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ORIGINAL ARTICLE

Trends in HRT and anti-osteoporosis medication prescribing in a European population after the WHI study

L. Huot · C. M. Couris · V. Tainturier · S. Jaglal · C. Colin · A.-M. Schott

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Abstract
Summary To assess the prescription patterns of anti-osteoporosis medications, three cross-sectional analyses were performed between 2004 and 2006. Women aged 50 and older were identified from the health insurance claims database of the Rhône-Alpes area. HRT prescriptions decreased while bisphosphonates and raloxifene prescriptions increased, respectively, in different age groups.

Introduction The objective of this study was to assess the prescription patterns of hormone replacement therapy (HRT) and anti-osteoporosis medications (AOM) in post-menopausal French women since the WHI and the revision of the French clinical practice guidelines in 2004.
Methods Three cross-sectional analyses were performed between 2004 and 2006. Women aged 50 and older who had at least one claim for a prescription for HRT, bisphosphonates or raloxifene were identified from health insurance claims database of the Rhône-Alpes area.
Results A 39% decrease in the number of women who had HRT was observed (67,241 to 41,024). Twenty-one percent and 18% increases were observed, respectively, for bisphosphonates (39,192 to 47,395) and raloxifene (10,263 to 12,060). HRT and raloxifene were mainly prescribed to women aged 55 to 64 (58% and 39%, respectively), bisphosphonates to women aged 65 to 84 (70%). Ninety-eight percent of women had HRT prescribed by a gynaecologist or a general practitioner (GP). Most AOM were prescribed by a GP; 13% of women had AOM prescribed by a rheumatologist.
Conclusion Prescriptions for HRT in post-menopausal French women have significantly decreased while bisphosphonates and raloxifene prescriptions have increased, respectively, in different age groups but to a lesser extent than the HRT decrease.

L. Huot · C. M. Couris · C. Colin · A.-M. Schott
Hospices Civils de Lyon,
Pole Information Médicale Evaluation Recherche,
Unité d'Epidémiologie,
Lyon F69003, France

L. Huot · C. M. Couris · C. Colin · A.-M. Schott
Université de Lyon,
Equipe d'Accueil 4129 Santé Individu Société,
Lyon F69003, France

L. Huot · C. M. Couris · C. Colin · A.-M. Schott
Université Lyon 1,
Lyon F69003, France

C. M. Couris · A.-M. Schott
INSERM Unité 831,
Lyon, France

V. Tainturier
Direction régionale du service médical de l'Assurance Maladie,
Lyon F69003, France

S. Jaglal
Department of Physical Therapy, University of Toronto,
Toronto, Canada

A.-M. Schott (✉)
Pôle Information Médicale Evaluation Recherche,
162 Avenue Lacassagne,
69424 LYON Cedex 03, France
e-mail: anne-marie.schott-pethelaz@chu-lyon.fr

Keywords Bisphosphonates · Guidelines · Hormone replacement therapy · Osteoporosis · Raloxifene

Introduction

The decreased production of ovarian steroids during menopause is responsible for climacteric complaints and

increases the risk of chronic and degenerative diseases such as osteoporosis. Until recently, hormone replacement therapy (HRT) used to be prescribed widely by the medical community for the treatment of menopausal symptoms and prevention of osteoporosis. Observational studies and randomized clinical trials have demonstrated that estrogens or estrogens plus progestin increase bone density and reduce the risk of fractures by preventing bone loss in both young and older post-menopausal women [1]. In July 2002, the Women's Health Initiative (WHI) trial produced evidence against the cardioprotective effect of HRT in older postmenopausal women and highlighted an increased risk of breast cancer associated with extended use [2].

