National Trends in Osteoporosis Visits and Osteoporosis Treatment, 1988-2003

Randall S. Stafford, MD, PhD; Rebecca L. Drieling, BA; Adam L. Hersh, MD, PhD

**Background:** Research is limited on physicians’ prescribing practices for osteoporosis treatment. We investigated patterns of pharmacotherapy from 1988 to 2003 and the impact of new medications on identification and treatment of patients with osteoporosis.

**Methods:** We tracked trends from 1988 through 2003 in the frequency of osteoporosis visits and patterns of pharmacotherapy associated with these visits using nationally representative data on prescribing patterns by office-based US physicians from the IMS HEALTH National Disease and Therapeutic Index.

**Results:** The number of physician visits for osteoporosis increased 4-fold between 1994 (1.3 million visits) and 2003 (6.3 million visits), whereas it had remained stable in prior years. This increase coincided with the availability of oral daily bisphosphonates and the selective estrogen receptor modulator raloxifene. The annualized percentage of osteoporosis visits where medications were prescribed increased from 82% in 1988 to 97% by 2003. Prior to 1994, the leading choices for osteoporosis therapy were calcium and estrogens, with lesser roles played by calcitonins and bisphosphonates. Between 1994 and 2003, the percentage of visits where bisphosphonates and raloxifene were prescribed increased from 14% to 73% and from 0% to 12%, respectively, while prescriptions for other medications declined.

**Conclusions:** New medications for osteoporosis offering improved efficacy and convenient dosing were associated with increased frequency of patient visits and treatment. This finding suggests that new drug therapy contributed to increased disease recognition and treatment.

Arch Intern Med. 2004;164:1525-1530

Osteoporosis is a condition of low bone mass and deterioration of bone microarchitecture leading to increased susceptibility to fracture and painful morbidity. The economic burden of osteoporotic fractures and its consequences is significant, as it was estimated at almost 14 billion direct medical dollars in 1995. Osteoporosis is determined clinically by bone mineral density (BMD) testing, and its prevalence in the United States was approximately 10% in 2000 using the World Health Organization definition of low BMD. The population at increased risk of fracture, and in whom treatment should be considered, may be substantially larger when additional risk factors such as age and health history—as specified by osteoporosis risk assessment tools—are assessed.

Despite evidence that osteoporosis is underdiagnosed, undertreated, and heavily concentrated among older women, routine screening in this population was not endorsed until 2002. Prior to these screening recommendations, there had been growing recognition of the public health significance of osteoporosis and evidence that treatment is effective in preventing osteoporotic fractures.

Substantial clinical trial evidence supports 5 major categories of antiosteoporosis medication (AOM). Bisphosphonates and calcitonins inhibit bone resorption by decreasing osteoclast activity; estrogens and the selective estrogen receptor modulator (SERM) raloxifene bind with estrogen receptors in bone to decrease bone loss; and calcium is a necessary nutrient for bone growth and maintenance. Estrogens, calcium supplements, calcitonins, and the cyclic bisphosphonate etidronate have been used for osteoporosis prevention and treatment since the 1980s. In recent years, AOM options changed with the availability of nasal calcitonin, the oral daily (or weekly) bisphosphonates alendronate and risedronate, and the SERM raloxifene.
The optimal choice of osteoporosis therapy requires considering the patient's specific factors, including age and competing risks. For example, estrogens effectively treat menopausal symptoms but increase breast cancer and cardiovascular disease risk.\textsuperscript{11,20,21} Raloxifene may induce hot flashes but decreases breast cancer risk and has beneficial effects on plasma lipid levels.\textsuperscript{9,18,22,23} Newer bisphosphonates may be selected for older patients at highest risk of fracture because of their superior effectiveness in preventing hip fractures, a level of benefit not achieved by etidronate.\textsuperscript{15,24}

