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### Caffeine Intake and Risk of Urinary Incontinence Progression Among Women

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#### Abstract

**Objective**—To estimate the association between long-term caffeine intake and risk of urinary incontinence (UI) progression over 2 years among women with moderate UI.

**Methods**—We conducted a prospective cohort study in 21,564 women with moderate UI enrolled in the Nurses' Health Study and Nurses' Health Study II. Incontinence progression was identified from questionnaires during 2 years of follow-up. Baseline caffeine intake (ie, average intake during the past year) and change in caffeine intake during the 4 years prior to baseline were measured using food frequency questionnaires. Odds ratios (ORs) for incontinence progression according to caffeine intake were calculated for each cohort separately, and then for both cohorts combined.

**Results**—The percentage of women with UI progression was similar across categories of baseline level of caffeine intake and change in caffeine intake prior to baseline. For example, percentages were 21% versus 22% comparing 450 mg or more to less than 150 mg of caffeine per day (adjusted OR 0.87, 95% confidence interval [CI] 0.70-1.08). Comparing women with increased caffeine intake to those with stable caffeine intake, percentages with progression were 22% versus 20% (OR 1.08, 95% CI 0.95-1.22). Results were similar in separate analyses of urgency and stress UI.

**Conclusion**—Long-term caffeine intake over one year was not associated with risk of UI progression over 2 years among women with moderate incontinence, although we could not examine acute effects of caffeine. Improved understanding of the effect of caffeine on the bladder is needed to better advise women with incontinence about caffeine intake.

#### INTRODUCTION

Reducing caffeine intake is a common recommendation for women with urgency urinary incontinence (UI).(1, 2) This recommendation is based on evidence that caffeine promotes diuresis(3, 4) and increases detrusor pressure(5), which, together, might increase the likelihood of urgency-related involuntary urine loss. Yet, the available data on caffeine restriction and UI, derived from several small, short-term trials, are equivocal. For example,

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a randomized crossover study(6) and randomized trial(7), each including less than 100 adults with lower urinary tract symptoms, found no statistically significant improvement in UI with caffeine reduction over a period of 14 to 30 days. In addition, in a 3-week randomized trial of 224 women with UI(8), there was no significant difference in episodes of UI among women who received counseling about multiple behavioral UI management strategies, including caffeine intake, compared to those who received no intervention, although interpretation of these results is difficult since caffeine intake was one of several simultaneous interventions.

Clearly, there is still much to learn about the impact of caffeine on UI among women with incontinence, and the current literature has focused on the acute rather than any potential longer-term impacts of caffeine intake. Therefore, we estimated the association between long-term caffeine intake and risk of subsequent UI progression over 2 years among 21,564 women with moderate UI enrolled in the Nurses' Health Study (NHS) and NHSII.

#### MATERIALS AND METHODS

The NHS began in 1976 when 121,700 female nurses, aged 30-55 years, returned a mailed questionnaire about their health and lifestyle. In 1989, the NHSII was initiated when 116,430 female nurses aged 25-42 years returned a similar questionnaire. Participants provided informed consent by returning their questionnaires. In both cohorts, updated information has been collected using biennial questionnaires. During each questionnaire cycle, full-length questionnaires are sent in initial mailings, followed by abbreviated questionnaires to maximize participation. Questions about UI were included on the full-length 2002 and 2004 questionnaires in NHS and 2003 and 2005 questionnaires in NHSII. The Institutional Review Board of Brigham and Women's Hospital approved these studies.