As long-term use of HRT is risky, physicians who have to treat women at increased risk of osteoporosis may replace HRT by other osteoporosis medications that seem safer [3]. Bisphosphonates were shown to be effective in preventing hip, wrist and spine fractures in the past decade [4]. Also new therapeutics such as raloxifene, a selective estrogen receptor modulator (SERM), are gaining acceptance. By suppressing bone turnover and preserving bone density in both young and older post menopausal women, raloxifene reduced the incidence of new vertebral fractures by 30–50% in a large prospective trial [5]. Furthermore, raloxifene seems to have a positive effect on cardiovascular risk, unlike estrogen [6]. Teriparatide, an analogue of the parathyroid hormone, is a new anabolic drug that improves the skeletal micro-architecture. Significant reductions in both vertebral and non-vertebral fractures were demonstrated in elderly women with at least one prevalent vertebral fracture before the onset of therapy [7].

Since the diffusion of the WHI and the Million Women Study (MWS) results [8], clinical practice guidelines on HRT use have been modified in most countries, including France [9], resulting in a significant decline in prescriptions for these treatments [10, 11]. What is not known from these studies is the impact of the guideline changes on prescriptions for anti-osteoporosis medications other than HRT. The aim of this study was to describe prescription patterns for HRT and other anti-osteoporosis medications (AOM) in a population of French post-menopausal women, a few years after the WHI study, regarding time trends, age of women and the specialty of the prescribers.

Methods

Study population

The study population included women aged 50 and older, living in the Rhône-Alpes area and affiliated with the French National Health Insurance (NHI) plan. The Rhône-Alpes area population, one of the three largest in France, was estimated at 5.9 million inhabitants on 01 January 2004, with 1,044,349 women aged 50 years and older [12]. The NHI covers approximately 80% of this population.

The total number of physicians in the Rhône-Alpes area in 2004 was 10,927 with 5,225 (47.8%) general practitioners (GP), 527 (4.8%) gynaecologists (medical or obstetric gynaecology) and 208 rheumatologists (1.9%; NHI data).

Database

Data were obtained from the NHI claims database of the Rhône-Alpes area. This database included individual level information on the patients (patient identification, date of birth, and sex) and on their claims for medical services and drugs. Information on claims included the name of the drugs prescribed, the Club Inter Pharmaceutical (CIP) index which is a seven-digit number identifying each marketed drug in France, and the WHO Anatomical Therapeutic Chemical (ATC) code of drugs, the date of prescription and the date of claim. Information on physician specialty was also available.

Data selection

The NHI database was used to identify women aged 50 and older who had at least one claim for a prescription for HRT (estrogen alone or estrogen plus progestin therapy), bisphosphonates or raloxifene or teriparatide, or both (HRT plus other AOM) during the study period. Only women with refunded treatments appear in the NHI claims database. In France, at the time of the study, etidronate was always refunded; raloxifene, risedronate 35 mg, alendronate 10 mg and 70 mg were refunded only for women with at least one previous fracture; and teriparatide was refunded if at least two vertebral fractures occurred. The physician was expected to add the mention "non-refundable" when prescribing those treatments in women without any previous fracture.

Drugs were selected using their ATC code (beginning with G03C for estrogens, G03D for progestin and G03F for estrogen-progestin combinations; M05BA for bisphosphonates), or their CIP index (one for each marketed drug containing raloxifene or teriparatide). No data on teriparatide were available in 2004, since it was marketed at the end of this year.

Variables and analysis

Three 3-month cross-sectional analyses (from January to March) were performed from 2004 to 2006. A three-month period was chosen from each year to provide a snapshot and obtain stable estimates.

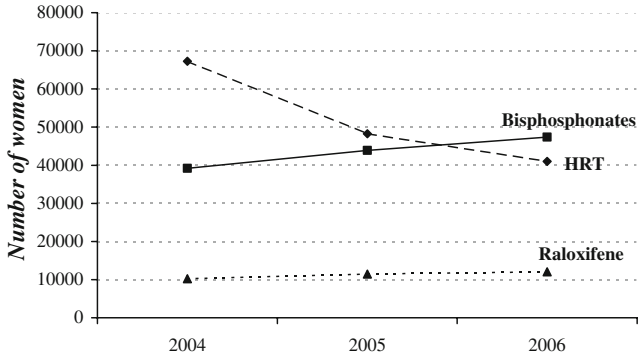

Fig. 1 Evolution of the total number of women with a prescription for hormone replacement therapy (HRT) or anti-osteoporosis medications in the Rhône-Alpes area between January 2004 and January 2006

