

## Factors associated with the use of hormone replacement therapy among older women

SIR—The long-term use of postmenopausal hormone replacement therapy (HRT) to prevent diseases has been recently questioned by the results of the Women's Health Initiative [1]. The discrepancy between data provided by observational studies and those from randomised controlled trials suggests that some apparent positive association between HRT use and long-term health benefits might be partially attributable to the presence of biases in the observational studies, such as selection [2] and compliance [3] biases. Data obtained in upper-middle class women [4, 5], early postmenopausal women [6] and women aged on average 65 years [7, 8] suggest that HRT users are healthier and more health conscious than the non-users. A recent study suggested a similar profile among older women [9], but without adjusting for the menopause status and/or hysterectomy, two determinants of HRT use [8]. The only population-based study assessing the determinants of HRT use in older women by taking into account the menopausal status was performed in the eighties [10].

The aim of our study was to determine the characteristics of HRT use among older women aged 70 or more who participated in the Swiss Study for the Evaluation of the Methods of Measurement of Osteoporotic Fracture Risk (SEMOF Study).

### Population and methods

The SEMOF Study is a prospective multi-centre study assessing the predictive value of bone ultrasound devices for hip fractures in a cohort of 7,609 women aged 70 and older [11, 12]. Briefly, participants were recruited from January 1998 to Summer 1999 from the Swiss official population-based listings in 10 areas across the country. We excluded those with a history of hip fracture, bilateral hip replacement, renal failure, active cancer or dementia.

Sociodemographic data included age, education, current partnership situation, and previous professional status. Clinical variables included report of previous and current medications, menopausal status, diagnosis of osteoporosis, personal history of hip fractures, current alcohol consumption, cigarette smoking, and level of physical activity. We measured weight and height to calculate the body mass index (BMI). HRT use was identified as any report of systemic (oral or transdermal medications) oestrogen, with or without progesterone. Current or past users were defined as women who reported use of HRT either at the time of the interview, or anytime in the past. Women whose only prescribed HRT was topical oestrogen creams were considered as never users.

We assessed the validity of the questionnaire information by comparing the participant's answers with the information provided by their primary care physician. We randomly selected 170 participants of one centre and

asked them permission to contact their physician, and 154 women agreed (91%). One hundred and twenty-four physicians answered the questionnaire (81% participation rate). The agreement between the self-reported information and the data obtained from the physician can be deemed as either good or excellent, since the kappa statistics ranged between 0.76 (diagnosis of osteoporosis) and 0.94 (vertebral fracture) for fracture events and between 0.69 (previous calcium supplementation) and 0.94 (current HRT use or calcium supplementation) for medication.

We performed bivariate analyses where current users of HRT were opposed to the others using the *t*-test for continuous and the Pearson chi-square test for categorical variables. The comparisons were also performed on three categories (current, past and never) using analysis of variance, Pearson chi-square, as well as a Wilcoxon-type test for trend. We conducted a multivariable logistic regression analysis of current users to adjust for potential confounding bias. Adjusted odds ratios and 95% confidence interval are reported. Statistical analyses were performed using STATA 7.0 statistical package.

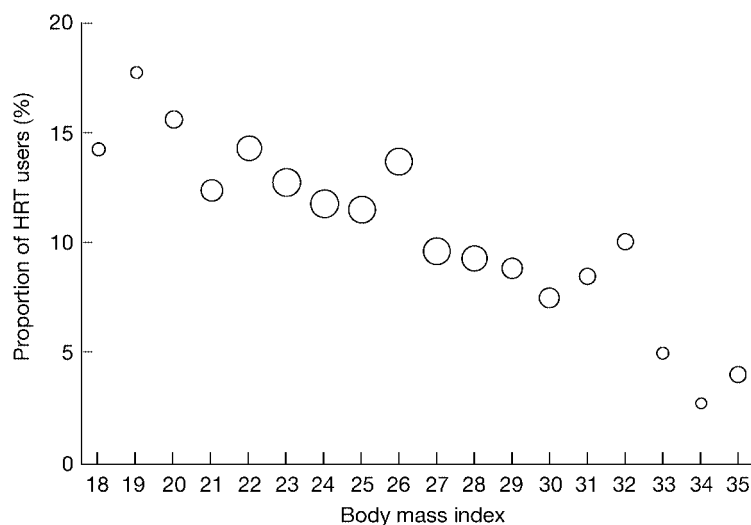
The ethics committee of the Swiss Academy of Medical Sciences approved the study protocol.