For these analyses, we defined baseline as 2002 (NHS) and 2003 (NHSII) since both UI and caffeine intake were assessed on those questionnaires. After excluding deaths prior to baseline (N=15,152 NHS; 1053 NHSII) and non-response to the full-length questionnaire (N=24,374 NHS; 37,583 NHSII) or the UI items at baseline (N=556 NHS; 144 NHSII), there were 81,619 NHS and 77,650 NHSII participants who provided baseline information on UI frequency. Since our focus was progression of prevalent incontinence, we excluded women who reported no UI or insignificant UI (N=42,350 NHS and 46,683 NHSII participants with no UI or UI <once per month) and women who already had frequent UI (N=24,315 NHS and 16.252 NHSII participants with UI once/week). Analyses utilized caffeine data from semi-quantitative food frequency questionnaires (FFQs) administered at baseline, and in additional analyses, 4 years prior to baseline. Thus, we excluded 1,134 NHS and 1,432 NHSII participants who did not provide caffeine intake data on the FFQs. In addition, we excluded women with major neurologic conditions (stroke, multiple sclerosis, Parkinson's disease, or amyotrophic lateral sclerosis) or functional limitations (defined as difficulty climbing a flight of stairs, walking 1 block, bathing, or dressing), which might cause UI, as well as women missing data on body mass index (BMI) and parity, which are important UI risk factors (N=1,596 NHS; 1,312=NHSII). Finally, after excluding women missing UI data on the follow-up questionnaire (N=1,214 NHS; 1,417 NHSII), there were 11,010 NHS and 10,554 NHSII participants available for analysis.

To measure caffeine intake, we used validated FFQs included on the NHS questionnaires in 1998 and 2002 and on the NHSII questionnaires in 1999 and 2003. Participants were asked about longer-term caffeine intake; specifically the FFQ inquired how often on average during the previous year they consumed various items, including coffee with caffeine ("1 cup"), tea with caffeine ("1 cup"), caffeinated soda ("1 glass, bottle or can"), and chocolate (e.g., "bar or packet"). There were 9 response options ranging from "none or less than 1/

month" to "6+/day". Using U.S. Department of Agriculture food composition data supplemented with other sources(9-12), estimated caffeine contents were 137 mg per cup of coffee, 47 mg per cup of tea, 46 mg per can/bottle of cola beverage, and 7 mg per serving of chocolate. We calculated total caffeine intake by summing the caffeine content for specific items multiplied by weights proportional to the frequency of use of each item.

The reproducibility and validity of the FFQs have been reported previously.(13) In an NHS validation study, there was a strong linear association between intakes assessed with the FFQ and intakes reported on four 1-week diet records completed over a 1-year period. For example, Pearson correlation coefficients were 0.78 for coffee, 0.93 for tea, and 0.84 for cola drinks.(14)

Questions about UI were included on the 2002, and 2004 questionnaires in the NHS and the 2003, and 2005 questionnaires in the NHSII. Participants were asked, "During the last 12 months, how often have you leaked or lost control of your urine?" Response options were never, less than once per month, 2-3 times per month, about once per week, and almost every day.(15) A reliability study among 200 participants demonstrated high reproducibility of response to this question.(16)

UI progression cases were women whose incontinence frequency increased from 1-3 times per month at baseline (i.e., 2002 in NHS and 2003 in NHSII) to at least once per week 2 years later. Non-cases were women whose UI frequency stayed the same or decreased over the 2-year period.

UI type was assessed on the 2004 NHS and 2005 NHSII questionnaires. Women were asked, "When you lose urine, what is the usual cause?" Urgency UI was defined as leaking usually caused by a sudden and urgent need to go to the bathroom. Stress UI was defined as leaking usually caused by coughing, sneezing, laughing, or doing physical activity. UI type was classified as mixed when stress and urgency UI symptoms were equally common.

We examined both baseline level of caffeine intake and prior change in caffeine intake in relation to risk of UI progression. For the analyses of level of caffeine intake, we categorized baseline intake into categories roughly corresponding to the amount of caffeine in 1, 2, 3, or 4 cups of coffee (0-149, 150-299, 300-449, 450-965 mg/d). For the analyses of change in caffeine intake, we first categorized caffeine intake at baseline and 4 years earlier into 5 finer categories (0-149, 150-299, 300-449, 450-599, and 600-965 mg/d). We then defined caffeine intake as "stable" when the intake category remained the same at both time-points. Women were considered to have increased their caffeine intake if they moved into a higher category, or decreased their intake if they moved into a lower category.

