

## CAFFEINE INTAKE AND RISK OF STRESS, URGENCY, AND MIXED URINARY INCONTINENCE

### Hypothesis / aims of study

In this prospective study, we investigated the relationship between caffeine intake and incident urinary incontinence in 65,176 women 37 to 79 years old enrolled in the Nurses' Health Study and Nurses' Health Study II. Based on likely mechanisms of action, we hypothesized that caffeine intake would be particularly related to urgency incontinence.

### Study design, materials and methods

Daily caffeine intake from food and beverages was calculated for each participant using dietary data reported on validated food frequency questionnaires administered every 4 years between 1980 and 2000 in the Nurses' Health Study and between 1989 and 2001 in the Nurses' Health Study II. The food frequency questionnaires distinguish between caffeinated and caffeine-free coffee and soda. To reduce measurement error and to better represent long-term habits, caffeine intake was defined as average intake across all the food frequency questionnaires from 1980-2000, or 1989-2001. New onset of urinary incontinence was identified from 2000 to 2004 in the Nurses' Health Study and 2001 to 2005 in the Nurses' Health Study II. We pooled data from the 2 cohorts and calculated multivariable-adjusted hazard ratios and 95% confidence intervals of the relation between caffeine intake and urinary incontinence risk, using Cox proportional hazard models adjusting for major incontinence risk factors, including age, body mass index, physical activity, total fluid intake, race, parity, cigarette smoking, and diabetes.

### Results

Women with higher levels of daily caffeine intake had a statistically significant 9 to 24% increased risk of developing urinary incontinence at least weekly (adjusted RR 1.10, 95% CI 1.01 - 1.18 for 150-299 mg/day; RR 1.09, 95% CI 1.00 - 1.19 for 300-449 mg/day; RR 1.24, 95% CI 1.12 - 1.38 for  $\geq 450$  mg/day) compared to those with the lowest level of caffeine intake, 0-149 mg/day (Table 1). This increase appeared largely explained by a significantly greater risk for incident urgency and mixed urinary incontinence (RR 1.28, 95% CI 1.00 - 1.63 for urgency incontinence; RR 1.44, 95% CI 1.14 - 1.81 for mixed incontinence, for  $\geq 450$ mg/day). There was also a significant trend of increasing risk of urgency and mixed UI ( $p$  for trend = 0.05 and 0.01, respectively) with increasing caffeine intake. There was no significant association between caffeine and stress urinary incontinence ( $p$  for trend = 0.22)

### Interpretation of results

In this analysis of 2 large prospective studies, we observed modest increased risks of urgency and mixed urinary incontinence in women with higher daily caffeine intakes. This risk increased continuously with the amount of caffeine consumed. These findings are consistent with caffeine's known ability to stimulate smooth muscle contractions by mobilizing intracellular calcium stores. While previous epidemiological studies generally do not support caffeine as a risk factor for urinary incontinence, these studies have largely been cross-sectional, which could lead to bias if women with urinary incontinence reduce their caffeine consumption to improve their symptoms. By examining incident incontinence, our prospective study is substantially less vulnerable to this source of bias. In addition, the majority of the previous studies focused on the consumption of individual beverages (e.g. coffee), which may underestimate an individual's total exposure to caffeine (e.g. from coffee plus caffeinated soda). Finally, few studies have examined associations separately by type of incontinence, which is important because as we have shown, caffeine may increase risk of one type incontinence, but not others. Some limitations of this study include reliance on self-reported data, potential residual confounding, and potential limited generalizability of the results to minority women, since our cohort is approximately 95% Caucasian.

### Concluding message

In our large, prospective study, findings suggest that higher daily caffeine intake is associated with modest increased risks for urgency and mixed urinary incontinence in women. If this association is confirmed in future studies, self-monitoring and counselling to reduce caffeine intake may be cost effective methods to prevent some of the burden of urinary incontinence in women.

**Table 1. Multivariable-adjusted relative risks for incident weekly urinary incontinence, by incontinence type according to caffeine intake**

	Caffeine intake (mg/d)				P trend
	0-149	150-299	300-449	≥ 450	
Any incontinence					
No. cases	1,419	1,316	1,013	676	
RR (95% CI)*	1.00 (reference)	1.09 (1.01 - 1.18)	1.09 (1.00 - 1.19)	1.24 (1.12 - 1.38)	<0.001
Stress incontinence					
No. cases	580	534	389	253	
RR (95% CI)*	1.00 (reference)	1.14 (1.00 - 1.28)	1.05 (0.91 - 1.20)	1.14 (0.96 - 1.34)	0.22
Urgency incontinence					
No. cases	254	227	185	120	
RR (95% CI)*	1.00 (reference)	1.01 (0.84 - 1.22)	1.12 (0.91 - 1.37)	1.28 (1.00 - 1.63)†	0.05†
Mixed incontinence					
No. cases	265	233	186	142	
RR (95% CI)*	1.00 (reference)	1.04 (0.86 - 1.24)	1.06 (0.87 - 1.29)	1.44 (1.14 - 1.81)	0.01

Urinary incontinence defined as urine leakage at least once per week.

\* All relative risks adjusted for age, body mass index, physical activity, total fluid intake, race, parity, cigarette smoking, and diabetes.

† Values were rounded to 2 significant digits. However, lower limit of confidence interval is greater than 1.00 and p value is less than 0.05. Both relative risk and p trend are statistically significant.

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<b><i>What were the subjects in the study?</i></b>	<b>HUMAN</b>
<b><i>Was this study approved by an ethics committee?</i></b>	<b>Yes</b>
<b><i>Specify Name of Ethics Committee</i></b>	<b>IRB of Brigham and Women's Hospital</b>
<b><i>Was the Declaration of Helsinki followed?</i></b>	<b>Yes</b>
<b><i>Was informed consent obtained from the patients?</i></b>	<b>Yes</b>