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The global burden of fragility fractures – what are the differences, and where are the gaps

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The global burden of fragility fractures – what are the differences, and where are the gaps

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A B S T R A C T

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The current burden of fragility fractures is enormous, and it is set to increase rapidly in the coming decades as humankind enters a new demographic era. The purpose of this review is to consider, in different settings:

- The human and economic toll of fragility fractures.
- Risk factors for fragility fractures.
- Current acute management of fragility fractures.
- Current care gaps in both secondary and primary fracture prevention.

A summary of global, regional, and national initiatives to improve the quality of care is provided, in addition to proposals for the research agenda. Systematic approaches to improve the acute care, rehabilitation and prevention of fragility fractures need to be developed and implemented rapidly and at scale in high-, middle- and low-income countries throughout the world. This must be an essential component of our response to the ageing of the global

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The global burden of fragility fractures

In 2021, for the first time, estimates of the epidemiology and burden imposed by fractures at all ages were published for 204 countries and territories throughout the world. A systematic analysis of the Global Burden of Disease (GBD) Study reported the following key findings for 2019 [1]:

- 178 million (95% uncertainty interval [UI], 162–196) new fractures, an increase of 33.4% (95% UI, 30.1–37.0) since 1990.
- 455 million (95% UI, 428–484) prevalent cases of acute or long-term symptoms of a fracture, an increase of 70.1% (95% UI, 67.5–72.5) since 1990.
- 25.8 million (95% UI, 17.8–35.8) years lived with disability (YLDs), an increase of 65.3% (95% UI, 62.4–68.0) since 1990.

While the GBD Study did not include sub-analyses to differentiate between high- and low-trauma fractures, the authors noted that older people were the most likely to have new fractures, with increases in age-specific incidence becoming evident after age 50 years in females and age 65 years in males. The overall age-standardised incidence rate of new fracture was 2296 per 100,000 populations in 2019, as compared to 15,381 per 100,000 populations in those aged 95 years or older. The breakdown by skeletal site reported 14.2 million hip fractures, 14.6 million fractures of the femur other than at the femoral neck, and almost 8.6 million fractures of the vertebral column.

Studies published during the last five years have characterised the burden of fractures among older people in Asia-Pacific, Eurasia, Europe, Latin America and the United States of America.

In 2018, the Asian Federation of Osteoporosis Societies (AFOS) updated estimates of hip fracture incidence in 2018 and 2050 for China, Hong Kong SAR, India, Japan, Korea, Malaysia, Singapore, Taiwan and Thailand [2]. The total population of these countries and regions represented 42% of the global population at the time. The authors predicted that the 1.1 million cases of hip fractures that occurred in 2018 would increase to 2.5 million cases by 2050, with direct costs projected to increase from US\$7.4 billion in 2018 to almost US\$13 billion in 2050.

In 2020, the *Working Group for the Audit on the Burden of Osteoporosis in the Eurasian Region* estimated hip fracture incidence in 2015 and projections for 2050 for Armenia, Belarus, Kazakhstan, Kyrgyz Republic, Moldova, Russian Federation and Uzbekistan [3]. Projected increases ranged from 60% in Belarus and 70% in Moldova to 310% in Kyrgyz Republic and 360% in Uzbekistan.

In 2021, the SCOPE 2021 Report provided a new scorecard for osteoporosis for the 27 countries of the European Union plus Switzerland and the United Kingdom (EU27 + 2) [4]. There were estimated to be 4.3 million new fragility fractures in this region in 2019, including almost 827,000 hip fractures. The direct cost of new fractures in the EU27 + 2 in 2019 was Euro 36.3 billion (US\$38.8 billion). The cost of long-term disability incurred in 2019 for fractures that occurred in prior years was an additional Euro 19 billion (US\$20.3 billion), and the cost of pharmacological assessment and treatment was Euro 1.6 billion (US\$1.7 billion). Thus, the total direct cost in the EU27 + 2 in 2019 was Euro 56.9 billion (US\$60.8 billion).

In 2019, Aziziyeh et al. characterised the burden of fragility fractures among people aged 50–89 years in Argentina, Brazil, Columbia and Mexico [5]. It was estimated that 840,000 fractures occurred in the four countries during 2018 at a total cost of almost US\$1.2 billion. The one-year cost burden ranged from US\$411 million in Mexico to US\$94 million in Columbia.

In 2019, the National Osteoporosis Foundation (now the Bone Health and Osteoporosis Foundation) commissioned the consulting company Milliman to determine the cost of fragility fractures to the Medicare system in the United States of America [6]. The analysis reported that in 2015 a total of 2

million Medicare fee-for-service and Medicare Advantage beneficiaries sustained a total of 2.3 million fractures. Fractures of the hip and spine were the most common fracture types identified (40%), and females had 79% higher fracture rates than males. Notably, about 15% of Medicare fee-for-service beneficiaries who sustained an initial fracture experienced at least one or more subsequent fractures within a year of the initial fracture. Among Medicare fee-for-service beneficiaries who survived for at least 180 days after sustaining a subsequent fracture, the estimated total costs to Medicare during a two-to-three year follow-up period were US\$6.3 billion.