The impact of new AOMs on patterns of osteoporosis pharmacotherapy and the number of patients receiving treatment is unknown. One study reported bisphosphonates and calcitonin as the combined leading category of AOMs in 1997, but that only 55% of patients received treatment.\textsuperscript{25} The current interest of these results is limited, in part, because data from more recent years that include the use of SERMs as a new AOM option.\textsuperscript{25} Another study reported estrogens as the leading category of AOMs prescribed at visits to ambulatory care physicians in 1997 and 1998.\textsuperscript{7} These results were not sufficient to make a statement about osteoporosis treatment, however, because the use of these medications was not linked directly to patients diagnosed with osteoporosis. This issue is particularly important for estrogens, whose use to treat menopausal symptoms may greatly outweigh their specific use for osteoporosis.

Our objective was to use nationally representative data on patient visits to physicians from 1988 through 2003 to describe trends in medications prescribed specifically for osteoporosis. In particular, we sought to gauge the impact of new osteoporosis treatment options.

### METHODS

#### DATA SOURCE

Data for this study were extracted from the Diagnosis Reference File 1988-2003 of the National Disease and Therapeutic Index (NDTI). The NDTI is a continuing physician survey conducted by IMS HEALTH, a health care information company in Plymouth Meeting, Pa, that provides nationally representative diagnostic and prescribing information on patients treated by office-based physicians in the continental United States. A random sample of office-based physicians is selected from the master lists of the American Medical Association and the American Osteopathic Association (both in Chicago, Ill) through random stratified sampling by specialty and geographic area. Approximately 3500 physicians participate in the survey each calendar quarter and each physician is randomly assigned 2 consecutive workdays per quarter for data collection. The geographic and specialty distribution of the participants closely matches national patterns.

Physicians provide information on each patient encountered during their data collection period. Each reported diagnosis generates a unique record on the condition and the medication therapies prescribed for it. A single patient may generate multiple diagnosis records, each of which listing multiple medications. Diagnosis records also may list no medications if none were prescribed for the specific condition. Medication reporting reflects the physician's best knowledge of new or continuing prescription and nonprescription medications. The NDTI does not capture information on patient adherence or unreported self-medication. Unreported self-medication may be particularly important to know when assessing the use of over-the-counter medications such as calcium-containing products.

Osteoporosis visits were reported under the International Classification of Diseases, Ninth Revision (ICD-9) code 733.0. We report both the annual number of patient visits for osteoporosis and the number of individual patients with osteoporosis accounting for these visits. The number of patients is derived from the number of visits and the number of times each patient is seen in a given year. Annual sample sizes for osteoporosis visits in the NDTI increased from 282 in 1988 to 1931 in 2003. For these sample sizes, the 95% confidence intervals around our estimates of annual medication use rates and patient visits are estimated to be less than ±15% for 1995 through 2003 and ±20% before 1995. This study reports annual estimates that were extrapolated from the sample data. Extrapolation accounts for the 2-stage stratified cluster-sampling method used in the NDTI where office-based physicians are sampled by specialty and geographic area, and then workdays are sampled for participating physicians. Annual data are presented as the aggregate of the quarterly surveys conducted within each year.

Annual data for osteoporosis visits were available for 1988 through 2003. We reported the annual number of visits for osteoporosis, the annual number of patients, and the percentage of new patients. We examined annual prescribing data to present the percentage of osteoporosis visits where individual medications or medication classes were prescribed as specific treatment for osteoporosis. All reported brand and generic names for a specific medication were combined into a single generic name.