The number of women who had prescriptions for HRT or AOM was extracted from the database for each study period. The proportion of women aged 50 and older living in the Rhône-Alpes area who were on HRT or AOM was calculated using the estimated number of women that were in the NHI database on 01 January 2004. Results were reported for each treatment as numbers and percentages of women by 5-year age groups over the three study periods. The specialty of physicians who prescribed HRT and AOM was also analyzed and results were reported for each type of prescriber as numbers and percentages of women by 5-year age group over the three study periods for prescriptions for HRT on the one hand and for prescriptions for AOM on the other hand. The average number of women per prescriber specialty and type of treatment was estimated.

Results

On 01 January 2004, approximately 835,479 women aged 50 and older had drug coverage by the NHI in the Rhône-Alpes area. Of these women, 67,241 (8.0%) had a prescription for HRT in 2004. This number fell to 41,024 (4.9%) in 2006. That represented a 39% decrease over the three study periods and an absolute reduction of 26,217 women (Fig. 1). For the other AOM, the overall number of women with a prescription rose from 49,455 in 2004 to 59,455 in 2006 representing an increase of 10,000 women (+20.0%). Very few women had a prescription for teriparatide (104 in 2005 and 228 in 2006). Increases of 20.9%, 17.5% and 1.2% were, respectively, observed for the number of women on bisphosphonates, raloxifene or teriparatide between 2004 and 2006. Overall almost 16,000 women were no longer on HRT in 2006 without being replaced with other AOM. A small number of women were treated with both HRT and other AOM, and this number of women decreased over the three study periods.

The number of women who had a prescription for HRT decreased for all age groups from 2004 to 2006 (Table 1). The number of women on HRT dropped by 21,951 in the total 50–64 age group – representing 83.7% of the decrease. This decrease was less striking for the 50–54 age group. Figure 2a shows that the pattern of HRT prescribing was similar for the three periods, with a peak for women aged 55 to 59. Almost 95% of the women who had a prescription for HRT were younger than 70. The number of women on AOM increased but with a smaller magnitude and different age patterns. An increase of 4,278 women was observed in the age-group 50–64 and represented 42.8% of the total increase. For age-group 70–74 and over, the increase of women on AOM was higher than the decrease of women on HRT (+2,411 versus -1,451, respectively). The number of women who had a prescription for bisphosphonates increased similarly among all age groups. Figure 2b shows the increase of bisphosphonate prescribing with a similar pattern for the three periods. There was a peak for women aged 65 to 84, who represented almost 70% of the women who had a prescription for bisphosphonates. The number of women younger than 75 who had a prescription for raloxifene increased over the three periods. The number and percent of those aged 50 to 64 increased from 4,350 (42.3%) in 2004 to 5,862 (48.6%) in 2006. Eighty-five percent of women who had a prescription for raloxifene were aged 55 to 79 (Fig. 2c). The prescription patterns of raloxifene tended to change between 2004 and 2006 with an increasing proportion of younger women treated (aged 55 to 59).