In summary, the current human burden and associated financial costs of fragility fractures are enormous throughout the world and are set to increase sharply as humankind enters a new demographic era.

Risk factors for fragility fracture in different settings

The International Orthopaedic Multicentre Study in fracture care (INORMUS) is an observational study that collects data from patients in low- and middle-income countries (LMICs) who have sustained a fracture or musculoskeletal injury [7]. In 2019, the INORMUS investigators explored differences in sites of fracture, mechanisms of injury and demographics for females ($n = 9878$) who sustained a fracture in 17 LMICs, including China and India, and 15 other countries in Africa, other Asian countries and Latin America [8]. Almost two-thirds (65.6%) of fractures occurred in patients aged 50 years or older and the majority (51.7%) resulted from a fall from standing height. Overall, the most common fracture was hip (26.8%), followed by tibia/fibula (12.6%) and spine (9.7%). Regional differences were evident, with the proportion of patients who fell from standing height being more common in China (64.1%) and Latin America (66.8%) than Africa (35.5%), India (39.2%) and the other Asian countries (42.3%).

In 2021, Veronese et al. assessed the association between sarcopenia and falls and fractures in individuals aged 65 years or over ($n = 13,101$) in five LMICs (China, India, Ghana, Mexico and Russia) [9]. Sarcopenia was defined as having low skeletal muscle mass, as reflected by lower skeletal mass index and either a slow gait speed or weak handgrip strength. Overall, the prevalence of sarcopenia and fall-related injuries was 13.5% and 4.9%, respectively, and the prevalence of fall-related injury was higher for individuals with sarcopenia than in individuals without the condition. As illustrated in Fig. 1, this association was evident in all countries, being most pronounced in Mexico. A diagnosis of sarcopenia conferred almost a doubling of risk of fall-related injury (Odds ratio [OR], 1.85; 95% Confidence interval [CI], 1.24–2.77), and the level of between-country heterogeneity was low (Higgins's I^2 , 39.3%). In terms of the limitations of the study, the authors noted that on account of the cross-sectional nature of the study that reverse causality was possible, whereby individuals who frequently fall may have a higher risk of sarcopenia. Thus, longitudinal studies should be designed and undertaken to confirm that sarcopenia can be considered as a risk factor for falls in LMICs.

Bars denote 95% confidence interval.

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In 2022, Shlisky et al. published a report of a Calcium Task Force convened by the Nutrition Science Program of the New York Academy of Sciences and the Children's Investment Fund Foundation [10]. The report focused on the global prevalence of inadequate calcium intakes and related health outcomes. Key observations included:

- Approximately 90% of people at risk of inadequate calcium intake live in Africa and Asia.
- Fortification of wheat flour, breakfast cereals and fruit juices are less common in LMICs than in high-income countries.
- The lack of well-validated, specific biomarkers of calcium status that are feasible for population-level usage in LMICs presents a barrier to widespread assessment.
- Randomised controlled trials are required to evaluate the effects of calcium on bone health in understudied regions of the world.

In 2021, Jiang et al. evaluated the prevalence of vitamin D deficiency in Asia in a systematic literature review and meta-analysis [11], which included 472 studies with 746,564 participants from 30 Asian

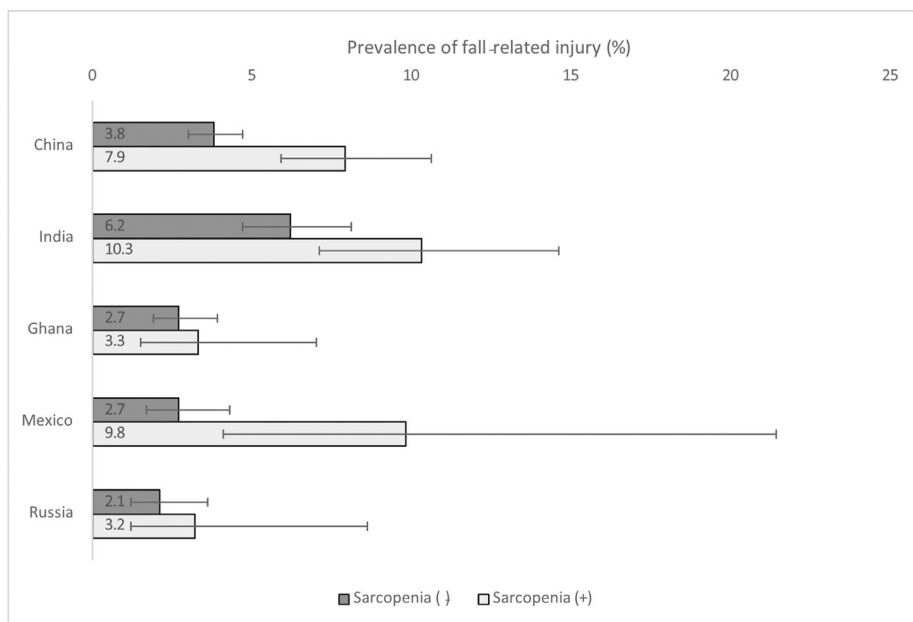


Fig. 1. Prevalence of fall-related injury by sarcopenia status in five low- and middle-income countries [9].

countries. Based on a definition of vitamin D deficiency as a 25-hydroxyvitamin D level less than 50 nmol/L, 54% of participants were deficient. The authors noted that this finding compares unfavourably with studies from Africa (34%), Europe (40%) and the United States of America (18–30%). Significant risk factors for vitamin D deficiency included gender (i.e., highest among females), age (i.e., highest among infants), region (i.e., highest in Southeast Asia and lowest in Central Asia) and altitude (i.e., highest among people at lower altitudes [≤ 500 m]). The presence of specific diseases was also significantly related to 25-hydroxyvitamin D levels, including anaemia, cancer, dermatitis, diabetes, fatty liver/hepatitis, obesity/metabolic diseases and systemic lupus erythematosus. The authors concluded that more detailed public health strategies and policies were required across the region to address this ubiquitous issue.

