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Vitamin D intake and the 10-year risk of urgency urinary incontinence in women

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Abstract

Evidence indicates that higher serum 25-hydroxy vitamin D levels may be associated with decreased prevalence of urgency urinary incontinence (UI), but the impact of vitamin D consumption on development of urgency and mixed UI is unclear. The objective was to assess whether greater vitamin D intake was associated with decreased risk of incident urgency and mixed UI over 10 years using 2 large prospective cohorts of middle-aged and older women. We analyzed 38,101 women from the Nurses' Health Study I (NHS I) and 35,190 women from NHS II who were free of UI at baseline. We followed incident UI, defined as new UI occurring at least monthly, separately by subtype (urgency, mixed, stress UI), from 2002–2012. We categorized vitamin D intake from supplements and diet. We estimated relative risk for developing UI according to vitamin D intake using Cox-proportional hazard models with adjustment for covariates. Median vitamin D intake was 580IU in the older women in NHS I (age range 56–71 at baseline) and 487IU in middle-aged women in NHS II (age range 40–57). Among women taking ≥ 1000 IU of vitamin D, median intake in the older women was 1252IU and 1202IU in the middle-aged women. Among the older women, we found no relation of vitamin D intake to risk of developing UI, across all UI subtypes. In multivariable-adjusted analysis for middle-aged women, the relative risk of developing mixed UI among women taking ≥ 1000 IU was 0.79 (0.63, 0.99) and for urgency UI was 0.88 (0.71, 1.07), versus < 200 IU. Risks of developing stress UI were not

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Declaration of Competing Interest

ADM, FG, CV, AH and VT have no COI to disclose.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jsbmb.2020.105601>.

related to vitamin D intake categories. Overall, we did not find a relationship between vitamin D intake and UI incidence in middle-aged and older women; however, the reported intake was moderate.

Keywords

Urinary incontinence; Women; Epidemiology; Longitudinal; Vitamin D

1. Introduction

Up to half of women report urinary incontinence (UI), and the prevalence increases with age. Urgency UI (UUI) is defined as UI that is preceded by the sudden, compelling need to void that is difficult to defer, and mixed UI (MUI) is a combination of UUI and stress UI [1]. UUI and MUI are more likely to produce severe symptoms with advanced age than stress UI [2]. The medical and psychosocial sequelae of UI, especially UUI and MUI, are considerable and complex. Both are associated with urinary tract infections [3], poor physical performance [4], falls [5,6], and physical functional decline [7]. UUI and MUI lead to changes in lifestyle, intimacy, and relationships [8,9], impact caregivers and family members, and have been linked to nursing home placement [10,11]. Moreover, UI often exacerbates comorbid psychiatric disorders [12]; many people with UI report elevated levels of depression [9,13,14], which negatively impacts quality of life [9,15,16].

One possible factor that may influence the development of UI in older women is vitamin D deficiency. Vitamin D receptors have been found in many different cell types throughout the body, including the bladder detrusor muscle [17]. In particular, vitamin D may improve skeletal and smooth muscle function, while decreasing inflammation. Vitamin D may be important for adequate bladder control through direct effects on improving detrusor muscle function and decreasing the sensation of urgency. Vitamin D insufficiency has been associated with incident UI in a cohort of older community dwelling adults [18]. Furthermore, a pilot study suggested improvement in UUI in older African-American women [19].

Treatment options for UUI and MUI include non-pharmacologic and pharmacologic interventions that rarely ameliorate all symptoms [20]. Thus, targeting prevention or early intervention strategies to prevent worsening bladder symptoms and severity is important [21]. We sought to evaluate vitamin D intake as a possible prevention strategy to reduce UI, specifically UUI as well as MUI, among middle-aged and older women.

To accomplish this objective, we analyzed data from the Nurses' Health Studies (NHS) I and II. These large observational studies include questionnaires assessing a wide range of vitamin D supplement doses, food frequency questionnaires (FFQ) to assess dietary intake, as well as data on UI and subtypes over a 10-year period. Specifically, our objective was to assess whether vitamin D intake from supplementation and foods decreases development of UI over 10 years in older women and middle-aged women from the NHS I and II. We hypothesized that higher levels of vitamin D intake would be related to lower rates of UUI in women and possibly MUI.

