Published in final edited form as:

Ann Rheum Dis. 2010 July ; 69(7): 1305–1309. doi:10.1136/ard.2009.109884.

Menopause, Postmenopausal Hormone Use and Risk of Incident Gout

A. Elisabeth Hak, MD, PhD^{1,2}, Gary C. Curhan, MD, ScD², Francine Grodstein, ScD², and Hyon K. Choi, MD, DrPH^{2,3,4}

¹Department of Internal Medicine, Division of Clinical Immunology, Erasmus MC University Medical Center, Rotterdam, The Netherlands ²Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, USA ³Department of Medicine, Division of Rheumatology, Arthritis Research Centre of Canada, Vancouver General Hospital, University of British Columbia, Vancouver, Canada ⁴Section of Rheumatology and the Clinical Epidemiology Unit, Boston University School of Medicine, Boston, MA, USA

Abstract

Objective—To prospectively study the relation between menopause, postmenopausal hormone use and risk of gout, since female sex hormones have been postulated to decrease gout risk among women.

Methods—In the Nurses' Health Study, we examined the association between menopause, age at menopause, postmenopausal hormone use and risk of self-reported physician diagnosed incident gout among 92,535 women without gout at baseline. We used multivariate proportional hazards regression analysis to adjust for other risk factors for gout such as age, body mass index, diuretic use, hypertension, alcohol intake and dietary factors.

Results—During 16 years of follow-up (1,240,231 person-years), we documented 1,703 incident gout cases. The incidence rate of gout increased from 0.6 per 1000 person-years in women <45 years of age to 2.5 in women ≥75 years of age (p for trend<0.001). Compared with premenopausal women, postmenopausal women had a higher risk of incident gout (multivariate-adjusted relative risk [RR], 1.26; 95% Confidence Interval [CI], 1.03 to 1.55). Among women with natural menopause, women with age at menopause <45 years had a RR of 1.62 (95% CI, 1.12 to 2.33) of gout compared with women with age at menopause 50 to 54 years. Postmenopausal hormone users had a reduced risk of gout (RR, 0.82; 95% CI, 0.70 to 0.96).

Conclusion—These prospective findings indicate that menopause increases the risk of gout, whereas postmenopausal hormone therapy modestly reduces gout risk.

Keywords

gout; women; menopause; postmenopausal hormone replacement therapy; epidemiology

Despite the increase of gout incidence in recent years,¹ and the substantial prevalence particularly in the older female population,² the risk factors for gout in women remain ill-defined. Sex hormones have been postulated to be associated with gout risk among women. Serum urate levels, which are closely associated with gout, increase substantially with age in

Corresponding author and address for reprints requests: Hyon Choi, MD, DrPH, Section of Rheumatology and the Clinical Epidemiology Unit, Boston University School of Medicine, 650 Albany Street, Suite 200, Boston, MA 02118, Tel) +1 617-638-5490; Fax) +1 617-638 5239, hchoius@bu.edu.

women, whereas among men urate concentrations are not significantly different between middle-and older age.³⁻⁵ In two surveys, a rise in urate levels among women was detected after middle age with a subsequent plateau.^{3, 4} Given the coinciding time periods, investigators inferred that this observation may be due to hormonal changes accompanying menopause.^{3, 4} Another survey, however, showed increasing uric acid levels with age from the 4th till the 8th decade and over in women.⁵ Nonetheless, small cross-sectional studies suggested that the vast majority of female gout cases were diagnosed after menopause.⁶⁻⁸ Furthermore, postmenopausal hormone therapy reduces uric acid levels among women.^{9, 10} Our recent data from a nationally representative sample of US women indicate that menopause is independently associated with higher serum uric acid levels, whereas postmenopausal hormone use is associated with lower uric acid levels among postmenopausal women.¹¹ Together, these reported findings suggest that menopause may increase the risk of gout, whereas postmenopausal hormone use may reduce gout risk among women. To date, no study has directly investigated these relations.

