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Global Health Effects of Osteopenia and Osteoporosis, 1990–2021

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ABSTRACT

Background and Aims: Osteopenia and osteoporosis present a significant global public health challenge. This study analyses the global, regional, and national burden of disease attributable to low bone mineral density, including both osteopenia and osteoporosis, across 204 countries and territories from 1990 to 2021.

Methods: Data were used to quantify deaths and disability-adjusted life years (DALYs) linked to osteopenia and osteoporosis.

Results: In 2021, osteopenia and osteoporosis were responsible for 459,661 deaths and 17.3 million DALYs globally, with population attributable fractions of 0.7% and 0.6%, respectively. The global age-standardized death rate was 5.7 per 100,000, while the age-standardized DALY rate was 205 per 100,000, reflecting declines of 9.4% and 14.8%, respectively, from 1990 to 2021. The highest age-standardized DALY rates were seen in Saudi Arabia and India, while the lowest were in Azerbaijan and Jamaica. Significant increases in DALY rates were noted in Lesotho and the Netherlands, whereas the largest decreases occurred in Hungary and Taiwan. DALY rates for osteopenia and osteoporosis were highest in the 95+ age group for both sexes, with females generally experiencing higher rates, particularly in older age groups. The main contributing causes varied by age, with falls being the leading cause in the 80–84 age group, road injuries in the 40–44 age group, and exposure to mechanical forces in the 50–54 age group. A negative correlation was observed between regional socio-demographic index and age-standardized DALY rates from 1990 to 2021.

Conclusion: Addressing the global burden of osteopenia and osteoporosis requires targeted interventions, further research, and efforts to reduce regional disparities and improve healthcare access.

Abbreviations: ASDR, age-standardized death rate; BMD, bone mineral density; DALYs, disability-adjusted life years; DXA, dual-energy X-ray absorptiometry; GBD, global burden of disease; LBMD, low bone mineral density; MET, metabolic equivalent task; MR-BRT, meta-regression bayesian, regularized, trimmed; NHANES, national health and nutrition examination survey; PAF, population attributable fraction; SDI, socio-demographic index; TMREL, theoretical minimum risk exposure level; UIs, uncertainty intervals; YLLs, years of life lost.

1 | Introduction

Bones are dynamic structures that are maintained through a delicate balance between resorption and formation, processes mediated by osteoclasts and osteoblasts. Disruption of this balance can lead to abnormal changes in mineral density, resulting in pathological conditions [1]. Low bone mineral density (LBMD), encompassing osteopenia and osteoporosis, is characterized by reduced bone mass due to impaired bone formation and/or increased resorption. These conditions affect millions worldwide, contributing significantly to the global health burden by increasing morbidity, disability, and mortality, as well as imposing substantial healthcare and socioeconomic costs [2, 3].

LBMD encompasses a range of conditions involving chronic reductions in bone density, which compromise bone strength and heighten susceptibility to fractures. It can be classified into two categories: osteopenia and osteoporosis, distinguished by standard deviation (T-score) values from the peak bone mineral density of healthy young adults. Osteopenia, the milder form, is characterised by a T-score between −1.0 and −2.5, while osteoporosis, the more severe condition, is defined by a T-score of −2.5 or lower [4, 5].

The etiology of osteopenia and osteoporosis is complex and multifactorial, involving genetic predisposition, hormonal changes, nutritional deficiencies, and lifestyle factors such as physical inactivity and smoking. Although these conditions primarily affect postmenopausal women and older adults, younger individuals with eating disorders, chronic diseases, or those undergoing prolonged medication use are also at considerable risk [6–8]. Risk factors differ across life stages and by sex. For example, declining estrogen levels in menopausal women and reduced testosterone levels in ageing men play critical roles in disease progression [6, 9]. Additional contributors include deficiencies in calcium and vitamin D, smoking, a sedentary lifestyle, excessive alcohol consumption, and systemic disorders such as chronic kidney disease [10, 11].

Epidemiological studies, including the Global Burden of Disease (GBD) 2019 study, estimate that osteopenia and osteoporosis were responsible for 16.6 million disability adjusted life years (DALYs) and 438,000 deaths globally, with substantial regional and national variations. These differences may reflect disparities in economic development, healthcare access, dietary patterns, and physical activity practices [12].

Osteopenia and osteoporosis markedly increase the risk of fracture, particularly among postmenopausal women, among whom a reduction in bone density is a key predictor of these injuries [13]. It has been reported that around 50% of all postmenopausal women will experience one or more fractures in their lifetime [14]. Of the 8.9 million fractures attributed to osteoporosis annually, 20%–25% occur in men [15]. Fractures are significant contributors to disability, and individuals with osteopenia or osteoporosis are especially prone to recurrent fractures; an adult who experiences one fracture is 50%–100% more likely to sustain another [16]. The insidious progression of these conditions often delays diagnosis and intervention, further exacerbating bone loss and fracture risk [17].

Management of osteopenia and osteoporosis involves both pharmacological and nonpharmacological strategies. Medications such as denosumab, a monoclonal antibody, have demonstrated efficacy in inhibiting bone resorption, particularly in postmenopausal women [18]. Nonpharmacological approaches focus on lifestyle modifications, including dietary improvements, weight-bearing exercises, and fall prevention. Early interventions, particularly in younger populations, can significantly mitigate future risks. However, there remain gaps in addressing the needs of specific groups, such as premenopausal women and individuals with secondary osteoporosis resulting from chronic illness or prolonged medication use [19].

Osteopenia and osteoporosis present a significant global public health challenge, acting as major risk factors for fractures, including those that can be life-threatening, such as hip and vertebral fractures. Addressing these issues requires up-to-date insights into their biological and epidemiological aspects. This study provides an updated overview of the epidemiology of osteopenia and osteoporosis, utilizing GBD 2021 data. The research focuses on deaths and DALYs, examining global and regional trends from 1990 to 2021, as well as associations with the socio-demographic index (SDI).

2 | Methods

2.1 | Overview

The GBD project, led by the Institute for Health Metrics and Evaluation (IHME), assesses the burden of diseases and injuries worldwide. GBD 2021 included 88 risk factors across 204 countries and territories from 1990 to 2021. The Comparative Risk Assessment approach was applied to estimate the burden of disease attributable to osteopenia and osteoporosis. Full methodological details, including model evaluation and selection criteria, are reported in the main GBD 2021 risk factors paper and its supporting materials [20].

2.2 | Case Definition and Data Sources

Bone mineral density (BMD) is a continuous variable that is assessed using dual-energy X-ray absorptiometry (DXA) at the femoral neck (FN), with results expressed in grams per square centimeter (g/cm^2) after adjustment for densitometer brand (sBMD). Low BMD is defined as the deviation of a population's BMD from the 99th percentile of a reference population of the same age and sex, known as the theoretical minimum-risk exposure level (TMREL). The burden associated with low BMD is estimated for those aged 20 and older [20].

A systematic review was initially conducted for GBD 2010 and subsequently re-run during GBD 2013 and 2015, utilizing exactly the same search criteria. There were no systematic reviews planned for GBD editions 2016, 2017, 2019, or 2020. The search's inclusion criteria required studies to be representative, population-based studies that reported quantitative BMD measured in grams per square centimetre (g/cm^2) using DXA at the FN region. Mean BMD was sometimes reported in subgroups, such as according to fracture status, rather than for the entire

sample. In these instances, the stratified means were combined to calculate an overall mean BMD at the population level for each specific sex or age category [20].

