ORIGINAL ARTICLE



Epidemiology and economic burden of fragility fractures in Austria

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Abstract

Summary Fragility fractures are a frequent and costly event. In Austria, 92,835 fragility fractures occurred in patients aged ≥ 50 years in 2018, accruing direct costs of > 157 million €. Due to demographic aging, the number of fragility fractures and their associated costs are expected to increase even further.

Introduction Fragility fractures are frequently associated with long hospital stays, loss of independence, and increased need for care in the elderly, with consequences often leading to premature death. The aim of this study was to estimate the number of fragility fractures and associated healthcare costs in Austria in 2018.

Methods The number of in-patient cases with relevant ICD-10 diagnoses in all Austrian public hospitals was derived from discharge documentation of diagnoses and procedures covering all public hospitals in Austria. Fractures resulting from falls from standing height in patients aged \geq 50 years were used as a proxy for fragility fractures, and the number of in-patient and out-patient cases was estimated. The direct costs of these cases were calculated using the average cost of the corresponding in-patient hospital stay and the average cost for the out-patient stay.

Results The present study estimated the number of fragility fractures (pelvis, thoracic and lumbar vertebra, hip, humerus, rib, forearm, and tibia) for 2018 at 92,835 or just over half of all fractures in patients aged \geq 50 years, corresponding to a prevalence of 2,600 per 100,000 inhabitants of this age group. A constant increase in the proportion of fragility fractures among all fractures was observed with increasing age in both men and women. These fractures amounted to direct costs of > 157 million ϵ .

Conclusion Fragility fractures are a frequent and costly event in Austria. Due to the aging of the population, the number of fragility fractures and their associated costs is expected to increase even further.

Keywords Burden of disease · Fragility fractures · Healthcare costs · Low-trauma fractures · Osteoporosis

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Introduction

According to the recommendations of a consensus development conference held in 1991, osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture [1]. A more operational definition is based on the so-called T-score for bone mineral density (BMD). Osteoporosis may thus be diagnosed in postmenopausal women and in men aged 50 years and above if the T-score of the lumbar spine, total hip, or femoral neck is -2.5 or less [2]. However, it should be noted that, although BMD contributes to an individual's fracture risk, the majority of osteoporosis by BMD [3].

Vertebral fractures, hip fractures, and fractures of the proximal humerus as well as the distal forearm are considered the most frequent types of osteoporotic fractures. Accordingly, they have also been referred to as major osteoporotic fractures (MOFs). The average lifetime risk of a 50-year-old woman to suffer a MOF has been estimated at close to 50%, and the respective risk in men has been estimated at 22% [4]. Osteoporotic fractures, however, can also occur at many other anatomical sites, such as the pelvis, the tibia, or the ribs. In general, the likelihood of experiencing an osteoporotic fracture is increasing with age.

In recent years, the term "osteoporotic fracture" has been interchangeably used with terms such as "fragility fracture," "low-trauma fracture," "low level fracture," "low-energy fracture," or "low impact fracture," denoting that fractures would not ordinarily result from low mechanical forces [5]. In general, such low mechanical forces have been quantified as equivalent to a fall from a standing height or less.

The Republic of Austria is located in the southern part of Central Europe. In 2018, Austria counted some 8.8 million inhabitants, thereof 3.6 million were aged \geq 50 years. Similar to other countries of the European Union, its age pyramid shows a narrow base and an increasing proportion of older individuals [6].

Incidence rates and trend analyses for the entire Austrian population 50 years and above have been published for hip fractures, proximal humeral fractures, and distal forearm fractures, and it has been shown that incidence rates for these types of fracture are among the highest worldwide [7–10]. However, the question of the proportion of fragility fractures in Austria and the associated economic burden — estimated at 2.5% of total healthcare spending in Austria in 2010 [11] — has not been comprehensively addressed so far in any of these studies.

The purpose of the present study was to assess the number of fragility fractures in the Austrian population including MOFs and fractures of the pelvis, ribs, and the tibia and to define the proportion of fragility fractures for each of these fracture types. Additionally, the direct healthcare costs associated with these fractures were estimated.

Methods

Study objectives

The primary objective of this study was to obtain recent data on the total number of fragility fractures in Austria and the corresponding standardized rate per 100.000 inhabitants. The secondary objective was to estimate the direct costs of in- and out-patient hospital stays related to these fractures. Exploratory objectives were to analyze the number and rate of fragility fractures by fracture site and subgroups of age, sex, and Austrian federal state and to estimate the proportion of in- and out-patient fracture treatments.