### Results

We included 7,609 women whose mean age ( $\pm$ SD) was 75.3 ( $\pm$ 3.1) years, and mean age at menopause was 49 ( $\pm$ 5.5) years. The vast majority (75%) reported a natural menopause, and 22% a post-surgery menopause (mainly due to a hysterectomy). Overall, 11% of the women reported current and 7% past use of HRT, with an average duration of 11.3 and 5.8 years, respectively. Among current users, the percent of women reporting unopposed oestrogen therapy was 27%. Current use of HRT declined with age and BMI (Figure 1).

As compared to never and past users, current users experienced significantly more frequently a surgical menopause (38.0% *versus* 21.3%), were younger (mean age 74.0 *versus* 75.4), more likely to have a BMI lower than the median (58.8% *versus* 49.1%), to live with a spouse or partner (56.0% *versus* 49.4%), to have a high education (13.2% *versus* 9.1%) and previous qualified professional level (60.6% *versus* 50.8%), to be supplemented with calcium (29.3% *versus* 19.3%) and vitamin D (19.6% *versus* 12.1%), as well as to report occasional alcohol consumption (62.6% *versus* 58.9%) and a diagnosis of osteoporosis (26.2% *versus* 17.6%). Smoking status, level of physical activity, history of vertebral or forearm fractures, and age of menopause did not differ between current HRT users and others.

When we compared the distribution of these variables among the HRT categories, we found a significant linear trend for age, BMI, diagnosis of osteoporosis, surgical menopause, living with a spouse, professional and educational level, calcium or vitamin D supplementation, and alcohol consumption (Table 1). Multiple logistic regression analyses including age and all variables statistically significant with a *P*-value  $<0.20$  in the bivariate analysis



**Figure 1.** Use of hormone replacement therapy among women aged 70 and older by body mass index (kg/m<sup>2</sup>). The areas of the symbols are proportional to the size of the population at that specific BMI.

revealed that the major determinants of current use of HRT were the following (Table 2): surgical menopause; calcium supplementation; diagnosis of osteoporosis; high socioeconomic status; lower weight; marital status.

**Discussion**

The proportion of current and past HRT users among these 7,609 older women was 11 and 7%, respectively. To our knowledge, this is the first study performed during the nineties taking into account the type of menopause and reporting the prevalence of HRT use and the health profile of the HRT users in older women.

After adjustment for age, the major determinant for the use of HRT was a post-surgery menopause, which

extends a similar association in younger women [8]. The current HRT users were different from former and never users with regard to disease prevention measures. After taking into account age, the report of post surgery menopause and the diagnosis of osteoporosis, current HRT users appear to be more likely to have a ‘health conscious’ profile (i.e., to be thinner and more likely to have calcium supplementation) and a higher socioeconomic status. The significant trends for several determinants in never, former, and current users, suggest that the more a woman is health conscious and has a high socioeconomic status, the more likely she is to keep on using HRT. Our results are in concordance with data obtained during the eighties [10, 13, 14]. These results extend data obtained in younger women [6–9, 13] and in older women but

**Table 1.** Analysis of the association between various factors and the use of hormone replacement therapy (n = 7,609)

Factors	Current (n = 841)	Past (n = 533)	Never (n = 6235)	P-value	P for trend
Age (mean ± SD), year	74.0 ± 2.9	74.4 ± 2.9	75.5 ± 3.0	<0.001	<0.001
BMI <sup>a</sup> (mean ± SD), kg/m <sup>2</sup>	24.9 ± 3.8	25.5 ± 4.0	26.1 ± 4.5	<0.001	<0.001
BMI <sup>a</sup> <25.5 kg/m <sup>2</sup> , %	58.8	54.4	48.5	<0.001	<0.001
Living with a spouse, %	56.0	54.6	48.9	<0.01	<0.01
High education <sup>b</sup> , %	13.2	11.8	8.9	<0.001	<0.001
Previous qualified job <sup>c</sup> , %	60.6	57.0	50.3	<0.001	<0.001
Post-surgery menopause, %	38.0	29.7	20.4	<0.001	<0.001
Diagnosis of osteoporosis, %	26.2	23.6	17.1	<0.001	<0.001
Ca supplementation, %	29.3	25.0	18.8	<0.001	<0.001
Vitamin D supplementation, %	19.6	17.7	11.6	<0.001	<0.001
Any alcohol consumption <sup>d</sup> , %	62.6	67.3	58.1	<0.001	<0.001
No sedentary lifestyle <sup>e</sup> , %	25.3	25.5	27.1	NS	–
No current smoking, %	91.6	93.4	92.0	NS	–
Any fracture in the past, %	53.0	54.2	51.0	NS	–

<sup>a</sup>BMI = body mass index (weight – kg/height<sup>2</sup> – cm).

<sup>b</sup>High education = having a university or equivalent degree (versus lower education level).

