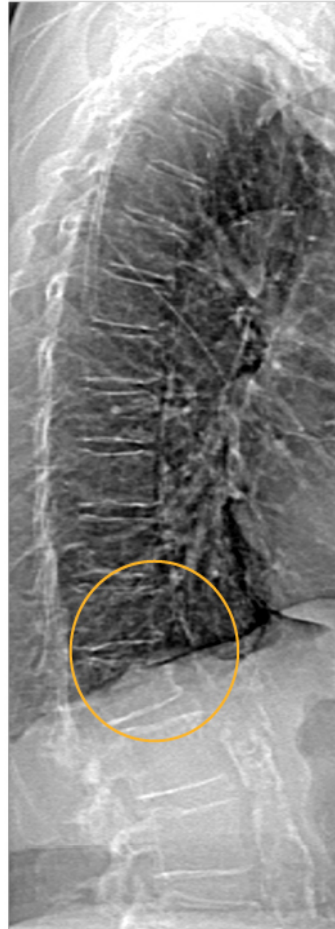


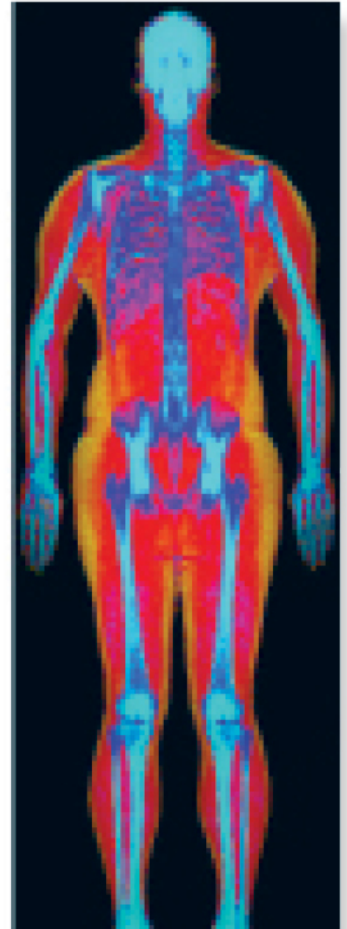
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Title: Global epidemiology of hip fractures: secular trends in incidence rate, post-fracture treatment, and all-cause mortality

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Data Availability Statement

Data sharing policy varies across the data custodians of the study sites. Individual authors for each country may be contacted for the availability of data access. The programming codes for the analysis of data is available upon request.

Abstract

In this international study, we examined the incidence of hip fractures, post-fracture treatment, and all-cause mortality following hip fractures, based on demographics, geography, and calendar year. We used patient-level healthcare data from 19 countries and regions to identify patients aged 50 years and older hospitalized with a hip fracture from 2005 to 2018. The age- and sex-standardized incidence rates of hip fractures, post-hip fracture treatment (defined as the proportion of patients receiving anti-osteoporosis medication with various mechanisms of action [bisphosphonates, denosumab, raloxifene, strontium ranelate, or teriparatide] following a hip fracture), and the all-cause mortality rates after hip fractures were estimated using a standardized protocol and common data model. The number of hip fractures in 2050 was projected based on trends in the incidence and estimated future population demographics. In total, 4,115,046 hip fractures were identified from 20 databases. The reported age- and sex-standardized incidence rates of hip fractures ranged from 95.1 (95% confidence interval [CI] 94.8-95.4) in Brazil to 315.9 (95% CI 314.0-317.7) in Denmark per 100,000 population. Incidence rates decreased over the study period in most countries; however, the estimated total annual number of hip fractures nearly doubled from 2018 to 2050. Within 1 year following a hip fracture, post-hip fracture treatment ranged from 11.5% (95% CI 11.1%-11.9%) in Germany to 50.3% (95% CI 50.0%-50.7%) in the United Kingdom and all-cause mortality rates ranged from 14.4% (95% CI 14.0%-14.8%) in Singapore to 28.3% (95% CI 28.0%-28.6%) in the United Kingdom. Males had lower use of anti-osteoporosis medication than females, higher rates of all-cause mortality, and a larger increase in the projected number of hip fractures by 2050. Substantial variations exist in the global epidemiology of hip fractures and post-fracture outcomes. Our findings inform possible actions to reduce the projected public health burden of

osteoporotic fractures among the ageing population.

Keywords: Osteoporosis, Hip fracture, Epidemiology, Fracture prevention, Mortality

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INTRODUCTION

Hip fracture, a major consequence of osteoporosis, remains a global public health concern because of the large number of fractures (over 10 million cases per year globally⁽¹⁾), which lead to a burden on patients, their families, and healthcare systems.⁽²⁾ Fortunately, many hip fractures and their sequelae are potentially preventable.^(3,4)

The pattern of hip fractures based on demographics, geography, and calendar year may reflect public health activities, healthcare policies, and underlying risk factors in populations. Temporal and geographic variations exist in the incidence rates of hip fracture.⁽⁵⁻⁸⁾ The International Osteoporosis Foundation (IOF) reported that the age-standardized incidence rates in females in Europe ranged from 246 in Romania in 2005-2009 to 677 in Denmark in 2004, per 100,000 population.⁽⁵⁾ Compared with Europe, countries in Asia reported lower age-standardized incidence rates in females, ranging from 133 in Philippines in 2001-2005 to 355 in Taiwan in 1996-2000, per 100,000 population.⁽⁶⁾ Stable or declining trends have been reported in Europe, Oceania, and North America, but increasing trends have been observed in Asia.^(7,8) The heterogeneous incidence rates could reflect genuine differences between populations or heterogeneity in data sources, study periods, and analytical approaches.^(6,7) To address this research gap and to inform clinical care guidelines, it is important to update the trend in incidences geographically using a standardized methodology.

We applied a unified methodology to analyse data in 20 healthcare databases from 19 countries and regions across Oceania, Asia, Western and Northern Europe, and North and South America. The main aims of this study were to examine secular trends from 2005 to 2018 for (i) the incidence rate of hip fracture, (ii) post-hip fracture treatment, defined as the proportion of patients receiving anti-osteoporosis medications (AOMs)

within 1 year following hip fracture, and (iii) the all-cause mortality rate within 1 year following hip fracture. We further aimed to project the number of hip fractures in 2050 based on trends in the incidence in 2005-2018 and the future population demographics.

