Effect of the Women’s Health Initiative on Osteoporosis Therapy and Expenditure in Medicaid

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ABSTRACT: Decreasing HRT use among postmenopausal women may have a reciprocal impact on other osteoporosis therapy. Time series analysis of prescribing trends for millions of Medicaid beneficiaries revealed a 57% decline in HRT without augmenting the pace of bisphosphonate use. Prescribing changes dramatically increased Medicaid spending on osteoporosis therapy over the last decade and requires further evaluation of cost effectiveness.

Introduction: Hormone replacement therapy (HRT) has been commonly prescribed to postmenopausal women, but its use is decreasing because adverse cardiac outcomes were reported by the Women’s Health Initiative (WHI) in July 2002. The reciprocal impact of the WHI on other osteoporosis medications use and expenditure is unknown.

Materials and Methods: We conducted a time series analysis on prescription data from 50 state Medicaid programs between 1995 and 2004. Five medication categories were used: HRT, bisphosphonates, calcium, calcitonin, and raloxifene.

Results: HRT was increasing before publication of the WHI, reaching 5 million prescriptions per year by mid-2002 (136 prescriptions per 1000 beneficiaries). Bisphosphonate prescribing rose in parallel until mid-2002. WHI publication was associated with a rapid reduction in HRT use, declining 57% by mid-2004 to an average of 59 prescriptions per 1000 beneficiaries (p < 0.01). WHI publication did not augment bisphosphonates’ nearly linear rate of rise (p = 0.43) as their prescribing pace continued, whereas HRT declined. Medicaid spending on osteoporosis therapy also changed dramatically during the last decade, as yearly expenditure increased 664% from $1465 to $9742 per 1000 beneficiaries. Over this period, a significant shift from daily to weekly bisphosphonates also occurred.

Conclusions: A dramatic decline in HRT and continued rise in bisphosphonate prescribing has occurred since the publication of the WHI. During this time, there have also been substantial increases in osteoporosis medication spending within Medicaid. Determining whether these trends are clinically appropriate and cost effective for osteoporosis therapy will have important implications for the development of future drug reimbursement programs, especially for elderly patients.

J Bone Miner Res 2006;21:765–771. Published online on January 30, 2006; doi: 10.1359/JBMR.060119

Key words: estrogen, bisphosphonate, osteoporosis, Medicaid, women’s health

INTRODUCTION

OSTEOPOROSIS IS ASSOCIATED with significant morbidity and mortality and imposes a substantial economic burden on the health care system.1–3 Unfortunately, osteoporosis therapy is often underused in high-risk patients.4–5

Until the publication of the Women’s Health Initiative (WHI) in July 2002, hormone replacement therapy (HRT) was a common pharmacologic approach to osteoporosis treatment in the United States.6–10 The WHI showed that HRT use increased the risk of breast cancer, cardiovascular disease, and dementia, despite its benefit in osteoporosis prevention.11 Accordingly, substantial reductions in HRT use have been documented.12–19

Little is known about the reciprocal impact of the WHI and subsequent revisions to HRT recommendations20,21 on the use of other drug treatments for osteoporosis. We analyzed data from state Medicaid programs to evaluate the effect of the WHI on trends in osteoporosis drug use and expenditure. We hypothesized that reductions in HRT use should be accompanied by accelerated increases in the

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use of other medications, most notably bisphosphonates. Because there is a marked cost difference between HRT and bisphosphonates, these changes in practice patterns may have profound economic implications.

MATERIALS AND METHODS

Sources of data

Our analysis used aggregate, state-level data on quarterly drug use by Medicaid recipients. Medicaid, an American health insurance entitlement program that is jointly funded by state and federal governments, provides health care services and prescription drug coverage for >16 million women in the United States. In 2004, this represented ~9% of American women and one third of all low-income women. To qualify for Medicaid, a woman must earn <200% of the federal poverty level (approximately $15,000) and be either pregnant, a mother of a child <18 years of age, ≥65 years of age, or have a physical impairment. Eighty percent of out-patient Medicaid prescription expenditures are for drugs consumed by enrollees ≥65 years of age and younger persons with disabilities and overall, 71% of Medicaid beneficiaries ≥65 years of age are women.