<sup>c</sup>Job requiring any form of training, such as apprenticeship or college (versus unqualified job).

<sup>d</sup>Any alcohol consumption = any level of consumption, i.e. occasional or regular (versus no drink at all).

<sup>e</sup>No sedentary lifestyle = any lifestyle or sports activities (versus no activity at all).

**Table 2.** Age-adjusted odds ratio for variables associated with current use of HRT

Variable	Odds ratio <sup>a</sup>	95% CI
Post surgery menopause	2.12	1.81–2.49
Calcium supplementation	1.49	1.23–1.80
Diagnosis of osteoporosis	1.48	1.22–1.80
High education	1.46	1.16–1.84
Body mass index <25.5 kg/m <sup>2</sup>	1.44	1.23–1.69
Previous qualified job	1.43	1.23–1.68
Living with a spouse	1.20	1.02–1.39

<sup>a</sup>Estimated from a multivariate model which included age, body mass index, type of menopause, diagnosis of osteoporosis, calcium and vitamin D supplementations, high education, previous qualified professional level, living with a spouse, and alcohol consumption.

without control for previous hysterectomy [13]. Such a ‘health-conscious’ profile has also been demonstrated in other preventive medicine areas [15].

Why this difference regarding health consciousness between current, past and never older HRT users? A self-selection by the women themselves is possible; the women with a health conscious profile might either have asked their physicians for or were compliant with HRT more frequently than other women. Current HRT users have been recently shown more likely to be worried about becoming less attractive, suggesting that they may have asked for or were compliant with HRT because of their desire to feel and look younger [8]. It is also possible that physicians themselves selected among their patients the candidates for such therapy according to their lifestyle, current medications or socioeconomic status. Our data support the recommendations to share with the patient the pros and cons of HRT before prescribing this therapy to a postmenopausal woman [16].

We compared the distribution of some variables with data in the age-matched Swiss general population provided by the Swiss Health Survey [17]. The prevalence of smoking (8% *versus* 7%, respectively) and of hysterectomy (23% *versus* 21%) and the median BMI (25.5 *versus* 25.2 kg/m<sup>2</sup>) were similar. These comparisons indicate that our study population are not different from the source population. Furthermore, the age at the menopause and the proportion of natural menopause were concordant with previous data [18, 19].

Our study has limitations. First, we used self-reported data. However, the very good agreement between the report of the medications (including HRT use) and the history of fractures, and the data provided by the participant’s physician give credence to the validity of our data. The validity of information on medications and fractures has also been previously demonstrated [20–25]. Second, a recall bias is possible [26]. However, we did not find any differences between HRT users and the other women in their proportion to report other events, such as previous fractures.

We conclude that older women using HRT had more often a post-surgery menopause and a diagnosis of osteoporosis. Besides, they were more likely to have a ‘health

conscious’ profile, as well as to have a high socioeconomic status, than non-users.

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### Conflicts of interests

None declared.

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JACQUES CORNUZ<sup>1,2\*</sup>, MARC-ANTOINE KRIEG<sup>1</sup>,  
LORENZO SANDINI<sup>1</sup>, CHRISTIANE RUFFIEUX<sup>2</sup>,  
GUY VAN MELLE<sup>2</sup>, PETER BURCKHARDT<sup>1</sup>

<sup>1</sup>Department of Medicine, <sup>2</sup>Institute of Social and Preventive  
Medicine,

University Hospital, 1011 Lausanne, Switzerland

Fax: ( 41) 21 314 08 71

Email: Jacques.Cornuz@chuv.hospvd.ch

\*To whom correspondence should be addressed

For the SEMOF research group (alphabetical order):

D. Büche (State Hospital, St. Gall); M. Dambacher (Balgrist  
Clinic, Zürich);

F. Hartl (University Hospital, Basel); H. Häuselmann  
(University Hospital, Zürich);

K. Lippuner (University Outpatient clinic, Bern); M. Neff  
(Osteoporosis Center, Zürich);

P. Pancaldi (Osteoporosis Center, Locarno); R. Rizzoli  
(University Hospital, Geneva);

F. Tanzi (Osteoporosis Center, Lugano); R. Theiler (State  
Hospital, Aarau);

A. Tyndall (University Hospital, Basel); C. Wimpfheimer,  
(Private practice, Luzern)

1. 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.

2. Vandenbroucke JP. How much of the cardioprotective effect of postmenopausal estrogens is real? *Epidemiology* 1995; 6: 207–8.

3. Petitti DB. Coronary heart disease and estrogen replacement therapy: can compliance bias explain the results of observational studies? *Ann Epidemiol* 1994; 4: 115–8.