In separate analyses within each cohort, logistic regression models were used to calculate multivariable-adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) for UI progression according to caffeine intake, both overall and by UI type. Model covariates, which reflected participants' status as of the baseline questionnaire, were UI frequency (1/ month or 2-3 times/month) and potential UI risk factors identified from the literature, including age, parity, BMI, cigarette smoking, race, and total fluid intake. Total fluid intake included milk, juice, tea, coffee, soda, punch, alcohol, and water. Analyses of change in caffeine intake were additionally adjusted for initial level of caffeine intake. Further adjustment for other potential confounding factors, such as physical activity (metabolic equivalent hours/week), menopausal status, postmenopausal hormone use, diabetes, and diuretic use did not change the results and thus were not included in the final multivariable logistic regression models.

After calculating cohort-specific odds ratios, we combined the log odds ratios, weighted by the inverse of their variances, using a random effects model for meta-analysis. Between-study heterogeneity was tested by the Q statistic.(17)

We conducted several secondary analyses to further estimate the association between caffeine and incontinence progression. First, in addition to controlling for initial frequency of UI, to estimate whether the association between caffeine and UI progression was influenced by UI frequency at baseline, we conducted separate analyses among women with UI once per month at baseline and UI 2-3 times per month at baseline. In addition, to minimize the possibility of misclassification of UI progression, we repeated the analyses after defining UI progression more conservatively as a change from UI 1 to 3 times per month to daily UI; non-cases remained women whose UI frequency stayed the same or decreased and women with more moderate progression were excluded. To estimate the association between baseline level of caffeine intake and UI progression among those with the most stable caffeine intake over time, in whom the likelihood of misclassification may be lowest, we repeated the analyses after excluding 3,071 participants who decreased their caffeine intake by >1 category during the 4 years prior to baseline. Finally, if any negative impact of caffeine might be limited to women more predisposed to UI progression, we repeated the analyses among the oldest women with mental health or physical function limitations. Mental health limitations were defined as a score below 84 (the median value among women without UI) on the Short-Form 36 Health Status Survey (SF-36) mental health subscale(18) or self-reported regular use of anti-depressant medication or diagnosis of depression. Limited physical function was defined as a score below 90 (the median value among women without UI) on the SF-36 physical function subscale.(18)

For all analyses, two-tailed p-values <0.05 were considered statistically significant. Data were analyzed using SAS 9.2 (SAS Institute Inc, Cary, NC).

#### RESULTS

At baseline, NHS participants were age 56-81 years and NHSII participants were age 39-56. In general, characteristics of women were fairly similar across categories of caffeine intake, although women who consumed more caffeine had higher mean daily fluid intake and were more likely to have ever smoked cigarettes (table 1).

There was little change in the proportion of women with UI progression across categories of baseline level of caffeine intake (data not shown in tables). For example, among NHS and NHSII participants with UI 1-3 times per month at baseline, the percentage reporting an increase in UI frequency to at least weekly after 2 years of follow-up was 22%, 22%, 24%, and 21% in women consuming 0-149, 150-299, 300-449, and 450 mg or more of caffeine per day, respectively.

After adjusting for potential confounding factors, we found no association between baseline level of caffeine intake and subsequent odds of UI progression over two years (table 2). For example, among women in both cohorts, the OR for UI progression was 0.87 (95% CI 0.70-1.08) comparing the highest versus the lowest category of caffeine intake. Results were comparable when women with UI once per month at baseline were analyzed separately from women with UI 2-3 times per month (data not shown). In addition, when we repeated the analyses defining UI progression as an increase in UI frequency to daily rather than at least weekly (data not shown in table), results in the combined cohorts were similar to those reported above (OR 0.85, 95% CI 0.59-1.21 comparing 450 vs. 0-149 mg of caffeine per day).