Our data were provided by the Center for Medicare and Medicaid Services (CMS) and included the total number of prescriptions filled, total units of medication dispensed, and total Medicaid reimbursement for each medication. Data were available for 49 states and the District of Columbia. No data were available for Arizona. The CMS data, grouped by National Drug Code (NDC), were linked to the National Drug Data File to incorporate detailed information about drug strength, dose type (e.g., extended release capsule, tablet), and therapeutic class. We also obtained data on the number and demographic characteristics of Medicaid recipients. No data about individual patients were used in this analysis. This study was approved by the institutional review board of Brigham and Women’s Hospital.

Osteoporosis medication categories

We grouped osteoporosis medications into five categories: HRT, bisphosphonates, calcium, calcitonin, and the selective estrogen receptor modifier (SERM) raloxifene. HRT includes oral, transdermal, and injectable forms of estrogen alone and estrogen-progesterone combination therapies. Bisphosphonates include oral, intravenous, and injectable forms of etidronate, alendronate, risedronate, and pamidronate. Both daily and weekly oral dosing versions of alendronate and risedronate were included. The calcium category includes calcium supplements and calcium carbonate. Synthetic forms of vitamin D, PTH, and progesterone alone were excluded from our analysis. The number of prescriptions was reported quarterly by category from January 1995 through July 2004. The beginning of the study period was chosen to coincide with the first availability of a daily oral bisphosphonate.

Data analysis

Using the categories described above, we calculated the total number of prescriptions filled, units of medication dis-
pensed, and dollar expenditure by Medicaid nationwide in each calendar quarter for each category of medication. To account for changes over time in the number of Medicaid beneficiaries, we present medication use and spending per 1000 beneficiaries. We calculated the quarterly and annual rates of change in each of these measures of prescribing. For the bisphosphonates, we performed similar calculations to describe the total use of daily or weekly formulations of these agents.

We modeled the trends in use of HRT and bisphosphonates using autoregressive integrated moving average (ARIMA) models, incorporating a ramp function to estimate the effect of the publication of the WHI results and reporting significance at the \( p < 0.05 \) level. Models with both total prescriptions and total Medicaid spending as the dependent variable were developed. We controlled for changes in the age distribution of the Medicaid population by including the proportion of Medicaid beneficiaries who were \( >65 \) years of age as an additional independent variable in the ARIMA models. Data on the total number of beneficiaries and number of elderly beneficiaries were available on an annual basis. We used linear interpolation to generate the quarter specific proportion of elderly beneficiaries. Statistical analyses were conducted using STATA, version 8.0 (Stata Corp., College Station, TX, USA) and SAS software (version 8.0; SAS Institute, Cary, NC, USA).

**RESULTS**

The number of Medicaid beneficiaries included in our analysis increased from 36.3 million in 1995 to 54.6 million in 2004 (Table 1). During this time, the proportion of total female Medicaid beneficiaries was \(~60\%\) (63\% of dually eligible Medicaid/Medicare beneficiaries were female), whereas the percentage of beneficiaries \( \geq 65 \) years of age decreased from 11.6\% to 9.3\% between 1995 and 2004.

### Trends in drug use

During the study period, the annual number of prescriptions for osteoporosis medications that were filled increased from \(~2.9\) to 10.6 million. This represents a rise from 79 prescriptions per 1000 beneficiaries in 1995 to 194 prescriptions per 1000 beneficiaries in 2004 (246\%). Notably, total osteoporosis drug use peaked in 2002 (208 prescriptions per 1000 beneficiaries) and declined subsequently by 4.6\% in 2003 (199 prescriptions per 1000 beneficiaries) and a further 2.6\% in 2004 (194 prescriptions per 1000 beneficiaries).

