

# The global, regional, and national burden attributable to low bone mineral density, 1990–2020: an analysis of a modifiable risk factor from the Global Burden of Disease Study 2021



GBD 2021 Low Bone Mineral Density Collaborators\*

## Summary

**Background** Fractures related to osteoporosis and low bone mineral density lead to substantial morbidity, mortality, and cost to individuals and health systems. Here we present the most up-to-date global, regional, and national estimates of the contribution of low bone mineral density to the burden of fractures from falls and additional categories of injuries from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021.

**Methods** The burden of low bone mineral density was estimated from 1990 to 2020 in terms of years lived with disability (YLDs), disability-adjusted life years (DALYs), and deaths, for individuals aged 40 years and older, using data from population-based studies from 48 countries or territories (169 unique sources). Mean standardised femoral neck bone mineral density values were estimated by GBD location, age, and sex by meta-regression. Based on a separate meta-analysis of population-based studies from nine countries (12 unique sources), we also estimated the pooled relative risk of fractures per unit decrease in bone mineral density (g/cm<sup>2</sup>). The population-attributable fraction for low bone mineral density was calculated by comparing the observed distributions of standardised femoral neck bone mineral density to an age-specific and sex-specific counterfactual distribution, defined as the 99th percentile of five rounds of the National Health and Nutrition Examination Survey in the USA, by 5-year age group and sex. Hospital and emergency department data were used to derive the incidence of fractures for six categories of injury (road injuries, other transport injuries, falls, non-venomous animal contact, exposure to mechanical forces, and physical interpersonal violence) using ICD codes. Deaths due to fractures were estimated as the proportion of in-hospital deaths due to the specified injury causes for which a fracture (nature of injury code) was more severe than the cause of injury code. YLDs and DALYs attributable to low bone mineral density by cause of injury were also determined according to previous GBD methods.

**Findings** In 2020, 8.32 million (95% UI 5.58–10.84) YLDs, 17.2 million (14.1–20.2) DALYs, and 477 000 (411 000–536 000) deaths were attributable to low bone mineral density globally in individuals aged 40 years and older. Between 1990 and 2020, global YLDs, DALYs, and deaths attributable to low bone mineral density increased by 91.8% (88.5–95.1), 89.8% (81.5–99.0), and 127.1% (108.5–144.5), respectively. Over this period, the age-standardised global rates of YLDs, DALYs, and deaths attributable to low bone mineral density showed modest decreases. In 2020, falls accounted for 76.2% (95% UI 74.2–78.3) of YLDs, 65.2% (62.9–67.6) of DALYs, and 71.0% (67.4–72.8) of deaths attributable to low bone mineral density, and road injuries largely accounted for the remaining amount: 12.4% (11.1–13.6) of YLDs, 24.6% (22.5–27.1) of DALYs, and 23.1% (21.6–26.2) of deaths. As a proportion of all fall-related burden, low bone mineral density accounted for 26.6% (23.2–28.7) of YLDs, 25.6% (22.1–27.4) of DALYs, and 40.6% (35.4–44.0) of deaths in 2020. Of all road injury-related burden, 12.6% (10.8–13.5) of YLDs, 6.3% (5.4–6.9) of DALYs, and 8.9% (7.6–9.6) of deaths were attributable to low bone mineral density. In men, road injuries accounted for the largest proportion of DALYs attributable to low bone mineral density in those aged 40–59 years and the largest proportion of deaths in those aged 40–64 years. In women, road injuries were the leading cause of DALYs attributable to low bone mineral density in those aged 40–44 years and the leading cause of deaths attributable to low bone mineral density in those aged 40–54 years. In older age groups among both men and women, falls were the leading cause of the burden attributable to low bone mineral density.

**Interpretation** Low bone mineral density is a crucial modifiable risk factor for fractures, which are an important cause of morbidity and mortality particularly in ageing populations. This analysis highlights low bone mineral density as a cause of health loss not just from falls, but also from road injuries.

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### Research in context

#### Evidence before this study

Low bone mineral density is a reliably measurable and modifiable risk factor for fractures at the hip, spine, and other skeletal sites. Low bone mineral density is acknowledged as a risk factor for fractures related to falls and minor trauma, but few studies to date have explored the relationship between bone mineral density and major non-fall-related injuries. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) analyses low bone mineral density as a risk factor that directly contributes to quantifiable disease burden from fractures. For GBD 2015 we searched PubMed for population-based studies reporting femoral neck bone mineral density measured by dual-energy x-ray absorptiometry from Jan 1, 1980, to Dec 31, 2015, using the search terms (osteoporosis OR osteopenia OR osteopaenia OR bone mineral density OR radiolucency) AND (prevalen\* OR inciden\* OR cross-sectional OR cross sectional OR epidemi\* OR survey OR population-based OR population based OR population study OR population sample OR cohort OR follow-up OR follow up OR longitudinal OR regist\* OR data collection). Additional studies encountered opportunistically during data review were added for GBD 2016, 2017, 2019, and 2021. In parallel, a systematic search of PubMed done for GBD 2019 and updated for GBD 2021 identified studies published from Jan 1, 2010, to Dec 31, 2020, reporting the relative risk of hip or non-hip fracture per change in bone mineral density, using the search terms (bone mineral density[title/abstract] OR bone mineral densities[title/abstract]) OR bone

density[Mesh]) AND (mean[title/abstract] OR average[title/abstract]) AND risk[Mesh]) AND fracture[title/abstract]).

#### Added value of this study

This synthesis provides updated and comprehensive estimates of the global burden from fractures attributable to low bone mineral density from 1990 to 2020, and quantifies the contribution of six categories of injury (falls, road injuries, other transport injuries, exposure to mechanical forces, animal contact, and interpersonal violence) in men and women aged 40 years and older. An increase in burden related to low bone mineral density was observed, with a nearly two-times increase in years lived with disability and disability-adjusted life-years and a greater than two-times increase in deaths attributable to low bone mineral density. Among the types of injury, road injuries were the largest contributor to burden attributable to low bone mineral density among middle-aged men, and a main contributor among middle-aged women. In older individuals, falls represented the predominant cause of burden attributable to low bone mineral density.

#### Implications of all the available evidence

Low bone mineral density is an important predictor of fracture that is modifiable by existing prevention and treatment interventions. Strengthened policy and implementation strategies are needed to improve the uptake of evidence-based injury and fracture prevention approaches and to promote lifestyle strategies, to support bone health across the life-course.

### Introduction

Fractures related to osteoporosis represent a substantial burden and economic cost for societies across the world, and a steady increase in incidence is forecast over the coming decades.<sup>1,2</sup> In addition to the pain, functional impairment, and mortality risks associated with a fracture in the short term, the lasting consequences of bone fractures include chronic pain, permanent disability, and long-term institutionalisation.<sup>3,4</sup> A study of the Danish National Hospital Discharge Registry showed that 1 year after a hip fracture event, cumulative mortality was 37·1% in men and 26·4% in women, compared with 9·9% in men and 9·3% in women in the general population.<sup>5</sup> In the USA, approximately half of individuals who have osteoporotic fractures (also known as fragility fractures) never regain their pre-fracture level of physical function, and many lose their independence, requiring long-term care.<sup>6</sup> Furthermore, estimates show that fragility fractures lead to higher costs for individuals and health-care systems than other common disabling disorders such as myocardial infarction, stroke, Parkinson's disease, and rheumatoid arthritis.<sup>7,8</sup>

Cost-effective strategies exist for the identification and treatment of individuals with low bone mineral

density who are at high risk of fracture,<sup>9,10</sup> yet there is little awareness regarding these strategies among health professionals, public health institutions, and the general population, as highlighted in a report of EU countries.<sup>7</sup> Low bone mineral density has been consistently shown to predict fragility fractures at the hip and other sites.<sup>11</sup> Standard methods to measure bone mineral density exist using dual-energy x-ray absorptiometry (DXA), allowing for the comparison of values between different populations, and the establishment of diagnostic and treatment thresholds.<sup>12,13</sup>

We previously estimated the burden of falls attributable to low bone mineral density in persons aged 50 years and older as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2010.<sup>14</sup> In this updated and expanded analysis of the GBD 2021 dataset, which encompasses data from 1990 to 2020, we estimate the burden—including years lived with disability (YLDs), disability-adjusted life years (DALYs), and mortality—attributable to low bone mineral density in people aged 40 years and older in the setting of falls, road injuries and other transport injuries, exposure to mechanical forces, animal contact, and interpersonal violence.

## Methods

### Overview

This Article was produced as part of the GBD Collaborator Network and in accordance with the GBD Protocol. This study adheres to the GATHER statement<sup>15</sup> and follows the comparative risk assessment methodology used in the GBD, as previously described.<sup>14,16</sup> Briefly, by this methodology, the burden due to a risk factor is compared to a hypothetical counterfactual exposure level that would result in the lowest attributable burden, referred to as the theoretical minimum risk exposure level (TMREL; appendix 1 p 1).<sup>14,16</sup> Full details of the methods are included in appendix 1 (pp 14–31).

### Case definition and input data

The case definition for bone mineral density refers to bone mineral density measured at the femoral neck by DXA in g/cm<sup>2</sup>. A systematic review was done for GBD 2010 to identify all population-based studies published from Jan 1, 1980, to Dec 31, 2010, reporting femoral neck bone mineral density (mean [SD]) measured by DXA.<sup>14</sup> This search was last updated during GBD 2015, but with each successive round of the GBD up to GBD 2021, new sources suggested by collaborators within the GBD Network or identified in the Global Health Data Exchange database by GBD librarians (keywords: bone mineral density or osteoporosis) have been included. All sources up to GBD 2021 are available online in the GBD 2021 Sources Tool. Details of the search strategy, databases, inclusion and exclusion criteria, risk of bias assessment, and data extraction have been described previously.<sup>14,16</sup> All mean (SD) values for femoral neck bone mineral density from eligible studies, measured using DXA systems from different manufacturers, were extracted and standardised by international conversion formulas to mean standardised femoral neck bone mineral density and standardised SD.<sup>17</sup> Mean standardised femoral neck bone mineral density values were estimated as a continuous parameter for each GBD location, age, and sex, from 1990 to 2020 using DisMod-MR 2.1 (Disease Modelling Meta-Regression; version 2.1), a Bayesian meta-regression tool developed specifically for the GBD.<sup>18</sup> DisMod-MR 2.1 was chosen due to its ability to leverage information across locations, years, and heterogeneous age groups to generate estimates when data are sparse or missing. Estimates were generated for 204 countries and territories and for the GBD regions and super-regions. Age was modelled in 5-year intervals starting from 40–44 years, with the final category covering ages 95 years and older. Estimates were modelled up to 2020 to align with other papers in a recent musculoskeletal series by GBD collaborators.<sup>19</sup>

### Defining the TMREL for low bone mineral density

To select counterfactual exposure levels of bone mineral density, defined as the exposure level with no or very low exposure to low bone mineral density, the TMREL was

taken as the 99th percentile of the femoral neck bone mineral density values (mean [SD]), by 5-year age groups (from age 40–44 years up to ≥95 years) and sex, from five different cycles (years 1988–94, 2005–06, 2007–08, 2009–10, and 2013–14) of the US National Health and Nutrition Examination Survey,<sup>20–24</sup> as the most broadly accepted standard international reference. Low bone mineral density exposure was defined as the difference between the mean bone mineral density of a population and the TMREL at the same age and sex. This meant that low bone mineral density exposure in a population was quantified as the amount by which the population's mean bone mineral density fell below the TMREL for the same age and sex. If the mean bone mineral density was higher than the TMREL, the exposure was considered zero.

### Risk estimation

To establish the relationship between low bone mineral density and fracture risk we conducted a meta-analysis. A systematic review originally conducted for GBD 2019 and updated for GBD 2021 identified six studies that reported fracture risk per SD of bone mineral density.<sup>25–30</sup> Specifically, studies were eligible for inclusion if they: included representative, population-based longitudinal data; reported femoral neck bone mineral density measured by DXA as the exposure variable; reported relative risk of fractures per change in bone mineral density (most often captured as the per 1 SD decrease in bone mineral density); and included fractures (including type of fractures) as an outcome of interest. These studies were supplemented with six additional studies<sup>31–36</sup> meeting criteria for inclusion (from a larger meta-analysis of 12 studies that previously estimated the relative risk of fragility fracture associated with low bone mineral density<sup>11</sup>). The relationship between low bone mineral density and fracture risk was subsequently modelled using a meta-regression–Bayesian, regularised, trimmed meta-analysis.<sup>37</sup> Relative risks were estimated separately for hip and non-hip fractures (appendix 1 p 2).

### Estimate projections

The attributable burden of fractures due to low bone mineral density was calculated by comparing the observed distribution of standardised femoral neck bone mineral density to the counterfactual distribution for each age group, sex, location, year, and cause according to the following formula, as described previously:<sup>14</sup>

$$PAF_{oast} = \frac{\int_{x=0}^{11} RR_o(x) P_{ast}(x) dx - RR_o(TMREL_{as})}{\int_{x=0}^{11} RR_o(x) P_{ast}(x) dx}$$

where  $PAF_{oast}$  represents the population attributable fraction for outcome  $o$  (ie, hip or non-hip fracture), age group  $a$ , sex  $s$ , location  $g$ , and year  $t$ ;  $RR_o(x)$  is the relative risk at exposure level  $x$  for outcome  $o$  with the lowest

See Online for appendix 1

For the Global Health Data Exchange database see <http://ghdx.healthdata.org/>

For the GBD 2021 Sources Tool see <https://ghdx.healthdata.org/gbd-2021/sources>

observed exposure as  $l$  and the highest as  $u$ ;  $P_{\text{age}}(x)$  is the exposure at level  $x$  for age group  $a$ , sex  $s$ , location  $g$ , and year  $t$ ;  $\text{TMREL}_{\text{as}}$  is the TMREL for age group  $a$  and sex  $s$ .