2. Subjects and methods

2.1. Study population

NHS I was initiated in 1976 when female registered nurses ages 30–55 years responded to a mailed questionnaire about their medical history and lifestyle. Using similar methodology, NHS II of women between 25 and 42 years old was initiated in 1989; the upper age was selected to correspond with the lowest age in NHS I in that year. Both cohorts utilize identical methods for data collection and follow-up, including biennial mailed questionnaires to update health and lifestyle information. During each questionnaire cycle, full-length questionnaires are sent in initial mailings, followed by abbreviated questionnaires to maximize participation. To date, the follow-up in both cohorts is approximately 90 %. The Institutional Review Board of Brigham and Women's Hospital approved both NHS I and NHS II.

2.2. Vitamin D intake

The NHS questionnaires every two years request details of multivitamin supplements (including brand/type of multivitamin, to facilitate extraction of doses of specific vitamins), and specific vitamin D supplements and dose. In addition, starting in 1980, approximately every four years, the Willett Food Frequency Questionnaire (FFQ) was administered to collect information on intake of 130 foods; for each food, for specified portion sizes (e.g., 1 cup skim milk) women were asked to report frequency of intake over the previous year (never/almost never, 1–3 times a month, once a week, 2–4 times a week, 5–6 times a week, once a day, 2–3 times a day, 4–6 times a day, or >6 times a day) [22]. Dietary vitamin D intake was computed by multiplying the frequency of consumption of each unit of food and the vitamin D content of the specified portion. Nutrient values in foods are obtained from the USDA, using year-specific information to capture changes in fortification and nutrient content over time.

We calculated vitamin D intake by combining amounts from multivitamins, specific supplements, and foods (for years when the FFQ was not administered, food data were carried forward from the previous questionnaire – regardless, supplements provide substantially more vitamin D than foods for most participants). We previously documented the validity of this approach to measuring vitamin D intake in our cohorts. In a subset of participants, we compared the FFQ to 7-day diet diaries completed 4 times throughout a year; we found correlations of 0.81 for milk and 0.66 for fish, the two largest contributors to dietary vitamin D [23]. For supplements, the sensitivity and specificity of the FFQ was 78 and 93 %, respectively. Thus, vitamin D intake sources are well-reported by participants.

2.3. Urinary incontinence

In 2002 (NHS I) and 2003 (NHS II), women were asked, “During the past 12 months, how often have you leaked or lost control of your urine?” Response choices were never, < 1/month, 1/month, 2–3/month, approximately 1/week, and almost every day. A reliability study among a subgroup of these nurses demonstrated high reproducibility of responses [24]. UI subtype was ascertained from all women reporting UI on the questionnaires starting in 2004 (NHS I) and 2005 (NHS II). UI classifications were based on the participants’

reports of their dominant symptoms. Urine loss with a sudden feeling of bladder fullness or when a toilet was inaccessible was defined as ‘urgency UI’ or UUI. We defined ‘stress UI’ or SUI as report of leakage primarily occurring with coughing or sneezing, lifting things, laughing, or exercise. Women who reported that stress and urgency symptoms occurred equally were defined as cases of ‘mixed UI’ or MUI.

2.4. Measurement of demographic and health characteristics/covariates

We used data from the cohort questionnaires in 2002 (NHS I, older women) and 2003 (NHS II, middle-aged women), as well as subsequent questionnaires, to obtain and update information on covariates. We used their questionnaire report to assess demographic, health, and lifestyle covariates, including age, race, height and weight, parity, smoking, postmenopausal hormone use, thiazide diuretic use, hysterectomy, and reported diagnosis of depression. In addition, women reported the number of hours spent on various leisure activities (e.g., walking, running) during the past year, and total energy expenditure was calculated in metabolic-equivalent task hours per week, which has been previously described in detail [20]. Finally, women reported diagnoses of stroke, myocardial infarction, and type 2 diabetes on every questionnaire.

