.

In our study, smoking was associated with urgency and frequency. Earlier results concur with our findings. In a prospective study among British women, smoking was a risk factor for the onset of an overactive bladder (defined as having either urgency, UUI, or a combination of these) but not for SUI.¹⁹ Furthermore, in a Finnish study among elderly people, urgency was associated with current (age-adjusted OR of 2.8, CI 1.4–5.3) and former (OR 1.6, CI 1.0–2.7) smoking when information on both genders was combined.²⁰ However, in this study, the association was not statistically significant in women, probably as a result of the small sample size ($n=531$; OR 2.5, CI 0.8–8.2). Concordant with our findings, smoking has been shown to be associated with increased day-to-night ratio of urine production (but not with nocturia in the multivariable analyses) among elderly men.²¹

We found no association of nocturia with smoking. Not all earlier results are consistent, although in a Swedish study,²² nocturia was more common among smokers, but Austrian²³ and Japanese²⁴ studies reported opposite findings. Several studies corroborate our results with no association of smoking with nocturia.^{21,25,26}

The results regarding smoking and female UI are inconsistent.² In our study, smoking was not related to SUI. In a Norwegian population-based study among women,⁶ no clear association of smoking with SUI was found (ORs ranging from 0.8 to 1.1 in different analyses). However, slightly higher (and statistically significant) estimates were found for mixed UI (ORs between 1.2 and 1.5) and UUI (ORs between 1.1 and 1.2). Furthermore, substantially stronger associations were found for heavy smoking and mixed UI; eg, those smoking more than 20 cigarettes per day had an OR of 2.4 (CI 1.6–3.6) compared with never smokers.⁶ In contrast to our findings, current smoking has been associated with SUI in several studies, yet none of these studies was population-based.^{27–30}

Smoking was not related to UUI in our analyses. There were some indications of increased UUI among smokers (eg, OR 1.5 for current smoking and 1.7 for heavy smoking), but the findings were not statistically significant. The point estimates could be regarded as clinically meaningful, but because of limited statistical power, we could not exclude the possibility of this association being the result of chance. There is a dire lack of studies on this topic. In the baseline analysis of a weight loss trial,³¹ ever smoking was associated with UUI (OR 1.7, CI 1.2–2.2) but not with SUI (effect size not reported). These results agree with our findings.

The strengths of the current study include a study population representative of the general population in numerous aspects,^{8,10,16} assessment of bladder symptoms with validated instruments, a high response proportion and completeness of questionnaires, likewise consideration of a large number of relevant factors and systematic control for confounding. Furthermore, our material was unaffected by the selection bias typical of clinic-based studies as a result of treatment-seeking (overrepresentation of severe symptoms and subjects with abundant healthcare service use).

This study has some limitations. No information on pack-years of smoking was available here. If the effect of smoking on bladder symptoms is cumulative, this may have caused misclassification bias attenuating a true effect. However, the effect of smoking on these symptoms may also be transient (eg, caused by nicotine-induced bladder contractility), which is plausible given that we found the effect of smoking status and intensity. Despite extensive adjustment for potential confounders, we were unable to adjust for deliver mode. This may not be a major limitation; a recent systematic review suggested that although short term any SUI is reduced with a cesarean delivery (compared with vaginal delivery), more severe symptoms



are equivalent by mode of birth.³² Regarding other bladder symptoms than SUI, there is a paucity of studies on the effect of delivery mode. Although the response proportion was high, nearly one-third did not participate and the number of women with UII was insufficient for precise analyses. Finally, the validity of self-report has not been established for all the characteristics we considered, and the cross-sectional study design precludes conclusions about causality. These results from the Finnish population of women may not be generalizable to all other groups.

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