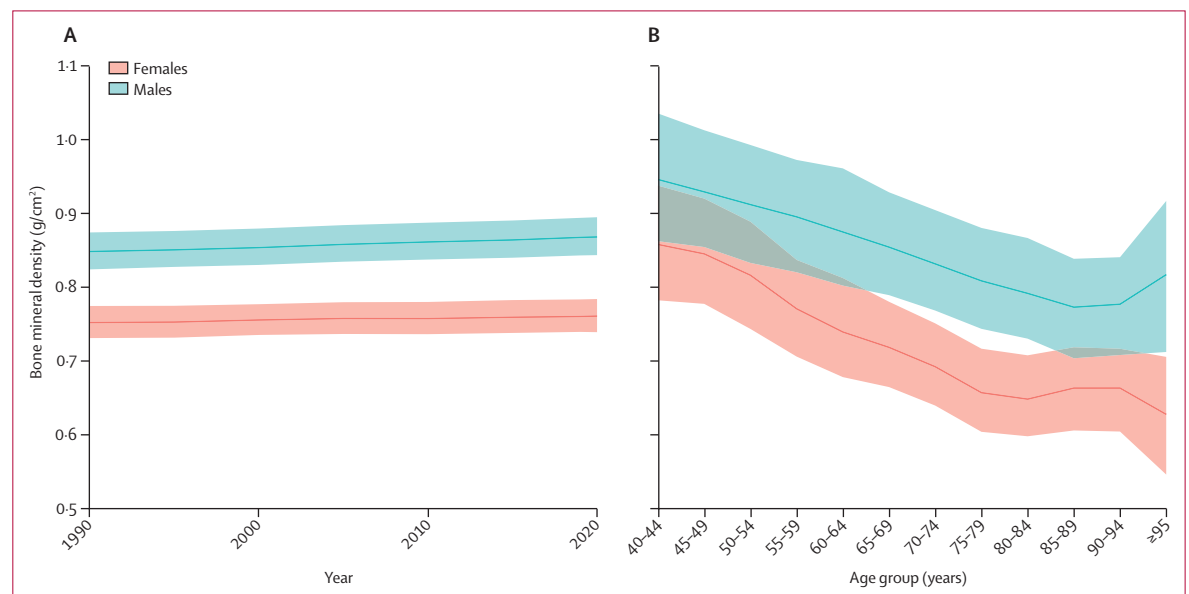
### Risk estimation for injuries

In view of the evidence showing the similar role of bone mineral density in both low-energy and high-energy trauma,<sup>38</sup> the estimation of burden attributable to low bone mineral density included fractures from unintentional injuries (falls, non-venomous animal contact, and exposure to mechanical forces [an aggregate of two causes: unintentional firearms and other exposure to mechanical forces]), from transportation injuries, including road injuries (pedestrian road injuries, cyclist road injuries, motorcyclist road injuries, motor vehicle road injuries) and other transport injuries (eg, trains, ferries, and aeroplanes), and interpersonal violence (physical violence by other means than firearms). The six distinct categories evaluated in the present analyses were road injuries, other transport injuries, falls, animal contact, exposure to mechanical forces, and interpersonal violence.

Methods to estimate the incidence of and deaths due to each injury have been described in detail previously,<sup>39</sup> with references for datasets available on the GBD 2021 Sources Tool. In summary, we utilised data from vital registration records, verbal autopsy, and police records for deaths, and from hospital and emergency or outpatient departments, insurance claims, and surveys that reported on injuries that warranted care for incidence. Death estimates were modelled with the Cause of Death Ensemble model tool,<sup>40</sup> which selects an ensemble of mixed-effects or spatiotemporal Gaussian

regression models of mortality rates or cause fractions. The hierarchical Bayesian meta-regression modelling tool, DisMod-MR 2.1, was used to estimate the incidence of each injury.<sup>18</sup> Years of life lost (YLLs) were the product of the number of deaths and standard life expectancy at each age of death,<sup>41</sup> and YLDs were the product of the disability weight corresponding to each ICD nature-of-injury code (N-code) and their probabilities of long-term and short-term impacts. DALYs were calculated as the sum of YLLs and YLDs.

There were two steps to estimate the fraction of fractures that were due to low bone mineral density for each injury. First, we estimated the fraction of each injury that resulted in a fracture. We calculated this across the six causes of injuries separately (by ICD external cause codes, E-codes) and then as a total. Briefly, we applied the ratio of fracture versus non-fracture injuries within each E-code. To derive these ratios, we used hospital and emergency department datasets with detailed diagnostic codes (ICD-9 and ICD-10) that were dual-coded with both the cause of injury (E-code; eg, falls or road injury) and nature of injury (N-code; eg, fracture or traumatic brain injury). We calculated the ratio of injuries attributable to fracture versus non-fracture injuries. These dual-coded data were available from 35 countries: Argentina, Brazil, Bulgaria, China, Chile, Colombia, Cyprus, Czech Republic, Denmark, Egypt, England, Estonia, Georgia, Hungary, Iceland, Iran, Italy, India, Kyrgyzstan, Latvia, Macedonia, Malta, Mauritius, Mexico, Mozambique, Netherlands, New Zealand, Norway, the Philippines, Portugal, Slovenia, Spain, Sweden, Uganda, the USA, and Zambia.<sup>39</sup> Second, we applied this ratio to the population attributable fractions for fractures by E-code



**Figure 1: Bone mineral density values for the global population by sex**

(A) Age-standardised mean bone mineral density values from 1990 to 2020. (B) Mean bone mineral density values in 2020 by 5-year age-strata. Shaded regions represent 95% UIs.

	Number of DALYs in 2020	Age-standardised rate of DALYs per 100000 in 2020	Percentage change in age-standardised rate of DALYs per 100000 from 1990 to 2020	Number of deaths in 2020	Age-standardised rate of deaths per 100000 in 2020	Percentage change in age-standardised rate of deaths per 100000 from 1990 to 2020
<b>Global</b>	<b>17200000</b> (14100000-20200000)	<b>207.6</b> (170.0-243.3)	<b>-12.7</b> (-16.5 to -8.6)	<b>477000</b> (411000-536000)	<b>6.0</b> (5.1-6.7)	<b>-4.0</b> (-10.9 to 3.5)
<b>Central Europe, eastern Europe, and central Asia</b>	<b>1170000</b> (878000-1460000)	<b>190.6</b> (142.3-236.0)	<b>-29.9</b> (-32.8 to -27.6)	<b>19100</b> (16200-21200)	<b>3.1</b> (2.6-3.4)	<b>-37.9</b> (-40.7 to -34.9)
Central Asia	97300 (73900-117000)	123.7 (94.3-148.3)	-31.5 (-34.9 to -28.6)	1510 (1280-1690)	2.2 (1.9-2.5)	-32.6 (-37.5 to -26.7)
Armenia	4100 (3270-4960)	102.2 (82.0-123.5)	-44.8 (-47.8 to -42.4)	78.8 (66.8-89.9)	2.0 (1.7-2.2)	-40.8 (-46.7 to -34.9)
Azerbaijan	8160 (5920-10000)	81.1 (59.3-98.7)	-41.7 (-46.8 to -37.2)	98.3 (77.4-119)	1.2 (0.9-1.5)	-53.6 (-62.8 to -43.4)
Georgia	12200 (9430-14500)	212.7 (164.5-255.0)	8.9 (2.1 to 14.5)	287 (237-324)	4.5 (3.7-5.1)	31.6 (17.8 to 43.3)
Kazakhstan	27400 (21400-33200)	149.2 (116.0-180.3)	-23.8 (-30.2 to -18.2)	385 (321-449)	2.3 (1.9-2.6)	-34.2 (-43.3 to -24.7)
Kyrgyzstan	6200 (5070-7430)	120.5 (97.2-143.7)	-38.7 (-43.6 to -33.4)	104 (86.7-123)	2.2 (1.8-2.5)	-39.6 (-47.7 to -29.9)
Mongolia	5310 (4100-6510)	183.1 (141.5-222.7)	9.8 (-1.5 to 20.6)	79.2 (63.2-100)	3.1 (2.5-3.8)	-6.2 (-27.4 to 16.1)
Tajikistan	5560 (4250-6850)	96.9 (74.2-118.1)	-41.1 (-46.5 to -35.2)	76.8 (59.8-93.3)	1.7 (1.3-2.1)	-38.8 (-50.7 to -23.6)
Turkmenistan	3550 (2590-4450)	82.0 (59.8-102.2)	-37.2 (-44.1 to -31.6)	45.2 (35.9-55.3)	1.1 (0.9-1.3)	-49.0 (-57.6 to -37.9)
Uzbekistan	24800 (18800-30300)	104.0 (79.1-126.5)	-39.2 (-43.5 to -35.4)	357 (298-417)	2.0 (1.7-2.2)	-45.3 (-51.4 to -38.9)
Central Europe	431000 (319000-530000)	204.8 (151.3-252.6)	-38.7 (-42.4 to -35.7)	8380 (7050-9410)	3.8 (3.2-4.2)	-53.5 (-56.9 to -50.7)
Albania	6210 (4350-7930)	150.6 (105.2-192.8)	-22.3 (-27.4 to -17.9)	72.8 (58.5-90.2)	1.8 (1.4-2.2)	-26.6 (-39.1 to -9.3)
Bosnia and Herzegovina	7760 (5380-9900)	135.7 (94.2-173.4)	-31.1 (-34.7 to -26.5)	83.2 (58.6-104)	1.5 (1.1-1.9)	-41.7 (-52.0 to -27.5)
Bulgaria	24400 (17300-30900)	182.4 (129.5-230.2)	-24.1 (-29.0 to -19.6)	333 (283-386)	2.4 (2.1-2.8)	-39.9 (-45.8 to -32.1)
Croatia	24300 (18500-29400)	267.1 (201.9-324.1)	-24.8 (-29.5 to -19.6)	627 (517-730)	6.5 (5.3-7.6)	-34.7 (-42.3 to -24.9)
Czechia	47500 (35400-57800)	224.5 (165.6-274.6)	-50.4 (-54.8 to -46.6)	1090 (921-1250)	4.8 (4.1-5.5)	-65.5 (-69.7 to -60.9)
Hungary	44400 (33200-54400)	227.1 (169.0-277.1)	-56.0 (-60.4 to -52.5)	997 (804-1170)	4.7 (3.8-5.6)	-72.3 (-76.0 to -68.9)
Montenegro	1710 (1240-2120)	180.3 (130.4-224.7)	-12.3 (-19.1 to -5.2)	27.3 (21.6-33.2)	3.1 (2.5-3.8)	-4.9 (-22.8 to 20.4)
North Macedonia	4800 (3410-6030)	161.4 (116.4-203.8)	14.5 (4.9 to 22.4)	75.4 (59.5-90.2)	3.3 (2.5-4.0)	72.1 (37.6 to 103.2)
Poland	142000 (107000-177000)	206.2 (154.6-256.2)	-35.8 (-39.6 to -32.2)	2900 (2340-3360)	3.9 (3.1-4.5)	-46.7 (-52.1 to -40.5)
Romania	68400 (48900-87100)	193.5 (138.2-246.3)	-34.2 (-38.9 to -30.5)	1030 (851-1190)	2.7 (2.3-3.2)	-41.2 (-48.4 to -34.9)
Serbia	24100 (17900-30200)	162.2 (121.7-203.6)	-25.5 (-31.0 to -20.0)	393 (315-473)	2.9 (2.3-3.5)	-35.5 (-45.7 to -22.4)
Slovakia	20900 (15200-26400)	229.9 (165.2-290.0)	-33.3 (-41.0 to -27.3)	361 (300-444)	4.0 (3.3-4.9)	-44.7 (-54.7 to -31.3)
Slovenia	13800 (10300-16700)	292.4 (215.9-355.5)	-29.4 (-34.1 to -25.3)	391 (303-453)	6.9 (5.4-8.0)	-20.2 (-30.8 to -10.8)
Eastern Europe	646000 (480000-812000)	195.0 (144.8-244.4)	-23.3 (-26.3 to -20.8)	9170 (7580-10300)	2.7 (2.3-3.1)	-24.3 (-29.4 to -19.4)
Belarus	31300 (23000-39300)	202.9 (148.9-254.4)	-9.8 (-14.7 to -4.5)	448 (374-520)	2.8 (2.4-3.3)	-8.1 (-17.0 to 3.1)
Estonia	3860 (2770-4760)	155.1 (111.2-191.5)	-48.7 (-51.7 to -45.0)	68.9 (56.2-82.8)	2.4 (2.0-2.9)	-50.4 (-56.6 to -42.9)
Latvia	6940 (5120-8430)	187.3 (137.0-226.8)	-50.4 (-53.7 to -47.3)	139 (116-165)	3.3 (2.8-4.0)	-50.9 (-56.2 to -44.3)
Lithuania	11500 (8440-14000)	208.2 (152.1-254.1)	-33.5 (-37.9 to -30.1)	225 (184-263)	3.6 (3.0-4.2)	-26.6 (-34.9 to -18.4)
Moldova	8250 (6220-10300)	145.1 (109.2-181.0)	-46.7 (-50.1 to -43.6)	128 (104-149)	2.2 (1.8-2.6)	-50.3 (-56.0 to -45.0)
Russia	455000 (339000-572000)	200.4 (149.1-251.3)	-20.2 (-24.0 to -16.9)	6760 (5680-7660)	2.9 (2.5-3.4)	-20.6 (-26.6 to -14.0)
Ukraine	130000 (95500-164000)	180.5 (133.6-226.9)	-29.4 (-34.8 to -23.9)	1400 (1090-1720)	1.9 (1.5-2.4)	-37.4 (-47.9 to -25.3)
<b>High income</b>	<b>4260000</b> (3210000-5270000)	<b>191.6</b> (143.1-236.7)	<b>-15.7</b> (-17.8 to -14.1)	<b>107000</b> (86600-121000)	<b>4.0</b> (3.3-4.5)	<b>-12.8</b> (-17.6 to -9.9)
Australasia	126000 (93400-158000)	239.3 (175.3-301.6)	-3.1 (-5.6 to -0.7)	3040 (2470-3480)	5.0 (4.1-5.7)	23.7 (14.9 to 35.8)
Australia	106000 (78900-133000)	238.4 (175.3-300.5)	0.9 (-2.0 to 4.1)	2620 (2120-3010)	5.1 (4.1-5.8)	30.4 (19.7 to 44.4)
New Zealand	20000 (14500-25200)	242.7 (174.4-304.6)	-18.8 (-20.8 to -16.4)	424 (343-497)	4.5 (3.7-5.2)	-3.2 (-9.8 to 4.3)
High-income Asia Pacific	622000 (454000-788000)	133.2 (96.1-167.4)	-32.7 (-36.0 to -30.7)	13100 (10300-15300)	2.2 (1.8-2.5)	-32.3 (-39.8 to -27.3)
Brunei	632 (477-756)	209.0 (158.6-246.0)	-30.1 (-36.9 to -23.8)	9.38 (8.01-10.6)	4.8 (4.1-5.6)	-26.0 (-38.0 to -8.7)
Japan	426000 (312000-540000)	113.8 (81.9-143.7)	-31.9 (-34.1 to -30.7)	9700 (7530-11300)	1.8 (1.5-2.1)	-27.8 (-35.4 to -23.4)
Singapore	9280 (6440-11700)	114.3 (79.7-144.7)	-30.3 (-36.8 to -26.0)	104 (90-115)	1.4 (1.2-1.5)	-50.8 (-54.7 to -47.3)
South Korea	186000 (137000-233000)	203.9 (149.5-255.1)	-44.7 (-51.4 to -40.4)	3290 (2600-3890)	3.8 (3.0-4.5)	-50.3 (-65.2 to -40.1)
High-income North America	1410000 (1070000-1710000)	219.8 (167.4-267.5)	11.1 (7.6 to 14.1)	35000 (29000-39400)	5.0 (4.2-5.6)	50.1 (42.4 to 55.2)
Canada	152000 (115000-187000)	204.2 (154.2-252.9)	-0.6 (-3.3 to 3.1)	4530 (3700-5280)	5.4 (4.5-6.3)	18.0 (9.8 to 26.5)
Greenland	227 (181-278)	367.4 (295.7-442.5)	-16.7 (-25.8 to -8.5)	6.11 (4.32-7.61)	12.0 (8.2-15.1)	-10.2 (-28.8 to 10.8)
USA	1250000 (956000-1520000)	221.2 (168.7-268.6)	12.1 (8.4 to 15.6)	30500 (25300-34200)	5.0 (4.2-5.5)	53.3 (45.2 to 58.3)