2.3 | Data Processing and Modeling

The average bone mineral density (BMD) was modeled using DisMod-MR 2.1 as a continuous, single-parameter framework, taking into account sex and age across all GBD locations from 1990 to 2021. For further information on the modeling process, please refer to the supporting material.

2.4 | Data on Estimated Relative Risk

The theoretical minimum risk exposure level (TMREL) was determined using the age- and sex-specific 99th percentile of BMD from five cycles of the NHANES study, with this reference population serving as the baseline. Additional details can be found in the supporting material.

2.5 | Estimating the Proportion of Disease and Injury Due to Osteopenia and Osteoporosis

The estimation of deaths and DALYs related to osteopenia and osteoporosis was conducted by multiplying the PAFs by the number of deaths or DALYs reported in GBD 2021, categorized by sex, age group, country, year, and disease type. To account for uncertainty, 95% uncertainty intervals (UIs) were calculated by performing 1000 draws at each stage of the modeling process, with the UIs defined as the 25th and 975th percentiles of the ordered draws.

All estimates were standardized to the GBD reference population and presented as numbers, proportions (PAFs), and age-standardized rates (per 100,000), along with 95% UIs. In addition to these calculations, the current study investigated the relationship between DALYs attributable to osteopenia and osteoporosis and the Socio-Demographic Index (SDI). The SDI is a composite index reflecting a country's socio-demographic development, incorporating total fertility rate, educational attainment, and average income per person, with values ranging from 0 (lowest development) to 1 (highest development).

3 | Results

3.1 | Global Level

In 2021, there were 459,661 (95% UI: 383,676–519,475) deaths attributable to osteopenia and osteoporosis globally, accounting for 0.7% (0.6–0.8) of all deaths (Table 1). Of these, 225,632 (95% UI: 194,050–250,804) deaths occurred among males, with a population attributable fraction (PAF) of 0.6% (0.5–0.7), and an age-standardized death rate of 6.5 (5.5–7.2) per 100,000. Among females, 234,029 (95% UI: 183,949–272,651) deaths were attributable to osteopenia and osteoporosis, representing a PAF of 0.8% (0.6–0.9) and an ASDR of 5.0 (3.9–5.8) per 100,000 (Table S1).

In 2021, osteopenia and osteoporosis was responsible for an estimated 17.3 million (95% UI: 14.3–20.5 million) DALYs globally, accounting for 0.6% (0.5–0.7) of all DALYs (Table 1). The age-standardized DALY rate due to osteopenia and osteoporosis was 205 (95% UI: 168.9–243) per 100,000 in 2021, reflecting a decrease of 14.8% (95% UI: −18.5% to −11.8%) from the 1990 level (Table S2). Among males, the estimated DALYs attributable to osteopenia and osteoporosis in 2021 were 8.2 million (95% UI: 6.9–9.6 million), with a PAF of 0.5% (0.5–0.6) and an age-standardized rate of 211 (95% UI: 177.7–245.9) per 100,000. For females, the DALYs were 9.1 million (95% UI: 7.3–11.2 million), with a PAF of 0.7% (0.6 –0.8) and an age-standardized rate of 196.4 (95% UI: 158.8–241.2) per 100,000 (Table S2).

3.2 | Regional Level

The regions with the highest counts of osteopenia and osteoporosis-related deaths were South Asia (134,563 [110,934–153,587]), East Asia (90,971 [65,433–115,323]), and Western Europe (50,732 [39,172–58,328]). In contrast, the regions with the lowest counts of osteopenia- and osteoporosis-related deaths were Oceania (283 [206–373]), Central Asia (1422 [1158–1622]), and Andean Latin America (2415 [1900–2974]) (Table 1). The top three contributors to osteopenia and osteoporosis-attributable deaths differed across regions. South Asia and Western Europe displayed a similar pattern, with falls, road injuries, and other transport injuries as the leading contributors. In contrast, in East Asia, the leading contributors were exposure to mechanical forces, falls, and road injuries (Figure S1). The proportion of deaths due to osteopenia and osteoporosis varied globally, with PAFs ranging from 0.2% to 1.4%. The highest PAFs were observed in Australasia (1.4% [1.1–1.7]), Western Europe (1.1% [0.9–1.3]), and High-income North America (0.9% [0.7–1.0]). Conversely, the smallest PAFs were observed in Central Asia (0.2% [0.2–0.2]), Eastern Europe (0.3% [0.2–0.3]), and Oceania (0.3% [0.2–0.3]) (Table 1).

In 2021, the age-standardized mortality rates for deaths due to osteopenia and osteoporosis (per 100,000) were highest in South Asia (11.6 [9.5–13.4]), Eastern Sub-Saharan Africa (10.7 [9.0–12.4]), and Central Sub-Saharan Africa (9.8 [7.7–12.6]). Conversely, the smallest rates were seen in Central Asia (1.8 [1.5–2.1]), high-income Asia Pacific (2.1 [1.6–2.4]), and Eastern Europe (2.6 [2.2–3.0]) (Table 1).

The majority of GBD regions showed changes in the age-standardized mortality rates of osteopenia and osteoporosis from 1990 to 2021, with the biggest increases observed in High-income North America (49.2% [40.9–54.5]) and Australasia (19.1% [8.8–29.1]). The greatest decreases were observed in Central Europe (−54.8% [−57.5 to −51.8]), Central Latin America (−48.7% [−53.3 to −44.0]), and Central Asia (−37.9% [−43.4 to −31.3]) (Table 1). Figure S2 presents the age-standardized mortality rates due to osteopenia and osteoporosis in 2021 by sex and region, whereas Figure S3 presents the changes from 1990 to 2021, by sex and region.

In 2021, the regions with the highest DALY counts attributable to osteopenia and osteoporosis were South Asia (4,145,067

TABLE 1 | Burden of diseases and injuries attributable to low bone mineral density in 2021 by GBD region.

