Outpatient Care for Osteoporosis Patients in Germany
Results of the BoneEVA study

Bertram Häussler, Holger Gothe, Sandra Mangiapane, Gerd Glaeske, Ludger Pientka, Dieter Felsenberg

SUMMARY
Introduction: In Germany, accurate data on prevalence and treatment of osteoporosis are not available. The aim of this study was to investigate how frequently osteoporosis occurs, who makes the diagnosis and how osteoporosis is treated in the outpatient setting. Methods: A retrospective cohort study was performed using routine data from a German health insurance company and billing data for outpatient visits for the years 2000 to 2003. Patients were included, if they were at least 50 years old and had at least one mention of osteoporosis or an osteoporosis related fracture or of osteoporosis specific medication. Results: Only 20 per cent of the projected 7.8 million osteoporosis patients were treated with osteoporosis specific drugs. Although the prevalence of osteoporosis increases with age, the treatment prevalence decreased in higher age groups in this study. Discussion: The study shows that osteoporosis treatment in Germany needs improvement. The high rates of undertreatment and non-compliance suggest a need for improved treatment strategies. Dtsch Arztebl 2006; 103(39): A 2542–8.

Key words: osteoporosis, fracture, drug prescription, diagnosis, health services research

Osteoporosis is a chronic skeletal disorder that is characterized by reduced bone mass, breakdown of the microarchitecture of the bones, and an increased risk of fracture. Especially postmenopausal women are at risk of developing osteoporosis. According to 1994 data from the World Health Organization, some 30% of postmenopausal women worldwide have osteoporosis. In Germany, an estimated 4 to 7 million people are affected by osteoporosis, but the exact prevalence of the disease is not known (1-5). The enormous social and economic consequences are caused primarily by osteoporosis-related fractures. These complications are responsible for more hospital bed days per year than diabetes, myocardial infarction, or breast cancer (6-7). Numerous studies found a fracture-reducing effect in several drugs, including bisphosphonates, raloxifene, and oestrogens, especially in patients who have had a fracture and in patients with a 10-year risk of fracture of more than 30%. The average number needed to treat (NNT) for three to five years is 15 to 30 (8-11). The extent to which calcium and vitamin D can lower susceptibility to fractures is not clear (12-13). Early identification of people with a high risk of developing the disease is vitally important, as is educating them about preventive measures; equally important is early identification of people who already have the disease and initiating treatment.

Research question
The BoneEVA study (Bone EVA: bone, epidemiology, validation of health care delivery) aimed to investigate the treatment of osteoporosis patients in Germany. In particular, answers to the following questions were sought: How common is osteoporosis in Germany? Who makes the diagnosis in the outpatient setting? Which medical expert teams use which medical drugs for which patients, and to what extent?
Methods

Data sources
Routine data from the Gmünder Ersatzkasse health insurance company (GEK, where circa 1.5 million people are insured) for the years 2000 to 2003. To obtain additional data about the services accessed in the outpatient setting, billing data from the Zentralinstitut für die Kassenärztliche Versorgung (ZI, the central institute for outpatient care provision; circa 600 000 patients) for 2003 were analyzed. All analyses done with the dataset from GEK and ZI data relate to the year 2003. The GEK data used include the following information:

- Age and sex of the insured person
- Start of insurance policy
- Prescribed medications
- Hospitalizations (including diagnoses according to ICD-10 and date of admission and discharge)
- Unfitness to work (including diagnoses according to ICD-10 and number of days)
- Rehabilitation
- Prescribed curative substances and devices

The ZI data come from a representative sample of doctors’ practices in the outpatient care setting (doctors’ panel) in the insurance district of North Rhine. The panel includes patient data from 7 911 doctors covering 14 specialties. The following information was collected for the year 2003:

- The patient’s identification number
- Date of birth and sex of the insured person
- Diagnosis (ICD-10)
- Medical specialty
- Billed services
- Date of treatment
- Number of doctor’s visits

Study population
The study population on which the national prevalence estimates for disease and treatment was based included people insured in the GEK on the one hand, who were insured for a consecutive 360 days in the period from 1 January 2000 to 31 December 2003 and who were at least 50 years of age in 2000. To identify osteoporosis patients among this group, the authors additionally used the following criteria:

- At least one diagnosis of osteoporosis (hospital diagnosis or diagnosis of being unfit to work in 2000 to 2003 according to ICD-10 (M80/M81)). Patients with a diagnosis of Paget’s disease (ICD-10 M88) and/or hypocalcaemia (ICD-10 E83.5*) and/or fractures in case of neoplasms (ICD-10 M90.7*) were excluded from the analysis.
- At least one fracture as a result of osteoporosis (hospital diagnosis or diagnosis of being unfit to work) in 2000 to 2003 according to ICD-10 or
- At least one prescription of a medical drug indicated in osteoporosis between 2000 and 2003. This includes calcium/vitamin D, certain hormone preparations, calcitonin, selective oestrogen receptor modulators (SERM), fluorides, anabolic steroids, bisphosphonates, raloxifene, teriparatide, and nandrolone).