METHODS

Study design

We analyzed patient-level data obtained from electronic health databases and registries using a standard protocol and a common data model (CDM). The study protocol has been published.⁽⁹⁾ Details of the CDM, data analysis workflow, and modifications made in site-specific analyses are described in the Supplementary Methods.

Data sources

This large-scale global study included databases from Oceania (State of Victoria in Australia, New Zealand), Asia (Hong Kong, Japan, Singapore, South Korea, Taiwan, Thailand), Northern and Western Europe (Denmark, Finland, the United Kingdom [UK], France, Germany, Italy, the Netherlands, Spain), and North and South America (Canada, the United States [US], Brazil). In the US, two large representative databases covering Medicare Fee-for-Service (Medicare), and Medicare Advantage–insured and commercial-plan–insured (Optum) populations were included. In total, 20 healthcare databases were included in the analysis (A brief description of each database is provided in the Supplementary Methods). The characteristics of the databases and data availability have been reported.⁽⁹⁾ Twelve databases covered over 90% of the population in their country or region, while the remaining eight covered 5%-70% of the population (Table1 and STable1).

Study populations

Patients aged ≥ 50 years at the time of hip fracture with data available on sex were identified in each calendar year from 2005 to 2018. In claims or primary care databases, we further selected those who met the following criteria on January 1 of a given calendar year: (i) still enrolled in the database and (ii) had at least a 1-year observation period.

To estimate post-hip fracture treatment and mortality, we excluded patients with a previous diagnosis of hip fracture at least 1 year before 2005. The rationale was that patients with a history of hip fracture are more likely to receive treatment and have a higher risk of death, than those without this history.

Outcome assessment

Hip fracture events were defined using inpatient diagnoses with International Classification of Diseases, Ninth/Tenth Revision codes or equivalent codes used in other diagnostic coding systems for hip fractures. The list of diagnosis codes has been reported.⁽⁹⁾ For primary care databases without inpatient diagnoses, we used general practice diagnoses. Each patient could have had multiple hip fracture events during the study period. These could represent multiple fracture events or complications, and follow-up visits after a single fracture event. To avoid repeat counting of the same episode, we applied a washout period of 180 days, based on clinical expertise, to define a new hip fracture event, (i.e., two hip fracture diagnoses occurring within 180 days of each other were considered a single event). Baseline characteristics including age, sex,

and receipt of AOMs within 1 year before fracture were described. To investigate whether the 180-day washout period would bias the incidence estimate, we used a shorter (90-day) and a longer (365-day) washout period in sensitivity analyses.

Post-hip fracture treatment was defined as the proportion of patients receiving a prescription for or being dispensed an AOM within 1 year of the initial hip fracture. AOM includes bisphosphonates, denosumab, raloxifene, strontium ranelate, or teriparatide; a list of AOMs has been reported elsewhere.⁽⁹⁾ Prescription or dispensing records were classified using World Health Organization Anatomical Therapeutic Chemical classification system codes or equivalent codes from other drug-coding systems, as used in the databases.

All-cause mortality was defined as all deaths occurring within 1 year following an initial hip fracture.

Statistical analysis

The methodologies used to estimate the incidence rates, post-hip fracture treatment, all-cause mortality rates, secular trends, and the projected number of hip fractures are described in the Supplementary Methods. The 2020 United Nations world population estimates (<https://population.un.org/wpp/Download/Standard/Population/>) was used for age- and sex-standardization. All analyses were conducted using SAS (SAS institute, Cary, NC, USA) or R (R Foundation for Statistical Computing, Vienna, Austria) software.

RESULTS

Overall, 4,115,046 hip fractures were identified from 20 databases. Over 70% of fractures occurred in females and more than 40% occurred in people aged ≥ 85 years (Table 1). Fourteen databases reported a median of 10.2% (range 2.3%-17.6%) of the patients being prescribed or dispensed an AOM within 1 year before a hip fracture event.

Hip fracture incidence rate in patients aged 50 years and older

All the databases reported the incidence rates of hip fractures. The highest age- and sex-standardized incidence rate per 100,000 population was observed in Denmark (315.9), followed by Singapore (314.2) and Taiwan (253.4) (Table 2 and SFigure1), and the lowest incidence rate was observed in Brazil (95.1), followed by Thailand (95.2) and the UK (134.0). The age-standardized incidence rates were higher in females than in males in all populations (Table 2). The incidence of hip fractures increased markedly with increasing age (STable2 and Sfigure2).

A decreasing trend (95% confidence Interval for the trend did not cross zero; see Supplementary Methods) was observed in age- and sex-standardized incidence rates over time in 11 databases, an increasing trend in five, and no substantial change in four (Figure 1, STable3 and Table 3). The declines were most prominent in Singapore (average annual percent change [AAPC]: -2.8; see Supplementary Methods), Denmark (AAPC: -2.8), and Hong Kong (AAPC: -2.4), while the largest increase was noted in the Netherlands (AAPC: 2.1). Trends in South Korea and France initially increased and subsequently declined in recent years.

Trends were similar in females and males, but in general, the magnitude of the decline was smaller in males than that in females (sFigure3 and STable4). Trends in the population aged 50-74 years increased in some databases, while the rates in the oldest

population (aged ≥ 75) generally showed a declining trend (STable5, sFigure4 to sFigure6). The trends did not change meaningfully in the sensitivity analyses when a shorter or a longer washout period was used to define a new fracture event (data not shown).

Post-hip fracture treatment in fracture prevention

Information on use of AOMs was available in 15 databases. Over the study period, less than 40% (11.5% to 37.0%) of patients at all sites except the UK (50.3%) received an AOM within 1 year after hip fracture, and a lower proportion of males (5.1% to 38.2%) versus females (15.0% to 54.7%) received AOM (STable6). Trends in post-hip fracture treatment varied across study sites and by years, with an increasing trend noted in four databases (AAPCs: Hong Kong, 12.7; Australia, Victoria, 6.8; Denmark, 4.3; the UK, 2.0), a declining trend in six (AAPCs ranging from -2.3 in Germany to -9.6 in France), and no substantial change in five (Figure 2, STable7 and STable8).

