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Global epidemiology and burden of osteoporosis among postmenopausal women: insights from the Global Burden of Disease Study 2021

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Osteoporosis, primarily characterized by low bone mineral density (LBMD), is a major skeletal disorder among postmenopausal women (PMW), yet its global burden remains poorly quantified. Leveraging data from the Global Burden of Disease (GBD) Study 2021, we assessed the LBMD burden in PMW across 204 countries and territories between 1990 and 2021. Metrics included deaths, disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs), with temporal trends evaluated via estimated annual percentage change (EAPC). We found that in 2021, LBMD was responsible for 219,552 deaths and 7.76 million DALYs in PMW globally, with age-standardized DALY rates reaching 979.2 per 100,000 population. Compared to premenopausal women, PMW experienced a 15.17-fold higher mortality, a 5.84-fold higher burden in DALYs, and a 6.29-fold higher burden in YLDs. While age-standardized rates (ASR) for deaths and DALYs showed slight declines from 1990 to 2021, the absolute number of LBMD-related deaths more than doubled, increasing from 91,941 in 1990 to 219,552 in 2021, largely driven by global population aging. South Asia experienced the greatest burden, with India reporting the highest DALYs rates. The burden was highest in women aged ≥80 years and increased most rapidly in those aged ≥95. Regions with a high Socio-demographic Index (SDI) exhibited lower mortality rates but disproportionately higher levels of disability, whereas low-SDI regions bore a greater burden of mortality. Projections to 2045 suggest a sustained rise in deaths and disability, despite modest rate reductions. These findings underscore the urgent need for age-tailored, equity-focused interventions to mitigate fracture risk and improve musculoskeletal health among aging female populations worldwide.

LBMD, encompassing both osteopenia and osteoporosis, is a common aging-related condition characterized by reduced bone mass and micro-architectural deterioration, leading to increased skeletal fragility and fracture risk[1,2]. Recognized as a major global public health issue, LBMD currently affects approximately 200 million women worldwide, including more than 10 million in the United States[3]. Meanwhile, due to its strong association with fragility fractures, LBMD not only affects a large population but also imposes a heavy and growing economic burden. In the United States alone, the annual cost of osteoporotic fractures exceeds $20 billion, while the European Union faces a comparable burden of approximately €30 billion[4,5]. As global population aging accelerates, individuals with LBMD are increasingly affected by high treatment costs, fracture-related disability,

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psychological distress, and long-term care needs[6,7]. Understanding the evolving burden of LBMD is therefore essential for guiding targeted public health interventions, informing resource allocation, and narrowing health disparities in aging populations worldwide.

PMW, characterized by estrogen deficiency as a defining biological feature, are widely recognized as a high-risk population for osteoporotic fractures[8–10]. Estrogen deficiency following menopause induces a cascade of physiological alterations—accelerated bone turnover, trabecular thinning, and increased cortical porosity—all of which have been extensively elucidated in mechanistic studies[11–14]. Furthermore, molecular and clinical investigations have firmly linked menopause-associated hormonal changes with dysregulation in bone remodeling pathways, including the RANK/RANKL/OPG axis, Wnt/β-catenin signaling, and increased oxidative stress, leading to compromised bone quality and microarchitectural deterioration[15–18]. Nevertheless, a major evidence gap persists: while mechanistic and interventional research has been robust, there remains a lack of comprehensive, population-level epidemiological data that accurately reflect the burden and distribution of LBMD in PMW across regions and time.

This study investigates the trends in LBMD disease burden across 204 countries and territories, considering variations in SDI levels and geographical factors. It utilizes a range of key indicators—such as death, DALYs, YLLs, and YLDs—to assess the overall impact of LBMD. The study also examines health inequalities in both absolute and relative terms, with a focus on how disease burden correlates with economic development. This is done through the application of the Inequality Slope Index and Concentration Index. Additionally, the Bayesian age-period-cohort (BAPC) model is used to forecast potential public health challenges related to LBMD by 2045 (Fig. 1). The insights from this research offer critical epidemiological data that can guide healthcare policymakers, clinicians, and epidemiologists in refining health strategies and optimizing resource allocation. These findings are essential for shaping effective, region-specific policies aimed at alleviating the global burden of LBMD.