(Table continues on next page)

	Number of DALYs in 2020	Age-standardised rate of DALYs per 100000 in 2020	Percentage change in age-standardised rate of DALYs per 100000 from 1990 to 2020	Number of deaths in 2020	Age-standardised rate of deaths per 100000 in 2020	Percentage change in age-standardised rate of deaths per 100000 from 1990 to 2020
(Continued from previous page)						
Southern Latin America	142000 (108000–173000)	169.2 (128.4–205.9)	-16.3 (-19.7 to -13.7)	2710 (2280–2960)	3.1 (2.6–3.4)	-24.4 (-27.9 to -21.7)
Argentina	84200 (64100–102000)	155.6 (118.4–188.9)	-19.7 (-22.7 to -17.1)	1510 (1280–1660)	2.7 (2.3–3.0)	-30.9 (-34.8 to -27.8)
Chile	47500 (35800–58100)	194.4 (146.4–237.4)	-12.8 (-18.1 to -8.5)	942 (785–1060)	3.9 (3.2–4.3)	-19.6 (-24.5 to -13.9)
Uruguay	10500 (8090–12900)	193.0 (146.9–236.8)	-11.5 (-14.0 to -9.0)	250 (209–280)	3.9 (3.3–4.3)	-3.7 (-8.5 to 2.8)
Western Europe	1970000 (1470000–2430000)	200.0 (148.2–247.9)	-21.1 (-23.9 to -19.4)	52700 (42300–60500)	4.4 (3.5–5.0)	-24.8 (-29.1 to -21.8)
Andorra	460 (332–577)	301.6 (218.0–375.7)	4.4 (-8.8 to 13.4)	7.64 (5.81–9.75)	4.5 (3.5–5.8)	-19.7 (-39.2 to 4.8)
Austria	43000 (32400–52800)	225.3 (167.4–277.5)	-26.9 (-29.8 to -24.7)	1140 (930–1310)	5.0 (4.1–5.7)	-28.8 (-34.0 to -24.3)
Belgium	68600 (50700–84800)	279.2 (203.6–346.8)	1.2 (-1.8 to 4.5)	1640 (1350–1890)	5.4 (4.5–6.2)	-2.7 (-8.8 to 4.9)
Cyprus	4290 (3200–5260)	233.3 (174.9–285.4)	-45.3 (-52.1 to -39.8)	97.9 (76.3–120)	6.6 (4.7–8.0)	-64.1 (-73.4 to -55.6)
Denmark	21100 (15600–25900)	176.7 (130.7–216.7)	-43.0 (-46.3 to -40.2)	540 (431–615)	4.0 (3.2–4.5)	-55.3 (-58.8 to -52.3)
Finland	33900 (24900–41900)	263.8 (191.8–324.8)	-22.3 (-26.4 to -19.2)	789 (656–913)	5.1 (4.3–5.9)	-30.0 (-35.1 to -25.0)
France	371000 (273000–463000)	242.7 (177.9–303.9)	-25.8 (-30.3 to -22.6)	10400 (8100–12200)	5.1 (4.0–5.9)	-41.1 (-45.9 to -37.6)
Germany	427000 (323000–523000)	206.7 (154.1–253.9)	-15.6 (-18.7 to -13.2)	12400 (9910–14600)	5.1 (4.1–6.0)	-13.1 (-20.8 to -7.6)
Greece	36800 (27700–45200)	156.7 (116.1–192.5)	-30.2 (-32.1 to -28.7)	909 (757–1020)	2.9 (2.4–3.2)	-19.1 (-24.7 to -14.7)
Iceland	1120 (844–1370)	188.4 (140.1–230.2)	-14.1 (-17.6 to -10.6)	31.4 (24.7–37.3)	4.4 (3.5–5.2)	5.6 (-5.7 to 17.0)
Ireland	12400 (8980–15600)	162.1 (116.9–203.0)	-24.4 (-28.9 to -21.0)	217 (176–252)	2.7 (2.2–3.1)	-45.0 (-49.6 to -40.9)
Israel	15900 (11600–19700)	132.3 (96.3–163.3)	-21.9 (-26.3 to -18.9)	322 (262–371)	2.4 (1.9–2.7)	-35.4 (-39.8 to -31.5)
Italy	302000 (227000–373000)	194.6 (143.7–240.7)	-34.5 (-36.6 to -32.8)	7960 (6440–9170)	4.0 (3.2–4.5)	-41.8 (-44.6 to -40.0)
Luxembourg	2450 (1830–3030)	224.9 (167.1–277.5)	-21.9 (-25.2 to -18.4)	63.1 (52.1–71.8)	5.0 (4.2–5.7)	-17.2 (-24.3 to -9.2)
Malta	1690 (1230–2110)	178.6 (128.2–222.0)	-21.5 (-24.7 to -18.6)	37 (29.8–42.4)	3.4 (2.8–3.9)	-32.5 (-37.3 to -26.8)
Monaco	135 (96.1–171)	141.2 (98.8–175.5)	-8.4 (-14.2 to -2.3)	2.57 (1.94–3.22)	2.1 (1.6–2.6)	-14.4 (-30.2 to 17.0)
Netherlands	87600 (67800–106000)	236.9 (181.4–288.6)	24.2 (19.6 to 28.9)	3170 (2520–3690)	7.9 (6.3–9.1)	52.3 (42.0 to 65.1)
Norway	24200 (18300–29500)	227.0 (169.8–278.3)	-28.8 (-31.7 to -26.8)	786 (623–910)	6.3 (5.1–7.3)	-19.5 (-25.9 to -15.5)
Portugal	37800 (28500–46400)	153.1 (114.9–187.6)	-40.7 (-43.3 to -38.0)	981 (794–1120)	3.3 (2.7–3.7)	-36.8 (-42.2 to -32.5)
San Marino	107 (76.2–134)	160.4 (113.1–201.0)	-10.6 (-17.8 to -3.6)	2.04 (1.52–2.61)	2.4 (1.8–3.1)	-14.7 (-31.1 to 8.8)
Spain	158000 (114000–196000)	158.1 (113.2–196.4)	-17.3 (-22.8 to -11.3)	2890 (2350–3340)	2.3 (1.9–2.6)	-26.8 (-32.0 to -21.7)
Sweden	44100 (33200–54100)	191.8 (142.2–237.2)	-17.4 (-19.5 to -15.2)	1230 (1030–1420)	4.5 (3.7–5.1)	-8.0 (-13.2 to -3.2)
Switzerland	48100 (35700–60100)	247.8 (181.9–308.7)	-32.9 (-35.7 to -30.9)	1270 (1000–1500)	5.3 (4.2–6.2)	-41.7 (-47.3 to -37.0)
UK	224000 (167000–278000)	169.8 (125.5–211.3)	-1.6 (-3.1 to 0.2)	5800 (4720–6540)	3.8 (3.1–4.3)	25.9 (20.7 to 29.5)
<b>Latin America and Caribbean</b>	<b>1070000 (861000–1230000)</b>	<b>177.7 (142.6–204.1)</b>	<b>-26.3 (-28.6 to -23.9)</b>	<b>27600 (23100–30700)</b>	<b>4.7 (3.9–5.3)</b>	<b>-23.6 (-27.2 to -20.1)</b>
Andean Latin America	93300 (75300–110000)	159.2 (128.6–187.8)	-10.8 (-19.4 to -0.7)	2640 (2170–3170)	4.7 (3.9–5.6)	-6.0 (-19.9 to 8.6)
Bolivia	16300 (12500–20400)	180.3 (139.6–225.7)	-22.2 (-34.4 to -7.0)	448 (346–577)	5.6 (4.4–7.2)	-22.7 (-37.8 to -3.3)
Ecuador	28700 (22800–34200)	187.1 (148.5–221.8)	-10.6 (-20.3 to 1.1)	824 (637–1000)	6.1 (4.7–7.3)	0.5 (-15.1 to 19.1)
Peru	48300 (38700–57800)	142.4 (114.0–170.7)	-6.2 (-17.4 to 9.6)	1370 (1080–1690)	4.0 (3.2–5.0)	-0.6 (-19.5 to 22.9)
Caribbean	93800 (75200–109000)	176.9 (142.1–206.2)	-4.9 (-11.1 to 0.5)	3320 (2720–3810)	6.2 (5.1–7.1)	-5.9 (-13.1 to 0.8)
Antigua and Barbuda	100 (77–122)	98.5 (76.8–120.3)	-3.2 (-8.9 to 3.6)	2.34 (1.98–2.66)	2.7 (2.3–3.0)	14.9 (5.1 to 26.9)
The Bahamas	506 (410–616)	126.1 (102.5–152.4)	-13.3 (-23.5 to 1.0)	13.9 (11.5–16.8)	3.9 (3.2–4.8)	-3.3 (-19.2 to 17.0)
Barbados	452 (357–551)	93.5 (73.6–113.8)	-2.0 (-10.6 to 8.5)	14.5 (11.6–17.7)	3.0 (2.4–3.6)	5.8 (-7.6 to 20.5)
Belize	414 (330–485)	136.5 (108.8–160.5)	10.5 (3.1 to 18.1)	10.0 (8.45–11.5)	3.7 (3.1–4.3)	14.1 (1.3 to 24.7)
Bermuda	115 (88.4–138)	88.8 (68.6–106.7)	-35.4 (-42.2 to -29.3)	3.55 (2.99–4.27)	2.5 (2.0–3.0)	-41.6 (-48.0 to -33.1)
Cuba	48200 (39200–56100)	236.9 (192.7–275.0)	0.3 (-6.3 to 7.8)	2070 (1710–2400)	9.5 (7.9–11.0)	2.6 (-6.9 to 13.5)
Dominica	98.7 (78.2–117)	111.2 (88.2–131.7)	-4.0 (-15.7 to 7.2)	3.13 (2.49–3.81)	3.5 (2.8–4.2)	1.6 (-19.9 to 20.7)
Dominican Republic	13000 (9770–15200)	133.7 (100.8–157.7)	-6.3 (-21.0 to 7.6)	326 (240–402)	3.6 (2.7–4.5)	-22.1 (-42.3 to -5.1)
Grenada	153 (126–180)	144.1 (118.3–168.8)	13.4 (5.6 to 20.6)	4.93 (4.28–5.62)	5.5 (4.7–6.3)	39.2 (25.5 to 52.9)
Guyana	1200 (942–1420)	196.6 (155.3–229.5)	1.1 (-10.0 to 16.6)	35.0 (28.1–42.7)	7.2 (5.8–8.5)	5.0 (-12.5 to 24.7)
Haiti	12400 (9150–15900)	170.2 (127.8–215.2)	-16.8 (-32.6 to 1.4)	334 (241–428)	6.0 (4.5–7.7)	-11.5 (-33.4 to 12.0)
Jamaica	2500 (1910–3070)	79.9 (61.1–98.4)	13.8 (4.8 to 24.8)	69.8 (55.3–84.9)	2.0 (1.6–2.5)	37.9 (15.8 to 67.2)
Puerto Rico	8090 (6170–9690)	113.1 (86.1–135.8)	-17.2 (-24.4 to -11.6)	221 (178–254)	2.6 (2.1–3.0)	-37.2 (-44.6 to -29.1)
Saint Kitts and Nevis	78.4 (61.5–95.1)	124.0 (98.9–149.6)	-14.9 (-21.7 to -8.9)	1.97 (1.64–2.26)	3.9 (3.3–4.5)	-13.4 (-21.5 to -3.9)