Fragility fracture management in high-, middle- and low-income countries

The science of medicine has progressed dramatically from the turn of the century and remarkable improvements in global health have been achieved in the last 25 years. However, provision of healthcare across the world has not been uniform and greatly influenced by a country's resources and socio-economic status. In 2015, an article from *The Lancet* Commissions stated that 5 billion people do not have access to safe, affordable surgical and anaesthesia care when needed, and access is worst in LMICs. Moreover, 143 million additional surgeries are needed in LMICs to save lives and prevent disability, especially in eastern, western, and central sub-Saharan Africa and south Asia [12]. In the USA, the majority of surgical procedures done were for musculoskeletal disorders and unintentional injuries in the non-communicable and injuries categories of the GBD [13], which included fragility fractures in the elderly. The same is true for LMICs as lower extremity fragility fractures like hip, femur and tibial fractures are mostly managed with surgery, and depending on the country where the patient lives and socio-economic status, treatment may vary [8,12].

Surgical management of lower extremity fragility fractures is expensive, and there is a stark difference of costing between a high-income country (HIC) vs a low-income country. Hip fractures were the costliest fragility fractures to treat in Europe, and they account for 57% of the total cost of fragility

fractures in Europe [14]. The average cost of hip fracture care in an HIC such as Australia was US\$750 million annually in 2016 [15], while in an LMIC such as the Philippines, the economic burden was computed to be \$22 million per year [16]. Part of the reason why there is a big difference in cost would be that in HICs hip fractures are mostly managed surgically. In the Australian registry, 97% of the patients underwent surgery, but in the Philippines from 2007 to 2012, less than half (25–50%) of elderly patients with hip fractures underwent surgery [17]. Still in 2021 in the Philippines, a multicentre study reported that only 80% of the admitted patients underwent surgery for their hip fractures [18]. A retrospective study in Nepal from 2016 to 2017 also reported that 96 out of 480 patients (20%) were treated conservatively, and 28 patients (5.7%) left against medical advice; only 340 of 480 patients (70.8%) were operated [19].

In terms of implants used in the Australian and New Zealand hip registry, there was an increasing number of total hip replacements (19.7%–26.4%) between 2000 and 2016. The use of bipolar hemiarthroplasty and intramedullary nailing for intertrochanteric fractures has also increased [15]. In a similar manner, in the Philippines, surgeons tend to use more hemiarthroplasty (24–35%) and intramedullary implants (21–29%) for elderly hip fractures [18]. In Nepal, the hemiarthroplasty implant of choice was the Austin-Moore prosthesis, and the Thomson prosthesis was also used for intertrochanteric fractures, along with dynamic hip screws and intramedullary nails [19].

Time to surgery for fragility hip fractures is recommended to be between 24 and 48 h. Delays in surgery result in significantly more hospital expenses, more complications, delayed mobilisation and recovery, and significant mortality rates [19–24]. In the Australian 2018 registry, the median time to surgery was 30 h, and this is comparable to the UK, wherein 97% of patients had their surgeries within 48 h [15]. In Beijing, China from 2009 to 2011, only 8% of the patients had their surgeries done within 48 h [25]. However, from 2012 to 2017 and with the adaptation of the orthogeriatric multidisciplinary model of care, the percentage of patients who underwent surgery within 48 h increased to 50% [26]. In LMICs, such as the Philippines, in 2021, the average time from admission to surgery was at least 5 days. The main reasons for the delay were protracted cardio-pulmonary clearance and a lack of hospital resources for facilitating an earlier surgery [18]. Similarly, in Sri Lanka, the average time to surgery was 11 days (7–21 days) [27], and in Nepal, it was 9.5 days [19]. Another factor contributing to prolonged surgery times is the delay in admissions of patients with fractures in LMICs. From 2014 to 2019, the INORMUS study reported that 71.9% of open fractures were admitted more than 2 h from injury, and 27.5% of closed fractures were admitted more than 24 h from injury [28]. In the Philippines, the average time from injury to admission in elderly patients with hip fractures was 3.54 days, and only 24% of the patients were able to seek medical attention within 24 h after injury [18]. Similar findings were reported from a military hospital in India in 2019, wherein more than 50% of the patients came in more than 48 h post-injury [29].