Data sources and case calculations

All data were calculated by the Austrian National Public Health Institute (Gesundheit Österreich GmbH, GÖG). This institution is responsible for researching and planning public healthcare in Austria. It also acts as the national competence and funding center for the promotion of health. As a public non-profit limited liability company fully owned by the Republic of Austria, it has the federal government as its sole shareholder, represented by the Ministry of Health.

Two main data sources were used: (1) the "DLD" (Diagnose- und Leistungsdokumentation; English translation, diagnosis and procedure documentation) hospital discharge database documenting diagnoses and medical procedures and covering all discharges from Austrian public hospitals and (2) the "MEDOK" (medizinische Dokumentation; English translation, medical documentation) database of the Austrian Workers' Compensation Board (AUVA, Allgemeine Unfallversicherungsanstalt). AUVA trauma hospitals are also open to the public, and taken together, they cover an approximate catchment area of >4 million people and represent the Austrian urban and rural population at all stages of life [7]. The documentation in DLD is the basis for the diagnosis-related group (DRG)-based hospital accounting, and therefore, the data are available for all public hospitals (including the AUVA-operated hospitals) fully documenting all in-patient stays. It uses diagnostic codes from the ICD-10 diagnostic groups. However, codes related to fragility fractures are documented only as a secondary diagnosis of "change in bone mineral density and structure (M80-85)," and documentation is too incomplete to be used for further calculations. In addition, the DLD provides data for the outpatient setting, but again the documentation of diagnoses is incomplete. The DLD database was used to obtain data on in-patient stays in 2018 from all public hospitals by ICD-10 codes for all fracture types (supplemental Table S1), age group, sex, and diagnosis.

The MEDOK database lists "fall from standing height (or ≤ 1.5 m)" as a diagnostic code. This code, in combination with the relevant fracture location and age ≥ 50 years, was used to identify the proportion of fragility fractures among all documented fractures for a given patient category (age group, sex, diagnosis, and year). In order to obtain an estimate for the out-patient setting, which is incompletely documented in the DLD, the MEDOK was also used to define an "out-patient correction factor" defined as 1 + (out-patient cases / in-patient cases) for each patient category using the average over the years 2011–2015 in order to avoid random variations due to small sample sizes in patient categories of a single year (see supplement Table S3). To estimate the total number of fragility fractures in Austria, (i) in-patient cases were used from the DLD using all inpatient fracture cases documented in 2018 multiplied by the proportion of fragility fractures among all fractures; (ii) outpatient cases were derived using in-patient fragility facture cases multiplied by the out-patient correction factor. The sum of in-patient and out-patient cases was considered as a surrogate for their incidence in Austria. Fracture patients younger than 50 years were excluded from data interpretation but included in some of the calculations as a sensitivity analysis to ascertain the 50-year age cut-off for fragility fractures. Incidence calculations are based on a population of 8,822,267 inhabitants in 2018 with 3,563,125 aged 50 years or older [12].

A full definition of all outcome variables, an overview of the mapping of MEDOK codes, and ICD-10 diagnostic groups, as well as the results for the proportion of fragility fractures among all fractures and for the out-patient correction factor are listed in the online supplement.

Health economic estimates

For the assessment of costs associated with in-patient stays, the estimated number of in-patient cases was multiplied by the average duration of hospitalization by age category, sex, and ICD-10 diagnostic code. The resulting total number of days of hospitalization were multiplied by the average costs of one hospital day. The primary costs per hospital day were composed of staff costs, costs for medicinal and non-medicinal products, costs for contracted medical and non-medical services, energy, fees, contributions, and other costs. These costs were averaged across all Austrian hospital departments of trauma surgery, orthopedics, orthopedic surgery, traumatology, internal medicine, neurology, and general surgery. This mean cost per day was estimated at 346 € for the year 2018 (minimum, 128,50 €; maximum, 378,50 €). For outpatient stays, a similar model was used to derive costs on the basis of trauma surgery, orthopedics, and traumatology departments. Costs for public hospitals were obtained from DRG-based accounting and hospital statistics; for AUVAoperated public hospitals, not cost data were available. The mean costs per stay were estimated at 152 € for 2018 (minimum, 141,84 €; maximum, 185,39 €).