### OSTEOPOROSIS MEDICATION CATEGORIES

We defined 5 medication categories: bisphosphonates, estrogen-containing medications, calcium, calcitonins, and SERMs. We accessed quarterly data that listed both individual medications and drug classes by the frequency of drug mentioned at visits with a report of a diagnosis of osteoporosis. Bisphosphonates reported in the NDTI include etidronate, the first bisphosphonate, which was delivered either as a cyclic oral drug or intravenously, as well as newer bisphosphonates, including second-generation alendronate and third-generation risedronate, both delivered in a daily or weekly oral dose. The bisphosphonate pamidronate, which was first reported in the NDTI in 2003, is not included in our analysis because it is reported in less than 0.5% of osteoporosis visits. The calcium group includes calcium supplements and calcium carbonate. The group of estrogen-containing medications includes oral, transdermal, and injectable forms of estrogen alone and estrogen-progesterone combination therapies. Synthetic forms of vitamin D are frequently used in combination products, and we excluded it from our analysis because of uncertainty about the completeness of its reporting. Although reporting on progestogenes is available, we do not report on this category of medications; progesterone is generally prescribed in combination with estrogen and not widely recommended alone for osteoporosis therapy.

### PATIENT VISIT CHARACTERISTICS

Most of the osteoporosis visits occur in outpatient settings. In 2003, 92% were office visits whereas 4% were conducted by telephone, 3% in nursing homes, and 1% in hospitals. The NDTI provides additional information on osteoporosis visits, including physician specialty. Patient demographic information, including sex and age, is recorded quarterly.
The estimated number of visits to US physicians for osteoporosis increased nearly 5-fold from 1994 to 2003 (annualized), whereas it remained stable in the years prior to 1994 (Table 1). The initiation of this trend coincided with the availability of the first oral daily bisphosphonate, alendronate, first released in 1995. The availability of new therapeutic options then coincided with increases in the percentage of visits where physicians prescribed medications, especially bisphosphonates. While in 1988 bisphosphonates were prescribed in 1% of osteoporosis visits, by 2003 their prescription was recorded in 73% of these visits.

### PATIENT VISITS

Between 1988 and 1994, the number of physician visits for osteoporosis showed little variation (Table 1) and patients visited physicians for osteoporosis a mean of 5.0 times per year. Between 1994 and 2003, a substantial increase was observed in the number of such patient visits (>300%), while the mean number of visits for osteoporosis per individual patient per year declined, reaching 3.0 by 2003. The percentage of new patients visiting a physician for osteoporosis increased from 27% in 1990 to 41% in 2003. The largest annual increases (of 76% and 46%, respectively) in osteoporosis visits occurred in 1996 and 1998. These increases coincided with the release of alendronate (September 1995) and raloxifene (December 1997). In the same way, the number of patients identified with osteoporosis also increased from 0.5 million in 1994 to 3.4 million in 2003, an increase of 500%.

### DRUG TREATMENTS

The medical treatment of osteoporosis changed during the 1990s as new therapeutic options became available. The percentage of osteoporosis visits where 1 or more AOM medications were prescribed increased from 83% to 97% during the 1990s (Table 1), for an average of approximately 1.3 drugs per visit throughout this period. We observed changes in the specific medications prescribed. Prior to 1996 estrogen and calcium therapy dominated osteoporosis treatment, whereas bisphosphonates and calcitonins played lesser roles. Between 1994 and 1996 the number of visits where a bisphosphonate was prescribed increased from 14% to 48%, which coincided with the release of alendronate, and remained stable until 1998. Between 1998 and 2003 bisphosphonate use increased further, which coincided with the release of risedronate (Figure). The use of raloxifene began in 1998 and the number of visits where estrogen was prescribed declined from 27% in 1994 to 3% in 2003, while smaller declines were observed for calcium prescriptions. In 1997 a 48% increase was observed in visits where calcitonin prescriptions, which coincided with the release of nasal calcitonins. This increase was not sustained, however, and calcitonins subsequently declined.