Additionally, the study population included patients from the ZI dataset, who met the following criteria in 2003:

- At least one outpatient diagnosis of osteoporosis according to ICD-10 (M80/M81). Patients with a diagnosis of Paget’s disease (ICD-10 M88) and/or hypercalcaemia (ICD-10 E83.5*) and/or fractures in neoplasms (ICD-10 M90.7*) were excluded from the analysis.
- At least one fracture as a result of osteoporosis according to ICD-10.

Diagnosis
Bone density scanning is a procedure used to identify patients at high risk of osteoporosis. On the basis of the ZI dataset we analyzed how many patients had had this investigation in 2003. In Germany, bone density scans can be billed to the statutory sickness fund (health insurance) only once a fracture is present. This means that we captured only treatments eligible for reimbursement, and not those that patients had paid for themselves.
Drugs

Seven categories of drugs relevant to the treatment of osteoporosis were defined. Basic therapy (calcium/vitamin D), hormone replacement therapy (oestrogen mono-preparations and combined preparations containing oestrogen and progesterone), bisphosphonates, calcitonin, selective oestrogen receptor modulators (SERM), fluoride, and anabolic steroids. Since a mention of hormone preparations only is not specific enough to indicate a case of osteoporosis, at least one prescription from the “basic therapy” category had to be recorded in order for an insured patient to be regarded as an osteoporosis patient. Studies from the USA (15) and the Netherlands (16) show a lack of compliance with treatment with bisphosphonates; compliance improves with weekly administration compared with daily administration; something that we also investigated in this study. To this end, we looked at a sample of the entire study population who had not received a prescription for bisphosphonates in the six months before the “index” prescription. The prescribing data were analyzed for 12 months after the index prescription to identify how many patients had stopped treatment. If no new prescription for bisphosphonates was issued within 90 days after the prescribed drug had been used up or during the current prescription, treatment was regarded as stopped. Patients who changed therapies were excluded from the analysis.

Statistical analysis

Fractures can have many causes other than osteoporosis. For this reason, the fractures identified in the GEK and ZI datasets were assigned to the age-specific and sex-specific weightings of osteoporosis according to Brecht and Schädlich (14) (table 1). The prevalences of osteoporosis as shown by the GEK and ZI datasets were adjusted according to Germany’s age and sex distribution (Federal Statistical Office, 2004), and projected to the entire Federal Republic of Germany according to the distribution of medical specialty groups (Kassenärztliche Bundesvereinigung (KBV), National Association of Statutory Health Insurance Physicians, 2004) and combined in the sense of an ecological study. The drug treatment prevalence calculated from the GEK dataset and the number of bone density scans performed as per the ZI dataset were also adjusted by Germany’s age and sex distribution and projected to all of Germany according to distribution of medical specialty groups. The influence of the bisphosphonate therapy regimen on the duration of the prescriptions was studied in a survival analysis (Kaplan-Meier curves). All statistical analyses were done with SPSS software, version 12.0.

Results

According to our projection, 7.8 million people aged 50 or older in Germany had osteoporosis in 2003. This corresponds to about a quarter of the population in this age bracket.
The prevalence is markedly higher in women than in men (6.5 million vs. 1.3 million) and increases with age in women as well as in men (Table 2).

**Osteoporosis related fractures**

According to our estimates, 333,322 (4.3%) of the 7.8 million osteoporosis patients in Germany had a fracture in 2003. Fractures of the hip joint (99,973 patients), wrist (42,242 patients), and vertebrae (40,741 patients) were the most common types. Although according to earlier estimates, at least 60% of all vertebral and hip fractures in people older than 45 and in 85% of people older than 85 are caused by osteoporosis (17), our study showed that in the outpatient setting, fractures are rarely associated with osteoporosis. The treating doctors made a diagnosis of osteoporosis in only 37% of patients with a fracture of the lumbar spine or the pelvis. Such fractures are, however, associated with osteoporosis in 62 to 78% of cases (Brecht & Schädlich [14]).