To address these issues, we prospectively examined the association between menopause, age at menopause and postmenopausal hormone use and incident gout in the Nurses' Health Study.

Subjects and Methods

Nurses' Health Study

The Nurses' Health Study (NHS) is a cohort study of 121,700 female U.S. nurses aged 30–55 years in 1976 at study inception.¹² The study was designed to prospectively examine the relations of lifestyle factors to chronic diseases, particularly cancer and cardiovascular disease. Information regarding diseases, lifestyle, and health practices is collected via biennial mailed questionnaires. The follow-up rate exceeds 90% for each 2-year period.

Assessment

On each questionnaire, menopausal status was determined by asking whether the participants' menstrual periods had ceased permanently and, if so, at what age and for what reason (occurring naturally or after radiation therapy or surgery). If menopause was due to surgery, the subject was asked to report the number of ovaries removed. Self-reported type of menopause and age at time of menopause in this cohort were highly accurate compared to medical records.¹³ From baseline onwards, all participants were asked whether they used postmenopausal hormone therapy.

Women were defined as menopausal from the self-reported time of natural menopause or bilateral oophorectomy (surgical menopause). Women with indeterminable age at menopause were women who underwent hysterectomy without bilateral oophorectomy, women with incomplete availability of data on the extent of pelvic surgery, women with permanent cessation of menses due to radiation therapy, and women who did not report the age of onset of menopause. Women with indeterminable age at menopause were considered menopausal when they reached the age at which natural menopause occurred in 90% of the cohort (54 years for smokers and 56 years for nonsmokers).¹⁴

Information on smoking status (never, past, or current) was assessed at baseline and updated every 2 years. Body mass index was computed for each two-year time interval using the most recent weight in kilograms divided by height in meters squared as reported at baseline. A study participant was considered to have hypertension from the time it was first reported on the questionnaire. Similarly, at baseline and every 2 years thereafter, the participants provided information on regular use of medications, including use of diuretics. To assess dietary intake, a self-administered semi-quantitative food frequency questionnaire (SFFQ)

was used that inquired about the average use of more than 130 foods and beverages, including alcohol, during the previous year.^{15, 16} The baseline SFFQ was completed in 1980, and updated every four years. The reproducibility and validity of this dietary questionnaire in this cohort have been previously reported.^{15, 16}

Starting with the 1982 questionnaire, and biennially up to 1988, participants were asked whether they had received a diagnosis of gout from a physician, and if so, the date of first diagnosis. In 2002, the question was posed again and women were then asked to report gout diagnosis since 1996. In 2004, we inquired about gout diagnosis between 2002 and 2004. Therefore, information regarding self-reported physician-diagnosed gout and its diagnosis date was available from 1980 to 1988, and from 1996 through 2004.

Study Population

After we excluded prevalent gout cases and women with indeterminable age at menopause in 1980, 92,535 women were included in the analyses of menopause and risk of incident gout for the 1980–1988 period. Since the question asking for gout occurrence from 1996 to 2002 was posed in the 2002 questionnaire, we restricted the analyses for the 1996 period onwards to women answering the 2002 questionnaire. Thus, after excluding prevalent gout cases from 1988 to 1996, we resumed our follow-up among 64,966 women for the analyses from 1996 onwards.

The analysis of age at menopause and risk of gout was restricted to women who had experienced natural menopause. Women who reported use of postmenopausal hormones were excluded from this analysis since use of postmenopausal hormones causes withdrawal bleeding and therefore makes it difficult for women to identify their exact age at menopause. As of 1980, and subsequently from 1996 onwards, 14,715 and 16,317 women were included in the analysis, respectively.