Results

Global disparities in the burden of LBMD among PMW

According to United Nations data, PMW accounted for 20% of the total female population in 2021, up from 13.75% in 1990. According to the GBD 2021, the burden of LBMD among PMW accounted for more than 20% of the total LBMD burden among the female population. Specifically, PMW were responsible for 93.81% of LBMD-related deaths, 85.39% of DALYs, 86.28% of YLDs, and 84.19% of YLLs among all age groups of women, as shown in Fig. 2A. These findings indicate that PMW bear a disproportionately high burden of LBMD and are significantly more susceptible to the disease compared to women of other age groups.

From 1990 to 2021, the global burden of LBMD among PMW demonstrated a diverging trend between absolute numbers and ASR. The global age-standardized death rate decreased slightly from 29.34 per 100,000 population in 1990 to 27.51 in 2021, with an EAPC of -0.05, while the total number of deaths more than doubled from 91,941 to 219,552 cases. A similar pattern was observed in DALYs, where the ASR declined from 1,074.43 to 979.20 per 100,000 population (EAPC = −0.30), despite the absolute number of DALYs rising markedly from 4 million to 8 million cases over the same period. This downward shift in DALY rates was driven by reductions in both non-fatal and fatal components: the ASR of YLDs rate declined from 623.50 to 567.51 (EAPC = −0.36), while the ASR of YLLs rate