### Table 1. Patient Visits and Pharmacotherapy for Osteoporosis, 1988 Through 2003*

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients, millions</th>
<th>Patient visits Total, millions</th>
<th>With medications prescribed, %</th>
<th>With new patients, %</th>
<th>Drugs prescribed, %</th>
<th>Bisphosphonates, total</th>
<th>Alendronate</th>
<th>Risedronate</th>
<th>Etidronate</th>
<th>Calcium</th>
<th>Calcitonsin</th>
<th>Estrogens</th>
<th>SERMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>NA</td>
<td>1.5</td>
<td>82</td>
<td>NA</td>
<td>1.9</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>39</td>
<td>35</td>
<td>35</td>
<td>5</td>
</tr>
<tr>
<td>1990</td>
<td>0.6</td>
<td>1.4</td>
<td>83</td>
<td>31</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>1992</td>
<td>0.6</td>
<td>1.3</td>
<td>82</td>
<td>31</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>1994</td>
<td>0.5</td>
<td>1.3</td>
<td>91</td>
<td>35</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>1996</td>
<td>1.2</td>
<td>2.5</td>
<td>91</td>
<td>35</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>1998</td>
<td>2.0</td>
<td>4.0</td>
<td>92</td>
<td>34</td>
<td>34</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>2000</td>
<td>2.6</td>
<td>4.9</td>
<td>97</td>
<td>43</td>
<td>43</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>2002</td>
<td>2.8</td>
<td>5.3</td>
<td>97</td>
<td>43</td>
<td>43</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>2003</td>
<td>3.6</td>
<td>6.3</td>
<td>97</td>
<td>43</td>
<td>43</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>33</td>
<td>25</td>
<td>9</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not available; SERMs, selective estrogen receptor modulators.

*Data are from the National Disease and Therapeutics Index, IMS HEALTH.
Our results indicate that, for osteoporosis treatment, physicians rapidly adopted new medications with proven effectiveness in fracture prevention. In addition, our results suggest that increased numbers of new patients are being diagnosed with and prescribed medical treatment for osteoporosis. In 1994, the population of US women 65 years and older was 20 million. Based on our estimates of the number of women visiting physicians for osteoporosis, 2% of the female population was recognized with osteoporosis. In 2003, the female population 65 years and older was 21 million, and the percentage of these women recognized with osteoporosis, which had increased to 13%, will likely increase further in 2004. Although this falls short of the estimated 29% prevalence, new guidelines recommending universal screening for women aged 65 years and older may promote further improvements in detection and treatment for this high-risk population.

Our results suggest a relationship between drug development and increased disease identification and patient treatment. Alendronate permitted more convenient daily or weekly dosing and offered improved efficacy compared with previously available cyclically delivered bisphosphonates. These obvious improvements likely contributed to the shift in treatment toward bisphosphonates. Furthermore, the rapid increase in the number of patient visits for osteoporosis associated with use of alendronate suggests that its availability influenced the likelihood that osteoporosis was recognized and treated by physicians. The development of new medications may broaden the spectrum of potentially treatable diseases and/or create entirely new disease entities—and, in so doing, induce marginally indicated treatment. The increases in osteoporosis therapy that we observed, however, are likely beneficial to patients based on the evidence that osteoporosis is undertreated and on the evidence that oral daily treatments with bisphosphonates and raloxifene are effective.

Although alendronate offered distinct advantages, it did not represent an innovation in drug mechanism because prior bisphosphonates existed. On the other hand, as the first SERM indicated for osteoporosis, raloxifene was a definite therapeutic innovation. Based on our analysis, however, its impact on osteoporosis therapy was much less significant than alendronate. This suggests the possibility that physicians are more receptive to refinements and improvements within a familiar drug class than to more novel alternatives. Other factors such as revisions in clinical guidelines and the relative intensity of product promotion, as well as the availability of and advancements in BMD screening, may have contributed to the trends that we observed. There is increasing evidence that advertising influences both patients’ demand for drugs and physicians’ prescribing patterns. Raloxifene and alendronate were among the 100 promoted drugs in 1998 and the intense level of advertising may have contributed to the large increase in osteoporosis visits that year. Testing equipment for BMD also became more widespread, which may have contributed to the growing number of patients diagnosed with osteoporosis. However, many patients identified with low BMD are not treated for osteoporosis. Even with the ad-

---

**Specific Treatments by Formulation**

Prior to 1996, etidronate, available in cyclic oral and intravenous formulations, was the most commonly prescribed bisphosphonate. Since 1996 the bisphosphonate class has been dominated by alendronate, with lesser roles for risedronate and etidronate (Table 1). Of note, however, 52% of the increase in bisphosphonate use we observed from 1998 to 2003 was accounted for by prescriptions for risedronate. Among estrogens, conjugated equine estrogens were the leading formulation (>90% of all estrogens prescribed).