The downward trend in prescriptions for HRT was not related to the medical specialty of the prescribers (Table 2). Between 2004 and 2006, a 39.9% decrease was observed for GPs, 36.9% for gynaecologists, 54.6% for rheumatologists. Among the women who were prescribed HRT in 2006, 97.5% had their prescription from a GP or a gynaecologist (45.7% and 51.8%, respectively). However, on average, in 2006 a GP prescribed HRT to 5 women versus 52 for a gynaecologist. Rheumatologists prescribed almost no HRT. For AOM (Table 3), the number of women who had a prescription increased between 2004 and 2006 for all physician specialties except for the rheumatologists: +26.5% for GPs, +15.0% for gynaecologists, +10.1% for other medical specialties, and -8.4% for rheumatologists. Among women who were prescribed AOM, most received it from a GP (79.0% in 2006), fewer from a rheumatologist (11.6% in 2006) or a gynaecologist (7.1% in 2006). Sixty percent of women aged 65 and older on AOM received their prescription from a GP with a high increase between 2004 and 2006 (29,622 to 36,192) versus 10% from a rheumatologist with a decreasing trend over time (5,615 in 2004 versus 4,831 in 2006). In average, in 2006 a GP prescribed AOM to nine women in 2006 versus 34 for a GP and eight for a gynaecologist.

Table 1 Number of women with a prescription for hormone replacement therapy or anti-osteoporosis medications in the Rhône-Alpes area between January 2004 and January 2006

Age groups (years)	2004				2005				2006			
	HRT[a]	AOM[b]		Both[d]	HRT	AOM		Both	HRT	AOM		Both
	n (%)	BP[c] n (%)	Raloxifene n (%)	n (%)	n (%)	BP n (%)	Raloxifene n (%)	n (%)	n (%)	BP n (%)	Raloxifene n (%)	n (%)
50–54	16,856 (25.1)	1,166 (3.0)	606 (5.9)	172 (11.8)	15,082 (31.3)	1,738 (4.0)	933 (8.1)	192 (16.0)	11,975 (29.2)	1,747 (3.7)	943 (7.8)	156 (14.6)
55–59	26,949 (40.1)	3,265 (8.3)	1,738 (16.9)	406 (27.9)	18,361 (38.0)	3,946 (9.0)	2,191 (19.1)	369 (30.8)	15,834 (38.6)	4,439 (9.4)	2,475 (20.5)	320 (30.0)
60–64	13534 (20.1)	4,265 (10.9)	2,006 (19.5)	344 (23.7)	8,565 (17.7)	4,916 (11.2)	2,279 (19.9)	259 (21.6)	7,579 (18.5)	5,276 (11.1)	2,444 (20.3)	268 (25.1)
65–69	6,243 (9.3)	6,041 (15.4)	2,111 (20.6)	244 (16.8)	3,888 (8.1)	6,815 (15.5)	2,296 (20.0)	187 (15.6)	3,428 (8.4)	7,003 (14.8)	2,349 (19.5)	146 (13.7)
70–74	2,688 (4.0)	8,108 (20.7)	1,821 (17.7)	197 (13.6)	1,732 (3.6)	9,017 (20.5)	1,895 (16.5)	129 (10.8)	1,569 (3.8)	9,338 (19.7)	1,899 (15.7)	111 (10.4)
75–79	785 (1.2)	8,011 (20.4)	1,167 (11.4)	75 (5.2)	512 (1.1)	8,729 (19.9)	1,140 (9.9)	52 (4.3)	516 (1.3)	9,532 (20.1)	1,185 (9.8)	51 (4.8)
80–84	165 (0.2)	5,777 (14.7)	554 (5.4)	14 (1.0)	105 (0.2)	6,193 (14.1)	523 (4.6)	11 (0.9)	103 (0.3)	6,842 (14.4)	538 (4.5)	14 (1.3)
85–89	15 (0)	1,639 (4.2)	160 (1.6)	0 (0)	11 (0)	1,646 (3.8)	135 (1.2)	0 (0)	18 (0)	2,293 (4.8)	154 (1.3)	2 (0.2)
≥90	6 (0)	920 (2.3)	100 (1.0)	1 (0)	2 (0)	880 (2.0)	86 (0.7)	0 (0)	2 (0)	925 (2.0)	73 (0.6)	0 (0)
Total	*67,241*	*39,192*	*10,263*	*1,453*	*48,258*	*43,880*	*11,478*	*1,199*	*41,024*	*47,395*	*12,060*	*1,068*