In certain countries, trends shifted over time: post-hip fracture treatment in the UK increased initially (annual percent change [APC] 9.2), but then declined after 2011 (APC -3.3). In contrast, post-hip fracture treatment in New Zealand and the US (as shown in both the Medicare and Optum databases) declined initially, and then plateaued afterward.

Trends were similar in females and males (SFigure7). Data on drug-specific trends were available in 14 databases (SFigure8).

One-year all-cause mortality rate

One-year post-hip fracture all-cause mortality rates were available in 18 databases. However, mortality rates could not be compared among Japan, US Medicare, Italy, and South Korea. The study population in Japan and US Medicare did not cover all persons aged 50 years and older, while Italy and South Korea reported only in-hospital mortality. Excluding these four databases, 1-year all-cause mortality rates over time across the sites ranged from 12.1% to 25.4% in females and from 19.2% to 35.8% in males (STable9). Mortality rates were consistently higher in males than in females throughout the study period (Figure 3 and STable10). Declining trends were noted in seven databases, with AAPCs ranging from -1.4 (Taiwan) to -4.3 (Singapore) (STable11); no substantial changes were observed in other databases. Among the sites, Denmark had the highest age- and sex-standardized mortality rate over the study period (females 13.3%, males 17.2%), whereas the Netherlands had the lowest (females 5.8%, males 8.2%) (STable12 and STable13).

Projection of hip fractures through 2050

All databases contributed to the projected number of hip fractures in 2030, 2040, and 2050 (Table 4 and STable14). Excluding Japan and the US Medicare populations (due to incommensurable populations), the total number of hip fractures in all databases projected in 2050 is nearly double the number in 2018 (1.9-fold increase). The increase in males (2.4-fold increase) was relatively larger than that in females (1.7-fold increase) (Table 4). Only in Denmark fewer hip fractures were projected in 2050 than in 2018.

DISCUSSION

Our study examined secular trends in hip fracture incidence, post-hip fracture treatment, and all-cause mortality following hip fracture from 2005 to 2018 in 19 countries and regions. Age- and sex-standardized hip fracture incidence rates have declined in recent years in most countries and regions. However, as the global population ages, the burden of hip fractures will increase with the number of hip fractures projected to double by 2050. A large post-hip fracture treatment gap in fracture prevention was observed across all countries throughout the study period. The 1-year all-cause mortality rates after hip fractures either declined or stabilized; however, this remains a concern in some countries. The burden of hip fractures, in terms of post-hip fracture treatment and mortality, was more pronounced in males than in females.

Hip fracture incidence

With updated data derived using a standardized methodology, our findings support published global studies showing geographical variations in hip fracture incidence across countries.^(5,6,10) However, we observed that the standardized incidence rates in European countries were generally lower than those reported in the IOF scorecard for osteoporosis in Europe (SCOPE) report.⁽⁵⁾ This discrepancy could be because of those studies in the IOF report being published over a decade ago, while hip fracture incidence rates declined in recent years. In addition, we also compared the risk category of incidence of hip fracture with the previous systematic review of hip fracture incidence⁽¹¹⁾ and found that there were substantial changes (STable15). For example, the UK is now one of the countries/regions having the lowest hip fracture incidence, while the UK was in the top 3 countries/regions with the highest hip fracture incidence in women in the previous systematic review.⁽¹¹⁾

It is noteworthy that the Global Burden Disease (GBD) study⁽¹⁾ reported a global age- and sex-standardized incidence rate of 183 per 100,000 population in 2019 in all ages and a rate of 681 per 100,000 population in aged ≥ 55 in 2019. Compared with our study, the number of hip fracture among people aged ≥ 50 years estimated in the GBD study was higher (Table 16). This discrepancy might be explained by the methodological differences that GBD study estimated the number of hip fracture based on statistical modelling on the data from heterogeneous sources, whereas our study reported the actual number of hip fracture recorded in the healthcare databases.

Most countries showed declining trends in the hip fracture incidence, regardless of sex while the characteristics of mean age of hip fracture have been relatively stable over time (Table 17). Since the causes of hip fracture are multifactorial, the secular trends observed in different countries were results of varying factors in each population. These factors include improved post-hip fracture care, improved lifestyle (such as reduced prevalence of smoking⁽¹²⁾ and alcohol consumption⁽¹³⁾), increasing body mass index^(14,15), and increasing use of calcium and vitamin D.⁽¹⁶⁾ Detailed discussion is provided in Supplementary Discussion.

As most hip fractures occur after a fall, implementing fall prevention programmes could be another key factor underlying the declining trend. A group of European experts has been studying drugs associated with risk of falls to heighten awareness of the need for judicious prescribing of these drugs in older people.⁽¹⁷⁾ Successful efforts taken to prevent falls could in turn reduce the occurrence of hip fractures.

We observed that declining hip fracture trends slowed down or stabilized in recent years in the US and New Zealand. These findings are consistent with research conducted by

Lewiecki et al. who reported a plateau in the age-standardized incidence of hip fractures in the US in 2013-2015.⁽¹⁸⁾ We found that the plateau in the US continued until 2018. One hypothesis for the plateau is the decreased reimbursement of dual-energy x-ray absorptiometry since 2007 in the US, which resulted in fewer diagnoses of osteoporosis and associated prescriptions for AOMs.⁽¹⁸⁾ In New Zealand, the reason for a slowdown in the declining hip fracture trends since 2013 is less clear, but decreased use of AOMs, as shown in our study, may be a contributing factor.

Despite declining trends in hip fracture incidence, the projected number of hip fractures will markedly increase by 2050, largely due to the aging of the population. As reported by the WHO,⁽¹⁹⁾ the global population aged ≥ 85 will increase 4.5-fold from 2010 to 2050. Thus, the current declines in hip fracture incidence we identified in most countries may be insufficient to offset the impact of the aging population and the attendant high risk of hip fractures in the older population. Larger or collaborative efforts focused on hip fracture prevention, such as the Capture the Fracture® global program⁽²⁰⁾ led by the IOF, and community screening of high-risk people using risk assessment tools,⁽²¹⁾ are needed to address the growing burden of hip fractures and osteoporosis across the globe.