The analysis of postmenopausal hormone use and incident gout included all postmenopausal women. Women with missing data on postmenopausal hormone use or use of hormones other than oral estrogen with or without progestin (e.g. unknown type or vaginal preparations) were excluded. As of 1980, and subsequently from 1996 onwards, 26,520 and 52,976 women were included in the analysis, respectively. Participants who later reached menopause during the follow-up were included beginning at the time of their menopause. We repeated our analysis after excluding women with a history of cardiovascular disease (myocardial infarction, angina, or revascularization) or cancer (except nonmelanoma skin cancer) at baseline and on subsequent questionnaires, because these conditions may have caused them to alter their use of hormones.

Statistical Analysis

We computed the person-time of follow-up for each woman as the interval between the date on which the 1980 questionnaire was returned and the date of the first report of physician diagnosed gout, death, or return of the 1988 questionnaire, and subsequently as the interval between the date of return of the 1996 questionnaire and diagnosis date of gout, date of death, or end of the study period, whichever came first. Person-time was allocated to menopausal status or postmenopausal hormone use status according to the 1980 questionnaire and then updated with each subsequent biennial questionnaire up to 1988, and subsequently from 1996 onwards.

Person-time for each exposure category was accumulated, and incidence rates were calculated by dividing the number of events by person-time of follow-up in each category. We used proportional hazards models to determine the independent association between menopause and postmenopausal hormone use and risk of incident gout while simultaneously

adjusting for other risk factors. The Anderson-Gill data structure was used to handle time-varying covariates efficiently,¹⁷ where a new data record is created for every questionnaire cycle at which a participant is at risk, with covariates set to their values at the time that the questionnaire is returned. In these analyses, we used time-varying information from each two-year interval to analyze the risk of gout in the next two-year cycle from 1980 up to 1988, and subsequently from 1996 onwards. Using the SFFQ,^{15, 16} we calculated intake of alcohol (gram/day), meat, seafood, total dairy and coffee (servings/day), total calories, energy-adjusted fructose (gram/day), and vitamin C (milligram/day).

Risk factors for gout included in the multivariate proportional hazards models were age (continuous), body-mass index (less than 21, 21 to 22, 23 to 24, 25 to 27.5, 27.6 to 29, 30 to 31, or 32 or more), smoking (never, past, current), use of diuretics (thiazide or furosemide; yes or no), history of hypertension (yes or no), alcohol intake (non-drinker, up to 4.9 g per day, 5.0 to 9.9 g per day, 10.0 to 14.9 g per day, 15.0 to 29.9 g per day, or 30.0 g per day or more), daily average intake of meats, seafood, dairy, coffee, energy-adjusted fructose and vitamin C (each in quintiles), and total energy intake. In the analyses of postmenopausal hormone use and risk of gout among menopausal women, we also controlled for age at menopause (continuous) and type of menopause (natural, surgical, other). All analyses were performed using SAS software (SAS Statistical Software, Inc).

The Partners Health Care System Institutional Review Board (IRB) approved this study. Return of a completed questionnaire was accepted by the IRB as implied consent.

Results

During 16 years of follow-up (1,240,231 person-years), we documented 1,703 incident self-reported physician diagnosed gout cases. The incidence rates of gout per 1000 person-years according to age categories (<45, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, and 75 years) were 0.6, 1.1, 1.4, 1.5, 1.2, 1.7, 2.2, and 2.5, respectively (P for trend <0.001).

The characteristics of the participants included in the analysis on menopause and risk of gout are shown in Table 1. Surgical menopausal women had the highest body mass index, reported use of diuretics and hypertension most often, and tended to consume less alcohol. Intake of meat, seafood and dairy was not consistently different between premenopausal and postmenopausal women. The consumption of meat and dairy products tended to be lower, whereas the consumption of seafood and vitamin C tended to be higher in 1996 compared to 1980.