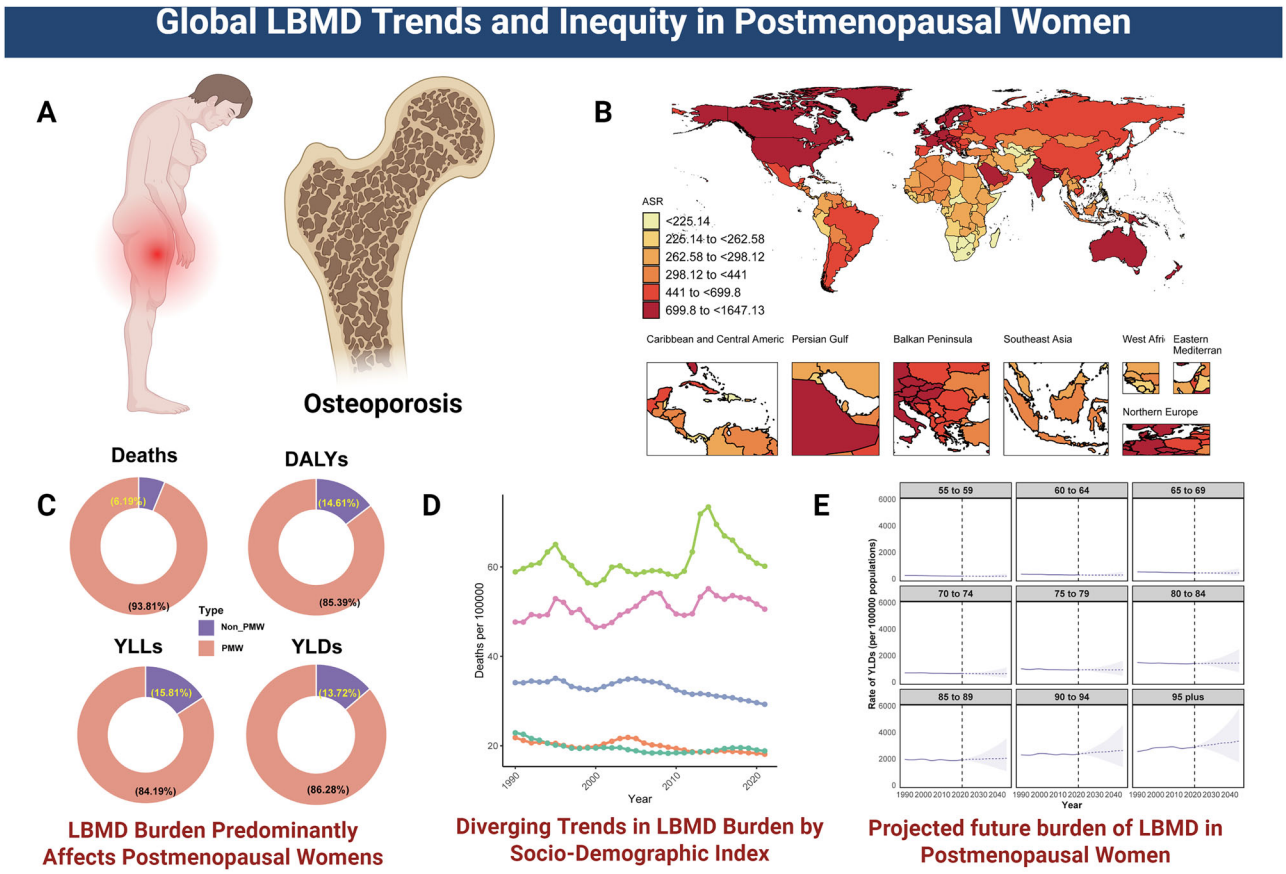

Fig. 1 | Overview of global LBMD burden and inequalities among PMW. A: Schematic representation of the study population, focusing on LBMD in PMW. **B**: Global distribution of LBMD burden in PMW across 204 countries/territories in 2021, showing variations in the burden by region. **C**: Comparison of LBMD disease burden proportions between premenopausal women and PMW in terms of deaths, DALYs, YLLs,and YLDs. **D**: The relationship between economic burden and LBMD in PMW across different global regions. **E**: Projected future trends in LBMD-related disease burden in PMW, highlighting changes from 1990 to 2045 across different age groups.