Post-hip fracture treatment gap in fracture prevention

A gap in the post-hip fracture treatment needed to prevent future fractures has been widely reported in many countries.^(22,23) Studies in the UK and the US have indicated that use of AOMs has declined since the 2010s.^(24,25) Our study further shows that the treatment rate is still lagging. Notably, if we only look at the patients who were not on treatment before hip fracture, the treatment gap is even larger (STable18).

The large treatment gap in some countries may stem from concerns about adverse events associated with anti-resorptive therapies, including osteonecrosis of the jaw and atypical femur fracture.⁽²⁵⁾ The US Food and Drug Administration issued a safety communication for bisphosphonates following a report on atypical femoral fractures in 2010.⁽²⁶⁾ Although these adverse effects are uncommon, concerns among patients and clinicians could contribute to a reluctance in prioritising treatment to reduce the fracture risk. These reactions may be exacerbated by media reports on the safety of bisphosphonates,⁽²⁵⁾ although comparisons of treatment risks and benefits clearly favours treatment.⁽²⁷⁾

Apart from concerns about adverse drug effects, the apparent decline in AOM use in some countries may stem from an increased use of parenteral bisphosphonate therapies, such as intravenous zoledronic acid, and subcutaneous denosumab. These drugs are administered in the hospital or clinic setting which would not be captured in the databases of some countries (such as in New Zealand and the UK). At the same time, some patients, particularly those with frailty and poor cognitive function, may not be prescribed AOMs because of the difficulty in taking oral bisphosphonates correctly (i.e. maintaining an upright position for at least 30 minutes after ingestion to avoid gastroesophageal irritation) or a perceived limited life expectancy. Notably, even the patients are prescribed AOMs, they may refuse to take them.

Several international societies have called for increased urgency in addressing the treatment gap.⁽²⁸⁾ Some countries have attempted to reduce or close this gap by improving post-hip fracture care and FLS. For example, the UK is leading the way to establish an FLS Database to monitor the national audit of secondary fracture prevention. The role of general practitioners, endocrinologists or other specialists is influential when patients decide whether or not to initiate treatment. Thus, clinical

education programmes to enhance the communication with patients about treatment options and their associated risks and benefits may reduce the treatment gap.

All-cause mortality after hip fractures

A systematic review of the literature from 36 countries (most published between 2015 and 2017) reported a median 1-year mortality rate of 22.8% after a hip fracture.⁽²⁹⁾ Our study had a similar result of 22.4% median 1-year mortality rate across the included countries. Several countries showed a downward trend that could be attributed to several factors. First, advances in post-hip fracture care could have a positive impact on mortality. FLS programmes have been shown to reduce post-hip fracture mortality and subsequent fracture rates.⁽³⁰⁾ The IOF has published guidance to assess the performance of and improve the quality of FLS at the local level.⁽³¹⁾ Second, some countries and regions, such as Australia, Denmark and Hong Kong, have implemented quality indicators for post-hip fracture care such as early surgery and preoperative optimisation. Fulfilment of these quality indicators has been associated with reduced post-hip fracture mortality. Despite declines in all-cause mortality, the rates remain a concern in some countries. For instance, New Zealand and the UK have a significant post-hip fracture mortality burden, with one in four females and one in three males dying within 1 year. Thus, focused efforts to improve fracture prevention and post-hip fracture care are warranted.

Preventing hip fractures in males: an unmet need

Our study found that approximately 30% of all hip fractures occurred in males, which

is consistent with that reported in the literature.⁽³²⁾ However, prevention, diagnosis, and treatment in males have been overlooked for years. In general, postmenopausal women are treated for primary prevention of osteoporotic fractures, while males are treated for secondary prevention when they had a fracture. In our study, we observed a sex disparity in post-hip fracture treatment, with males having 29.8%-66.5% lower use of AOMs than females. Compared with females, males have a poorer prognosis after hip fracture, including the higher mortality shown in this study, and greater loss of independence.⁽³³⁾ In addition, our study suggests that by 2050 males may have a larger increase in the projected number of hip fractures than females. This is likely explained by the smaller decline in the incidence rate in males than in females, and a larger treatment gap in males. Another contributing factor could be the larger increase in life expectancy by 2050 in males than in females as estimated by the United Nations.⁽³⁴⁾ By 2050, estimated life expectancy in males will likely surpass 75 years, an age at which our study showed a high risk of hip fracture. Thus, an increasing number of males is expected to experience hip fracture, and more attention should be paid to post-hip fracture care in males.

Our study has several limitations. First, changes in coding and recording of fractures in the databases over time might influence trends within a study site. However, our findings were consistent with the published literature (where available), and most study sites showed constantly declining trends, suggesting that any coding changes had a minimal impact on the trend analysis. Second, for higher accuracy in identifying hip fracture cases, the study did not include hip fractures occurring outside the hospital, including those occurring in nursing homes without hospital admission. Thus, our incidence and mortality rates may be slightly underestimated. Third, our findings are based on a descriptive analysis of retrospective datasets, and the reasons for the

observed trends would require further in-depth research. Fourth, site-specific limitations stemming from the characteristics of the databases are discussed in the Supplementary Methods. Fifth, there are several factors affecting the hip fracture incidence, such as the use of fracture liaison service, lifestyle, diet, comorbidities, and societal changes in the population. However, it is difficult to evaluate all these factors on hip fracture incidence in one single study and it may need different data sources which include lifestyle information. Future studies are warranted to examine how these factors may influence the trends of hip fracture incidence. Sixth, since the COVID-19 pandemic started in 2019 and several study sites did not have data from 2019 onward due to lags in administrative data collection or data availability, the current study only evaluated the hip fracture epidemiology up to 2018. There is a possibility that undertreatment during the pandemic could result in surge of initial hip fractures. Future study evaluating the impact of COVID-19 pandemic on the hip fracture incidence is warranted. Finally, there could be some countries and regions having fewer hip fractures in the future despite a significant increase in the population aged 50 years or above, in addition to Denmark. However, we expect that a majority of the countries and regions will still have increased numbers of hip fracture in the future, if the incidence of hip fracture is not further reduced.