The risk of incident gout according to menopause is shown in Table 2. Menopause was associated with an increased risk of gout (age-adjusted relative risk [RR] 1.33, 95% confidence interval [CI] 1.08 to 1.63). After adjusting for other covariates including body-mass index, use of diuretics, hypertension, smoking, and intake of alcohol, meat, seafood, dairy, coffee, fructose, vitamin C, and total energy the RR was slightly attenuated. When we examined type of menopause, the risk of incident gout tended to be higher for surgical than natural menopause (Table 2).

Among women who had experienced natural menopause and had never used postmenopausal hormones, women with age at menopause younger than 45 years had a multivariate-adjusted RR of 1.62 (95% CI, 1.12 to 2.33) of incident gout compared with women with age at menopause 50 to 54 years (Table 3).

The age-adjusted relative risk of gout among current postmenopausal hormone users (estrogen alone or with progestin) compared with postmenopausal women who had never used postmenopausal hormones was 0.81 (95% CI, 0.70 to 0.94) (Table 4). Multivariate

adjustment including age at menopause, type of menopause, body-mass index, use of diuretics, hypertension, smoking and intake of alcohol, meat, seafood, dairy, coffee, fructose, vitamin C, and total energy did not influence this result. The results were not materially different for users of estrogen alone (n=238, multivariate-adjusted RR, 0.86; 95% CI, 0.72 to 1.02) or estrogen with progestin (n=73, multivariate-adjusted RR, 0.74; 95% CI, 0.57 to 0.96). We found no association between duration of postmenopausal hormone use among current users (p for trend=0.37) or interval since last postmenopausal hormone use among past users and risk of gout (p for trend=0.69). Exclusion of women with a history of cardiovascular disease or cancer did not materially affect the results.

Discussion

In this large prospective study of female registered nurses, we found that menopause was associated with a 26% increased risk of gout. This increase in the risk of gout tended to be more evident among women with surgical menopause and among women with younger age at natural menopause. We also found that postmenopausal hormone use was associated with an 18% lower risk of incident gout among postmenopausal women. These associations were independent of dietary and other risk factors for gout such as age, body mass index, diuretic use and hypertension. The current study provides the first prospective evidence for the long-suspected hypothesis that menopause and postmenopausal hormone use affect the risk of gout among women.

A biological mechanism that has been postulated to underlie the relation between menopause, postmenopausal hormone use and the risk of gout is the effect of estrogens and progesterone on a more efficient renal clearance of urate.^{18–20} In contrast to men who attain their “adult levels” of serum urate around the time of puberty, women persist with “juvenile levels” of serum urate throughout most of young adulthood and do not reach their maximum urate levels until after menopause. Thus, incident gout among women has been speculated to be simply a reflection of degree and duration of female hormonal influence. We found the highest risk of gout among women experiencing surgical menopause, in whom loss of ovarian hormone production is sudden and complete,²¹ providing support for a causal role of female sex hormone depletion. Age of menarche and period of relative estrogen deficiency (e.g. illness, athletic training, or eating disorders) might also affect the risk of incident gout in women, although these factors were not a focus of this study. In parallel with our results, among women enrolled in the Heart and Estrogen-Progestin replacement Study, treatment with postmenopausal hormones resulted in a slight lowering of serum uric acid levels compared with placebo (0.2 mg/dl at one year of follow-up).¹⁰ However, the risks of hormone replacement therapy, including breast cancer and stroke,²² should dampen the potential utility of this option as a means to lower serum uric acid levels and the risk of gout.