Statistical analysis

The statistical analysis was descriptive in nature; no formal hypothesis was tested. For categorical variables, the number and percentage of patients in each category were reported. Patients with malignancies were excluded. Menopausal status was not assessed. Patients with more than one relevant fracture were only counted once. Patients with more than one fracture-related hospital stay during 2018 were counted once

for each stay. Stays were counted as out-patient when treatment was exclusively delivered on an out-patient basis. Cases with mixed in-patient and out-patient treatment were counted as in-patient. Since our results are not based on a random sample but the population itself covering all cases in Austria in 2018, no measurement of statistical precision is reported [13]. The following software was used: StataCorp (2013), Stata statistical software, and Release 13 (College Station, TX, StataCorp LP; Microsoft Corporation (2018), Microsoft Excel, retrieved from https://office.microsoft.com/excel).

Results

Estimate of fragility fractures in 2018 (primary objective)

In the year 2018, the integral collection of in-patient stays from AUVA-operated and other public hospitals yielded a total of 99,340 fractures, 39,147 of which were documented as fractures from falls from standing height, i.e., fragility fractures; 37,128 of these occurred in persons aged 50 years or older (supplemental Table S3). Figure 1A shows the percentage of fragility fractures among all fractures in the in-patient setting by age, showing a rapid increase of the proportion of fragility fractures in both male and female individuals starting at the age of 50 years. In the age group of 50–59 years, the proportion of fragility fractures was 31% in women, increasing by approximately 15% steps during each decade. Men showed an equally steep increase but lagging approximately 10 years behind women.

Based on the numbers of in-patient cases, the number of out-patient cases was calculated using the sex- and agespecific out-patient correction factors of each ICD-code (supplemental Table S2). This calculation yielded a total of 115,309 patients with relevant fractures from falls from standing height in all age groups and 92,835 relevant fractures in persons aged 50 years or older, considered fragility fracture cases of osteoporotic origin (Table S4, Figure S1). These 92,835 fractures translate into an incidence of 2,600/100,000 inhabitants aged 50 years or older suffering from fragility fractures in Austria. Generally, the incidence was higher in women than men and strongly increased with age (Fig. 1B).

Costs associated with fragility fractures (secondary objective)

The total costs of fragility fracture-associated in-patient stays in Austria were estimated at 148,777,296 \in for 2018 (minimum, 55,273,166 \in ; maximum, 162,808,507 \in). Additionally, costs of fractures treated on an out-patient basis were estimated at 8,467,525 \in (minimum, 7,901,481 \in ; maximum, 10,327,521



<Fig. 1 Fragility fractures across all age groups. A Percentage of fragility fractures among all fractures in the in-hospital setting in 2018, by sex and age (N=39,147 in-hospital cases with documented falls from standing height) (**a**). **a** The figure covers in-patient cases only, since data on diagnosis is not available in the out-patient sector. **B** Incidence of fragility fractures per 100,000 inhabitants in 2018, by sex and age (N=115,309 in-patient and out-patient cases with falls from standing height) (**b**). **b** Incidence calculations are based on a population of 8,822,267 inhabitants in 2018, 4,338,518 men and 4,483,749 women [6]

€). Direct healthcare costs for 1 year were thus $157,244,822 \in (\text{minimum}, 63,174,647 \in; \text{maximum}, 173,136,028 €)$. Costs increased with patients' age and were substantially higher in women due to longer average hospital stays. Hip fractures incurred the highest costs in the in-patient setting with 76,892,113 €, while forearm fractures were responsible for the highest costs in the out-patient setting with 3,400,006 € (Fig. 2; Table S5).

Exploratory objectives

Overall, the most frequently affected fracture site was the forearm with 25,795 fractures, followed by rib fractures (n=16.868) and hip fractures (n=16.466; Fig. 3). Fractures occurred more frequently in women (n=67,331) than men (n=25,504). Men and women were also affected differently with regard to the fracture location with fractures arising more frequently in women at all sites, except the ribs (n=9,063 in men, n=7,805 in women). Forearm fractures occurred approximately 6 times more frequently in women (n=21,952) than men (n=3,843); pelvic fractures occurred approximately five times more frequently (n=8,899 in women; n=1,870 in men).