We also conducted analyses of specific types of UI progression. Comparing those in the highest versus lowest caffeine intake category, there was no indication of significant increased odds of urgency UI progression with higher caffeine intake (combined cohorts OR 0.84, 95% CI 0.57-1.25) (table 2). Higher caffeine intake was also not associated with odds of stress or mixed UI progression (data not shown in table). For example, odds ratios comparing the highest versus lowest caffeine intake categories were 0.93 (95% CI 0.69-1.25) for women with stress UI and 0.68 (95% CI 0.45-1.04) for women with mixed UI.

In secondary analyses, we restricted the study population to women with stable caffeine intake over the previous four years; results were similar to those reported above (data not shown). In addition, results were comparable to those in the main analyses when we restricted the study population to older women in the NHS with depressive symptoms or limited physical function.

We were also interested in assessing the relation between change in caffeine intake and subsequent risk of UI progression. In unadjusted analyses, the percentage of women with UI progression was similar among women with stable caffeine intake (22%) and those who increased (20%) or decreased (22%) their caffeine intake during the 4 years prior to baseline. After adjusting for potential confounding factors, odds of subsequent UI progression were similar among women who increased (combined cohorts OR 1.08, 95% CI 0.95-1.22) or decreased their caffeine intake (OR 1.16, 95% CI 1.02-1.31) compared to women with stable caffeine intake (table 3). When we separately examined women with UI once per month versus 2-3 times per month at baseline, results were similar to those in the primary analyses (data not shown in table). For example, comparing women who increased their caffeine intake to those who remained stable, odds ratios were 1.01 (95% CI 0.78-1.31) for women with UI once per month and 1.10 (95% CI 0.89-1.37) for women with UI 2-3 times per month. In addition, results in analyses using a stricter definition of UI progression (i.e., an increase to daily UI) were consistent with those reported above (data not shown).

When we looked specifically at women with urgency UI progression (table 3), there was no indication of an association between increased (combined cohorts OR 1.10, 95% CI 0.85-1.43) or decreased caffeine intake (combined cohorts OR 1.15, 95% CI 0.90-1.45) and UI progression. In addition, there was no association between increased or decreased caffeine intake and risk of stress or mixed UI progression (data not shown).

#### DISCUSSION

Overall, we observed no association between longer-term caffeine intake, defined as average intake during the past year, or previous change in caffeine intake and subsequent odds of UI progression, including urgency UI progression, over two years among women with moderate UI. Although these data do not address acute effects of caffeine on continence mechanisms, they indicate that longer-term caffeine levels, or long-term changes in caffeine intake, are not related to UI progression. Compared to other large U.S. studies(19, 20), caffeine intake among the women in our cohorts was comparable or slightly lower (lower intake in our study might be expected since all women had moderate UI at baseline), thus our findings on levels of caffeine intake are not likely to vary from other populations.

Our results are consistent with data from two small randomized trials(6, 7). For example, Swithinbank et al. observed no change in UI over 2 weeks after an intervention to replace caffeinated with decaffeinated beverages in 69 women (mean age 55 years) with stress incontinence or idiopathic detrusor overactivity.(6)

Several mechanisms have been hypothesized to link caffeine intake with exacerbation of UI, such as increased diuresis(3, 4) and increased detrusor pressure during bladder filling(5), which could promote urgency, and possibly urgency incontinence, particularly in women with underlying detrusor overactivity. It is unknown how long-term versus acute caffeine intake may influence these mechanisms. Nonetheless, the results of our study and other epidemiologic studies of acute caffeine reduction do not support the hypothesized mechanisms.