(Table continues on next page)

	Number of DALYs in 2020	Age-standardised rate of DALYs per 100000 in 2020	Percentage change in age-standardised rate of DALYs per 100000 from 1990 to 2020	Number of deaths in 2020	Age-standardised rate of deaths per 100000 in 2020	Percentage change in age-standardised rate of deaths per 100000 from 1990 to 2020
(Continued from previous page)						
Saint Lucia	228 (180–272)	103.3 (81.6–122.9)	-29.2 (-35.9 to -22.0)	5.92 (4.85–6.89)	2.9 (2.3–3.3)	-37.7 (-46.5 to -27.8)
Saint Vincent and the Grenadines	162 (130–191)	122.8 (99.5–144.4)	5.4 (-0.7 to 13.3)	5.09 (4.41–5.73)	4.4 (3.8–4.9)	19.3 (10.0 to 31.3)
Suriname	861 (685–998)	139.9 (111.0–161.7)	-8.2 (-16.6 to 1.5)	25.1 (21.1–29.7)	4.4 (3.6–5.2)	-9.5 (-22.4 to 5.3)
Trinidad and Tobago	1890 (1490–2270)	103.0 (81.4–123.7)	-23.6 (-31.3 to -15.1)	53.7 (42.7–63.9)	3.0 (2.4–3.6)	-35.1 (-44.3 to -23.6)
Virgin Islands	211 (171–251)	125.5 (100.7–150.4)	-11.5 (-21.3 to -0.6)	5.97 (4.99–7.17)	3.8 (3.1–4.6)	-25.9 (-38.9 to -11.7)
Central Latin America	385000 (298000–450000)	156.7 (121.5–183.1)	-39.9 (-43.1 to -37.1)	8510 (7390–9550)	3.6 (3.1–4.0)	-46.4 (-49.9 to -42.4)
Colombia	66200 (51000–78900)	120.8 (93.0–144.1)	-40.5 (-44.8 to -36.5)	1530 (1260–1810)	2.7 (2.2–3.2)	-44.7 (-51.1 to -38.4)
Costa Rica	8870 (6870–10500)	167.3 (129.9–198.3)	-25.4 (-30.9 to -20.0)	259 (209–297)	4.8 (3.9–5.5)	-30.5 (-39.0 to -21.9)
El Salvador	11600 (9290–13600)	188.1 (151.2–221.5)	-19.8 (-27.4 to -13.3)	320 (264–376)	5.0 (4.1–5.7)	-23.2 (-34.3 to -11.4)
Guatemala	21000 (16600–24700)	183.1 (145.1–215.1)	-19.2 (-25.2 to -13.5)	436 (375–493)	4.4 (3.7–4.9)	-41.4 (-47.9 to -36.3)
Honduras	11600 (9190–13900)	182.2 (145.3–214.3)	-3.8 (-14.8 to 10.8)	301 (248–362)	5.4 (4.6–6.4)	6.2 (-11.3 to 27.0)
Mexico	203000 (158000–239000)	167.7 (130.8–197.5)	-47.0 (-50.1 to -44.5)	4250 (3530–4830)	3.8 (3.1–4.3)	-54.8 (-58.1 to -50.6)
Nicaragua	6310 (4970–7360)	145.1 (114.3–169.5)	-18.0 (-24.2 to -10.4)	149 (121–171)	4.1 (3.4–4.9)	-16.2 (-28.8 to -1.4)
Panama	4570 (3500–5480)	105.0 (80.5–126.1)	-38.4 (-43.9 to -33.3)	96.7 (79.2–111)	2.2 (1.8–2.5)	-48.4 (-54.4 to -41.5)
Venezuela	52000 (39800–63700)	170.2 (130.3–208.1)	-21.2 (-30.2 to -9.6)	1160 (910–1440)	4.0 (3.1–4.9)	-26.3 (-39.1 to -9.5)
Tropical Latin America	503000 (411000–582000)	202.2 (165.8–234.3)	-19.8 (-22.5 to -17.9)	13100 (10800–14700)	5.5 (4.6–6.2)	-6.4 (-12.4 to -2.5)
Brazil	493000 (403000–572000)	202.9 (166.2–235.6)	-20.4 (-23.0 to -18.4)	12900 (10600–14400)	5.6 (4.6–6.2)	-7.3 (-13.1 to -3.3)
Paraguay	9810 (7750–11900)	169.4 (134.4–205.4)	15.0 (0.1 to 35.3)	255 (189–323)	4.6 (3.4–5.8)	43.4 (5.5 to 86.3)
<b>North Africa and Middle East</b>	<b>792000 (652000–913000)</b>	<b>168.6 (139.1–193.8)</b>	<b>-24.2 (-28.3 to -20.3)</b>	<b>18100 (15800–20400)</b>	<b>4.6 (4.1–5.2)</b>	<b>-26.1 (-31.5 to -19.3)</b>
Afghanistan	39900 (31800–50200)	266.7 (212.5–327.1)	3.0 (-14.6 to 33.6)	1110 (837–1370)	10.7 (7.5–13.4)	4.1 (-13.8 to 33.4)
Algeria	57600 (46200–69800)	161.7 (129.8–195.0)	-31.1 (-38.8 to -21.3)	1290 (1060–1580)	4.4 (3.6–5.3)	-25.2 (-37.7 to -8.1)
Bahrain	1240 (964–1470)	102.8 (82.0–121.3)	-36.8 (-44.2 to -30.2)	20.3 (16.4–23.5)	3.4 (2.8–4.0)	-40.8 (-50.3 to -31.5)
Egypt	74600 (56200–87000)	110.7 (85.1–130.6)	-22.6 (-28.6 to -16.5)	1270 (1020–1570)	2.4 (1.9–3.1)	-24.9 (-38.2 to -13.2)
Iran	131000 (109000–152000)	165.5 (136.4–192.5)	-42.2 (-45.8 to -38.6)	3050 (2670–3500)	4.3 (3.7–5.0)	-41.8 (-46.7 to -36.6)
Iraq	43100 (33600–52500)	158.3 (124.5–188.8)	-24.3 (-36.1 to -10.8)	869 (683–1110)	3.8 (3.0–4.6)	-16.4 (-36.1 to 6.6)
Jordan	7650 (6170–9070)	103.1 (82.8–122.2)	-40.9 (-49.4 to -32.9)	154 (124–186)	2.8 (2.2–3.4)	-46.7 (-57.2 to -35.4)
Kuwait	4050 (3100–4830)	123.4 (95.9–145.9)	-33.5 (-39.6 to -27.7)	88.7 (71.7–104)	3.8 (3.0–4.4)	-23.1 (-32.4 to -12.9)
Lebanon	5950 (4800–7020)	113.1 (91.3–133.3)	-45.5 (-51.9 to -37.6)	174 (146–206)	3.4 (2.9–4.0)	-57.6 (-66.2 to -39.0)
Libya	14600 (11700–18100)	234.8 (185.7–296.9)	4.3 (-17.3 to 39.4)	361 (268–494)	6.6 (4.9–9.4)	12.2 (-22.0 to 77.4)
Morocco	55900 (41500–68900)	173.8 (130.2–213.3)	-22.3 (-32.1 to -9.5)	1250 (919–1580)	4.5 (3.3–5.7)	-17.8 (-33.7 to 5.3)
Oman	5600 (4560–6530)	269.5 (220.5–312.0)	-47.3 (-57.3 to -34.5)	123 (99.8–147)	9.3 (7.5–10.9)	-40.6 (-52.9 to -20.5)
Palestine	2700 (2150–3170)	113.9 (92.0–133.2)	-25.0 (-35.6 to -16.2)	55.7 (47.9–64.4)	3.2 (2.7–3.6)	-36.3 (-48.2 to -24.7)
Qatar	2820 (2130–3530)	193.8 (148.6–237.5)	-37.1 (-49.7 to -22.9)	51.2 (38.7–66.5)	6.8 (5.1–8.5)	-50.8 (-62.4 to -36.3)
Saudi Arabia	99800 (78500–120000)	385.4 (304.4–459.4)	-13.2 (-26.3 to 2.1)	1680 (1300–2100)	7.8 (6.2–9.3)	-23.9 (-40.0 to -1.5)
Sudan	37300 (29400–45100)	184.7 (147.3–221.8)	-28.5 (-38.7 to -14.1)	972 (765–1220)	5.7 (4.5–7.1)	-29.0 (-42.0 to -8.9)
Syria	15400 (11900–19200)	120.2 (94.6–147.7)	-15.0 (-27.8 to 1.1)	314 (239–396)	3.2 (2.5–3.8)	-15.2 (-34.7 to 9.0)
Tunisia	20300 (16400–25800)	155.4 (126.4–197.7)	-23.3 (-34.9 to -6.1)	476 (346–638)	4.0 (2.9–5.4)	-28.6 (-47.0 to -3.9)
Türkiye	118000 (95800–140000)	133.4 (108.1–159.0)	-17.9 (-27.4 to -5.5)	3630 (2860–4440)	4.4 (3.4–5.4)	-24.3 (-39.3 to -0.1)
United Arab Emirates	12300 (9290–15200)	184.3 (143.1–224.4)	-41.1 (-52.5 to -27.9)	159 (122–209)	5.3 (4.2–6.6)	-47.3 (-59.6 to -30.5)
Yemen	40800 (31300–51700)	261.1 (204.3–324.4)	-26.2 (-43.7 to -6.5)	1010 (762–1320)	7.8 (6.0–10.0)	-23.5 (-44.3 to 2.2)
<b>South Asia</b>	<b>4120000 (3510000–4620000)</b>	<b>312.3 (266.5–350.2)</b>	<b>1.9 (-6.5 to 9.7)</b>	<b>140000 (119000–157000)</b>	<b>12.5 (10.6–14.1)</b>	<b>6.3 (-8.6 to 19.9)</b>
Bangladesh	112000 (90400–142000)	83.9 (67.2–106.6)	-5.8 (-21.3 to 8.0)	3110 (2280–4330)	2.7 (2.0–3.8)	-6.0 (-25.2 to 17.8)
Bhutan	1430 (1060–1830)	274.2 (202.6–351.1)	-13.2 (-33.1 to 9.9)	54.6 (35.1–76.2)	12.1 (7.6–17.0)	-18.1 (-39.3 to 15.3)
India	3780000 (3220000–4260000)	354.6 (302.5–399.4)	1.0 (-7.3 to 9.5)	129000 (110000–146000)	14.2 (12.0–16.2)	5.8 (-9.2 to 19.9)
Nepal	46500 (34700–61300)	229.6 (172.0–305.9)	2.0 (-12.8 to 18.4)	1330 (959–2080)	8.6 (6.2–13.1)	4.7 (-19.3 to 36.3)
Pakistan	178000 (142000–213000)	162.3 (127.6–195.2)	-8.9 (-23.6 to 7.5)	5810 (4500–7130)	7.1 (5.3–8.8)	-18.5 (-36.5 to 3.3)

(Table continues on next page)