2.5. Population for analysis

Of the 81,593 NHS I participants who provided UI information at our analytic baseline in 2002, we excluded 39,257 with prevalent UI leaking once per month or more, 2210 women missing information on vitamin D intake, 982 women who reported a history of stroke or Parkinson Disease and 1043 women who either died or were lost to follow-up between 2002–04. Thus, 38,101 women were included in analyses Fig. 1. Of the 81,055 NHS II participants who provided UI information at our analytic baseline in 2003, we excluded 33,624 with prevalent UI leaking once per month or more, 9936 women missing information on vitamin D intake, 335 women who reported a history of stroke or Parkinson Disease and 1970 women who either died or were lost to follow-up between 2003–05. Thus, 35,190 women were included in analyses. Subsequent to the first time-period, women were censored at onset of UI, at loss-to-follow up, or at death, whichever came first.

2.6. Statistical analysis

We identified participants’ intake of vitamin D at study baseline (ie, 2002 in NHS I and 2003 in NHS II), and updated information at the start of each two-year follow-up period. Vitamin D intake was categorized as <200IU, 200–399, 400–599, 600–799, 800–999, and 1000 +. Multivariable-adjusted relative risks of UI, estimated by hazard ratios, were calculated using Cox proportional hazard models across categories of vitamin D intake. We calculated 95 % confidence intervals for all relative risk estimates, and conducted tests of linear trend using an ordinal variable representing the median value of each vitamin D category. To control for potential confounding, models were stratified by age (in months) and two-year time period, and in models we included covariates that were identified from the existing literature as potential risk factors for UI, and were related to vitamin D in our cohorts: parity (none, 1–2, 3+ children), body-mass index (continuous), cigarette smoking (never, current, past), type 2 diabetes (yes, no), post-menopausal hormone therapy (never, current, and past use, and a dummy variable for premenopausal women), and physical activity (quintiles). In analyses of

UI type, three separate models were constructed for each UI type, UUI, MUI, and SUI, and women were censored at development of any UI type. All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC).

3. Results

Among the 38,101 older women (age range 56–71 years at baseline) in NHS I, 21 % of women reported a daily vitamin D intake of at least 800 IU per day (Table 1). Among the 35,190 middle-aged women (age range 40–57 years at baseline) in NHS II, 17 % of women reported a daily vitamin D intake of at least 800 IU or more per day (Table 2). Key similarities between the older and middle-aged women at baseline included similar race/ethnicity (97 % Non-Hispanic White) across all vitamin D categories, with a somewhat lower mean BMI for the highest intake level >1000 IU (25 kg/m^2) and for the lowest intake <200 IU (27 kg/m^2). Current cigarette smoking was lower with greater vitamin D intake among older women (e.g., 5 % of those with ≥ 1000 IU/day versus 13 % of those with <200 IU/day) and among middle-aged women (e.g., 5 % of those with ≥ 1000 IU/day of vitamin D versus 10 % of women with <200 IU/day of vitamin D).

Older women reported higher prevalence of physical activity with ≥ 1000 IU/day of vitamin D (22 (SD ± 26) MET-hours/week) versus older women with <200 IU/day (average 15 (SD ± 21) MET-hours/week). Physical activity level was higher in those with greater vitamin D intake level (e.g., 30.7 (SD ± 39.1) MET-hours/week in those with ≥ 1000 IU/day of vitamin D versus 20.1 (SD ± 30.0) MET-hours/week in women with <200 IU/day of vitamin D). Postmenopausal hormone use was slightly more common for higher vitamin D intake categories compared to low intake categories for older women (e.g., 34 % of those with vitamin D intake ≥ 1000 IU/day versus 29 % of women with vitamin D intake <200 IU/day versus) and middle-aged women (e.g., 16 % of those with ≥ 1000 IU/day of vitamin D versus 12 % of those with <200 IU/day).

Between 2002 and 2014, a total of 16,442 incident UI cases were identified among older women (Table 3). Between 2003 and 2013, a total of 8052 incident UI cases were identified among middle-aged women (Table 4). Median vitamin D intake over follow-up was 580 IU in the older women and 487 IU in the middle-aged women (data not shown in table); among women taking at least 1000 IU of vitamin D, median intakes were 1252 IU in the older women and 1202 IU in the middle-aged women.