	Deaths (95% UI)				DALY (95% UI)			
	Counts (2021)	PAF (2021)	ASRs (2021)	% change in ASRs 1990–2021	Counts (2021)	PAF (2021)	ASRs (2021)	% Change in ASRs 1990–2021
Global	459,661 (383676, 519475)	0.7 (0.6, 0.8)	5.6 (4.7, 6.4)	−9.4 (−16.4, −2.9)	17,310,085 (14294592, 20511120)	0.6 (0.5, 0.7)	205 (168.9, 243)	−14.8 (−18.5, −11.8)
High-income North America	35,000 (28065, 39458)	0.9 (0.7, 1)	4.9 (4, 5.4)	49.2 (40.9, 54.5)	1,451,886 (1151099, 1809286)	1.1 (0.9, 1.2)	219.9 (174.6, 273.2)	11.5 (7.9, 14.9)
Australasia	3018 (2388, 3480)	1.4 (1.1, 1.7)	4.7 (3.7, 5.4)	19.1 (8.8, 29.1)	132,173 (102468, 168950)	1.6 (1.4, 1.9)	237 (182.5, 302.7)	−2.4 (−5.3, 0.4)
High-income Asia Pacific	13,188 (9846, 15311)	0.7 (0.5, 0.9)	2.1 (1.6, 2.4)	−33.8 (−40.4, −29.1)	634,735 (493310, 813938)	1.2 (1, 1.4)	132.5 (102.4, 170.7)	−33.5 (−36.3, −31.1)
Western Europe	50,732 (39172, 58328)	1.1 (0.9, 1.3)	4 (3.2, 4.6)	−28.5 (−33.1, −25.4)	1,990,717 (1543915, 2507922)	1.4 (1.2, 1.7)	197.4 (152.1, 248.6)	−22.5 (−25.2, −20.3)
Southern Latin America	2479 (2044, 2766)	0.4 (0.4, 0.5)	2.8 (2.3, 3.1)	−31.5 (−35.2, −28.6)	143,132 (112241, 180060)	0.7 (0.6, 0.8)	165.3 (129.6, 208.2)	−18.2 (−21.8, −14.9)
Eastern Europe	8905 (7492, 10073)	0.3 (0.2, 0.3)	2.6 (2.2, 3)	−26.4 (−31.2, −21.3)	642,558 (500399, 817972)	0.6 (0.5, 0.7)	193.3 (149.9, 245.7)	−24.2 (−27.2, −21.5)
Central Europe	8316 (6885, 9348)	0.5 (0.4, 0.5)	3.6 (3, 4)	−54.8 (−57.5, −51.8)	435,983 (335673, 549767)	0.9 (0.7, 1)	201.9 (155, 254.9)	−39.8 (−43.1, −36.8)
Central Asia	1422 (1158, 1622)	0.2 (0.2, 0.2)	1.8 (1.5, 2.1)	−37.9 (−43.4, −31.3)	98,630 (77969, 122018)	0.3 (0.3, 0.4)	115.9 (91.7, 143.3)	−31.5 (−35.2, −27.6)
Central Latin America	8456 (7105, 9634)	0.4 (0.3, 0.5)	3.5 (2.9, 4)	−48.7 (−53.3, −44)	396,157 (318364, 469391)	0.5 (0.4, 0.5)	157.2 (126.4, 186.4)	−40.2 (−43.6, −36.9)
Andean Latin America	2415 (1900, 2974)	0.4 (0.4, 0.5)	4.2 (3.3, 5.1)	−14.7 (−28.2, 1.9)	91,865 (73108, 109619)	0.4 (0.3, 0.5)	153.1 (121.9, 182.3)	−14 (−22.9, −2.7)
Caribbean	3344 (2749, 3839)	0.7 (0.5, 0.8)	5.9 (4.9, 6.8)	−5 (−14.1, 4.8)	96,677 (76515, 114460)	0.5 (0.4, 0.6)	177.6 (140.6, 210.7)	−4.3 (−11, 2.1)
Tropical Latin America	12,866 (10427, 14459)	0.7 (0.6, 0.8)	5.2 (4.2, 5.9)	−10 (−15.4, −5.9)	515,136 (418931, 606221)	0.6 (0.5, 0.7)	201.1 (163.6, 236.4)	−20.7 (−23.4, −18.8)
East Asia	90,971 (65433, 115323)	0.8 (0.5, 0.9)	5 (3.5, 6.4)	−10.8 (−40.7, 17.1)	3,567,799 (2868063, 4352948)	0.9 (0.7, 1)	174.4 (139.4, 212.9)	−10.1 (−26, 5.6)
Southeast Asia	33,100 (26617, 38255)	0.6 (0.5, 0.7)	6.1 (4.8, 7.2)	−20.7 (−31.6, −9.2)	1,148,904 (982773, 1312081)	0.5 (0.4, 0.5)	183.7 (154.8, 211)	−20.4 (−26.7, −13.4)
Oceania	283 (206, 373)	0.3 (0.2, 0.3)	4.9 (3.5, 6.6)	−7.5 (−25.5, 15.5)	13,240 (10728, 16244)	0.2 (0.2, 0.3)	181 (146, 222.6)	2.9 (−11.3, 17.9)
North Africa and Middle East	17,731 (14883, 20211)	0.4 (0.4, 0.5)	4.5 (3.8, 5.1)	−29.7 (−35.5, −22.6)	798,485 (660974, 939982)	0.4 (0.3, 0.5)	167.6 (139, 197.2)	−25.9 (−30.1, −21.6)

(Continues)

TABLE 1 | (Continued)

	Deaths (95% UI)				DALY (95% UI)			
	Counts (2021)	PAF (2021)	ASRs (2021)	% change in ASRs 1990–2021	Counts (2021)	PAF (2021)	ASRs (2021)	% Change in ASRs 1990–2021
South Asia	134,563 (110934, 153587)	0.9 (0.8, 1)	11.6 (9.5, 13.4)	−0.9 (−15.4, 15.4)	4,145,067 (3509461, 4770996)	0.6 (0.5, 0.7)	308.4 (260.6, 353.8)	−2.1 (−11.1, 7.9)
Southern Sub-Saharan Africa	2728 (2317, 3030)	0.3 (0.2, 0.3)	4.7 (4, 5.2)	−12.9 (−21.9, −2.9)	113,632 (96124, 128418)	0.2 (0.2, 0.3)	176.1 (148.9, 199.2)	−19.6 (−25.2, −13.4)
Western Sub-Saharan Africa	13,147 (11043, 15058)	0.3 (0.3, 0.4)	9.3 (7.9, 10.7)	−8 (−19.2, 5.2)	382,035 (320288, 441084)	0.1 (0.1, 0.2)	211.8 (178.8, 240.8)	−9.5 (−19.1, 1.6)
Eastern Sub-Saharan Africa	12,735 (10918, 14472)	0.4 (0.3, 0.4)	10.7 (9, 12.4)	−14.3 (−24, −2.7)	361,026 (310636, 406082)	0.2 (0.2, 0.2)	234.7 (201.5, 264.9)	−18 (−25.6, −8.9)
Central Sub-Saharan Africa	4262 (3371, 5288)	0.4 (0.3, 0.5)	9.8 (7.7, 12.6)	−2.9 (−22.7, 19.5)	150,248 (120725, 182007)	0.2 (0.2, 0.3)	259.5 (208.3, 311.3)	−5.8 (−22.2, 12.8)

Abbreviations: ASRs, age-standardized rates; DALY, disability adjusted life year; GBD, global burden of disease.

[3,509,461–4,770,996]), East Asia (3,567,799 [2,868,063–4,352,948]), and Western Europe (1,990,717 [1,543,915–2,507,922]). Conversely, the regions with the lowest DALY counts were Oceania (13,240 [10,728–16,244]), Andean Latin America (91,865 [73,108–109,619]), and the Caribbean (96,677 [76,515–114,460]) (Table 1). The leading causes of osteopenia and osteoporosis-attributable DALYs varied across regions. In South Asia, road injuries, falls, and other transport injuries were the top contributors. In contrast, both East Asia and Western Europe showed a similar pattern, with exposure to mechanical forces, road injuries, and falls as the primary contributors (Figure S4).

The PAF for DALYs varied significantly across regions, with the highest values observed in Australasia (1.6% [1.4–1.9]), Western Europe (1.4% [1.2–1.7]), and High-income Asia Pacific (1.2% [1.0–1.4]). In contrast, the lowest PAF values were seen in Western Sub-Saharan Africa (0.1% [0.1–0.2]), Eastern Sub-Saharan Africa (0.2% [0.2–0.2]), and Oceania (0.2% [0.2–0.3]) (Table 1).