The main strengths of our study are its direct access to patient-level data and use of a standardized methodology for data analysis. Another strength is inclusion of a large number of countries and regions across Asia, Oceania, Europe, and the Americas. Most study sites provided more than 10 years of nationwide data to inform secular trends. Importantly, we have been able to establish a global routine clinical care data platform to facilitate collaboration across multiple institutions for future epidemiological studies.

CONCLUSION

This study provides an update on the global epidemiology of hip fractures. Globally, hip fractures remain an important public health condition with severe morbidity and mortality. The declining incidence of hip fractures in many countries in recent years is insufficient to offset the impact of the growing aging population. Consequently, the number of hip fractures is projected to nearly double over the next 20-30 years. Interventions are needed to prevent hip fractures, improve the treatment gap, and provide post-hip fracture care to achieve better patient outcomes and fewer future hip fractures, particularly in males.

Ethics statement

Each participating site adhered to the relevant local ethics and regulatory framework for study approval. The status of ethics approval at each site was provided in the previous publication.⁽⁹⁾

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Contributors

C-WS co-developed the study, analyzed the data, and draft the manuscript. T-CL, CB, JLL, JM, JOK, and TT co-developed the study, visualized the data, and critically

reviewed and commented on the manuscript. SB, JSB, KB, PB-L, BDB, AHYC, MC, CC, MdR, CYD, CD-P, GG, SH, JI, HEJ, DPK, KK, EC-CL, EML, JuL, JnL, MMdA, NO, ABP, AP-U, DP-A, SXQ, J-YS, HTS, KBT, A-MT, KMCV, GH-MW, SW, and SJW analyzed the data, and critically reviewed and commented on the manuscript. C-LC and ICKW are the principal investigators of this study and academic contributors and take responsibility for its integrity of the study; they co-developed the protocol and critically reviewed and commented on the manuscript.

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Tables

Table 1: Age and sex distribution of hip fractures during the study period in people aged 50 years and older

Site	Database coverage	Study period	Total number of hip fractures during the study period, frequency and percentage, presented as “n (%)”										
			Overall	Female	Male	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Oceania													
Australia, Victoria	26%, 100% ^a	2014-2017	24,938	17,207 (69.0)	7,731 (31.0)	423 (1.7)	660 (2.6)	916 (3.7)	1,377 (5.5)	1,995 (8.0)	3,128 (12.5)	4,795 (19.2)	11,644 (46.7)
New Zealand	98%	2008-2018	41,963	29,143 (69.4)	12,820 (30.6)	623 (1.5)	951 (2.3)	1,436 (3.4)	2,203 (5.2)	3,378 (8.0)	5,338 (12.7)	8,597 (20.5)	19,437 (46.3)
Asia													
Hong Kong	90%	2005-2018	85,701	58,172 (67.9)	27,529 (32.1)	924 (1.1)	1,596 (1.9)	2,413 (2.8)	3,760 (4.4)	6,919 (8.1)	13,079 (15.3)	19,857 (23.2)	37,153 (43.4)
Japan	6%	2013-2018	1,457	949 (65.1)	508 (34.9)	234 (16.1)	357 (24.5)	325 (22.3)	255 (17.5)	286 (19.6)
Singapore	100%	2005-2018	38,902	26,560 (68.3)	12,342 (31.7)	703 (1.8)	1,203 (3.1)	2,095 (5.4)	3,396 (8.7)	5,113 (13.1)	7,285 (18.7)	7,881 (20.3)	11,226 (28.9)
South Korea	97%	2008-2018	335,385	240,671 (71.8)	94,714 (28.2)	85,49 (2.5)	12,358 (3.7)	15,055 (4.5)	23,007 (6.9)	42,864 (12.8)	67,720 (20.2)	76,112 (22.7)	89,720 (26.8)
Taiwan	99%	2005-2018	263,249	161,442 (61.3)	101,807 (38.7)	7,644 (2.9)	11,059 (4.2)	14,268 (5.4)	19,698 (7.5)	30,165 (11.5)	47,550 (18.1)	57,735 (21.9)	75,130 (28.5)
Thailand	67%	2016-2018	53,946	38,272 (70.9)	15,674 (29.1)	2,461 (4.6)	3,318 (6.2)	4,376 (8.1)	6,053 (11.2)	7,027 (13.0)	9,368 (17.4)	10,243 (19.0)	11,100 (20.6)
Northern and Western Europe													
Denmark	100%	2005-2018	119,868	82,683 (69.0)	37,185 (31.0)	2,247 (1.9)	3,882 (3.2)	5,948 (5.0)	8,387 (7.0)	11,802 (9.8)	16,645 (13.9)	22,849 (19.1)	48,108 (40.1)
Finland	100%	2005-2018	94,299	64,510 (68.4)	29,789 (31.6)	1,575 (1.7)	2,932 (3.1)	4,372 (4.6)	5,841 (6.2)	8,308 (8.8)	13,240 (14.0)	19,772 (21.0)	38,259 (40.6)
UK	24%	2005-	116,044	84,084	31,960	1,447	2,312	3,719	5,725	9,352	15,749	24,822	52,918