In age-adjusted analyses of older women, no associations between vitamin D intake levels and incidence of UI were observed (Table 3), across incidence of UUI, MUI, or SUI types. Results were similar in multivariable models that further adjusted for parity, physical activity, cigarette smoking, history of type 2 diabetes, history of vascular disease, and use of postmenopausal hormone therapy.

In age-adjusted analyses of middle-aged women (Table 4, women with vitamin D intake levels of ≥ 1000 IU/day had an estimated 27 % lower rate of incident MUI, relative to those with vitamin D intake levels <200 IU/day. In multivariable analyses, the relative risk for incident MUI among women with vitamin D intake ≥ 1000 IU/day versus <200 IU/day was

0.79 95 %CI 0.63, 0.99). No differences in incident rates for UUI or SUI were observed by vitamin D intake level, although women with vitamin D intake ≥ 1000 IU/day had a relative risk of incident UUI of 0.88 (95 % CI 0.71, 1.07), and we found nonsignificant trends of decreasing risk of UUI and MUI with increasing vitamin D intake (p-trend = 0.1 for both).

We conducted secondary analyses to examine vitamin D intake ≥ 2000 IU; these were conducted only among the older women, since so few younger women had these higher levels of vitamin D intake. Among older women, the number of incident UI cases among women with ≥ 2000 IU of vitamin D intake was 28 for UUI, 16 for SUI, and 58 for MUI. However, no differences in UI incidence were detected between women with ≥ 2000 IU versus < 200 IU per day intake, regardless of subtype. In multivariable models, we found relative risks of 0.74 (95 % CI 0.50, 1.12) for UUI, of 0.71 (95 % CI 0.42, 1.20) for SUI, while for MUI, the relative risk was 1.19 (95 % CI 0.89, 1.60).

Since vitamin D bioavailability is lower in obese women, and thus higher vitamin D intake may be especially relevant in this population, we also conducted secondary analyses specifically in women with BMI ≥ 30 kg/m² (data not shown in table). In general, findings in obese women were consistent with those in all women. For example, in the older women with BMI ≥ 30 kg/m², the relative risks of UUI, SUI, and MUI among those with vitamin D intake ≥ 1000 IU/day versus < 200 IU/day were 1.05 (95 % CI 0.77, 1.42), 0.89 (95 % CI 0.64, 1.24), and 1.00 (95 % CI 0.73, 1.37), respectively. In the middle-aged women with BMI ≥ 30 kg/m², the relative risks of UUI, SUI, and MUI among those with vitamin D intake ≥ 1000 IU/day versus < 200 IU/day were 1.19 (95 % CI 0.82, 1.74), 1.01 (95 % CI 0.74, 1.31), and 0.85 (95 % CI 0.56, 1.29), respectively.

4. Discussion

This study provides some of the first prospective data to examine associations between vitamin D intake and UI incidence over a 10-year time period.

Overall, we found little evidence of a relationship of vitamin D intake to development of UI, including UI subtypes, in older and middle-aged women. Thus, our findings do not support our hypothesis that higher vitamin D intake would be associated with lower rates of UUI and MUI. We did not find that women with vitamin D intake at least 1000 IU/day had any association with the development of UUI or MUI, including secondary analysis at even higher intake levels of vitamin D ≥ 2000 IU/day. And, we did not find a 'dose-effect' with increasing levels of vitamin D intake on decreasing risk of MUI or UUI, including sensitivity analysis at even higher intake levels of vitamin D ≥ 2000 IU/day, and the overall trend was not significant across vitamin D intake categories.