Considerable differences in prescribing among osteoporosis medication categories were observed (Table 1). Before the publication of the WHI, prescriptions dispensed for HRT had increased steadily, peaking at \(~5\) million per year (136 prescriptions per 1000 beneficiaries) in 2002. After the release of the WHI in July 2002, HRT prescribing declined rapidly, representing a 57\% reduction by mid-2004 to 59 prescriptions written per 1000 beneficiaries (Fig. 1; \( p = 0.01 \)). Prescribing rates for bisphosphonates rose approximately in parallel with HRT prescriptions after the introduction of a daily oral formulation in 1995. Bisphosphonate prescribing rates have continued to steadily increase without any change in their rate of rise after publication of the WHI (\( p = 0.43 \)).

Changes in the types of bisphosphonates prescribed during the study period were also observed. By 2001, both alendronate and risedronate were made available in once-weekly oral formulations, and both versions rapidly rose in market share from 19\% in 2001 to 88\% by mid-2004. Reciprocally, the use of once-daily alendronate and risedronate sharply declined from \(~74\%) to 8\% of market share. Etidronate and pamidronate were minimally prescribed between 1991 and 2004. The rise in use of once-weekly oral bisphosphonates did not significantly change as a result of the WHI publication.

Slower rates of growth were observed for calcium, raloxifene, and calcitonin between 1995 and 2004 (Fig. 1). Calcium prescribing peaked at 31 prescriptions per 1000 beneficiaries in 2001, but the rate of growth of calcium prescribing has slowed to 3\% in 2004 (37 prescriptions per 1000 beneficiaries). Calcitonin prescribing peaked in 2001 at 18 prescriptions per 1000 beneficiaries and has subse-
Tends in drug expenditure

The annual expenditure on osteoporosis medications increased from approximately $53 to $532 million, representing a 664% rise from $1465 to $9742 per 1000 beneficiaries. Trends in the cost of osteoporosis therapy are presented in Table 2. Steady increases in expenditure for each class of medications were observed before the publication of the WHI (Fig. 2). The publication of the WHI in July 2002 was associated with a rapid decline in HRT expenditure ($7.28 to $3.22 per 1000 beneficiaries, p = 0.0006) but had no effect on the rise in bisphosphonate expenditures ($15.00 to $28.07 per 1000 beneficiaries, p = 0.21). Bisphosphonate spending increased from $2540 per 1000 beneficiaries per year in 2001 when once-weekly oral bisphosphonates were first made available to $5400 per 1000 beneficiaries per year in 2004.

DISCUSSION

In the United States Medicaid program, we observed substantial reductions in HRT prescribing after the publication of the WHI. These results are consistent with previously published findings and show a persistent decline in HRT use through 2004. We expected that decreased hormone therapy after the report of the WHI would be accompanied by a reciprocal acceleration in the rate of bisphosphonate prescribing, presumably because a proportion of those patients on HRT were benefiting from osteoporosis protection. Although prescriptions for bisphosphonates, raloxifene, and calcium did rise after the WHI, our results indicate that the publication of the WHI did not augment their rate of increase. In addition, overall rates of osteoporosis drug use may have declined slightly in the past 2 years.

Nevertheless, we did observe an increase in the overall rate of bisphosphonate prescribing within our observation period and a significant shift since 2000 from once-daily bisphosphonates toward once-weekly formulations, presumably based on the assumption that less frequent administration of an ongoing medication may improve patient compliance. This overall increase in medication use, if appropriate, is likely cost-saving to the health care system because of avoided fractures and their complications. However, whether the rate of bisphosphonate prescribing effectively compensates for decreases in HRT use is unclear.