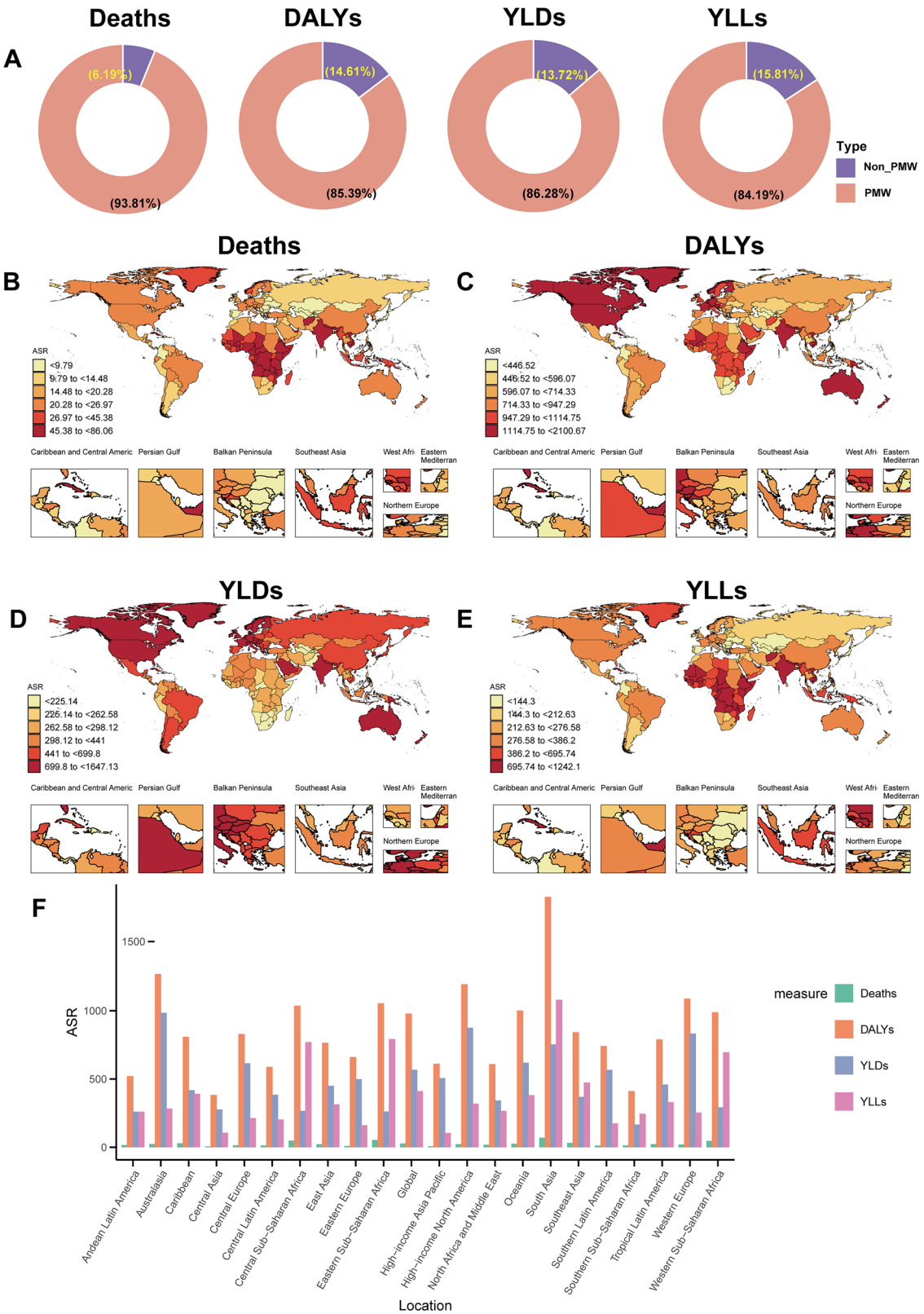

Fig. 2 | Comparison of LBMD between premenopausal women and PWM across global regions in 1990 and 2021, with global distribution of LBMD burden in terms of ASR. A In 2021, the number of deaths, DALYs, YLDs and YLLs for PMW as a percentage of the total female population. B-E: The global age-standardized deaths, DALYs, YLDs and YLLs rates for LBMD in PMW across 204 countries/territories in 2021. Panels (**B**), (**C**), (**D**–**E**) represent the age-standardized deaths, DALYs, YLDs and YLLs rates in 2021, respectively. **F**: The age-standardized death rates, DALYs, YLDs, and YLLs of LBMD among PMW in 2021 across 21 GBD regions.