Compared to other existing cohort studies that have evaluated the relationship of vitamin D and UI, our study had a very large sample size and assessed food and supplement intake repeatedly over 2-year intervals to test our hypothesis with maximum power and accuracy. Dallosso and colleagues longitudinally investigated the association between nutrient composition of the diet and the onset of overactive bladder OAB symptoms and UI in 5816 community-dwelling women [25]. After one year, a higher intake of vitamin D ($p = 0.008$),

was associated with a decreased risk of onset of OAB and UI among women [25], but not among men [26]; OAB is similar to UUI but does not require urine leaking and thus may have different risk and predisposing factors. In observational studies using serum levels of vitamin D [18,27,28], Badalian and Rosenbaum characterized the prevalence of vitamin D deficiency in women with pelvic floor disorders from the 2005–2006 NHANES cycle [27]. The investigators found the likelihood of UI was lower in women 50+ years with serum 25-hydroxy vitamin D levels ≥ 30 ng/mL (AOR = 0.55; 95 % CI, 0.34–0.91, adjusted for age, race, education, body mass index, and parity) [27] in comparison to deficient women. In contrast, Parker-Autry and colleagues did not detect a relationship between low serum 25-hydroxy vitamin D levels and incident UI over 4-years in an older cohort of women (n = 673);[28] whereas another smaller study of older adults found increased UI incidence rates in older men and women with low 25-hydroxy vitamin D levels over a 3.5-year period (n = 175) [18]. Thus, in general, findings are mixed from observational studies.

A recent pilot study suggests high-dose vitamin D supplementation may be more likely to improve UUI in non-Hispanic black women compared to non-Hispanic white women [19]. This pilot study randomized 56 post-menopausal women with low 25(OH)D and UUI to high-dose cholecalciferol (50,000 IU weekly for twelve weeks) or placebo. Perhaps, certain racial/ethnic groups and women with low 25(OH)D levels may be target populations for improving UUI as well as other lower urinary tract symptoms, such as urgency and frequency, with vitamin D supplementation. While the NHS is derived from a geographically diverse pool, the cohort is not representative of the racial/ethnic diversity of the US population (both cohorts are representative of the general nursing population at the time they were initiated, with few minorities). Other nested case control studies using NHS data did not find associations with vitamin D serum status measured in 1989–1990 and the development of colorectal cancer risk [29], breast cancer [30], and lymphoma [31]. However, these nested case-control studies did not have adequate participants with incident UUI to enable rigorous research on UI. More research in specific racial/ethnic groups should be conducted, as well as among women with low 25(OH)D levels.

Strengths of this study include the large sample size, strong response rate, and longitudinal follow-up over several time intervals, of UI as well as vitamin D intake. Other study weaknesses include the limited use of high-dose vitamin D, because the study period occurred before many persons began taking high-dose, over-the-counter vitamin D supplements as a result of increasing public interest in the potential health effects of vitamin D [32]. Thus, we could not examine the hypothesis that high levels of vitamin D may be related to lower rates of UI.

In conclusion, our study did not find evidence that low vitamin D intake, even at moderate levels, as a risk factor for developing UI in middle-aged and older women.

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The authors responsibilities were as follows: ADM, FG, CV, AH and VT designed research; FG conducted research and provided essential materials; ADM and FG analyzed data or performed statistical analysis; ADM, FG, CV, AH

and VT wrote the paper; ADM had primary responsibility for final content; and all authors read and approved the final manuscript.

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Abbreviations

NHS	Nurses Health Study I
NHSII	Nurses Health Study II
UI	Urinary Incontinence
IU	International Unit
UUI	Urgency Urinary Incontinence
MUI	Mixed Urinary Incontinence
FFQ	Food Frequency Questionnaire
SUI	Stress Urinary Incontinence
OAB	Overactive Bladder