In the in-patient setting, a clear trend was observed towards an increasing incidence of fragility fracture cases as patients get older, especially with hip fractures in the 70 to 79 and 80+years age groups (Figure S2A). In the out-patient setting, no clear trend was observed (Figure S2B), except for a peak of distal forearm fractures at age 60 to 69 years and an increase with age in the number of rib fractures. Pelvic fractures show an increase after age 60 to 69, although only selected types of pelvic fractures are treated on an out-patient basis at all.

The distribution of fragility fractures across all nine Austrian federal states is shown in the supplement. In summary, a markedly higher incidence is shown in the Western half of Austria, in Salzburg and Tyrol, followed by Upper Austria, Vorarlberg and Carynthia (Figure S3).

Discussion

This integral collection of fragility fractures associated with osteoporosis in Austria found a high number of relevant fractures (n = 92,835) in persons aged 50 years or older,

accounting for more than 157 million \in of direct treatment costs. Both sexes were affected already at an unexpectedly young age beginning at 50 years, with women leading the steep increase over men by a lag of about 10 years. Importantly, all investigated anatomical fracture sites were affected, not only the common sites known as the MOFs, i.e., vertebral, hip, proximal humerus, and distal forearm fractures.

Fragility fractures are thus frequent and costly events with an incidence increasing with age. This is an important finding given the demographic development towards an ever-increasing proportion of individuals aged 50 years or older in developed nations. In Austria, the number of individuals aged 65 or older is expected to increase and plateau at around 2.7 to 2.8 million from 2060 onward, while the 25- to 65-year-olds are expected to decrease from 2020 onward. All other age groups are projected to remain stable [14]. Osteoporosis-related fragility fractures thus need to be counted among those chronic diseases related to aging that will exacerbate the societal burden in the coming decades. According to the WHO definition of osteoporosis, i.e., a T-score < -2.5, the prevalence of osteoporosis in Austria is estimated at approximately 460,000 individuals with 370,000 women and 90,000 men [11]. The number of 93,835 fragility fractures in 2018 alone compares in dimension with other chronic diseases. According to recent data from the Austrian Central Statistical Office, among Austrians aged \geq 45 years, approximately 150,000 individuals (4%) have chronic kidney disease, 221,000 (5%) have coronary heart disease or angina pectoris, 121,000 (3%) have heart attacks or chronic sequelae thereof, 113,000 (3%) have strokes or their chronic sequelae, and 1,190,000 (28%) have hyperlipidemia [15–17]. The number of inhabitants aged 65 or older, which is the age cut-off used in the available demographical prognoses [14, 18], is projected to steadily increase from 1.7 million in 2019 to 2.7 in 2060 [14]. Importantly, the size of the potential workforce (age cohort 25 to 64 years) will be decreasing [14]. From the demographic development, an increase in health expenditure pertaining to chronic diseases of the elderly is expected, while the number of individuals of working age that actively contribute to the health insurance system will decrease. It is expected that this development will present an enormous strain on a health insurance system based on the generational contract, such as in Austria.

Although fractures of the feet, toes and fingers, skull, facial bones, and neck usually are not considered as fragility fractures [19], we have included them as "other diagnoses" in the initial count of all fractures in the in-patient setting (Table S3). Of the total fracture count, 43,645 fractures considered "other diagnoses" as well as 27,328 relevant fractures and other diagnoses occurring in individuals younger than 50 years of age were subsequently excluded according





◄Fig. 2 Healthcare costs associated with fragility fractures in patients aged 50 years or older, by treatment setting, sex, and fracture site. A In-patient setting. B Out-patient setting

to our fragility fracture definition. Interestingly, of relevant fracture types, 2,020 fractures (7%) occurred in individuals younger than 50 years. This group was not further assessed, and the causes of their fractures are unknown. "Other diagnoses" occurred at a similar frequency in younger and older persons (5:6 ratio), while "relevant fractures" occurred almost six times more frequently in older than younger individuals.

The estimated annual costs of all fragility fractures exceeded the sum of 157 million \in . These costs do not include any secondary costs for rehabilitation, work time lost, or other economic burden to the individual, third persons, and to society. In Austria, the percentage of all direct and indirect fracture costs amounts to 2.5% of the annual healthcare spending budget, which corresponded to 10.3% of the 2018 gross domestic product [20]. Taken into account that the whole cost of osteoporotic fractures is approximately 775 million \notin /year, the sum of 157 million \notin for medical care after fracture amounts to 20% [11].