The striking rise in drug expenditures that we observed highlights the concern that certain bisphosphonate formulations can be cost-prohibitive drug choices when absolute risk reduction and compliance are considered. These trends likely represent the natural result of removing HRT as a choice in the pharmacological armamentarium for osteoporosis treatment and provide insight into the consequences of eliminating a member of a therapeutic class on rates of use and expenditures for other drugs within the class. For example, the recent withdrawal of rofecoxib and valdecoxib could lead to reductions in expenditures of os-
Osteoarthritis therapy through the greater use of acetaminophen and nonselective nonsteroidal anti-inflammatory drugs, assuming that there are no changes in rates of use of gastroprotective agents.

Osteoporosis therapy expenditure trends may strain the sustainability of drug insurance programs for the elderly, in particular those that are publicly funded. The increasing number of eligible Medicaid recipients and the implementation of the new Medicare Part D drug benefit program may add to the challenge. Therefore, cost-containment strategies that include rational policies for osteoporosis drug use, such as the recently announced decision to use preferred drug lists within the new Medicare drug benefit program, should be further considered.

Reported trends in HRT use within the largest U.S. health insurer are consistent with findings among international public health insurance programs. Within a year of the WHI publication, significant HRT declines of 30–60% were shown within Canada, New Zealand, Australia, Chile, Hong Kong, and Israel. Two of these studies were large provincial cohorts that analyzed HRT use over time and as a function of age, although neither compared trends in HRT use in the context of other osteoporosis medication. Analyses of nationally representative U.S. databases detailing retail prescribing and physician office visits for HRT and osteoporosis treatment found that HRT use for osteoporosis treatment began to decline after bisphosphonates were introduced in 1994 and that HRT use overall declined 38% in the first year after publication of the WHI. Therefore, whereas our results are suggestive, we are limited in our ability to comment on whether the observed trends are clinically appropriate. In addition, we cannot adjust for variability in individual consumption or distinguish between medication use for other indications, particularly estrogen use for menopausal symptoms. However, ~38% of postmenopausal women in the United States used HRT to manage symptoms of menopause by the end of the 1990s, and the potential preventive effects of HRT on osteoporosis and cardiovascular outcomes were increasingly a consideration for its continuation.

Our study was limited to Medicaid beneficiaries, which is largely composed of low-income women, one fifth of whom are ≥65 years of age. Low-income women are reported to use HRT less frequently for menopausal symptom relief than other American women. As a result, their use of HRT for osteoporosis therapy may differ slightly from those of other elderly American women.

Finally, the apparent lag in calcium use as an adjunct to other appropriate osteoporosis prescribing may be an artifact of our inability to evaluate nonprescription calcium use. That said, if Medicaid calcium coverage policies have remained constant over the study period, presumably this...

FIG. 2. Quarterly Medicaid spending on osteoporosis therapy by drug class, January 1995 to July 2004. ■, HRT; ◊, bisphosphonates; X, calcium; ○, calcitonin; ▲, raloxifene.
under-reporting bias should have remained constant as well,\(^{(38)}\) and therefore, it is possible that calcium is being underused.

In summary, because publication of the WHI made clear that HRT was not ideal pharmacotherapy for osteoporosis, a dramatic decline in its use has occurred within Medicaid. In contrast, the WHI did not augment the steady rate of rise in bisphosphate prescribing. Nevertheless, substantial increases in spending on osteoporosis medication have also occurred. This trend has had an unintended, and perhaps unavoidable, impact on medication spending by state Medicaid programs as more costly forms of osteoporosis medication are used. Whether this trend in drug use compensates postmenopausal women at risk for osteoporotic fracture is unclear. Future research and policy planning should consider trends in drug use and total expenditures when developing osteoporosis therapy strategies for patients and drug-reimbursement programs, especially for elderly patients.

**ACKNOWLEDGMENTS**

Dr Choudhry had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr Udell was supported by a Canada-United States Fulbright Fellowship. Dr Solomon was supported by National Institutes of Health Grant K23AR48616. The Fulbright Program and National Institutes of Health had no involvement in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

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Received in original form October 22, 2005; revised form January 17, 2006; accepted January 26, 2006.