In 2021, the age-standardized DALY rates for osteopenia and osteoporosis were highest in South Asia (308.4 [260.6–353.8]), Central Sub-Saharan Africa (259.5 [208.3–311.3]), and Australasia (237 [182.5–302.7]), while the lowest rates were seen in Central Asia (115.9 [91.7–143.3]), High-income Asia Pacific (132.5 [102.4–170.7]), and Andean Latin America (153.1 [121.9–182.3]) (Table 1). Figure S5 presents the age-standardized DALY rates due to osteopenia and osteoporosis in 2021, detailed by sex. From 1990 to 2021, high-income North America was the only region to experience an increase in age-standardized DALY rates, rising by 11.5% (95% CI: 7.9–14.9). The largest reductions were seen in Central Latin America (−40.2% [−43.6 to −36.9]), Central Europe (−39.8% [−43.1 to −36.8]), and high-income Asia Pacific (−33.5% [−36.3 to −31.1]) (Table 1). Figure S6 reports the percentage changes in the age-standardized DALY rates attributable to osteopenia and osteoporosis, broken down by sex in 2021.

3.3 | National Level

In 2021, the proportion of deaths due to osteopenia and osteoporosis varied significantly between countries. The highest PAFs were observed in the Netherlands (1.9% [1.5−2.2]), Norway (1.9% [1.4−2.1]), and Switzerland (1.7% [1.3−2.0]). Conversely, the smallest PAFs were seen in Azerbaijan (0.1% [0.1−0.1]), Tajikistan (0.1% [0.1−0.1]), and Turkmenistan (0.1% [0.1−0.1]) (Table S3). The proportion of deaths attributable to osteopenia and osteoporosis, stratified by sex, is reported in Table S1.

The age-standardized death rates for osteopenia and osteoporosis in 2021 varied widely, ranging from 1.0 to 16.1 per 100,000. The highest rates were recorded in India (13.2 [10.8−15.2]), Burkina Faso (13.1 [10.1−15.9]), and Eritrea (12.9 [9.8−16.1]). Conversely, the smallest rates were observed in Azerbaijan (1.0 [0.7−1.2]), Turkmenistan (1.1 [0.9−1.4]), and Bosnia and Herzegovina (1.2 [0.8−1.6]) (Table S3). Table S1 provides a breakdown of the age-standardized mortality rate for osteopenia and osteoporosis in 2021 by sex. Throughout the

measurement period, several countries and territories experienced increases in age-standardized death rates associated with osteopenia and osteoporosis. The Netherlands (53.8% [42.1−64.3]), the United States of America (45.2% [40.9−54.5]), and Lesotho (44.5% [4.9−99.9]) had the largest rises in age-standardized mortality rates from 1990 to 2021. Conversely, Hungary (−74.3% [−77.4 to −71.2]), Czechia (−67.3% [−70.7 to −63.3]), and Guam (−66.3% [−73.3 to −59.5]) had the largest declines over the measurement period (Table S3).

In 2021, the proportion of DALYs due to osteopenia and osteoporosis varied significantly between countries. Switzerland (2.1% [1.7–2.4]), Andorra (2.0% [1.6–2.4]), and Finland (2.0% [1.6–2.3]) recorded the largest PAFs for osteopenia and osteoporosis. Conversely, the smallest PAFs were observed in Kiribati (0.1% [0.1–0.1]), Botswana (0.1% [0.1–0.2]), and Zimbabwe (0.1% [0.1–0.2]) (Figure 1A and Table S4). The proportion of all DALYs attributable to osteopenia and osteoporosis for males and females are reported in Figures 1B and 1C.

The age-standardized DALY rate for osteopenia and osteoporosis in 2021 ranged from 77.5 to 462.1 per 100,000. Saudi Arabia (379.2 [305.9–462.1]), India (349.8 [293.8–403.2]), and Greenland (329.5 [259.6–409.2]) had the largest age-standardized DALY rates. Conversely, the smallest rates were observed in Azerbaijan (77.5 [60–98]), Jamaica (80.1 [61.8–100]), and Turkmenistan (82.3 [62.6–104.5]) (Figure 2A and Table S4). Figure 2B,C present the sex-specific age-standardized DALY rates for osteopenia and osteoporosis in 2021. During the measurement period, several countries and territories saw increases in age-standardized DALY rates for osteopenia and osteoporosis. Lesotho (53.9% [19.2–99.7]), the Netherlands (24.2% [19.5–29]), and Jamaica (13.5% [3.2–27.9]) had the biggest increases in age-standardized DALY rates from 1990 to 2021. Conversely, Hungary (−57.5% [−61.2 to −53.6]), Taiwan (−53.9% [−56.6 to −51.5]), and Czechia (−52% [−55.4 to −48.3]) saw the largest decreases over this period (Table S4).

3.4 | Sex and Age Patterns

In 2021, the global number of osteopenia and osteoporosis-related deaths began to rise from the 65–69 age group and reached its peak in the 85–89 age range for both sexes. Similarly, the death rate for osteopenia and osteoporosis increased from the 40–44 age group, reaching its peak among those aged 95+ for both sexes. Significant sex differences were observed, with males typically experiencing higher death rates across all ages, especially in the older age groups (Figure 3A). The analysis of mortality by cause revealed that deaths from osteopenia and osteoporosis-related causes began to rise from the 40–44 age range, peaking in the 85–89 age range before gradually declining in the oldest age categories. The leading contributors to osteopenia and osteoporosis-attributable deaths were exposure to mechanical forces, road injuries, and falls. Additionally, the death rate from osteopenia and osteoporosis-related falls began to rise from the 40–45 age group, reaching its peak among individuals aged 95 and older (Figure 3B).

In 2021, the global DALYs due to osteopenia and osteoporosis peaked at ages 40–44 for males and 80–84 for females. Up to age 65, DALY counts were higher among males, after which they were surpassed by those of females through to the oldest age groups. Similarly, the DALY rate for osteopenia and osteoporosis began rising from the 40–44 age group, reaching its peak in the 95+ age group for both sexes. Notably, substantial differences existed between males and females, with females generally experiencing higher DALY rates across most age groups, particularly in the older age groups (Figure S7). DALYs attributable to osteopenia and osteoporosis from all causes began to rise from the 40–44 age group, peaking in the 70–74 age range and then gradually declining in the older age categories. The primary contributing causes varied by age: falls were the leading cause in the 80–84 age group, road injuries in the 40–44 age category, and exposure to mechanical forces in the 50–54 age range. Furthermore, the DALY rate attributable to osteopenia and osteoporosis from falls displayed a steady upward trend across age groups, reaching its peak in the oldest age category (Figure S8).

3.5 | Disease and Injury Burden Due to Osteopenia and Osteoporosis by SDI

From 1990 to 2021, a generally negative correlation was observed between regional SDI and age-standardized DALY rates due to osteopenia and osteoporosis. Throughout this period, most GBD regions experienced a decline in age-standardized DALY rates. South Asia and Tropical Latin America experienced a larger than expected burden throughout the entire period. Conversely, Southern Latin America, Southeast Asia, East Asia, and Southern Sub-Saharan Africa achieved a lower than expected burden towards the end of the measurement period. Additionally, Western Sub-Saharan Africa, Oceania, the Caribbean, Andean Latin America, Central Asia, and High-income Asia Pacific consistently exhibited a lower than expected burden from 1990 to 2021 (Figure 4).