As a consequence, ways need to be found to reduce the fracture risk resulting from osteoporosis and thus help to identify persons at risk and engage them in prevention programs. This is even more important during the current COVID-19 pandemic period that forces large parts of the population, especially older persons but also the young in whom bone strength is still building up, into a state of reduced physical activity and reduced sun exposure and thus lower production of endogenous vitamin D. Physical inactivity was shown to very rapidly lead to loss of bone strength, while recovery takes disproportionately long [21, 22]. Due to repetitive lockdowns and temporary closures of medical facilities in conjunction with the fear of patients to meet a physician at a hospital or ambulance, an unfavorable increase of patients with osteoporosis is expected. Recent data suggest that COVID-19 has the potential to act directly on bone resorption units with unfavorable long-term effects on bone metabolism and a possibly increased risk of fragility fractures [23]. In the first months of the COVID-19 pandemic, the number of online FRAX fracture risk assessment sessions fell by at least 50% in the majority of European countries and up to 58% globally, demonstrating a dire impact on osteoporosis management [24]. To date, approximately 7% of the total Austrian population were tested positive on this new disease with an increasing number of younger patients [25].

In Austria, the proportion of the population aged 50–89 years with a 10-year probability of sustaining a MOF is close to 35% [11]. The findings of this investigation with an approximately 15% increase of fragility fracture

occurrence per decade of life in both sexes confirm the magnitude of the population burden in this country. Except for rib fractures, women were affected substantially more frequently, especially at locations such as the forearm (1:6 ratio) and the pelvis (1:5 ratio), which is in line with recently reported data from France [26].

The incidence of distal radius fractures was expectedly high in female patients at the sixth and seventh decades of age with a known decline at higher age. Between 1989 and 2008, a 1.7-fold increase in humerus fractures was observed and women aged > 50 years, with a 1.2-fold increase in men [9]. In this investigation, the proximal humerus fracture incidence was more than threefold higher in females, reaching a plateau at the seventh decade of life. In Germany, the incidence of this type of fragility fracture increases in both sexes with age, which is in contrast to this investigation. Other countries such as Finland report a stabilized incidence. The reasons for these differences between European countries remain ambiguous. Cohort effects towards a healthier aging population are discussed; measures to prevent falls, enhanced fall security, and training/countermeasures may contribute to this observation [27, 28].

Pelvic fragility fractures continuously increased after the age of 60 years and to a higher extent in the female population. This increase was even higher at the hip. Since the number of this type of fragility fracture is globally on the rise, there is cause for concern. These injuries have a high morbidity and mortality burden and are challenging not only for patients and their families but also for healthcare providers and the healthcare systems in which they operate. Given their diminished physiologic reserve in conjunction with muscle loss, the increasing incidence of low-energy pelvic ring fractures is particularly concerning in the older, frailer population [29]. Studies report a continuous rise from 1970 caused by demographic changes but also mention previous internal fixation of the proximal femur or hip arthroplasty and female sex as risk factors [30]. Fractures of the pelvis and fractures of the vertebrae are associated with increased mortality of similar magnitude [31].

This study identified a continuous increase of rib fractures at the age of 70 years or older in both sexes, but this anatomical site was more frequent in male patients. Low-trauma rib fractures are a class of fracture that has not yet been widely studied. Often multiple, even single rib fractures are associated with an increased risk for refracture and even mortality [32, 33]. There is cause for concern that this respective type of fracture is associated with chronic lung diseases such as chronic obstructive pulmonary disease (COPD) or asthma. Although males sustained rib fractures more frequently, the proportion of females at this respective fracture type accounted for 46% in the whole population, owing the fact that smoking in the female population increased over the last decades. To date, there is less awareness on comorbidities



Fig. 3 Fragility fractures in patients aged 50 years or older, by sex and fracture site (N=92,835 in- and out-patients)

and the clinical impact of co-existing diseases, the impact of a chronic inflammatory state, and necessary medications such as glucocorticoids [33, 34].