Site	Database coverage	Study period	Total number of hip fractures during the study period, frequency and percentage, presented as “n (%)”										
			Overall	Female	Male	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
		2018		(72.5)	(27.5)	(1.2)	(2.0)	(3.2)	(4.9)	(8.1)	(13.6)	(21.4)	(45.6)
France	99% ^b	2007-2018	113,860	85,192 (74.8)	28,668 (25.2)	1,688 (1.5)	2,814 (2.5)	3,783 (3.3)	4,935 (4.3)	7,040 (6.2)	12,348 (10.8)	22,297 (19.6)	58,955 (51.8)
Germany	5%	2012-2018	25,272	15,984 (63.2)	9,288 (36.8)	655 (2.6)	1,002 (4.0)	1,345 (5.3)	1,678 (6.6)	2,533 (10.0)	4,720 (18.7)	5,332 (21.1)	8,007 (31.7)
Italy	100%	2011-2018	776,138	577,976 (74.5)	198,162 (25.5)	9,029 (1.2)	13,952 (1.8)	20,592 (2.7)	33,755 (4.3)	57,159 (7.4)	105,952 (13.7)	169,719 (21.9)	365,980 (47.2)
The Netherlands	10%	2009-2018	8,654	5,971 (69.0)	2,683 (31.0)	289 (3.3)	396 (4.6)	523 (6.0)	734 (8.5)	928 (10.7)	1,174 (13.6)	1,553 (17.9)	3,057 (35.3)
Spain	99%	2005-2018	674,675	502,424 (74.5)	172,251 (25.5)	7,810 (1.2)	11,046 (1.6)	15,400 (2.3)	23,854 (3.5)	44,485 (6.6)	88,753 (13.2)	156,325 (23.2)	327,002 (48.5)
North and South America													
Canada	97%	2005-2016	323,530	230,010 (71.1)	93,540 (28.9)	5,710 (1.8)	9,460 (2.9)	13,280 (4.1)	18,040 (5.6)	25,790 (8.0)	40,860 (12.6)	63,300 (19.6)	147,190 (45.5)
US (Medicare)	Approx. 65% ^c	2008-2018	381,588	276,855 (72.6)	104,733 (27.4)	17,704 (4.6)	35,539 (9.3)	53,905 (14.1)	80,073 (21.0)	194,367 (50.9)
US (Optum)	30%	2009-2018	172,198	122,556 (71.2)	49,642 (28.8)	2,034 (1.2)	3,832 (2.2)	6,025 (3.5)	10,437 (6.1)	17,977 (10.4)	24,326 (14.1)	..	107,567 (62.5)*
Brazil	70%	2008-2018	463,359	301,551 (65.1)	161,808 (34.9)	22,206 (4.8)	29,841 (6.4)	35,554 (7.7)	43,264 (9.3)	55,653 (12.0)	73,381 (15.8)	82,203 (17.7)	121,257 (26.2)

* Aged 80 years and older. UK=United Kingdom; US=United States.

^a Population coverage is 26%, and the state coverage is 100%

^b The data used for this study represent a 10% random sample

^c Medicare covers more than 90% of the population aged 65 or above; approximately 70% of the beneficiaries are in the Medicare Fee-for-Service program. The data used for this study represent a 20% random sample of Medicare FFS, which includes FFS coverage of Medicare Parts A, B, and D.

Table 2: Age- and sex-standardized[^] incidence rates of hip fractures during the study period in people aged 50 years and older

Site	Study period	Standardized incidence rate per 100000 population (95% CI)			Female to male ratio
		Overall	Female	Male	
Oceania					
Australia, Victoria	2014-2017	224.2 (221.3, 227.1)	297.3 (292.7, 301.9)	144.1 (140.8, 147.6)	2.1
New Zealand	2008-2018	189.8 (187.9, 191.6)	252.4 (249.5, 255.4)	121.1 (119.0, 123.3)	2.1
Asia					
Hong Kong	2005-2018	190.4 (189.1, 191.7)	245.5 (243.4, 247.5)	130.2 (128.6, 131.7)	1.9
Japan*	2013-2018	54.8 (51.6, 58.2)	79.4 (73.8, 85.3)	29.1 (26.1, 32.4)	2.7
Singapore	2005-2018	314.2 (311.0, 317.4)	418.1 (412.9, 423.3)	200.4 (196.8, 204.1)	2.1
South Korea	2008-2018	189.5 (188.8, 190.1)	244.1 (243.2, 245.1)	129.6 (128.8, 130.5)	1.9
Taiwan	2005-2018	253.4 (252.4, 254.4)	319.4 (317.8, 320.9)	181.1 (180.0, 182.3)	1.8
Thailand	2016-2018	95.2 (94.4, 96.0)	128.2 (126.9, 129.5)	59.2 (58.2, 60.1)	2.2
Northern and Western Europe					
Denmark	2005-2018	315.9 (314.0, 317.7)	401.9 (399.1, 404.7)	221.6 (219.3, 223.9)	1.8
Finland	2005-2018	226.5 (225.0, 228.0)	271.3 (269.1, 273.5)	177.5 (175.5, 179.6)	1.5
UK	2005-2018	134.0 (133.2, 134.9)	183.3 (182.0, 184.6)	80.0 (79.1, 81.0)	2.3
France	2007-2018	239.4 (237.9, 240.9)	318.4 (316.1, 320.7)	152.9 (151.1, 154.8)	2.1
Germany	2012-2018	178.5 (176.2, 180.8)	224.0 (220.4, 227.5)	128.7 (126.0, 131.4)	1.7
Italy	2011-2018	227.2 (226.7, 227.7)	309.6 (308.8, 310.5)	136.9 (136.3, 137.6)	2.3
The Netherlands	2009-2018	147.0 (144.5, 150.9)	192.0 (187.0, 197.1)	99.1 (95.3, 103.1)	1.9
Spain	2005-2018	176.8 (176.4, 177.3)	240.2 (239.5, 240.9)	107.4 (106.9, 108.0)	2.2
North and South America					
Canada	2005-2016	157.8 (157.2, 158.3)	209.6 (208.7, 210.5)	100.9 (100.3, 101.6)	2.1
US (Medicare)*	2008-2018	487.9 (486.2, 489.6)	624.0 (621.4, 626.5)	321.0 (318.8, 323.1)	1.9
US (Optum)	2009-2018	237.3 (236.1, 238.5)	315.8 (313.9, 317.7)	151.2 (149.8, 152.7)	2.1
Brazil	2008-2018	95.1 (94.8, 95.4)	116.9 (116.5, 117.3)	71.2 (70.9, 71.5)	1.6

[^]The 2020 United Nations world population estimates was used for standardization

*The population in Japan included people aged <75 years only; Medicare database in the US included people aged >65 years only.

CI=confidence interval; UK=United Kingdom; US=United States.

Table 3: Secular trends for age- and sex-standardized incidence rates of hip fractures estimated using segmented linear regression.