A critical aspect in the management of elderly hip fractures is the establishment of an efficient and functioning orthogeriatric multidisciplinary team. The only way to facilitate early admission, comorbidities treatment, surgery within 48 h, complications prevention, bone protection treatment and falls prevention is to have an intricate pathway of care starting from the emergency room up until the care at home. In LMICs, the adaptation of the concept of orthogeriatrics was quite late compared to when it was first started in HICs such as Australia, the UK and the USA. In the Philippines, the concept was first implemented in 2017, and until the present day, most institutions still vary in the orthogeriatric services offered. Only COVID-19 screening and co-morbidity assessment/co-management services were routinely present. Peri-operative pain assessment, anti-coagulation management, inpatient mobilisation, falls assessment, osteoporosis management and even coordinated patient monitoring services were clearly lacking or inconsistent and would need further improvements [18]. The same situation was also mentioned in one centre in Thailand when they adopted a fast-track multidisciplinary program from 2016 to 2018 in which involvement of other specialties remained low, thus explaining why their desired outcomes were not what they observed [30]. A more alarming issue is that there is still no established national policy or agenda to improve musculoskeletal health for fragility fractures in many LMICs like in the Philippines [18] and Malaysia [31].

In terms of patient outcomes, mortality rates after hip fractures are still high even in HICs but have improved. A recent systematic review in 2019 in 8 national registries and 36 countries reported a 1-year average mortality rate of 22% (2.4–34.8%), compared to 30% as reported in 2005 [32,33]. There

is a paucity of data with regards to outcomes in LMICs, but generally mortality rates are at par with data from HICs. Mortality rates in Sri Lanka after hip fractures were around 20–26% at 1-year post-operatively [27], 7.7–21.5% in India [29,34], 26% in Malaysia [31,35], 30–35% in Brazil [36,37], 33.9% in Pakistan [38], 26.98% in Saudi Arabia [39], 16.7% in Sudan [40] and 19% in Thailand [41]. However, in Egypt, it was reported to be unexpectedly high at 52.8% in a level one trauma centre [42]. The high rates were attributed to varied postoperative protocols, lack of specialised orthogeriatric care, poor follow-up rates and low socio-economic status of the included patients. Advanced age, poor pre-fracture mobility, delays in surgery, male gender and significant co-morbidities were consistently reported to have higher mortality rates. Disability after hip fracture was also similar between HICs and LMICs. In the Baltimore hip studies, despite steady improvements in disability from 2 to 24 months post-injury; still around 55% of patients remained dependent on activities after 24 months [43]. In one report in Sri Lanka, at least 80% of patients pre-injury were fully independent, but only 40% were fully independent at 12 months post-surgery [27]. The same finding was also reported in Malaysia, wherein 59% of the patients were dependent for their activities of daily living after hip fracture [35].

Secondary and primary fracture prevention in high-, middle- and low-income countries

Secondary fracture prevention

In 2017, Harvey et al. published a review that focused on the following themes [44]:

1. Case finding and management of individuals at high risk of fracture
2. Public awareness of osteoporosis and fragility fractures
3. Reimbursement and health system policy
4. Epidemiology of fracture in the developing world

The authors stated, “*Secondary fracture prevention is an obvious first step in the development of a systematic approach to the prevention of all fragility fractures caused by osteoporosis.*” This statement is supported by meta-analyses that have demonstrated that individuals with an index fracture are approximately twice as likely to sustain subsequent fractures compared to fracture-free peers [45,46]. From the obverse perspective, we have known since the 1980s that up to half of individuals who sustain a hip fracture experience a previous fracture in the months or years before breaking their hip [47–50]. Given that safe and effective pharmacological treatments that significantly reduce the incidence of secondary fractures have been available since the 1990s, the care gap documented by Harvey et al. for all world regions is all the more remarkable. Disappointingly, as noted in the second edition of the IOF Compendium of Osteoporosis published in 2019 [51], the post-fracture care gap has proven to be both persistent and pervasive. A summary of recent, primarily large-scale care gap studies published during the last three years (mid-2019 to mid-2022) follows, and thereafter a summary of links to global, regional and national initiatives intended to promote optimal post-fracture care.

The global secondary fracture prevention care gap

In 2021, Wong et al. described a study protocol using a common analytical platform to evaluate secular trends in hip fracture incidence, mortality and the use of post-fracture pharmacological treatment across Asia, Oceania, North and South America and Western and Northern Europe during the period 2005 to 2018 [52]. Initial findings presented as a late breaking abstract at the 2021 American Society for Bone and Mineral Research Meeting noted that the overall treatment rate prior to hip fracture was one-fifth or less, and 12 months after hip fracture varied from 11.5% to 50.3% [53]. By 2018, the treatment rate in the majority of countries and regions evaluated remained below 40%.

The secondary fracture prevention care gap in Asia Pacific

In 2020, Shimodan et al. described the post-fracture care for 4764 men and women who presented with hip fracture to seven hospitals in Hokkaido prefecture, Japan, during the period 2008 to 2017 [54]. Prior to hip fracture, 8.4% of patients were receiving osteoporosis-specific therapy, which included

bisphosphonates, selective estrogen receptor modulators, teriparatide and denosumab. After surgery, the treatment rate increased to 34.2%, the majority (>80%) being treated with bisphosphonates. Also, prior to surgery, 6.3% of patients were taking active vitamin D3 or calcium preparations, which increased to 12.6% after surgery. Notably, treatment rates in the hospitals that introduced Osteoporosis Liaison Services (OLS) [55] were four times higher than that recorded in the hospitals without an OLS.