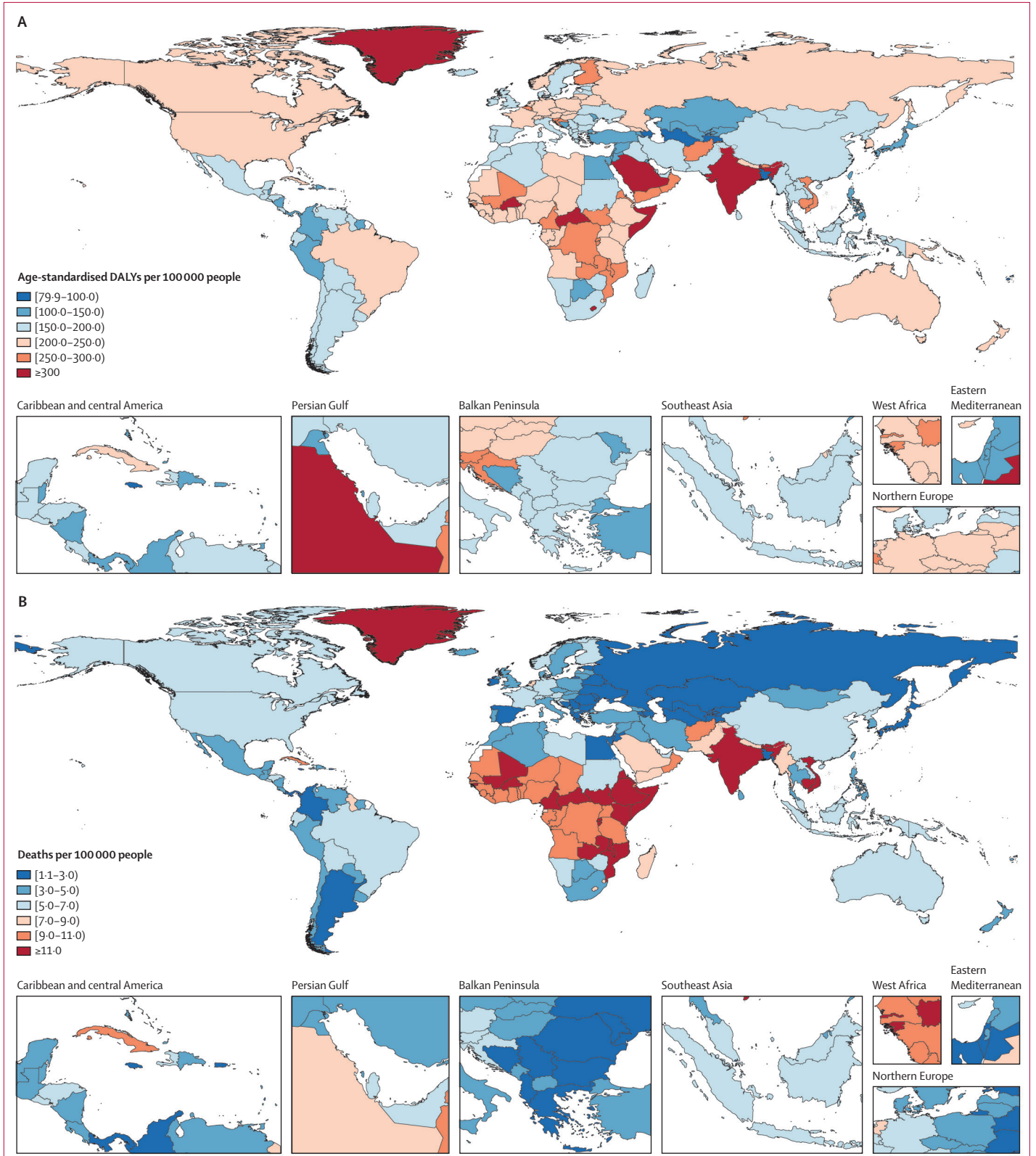
	Number of DALYs in 2020	Age-standardised rate of DALYs per 100000 in 2020	Percentage change in age-standardised rate of DALYs per 100000 from 1990 to 2020	Number of deaths in 2020	Age-standardised rate of deaths per 100000 in 2020	Percentage change in age-standardised rate of deaths per 100000 from 1990 to 2020
(Continued from previous page)						
<b>Southeast Asia, east Asia, and Oceania</b>	<b>4760000 (3960000–5700000)</b>	<b>178.2 (146.8–214.4)</b>	<b>-8.3 (-21.8 to 4.8)</b>	<b>131000 (99 600–160 000)</b>	<b>5.5 (4.1–6.8)</b>	<b>-2.6 (-28.3 to 19.2)</b>
East Asia	3650000 (3020000–4440000)	177.2 (146.0–216.4)	-3.2 (-22.8 to 15.4)	98000 (71700–123000)	5.3 (3.8–6.7)	9.6 (-31.5 to 44.3)
China	3540000 (2920000–4320000)	178.8 (146.8–219.1)	-2.0 (-22.4 to 17.4)	94900 (68600–120000)	5.3 (3.8–6.8)	11.3 (-31.5 to 48.0)
North Korea	55500 (43800–69200)	168.2 (134.3–209.0)	6.7 (-13.7 to 28.1)	1590 (1280–2090)	5.3 (4.3–6.9)	20.0 (-8.8 to 55.6)
Taiwan (province of China)	45900 (36500–52500)	113.3 (90.1–129.4)	-53.3 (-57.5 to -49.5)	1520 (1210–1730)	3.6 (2.9–4.1)	-45.6 (-52.5 to -39.3)
Oceania	13100 (10800–15800)	187.2 (152.5–225.0)	-0.8 (-13.1 to 13.2)	291 (223–376)	5.3 (4.0–7.0)	-9.7 (-27.8 to 16.6)
American Samoa	54.7 (43.8–62.9)	120.5 (96.8–137.9)	-8.3 (-19.0 to 3.9)	1.56 (1.28–1.88)	4.1 (3.3–5.0)	-5.5 (-25.5 to 20.4)
Cook Islands	29.4 (23.5–34.6)	120.6 (96.3–142.1)	-28.8 (-39.0 to -16.9)	0.778 (0.619–0.966)	3.3 (2.6–4.1)	-38.1 (-50.3 to -22.0)
Federated States of Micronesia	114 (88.9–141)	176.5 (137.2–214.3)	3.0 (-14.2 to 29.8)	3.02 (2.29–3.79)	6.5 (5.0–8.0)	11.7 (-11.8 to 49.4)
Fiji	672 (531–804)	97.9 (78.5–117.1)	-9.9 (-21.3 to 6.0)	17.9 (13.9–20.8)	3.5 (2.8–4.2)	-0.9 (-21.6 to 24.7)
Guam	189 (151–221)	98.7 (79.0–115.0)	-23.6 (-31.8 to -16.8)	5.76 (4.79–6.72)	3.0 (2.5–3.5)	-33.2 (-47.0 to -19.1)
Kiribati	57.1 (44.4–69.1)	84.0 (67.4–99.8)	5.8 (-9.5 to 24.0)	1.19 (0.91–1.49)	2.5 (1.9–3.1)	28.4 (-0.4 to 63.2)
Marshall Islands	53.9 (40.9–65.7)	161.7 (125.4–193.2)	1.9 (-12.4 to 16.6)	1.33 (1.03–1.67)	5.9 (4.5–7.2)	7.1 (-12.5 to 31.2)
Nauru	10.5 (7.7–13.4)	208.6 (158.2–260.2)	-17.7 (-31.9 to 2.0)	0.220 (0.157–0.294)	6.4 (4.7–8.9)	-36.3 (-50.0 to -14.9)
Niue	2.69 (2.09–3.35)	126.0 (97.8–157.5)	-4.9 (-18.7 to 11.2)	0.0875 (0.0685–0.112)	4.2 (3.3–5.3)	-1.9 (-27.2 to 28.4)
Northern Mariana Islands	77.4 (60.2–93.7)	161.1 (126.6–192.7)	-12.2 (-25.8 to 2.2)	1.74 (1.46–2.16)	5.0 (4.0–6.0)	-14.2 (-31.8 to 7.9)
Palau	44.5 (36.2–53.3)	242.4 (204.5–282.6)	-6.3 (-19.3 to 8.7)	1.21 (0.99–1.48)	9.7 (8.0–12.0)	-0.3 (-21.2 to 25.5)
Papua New Guinea	9910 (7970–12 200)	211.9 (170.1–260.1)	-3.8 (-20.1 to 15.1)	214 (154–287)	5.8 (4.0–8.2)	-13.5 (-37.9 to 21.8)
Samoa	211 (165–250)	146.7 (116.2–172.9)	4.5 (-10.4 to 23.0)	6.19 (4.99–7.53)	4.9 (3.9–6.0)	4.2 (-20.4 to 31.3)
Solomon Islands	758 (589–956)	242.1 (191.5–298.2)	-4.7 (-20.5 to 16.5)	13.8 (10.3–18.1)	5.9 (4.3–7.9)	-15.2 (-35.4 to 15.8)
Tokelau	1.62 (1.25–2.03)	123.8 (96.7–153.5)	-24.8 (-35.2 to -9.9)	0.0498 (0.0374–0.0667)	4.2 (3.2–5.5)	-37.0 (-50.8 to -16.7)
Tonga	79.9 (63.0–95.5)	99.8 (79.1–119.3)	-12.0 (-25.1 to 5.1)	2.64 (2.06–3.34)	3.4 (2.7–4.3)	-8.6 (-31.4 to 19.7)
Tuvalu	15.6 (12.8–18.5)	162.5 (132.7–192.8)	-13.5 (-23.2 to -0.2)	0.451 (0.343–0.556)	5.6 (4.1–6.9)	-16.6 (-32.9 to 4.6)
Vanuatu	252 (195–301)	145.8 (113.6–174.2)	-2.9 (-19.0 to 17.5)	6.72 (5.06–8.15)	5.0 (3.7–6.0)	1.2 (-19.8 to 30.9)
Southeast Asia	1100000 (922000–1250000)	183.8 (151.4–208.5)	-21.0 (-26.9 to -15.1)	32800 (26800–37800)	6.4 (5.0–7.5)	-21.2 (-31.7 to -11.0)
Cambodia	31900 (25700–38200)	288.8 (234.3–343.1)	11.1 (-4.9 to 27.8)	1060 (810–1290)	11.8 (8.8–14.5)	16.9 (-6.9 to 41.9)
Indonesia	351000 (289000–411000)	173.1 (141.3–204.5)	-25.6 (-35.8 to -17.0)	10300 (8270–12200)	6.5 (4.9–7.8)	-14.6 (-32.1 to 1.4)
Laos	7130 (5790–8730)	161.7 (131.6–196.0)	-19.6 (-34.2 to 2.1)	202 (161–251)	5.7 (4.6–7.0)	-15.1 (-32.6 to 16.4)
Malaysia	48100 (39400–56300)	176.6 (145.2–206.8)	-10.1 (-20.4 to 3.0)	1370 (1120–1630)	5.6 (4.6–6.7)	-8.0 (-22.9 to 8.7)
Maldives	302 (237–365)	101.1 (79.7–122.4)	-25.5 (-36.5 to -12.0)	7.35 (6.05–9.21)	3.0 (2.3–3.7)	-27.0 (-43.0 to 1.8)
Mauritius	1750 (1410–2040)	98.4 (79.1–114.2)	-8.3 (-17.4 to 0.3)	41.8 (34.6–48.3)	2.4 (2.0–2.8)	-7.0 (-19.0 to 5.2)
Myanmar	87000 (72500–107000)	194.8 (160.3–233.0)	-23.3 (-35.0 to -8.6)	2630 (2170–3230)	7.0 (5.6–8.5)	-24.5 (-41.1 to -3.5)
Philippines	99700 (82200–116000)	126.7 (103.8–146.0)	-4.4 (-14.3 to 4.3)	2580 (2150–2970)	4.0 (3.2–4.6)	7.0 (-12.3 to 26.0)
Seychelles	129 (103–148)	109.1 (87.1–125.0)	-15.5 (-23.4 to -0.7)	3.03 (2.51–3.65)	2.8 (2.4–3.4)	-18.2 (-30.2 to 8.4)
Sri Lanka	40600 (32400–51200)	163.8 (130.5–205.6)	-20.6 (-33.7 to -7.1)	983 (717–1240)	4.4 (3.3–5.4)	-42.5 (-58.4 to -25.5)
Thailand	171000 (140000–200000)	161.4 (131.7–189.4)	-30.4 (-40.1 to -20.1)	4240 (3290–5300)	4.1 (3.1–5.1)	-41.6 (-53.5 to -26.5)
Timor-Leste	1160 (953–1430)	148.0 (122.5–181.2)	3.1 (-16.0 to 27.1)	34.9 (27.2–44.2)	5.3 (4.1–6.6)	9.2 (-18.0 to 43.6)
Viet Nam	264000 (210000–318000)	292.0 (225.8–351.8)	-2.1 (-17.7 to 14.6)	9340 (5950–12300)	11.8 (7.0–16.1)	-1.8 (-24.4 to 27.5)
<b>Sub-Saharan Africa</b>	<b>1040000 (907000–1160000)</b>	<b>224.8 (197.9–250.5)</b>	<b>-9.5 (-18.2 to -1.6)</b>	<b>35300 (31300–39500)</b>	<b>9.8 (8.6–10.9)</b>	<b>-2.2 (-12.8 to 8.2)</b>
Central sub-Saharan Africa	151000 (125000–181000)	260.1 (215.7–311.0)	-3.0 (-19.4 to 15.9)	4460 (3460–5440)	10.1 (7.9–12.8)	3.2 (-17.4 to 24.1)
Angola	29400 (23200–36400)	242.7 (199.2–291.9)	-18.3 (-34.9 to 3.7)	847 (667–1040)	9.7 (8.0–11.8)	-12.7 (-30.0 to 10.1)
Central African Republic	8730 (6780–11300)	338.6 (266.3–425.1)	-7.3 (-24.6 to 15.0)	238 (182–309)	12.5 (9.8–15.7)	-5.1 (-23.1 to 14.2)
Congo (Brazzaville)	7210 (5410–9050)	241.2 (187.7–293.6)	-25.6 (-41.7 to -6.6)	209 (157–264)	9.4 (7.1–11.9)	-21.8 (-38.2 to -3.1)
DR Congo	102000 (80300–127000)	263.7 (208.9–324.8)	6.0 (-16.9 to 29.0)	3050 (2230–3830)	10.1 (7.5–13.5)	13.1 (-14.5 to 40.4)
Equatorial Guinea	1080 (791–1430)	209.0 (155.0–266.9)	-33.1 (-50.9 to -9.0)	33.1 (23.3–44.2)	8.2 (5.9–11.0)	-28.4 (-50.0 to 0.7)
Gabon	2650 (2080–3280)	240.1 (191.2–293.7)	-12.5 (-28.2 to 10.9)	83.4 (64.6–105)	9.3 (7.2–11.9)	-4.5 (-22.8 to 23.1)