4. Barret-Connor E. Postmenopausal estrogen and prevention bias. *Ann Intern Med* 1991; 115: 455–6.

5. Barrett-Connor EL, Cohn BA, Wingard DL, Edelstein SL. Why is diabetes mellitus a stronger risk factor for fatal ischemic heart disease in women than in men? The Rancho Bernardo Study. *JAMA* 1991; 254: 627–31.

## Research letters

6. Matthews KA, Kuller LH, Wing RR, Meilahn EN, Plantinga P. Prior to use of estrogen replacement therapy, are users healthier than nonusers? *Am J Epidemiol* 1996; 143: 971–8.
7. Brett KM, Madans JH. Use of postmenopausal hormone replacement therapy: estimates from a nationally representative cohort study. *Am J Epidemiol* 1997; 145: 536–45.
8. Keating NL, Cleary PD, Rossi AS, Zaslavsky AM, Ayanian JZ. Use of hormone replacement therapy by postmenopausal women in the United States. *Ann Intern Med* 1999; 130: 545–53.
9. Rödström K, Bengtsson C, Lissner L, Björkelund C. Pre-existing risk factor profiles in users and non-users of hormone replacement therapy: prospective cohort study in Gothenburg, Sweden. *Br Med J* 1999; 319: 890–3.
10. Cauley JA, Cummings SR, Black DM, Mascioli SR, Seeley DG. Prevalence and determinants of estrogen replacement therapy in elderly women. *Am J Obstet Gynecol* 1990; 163: 1438–44.
11. Cornuz J, Krieg MA, Burckhardt P. Evaluation suisse des méthodes de mesure du risque de fracture ostéoporotique. *Bull méd suisses* 1999; 80: 352–5.
12. Krieg MA, Cornuz J, Büche D *et al.* Quality controls for two heel bone ultrasound used in the SEMOF study. *J Clin Densitom* 2002; 5: 335–41.
13. Handa VL, Landerman R, Hanlon JT, Harris T, Cohen HJ. Do older women use estrogen replacement? Data from the Duke established populations for epidemiologic studies of the elderly (EPESE). *J Am Geriatr Soc* 1996; 44: 1–6.
14. Sourander L, Rajala T, Rähä I, Mäkinen J, Erkkola R, Helenius H. Cardiovascular and cancer morbidity and mortality and sudden cardiac death in postmenopausal women on estrogen replacement therapy. *Lancet* 1998; 352: 1965–69.
15. Ervin RB, Wright DW, Kennedy-Stephenson J. Use of dietary supplements in the United States, 1988–1994. *Vital Health Stat* 2000; 11: 244–56.
16. Mosca L, Collins P, Herrington DM *et al.* Hormone replacement therapy and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001; 104: 499–503.
17. Office fédéral de la statistique. Swiss Health Survey. Neuchâtel: Office fédéral de la statistique, 1999.
18. Luoto R, Kaprio J, Uuetela A. Age at natural menopause and sociodemographic status in Finland. *Am J Epidemiol* 1983; 117: 651–8.
19. Levi F, Lucchini F, Pasche C, La Vecchia C. Oral contraceptives, menopausal hormone replacement treatment and breast cancer risk. *Eur J Cancer Prev* 1996; 5: 259–66.
20. Colditz GA, Martin P, Stampfer MJ *et al.* Validation of questionnaire information on risk factors and disease outcome in a prospective cohort study of women. *Am J Epidemiol* 1986; 123: 894–900.
21. Goodman MT, Nomura AMY, Wilkens LR, Kolonel LN. Agreement between interview information and physician records on history of menopausal estrogen use. *Am J Epidemiol* 1990; 131: 815–25.
22. Jannaussch Sowers MR. Consistency of perimenopausal estrogen use reporting by women in a population-based study. *Maturitas* 1992; 14: 161–9.
23. Honkanen K, Honkanen R, Heikkinen L, Heikki K, Saarikoski S. Validity of self-reports of fractures in perimenopausal women. *Am J Epidemiol* 1999; 150: 511–16.
24. Jain MG, Rohan TE, Howe GR. Agreement of self-reported use of menopausal hormone replacement therapy with physician reports. *Epidemiology* 1999; 10: 260–3.
25. Merlo J, Berglund G, Wirfält E *et al.* Self-administrated questionnaire compared with a personal diary for assessment of current use of hormone therapy: an analysis of 16,060 women. *Am J Epidemiol* 2000; 152: 788–92.
26. Yaffe K, Sawaya G, Lieberburg I, Grady D. Estrogen therapy in postmenopausal women: effects on cognitive function and dementia. *JAMA* 1998; 279: 688–95.