Site	Year	AAPC (95% CI)	Year	APC (95% CI)
Oceania				
Australia, Victoria	2014-2017	0.17 (-1.08, 1.44)
New Zealand	2008-2018	-0.86 (-1.15, -0.57)	2008-2012	-2.25 (-3.27, -1.22)
			2013-2018	0.19 (-0.61, 0.98)
Asia				
Hong Kong	2005-2018	-2.43 (-2.73, -2.14)
Japan	2013-2018	-2.30 (-6.24, 1.80)
Singapore	2005-2018	-2.84 (-3.30, -2.38)
South Korea	2008-2018	1.24 (1.01, 1.48)	2008-2011	7.16 (5.91, 8.41)
			2012-2018	-1.59 (-2.08, -1.11)
Taiwan	2005-2018	-2.10 (-2.33, -1.87)
Thailand	2016-2018	1.17 (-9.20, 12.72)
Northern and Western Europe				
Denmark	2005-2018	-2.77 (-3.02, -2.52)
Finland	2005-2018	-1.50 (-1.75, -1.24)
UK	2005-2018	-1.38 (-1.70, -1.06)
France	2007-2018	1.02 (0.41, 1.63)	2007-2009	9.14 (3.80, 14.75)
			2010-2018	-1.65 (-2.55, -0.75)
Germany	2012-2018	0.77 (0.14, 1.40)
Italy	2011-2018	-1.48 (-2.27, -0.67)
The Netherlands	2009-2018	2.07 (0.18, 4.00)
Spain	2005-2018	-1.18 (-1.38, -0.97)
North and South America				
Canada	2005-2016	-0.90 (-1.25, -0.55)
US (Medicare)	2008-2018	-1.18 (-1.45, -0.91)	2008-2012	-2.66 (-3.61, -1.70)
			2013-2018	-0.03 (-0.77, 0.71)
US (Optum)	2009-2018	-0.25 (-0.72, 0.22)
Brazil	2008-2018	0.67 (0.12, 1.22)

AAPC=average annual percent change; APC=annual percent change; CI=confidence interval; UK=United Kingdom; US=United States.

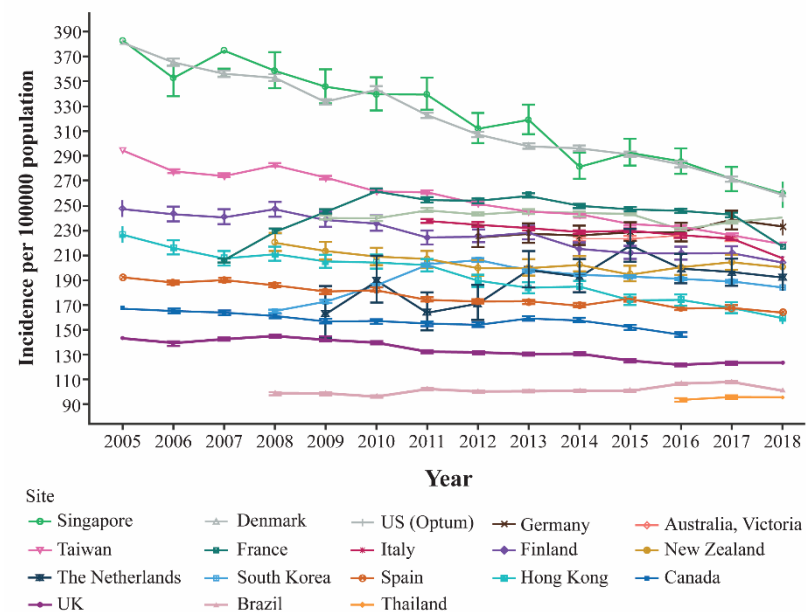
Table 4: Projection of hip fractures in 2050 in people aged 50 years and older

Site*	2018 (or the most recent year [†])			2050			Fold change (2050/2018)		
	All	Female	Male	All	Female	Male	All	Female	Male
Oceania									
Australia	25,219	16,757	8,462	108,260	35,585	72,675	4.29	2.12	8.59
New Zealand	4,215	2,870	1,345	9,305	5,636	3,669	2.21	1.96	2.73
Asia									
Hong Kong	6,600	4,398	2,202	9,820	6,947	2,873	1.49	1.58	1.30
Singapore	3,146	2,092	1,054	8,196	4,911	3,285	2.61	2.35	3.12
South Korea	38,679	27,971	10,708	102,257	83,843	18,414	2.64	3.00	1.72
Taiwan	20,629	13,176	7,453	34,372	20,219	14,153	1.67	1.53	1.90
Thailand	21,478	15,055	6,423	96,246	56,284	39,962	4.48	3.74	6.22
Northern and Western Europe									
Denmark	7,800	5,176	2,624	3,960	1,695	2,265	0.51	0.33	0.86
Finland	7,083	4,768	2,315	7,929	5,069	2,860	1.12	1.06	1.24
UK	45,781	32,001	13,780	54,147	35,010	19,137	1.18	1.09	1.39
France	97,377	72,187	25,190	119,702	87,985	31,717	1.23	1.22	1.26
Germany	126,329	85,896	40,433	222,708	115,523	107,185	1.76	1.34	2.65
Italy	93,636	69,566	24,070	97,710	71,679	26,031	1.04	1.03	1.08
The Netherlands	17,177	11,739	5,438	67,346	35,096	32,250	3.92	2.99	5.93
Spain	51,936	37,529	14,407	78,520	49,983	28,537	1.51	1.33	1.98
North and South America									
Canada	28,030	19,350	8,680	47,486	31,431	16,055	1.69	1.62	1.85
US (Optum)	337,348	232,635	104,713	605,966	370,679	235,287	1.80	1.59	2.25
Brazil	50,593	32,903	17,690	199,148	131,386	67,762	3.94	3.99	3.83
All sites	983,056	686,069	296,987	1,873,078	1,148,961	724,117	1.91	1.67	2.44

*The projection of hip fractures in Japan (people aged <75 years only) and the US Medicare database (people aged >65 years only) is shown in STable8. †The most recent year is 2017 in Australia and 2016 in Canada. UK=United Kingdom; US=United States.