In 2021, Nakatoh et al. undertook a big data approach to analyse secondary fracture prevention in Japan for a very large sample of men and women with hip fractures ($n = 941,483$), vertebral fractures ($n = 954,789$) and mixed fractures, i.e., the individual had sustained two fractures on the same day ($n = 4669$) [56]. The analysis was conducted on medical insurance data from the National Database of Health Insurance Claims and Specific Health Checkups of Japan for the period April 2012 to March 2019. Osteoporosis-specific therapies included bisphosphonates, denosumab, teriparatide, selective estrogen receptor modulators, active vitamin D3 single-agent (eldecalcitol) and others (alfacalcidol and menatetrenone). In total, prior to the fracture, 27.4% ($n = 520,222$) patients received treatment, which increased to 46.9% ($n = 891,443$) within 1 year of registration of the fracture. Differences in post-fracture treatment rate were evident by fracture type, with 31.9%, 61.7% and 46.6% of hip fracture, vertebral fracture and mixed fracture groups treated, respectively.

In 2019, Kim et al. evaluated diagnosis of osteoporosis in a large sample ($n = 77,209$) of men and women who sustained a distal radius fracture in Korea [57]. Data were obtained from the Korean Health Insurance Review and Assessment Service nationwide claims database for the period 2010 to 2016. Patients with multiple fractures, Paget's disease and cancer, and those who had undergone an osteoporosis examination before the fracture were excluded. Overall, one quarter ($n = 19,305$) of patients underwent diagnostic assessment for osteoporosis within six months of fracture, with the majority of assessments being bone mineral density (BMD) alone (74.2%) and a minority being quantitative computed tomography (QCT) alone (17.3%) or BMD plus QCT (8.5%). The proportion of patients assessed by BMD alone increased from 64.0% in 2011 to 87.0% in 2016. Assessment rates were higher among patients aged 70–79 years (39.9%) and among those who attended a tertiary hospital (32.9%), while males were less likely to be assessed than women (10% vs 30%).

In 2020, Wang et al. undertook a retrospective cohort study of post-fracture osteoporosis treatment among men and women ($n = 27,342$) aged over 50 years who presented with fragility fracture to hospitals in Fujian, China, during the period 2010 to 2016 [58]. Data were obtained from the National Healthcare Big Data electronic health record database, which contains information on more than 23 million patients managed in 37 hospitals. Osteoporosis-specific therapies included bisphosphonates, calcitonin, selective estrogen receptor modulators, estrogens and strontium ranelate. Overall, 15.6% ($n = 4272$) of patients received osteoporosis-specific treatment within 90 days of the first fracture diagnosis, which did not increase markedly at 1 year (16.7%, $n = 4554$). At 1 year, treatment rates were 24.5%, 14.2% and 2.3% for hip fracture, vertebral fracture and wrist fracture, respectively. In addition, 35.7% of all fracture patients received calcium or vitamin D within 1 year. Notably, the proportion of patients receiving osteoporosis specific treatment declined from 18.0% in 2010 to 13.2% in 2016.

Information on delivery of secondary fracture prevention in lower-middle and low-income countries in the Asia Pacific region is sparse. In 2021, Arshad et al. evaluated the post-fracture osteoporosis treatment of men and women ($n = 210$) aged 50 years or older who presented with a hip fracture to a university hospital in Karachi, Pakistan, between mid-2015 and mid-2018 [59]. None of the patients were taking osteoporosis-specific treatments on admission or discharge from the hospital.

The secondary fracture prevention care gap in Europe

The secondary fracture prevention care gap is well documented in Europe, with recent studies describing sub-optimal levels of post-fracture care in Austria [60], Denmark [61,62], France [63,64], Germany [65,66], Malta [67], Spain [68] and Sweden [69]. Summaries of the findings of several very large-scale studies follow.

In 2021, Skjodt et al. utilised data from the Danish Health Registries to evaluate the post-fracture osteoporosis treatment of men and women aged 50 years or older who sustained at least one major osteoporotic fracture (MOF) during the period 2005 to 2014 [62]. For each calendar year, a cross-sectional design enabled the generation of cohorts of patients who sustained a first MOF, hip, vertebral, humerus or forearm fracture, which included a total of 236,180 fracture events.

Osteoporosis-specific treatment was defined as bisphosphonates, raloxifene, teriparatide, denosumab or strontium ranelate. Little change was evident during the study period in the treatment gap for the MOF cohorts, which decreased from 85% in 2005 to 79% in 2014. Notably, the 6% decline in the treatment gap was primarily attributable to a higher proportion of fracture patients being on osteoporosis treatment when they sustained their fracture, at 8% in 2005 and 12% in 2014. The proportion of patients being initiated on treatment within 1 year of fracture was just 7% and 9% in 2005 and 2014, respectively.