Although we observed an independent association between menopause and risk of gout, gout incidence increased before menopause and continued to increase until old age (≥ 75 years). This sharp increase of gout incidence with age among women corresponds with results from the United Kingdom General Practice Research Database.²³ The gout incidence among women reported in this UK study using primary care physician data was comparable with the self-reported physician-diagnosed gout incidence in our population (up to 2.7 versus 2.5 per 1000 person-years in the oldest age-groups, respectively). These incidence rates of gout among elderly women have been reported to be approximately half of those among men.²³

Strengths and limitations of our study deserve comment. A major strength of our study is its prospective design with biennial update of menopause, postmenopausal hormone use and other covariates, which reduces misclassification of these exposures. It has been shown, for

example, that the validity of reported age at menopause, which can only be determined in retrospect, increases with decreasing number of years since menopause.²⁴ Furthermore, the high level of education and the strong health interest of the women in our cohort favorably influenced the quality and accuracy of information reported. Participants of our study are not a random sample of US women, so our findings may not be directly generalizable to the entire US population. However, it seems unlikely that the basic biological relationships among our participants would differ from the population in general. A limitation of our study is that the end-point was self-reported physician-diagnosed gout. Since these self-reports were not verified, the incidence rates presented are likely to be overestimates.²⁵ However, any misclassification introduced by using self-reported physician-diagnosed gout is likely to be non-differential with regard to menopause and postmenopausal hormone use, and may thus only have led to an underestimate of the association between menopause, postmenopausal hormone use and risk of gout. Notably, our results with incident gout as the outcome agreed well with the recent data with the outcome of serum uric acid levels based on a nationally representative study of US women.¹¹

In conclusion, our findings provide prospective evidence that menopause increases the risk of gout among women, whereas postmenopausal hormone therapy modestly reduces gout risk among postmenopausal women. The impact of menopause on the risk of gout may be larger among women with surgical menopause and younger age at natural menopause.

Acknowledgments

Grant support: This research was supported by grant AR056042 from the National Institutes of Health.

Dr. Hak is the recipient of an Erasmus MC Fellowship (Erasmus MC University Medical Center, Rotterdam, The Netherlands) and has been supported by the Foundation 'Vereniging Trustfonds Erasmus Universiteit Rotterdam', The Netherlands.

The authors gratefully acknowledge the participants in the NHS for their continuing cooperation and thank Elaine Coughlan-Gifford for her assistance.

References

1. Roddy E, Zhang W, Doherty M. The changing epidemiology of gout. *Nature clinical practice*. 2007; 3:443–9.
2. Kramer HM, Curhan G. The association between gout and nephrolithiasis: the National Health and Nutrition Examination Survey III, 1988–1994. *Am J Kidney Dis*. 2002; 40:37–42. [PubMed: 12087559]
3. Mikkelsen WM, Dodge HJ, Valkenburg H. The distribution of serum uric acid values in a population unselected as to gout or hyperuricemia: Tecumseh, Michigan 1959–1960. *The American journal of medicine*. 1965; 39:242–51. [PubMed: 14320691]
4. Sturge RA, Scott JT, Kennedy AC, Hart DP, Buchanan WW. Serum uric acid in England and Scotland. *Ann Rheum Dis*. 1977; 36:420–7. [PubMed: 921341]
5. Akizuki S. Serum uric acid levels among thirty-four thousand people in Japan. *Ann Rheum Dis*. 1982; 41:272–4. [PubMed: 7092340]
6. Lally EV, Ho G Jr, Kaplan SR. The clinical spectrum of gouty arthritis in women. *Archives of internal medicine*. 1986; 146:2221–5. [PubMed: 3778053]
7. Puig JG, Michan AD, Jimenez ML, et al. Female gout. Clinical spectrum and uric acid metabolism. *Archives of internal medicine*. 1991; 151:726–32. [PubMed: 2012455]
8. De Souza AW, Fernandes V, Ferrari AJ. Female gout: clinical and laboratory features. *J Rheumatol*. 2005; 32:2186–8. [PubMed: 16265700]
9. Sumino H, Ichikawa S, Kanda T, Nakamura T, Sakamaki T. Reduction of serum uric acid by hormone replacement therapy in postmenopausal women with hyperuricaemia. *Lancet*. 1999; 354:650. [PubMed: 10466673]