[a] HRT: Hormone replacement therapy
[b] AOM: Anti-osteoporosis medications
[c] BP: Bisphosphonates
[d] Both: Hormone replacement therapy and anti-osteoporosis medications prescribed simultaneously
%: number of women in an age group related to total number of women in each treatment category

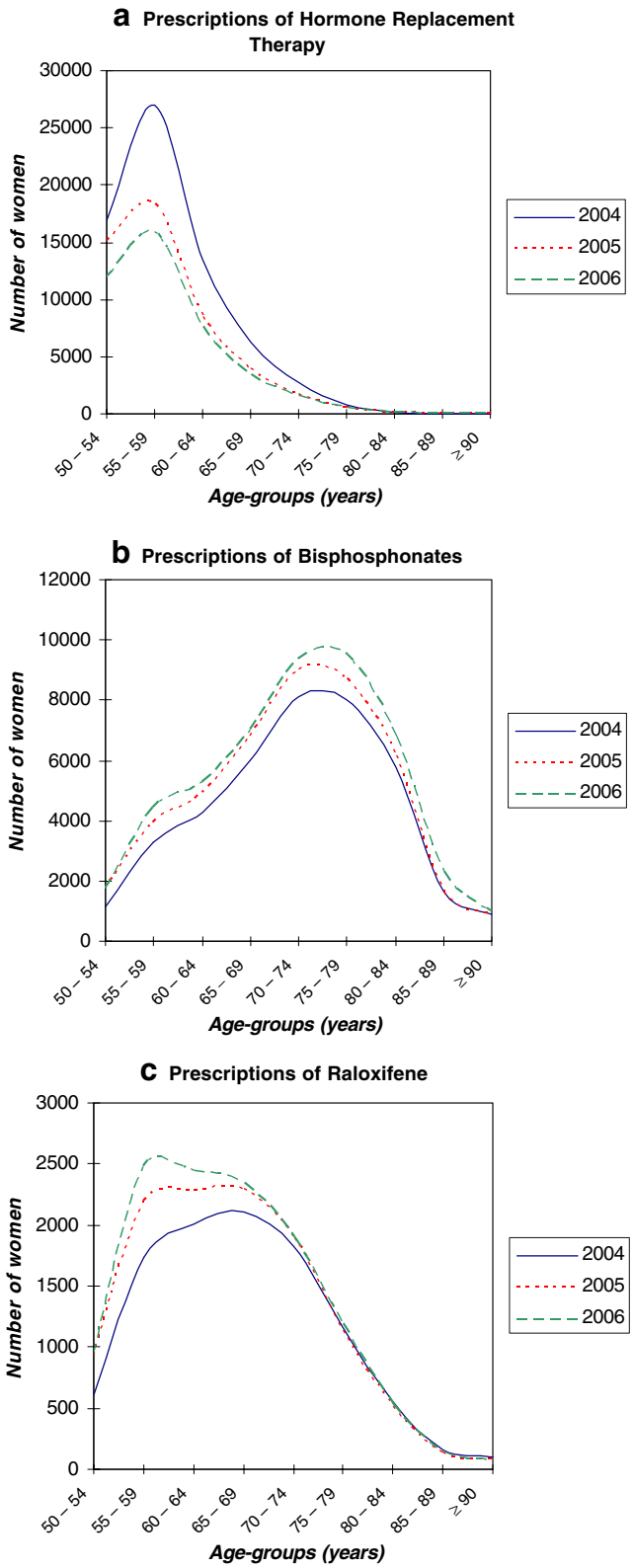

Fig. 2 Evolution of the number of women with a prescription for hormone replacement therapy, bisphosphonates and raloxifene by age groups in the Rhône-Alpes area between January 2004 and January 2006. Please note that the Y-axis scales are different in the three graphs

Discussion

This study outlines a decrease in HRT prescribing and a concurrent increase in AOM prescribing for women aged 50 and older in the Rhône-Alpes area of France between 2004 and 2006. This change in the prescription patterns can be interpreted as a consequence of the publication of the WHI and MWS results in 2002 and 2003 [2, 8]. These two studies led to the publication of revised French guidelines for the use of HRT and the management of osteoporosis in post-menopausal women in 2004 [9, 13].