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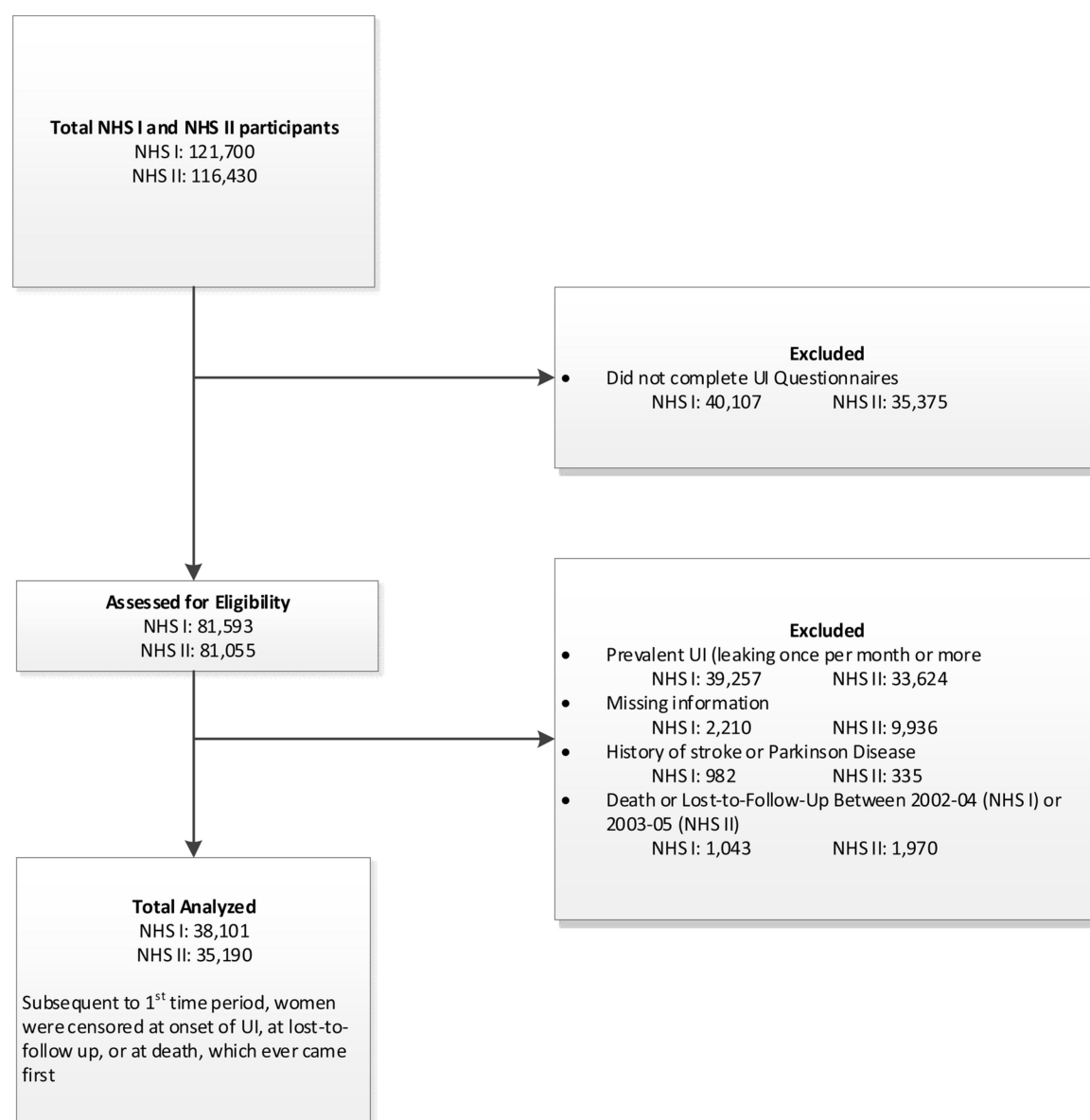


Fig. 1.
STROBE diagram for NHS I and NHS II for vitamin D intake and the risk of urgency urinary incontinence in women.

Table 1

NHSI age-standardized baseline characteristics^{1,2}, n = 38,101.

	Vitamin D total (IU), 6 categories					
	0– < 200 (n = 6472)	200– < 400 (n = 6208)	400– < 600 (n = 9421)	600– < 800 (n = 8146)	800– < 1000 (n = 3942)	> = 1000 (n = 3912)
<i>Demographics</i>						
Age, * mean (SD)	67 (7)	67 (7)	67 (7)	68 (7)	67 (7)	68 (7)
Race/Ethnicity						
White, %	97	97	97	97	97	97
Black, %	2	2	2	2	2	2
Asian, %	1	1	1	1	1	1
Other, %	0	0	0	0	0	0
<i>Health and Lifestyle</i>						
BMI (kg/m ²), mean ± SD	27 (5)	26 (5)	26 (5)	26 (5)	26 (4)	25 (4)
Physical activity (METS) ³ , mean ± SD	15 (21)	18 (21)	19 (23)	20 (22)	21 (25)	21 (26)
Cigarette Smoking						
never, %	43	45	45	47	46	47
past, %	44	45	47	46	48	48
current, %	13	9	8	7	6	5
<i>Medical Comorbidities</i>						
Thiazide Diuretic usage, %	13	13	14	15	14	14
Type 2 Diabetes, %	7	7	5	6	6	5
Vascular disease, %	3	2	2	2	1	2
Depression, %	5	5	6	5	6	6
<i>Obstetrical and Gynecological</i>						
Parity						
0, %	5	6	6	6	6	7
1–2, %	36	36	36	37	36	38
3+, %	58	58	58	58	58	55
Hysterectomy, %	38	39	38	39	39	38
Post-menopausal hormone use						
never, %	34	30	26	26	24	23