Several limitations of our study should be considered when interpreting the results. First, caffeine intake and UI data were self-reported rather than objectively measured, and thus absolute caffeine intake and prevalence of UI progression may be underestimated or overestimated. However, validation of the main contributors to caffeine intake among these women (coffee, tea, and soda) indicated that self-reports are reasonably accurate in ranking individuals according to intake level and thus not likely a major source of bias.(14) Regarding UI, previous studies have demonstrated high reliability(21) and validity(22) of self-reported UI; moreover, there is high specificity of self-reported UI type compared with clinical diagnoses(23), which is key to valid risk factor estimation. Second, we did not have information on caffeine consumption patterns (e.g., consuming large quantities at once versus moderate quantities throughout the day) and thus could not examine this aspect of caffeine intake in relation to UI progression. Third, in a large epidemiologic study, measurement of acute caffeine intake is not feasible, and our food frequency questionnaire requests information about longer-term food and beverage consumption (i.e., average intake over the past year). Nonetheless, understanding the relation between longer-term caffeine habits and UI progression is important, and information on the role of caffeine in worsening UI is largely based on a few small studies. In addition, we did not assess UI treatment among women in current analysis and thus it is unclear how treatment may have affected our UI progression estimates. However, data from previous studies in these cohorts indicate that a minority of women seek treatment. (24, 25) Furthermore, it is unlikely that treatment is related to caffeine intake, suggesting lack of treatment data would not bias our results. In addition, we did not collect data on urinary symptoms other than UI, such as urgency, daytime frequency, and nocturia, and thus cannot make any conclusions about their potential associations with long-term caffeine intake. Finally, >95% of our study participants are white; thus, our findings may not be generalizable to nonwhite women, in whom UI progression rates may be different from those in white women.(26)

In conclusion, if confirmed in other studies, these results suggest that women with moderate UI should not be concerned that their regular caffeine consumption, defined here as intake over one year, will influence their risk of developing more frequent UI. In addition, these data do not support an association between long-term increases or decreases in caffeine intake and risk of UI progression over two years.

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# Table 1

Characteristics of Nurses' Health Study and Nurses' Health Study II Participants With Moderate Urinary Incontinence at Baseline According to Caffeine Intake Over the Previous Year\*

			c	affeine Inta	ike (mg/day)			
		Nurses' Hea	alth Study		I	Nurses' Heal	th Study II	
Variable	0-149 (N=7055)	150-299 (N=3113)	300-449 (N=616)	450 (N=226)	0-149 (N=6151)	150-299 (N=3254)	300-449 (N=792)	450 (N=357)
				Me	ans			
Age, yrs	67.8	67.0	65.9	64.8	48.6	48.7	48.5	48.6
Body mass index, kg/m <sup>2</sup>	26.5	26.4	26.5	27.4	27.3	26.9	27.1	27.4
Total fluid intake, L/day	2.0	2.1	2.3	2.4	1.8	2.1	2.4	2.6
Caffeine intake, mg/day	58.0	245.9	388.1	527.5	65.0	242.8	368.1	524.0
				Percer	ntages			
Parity								
0 live births	5.2	5.3	4.5	6.7	15.6	15.6	13.5	15.4
1-2 live births	35.7	33.6	33.8	33.6	56.0	56.0	55.8	56.9
3 or more live births	59.1	61.1	61.7	59.7	28.4	28.4	30.7	27.7
Race								
White	98.0	0.66	0.66	98.7	97.2	98.0	98.5	98.6
Black	0.9	0.4	0.3	0.4	1.1	0.6	0.5	0.3
Asian	0.8	0.2	0.7	6.0	1.3	0.7	0.4	0.3
Other or missing data	0.3	0.4	0.0	0.0	0.4	0.7	0.6	0.8
Cigarette smoking								
Never	50.2	40.5	39.6	31.0	73.9	58.3	51.6	43.7
Past	45.3	50.4	44.1	46.0	21.7	32.9	34.0	34.4
Current, cigarettes per day								
1-14	2.7	4.9	7.0	7.5	2.4	4.6	7.8	7.6
15-24	1.4	3.1	6.7	10.6	1.4	3.3	4.8	10.4
25 or more	0.4	1.1	2.6	4.9	0.6	0.9	1.8	3.9
UI frequency								
Once/month	33.6	32.7	34.6	34.5	35.6	35.7	32.3	28.0