In 2021, the relationship between each country's SDI and the age-standardized DALY rate due to osteopenia and osteoporosis followed a nonlinear pattern. For SDI values up to approximately 0.7, the association was generally negative; however, beyond this point, the trend began to increase (Figure S9). Several countries and territories, including Saudi Arabia, India, Greenland, Vietnam, and the Central African Republic, exhibited significantly higher than expected burden levels. Conversely, countries such as Jamaica, Azerbaijan, Tajikistan, Bangladesh, and Niger had markedly lower than expected burdens (Figure S9).

4 | Discussion

This study provides an in-depth examination of the global, regional, and national impacts of diseases and injuries linked to osteopenia and osteoporosis over the period 1990 to 2021. The burden varied considerably across different regions, countries, sexes, age groups, and levels of socio-demographic development. Although the overall global osteopenia and osteoporosis burden decreased during this period, some countries, particularly high income countries, experienced an increase. In all age categories, males had higher death rates than females, with

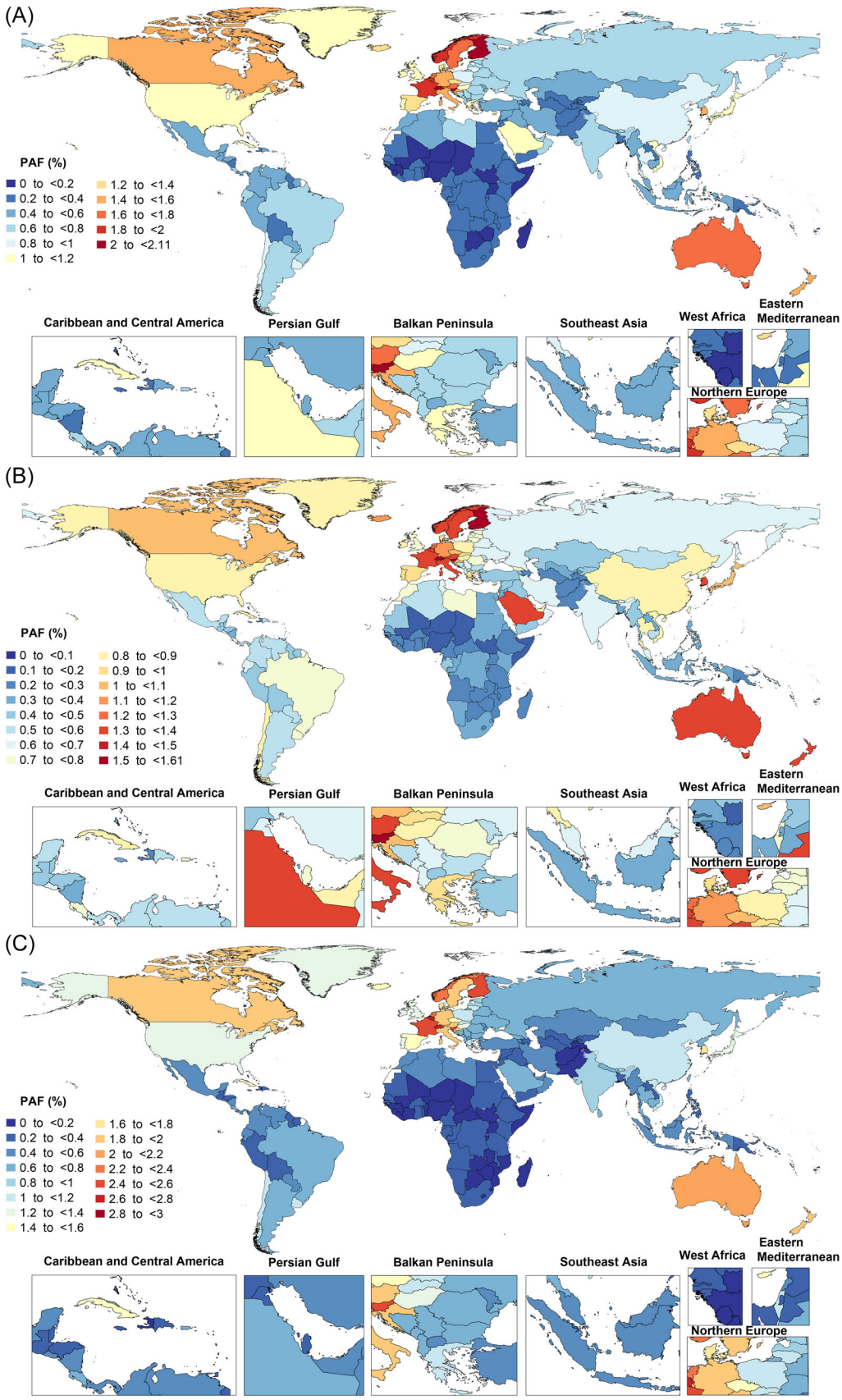

FIGURE 1 | Population attributable fraction of deaths attributable to osteopenia and osteoporosis for both sexes (A), males (B), and females (C) in 2021, by country. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool).