In 2022, Fardellone et al. utilised data from the French Health Insurance Database to undertake a retrospective cohort study on post-fracture care of men and women ($n = 574,133$) who had a hospital discharge diagnosis of osteoporosis with fracture or a fragility fracture during the period 2011 to 2014 [64]. Osteoporosis-specific treatments included bisphosphonates, denosumab, strontium ranelate, teriparatide and certain selective estrogen receptor modulators. Key findings included:

- Bone mineral density was measured in 5.1% of males and 14.5% of females following the index fracture.
- Within 1 year of the index fracture, 4.1% of males and 14.0% of females received osteoporosis treatment.

In 2022, Freyschuss et al. published results of a real-world effectiveness (RWE) analysis of anti-resorptive treatment in Swedish men and women ($n = 9840$) aged 50 years or older with incident fragility fracture [69]. The virtually complete coverage of electronic medical records in Sweden provides a unique environment in which to conduct RWE analyses. The study was conducted in the Stockholm region and included 1640 cases who received anti-resorptive treatment after sustaining a fracture and 8200 controls who did not receive such treatment. A key finding of the study was that in a region comprising a quarter of the Swedish population less than 10% of patients received anti-resorptive treatment within 1 year after fragility fracture.

The secondary fracture prevention care gap in Latin America

In 2021, Macias-Hernandez et al. described a retrospective chart review of post-fracture osteoporosis management of men and women ($n = 838$) aged over 50 years who presented with fragility fracture to the National Rehabilitation Institute in Mexico City between January 2014 and October 2016 [70]. Overall, on discharge from the hospital, 17.2% of patients were receiving osteoporosis-specific treatment, defined as a bisphosphonate or denosumab, which subsequently declined to 8.4% and 11.4% at 1 year and 3 years after the incident fracture, respectively.

The secondary fracture prevention care gap in North America

Several recent studies have documented the post-fracture osteoporosis treatment care gap in Canada [71] and the United States of America [72–74]. A summary of one study from each country follows.

In 2022, Bell et al. conducted a retrospective chart review of Canadian men and women ($n = 778$) with an index fragility fracture that occurred between 2014 and 2016 [71]. Patients were identified from 76 primary care centres in Canada and followed-up until January 2018. Osteoporosis-specific treatments included bisphosphonates, denosumab, teriparatide, menopausal hormone therapy, calcitonin and selective estrogen receptor modulators. Data were collected on all osteoporosis treatments prescribed within 1 year prior to the index fracture and for the duration of post-fracture follow-up. Key findings included:

- Overall, 27.6% ($n = 215$) continued on a treatment that had been initiated prior to the index fracture, and 28.8% ($n = 224$) were initiated on osteoporosis treatment after their index fracture.
- Overall, 11.6% ($n = 90$) had undergone a FRAX® or CAROC fracture risk assessment within 5 years before their index fracture, and 16.8% ($n = 131$) underwent fracture risk assessment after their index fracture.
- Overall, 11.5% ($n = 86$) of patients with an index fracture sustained a subsequent fracture.

In 2022, Liu et al. undertook a retrospective cohort study of women ($n = 43,193$) who had an outpatient visit in 2011 and had sustained a fracture within 2 years prior to the visit [74]. The Medicare 20% database was used, which comprises a one-fifth random sample of the national Medicare population in the United States of America. Osteoporosis-specific treatments included bisphosphonates, teriparatide, denosumab, calcitonin and raloxifene. Study outcomes included subsequent fracture risk, all-cause and fracture-related healthcare resource utilisation and cost, and osteoporosis medication use in the 5 years after the visit. The rate of osteoporosis treatment decreased from 29.1% in year 1–16.9% by year 5. Notably, when compared to the 10-year fracture probability thresholds designated as very high risk in the 2020 American Association of Clinical Endocrinologists clinical practice guidelines [75], the observed 5-year fracture probability for patients in the MOF and hip fracture cohorts in the current study was markedly higher, at 0.36 vs 0.30 for MOF and 0.17 vs 0.045 for hip fracture, respectively.

The secondary fracture prevention care gap and solutions

The studies described above provide a stark illustration of the breadth and depth of the secondary fracture prevention care gap throughout the world. Subsequent chapters in this issue of *Best Practice Research and Clinical Rheumatology* provide the reader with a comprehensive review of solutions to overcome the care gap. A brief summary of initiatives that have been devised to promote best practice in post-fracture care follows:

- **Global:**

- **Fragility Fracture Network (FFN):** The FFN Clinical [76] and Policy Toolkits [77] provide practical, stepwise advice on establishing systems to implement optimal acute multidisciplinary care, rehabilitation and secondary fracture prevention for people who sustain fragility fractures. The second edition of the textbook on orthogeriatrics provides a comprehensive commentary on the state-of-the-art in all aspects of orthogeriatric care [78].
- **International Osteoporosis Foundation (IOF):** The IOF Capture the Fracture® (CtF) programme was launched with the publication of the 2012 World Osteoporosis Day thematic report [79] and has become an IOF flagship initiative during the ensuing decade. In 2013, the IOF CtF Best Practice Framework [80] set - for the first time - an international benchmark for Fracture Liaison Services (FLS), which defines essential and aspirational elements of service delivery. As of July 2022, 755 FLS from 50 countries feature on the IOF CtF Map of Best Practice [81].