The decrease of HRT use has been observed in the United States, Canada and in other European countries [10, 11, 14–17]. These studies provided data until 2004 and highlighted the short-term impact of the WHI and MWS results on prescription patterns. Our findings show that there is a continuous downward trend in HRT prescriptions in France. Regarding the increase in prescriptions for other AOM, only one Irish study reported an increase use of bisphosphonates between 2001 and 2004 [18]. In 2004, a report from the French NHI showed that the number of annual bisphosphonates and raloxifene treatments increased in France between 2001 and 2004 [19]. In our study, bisphosphonates were mostly prescribed in women aged 70 and older. This is consistent with the age of women that were included in randomized trials on bisphosphonates [20–22]. Furthermore, these women are at higher risk of fracture and according to the 2004–2006 French guidelines, they had to be treated with bisphosphonates as a first line treatment. Our data show that raloxifene was increasingly prescribed in younger women who could have previously been on HRT. This is consistent with a recent review that suggests that raloxifene should mainly be used in postmenopausal women with less severe osteoporosis or in those with predominantly spinal osteoporosis [23]. As expected, teriparatide was not much prescribed since women must have severe osteoporosis to be eligible for this treatment. The route of administration (subcutaneous injections) might also reduce prescriptions [9].

This study shows a net loss of 16,000 women prescribed bone-sparing medications over three years (i.e., that were no longer on HRT without being replaced with AOM). The new guidelines issued in France restricted the use of HRT as follows: no HRT if neither climacteric syndromes nor risk factors for osteoporosis; HRT possible but carefully followed if climacteric syndromes; and for women who suffered an osteoporotic fracture, the only recommended treatment was other AOM unless they were contraindicated. Although these guidelines were mostly debated in France mainly because HRT formulas used are different from that used in the USA, our results suggest that physicians have followed them. In our study, the reduction of HRT prescriptions was more pronounced for perimenopausal

Table 2 Medical specialties of the prescribers of hormone replacement therapy in the Rhône-Alpes area between January 2004 and January 2006

Age groups (years)	General practitioner			Gynaecologist			Rheumatologist			Other medical specialties*		
	2004 n (%)	2005 n (%)	2006 n (%)	2004 n (%)	2005 n (%)	2006 n (%)	2004 n (%)	2005 n (%)	2006 n (%)	2004 n (%)	2005 n (%)	2006 n (%)
50–54	11,608 (28.5)	10,612 (36.3)	8,537 (34.9)	14,505 (32.9)	12,849 (40.2)	10,717 (38.6)	32 (22.7)	20 (24.4)	17 (26.6)	661 (31.7)	618 (38.0)	417 (33.9)
55–59	15,128 (37.1)	10,045 (34.4)	8,418 (34.4)	16,946 (38.5)	11,097 (34.8)	9,863 (35.5)	31 (22.0)	24 (29.3)	21 (32.8)	750 (36.0)	554 (34.1)	448 (36.4)
60–64	7,884 (19.3)	4,831 (16.5)	4,175 (17.0)	7,408 (16.8)	4,686 (14.7)	4,219 (15.2)	28 (19.9)	14 (17.1)	12 (18.8)	381 (18.3)	262 (16.1)	213 (17.3)
65–69	3,802 (9.3)	2,256 (7.7)	1,966 (8.0)	3,303 (7.5)	2,093 (6.6)	1,856 (6.7)	24 (17.0)	11 (13.4)	10 (15.6)	171 (8.2)	115 (7.1)	86 (7.0)
70–74	1,708 (4.2)	1,043 (3.6)	973 (4.0)	1,421 (3.2)	895 (2.8)	815 (2.9)	14 (9.9)	6 (7.3)	2 (3.1)	84 (4.0)	59 (3.6)	42 (3.4)
75–79	509 (1.2)	342 (1.2)	320 (1.3)	400 (0.9)	258 (0.8)	263 (0.9)	7 (5.0)	5 (6.1)	1 (1.6)	29 (1.4)	13 (0.8)	19 (1.5)
80–84	127 (0.3)	80 (0.3)	86 (0.4)	73 (0.2)	46 (0.1)	43 (0.2)	5 (3.5)	2 (2.4)	1 (1.6)	7 (0.3)	3 (0.2)	2 (0.2)
85–89	14 (0)	9 (0)	17 (0.1)	6 (0)	3 (0)	7 (0)	0 (0)	0 (0)	0 (0)	1 (0)	3 (0.2)	1 (0.1)
≥90	5 (0)	3 (0)	3 (0)	5 (0)	2 (0)	2 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.2)
Total	*40,785*	*29,221*	*24,495*	*44,067*	*31,929*	*27,785*	*141*	*82*	*64*	*2,084*	*1,627*	*1,230*