10. Simon JA, Lin F, Vittinghoff E, Bittner V. The relation of postmenopausal hormone therapy to serum uric acid and the risk of coronary heart disease events: the Heart and Estrogen-Progestin Replacement Study (HERS). *Ann Epidemiol.* 2006; 16:138–45. [PubMed: 16039873]
11. Hak AE, Choi HK. Menopause, postmenopausal hormone use and serum uric acid levels in US women - The Third National Health and Nutrition Examination Survey. *Arthritis Res Ther.* 2008; 10:R116. [PubMed: 18822120]
12. Colditz GA, Manson JE, Hankinson SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. *Journal of women's health/the official publication of the Society for the Advancement of Women's Health Research.* 1997; 6:49–62. [PubMed: 9065374]
13. Colditz GA, Stampfer MJ, Willett WC, et al. Reproducibility and validity of self-reported menopausal status in a prospective cohort study. *Am J Epidemiol.* 1987; 126:319–25. [PubMed: 3605058]
14. Willett W, Stampfer MJ, Bain C, et al. Cigarette smoking, relative weight, and menopause. *Am J Epidemiol.* 1983; 117:651–8. [PubMed: 6859020]
15. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *Am J Epidemiol.* 1992; 135:1114–26. discussion 27–36. [PubMed: 1632423]
16. Willett, W.; Lenart, E. Reproducibility and validity of food-frequency questionnaires. In: Willett, W., editor. *Nutritional epidemiology.* New York: Oxford University Press; 1998. p. 101-47.
17. Therneau, TM. Extending the Cox model. In: Lin, DY.; Flemin, TR., editors. *Proceedings of the First Seattle Symposium in Biostatistics: Survival Analysis.* New York, NY: Springer Verlag; 1997. p. 51-84.
18. Nicholls A, Snaith ML, Scott JT. Effect of oestrogen therapy on plasma and urinary levels of uric acid. *Br Med J.* 1973; 1:449–51. [PubMed: 4689833]
19. Adamopoulos D, Vlassopoulos C, Seitanides B, Contoyiannis P, Vassilopoulos P. The relationship of sex steroids to uric acid levels in plasma and urine. *Acta Endocrinol (Copenh).* 1977; 85:198–208. [PubMed: 577077]
20. Atallah AN, Guimaraes JA, Gebara M, Sustovich DR, Martinez TR, Camano L. Progesterone increases glomerular filtration rate, urinary kallikrein excretion and uric acid clearance in normal women. *Braz J Med Biol Res.* 1988; 21:71–4. [PubMed: 3179582]
21. Bachmann G. Physiologic aspects of natural and surgical menopause. *J Reprod Med.* 2001; 46:307–15. [PubMed: 11310451]
22. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA.* 2002; 288:321–33. [PubMed: 12117397]
23. Mikuls TR, Farrar JT, Bilker WB, Fernandes S, Schumacher HR Jr, Saag KG. Gout epidemiology: results from the UK General Practice Research Database, 1990–1999. *Ann Rheum Dis.* 2005; 64:267–72. [PubMed: 15647434]
24. den Tonkelaar I. Validity and reproducibility of self-reported age at menopause in women participating in the DOM-project. *Maturitas.* 1997; 27:117–23. [PubMed: 9255746]
25. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum.* 2008; 58:26–35. [PubMed: 18163497]

Table 1
Age-standardized distribution of characteristics among women participating in the Nurses' Health Study by menopausal status