- **Regional:**

- **Asia Pacific Fragility Fracture Alliance (APFFA):** The APFFA-FFN Hip Fracture Registry Toolbox provides a distillation of learning from established registries throughout the world and summarises essential components of national quality improvement (QI) programs for hip fracture care [82]. The Hip Fracture Registry Toolbox is currently available in English, simplified and traditional Chinese, Japanese and Korean. The APFFA Primary Care Physician (PCP) Education Toolkit provides PCPs with practical resources to improve the identification, assessment and ongoing management of individuals at risk of fractures [83].

- **National:**

- **Clinical Standards for FLS:** National clinical standards for FLS are available in Canada [84], Egypt [85], Japan [86], New Zealand [87], Spain [88] and the United Kingdom [89].
- **Secondary fracture prevention registries:** National registries for secondary fracture prevention/FLS have been established in Australia [90], Canada [91], Egypt [85], New Zealand [92], the United Kingdom [93] and the United States of America [94].

Primary fracture prevention

In addition to describing care gaps and solutions relating to secondary fracture prevention, Harvey et al., 's 2017 review [44] also proposed a pragmatic approach to undertake primary fracture prevention in a systematic fashion, "Equipped with knowledge of which medicines induce osteoporosis, which other diseases have osteoporosis as a common comorbidity and online access to absolute fracture risk calculators

to stratify fracture risk in the population, the necessary case-finding tools are now available to develop effective models of care to prevent the first fracture.” The review summarised studies that evaluated rates of assessment, diagnosis and/or treatment to prevent bone loss among individuals treated with glucocorticoids, androgen deprivation therapy and aromatase inhibitors. Summaries of two recent studies follow that sought, at least in part, to identify gaps in primary fracture prevention.

In 2021, McCloskey et al. evaluated the osteoporosis treatment gap in women aged 70 years or older in primary care in 8 European countries [95]. The primary outcome of the study was the proportion of women who were at increased risk of fragility fracture who were not receiving osteoporosis treatment. Increased risk was defined as the presence of at least one of the following three criteria: a history of fracture after the age 50 years, a 10-year probability of fracture above country-specific FRAX® thresholds or a bone mineral density DXA T-score ≤ -2.5 standard deviations below the young adult normal. Approximately 500 patients were enrolled across 18 to 25 sites in each country, with the exception of Switzerland, in which 205 patients were enrolled across 6 sites. Key findings included:

- Among the 3798 enrolled patients, 2077 (55%) met one or more of the criteria for increased risk of fracture, including more than half ($n = 1200$) with a prior fracture history.
- Overall, 804 patients (21.2%) had a recorded diagnosis of osteoporosis, most of whom were at increased fracture risk.
- Across all 8 countries, the treatment gap was 74.6%, ranging from 53% in Ireland to 91% in Germany.

Of the 877 women without a history of fracture, 79% ($n = 693$) were not treated. Accordingly, 71.4% ($n = 343$) of the 1200 women with a history of fracture were also not treated, highlighting the secondary fracture prevention management gap described previously.

In 2022, Cortet et al. described trends in pharmacological management of osteoporosis among French postmenopausal women during the period 2007 to 2016 [96]. Data were analysed from a nationwide claims database comprising a 1 in 97 representative sample of the population insured by the primary French public health insurance schemes, equating to a sample of approximately 600,000 individuals. The outcome that could provide an indication of the primary fracture prevention care gap was the initiation of osteoporosis-specific treatment for women with high-dose use of corticosteroids. Osteoporosis-specific treatments were defined as bisphosphonates, selective estrogen receptor modulators, strontium ranelate, teriparatide or denosumab. The proportion of women with high-dose steroid usage who initiated any osteoporosis-specific treatment increased from 2.9% in 2007 to 8.4% in 2016.

The primary fracture prevention care gap and solutions

In comparison to the plethora of studies that document sub-optimal care after fragility fracture worldwide, there is a paucity of data relating to the delivery of evidence-based primary fracture prevention for individuals at high risk of sustaining a first fragility fracture. As for the secondary fracture prevention section above, subsequent chapters in this issue of *Best Practice Research and Clinical Rheumatology* provide the reader with a comprehensive review of solutions to overcome the care gap. A brief summary of initiatives that have been devised to promote best practices in primary fracture prevention follows.

In 2019, the second edition of the IOF Compendium on Osteoporosis [51] proposed 9 key priorities, of which three related specifically to primary fracture prevention:

- **IOF Compendium Priority 2 - Osteoporosis induced by medicines:** “Where treatments are licensed to prevent osteoporosis induced by medicines, and guidelines have been published to inform best clinical practice, osteoporosis management must become a standard consideration for clinicians when prescribing medicines with bone-wasting side effects.”
- **IOF Compendium Priority 3 - Primary fracture prevention:** “National osteoporosis societies to incorporate messaging regarding self-assessment of fracture risk with FRAX® into public awareness and education initiatives, as advocated in Priority 6. National osteoporosis societies to collaborate with healthcare professional organisations for primary care providers (PCPs) to jointly advocate for PCPs to routinely undertake fracture risk assessment when interacting with patients aged 50 years and over.”

- **IOF Compendium Priority 6 - Priority 6: Public awareness and education:** “National osteoporosis societies, healthcare professional organisations, policymakers and regulators to collaborate to develop impactful public awareness campaigns that will empower consumers to take ownership of their bone health.”