Nurses' Health Study         Nurses' H           Variable         0-149         150-299         300-449         450         0-149         150-29           Variable         (N=7055)         (N=3113)         (N=616)         (N=226)         (N=6151)         (N=325           2-3 times/month         66.4         67.3         65.4         65.5         64.4         64.3				0	affeine Inta	ake (mg/day)			
ariable $0-149$ 150-299         300-449         450 $0-149$ 150-29 $(N=7055)$ $(N=3113)$ $(N=616)$ $(N=226)$ $(N=6151)$ $(N=325)$ $2-3$ times/month $66.4$ $67.3$ $65.4$ $65.5$ $64.4$ $64.3$			Nurses' Hea	lth Study			Nurses' Heal	th Study II	
2-3 times/month 66.4 67.3 65.4 65.5 64.4 64.3	ariable	0-149 (N=7055)	150-299 (N=3113)	300-449 (N=616)	450 (N=226)	0-149 (N=6151)	150-299 (N=3254)	300-449 (N=792)	450 (N=357)
	2-3 times/month	66.4	67.3	65.4	65.5	64.4	64.3	67.7	72.0

UI, urinary incontinence.

\* Caffeine intake was measured using semi-quantitative food frequency questionnaires, in which women were asked how often on average during the past year they consumed various items, administered in 2002 in Nurses' Health Study and 2003 in Nurses' Health Study II.

#### Table 2

Odds Ratios (95% Confidence Intervals) for Urinary Incontinence Progression According to Caffeine Intake at Baseline Among Women With Moderate Urinary Incontinence

	Caffeine Intake (mg/day)				
Cohort	0-149	150-299	300-449	450 or higher	
All UI progression					
Nurses' Health Study					
Cases	1,541	713	125	43	
Age adjusted OR	1.00 (reference)	1.07 (0.97- 1.19)	0.93 (0.76- 1.15)	0.87 (0.62- 1.23)	
Fully adjusted OR *	1.00 (reference)	1.08 (0.98- 1.20)	0.96 (0.78- 1.18)	0.88 (0.62- 1.24)	
Nurses' Health Study					
Cases	1,392	698	206	82	
Age-adjusted OR	1.00 (reference)	0.93 (0.84- 1.04)	1.20 (1.01- 1.42)	1.02 (0.79- 1.31)	
Fully adjusted OR	1.00 (reference)	0.91 (0.81- 1.01)	1.10 (0.92- 1.32)	0.87 (0.66- 1.13)	
Combined cohorts <sup>†</sup>					
Cases	2,933	1,411	331	125	
Age-adjusted OR	1.00 (reference)	1.00 (0.87- 1.15)	1.07 (0.83- 1.36)	0.96 (0.79- 1.18)	
Fully adjusted OR	1.00 (reference)	0.99 (0.83- 1.18)	1.04 (0.91- 1.19)	0.87 (0.70- 1.08) <sup>‡</sup>	
Urgency UI progression					
Nurses' Health Study					
Cases	540	255	42	12	
Age-adjusted OR	1.00 (reference)	1.12 (0.96- 1.31)	0.94 (0.68- 1.31)	0.76 (0.42- 1.37)	
Fully adjusted OR	1.00 (reference)	1.14 (0.97- 1.34)	0.99 (0.71- 1.38)	0.80 (0.44- 1.46)	
Nurses' Health Study II					
Cases	268	146	37	17	
Age-adjusted OR	1.00 (reference)	1.02 (0.82- 1.25)	1.12 (0.79- 1.60)	1.10 (0.66- 1.82)	
Fully adjusted OR	1.00 (reference)	0.98 (0.79- 1.21)	1.02 (0.70- 1.47)	0.88 (0.52- 1.50)	
Combined cohorts					
Cases	808	401	79	29	
Age adjusted OR	1.00 (reference)	1.08 (0.95- 1.22)	1.02 (0.80- 1.30)	0.94 (0.64- 1.38)	
Fully adjusted OR	1.00 (reference)	1.08 (0.93- 1.25)	1.00 (0.78- 1.28)	0.84 (0.57- 1.25)§	

UI, urinary incontinence; OR, odds ratio.