**Patient Characteristics and Physician Specialty**

The distribution of osteoporosis visits by sex and age remained stable from 1988 to 2003. Most patients were women (91%-96%) and older than 65 years (70%-80%). The most common comorbidities reported for this population were hypertension and osteoarthritis. During the study period, patient visits for osteoporosis were mostly to primary care physicians. Between 1988 and 2003 approximately 48% of visits were to internists and approximately 27% were to other primary care physicians. Osteoporosis visits to obstetricians and gynecologists increased during the study period (Table 2).

**Comment**

The number of patient visits for osteoporosis and the likelihood of treatment with an AOM has increased significantly since 1996, and the beginning of this increase has coincided with the availability of the first oral daily bisphosphonate, alendronate. The subsequent development of the bisphosphonate risedronate and the SERM raloxifene likely contributed to further increases in osteoporosis treatment. By 2003 osteoporosis therapy was dominated by bisphosphonates, which were prescribed in 73% of patient visits. This was a significant change from the 1988 to 1995 period when calcium and estrogens were the leading medications. In recent years, estrogen use for osteoporosis has declined markedly.

---

**Table 2. Patient Age and Physician Specialty for Osteoporosis Visits, 1990 and 2003**

<table>
<thead>
<tr>
<th>Patient visits, millions</th>
<th>1990</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 39 y</td>
<td>1.5</td>
<td>0.8</td>
</tr>
<tr>
<td>40-59 y</td>
<td>19.7</td>
<td>19.3</td>
</tr>
<tr>
<td>60-64 y</td>
<td>9.7</td>
<td>11.3</td>
</tr>
<tr>
<td>≥ 65 y</td>
<td>70.8</td>
<td>68.6</td>
</tr>
<tr>
<td>Women, %</td>
<td>91</td>
<td>94</td>
</tr>
<tr>
<td>Physician specialty, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internist</td>
<td>45</td>
<td>48</td>
</tr>
<tr>
<td>Other primary care</td>
<td>41</td>
<td>27</td>
</tr>
<tr>
<td>Obstetrician/gynecologist</td>
<td>6</td>
<td>18</td>
</tr>
</tbody>
</table>

*Data are from the National Disease and Therapeutic Index, IMS HEALTH.*
vances in therapy that we noted, adherence to AOMs remains an issue for some patients because of their possible adverse effects.9,10

We identified 2 areas of concern from a quality and clinical care perspective. First, the report that calcium use declined in association with the increase in bisphosphonates prescriptions at osteoporosis visits. Calcium use may be underreported in NDTI because it is available as a supplement without a prescription; however, we expect this bias to have remained constant. The decline in calcium use may reflect the need to separate bisphosphonate dosing from other drugs, such as calcium, to achieve maximum bisphosphonate absorption. However, adequate calcium intake may be especially important for bisphosphonates to achieve maximal effectiveness. Recent bisphosphonate trials ensured adequate calcium intake in both treatment and placebo groups.54

A second concern relates to the future of osteoporosis prevention, an area where estrogens have played an important role. Although we showed that estrogen use specifically for osteoporosis has declined, its overall use has increased since 1988, providing prevention for many women. Based on evidence from the Women's Health Initiative showing increased risk of cardiovascular disease,10 new guidelines recommend against long-term estrogen use for postmenopausal women55 despite its effectiveness in preventing hip fractures. Although overall prescriptions for estrogens declined significantly in the months following the publication of Women's Health Initiative results,38,39 prescriptions for estrogen use as a specific therapy for osteoporosis declined only slightly. This may reflect differences in the assessment of risks and benefits associated with estrogen use for patients with and without osteoporosis. For some women, changing from a SERM may be an acceptable alternative, as may be limiting estrogen exposure to the immediate postmenopausal years; however, the optimal role of medical therapy in osteoporosis prevention remains uncertain.