**Diagnosis**

In 2003, an extrapolated 115,229 bone density scans were billed. Compared with the estimated number of patients with osteoporosis related fractures (333,322), the rate of adequately diagnosed patients seems low. 87% of scans were done in women; the number of procedures drops with age, in men more than in women (table 1). And in 85% of people older than 85 are caused by osteoporosis (17), our study showed that in the outpatient setting, fractures are rarely associated with osteoporosis. The treating doctors made a diagnosis of osteoporosis in only 37% of patients with a fracture of the lumbar spine or the pelvis. Such fractures are, however, associated with osteoporosis in 62 to 78% of cases (Brecht & Schädlich [14]).

**Drug therapy**

Only one in five osteoporosis patients (22%; 12% of male and 24% of female osteoporosis patients; projected n=1,692,281) received the drugs that are typically indicated in osteoporosis (figure 1). Calcium and vitamin D, and bisphosphonates were the most commonly prescribed substances for long term therapy (17% and 10%, respectively (figure 2)). This reflects the therapeutic guidelines valid in Germany at the time of the study (18, 19). 90% of patients took painkillers. Compared with age- and sex-matched patients without osteoporosis, of whom 61% received analgesia, osteoporosis patients received three times the amount of prescriptions for painkillers. A subgroup analysis showed that osteoporosis patients who were taking non-steroidal anti-inflammatory drugs (NSAIDs) were treated in hospital with an ulcer diagnosis more often than patients not taking these drugs (3.2% vs. 2.3%, P < 0.001). Extensive prescribing of NSAIDs thus incurs costs that might be avoidable through rational therapeutic action. In spite of a rising prevalence of the disease, the prevalence of treatment fell with increasing age. In women, the treatment rate fell from 31% in the 50 to 64 age group to 19% in the over-75s (figure 1). Only every 11th patient

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**TABLE 2**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Number of people with osteoporosis</th>
<th>Prevalence (%)</th>
<th>Number of bone density scans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>50–64</td>
<td>7 658 928</td>
<td>543 642</td>
<td>7.1</td>
</tr>
<tr>
<td></td>
<td>65–74</td>
<td>3 929 276</td>
<td>448 962</td>
<td>11.4</td>
</tr>
<tr>
<td></td>
<td>≥ 75</td>
<td>2 043 080</td>
<td>329 068</td>
<td>16.1</td>
</tr>
<tr>
<td>Total (Men)</td>
<td></td>
<td>13 630 284</td>
<td>1 321 672</td>
<td>9.7</td>
</tr>
<tr>
<td>Woman</td>
<td>50–64</td>
<td>7 759 628</td>
<td>1 809 571</td>
<td>23.3</td>
</tr>
<tr>
<td></td>
<td>65–74</td>
<td>4 537 484</td>
<td>2 119 505</td>
<td>46.7</td>
</tr>
<tr>
<td></td>
<td>≥ 75</td>
<td>4 316 049</td>
<td>2 553 010</td>
<td>59.2</td>
</tr>
<tr>
<td>Total (women)</td>
<td></td>
<td>16 613 161</td>
<td>6 482 086</td>
<td>39.0</td>
</tr>
<tr>
<td>Total (all)</td>
<td></td>
<td>30 243 445</td>
<td>7 803 758</td>
<td>25.8</td>
</tr>
</tbody>
</table>
aged 75 or older was treated with bisphosphonates (figure 1). This trend also showed in men: the older a male patient the more rarely he was prescribed bisphosphonates. The projected 1 556 056 prescriptions for bisphosphonates came from general practitioners in 46% of cases, 29% from orthopaedic specialists, 20% from specialists in internal medicine, and 5% from other specialties. Patients stopped treatment with bisphosphonates over a year more often when the drug was administered daily (58%) rather than on a weekly regimen (43%) (figure 3).

Percentage of osteoporosis patients receiving drug treatment (excluding analgesics) and bisphosphonate treatment. Calculations based on billing data from Gmünder Ersatzkasse (GEK) for the years 2000 to 2003

**Figure 1**

<table>
<thead>
<tr>
<th>Drug therapy</th>
<th>Bisphosphonate therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60–64</td>
<td>Age 65–74</td>
</tr>
<tr>
<td>Age ≥75</td>
<td></td>
</tr>
</tbody>
</table>

22% of all osteoporosis patients (n = 1 692 281)

10% of all osteoporosis patients (n = 734 727)

13% of men (n = 1 032 234)

24% of women (n = 529 047)

9% of men (n = 104 014)

16% of women (n = 639 713)

**Figure 2**

Percentage of osteoporosis patients receiving drug treatment by substance group (as many as apply). Calculations based on billing data from Gmünder Ersatzkasse (GEK) for the years 2000 to 2003

* All pharmaceutical drugs except analgesics, at least one drug indicated in osteoporosis; SERM, selective estrogen receptor modulator

*Analgesics, vitamin D, Bisphosphonate, Hormone therapy, Fluoride, Calcitriol, Selective oestrogen receptor modulators, Anabolic steroids, Other drugs*


Discussion
This study aimed to estimate the prevalence of osteoporosis in Germany and investigate osteoporosis treatment, and to analyse how this disease is diagnosed.