(Table continues on next page)

	Number of DALYs in 2020	Age-standardised rate of DALYs per 100000 in 2020	Percentage change in age-standardised rate of DALYs per 100000 from 1990 to 2020	Number of deaths in 2020	Age-standardised rate of deaths per 100000 in 2020	Percentage change in age-standardised rate of deaths per 100000 from 1990 to 2020
(Continued from previous page)						
Eastern sub-Saharan Africa	366000 (318000–409000)	237.7 (207.1–265.6)	-14.6 (-23.5 to -6.1)	13600 (12000–15200)	11.4 (10.0–12.7)	-8.4 (-18.8 to 3.3)
Burundi	10900 (8860–13400)	250.9 (202.4–305.5)	-22.5 (-39.4 to -1.5)	379 (296–473)	11.7 (9.2–14.7)	-20.7 (-39.3 to 1.0)
Comoros	1170 (931–1410)	243.4 (193.5–295.5)	-23.5 (-37.7 to -4.6)	47.8 (36.7–57.6)	11.3 (8.8–14.0)	-24.6 (-40.1 to -4.8)
Djibouti	1310 (1030–1680)	226.4 (182.2–282.8)	4.2 (-20.1 to 30.1)	42.8 (33.6–55.7)	10.7 (8.4–13.7)	13.1 (-15.2 to 46.3)
Eritrea	7640 (5890–9580)	287.8 (225.1–348.2)	3.2 (-13.0 to 23.0)	243 (182–302)	13.0 (10.0–15.5)	2.9 (-16.0 to 21.3)
Ethiopia	88900 (76200–100000)	231.1 (200.0–258.9)	-39.2 (-50.1 to -29.2)	3590 (3120–3970)	11.7 (9.9–13.1)	-32.1 (-45.0 to -17.6)
Kenya	48700 (41000–55900)	243.3 (208.1–281.1)	11.6 (-5.4 to 33.2)	1820 (1540–2160)	12.1 (10.2–14.2)	15.8 (-6.8 to 45.2)
Madagascar	18800 (15300–23200)	177.6 (144.7–215.0)	-7.7 (-23.8 to 14.2)	602 (488–752)	8.0 (6.4–9.8)	-3.5 (-23.8 to 22.4)
Malawi	17700 (14800–20600)	257.6 (216.2–298.6)	9.0 (-9.2 to 26.2)	685 (577–790)	12.6 (10.2–14.6)	18.3 (-3.2 to 40.9)
Mozambique	31400 (24000–40400)	294.7 (226.0–375.8)	16.2 (-6.2 to 44.0)	1110 (837–1480)	13.4 (9.9–18.1)	22.0 (-6.4 to 60.4)
Rwanda	14200 (11400–17300)	253.3 (206.6–309.6)	-33.3 (-48.0 to -16.7)	526 (419–657)	12.2 (9.5–15.7)	-28.9 (-45.4 to -8.7)
Somalia	21700 (16300–27700)	318.3 (246.6–389.3)	21.9 (-2.5 to 48.2)	687 (505–862)	14.3 (11.1–18.0)	36.9 (7.2 to 64.6)
South Sudan	9760 (7610–12300)	251.6 (198.6–312.5)	14.1 (-11.8 to 40.7)	352 (273–442)	11.7 (9.1–14.8)	18.5 (-8.1 to 47.4)
Tanzania	46900 (37900–57100)	201.0 (163.7–242.6)	-15.3 (-26.0 to 1.2)	1770 (1440–2180)	9.5 (7.7–11.8)	-14.2 (-26.9 to 4.5)
Uganda	30100 (24000–36900)	224.6 (179.5–274.5)	-3.9 (-25.5 to 20.8)	1100 (876–1380)	10.5 (8.3–13.0)	-2.4 (-24.9 to 31.5)
Zambia	17000 (13600–21000)	262.0 (212.0–319.0)	-5.6 (-23.7 to 14.0)	597 (467–732)	12.4 (9.7–15.1)	-4.3 (-21.3 to 16.0)
Southern sub-Saharan Africa	113000 (94200–125000)	177.0 (147.9–197.1)	-18.4 (-24.4 to -10.6)	2790 (2440–3060)	4.9 (4.3–5.4)	-8.7 (-19.2 to 6.1)
Botswana	1900 (1590–2330)	123.3 (104.1–149.3)	-28.4 (-42.8 to -11.1)	41.9 (34.8–52.9)	3.4 (2.8–4.1)	-40.6 (-55.7 to -20.8)
Eswatini	1710 (1280–2220)	246.9 (191.0–314.9)	14.9 (-8.9 to 56.7)	42.4 (31.6–56.4)	7.2 (5.6–9.5)	16.1 (-10.4 to 57.3)
Lesotho	4360 (3450–5550)	302.4 (243.1–382.0)	58.1 (24.0 to 100.0)	112 (88.3–142)	8.9 (7.1–11.1)	58.6 (18.8 to 106.9)
Namibia	2970 (2250–3820)	185.9 (142.7–234.4)	-7.3 (-26.3 to 11.8)	78.9 (59.7–105)	5.6 (4.4–7.2)	-6.6 (-27.2 to 14.9)
South Africa	87300 (74100–97900)	174.4 (147.8–195.2)	-24.4 (-30.3 to -17.5)	2110 (1830–2310)	4.6 (4.0–5.1)	-13.7 (-23.5 to 1.4)
Zimbabwe	14300 (10900–17500)	191.5 (147.6–231.9)	19.0 (-1.9 to 42.8)	407 (310–515)	6.9 (5.2–8.6)	35.3 (6.2 to 69.8)
Western sub-Saharan Africa	406000 (354000–459000)	223.5 (194.7–249.5)	-4.7 (-14.5 to 4.9)	14500 (12700–16300)	10.1 (8.8–11.4)	-0.4 (-10.8 to 12.5)
Benin	10800 (8650–13200)	223.0 (183.0–268.6)	-11.4 (-24.0 to 3.3)	377 (309–450)	9.7 (8.1–11.6)	-12.8 (-25.4 to 5.8)
Burkina Faso	27300 (23300–33700)	306.0 (259.7–364.6)	-9.8 (-23.8 to 9.0)	983 (824–1210)	14.0 (11.6–17.0)	-11.4 (-24.8 to 10.8)
Cabo Verde	545 (429–652)	123.3 (97.9–146.9)	12.1 (-5.6 to 34.1)	18.4 (14.7–24.5)	4.3 (3.4–5.7)	17.2 (-11.9 to 56.4)
Cameroon	31700 (25000–39100)	264.9 (212.7–324.7)	-10.3 (-26.3 to 15.6)	1070 (857–1350)	11.4 (9.3–14.4)	-12.0 (-30.0 to 15.9)
Chad	13300 (10900–15900)	241.7 (202.5–288.4)	15.8 (-3.3 to 48.0)	475 (391–578)	10.8 (8.9–12.9)	19.0 (-5.9 to 57.6)
Côte d'Ivoire	24400 (19300–30100)	233.3 (189.0–281.8)	-8.2 (-22.2 to 13.8)	808 (677–1000)	10.2 (8.6–12.4)	-7.8 (-24.8 to 14.4)
The Gambia	2340 (1880–2850)	256.1 (207.6–311.3)	4.7 (-14.8 to 27.7)	94.2 (74.6–116)	12.3 (9.7–15.0)	6.7 (-15.1 to 33.3)
Ghana	34500 (27300–41700)	223.8 (179.2–267.4)	2.8 (-17.5 to 26.5)	1210 (940–1490)	10.2 (7.8–12.5)	8.6 (-16.2 to 40.4)
Guinea	11800 (9700–14200)	221.6 (183.7–264.7)	7.5 (-15.5 to 36.4)	444 (363–537)	9.7 (8.2–11.8)	11.0 (-19.9 to 47.8)
Guinea-Bissau	1990 (1550–2450)	270.6 (218.2–327.1)	-7.9 (-26.3 to 12.9)	61.5 (46.9–74.2)	11.2 (8.7–13.6)	1.8 (-18.3 to 24.8)
Liberia	4310 (3460–5370)	208.5 (170.5–256.0)	6.2 (-16.4 to 31.9)	152 (122–194)	9.4 (7.6–11.8)	7.0 (-16.5 to 33.2)
Mali	20400 (16500–25000)	252.4 (203.7–306.0)	-8.9 (-23.5 to 7.2)	756 (595–912)	11.6 (9.0–13.8)	-0.7 (-20.1 to 20.1)
Mauritania	4680 (3840–5740)	224.0 (184.3–272.0)	-23.5 (-36.9 to -2.1)	169 (134–206)	9.4 (7.4–11.5)	-17.7 (-32.6 to 8.0)
Niger	16200 (12800–20000)	226.4 (177.9–281.7)	-2.9 (-20.7 to 20.4)	543 (414–713)	10.0 (7.4–13.4)	-0.5 (-24.3 to 31.8)
Nigeria	169000 (143000–201000)	205.1 (175.1–239.7)	-7.0 (-20.9 to 9.9)	6200 (5190–7180)	9.5 (7.9–11.0)	-0.7 (-15.9 to 18.2)
São Tomé and Príncipe	213 (181–256)	208.0 (176.8–244.9)	14.1 (0.5 to 31.3)	6.74 (5.54–8.17)	8.1 (6.5–10.2)	18.4 (-1.4 to 38.5)
Senegal	15800 (12900–19500)	220.9 (180.9–270.9)	-2.6 (-20.7 to 18.0)	601 (481–747)	10.0 (8.0–12.5)	-0.2 (-22.2 to 22.4)
Sierra Leone	7410 (5920–9330)	210.2 (171.5–257.3)	2.9 (-14.7 to 25.4)	265 (209–321)	9.2 (7.4–11.0)	2.6 (-15.5 to 24.0)
Togo	8630 (6930–10800)	229.7 (188.8–278.8)	4.7 (-14.9 to 34.8)	266 (205–334)	9.6 (7.4–11.5)	7.9 (-16.7 to 42.3)

Numbers in parentheses are 95% uncertainty intervals. Rates are provided per 100 000 of the population. Values are rounded to three significant figures (absolute numbers) or one decimal place (rates and percentage changes). DALYs=disability-adjusted life-years.

**Table: Absolute numbers and age-standardised rates of DALYs and deaths attributable to low bone mineral density in 2020, and percentage change in age-standardised rates from 1990 to 2020, globally and by super-region, region, and country or territory**



to quantify the magnitude of each burden measurement that resulted from low bone mineral density. We then aggregated the low bone mineral density-specific and total number of YLDs, DALYs, and deaths across E-codes to calculate the proportion of burden of each E-code that was due to low bone mineral density.

We observed that each cause of injury could result in multiple N-codes within each dataset, so we applied a series of logical and pragmatic decisions. First, we assumed that only hip fractures and some non-hip fractures, including vertebral, pelvic, and humeral fractures, were assumed to be potentially fatal. Second, we assigned the death to the fracture in the absence of a more severe injury code (N-code) that could better explain the death (ie, moderate to severe head trauma, spinal cord lesion, and intra-abdominal or thoracic organ damage).

For all measures, uncertainty was calculated by taking the final 100 draws from the posterior distribution. We report the 95% uncertainty intervals (UIs) as the 2.5th and 97.5th percentile values. Age-standardised rates and values were calculated with use of the GBD standard population.<sup>42</sup> We provide detailed data on DALYs but not always on YLDs because, for low bone mineral density, YLDs are nearly equivalent to DALYs. This is due to the age structure of low bone mineral density, which primarily affects older adults who contribute few YLLs.

### Decomposition analysis

A Das Gupta decomposition analysis was done to determine the relative contributions of four factors to the change in absolute DALYs and deaths attributable to low bone mineral density between 1990 and 2020. These factors were population growth, population ageing, changes in exposure to low bone mineral density, and changes in risk-deleted injury (ie, injury-related DALY or death rate after removing the effect of low bone mineral density on overall rate).<sup>43</sup>

### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

## Results

The current analysis is based on 169 unique sources (including some sources reporting bone mineral density in multiple countries) representing 48 countries or

territories and all seven GBD super-regions for mean bone mineral density, and on 12 sources representing nine countries and three super-regions for the meta-analysis establishing the relationship between low bone mineral density and risk of fracture (appendix 1 p 3).