Our results differ from those of prior reports describing osteoporosis pharmacotherapy and may reflect advantages in the database we used. Using the NDTI for our analysis enabled reporting trends through December 2003, while prior studies were limited to several years prior to their publication date. The NDTI design provides a large sample size and allows physicians to include an unlimited list of patient diagnoses and drugs prescribed. The reports are subsequently organized by individual diagnosis, overcoming a limitation of those prior studies where the specific indication for medication use was not clear. Gehlbach et al37 reported low recognition and treatment of osteoporosis at visits to physicians in from 1993 to 1997, but grouping bisphosphonates with calcitonin into a single treatment prevented from distinguishing these classes. That study reported that only 55% of patients with osteoporosis received medical therapy in 1997, and that bisphosphonate/calcitonin was the leading category of treatment at 27%. Subsequent reanalysis of this study showed that the reported number of visits was substantially underestimated.40 Although revised results suggested higher recognition of osteoporosis, revised estimates for pharmacotherapy trends were not presented.54 In contrast, our results for 1997 showed that 93% of patients with osteoporosis received treatment and that bisphosphonates were used in 51% of them.

Lee et al27 described AOM use for all visits to ambulatory care physicians and reported estrogen therapy as the leading treatment (it was prescribed in 80% of visits) in 1997 and 1998. However, the use AOMs was not specifically linked to patients with osteoporosis and therefore the results cannot distinguish between estrogen use for other indications, especially menopausal symptoms. Our analysis of NDTI data indicates that in 1998 only 4% of all estrogen use, overall, was specifically associated with osteoporosis. From our results, estrogen was prescribed at 12% of visits in 1998 and estrogen prescription has subsequently declined.

The use of NDTI to describe osteoporosis pharmacotherapy has certain limitations. The database depends on accurate reporting by physicians of the diagnosis reached and specific medications prescribed. Physicians may be more likely to report osteoporosis in patients receiving medical treatment than in patients not receiving treatment. This potential bias could lead to overestimating the percentage of patients receiving medical therapy. Focusing our analysis on patients with a specific diagnosis of osteoporosis rather than on patients potentially receiving AOMs may be another source of bias in our data set. We could therefore exclude significant numbers of patients with low, undiagnosed or unreported BMD, who were receiving effective therapy, especially estrogen therapy. Another area of potential underreporting concerns the use of supplements including calcium.41,42 As stated above, although this may lead to an underestimate, this bias is likely to remain constant. We were unable to report on concomitant prescriptions, eg, on the frequency with which calcium or estrogens were prescribed concomitantly to patients receiving bisphosphonates.

Treatment of osteoporosis has improved in recent years in association with the availability of new medications. Physicians are prescribing drugs with greater effectiveness and convenience, and recognition of osteoporosis is increasing. The future role of estrogens in osteoporosis treatment and prevention is uncertain despite their effectiveness in preventing osteoporotic fractures. As estrogens are no longer recommended for long-term use in postmenopausal women,8 greater attention to osteoporosis prevention is critical. This includes calcium use and physical activity as well as potential advancements in pharmacotherapy for osteoporosis prevention.

Accepted for publication September 25, 2003.

This study was supported by research grant R01-HS013405 from the Agency for Healthcare Research and Quality.

We thank Stan Finkelstein, MD, for his personal assistance. We also thank Merck & Co, Inc, for generously providing access to data from the IMS HEALTH National Disease and Therapeutic Index data and IMS HEALTH for authorizing their use.

Correspondence: Randall S. Stafford, MD, PhD, Stanford Prevention Research Center, Stanford University, Palo Alto, CA 94304 (rstafford@stanford.edu).
REFERENCES