According to our projections, 7.8 million people aged 50 or older in Germany have osteoporosis; 83% of these are women. The prevalence is thus higher than previously believed (1-5). In 2003, an extrapolated more than 333,000 patients had a fracture. Of these, 100,000 were hip fractures, which were the most common fracture type. The data that our calculations are based on are routine data from a health insurance company (Gmünder Ersatzkasse, GEK) and data from the Zentralinstitut der KV (ZI, the central institute for outpatient care provision; doctors' panel North Rhine) The advantage was that numerous treatments, distributed all over Germany, were included in the calculations. A disadvantage is the fact that we had no way of verifying coded diagnoses, for example, on the basis of radiographs or other clinical variables, such as was done in the EPOS study (3). This might be the reason why the number of vertebral fractures is lower in this study than anticipated.

It has to be pointed out that the samples used for the calculations are not representative for Germany as a whole. In the projections, differences in age and sex were adjusted for, but other relevant factors, such as the place of residence or the socioeconomic status, could not be included because no data were available.
Overall, it has to be borne in mind that the prevalence is only a “treatment prevalence” because only patients were included who had accessed medical services. Patients who had not seen a doctor, or patients who were not treated and in whom no diagnosis of osteoporosis was coded were not included. This may have resulted in an underestimate of the real prevalence of osteoporosis. On the other hand, the datasets used may include misdiagnoses and false positives. Calcium, vitamin D, and hormone preparations are not specific drugs to treat osteoporosis, so that this might have resulted in an overestimate of the prevalence.

Osteoporosis is under-recognized in Germany. The diagnosis, especially in connection with fractures, was made far more rarely than might have been expected. Those bone densitometries that were covered by the statutory sickness fund for diagnostic purposes in cases of existing fractures were rarely initiated. Doctors’ prescribing behaviour was extremely cautious. In the period under observation, only 22% of osteoporosis patients received specific treatment. Even when one bears in mind that such medication is indicated only in patients with a 10 year fracture risk of more than 30% or in patients who have actually had a fracture, patients were still not receiving medication to a sufficient degree. The treatment prevalence fell with increasing age, so that our results seem to show an under-treatment especially among older osteoporosis patients. This is all the more astonishing because the prevalence of hip fractures rises with age. Additionally, it is well known that drug therapy improves the quality of life notably and therefore reduces overall costs (20, 21).

In terms of compliance with bisphosphonate treatment, the weekly dosage regimen has been shown to be superior to the daily regimen, but on the whole, compliance with bisphosphonate treatment is in need of improvement. This result corresponds with international studies (15-16). Possible reasons for this are the insidious disease process, which does not alert patients to the need for drug treatment, as well as the fact that treatment effects are not noticed immediately. In addition, the specific administration modes and the side effects associated with bisphosphonates are a problem for compliance (22 – 24). Consequently, the success of the treatment is often unsatisfactory. This is why drug developments are to be welcomed that enable a reduction in the frequency of administration to a monthly or quarterly dosage regimen, so that patients’ compliance with the treatment can improve. However, it is also the task of doctors and pharmacists to educate those patients who are receiving drug treatment better about the necessity of continuing drug therapy and improve compliance in this way. Furthermore, patients have to be made aware to a higher degree of preventive measures such as a diet rich in calcium and enough exercise.

Acknowledgment
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Conflict of Interest Statement
Professor Häussler, Dr Gothe und Ms Mangiapane are advisers to Grünenthal, MSD Sharp & Dohme, Lilly Deutschland, Pfizer, Wyeth, Hoffmann-LaRoche and GlaxoSmith-Kline. Professor Glaseke has received funding from the Grünender Ersatzkasse. Professor Pientka has received honoraria for lectures and advisory activities from MSD Sharp & Dohme, Lilly Deutschland, Proctor & Gamble, Servier Deutschland, and Nycomed Pharma GmbH. Professor Felsenberg has received monies from MSD Sharp & Dohme, Sanofi-Aventis, Proctor & Gamble, Hoffmann-LaRoche, GlaxoSmithKline, Lilly Deutschland, Nycomed, Otto Bock, Novartis, Servier, SE Healthcare, Wyeth, Schering, Organon, and Pfizer for advice and/or lectures and/or studies.

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REFERENCES

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