*The main other medical specialties were endocrinology, internal medicine and general surgery
%: number of women in an age group related to total number of women for each study period
Note that the number of women treated is not exactly the same as in Table 1, as women can be counted more than once if the initial prescriber and the subsequent prescriber were not the same

Table 3 Medical specialties of the prescribers of anti-osteoporosis medications in the Rhône-Alpes area between January 2004 and January 2006

Age groups (years)	General practitioner			Gynaecologist			Rheumatologist			Other medical specialties*		
	2004 n (%)	2005 n (%)	2006 n (%)	2004 n (%)	2005 n (%)	2006 n (%)	2004 n (%)	2005 n (%)	2006 n (%)	2004 n (%)	2005 n (%)	2006 n (%)
50–54	1,126 (2.9)	1,733 (3.9)	1,807 (3.7)	332 (8.7)	505 (12.5)	506 (11.5)	322 (4.1)	460 (5.9)	410 (5.7)	74 (6.3)	101 (7.9)	97 (7.4)
55–59	3,277 (8.5)	4,140 (9.4)	4,874 (10.0)	988 (25.9)	1,160 (28.7)	1,257 (28.6)	854 (11.0)	956 (12.2)	921 (12.9)	148 (12.5)	170 (13.3)	194 (14.9)
60–64	4,449 (11.6)	5,305 (12.0)	5,797 (11.9)	951 (24.9)	944 (23.3)	1,066 (24.2)	1,001 (12.8)	1,041 (13.2)	969 (13.6)	186 (15.7)	195 (15.3)	198 (15.2)
65–69	6,131 (15.9)	7,156 (16.2)	7,500 (15.4)	842 (22.0)	790 (19.5)	835 (19.0)	1,281 (16.4)	1,278 (16.3)	1,136 (15.9)	208 (17.6)	206 (16.1)	210 (16.1)
70–74	7,943 (20.6)	9,042 (20.5)	9,523 (19.6)	488 (12.8)	457 (11.3)	500 (11.4)	1,628 (20.9)	1,527 (19.4)	1,347 (18.9)	220 (18.6)	224 (17.5)	214 (16.4)
75–79	7,580 (19.7)	8,358 (18.9)	9,349 (19.2)	184 (4.8)	159 (3.9)	181 (4.1)	1,499 (19.2)	1,450 (18.4)	1,290 (18.1)	178 (15.0)	203 (15.9)	210 (16.1)
80–84	5,420 (14.1)	5,876 (13.3)	6,610 (13.6)	34 (0.9)	25 (0.6)	44 (1.0)	935 (12.0)	901 (11.5)	804 (11.3)	126 (10.6)	137 (10.7)	133 (10.2)
85–89	1,596 (4.1)	1,601 (3.6)	2,256 (4.6)	3 (0.1)	3 (0.1)	7 (0.2)	210 (2.7)	184 (2.3)	208 (2.9)	31 (2.6)	32 (2.5)	41 (3.1)
≥90	952 (2.5)	904 (2.0)	954 (2.0)	0 (0)	1 (0)	1 (0)	62 (0.8)	63 (0.8)	46 (0.6)	13 (1.1)	10 (0.8)	7 (0.5)
Total	*38,474*	*44,120*	*48,670*	*3,822*	*4,044*	*4,397*	*7,792*	*7,860*	*7,131*	*1,184*	*1,278*	*1,304*