In 2020, 8.32 million (95% UI 5.58–10.84) YLDs, 17.2 million (14.1–20.2) DALYs, and 477 000 (411 000–536 000) deaths were attributable to low bone mineral density. From 1990 to 2020, age-standardised mean bone mineral density values in the global population remained stable in men (0.85 g/cm<sup>2</sup> [0.82–0.87] in 1990 vs 0.87 g/cm<sup>2</sup> [0.84–0.89] in 2020) and women (0.75 g/cm<sup>2</sup> [0.73–0.77] in 1990 vs 0.76 g/cm<sup>2</sup> [0.74–0.78] in 2020 (figure 1A). In 2020, mean bone mineral density was lower in women than in men across all age strata. In women, mean bone mineral density decreased from 0.86 g/cm<sup>2</sup> (0.78–0.94) at age 40–44 years to 0.65 g/m<sup>2</sup> (0.60–0.70) at age 80–84 years (figure 1B). The lowest mean bone mineral density was observed in women aged 95 years and older, although the 95% UIs widened due to the smaller size of this age group. Similarly, in men, mean bone mineral density decreased from 0.95 g/cm<sup>2</sup> (0.86–1.04) at age 40–44 years to 0.79 g/cm<sup>2</sup> (0.73–0.87) at age 85–89 years. Global, region, and country or territory level mean bone mineral density data in 2020, including change from 1990, by sex for all ages combined, are shown in appendix 1 (pp 4–7).

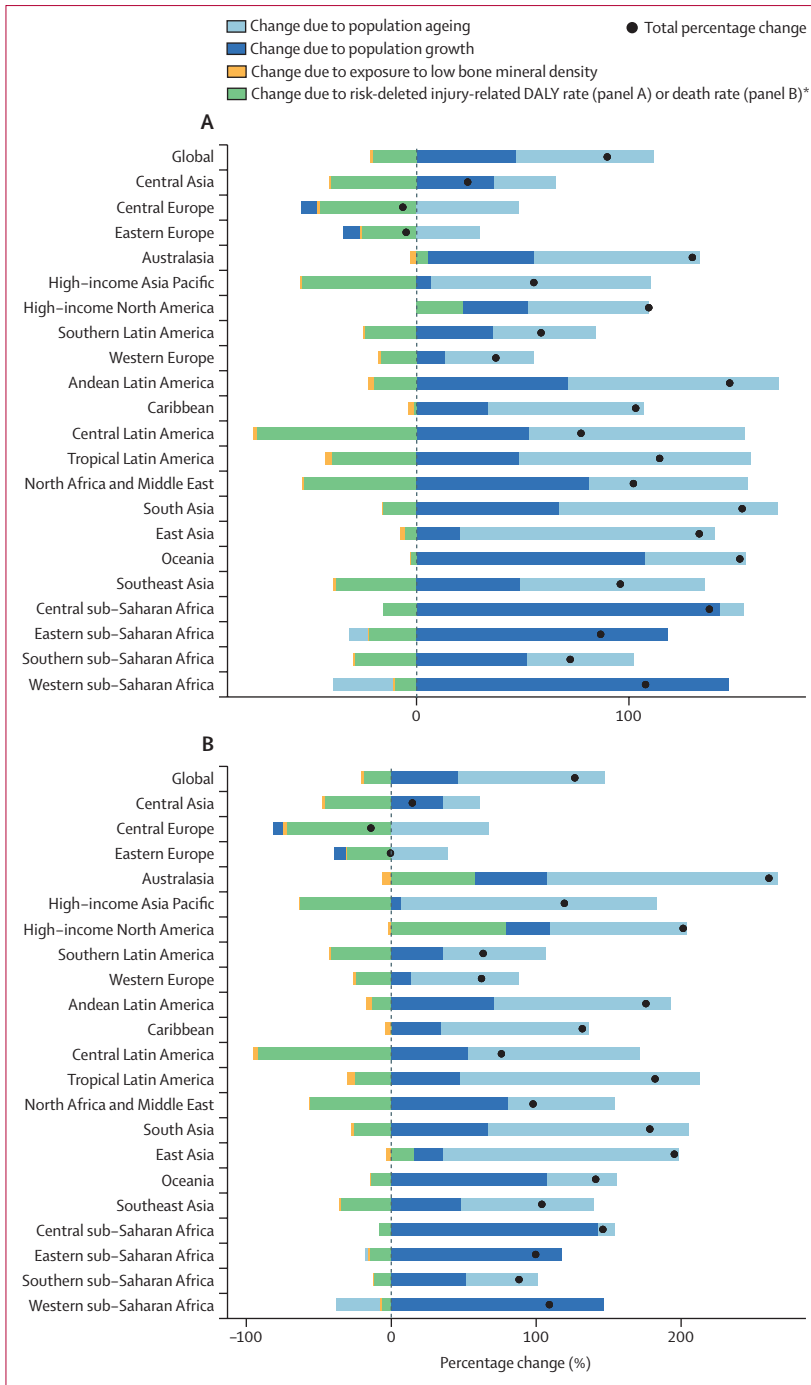
Between 1990 and 2020, global YLDs attributable to low bone mineral density increased by 91.8% (95% UI 88.5–95.1), DALYs increased by 89.8% (81.5–99.0), and deaths increased by 127.1% (108.5–144.5). After standardisation by age, global rates of YLDs, DALYs and deaths attributable to low bone mineral density showed modest decreases between 1990 and 2020 (–12.9% [–14.2 to –11.6] for YLDs, –12.7% [–16.5 to –8.6] for DALYs, and –4.0% [–10.9 to 3.5] for deaths; table).

Figure 2 illustrates the geographical differences in the age-standardised rates of DALYs and deaths attributable to low bone mineral density in 2020. The absolute and age-standardised burden by super-region, region, and country or territory in 2020, and percentage change from 1990 to 2020, are shown in the table. At the region level, for DALYs, south Asia had the highest age-standardised rate in 2020 (312.3 [266.5–350.2] per 100 000 of the population) and central Asia had the lowest rate (123.7 [94.3–148.3] per 100 000). The region with the highest age-standardised mortality in 2020 attributed to low bone mineral density was south Asia (12.5 [10.6–14.1] deaths per 100 000), and the regions with the lowest rate were high-income Asia Pacific (2.2 [1.8–2.5]) per 100 000 and Central Asia (2.2 [1.9–2.5] per 100 000). With respect to YLDs, Australasia had the highest age-standardised rate of YLDs in 2020 (173.8 [121.2–240.6] per 100 000) and southern sub-Saharan Africa had the lowest rate (43.7 [31.7–58.4] per 100 000).

A decomposition analysis by region showed the relative contribution of population growth, population

**Figure 2:** Map of age-standardised DALY rates (A) and death rates (B) for male and female sexes combined in 2020

Values are rounded to one decimal place. Rates are provided per 100 000 of the population. Intervals start at the lowest estimated rates (Jamaica for DALY rate and Turkmenistan for death rate; table). Areas with several small countries or details are magnified. DALYs=disability-adjusted life-years.



**Figure 3: Decomposition of change in the number of DALYs (A) and deaths (B) attributable to low bone mineral density from 1990 to 2020 for male and female sexes combined, globally and by region**  
 Note that scales on x-axes differ between plots. DALYs=disability-adjusted life-years. \*Injury-related DALY or death rate after removing the effect of low bone mineral density on the rate.

ageing, changes in exposure to low bone mineral density, and changes in risk-deleted injury-related DALY or death rates to the changes in absolute DALYs and deaths attributable to low bone mineral density from 1990 to 2020 (figure 3). Apart from population growth,

which was the main driver of increases in DALYs and deaths in central Asia, north Africa and the Middle East, Oceania, and sub-Saharan Africa, population ageing was the main driver of increases in estimates in all other regions that showed an increase in estimates in 2020. In most regions that showed increases in DALYs and deaths, the increases were partially countered by reductions in injury-related DALY and death rates. In high-income North America and Australasia, increased injury-related DALY and deaths rates contributed to increases in absolute DALYs and deaths attributable to low bone mineral density. DALYs and deaths attributable to low bone mineral density showed a slight decrease or remained stable in eastern Europe and central Europe, primarily due to declines in injury-related DALY and death rates.

In 2020, falls and road injuries represented the first and second largest contributors, respectively, to the burden from fractures that was attributable to low bone mineral density (figure 4). The proportion of global burden attributable to low bone mineral density resulting from falls in 2020 was 76.2% (95% UI 74.2–78.3) for YLDs, 65.2% (62.9–67.6) for DALYs, and 71.0% (67.4–72.8) for deaths. In comparison, the proportion of global burden attributable to low bone mineral density resulting from road injuries in 2020 was 12.4% (11.1–13.6) for YLDs, 24.6% (22.5–27.1) for DALYs, and 23.1% (21.6–26.2) for deaths. Appendix 1 (pp 8–13) presents the proportion of total fall-related burden and road injury-related burden attributable to low bone mineral density in 1990 and 2020, globally and by super-region, region, and country or territory. Globally, as a proportion of all fall-related burden, low bone mineral density accounted for 26.6% (23.2–28.7) of YLDs, 25.6% (22.1–27.4) of DALYs, and 40.6% (35.4–44.0) of deaths in 2020. Of all road injury-related burden, 12.6% (10.8–13.5) of YLDs, 6.3% (5.4–6.9) of DALYs, and 8.9% (7.6–9.6) of deaths were attributable to low bone mineral density. Compared with falls and road injuries, the relative burden from other causes was low and did not vary substantially over time (data not shown).

Counts of DALYs attributable to low bone mineral density due to falls were highest between age 70 and 84 years for men and women, and counts of fall-related deaths attributable to low bone mineral density were highest between age 80 and 94 years. In men, DALYs and deaths attributable to low bone mineral density due to road injuries were greatest at age 40–49 years and steadily decreased thereafter. In women, road injury-related DALYs were greatest at age 40–59 years and decreased thereafter, whereas road injury-related deaths were greatest at age 65–69 years and 75–79 years (figure 4). In men, road injuries accounted for the largest proportion of DALYs up to age 55–59 years, and deaths until age 60–64 years, after which falls became the primary driver of these outcomes. In women, road injuries were

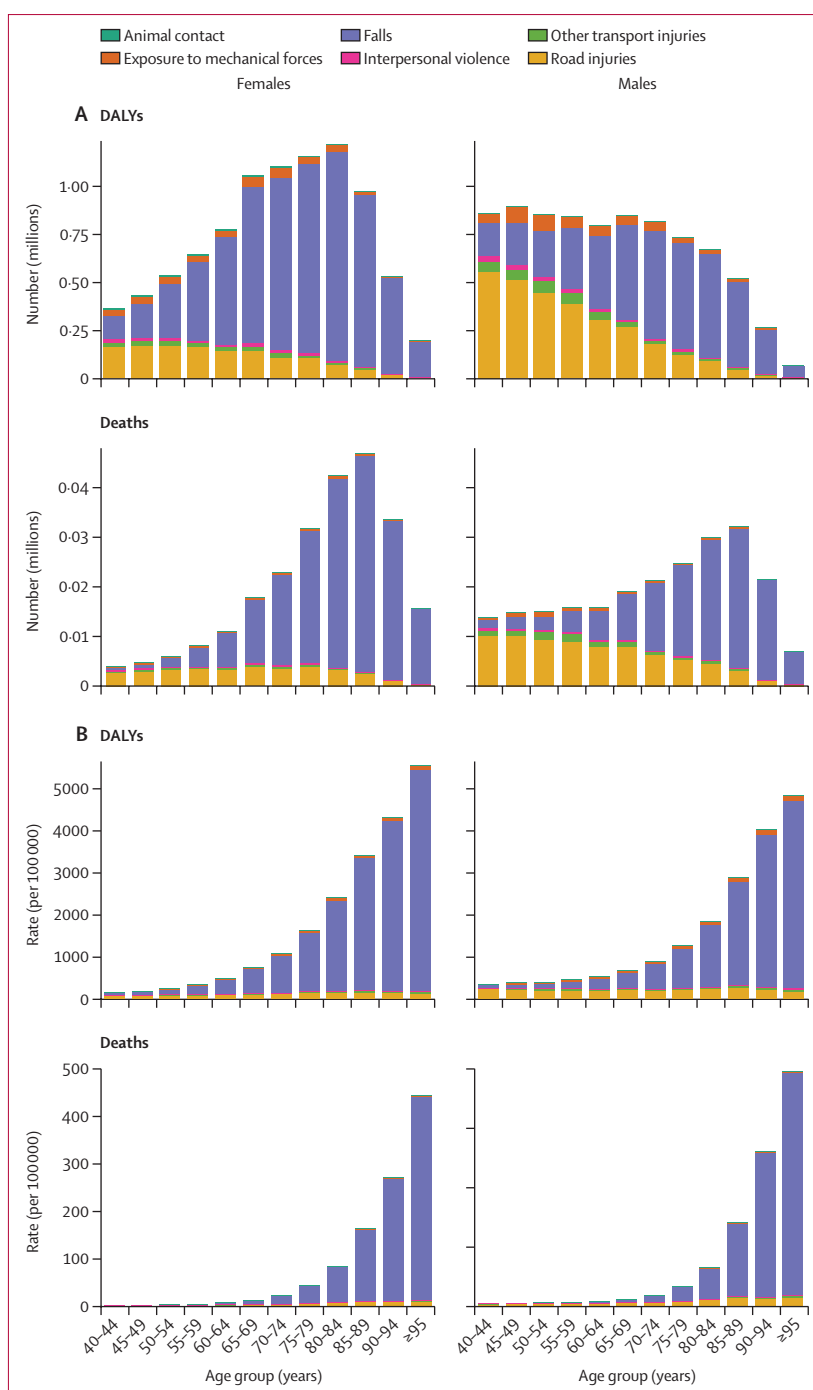
the leading cause of DALYs attributable to low bone mineral density in those aged 40–44 years, with the burden from falls predominating in older age groups. Road injuries were the primary driver of deaths attributable to low bone mineral density in women up to age 50–54 years, after which the burden from falls became the leading cause of attributable deaths.