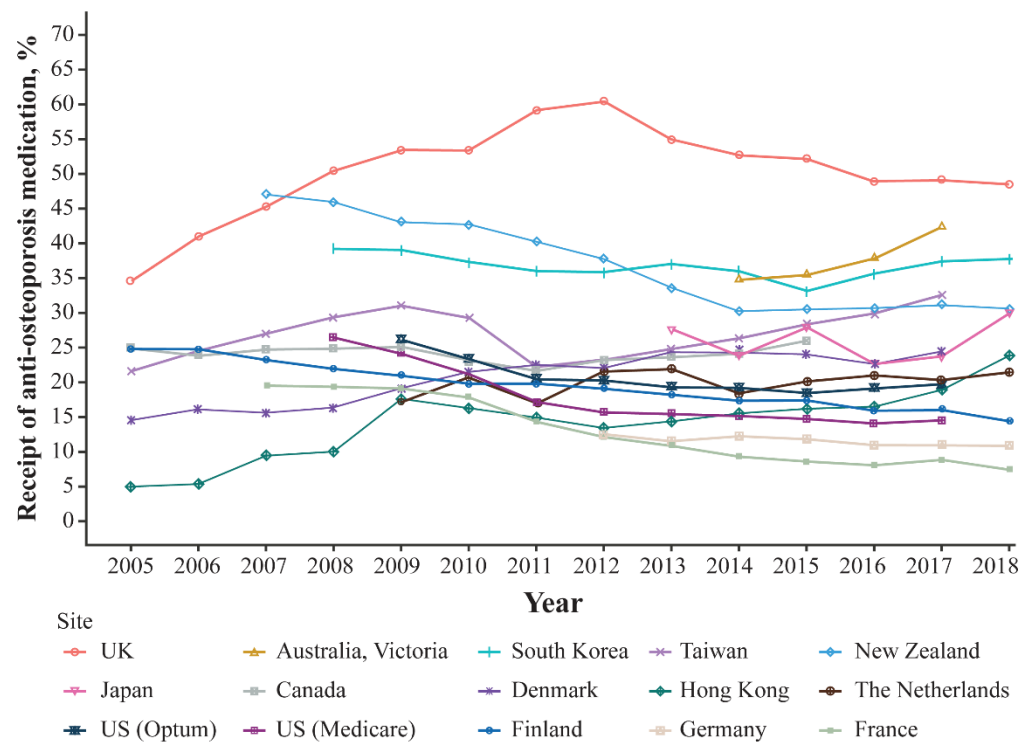
Figures

Figure 1: Age- and sex-standardized incidence rates of hip fractures from 2005 to 2018 among people aged 50 years and older



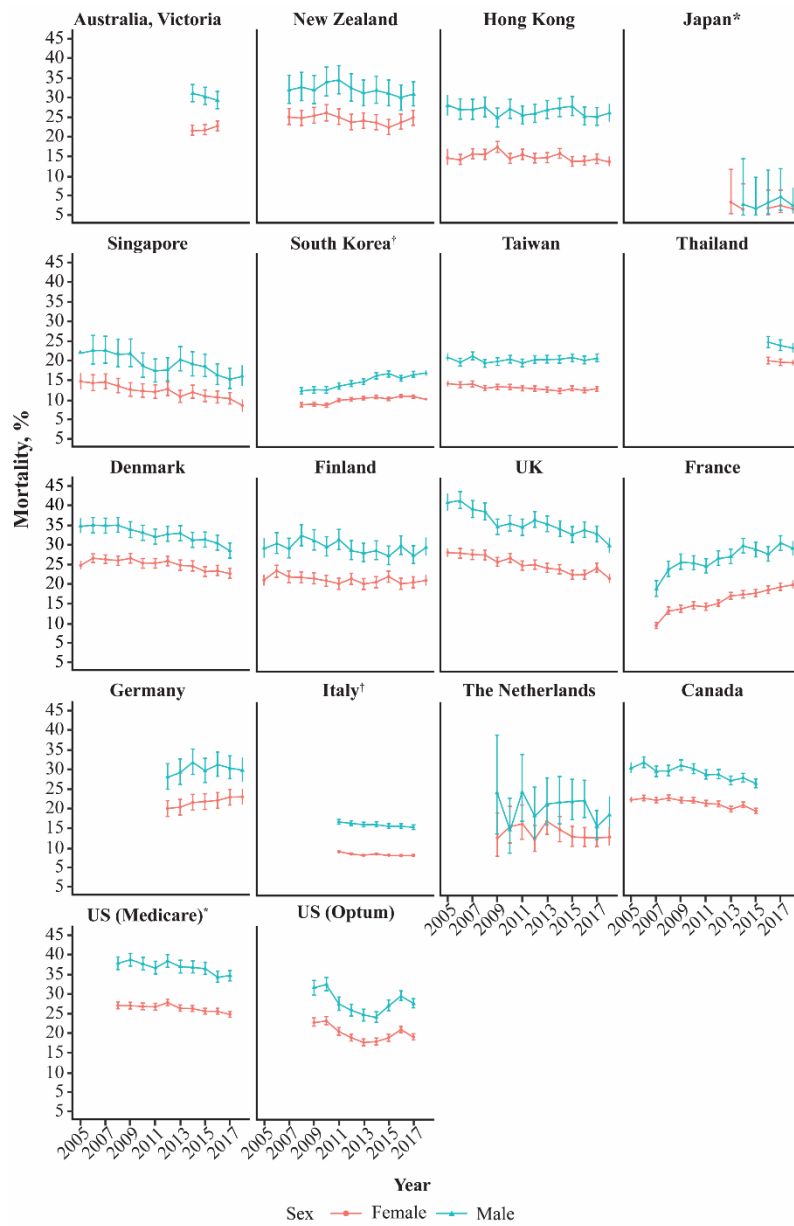
The 2020 United Nations world population estimates was used for standardization. Japan and US (Medicare) data are not shown because the age groups of the study population in the two databases were not comparable. The legend is ordered by the incidence (highest to lowest) in 2018 or the most recent year available in the database. UK=United Kingdom; US=United States.

Figure 2: Receipt of anti-osteoporosis medication within 1 year after a hip fracture from 2005 to 2018



The legend is ordered by the proportion of patients receiving treatment (largest to smallest) in 2018 or the most recent year available in the database. UK=United Kingdom; US=United States.

Figure 3: All-cause mortality rate within 1 year after a hip fracture from 2005 to 2018, stratified by sex



*The population in Japan included people aged <75 years only; the Medicare database in the US included people aged >65 years only. †South Korea and Italy reported in-hospital all-cause mortality. UK=United Kingdom; US=United States.