In 2022, Chotiyarnwong and McCloskey et al. published an IOF Epidemiology and Quality of Life Working Group Position Paper on the potential role of population screening for high hip fracture risk against well-established criteria [97,98]. The approach to the development of a screening program advocated by the UK National Steering Committee was employed. The authors concluded “... that evidence supports the proposal that screening for high fracture risk in primary care should strongly be considered for incorporation into many health care systems to reduce the burden of fractures, particularly hip fractures. The key remaining hurdles to overcome are engagement with primary care healthcare professionals and the implementation of systems that facilitate and maintain the screening program.”

In 2021, Chandran et al. published the Asia Pacific Consortium on Osteoporosis (APCO) Framework [99]. The APCO Framework is intended to support national osteoporosis clinical practice guidelines development groups to draft new, or revise existing, guidelines to be consistent with a set of clear, concise, relevant and pragmatic clinical standards. As has been done previously in the development of national clinical standards for FLS [86,87,89], the 16 APCO clinical standards are organised in accordance with so-called “5IQ” approach:

- **Identification:** Statements relating to which individuals should be identified.
- **Investigation:** Description of the types of investigations that will be undertaken.
- **Information:** Description of the types of information to be provided to patients and families.
- **Intervention:** Description of pharmacological interventions and falls prevention.
- **Integration:** Statements on the need for integration between primary and secondary care.
- **Quality:** Description of professional development, audit and peer-review activities.

In addition to addressing secondary fracture prevention in the first APCO clinical standard relating to individuals who sustain fragility fractures, three other APCO clinical standards recommend the identification of the primary fracture prevention population. This includes men and women with common risk factors for osteoporosis, those who take medicines that are associated with bone loss and/or increased fracture risk, and those who have conditions associated with bone loss and/or increased fracture risk. APCO has developed comprehensive modules to support peer-to-peer education relating to each of the 16 clinical standards, and it has recently launched the APCO Bone Health QI Tool Kit, which focuses on seven selected standards from the APCO Framework that are applicable to the clinical setting. All these resources are freely available from the APCO website at www.apcobonehealth.org.

Summary

As noted by the FFN [76] and the IOF [51], during the first half of the 21st century, humankind is en route to a new demographic era. A direct consequence of this dramatic change in the age structure of our global society will be a considerable increase in the number of older people living with chronic diseases, including osteoporosis and the fragility fractures that result from this condition, which is the most common bone disease in humans.

In 2018, the *Global Call to Action on Fragility Fractures* [100] made a case for urgent improvements in care of the acute fracture episode, rehabilitation and secondary fracture prevention for the many millions of people who sustain fragility fractures every year. While implementation of proven models of care that have been shown to improve processes and outcomes for fragility fracture patients has occurred in many countries, there is still much to do. Worldwide, a small minority of patients enjoy best clinical practice delivered by Orthogeriatric Services, Multidisciplinary Rehabilitation Teams and FLS. That must change within this United Nations – World Health Organization “Decade of Healthy Ageing”. There is still work to be done before primary fracture prevention becomes a reality for individuals with well-documented risk factors for sustaining a first fragility fracture. However,

advances in information technology to support case finding, a range of established and emerging diagnostic modalities and readily accessible online fracture risk assessment tools have made widespread implementation of primary fracture prevention measures in reach.

The time has come for care and prevention of fragility fractures to feature in national health and injury prevention strategies for high-, middle- and low-income countries. The subsequent chapters of this issue of *Best Practice Research and Clinical Rheumatology* equip the reader with clinical knowledge to provide best practice for people who sustain, or are at high risk of sustaining fragility fractures, and insights to changing the political priority for osteoporosis and fragility fractures in their countries.

Practice points

- Implementation of a multidisciplinary orthogeriatric approach to the management of individuals who sustain hip and other major fragility fractures enables the delivery of best practice throughout the pre-operative, surgical and post-operative phases of care.
- Analysis of current clinical pathways can help to identify issues, such as reasons for surgical delay, lack of early mobilisation or management of comorbidities.
- Throughout the world, every fragility fracture should be viewed as an opportunity to trigger osteoporosis management and falls prevention to prevent secondary fractures.
- Benchmarking against clinical standards provides a mechanism to critically evaluate performance and identify opportunities for improvement.

Research agenda

Fracture burden:

- In order to provide policymakers in LMICs that lack epidemiological data on the burden of fragility fractures, major studies such as the GBD Study could quantify the proportion of all fractures that occur at the national level among people aged under 50 years and over 50 years in the supplementary information tables provided for peer-reviewed publications.
- Government departments and public and private health insurance organisations should seek to quantify the financial burden of fragility fractures in LMICs using claims data.

Management of the acute episode:

- Evaluation of the impact of Clinical Standards for Orthogeriatric Services and Fragility Fracture Registries to enable benchmarking of acute fracture care.

Secondary and primary fracture prevention:

- Evaluation of the impact of Clinical Standards for FLS and Fragility Fracture Registries to enable benchmarking of secondary preventive care.
- Evaluation of systematic approaches to primary fracture prevention through the development of stratified approaches to case-finding and management, at scale, by primary healthcare professionals.

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