	1980				1996			
	Premenopausal		Postmenopausal		Premenopausal		Postmenopausal	
	(n=56,878)		Natural (n=24,624)	Surgical (n=11,033)	(n=5,395)		Natural (n=46,613)	Surgical (n=12,958)
Age, mean $\pm$ SD (y)	42.0 $\pm$ 5.3		54.1 $\pm$ 3.5	50.4 $\pm$ 5.7	51.9 $\pm$ 2.2		63.0 $\pm$ 6.8	62.5 $\pm$ 6.9
Body mass index (kg/m ²)	24.5		24.5	24.8	26.3		26.3	26.9
Diuretic use (%)	9.0		8.6	11.6	3.7		9.3	13.1
History of hypertension (%)	15.2		17.4	21.2	43.5		37.9	46.8
Alcohol intake (g/d)	6.3		6.2	5.7	5.4		5.3	4.4
Total meat intake (servings/day)	1.2		1.2	1.2	0.7		0.7	0.7
Seafood intake (servings/day)	0.2		0.2	0.2	0.3		0.3	0.3
Total dairy food intake (servings/day)	1.9		1.9	1.9	1.3		1.6	1.6
Total coffee intake (servings/day)	2.2		2.4	2.1	2.0		2.1	1.9
Total fructose intake (g/day)	21.3		21.8	22.5	22.3		21.1	21.4
Total vitamin C intake (mg/day)	299		292	326	476		366	374
Smoking status (%)								
Current	24.8		37.9	29.7	6.1		12.9	10.3
Former	27.9		24.6	25.5	49.1		43.3	43.1
Never	46.9		35.5	41.5	44.8		43.4	46.1
Age at menopause, mean $\pm$ SD (y)	Not applicable		48.8 $\pm$ 4.0	42.2 $\pm$ 6.5	Not applicable		50.0 $\pm$ 3.7	44.3 $\pm$ 6.3

Relative risk (RR) of self-reported physician diagnosed incident gout according to menopausal status among women participating in the Nurses' Health Study

Table 2

Menopausal status	Person years	No. of cases	Age-adjusted RR (95% CI)	Multivariate-adjusted RR* (95% CI)
Premenopausal	373,176	294	1.00 (ref)	1.00 (ref)
Postmenopausal	867,054	1,409	1.33 (1.08–1.63)	1.26 (1.03–1.55)
Natural	659,184	1,007	1.16 (0.94–1.44)	1.17 (0.95–1.45)
Surgical	207,870	402	1.54 (1.24–1.91)	1.37 (1.10–1.69)

* adjusted for age, body-mass index, smoking, use of diuretics, history of hypertension, alcohol intake, daily average intake of meats, seafood, dairy, coffee, energy-adjusted fructose and vitamin C, and total energy intake

Table 3

Relative risk (RR) of self-reported physician diagnosed incident gout according to age at natural menopause among women who never used postmenopausal hormones in the Nurses' Health Study

Age at menopause	Person years	No. of cases	Age-adjusted RR (95% CI)	Multivariate-adjusted RR* (95% CI)
<45	17,852	40	1.50 (1.05–2.16)	1.62 (1.12–2.33)
45–49	80,650	149	1.18 (0.95–1.46)	1.20 (0.97–1.49)
50–54	140,958	236	1.00 (ref)	1.00 (ref)
≥55	20,857	37	1.10 (0.77–1.56)	1.06 (0.75–1.51)

* adjusted for age, body-mass index, use of diuretics, history of hypertension, smoking, alcohol intake, daily average intake of meats, seafood, dairy, coffee, energy-adjusted fructose and vitamin C, and total energy intake

Relative risk (RR) of self-reported physician diagnosed incident gout according to postmenopausal hormone use among postmenopausal women in the Nurses' Health Study

Table 4

	Postmenopausal hormone use		
	Never Used	Used in Past	Current user
No. of gout cases	613	268	311
Person-years	328,322	136,342	239,954
Age-adjusted RR (95% CI)	1.00 (reference)	1.04 (0.89–1.20)	0.81 (0.70–0.94)
Multivariate-adjusted RR* (95% CI)	1.00 (reference)	0.99 (0.85–1.16)	0.82 (0.70–0.96)

* adjusted for age, age at menopause, type of menopause, body-mass index, use of diuretics, history of hypertension, smoking, alcohol intake, daily average intake of meats, seafood, dairy, coffee, energy-adjusted fructose and vitamin C, and total energy intake