*The main other medical specialties were endocrinology, internal medicine, and functional re-education
%: number of women in an age group related to total number of women for each study period
Note that the number of women treated is not exactly the same as in Table 1, as women can be counted more than once if the initial prescriber and the subsequent prescriber were not the same

women aged more than 55, suggesting that for younger women a number of prescriptions were probably motivated by climacteric symptoms and thus were still appropriate in 2006. Two factors may also have contributed to explain this apparently uncompensated loss. The first one was the absence of BMD tests coverage by the NHI throughout the study period. Women had to pay out of their pocket for it. That might have truly lowered the number of women on AOM since the French national guidelines recommended prescribing AOM on the basis of BMD results in addition to clinical evaluation of individual risk factors [9]. The second one was that most AOM (10 and 70 mg alendronate and 35 mg risedronate) could only be refunded when women had a history of osteoporotic fracture. Women with no prior fracture could get a prescription, but the physician was then supposed to specify the mention "unrefundable" on it [24]. Since non-refunded drugs are not filed in the NHI database, we would have, therefore, missed those prescriptions and underestimated the number of women on AOM. This underestimation depends on how thoroughly physicians followed the NHI billing rules. In 2002, a French survey showed that 35% to 58% of them did not follow this requirement and prescribed these medications to women without previous fracture [19], who were then able to get their prescription and a claim for it. The number of women who got the drugs without claim should also be limited by the fact that private insurances did not cover medications that were not refunded by NHI. HRT may also have been switched to low doses bisphosphonates (5 mg daily alendronate) that where not refunded in France at the time of the study.

Our study shows that at the population level, GPs are by far the most frequent prescribers of AOM although their individual rate of prescription is very low compared to rheumatologists. GPs dramatically increased their prescription of AOM, and we may think they were more comfortable with HRT prescribing that they knew for a long time than with AOM although we do not have survey on GPs knowledge about osteoporosis guidelines. This situation raises questions about the need for continuing medical education (CME) on osteoporosis management for GPs and their willingness [25]. In France most CME regarding osteoporosis is led by specialists and aimed at specialists. Our data suggest that France may need to increase CME efforts towards GPs. This becomes even more essential with the recent decision of the government (July 2006) to refund BMD tests in women with fractures or defined risk factors.

Several limitations of the present study should be noted. The French NHI cannot distinguish geriatricians as a medical specialty, and the proportion of these physicians is missing in our results since these physicians are increasingly involved in the management of elderly populations in France. Another limitation due to the cross-sectional design was the impossibility to obtain data on duration of treatments or on practice changes that occurred after the WHI release on an individual basis. We also did not have data on the reason for prescribing HRT from which we could have gained information on practices appropriateness.

In summary, this study provides information on changes over time of HRT and AOM prescribing patterns. The results of this large population-based study suggest that there is still a fall-off in overall HRT prescribing 4 years after the publication of the WHI and the MWS results. The findings regarding the coincident increase in use of other AOM, especially bisphosphonates, suggest that the therapeutical implications of HRT trials have been correctly perceived by physicians in terms of effective, bone-protective alternatives to HRT. The impact of such dramatic and rapid changes in prescriptions habits is yet unknown. Several countries have observed these last ten years a reversal trend in fracture incidence with a decrease of age-adjusted fracture incidence rates and they have suggested that it could be the effect of BMD testing and bisphosphonates prescription [26, 27]. The large amount of HRT prescribing might also have explained a part of this decrease. We should, therefore, follow-up health indicators especially fracture incidence rates at the population level to assess potential effects of these changes.

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