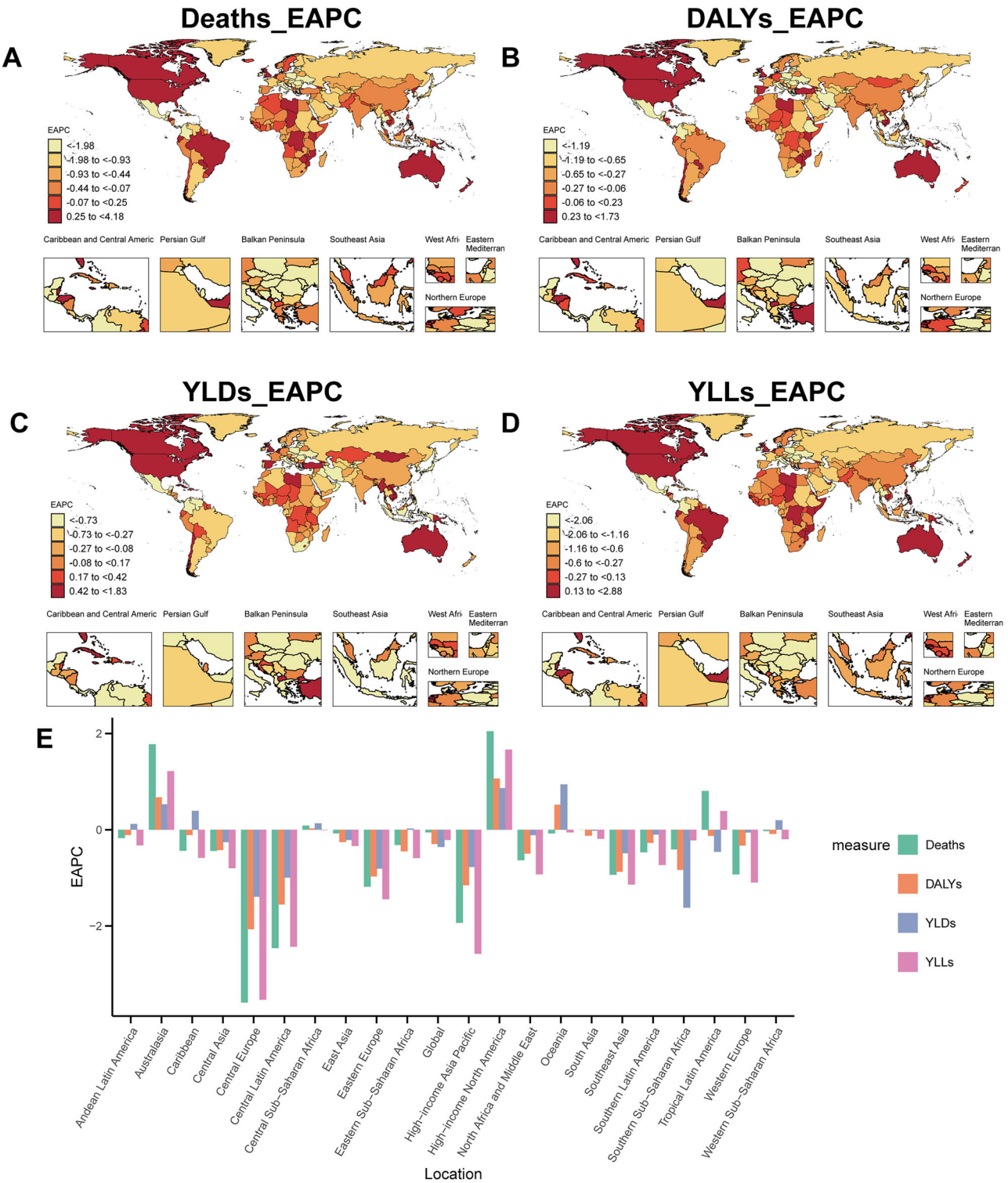

Fig. 3 | The EAPC from 1990 to 2021, globally and across 21 GBD regions. **A**–**D** The EAPC of age-standardized deaths (**A**), DALYs (**B**), YLDs (**C**) and YLLs (**D**) rates of LBMD among PMW from 1990 to 2021, globally. **E** The EAPC of age-standardized deaths, DALYs, YLDs and YLLs rates of LBMD among PMW from 1990 to 2021, in 21 GBD regions.

decreased from 450.92 to 411.69 per 100,000 population (EAPC = –0.21). (Fig. 2B–E, Fig. 3A–D, Tables 1, 2).

Regional variations in LBMD burden in PMW

In 2021, marked geographical heterogeneity was observed in the ASR of LBMD-related burden among PWM across the 21 GBD regions. South Asia exhibited the highest age-standardized death rate at 70.18 per 100,000 population, followed by Eastern Sub-Saharan Africa (54.10) and Central Sub-Saharan Africa (49.29). For DALYs, South Asia also ranked first with an ASR of 1833.32 per 100,000 population, significantly higher than that of Australasia (1268.62) and High-income North America (1194.14). While South Asia had the highest YLLs ASR (1079.51),

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Table 1 | Cases and ASR of deaths and DALYs with EAPC for LBMD, globally and by 21 GBD regions