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\* Adjusted for age (continuous), urinary incontinence frequency (1 per month, 2-3 per month), body mass index (continuous), parity (0, 1-2, 3 or more live births), cigarette smoking (never, past, current: 1-14, 15-24, 25 or more cigarettes per day), race (white, black, Asian, other or missing data), total fluid intake (continuous)

 $^{\dagger}\mathrm{Cohort}\text{-specific ORs}$  were combined using random effects meta-analysis.

<sup>‡</sup>Q-statistic=0.00, p-heterogeneity=0.9

 $^{\$}$ Q-statistic=0.05 , p-heterogeneity=0.8

#### Table 3

Odds Ratios (95% Confidence Intervals) for Urinary Incontinence Progression According to Change in Caffeine Intake During the 4 Years Prior to Baseline Among Women With Moderate Urinary Incontinence

Cohort	Stable	Increase	Decrease
All UI progression			
Nurses' Health Study			
Cases	1223	172	1027
Age-adjusted OR	1.00 (reference)	1.14 (0.95-1.37)	1.07 (0.89-1.30)
Fully adjusted OR $^*$	1.00 (reference)	1.15 (0.96-1.39)	1.08 (0.89-1.32)
Nurses' Health Study II			
Cases	1187	212	979
Age-adjusted OR	1.00 (reference)	1.06 (0.90-1.25)	1.16 (0.99-1.37)
Fully adjusted OR	1.00 (reference)	1.02 (0.86-1.21)	1.22 (1.03-1.44)
Combined cohorts <sup>†</sup>			
Cases	2410	384	2006
Age-adjusted OR	1.00 (reference)	1.10 (0.97-1.24)	1.12 (0.99-1.27)
Fully adjusted OR	1.00 (reference)	1.08 (0.95-1.22)	1.16 (1.02-1.31) <sup>§</sup>
Urgency UI progression			
Nurses' Health Study			
Cases	435	62	352
Age-adjusted OR	1.00 (reference)	1.20 (0.91-1.59)	1.16 (0.84-1.60)
Fully adjusted OR	1.00 (reference)	1.23 (0.93-1.64)	1.17 (0.84-1.61)
Nurses' Health Study II			
Cases	240	40	188
Age-adjusted OR	1.00 (reference)	1.00 (0.71-1.41)	1.04 (0.74-1.46)
Fully adjusted OR	1.00 (reference)	0.94 (0.66-1.34)	1.12 (0.79-1.59)
Combined cohorts			
Cases	675	102	540
Age-adjusted OR	1.00 (reference)	1.12 (0.90-1.39)	1.10 (0.87-1.39)
Fully adjusted OR	1.00 (reference)	1.10 (0.85-1.43)#	1.15 (0.90-1.45)

UI, urinary incontinence; OR, odds ratio.

\* Adjusted for age (continuous), urinary incontinence frequency (1 per month, 2-3 per month), body mass index (continuous), parity (0, 1-2, 3 or more live births), cigarette smoking (never, past, current: 1-14, 15-24, 25 or more cigarettes per day), race (white, black, Asian, other/missing), total fluid intake (continuous), initial level of caffeine intake (0-149, 150-299, 300-449, 450 or more mg per day)

<sup>†</sup>Cohort-specific ORs were combined using random effects meta-analysis.

 $\frac{1}{2}$ Q-statistic=0.90, p-heterogeneity=0.3

<sup>§</sup>Q-statistic=0.76, p-heterogeneity=0.4

¶Q-statistic=1.36, p-heterogeneity=0.2

<sup>¶</sup>Q-statistic=0.02, p-heterogeneity=0.9