## Discussion

This analysis updates and expands the evidence regarding the global burden attributable to low bone mineral density, an important modifiable risk factor for fractures related to injury. These data show an increase in burden related to low bone mineral density over time, with a nearly two-times increase in DALYs and YLDs and greater than two-times increase in deaths from 1990 to 2020. However, age-standardised rates showed slight decreases over this period, indicating that the numbers will continue to be driven by both population growth and population ageing. To our knowledge, this study highlights for the first time, the part that low bone mineral density plays in the global burden of fractures related to categories of injury other than falls, most notably road injuries.

We found that road injury-related deaths and disabilities constituted a substantial portion of burden associated with low bone mineral density, particularly in men. The data indicated that road injuries in women aged 40–54 years and men aged 40–64 years accounted for the largest proportion of deaths attributable to low bone mineral density, and also accounted for the largest proportion of DALYs attributable to low bone mineral density among women aged 40–44 years and men aged 40–59 years. Taken together, the data underscore the fact that the risk of death and disability attributable to low bone mineral density is not just an isolated problem among older women but also affects younger age groups and men.

South Asia was the region with the greatest burden attributable to low bone mineral density, with high overall rates of morbidity (DALYs) and mortality attributable to low bone mineral density (table). Although age-standardised rates of DALYs and deaths showed little change from 1990 to 2020 in this region, the rising absolute numbers of DALYs and deaths from fractures (figure 3) mean increasing costs to individuals and health systems.<sup>44–48</sup> The Asian Federation of Osteoporosis Societies has projected that direct medical costs for hip fractures alone will escalate from US\$9.5 billion in 2018 to \$15 billion by 2050.<sup>49</sup> Furthermore, infrastructure and capacity to adequately screen, diagnose, and manage low bone mineral density remain underdeveloped in many parts of Asia, with less than one DXA machine per million of the population in several countries or territories, and substantial gaps in health professional training and practice patterns.<sup>50</sup> To meet this growing burden, strong collaborative efforts by regional osteoporosis societies



**Figure 4:** DALYs and deaths attributable to low bone mineral density in 2020 by sex, cause of injury, and 5-year age strata

(A) Absolute number by cause of injury. (B) Rate per 100 000 of the population in each age group by cause of injury. Note that scales on y-axes differ between plots. DALYs=disability-adjusted life-years.

have spurred the generation of locally relevant evidence and guidelines, multidisciplinary health professional education and capacity building programmes, including secondary prevention fracture-liaison programmes, and public awareness and advocacy initiatives.<sup>48</sup>

Sub-Saharan Africa also had increases in absolute DALYs and deaths attributable to low bone mineral density in the context of substantial population growth, including growth in the absolute number of older individuals in some regions. There is a notable lack of access to diagnostics, care, and treatments for osteoporosis across sub-Saharan Africa, and low prioritisation by health-care systems compared with communicable diseases or other non-communicable disease priorities.<sup>51,52</sup> Importantly, the WHO Essential Medicines List does not include any oral formulations of bisphosphonates,<sup>53</sup> which are generally considered first-line agents for osteoporosis drug therapy, meaning in many low-income and middle-income countries (LMICs), including those in sub-Saharan Africa, availability might be limited. Intravenous zoledronic acid is on the Essential Medicines List, for the dosage recommended for adjuvant cancer treatment, but not for the formulation recommended for osteoporosis treatment.<sup>53</sup> These gaps present an opportunity for advocacy and awareness. In sub-Saharan Africa, where long-standing priorities such as HIV, tuberculosis, and malnutrition continue to dominate the health agenda and international funding, health systems have difficulty managing the concurrent rise of non-communicable diseases and their risk factors.<sup>54</sup> In this setting, there remains a paucity of high-quality regional epidemiological and health services data related to osteoporosis to inform evidence-based interventions.<sup>52</sup>

Although bone mineral density is a well established risk factor for fractures of all types, studies have consistently shown that the proportion of fractures attributable to osteoporosis alone, as defined by bone mineral density, is modest.<sup>55</sup> Therefore, fracture prediction tools typically incorporate other clinical risk factors with or without bone mineral density to improve fracture prediction.<sup>56,57</sup> However, unlike risk factors such as age, sex, and family history of fracture, bone mineral density is potentially modifiable through a range of non-pharmacological primary prevention and lifestyle modification approaches (eg, dietary calcium, vitamin D and protein intake, sunlight exposure, weight-bearing physical activity, optimisation of underlying comorbidities, and smoking and alcohol cessation) and pharmacological interventions.<sup>58,59</sup> Furthermore, bone mineral density can be measured by standard techniques that are objective, reproducible, non-invasive, and fast.<sup>13</sup> Evidence supports a correlation between change in bone mineral density with osteoporosis treatment and fracture risk reduction, albeit recognising that the full benefit derived from osteoporosis drug therapy goes beyond reductions in bone mineral density alone.<sup>60</sup>

Despite data supporting the screening, diagnosis, prevention, and management of osteoporosis, notable gaps exist between evidence-based guidelines and clinical practice, even in high-income regions where DXA imaging, osteoporosis treatments, and trained health

professionals are available.<sup>7,61</sup> These gaps are compounded in low-income and middle-income regions, where fundamental barriers to accessing such resources exist.<sup>62</sup> The critical role of policy and public health messaging in promoting best practices can be seen through key examples around the world. Crisp and colleagues reported a 20% and 13% decrease in age-standardised hip fracture incidence rates among men and women, respectively, in Australia between 1997–98 and 2006–07, a period during which there was active roll-out of public health initiatives focused on osteoporosis.<sup>63</sup> Screening and treatment for low bone mineral density is reimbursed by the Australian Government for all men and women aged 50 years and older who have sustained a fracture, and for all individuals aged 70 years and older whether they've sustained a fracture or not. By contrast, in the USA, Hayes and colleagues described associations between cuts in Medicare reimbursements for DXA and decreased provision of physician's office-based DXA services and prescriptions for US Food and Drug Administration-approved osteoporosis therapies 2 years later.<sup>64</sup> Age-adjusted hip fracture rates also plateaued in the USA from 2012 to 2015, following a decade of steady decreases, in the setting of decreased DXA testing and osteoporosis diagnosis, coupled with a reduction in bisphosphonate prescriptions due to fear of rare side-effects and misperceptions regarding the risk and benefits of treatment.<sup>65</sup>

The role of secondary prevention in osteoporosis also cannot be understated. Studies have shown that women aged 50 years and older with a history of fracture have as high as a four-times increase in the relative risk of future fractures compared to those without previous fractures.<sup>66</sup> Nevertheless, rates of initiation of osteoporosis treatment following a fracture are poor across regions and practice settings.<sup>67</sup> Fracture liaison services are coordinated multidisciplinary programmes aimed at identifying patients in the peri-hospitalisation period following a sentinel fracture, and linking patients to osteoporosis care.<sup>68,69</sup> Fracture liaison services have been shown to be effective at reducing both fracture rates and health-care costs compared with usual care or no care, and have been widely promoted by osteoporosis societies worldwide as the single most important step by health systems to prevent fracture-associated burden.<sup>67,70</sup>

The promotion of strategies to prevent falls and road traffic injuries is additionally important. Falls prevention strategies include individual-level or practice or hospital-level interventions that might comprise multifactorial components such as falls risk screening, education, exercise, home modifications, medication changes, referral to other health-care services, and recommended use of assistive devices or aids.<sup>71,72</sup> The effectiveness of road traffic injuries prevention strategies across the domains of legislation (eg, seat belt, helmet, and cell phone usage laws and increased penalties), enforcement (eg, specific groups and individuals subject to

enforcement and technology for enforcement), public awareness and education (eg, mass media campaigns against drunk driving), speed control (eg, speed bumps and other road designs to reduce speed), and road improvement (eg, repaving damaged roads) have been shown in high-income countries.<sup>73</sup> Data from LMICs are comparatively limited. However, given rapid urbanisation and motorisation in these settings, more research and advocacy are needed to guide and strengthen road safety enforcement policies, speed control efforts, and public education campaigns.<sup>74,75</sup>

Limitations associated with the comparative risk assessment methodology of the present analyses need to be acknowledged. In these analyses, uncertainty was estimated based on 100 draws where 1000 draws would have been preferable. The TMREL was based on US cohorts, which could lead to overestimation or underestimation of risk factor attribution in some world regions. For example, regions with lower average BMI compared with the USA might have lower age-specific and gender-specific bone mineral density, leading to higher attribution of fractures to low bone mineral density. Furthermore, the choice of a stringent TMREL (99th percentile) could have led to an overall overestimation of the burden of low bone mineral density.

The methodology to account for fracture-related deaths might also be susceptible to error in the estimation of true mortality attributable to low bone mineral density. We used hospital and emergency department data from 35 countries with double coding (ie, ICD codes for cause and nature of injury) to derive the proportion of in-hospital deaths attributable to the fracture event if a more severe life-threatening injury wasn't listed, an approach subject to variations in coding practices between hospitals and countries. In addition, the excess risk of mortality remains elevated beyond the initial evaluation or hospitalisation period for osteoporotic fractures, not just for hip fractures, but for other types of fragility fractures as well (vertebral, pelvis, distal femur, proximal tibia, proximal humerus, and multiple ribs) and might not be assigned to the fracture as the underlying cause.<sup>3,76,77</sup>

Furthermore, the 12 studies used in the meta-analysis from which we derived the relative risks for hip and non-hip fractures were largely based in high-income countries.<sup>25-36</sup> These studies represented diverse regions and showed some variability; however, the relationship between bone mineral density and fracture risk remains to be explored across all populations. More high-quality epidemiological data across racially, ethnically, and socioeconomically diverse populations is needed to better inform future analyses. In addition, variations in modifiable risk factors for low bone mineral density, as well as variations in attributable risk of low bone mineral density related to the social disadvantage index and access to diagnosis and treatment, were beyond the

scope of this paper but are important to consider for the future.

In summary, low bone mineral density is a key, modifiable risk factor for fractures related to injury. The present analysis highlights the contribution of low bone mineral density to DALYs and deaths resulting not only from falls in older adults, but also from fractures sustained in road injuries, particularly among middle-aged men. Although age-standardised rates of DALYs and deaths attributable to low bone mineral density decreased in many countries from 1990 to 2020, the increase in absolute numbers due to a growing and ageing global population places a substantial burden on health-care systems. LMICs are less equipped than high-income countries to handle this increasing demand and will thus face greater challenges. We advocate for the addition of oral bisphosphonates to the WHO Essential Medicines List, and for expansion of the eligibility for intravenous bisphosphonates on the Essential Medicines List to include management of low bone mineral density and individuals with high fracture risk aged 50 years and older. We also advocate for support for implementation strategies to improve the uptake of evidence-based injury and fracture prevention approaches, and recommend lifestyle strategies to improve bone health across the life-course.

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Please see appendix 2 (pp 10–12) for more detailed information about individual author contributions to the research, divided into the following categories: providing data or critical feedback on data sources; developing methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; and managing the estimation or publications process. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit the manuscript for publication. Members of the core research team for this topic area had full access to the underlying data used to generate estimates presented in this Article. All other authors had access to and reviewed estimates as part of the research evaluation process, which includes additional stages of formal review.

#### Declaration of interests

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Atheneum, Clearview Healthcare Partners, the American College of Rheumatology, Yale University, Hulo, Horizon Pharmaceuticals, DINORA, ANI/Exeltis USA, Frictionless Solutions, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two Labs, Adept Field Solutions, Clinical Care Options, Putnam Associates, Focus Forward, Navigant Consulting, Spherix, MediQ, Jupiter Life Science, UBM, Trio Health, Medscape, WebMD, Practice Point Communications, and the National Institutes of Health; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events as a member of the speaker's bureau of Simply Speaking; leadership or fiduciary roles in other board, society, committee, or advocacy groups, paid or unpaid, and support for attending meetings or travel, as a past steering committee member of OMERACT; participation on a data safety monitoring board or advisory board from the US Food and Drug Administration Arthritis Advisory Committee; stock or stock options in Atai Life Sciences, Kintara Therapeutics, Intelligent Biosolutions, Acumen Pharmaceutical, TPT Global Tech, Vaxart Pharmaceuticals, Atyu Biopharma, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics, Seres Therapeutics, Tonix Pharmaceuticals, Aebona Pharmaceuticals, and Charlotte's Web Holdings; and previous stock options in Amarin, Viking, and Moderna; all outside the submitted work. M Zielińska reports other financial or non-financial interests from Alexion, AstraZeneca Rare Disease as an employee outside the submitted work. All other authors declare no competing interests.

#### Data sharing

The findings of this study are supported by data available in public online repositories, data publicly available upon request of the data provider, and data not publicly available due to restrictions by the data provider. To download citations and metadata for the input data used in these analyses, please visit the Global Health Data Exchange GBD 2021 website (<https://ghdx.healthdata.org/gbd-2021/sources>). The data sources used in this analysis are listed in appendix 1 (pp 14–21).

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