Characteristics	1990		2021		1990–2021	1990		2021		1990–2021
	Deaths cases No. (95% CI)	ASR per 100,000 No. (95% CI)	Deaths cases No. (95% CI)	ASR per 100,000 No. (95% CI)	EAPC No. (95% CI)	DALYs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	DALYs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	EAPC No. (95% CI)
Global	91941 (74059 to 105912)	29.34 (23.43 to 34.00)	219552 (163828 to 261904)	27.51 (20.56 to 32.79)	−0.05(−0.12 to 0.01)	3648267 (2915423 to 4436624)	1074.43 (855.44 to 1307.56)	7763502 (6131195 to 9602497)	979.20 (773.82 to 1210.94)	−0.30(−0.32 to −0.27)
Andean Latin America	265 (206 to 325)	17.22 (13.26 to 21.25)	832 (595 to 1094)	16.28 (11.65 to 21.39)	−0.17(−0.28 to −0.06)	8782 (7020 to 10472)	538.37 (428.47 to 643.80)	26683 (20456 to 33064)	521.31 (399.87 to 645.87)	−0.11(−0.15 to −0.06)
Australasia	434 (339 to 510)	18.71 (14.55 to 22.05)	1614 (1145 to 2004)	24.06 (17.36 to 29.68)	1.78(1.51 to 2.05)	26483 (19765 to 34608)	1149.49 (855.60 to 1505.62)	71455 (52257 to 93662)	1268.62 (928.36 to 1672.26)	0.68(0.57 to 0.78)
Caribbean	588 (463 to 700)	29.53 (22.74 to 35.52)	1641(1195 to 2056)	29.65 (21.79 to 37.08)	−0.44(−0.64 to −0.24)	16485 (13054 to 19819)	773.94 (605.09 to 935.62)	42212 (31899 to 52762)	809.21 (614.90 to 1010.24)	−0.11(−0.22 to 0)
Central Asia	367 (301 to 410)	8.07 (6.60 to 9.05)	416 (336 to 479)	6.02 (4.84 to 6.94)	−0.44(−0.78 to −0.1)	22154 (17183 to 27570)	474.44 (367.45 to 590.61)	28759 (22143 to 36514)	383.55 (294.81 to 486.81)	−0.42(−0.56 to −0.28)
Central Europe	5419 (4489 to 6083)	41.49 (33.78 to 47.09)	4167 (3259 to 4849)	15.53 (12.22 to 18.02)	−3.59(−3.83 to −3.35)	212546 (167279 to 263005)	1479.66 (1158.72 to 1830.36)	200652 (150831 to 258640)	829.31 (623.27 to 1072.74)	−2.07(−2.15 to −1.99)
Central Latin America	1655 (1374 to 1844)	29.58 (24.16 to 33.35)	3006 (2346 to 3575)	13.60 (10.62 to 16.17)	−2.46(−2.71 to −2.21)	64257 (51201 to 77566)	1013.40 (803.45 to 1223.27)	131951 (101191 to 164560)	588.88 (451.37 to 734.41)	−1.55(−1.69 to −1.41)
Central Sub-Saharan Africa	540 (399 to 722)	48.10 (34.86 to 66.15)	1536 (1073 to 2157)	49.29 (33.77 to 70.62)	0.09(0.06 to 0.11)	15515 (12179 to 19442)	1028.81 (798.61 to 1312.14)	39666 (30152 to 51561)	1036.50 (780.23 to 1368.01)	0.03(0.01 to 0.05)
East Asia	12479 (9617 to 16633)	25.88 (19.55 to 34.39)	40373 (23757 to 55814)	23.00 (13.32 to 31.95)	−0.07(−0.46 to 0.32)	515439 (410814 to 635284)	813.38 (647.13 to 1001.63)	1451348 (1098120 to 1843021)	765.82 (576.43 to 974.32)	−0.26(−0.38 to −0.13)