Vitamin D total (IU), 6 categories						
	0– < 200 (n = 6472)	200– < 400 (n = 6208)	400– < 600 (n = 9421)	600– < 800 (n = 8146)	800– < 1000 (n = 3942)	> =1000 (n = 3912)
past, %	37	38	39	39	42	42
current, %	29	32	35	35	34	34

¹Values are means (SD) for continuous variables; percentages for categorical variables, and are standardized to the age distribution of the study population.

²Values of polytomous variables may not sum to 100 % due to rounding.

³Metabolic Equivalents (METs).

* Value is not age adjusted.

Table 2

NHSII age-standardized baseline characteristics^{1,2}, n = 35,190.

	Vitamin D total (IU), 6 categories					
	0– < 200 (n = 7555)	200– < 400 (n = 7657)	400– < 600 (n = 7839)	600– < 800 (n = 6214)	800– < 1000 (n = 2973)	> = 1000 (n = 2956)
<i>Demographics</i>						
Age, * mean (SD)	49 (5)	50 (5)	50 (5)	51 (5)	51 (4.5)	52 (4)
Race/Ethnicity						
White, %	97	97	97	97	97	96
Black, %	1	1	1	1	1	2
Asian, %	1	2	1	2	1	2
Other, %	1	1	1	0	0	1
<i>Health and Lifestyle</i>						
BMI (kg/m ²), mean (SD)	27 (6)	26 (6)	26 (6)	26 (5)	26 (6)	26 (6)
Physical activity (METS) ³ , mean ± SD	21 (30)	25 (30)	25 (29)	27 (30)	28 (34)	31 (39)
Cigarette Smoking						
never, %	64	66	68	68	68	68
past, %	25	27	26	27	27	27
current, %	10	7	6	6	4	5
<i>Medical Comorbidities</i>						
Thiazide Diuretic usage, %	8	7	8	8	8	7
Type 2 Diabetes, %	3	2	3	3	3	3
Vascular disease, %	0	0	0	0	0	0
Depression, %	11	10	11	11	11	13
<i>Obstetrical and Gynecological</i>						
Parity						
0, %	18	18	20	22	23	25
1–2, %	52	52	53	52	53	51
3+, %	30	30	27	26	24	24
Hysterectomy, %	20	20	21	21	21	24
Post-menopausal hormone use						
pre/never, %	74	74	72	71	70	68

Vitamin D total (IU), 6 categories						
0– < 200 (n = 7555)	200– < 400 (n = 7657)	400– < 600 (n = 7839)	600– < 800 (n = 6214)	800– < 1000 (n = 2973)	> = 1000 (n = 2956)	
past, %	14	13	15	16	15	16
current, %	12	12	13	14	15	16

¹Values are means (SD) for continuous variables; percentages for categorical variables, and are standardized to the age distribution of the study population.

²Values of polytomous variables may not sum to 100 % due to rounding.

³Metabolic Equivalents (METs).

*Value is not age adjusted.

Table 3

NURSES' HEALTH STUDY I: Relative Risk of UI¹, According to Vitamin D Intake from Food and Supplements.