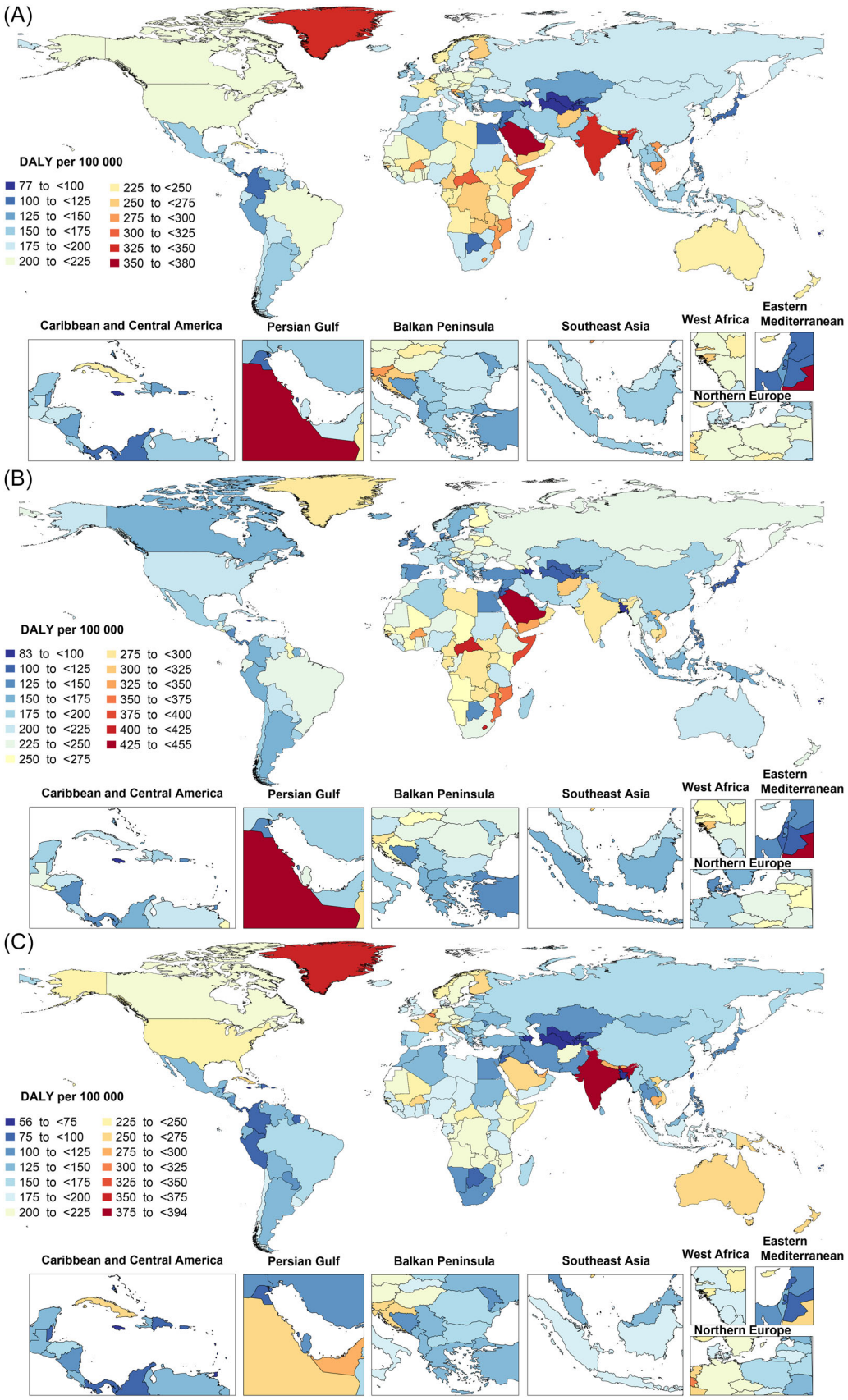

FIGURE 2 | Age-standardized death rates attributable to osteopenia and osteoporosis for both sexes (A), males (B), and females (C) in 2021, by country. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool).

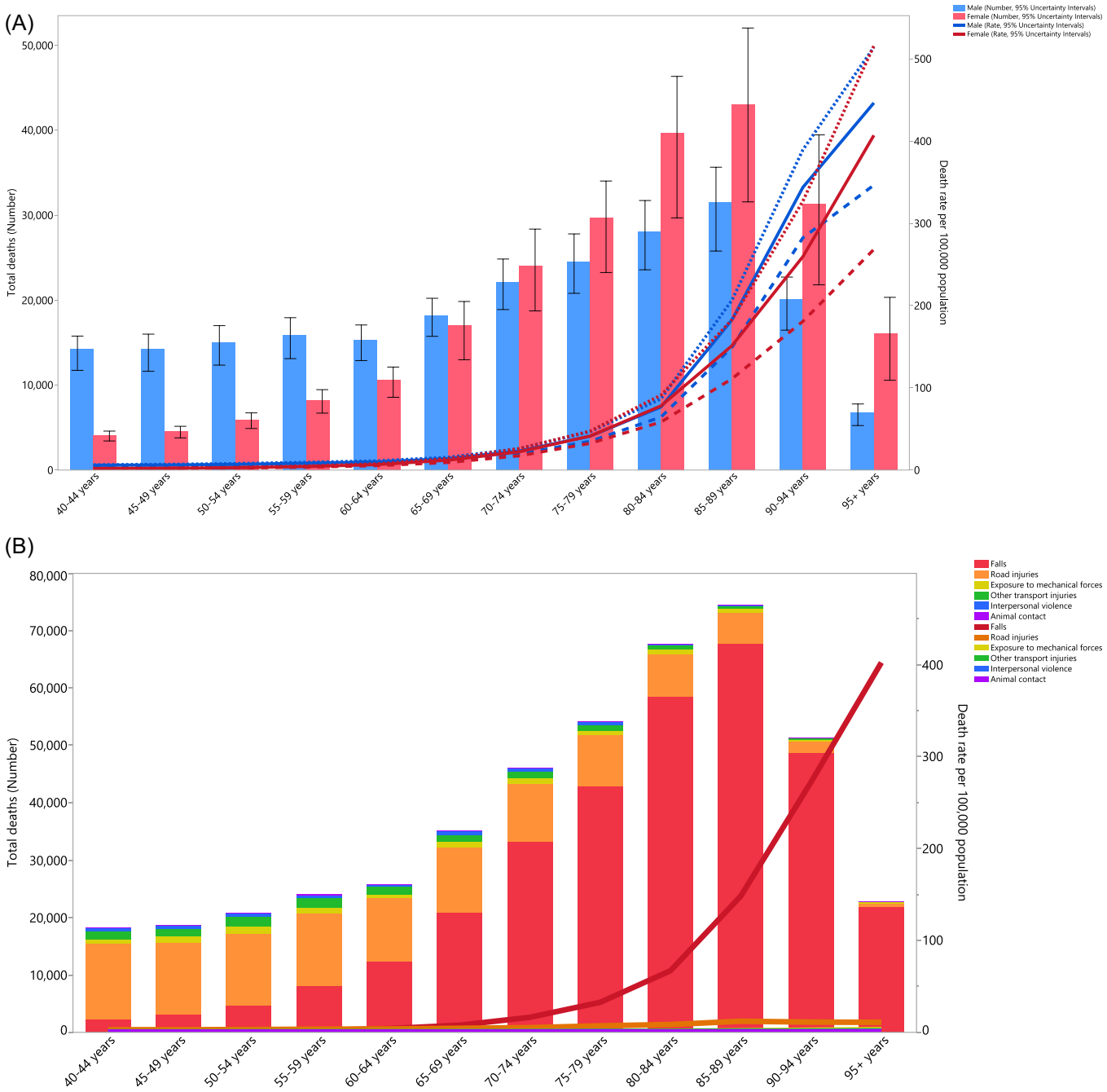

FIGURE 3 | Global number of deaths and death rate of diseases and injuries attributable to osteopenia and osteoporosis per 100,000 population by age and sex (A), and by age and cause (B) in 2021; Dotted and dashed lines indicate 95% upper and lower uncertainty intervals, respectively. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool).

osteopenia and osteoporosis-related death rates reaching a peak in the 85–89 age category for both sexes. Generally, our findings indicated a negative association between the regional SDI and DALY ASRs.

In 2021, osteopenia and osteoporosis accounted for approximately 459,661 deaths and 17.3 million DALYs worldwide, representing 0.7% of all deaths and 0.6% of total DALYs. These findings are consistent with the GBD 2019 data, which also reported a general global decrease in the osteopenia and osteoporosis burden [12]. From 1990 to 2021, there was a 14.8% decline in the global age-standardized DALY rate, likely reflecting advancements in diagnosis and management, greater awareness of bone health, and enhanced healthcare access worldwide. Nonetheless, the absolute numbers of deaths and DALYs remains high. As the global population grows and ages, further challenges in disease management and control are anticipated [21].