Eastern Europe	3652 (3074 to 3999)	11.94 (9.93 to 13.18)	3988 (3219 to 4607)	9.51 (7.69 to 10.99)	−1.18(−1.44 to −0.93)	258893 (198955 to 328700)	813.94 (623.99 to 1034.23)	264326 (199601 to 342227)	660.74 (498.75 to 856.13)	−0.97(−1.25 to −0.69)
Eastern Sub-Saharan Africa	2291 (1782 to 2883)	57.99 (44.12 to 74.51)	5173 (3972 to 6459)	54.10 (40.52 to 68.45)	−0.32(−0.36 to −0.27)	56724 (45921 to 68200)	1172.01 (938.31 to 1425.92)	118409 (96747 to 141063)	1054.82 (850.78 to 1270.22)	−0.45(−0.49 to −0.41)
High-income Asia Pacific	2293 (1842 to 2670)	12.42 (9.83 to 14.55)	6060 (3980 to 7698)	7.88 (5.42 to 9.83)	−1.94(−2.08 to −1.79)	157682 (119368 to 203494)	813.91 (614.86 to 1050.51)	321873 (236726 to 427447)	611.97 (449.58 to 818.56)	−1.15(−1.26 to −1.05)
High-income North America	5530 (4314 to 6318)	13.66 (10.71 to 15.55)	18095 (13425 to 21290)	23.50 (17.75 to 27.35)	2.05(1.93 to 2.17)	333923 (250312 to 435508)	892.61 (668.22 to 1166.38)	810020 (607926 to 1052584)	1194.14 (897.76 to 1555.68)	1.06(1.01 to 1.12)
North Africa and Middle East	2348 (1793 to 3011)	23.85 (17.77 to 31.16)	4959 (3725 to 6312)	18.30 (13.48 to 23.56)	−0.63(−0.77 to −0.49)	86219 (69067 to 104044)	725.84 (577.40 to 881.28)	194113 (152933 to 240933)	609.00 (478.44 to 757.55)	−0.5(−0.53 to −0.46)
Oceania	34 (22 to 50)	26.50 (17.35 to 39.95)	92 (59 to 137)	25.26 (15.94 to 38.45)	−0.08(−0.14 to −0.01)	1453 (1116 to 1894)	852.28 (651.43 to 1114.84)	4430 (3424 to 5710)	1001.87 (772.06 to 1294.86)	0.52(0.47 to 0.57)
South Asia	22115 (14815 to 28295)	71.47 (47.94 to 92.43)	70969 (50817 to 89206)	70.18 (49.99 to 89.26)	0(−0.21 to 0.22)	684518 (531406 to 832305)	1883.63 (1457.74 to 2303.82)	2042083 (1618758 to 2461335)	1833.32 (1448.87 to 2217.69)	−0.12(−0.2 to −0.04)
Southeast Asia	6758 (4178 to 8975)	40.58 (24.03 to 55.28)	15269 (9840 to 20017)	32.25 (20.26 to 42.77)	−0.93(−1.08 to −0.79)	197278 (150675 to 242887)	1038.72 (780.35 to 1295.56)	440132 (344911 to 535492)	843.34 (654.36 to 1030.97)	−0.87(−0.98 to −0.77)
Southern Latin America	746 (608 to 858)	18.55 (14.98 to 21.44)	1289 (997 to 1514)	13.00 (10.13 to 15.23)	−0.47(−0.7 to −0.24)	37025 (28758 to 46038)	859.95 (666.92 to 1068.42)	66716 (50436 to 85494)	742.15 (560.72 to 954.45)	−0.27(−0.34 to −0.2)
Southern Sub-Saharan Africa	333 (255 to 427)	15.21 (11.46 to 19.65)	665 (537 to 803)	13.88 (11.04 to 16.96)	−0.41(−0.76 to −0.05)	12362 (9997 to 14941)	520.12 (419.08 to 630.21)	21671 (17788 to 25488)	411.76 (336.15 to 486.27)	−0.83(−1.04 to −0.63)