Vitamin D	Cases	Person-years	Age-adjusted RR (95 % CI)	Multi-variable adjusted RR*
URGENCY UI				
0– < 200IU	543	17,242	1.0 (ref)	1.0 (ref)
200– < 400	536	16,347	1.04 (0.91,1.18)	1.05 (0.93,1.18)
400– < 600	863	25,380	1.06 (0.95,1.19)	1.08 (0.97,1.21)
600– < 800	775	22,106	1.08 (0.97,1.21)	1.09 (0.97,1.22)
800– < 1000	398	11,055	1.11 (0.97,1.27)	1.13 (0.99,1.29)
1000+	481	13,397	0.99 (0.87,1.13)	1.02 (0.88,1.16)
				p-trend = 0.5
MIXED UI				
0– < 200IU	475	18,448	1.0 (ref)	1.0 (ref)
200– < 400	448	17,300	1.06 (0.92,1.20)	1.06 (0.93,1.21)
400– < 600	689	27,097	0.99 (0.87,1.11)	1.00 (0.89,1.12)
600– < 800	631	24,088	0.97 (0.86,1.10)	0.98 (0.87,1.11)
800– < 1000	328	12,046	0.98 (0.85,1.13)	1.00 (0.86,1.16)
1000+	457	15,218	0.92 (0.82,1.05)	0.94 (0.82,1.08)
				p-trend = 0.2
STRESS UI				
0– < 200IU	489	17,496	1.0 (ref)	1.0 (ref)
200– < 400	430	16,707	0.91 (0.80,1.04)	0.91 (0.80,1.04)
400– < 600	711	26,206	0.98 (0.87,1.10)	0.98 (0.87,1.10)
600– < 800	625	23,364	0.98 (0.87,1.10)	0.98 (0.87,1.10)
800– < 1000	295	11,856	0.93 (0.80,1.08)	0.94 (0.81,1.09)
1000+	377	14,624	0.98 (0.86,1.13)	1.01 (0.87,1.16)
				p-trend = 0.7

¹Urinary Incontinence (UI).

* Multivariable model adjusted for age, history of type 2 diabetes, history of vascular disease, cigarette smoking, parity, use of postmenopausal hormone therapy, and physical activity.

Table 4

NURSES' HEALTH STUDY II: Relative Risk of UI^I, According to Vitamin D Intake from Food and Supplements.

Vitamin D	Cases	Person-years	Age-adjusted RR (95 % CI)	Multi-variable adjusted RR*
URGENCY UI				
0– < 200IU	350	34430	1.0 (REF)	1.0 (REF)
200– < 400	323	34542	0.93 (0.79,1.08)	0.95 (0.82,1.11)
400– < 600	325	35388	0.88 (0.76,1.03)	0.91 (0.78,1.06)
600– < 800	247	28066	0.82 (0.69,0.96)	0.84 (0.71,0.99)
800– < 1000	141	13677	0.93 (0.76,1.13)	0.96 (0.79,1.18)
1000+	136	14063	0.85 (0.70,1.04)	0.88 (0.71,1.07)
				P trend = 0.1
MIXED UI				
0– < 200IU	320	34470	1.0 (REF)	1.0 (REF)
200– < 400	279	34813	0.86 (0.73,1.00)	0.90 (0.76,1.05)
400– < 600	314	35510	0.95 (0.81,1.12)	1.01 (0.86,1.19)
600– < 800	250	28253	0.92 (0.78,1.09)	0.99 (0.84,1.18)
800– < 1000	112	13879	0.81 (0.65,1.01)	0.88 (0.71,1.10)
1000+	110	14362	0.73 (0.59,0.91)	0.79 (0.63,0.99)
				P trend = 0.1
STRESS UI				
0– < 200IU	666	32,692	1.0 (REF)	1.0 (REF)
200– < 400	699	32,718	1.06 (0.95, 1.18)	1.07 (0.96,1.19)
400– < 600	662	33,842	0.99 (0.89, 1.11)	1.01 (0.90,1.12)
600– < 800	552	26,798	1.06 (0.95, 1.19)	1.09 (0.97,1.23)
800– < 1000	246	13,127	0.98 (0.84, 1.14)	1.01 (0.87,1.17)
1000+	228	13,266	0.91 (0.78, 1.06)	0.94 (0.81,1.10)
				P trend = 0.6

^IUrinary Incontinence (UI).

* Multivariable models adjusted for age, body mass index, cigarette smoking, parity, use of postmenopausal hormone therapy, physical activity.