In the sex-specific analysis, males exhibited higher age-standardized death rates than females (6.5 vs. 5.0 per 100,000), whereas females had a slightly greater DALY burden (9.1 million vs. 8.2 million). One possible explanation is that postmenopausal women are more susceptible to bone loss due to

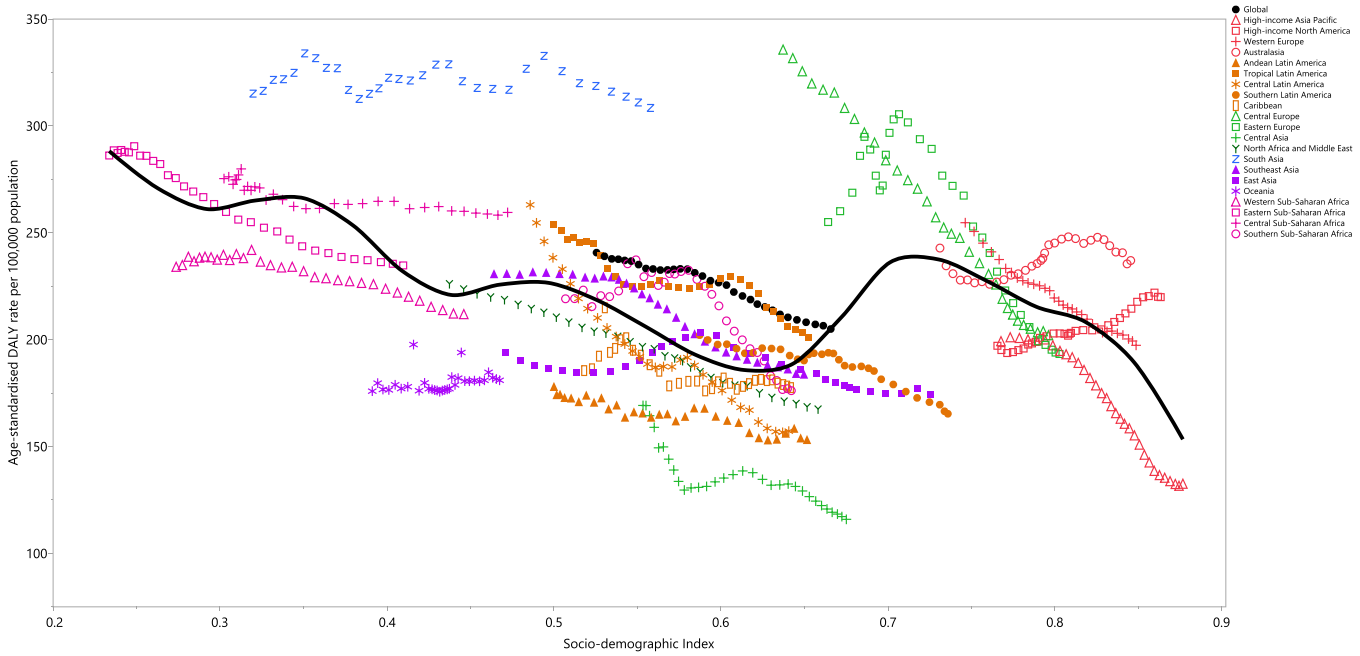

FIGURE 4 | Age-standardized DALY rate attributable to osteopenia and osteoporosis for the 21 Global Burden of Disease regions by Socio-demographic Index, 1990–2021; expected values based on Socio-demographic Index and disease rates in all locations are shown as the black line. Thirty points are plotted for each GBD region and show the observed age-standardized DALY rates from 1990 to 2021 for that region. Abbreviation: DALY= disability-adjusted-life-years. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool).

oestrogen deficiency, resulting in higher DALY rates [17, 18]. Conversely, osteopenia and osteoporosis in men has historically been neglected. Osteoporosis is generally perceived as a female-dominant disorder, leading to less frequent screening in men, delayed diagnosis, and higher mortality rates from osteopenia and osteoporosis-related complications. Although men are known to have stronger bones, they have been reported to have higher rates of secondary osteoporosis compared to women [15, 22].

In examining regional data, South Asia, East Asia, and Western Europe reported the largest numbers of deaths and DALYs attributable to osteopenia and osteoporosis, whereas Oceania, Central Asia, and Andean Latin America had the lowest. South Asia had the largest age-standardized death rate (11.6 per 100,000) and DALY rate (308.4 per 100,000). Falls, road injuries, and other transport injuries were the main contributors to the disease burden in this region. Moreover, factors such as nutritional deficiencies, limited access to healthcare, and socio-cultural practices affecting bone health may exacerbate the osteopenia and osteoporosis burden in this region [23]. A study by Bainbridge et al. highlighted the role of calcium and vitamin D deficiencies in contributing to the osteopenia and osteoporosis burden in low income regions [6]. Additionally, the rapid urbanization in South Asia has been linked to increased fall hazards and traffic-related injuries [24–26]. The substantial osteopenia and osteoporosis burden in this region not only affects individual and societal health and wellbeing but also significantly contributes to the health-related economic costs [27].

High-income regions, such as Australasia, High-income North America, and, Western Europe had higher PAFs for osteopenia and osteoporosis despite having lower overall age-standardized death and DALY rates. Ageing populations with increased life expectancy may contribute to the higher PAFs observed in these regions. This trend is likely combined with improved healthcare systems and greater access to screening programmes that facilitate the detection and reporting of osteopenia and osteoporosis-related conditions. Several studies have underscored the importance of early diagnosis and intervention in preventing osteopenia and osteoporosis-related fractures and injuries, practices that are more likely to be implemented in high-income settings [28, 29].

From 1990 to 2021, most regions experienced a reduction in age-standardized death and DALY rates attributable to osteopenia and osteoporosis, reflecting global improvements in healthcare and public health interventions. Central Europe, Central Latin America, and Central Asia showed ASDRs reductions of up to 54.8%, marking the most significant decreases. These trends may be attributed to improved access to osteoporosis treatments, lifestyle modifications, and preventive measures targeting bone health [30, 31]. However, over the same period, High-income North America and Australasia reported increases in osteopenia and osteoporosis-related ASDRs and DALY rates. These trends may be attributed to population ageing, a rising prevalence of chronic health conditions, including diabetes and obesity, and increasingly sedentary lifestyles [32, 33]. Furthermore, the higher rates of autoimmune disorders in these regions have led to greater use of medications such as glucocorticoids, which are known to induce secondary osteoporosis and may have contributed to the growing burden, as highlighted in numerous studies [34–37].

At the national level, the burden of osteopenia and osteoporosis varied widely, with the Netherlands, Norway, and Switzerland reporting the highest PAFs for osteopenia and osteoporosis-related deaths, while Azerbaijan, Tajikistan, and Turkmenistan

reported the lowest. These disparities may stem from differences in national healthcare systems, public health policies, and socioeconomic factors. Countries with the highest ASDRs and DALY rates, such as India, Burkina Faso, and Saudi Arabia, face challenges related to healthcare access, nutritional deficiencies, and coexisting health problems [38, 39]. Conversely, countries with the lowest rates, such as Azerbaijan and Jamaica, may benefit from more favorable demographic profiles, better self-care habits, and effective public health interventions targeting bone health [40, 41].

Consistent with previous findings, our study's age-specific analysis revealed that the burden of osteopenia and osteoporosis-related deaths and DALYs rose significantly with age, reaching peaks in the 85–89 and 95+ age categories, respectively [42–44]. Furthermore, Di Monaco et al. investigated the relationship bone density has with low lean muscle mass, finding that this association significantly impacts fracture risk among the elderly. Their study underscores the importance of adopting integrated approaches to geriatric care [45].