The following strength and limitations may warrant consideration. Our study is an integral collection of all in-patient fracture cases treated in Austrian public hospitals, extended to hospital-treated out-patients by model. It represents the most comprehensive accounting of fracture cases in Austria to date. The data exploration assumed a definition of fragility fractures occurring as a consequence of a fall from standing height in persons aged 50 years or older. Menopausal status was not assessed; patients with malignancies were excluded. The distribution of documented fractures resulting from falls from standing height in hospital in-patients across all ages clearly shows a steep increase in cases starting at the age of 50 years. This confirms the validity of the adopted fragility fracture definition. Our fragility fracture definition and the diagnostic codes that we were able to access only provide the presence of a fracture by location and do not allow to discern primary from secondary osteoporosis. We have only accounted for clinical fractures treated in hospitals on an inpatient or hospital-based out-patient basis with no accounting for chance findings during X-ray imaging. The high numbers we identified are thus likely to be underestimating the total fragility fracture numbers in Austria, particularly in regard to the so-called morphometric or radiographic vertebral fractures, which are known to account for almost 70% of all vertebral fractures and often remain undetected [35]. We have also not characterized patient characteristics beyond age and sex, with the impact of other risk factors, such as comorbidities or recurring fractures not reflected in the present study. The present study thus does not allow any identification of fracture-prone patient profiles. The cost estimates only take into consideration the direct costs associated with treatment provided in hospital (for both in- and out-patients). Costs occurring after discharge, e.g., for rehabilitation and secondary prevention, or costs for work hours lost or for care through third persons have not been taken into consideration, thus crossly underestimating the total burden associated with fragility fractures. Considering the fact that the fracture prevalence increases by age, post-discharge costs will be especially high in nursing home residents. The potential impact of periodic BMD and/or FRAX-based screening of the population at risk, e.g., persons aged 50 years or older, as part of preventive medical checkup programs, as well as the potential effect of osteoporosis treatment on the long-term development of the incidence of fragility fractures on a population scale, should be an important focus of future research.

The human skeleton can be viewed as an endocrine organ system with a supporting function and should be considered for periodic organ screening, similar to other preventive screening programs for the abovementioned and other diseases. Osteoporosis guidelines are continuously updated to include periodic FRAX assessment for the assessment of an individual fracture risk in order to prevent a fragility fracture. Therefore, the documentation of fractures including high-impact fractures is mandatory for each patient's medical history. A previous long-term study conducted in Austria found that also preceding hightrauma fractures increased the risk of future non-vertebral fragility fractures including hip [36]. Timely lifestyle interventions and — where indicated — drug treatment should be initiated to postpone or even halt the occurrence of fractures. According to results of the Austrian branch of the International Costs and Utilities Related to Osteoporotic Fractures Study (ICUROS), 68% of patients who presented with a fracture and who had a clear indication for osteoporosis treatment did not receive any such treatment. More importantly still, of patients who did not receive osteoporosis treatment at the time of fracture, 9 in 10 men and over 8 in 10 women were also not prescribed an adequate osteoporosis treatment thereafter [37]. In a study from France, only 16.7% received a specific osteoporosis treatment in the 12 months after a fracture. The refracture rate within the first year after fracture was 6.3%, with lower rates for multiple rib fractures (4.0%) and higher rates for pelvic fractures (7.8%) [26]. A recent study of the impact of antiosteoporotic drugs and calcium/ vitamin D on refracture in patients with previous fragility fractures showed that over a mean follow-up of 3 years, the risk of subsequent fractures was 44.4% lower in treated patients compared to untreated ones and 77.2% lower in treated patients who were adherent to medication [38]. It can thus be assumed that if the 92,835 Austrian patients with fragility fractures in 2018 subsequently received adequate treatment, the risk of refracture would be substantially decreased. A substantial number of initial fractures would even have been prevented, had these same individuals been identified through a screening program prior to their index fragility fracture and adequately been treated.

In conclusion, fragility fractures are a frequent, costly, and — above all — preventable event. Demographic developments will lead to an even higher burden in the future. Treatment guidelines and reimbursement regulations need to be focusing on prevention to avoid the high costs associated with fracture treatment and rehabilitation, especially keeping in mind that many patients will have recurring fractures.

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Data availability All authors had access to the source data. Qualified researchers may request data from the corresponding author upon reasonable request.

Code availability Not applicable.

Declarations

Ethics approval This study was approved by the ethics committee of the medical university of Vienna (ethics committee number: 1216/2021).

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest Christian Muschitz, Michael Hummer, Anton Hlava, Andreas H. Birner, and Hans Peter Dimai have no conflicts of interest to declare. Margit Hemetsberger has received consulting fees from Amgen outside scope of the present work and holds Amgen equity. Johannes Grillari is scientific advisor, co-founder, and shareholder of TAmiRNA GmbH and Evercyte GmbH.

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