In line with previous studies, we identified sex differences in the burden of osteopenia and osteoporosis. Males exhibited higher death rates, whereas females bore a greater burden of DALYs, particularly in older age groups. These findings align with earlier research that has documented sex-specific differences in physiological events, bone health, fracture risk, and health-seeking behaviors [12, 46]. These differences underscore the need for tailored screening approaches for both sexes [47]. While the higher DALY burden in females highlights the necessity for targeted interventions addressing postmenopausal bone loss and its related consequences, the increased mortality rates in males highlight the importance of enhancing osteoporosis screening and treatment efforts for men.

The analysis of osteopenia and osteoporosis burden by SDI revealed a broadly negative correlation between SDI and age-standardized DALY rates up to an SDI of 0.7, after which the trend reversed. This nonlinear pattern suggests that higher socioeconomic development is typically linked to improved bone health. However, factors such as urbanization, sedentary lifestyles, and ageing populations in high-SDI regions may negatively impact and offset the benefits of improved care.

Countries like Saudi Arabia and India exhibited higher-than-expected osteopenia and osteoporosis burdens, relative to their SDI levels. As discussed earlier, these results may be attributed to factors such as dietary habits, healthcare access, and cultural practices. In contrast, countries like Jamaica and Azerbaijan showed lower-than-expected burdens, which may indicate effective public health strategies, self-care practices, and disease awareness.

The primary pathway through which osteopenia and osteoporosis contribute to mortality and disability is fragility fractures, events associated with dramatically increase morbidity and mortality. Hip fractures, for instance, carry a 1-year mortality rate surpassing 30% in certain populations, a figure projected to rise annually by approximately 2% [48]. The prolonged immobilization following such fractures increases susceptibility to life-threatening complications like pressure ulcers, muscle atrophy, and deep vein thrombosis, further exacerbating mortality risk [49]. Consequently, addressing this global burden necessitates a comprehensive, multifaceted approach to prevention, encompassing primary, secondary, and tertiary interventions tailored to individual and population-level risk factors [50].

The results of this study have several important implications for policymakers and healthcare providers. Implementing early screening for osteoporosis and osteopenia and osteoporosis, especially among high-risk groups like postmenopausal women and older adults, could help mitigate the anticipated rising disease burden due to population ageing. Public health campaigns that promote disease awareness, weight-bearing exercises, adequate calcium and vitamin D intake, and fall prevention strategies could also help reduce the burden of osteopenia and osteoporosis. Integrating bone health management into primary care and chronic disease programmes can facilitate early detection and treatment. Additionally, greater involvement of endocrinologists, orthopedists, and rehabilitation specialists could provide comprehensive care for the affected population. It is crucial to address disparities in healthcare access, particularly in low- and middle-income countries, to decrease the global burden of osteopenia and osteoporosis.

5 | Strengths and Limitations of This Study

While this study provides valuable insights, it is not without limitations. As with other GBD studies, there was a lack of data, particularly from low- and middle-income countries. Although robust modeling techniques were employed to mitigate this issue, reliance on modeling and secondary data can introduce uncertainty. Furthermore, the study does not encompass the full range of factors influencing osteopenia and osteoporosis, such as genetic predisposition and environmental exposures. Additionally, in accordance with the GATHER checklist, we note that the underlying computational code is developed and maintained by the Institute for Health Metrics and Evaluation (IHME) and is not publicly available; however, all input data sources and output results are publicly available via the GHDx [20]. Furthermore, we did not separately analyze the burden associated with different stages of LBMD, including osteopenia and osteoporosis, despite the varying severity, diagnostic approaches, and treatment and rehabilitation strategies they entail. Future research should aim to address these gaps to improve our understanding of osteopenia and osteoporosis epidemiology.

6 | Conclusions and Policy Implications

Although the global burden of osteopenia and osteoporosis has decreased since 1990, there remain significant variations across regions, countries, sexes, and age groups, with some countries, including many high-income nations, experiencing an increase. The persistently high absolute burden underscores the need for sustained efforts to address the osteopenia and osteoporosis burden, particularly in regions that have shown an increase since 1990. Targeted interventions, improved healthcare access,

increased public awareness, as well as effecting screening and rehabilitation programmes, are essential to improve population health worldwide.

Author Contributions

S.S. and A.A.K. designed the study. S.S. analyzed the data and performed the statistical analyses. S.S., F.A., F.S., M.J.M.S., M.A.M., M.R., G.S.C. and A.A.K. validated, visualized, and drafted the initial manuscript. All authors reviewed the drafted the manuscript for critical content. All authors approved the final version of the manuscript. All authors reviewed the draft manuscript for critical intellectual content and approved the final version. S.S. and A.A.K. had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Data Availability Statement

The data used in this study are publicly available and can be accessed at http://ghdx.healthdata.org/gbd-results-tool.

Transparency Statement

The corresponding authors Saeid Safiri and Ali-Asghar Kolahi affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Figure S1: Number of deaths attributable to osteopenia and osteoporosis in 2021 across the 21 Global Burden of Disease regions, by cause. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S2:** Age-standardised death rate of diseases and injuries attributable to osteopenia and osteoporosis in 2021 across the 21 Global Burden of Disease regions, by sex. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S3:** Percentage change in the age-standardised death rate of diseases and injuries attributable to osteopenia and osteoporosis from 1990 to 2021 across the 21 Global Burden of Disease regions, by sex. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S4:** Number of DALYs attributable to osteopenia and osteoporosis in 2021 across the 21 Global Burden of Disease regions, by cause. DALY= disability-adjusted-life-years. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S5:** Age-standardised DALY rate of diseases and injuries attributable to osteopenia and osteoporosis in 2021 for 21 Global Burden of Disease regions, by sex. DALY=disability-adjusted-life-years. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S6:** Percentage change in the age-standardised DALY rate of diseases and injuries attributable to osteopenia and osteoporosis from 1990 to 2021 across the 21 Global Burden of Disease regions, by sex. DALY=disability-adjusted-life-years (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S7**: Global number of DALYs and DALY rate of diseases and injuries attributable to osteopenia and osteoporosis per 100,000 population, by age and sex, in 2021; Dotted and dashed lines indicate 95% upper and lower uncertainty intervals, respectively. DALY= disability-adjusted-life-years. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S8**: Global number of DALYs and DALY rate of diseases and injuries attributable to osteopenia and osteoporosis per 100,000 population, by age and cause, in 2021; Dotted and dashed lines indicate 95% upper and lower uncertainty intervals, respectively. DALY= disability-adjusted-life-years. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Figure S9**: Age-standardised DALY rates of diseases and injuries attributable to osteopenia and osteoporosis by socio-demographic Index for 204 countries and territories in 2021; expected values are shown as the black line. Each point shows observed age-standardised DALY rate for specified country in 2021. DALY=disability-adjusted-life-years. (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Table S1:** Deaths attributable to osteopenia and osteoporosis per 100,000 in 2021, by sex and location (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Table S2:** DALYs attributable to osteopenia and osteoporosis per 100,000 in 2021, by sex and location (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Table S3:** Deaths attributable to osteopenia and osteoporosis per 100,000 in 1990 and 2021, by location (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool). **Table S4:** DALYs attributable to osteopenia and osteoporosis per 100,000 in 1990 and 2021, by location (Generated from data available from http://ghdx.healthdata.org/gbd-results-tool).