Table 1 (continued) | Cases and ASR of deaths and DALYs with EAPC for LBMD, globally and by 21 GBD regions

Characteristics	1990		2021		1990–2021	1990		2021		1990–2021
	Deaths cases No. (95% CI)	ASR per 100,000 No. (95% CI)	Deaths cases No. (95% CI)	ASR per 100,000 No. (95% CI)	EAPC No. (95% CI)	DALYs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	DALYs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	EAPC No. (95% CI)
Tropical Latin America	1424 (1160 to 1606)	22.47 (17.91 to 25.72)	5754 (4277 to 6888)	23.55 (17.59 to 28.12)	0.81(0.46 to 1.16)	63320 (50350 to 76969)	871.87 (688.82 to 1061.48)	191082 (147994 to 236570)	789.76 (612.58 to 977.30)	−0.13(−0.22 to −0.04)
Western Europe	20105 (15720 to 23218)	29.92 (23.25 to 34.70)	28366 (20263 to 34363)	20.48 (14.97 to 24.49)	−0.93(−1.22 to −0.64)	815362 (619613 to 1034105)	1265.75 (956.77 to 1612.32)	1165709 (856314 to 1515781)	1088.04 (799.97 to 1423.75)	−0.33(−0.4 to −0.25)
Western Sub-Saharan Africa	2566(1959 to 3231)	47.56 (35.85 to 60.68)	5288 (3967 to 6715)	47.22 (35.23 to 60.13)	−0.03(−0.09 to 0.04)	61847 (50068 to 73584)	1012.15 (814.44 to 1212.92)	130212 (104429 to 158587)	988.53 (789.43 to 1205.99)	−0.09(−0.13 to −0.04)

followed by Eastern (792.56) and Central Sub-Saharan Africa (769.52), the burden of YLDs was more pronounced in high-income regions. Specifically, Australasia (985.02), High-income North America (875.36), and Western Europe (833.65) reported the highest YLD rates, indicating a greater proportion of non-fatal disability in these settings (Fig. 2F).

Temporal trends from 1990 to 2021, as measured by the EAPC, further revealed stark contrasts. High-income North America and Australasia were the only two regions where all four indicators—deaths, DALYs, YLDs, and YLLs—exhibited an upward trend. In contrast, Central Europe, Central Latin America, and High-income Asia Pacific experienced the most pronounced declines across all four metrics. Notably, the increase in DALYs in Western Sub-Saharan Africa, Oceania, Andean Latin America, Caribbean, and Central Sub-Saharan Africa was primarily driven by rising YLDs, suggesting that disability associated with LBMD is becoming an increasingly dominant contributor to disease burden in these regions. These regional variations underscore the interplay between healthcare capacity, aging demographics, and diagnostic availability in shaping LBMD outcomes across the globe (Fig. 3E, Tables 1, 2).

Cross-national differences in LBMD-related mortality and YLDs among PMW

In 2021, Palau (86.06 per 100,000) recorded the highest age-standardized death rate, whereas Azerbaijan (3.24 per 100,000) reported the lowest. India (2100.67 per 100,000) exhibited the highest age-standardized DALY rate, reflecting its large population size and substantial disease burden. For DALYs, the highest ASR were noted in India (2100.67), Andorra (1938.73), and Greenland (1894.41). The top countries for YLDs were Andorra (1647.13), Belgium (1316.99), and Greenland (1288.32), whereas the YLL burden was highest in India (1242.10), the United Arab Emirates (1161.93), and Palau (1053.44) (Fig. 2B–E).

In terms of temporal trends, the most pronounced increases in death rates were observed in the United Arab Emirates (EAPC = 4.18), Georgia (EAPC = 2.53), and the United States of America (EAPC = 2.03). For DALYs, the highest upward trends occurred in the Netherlands (EAPC = 1.73), United Arab Emirates (EAPC = 1.71), and Georgia (EAPC = 1.34). The most significant increases in YLDs were seen in Bhutan (EAPC = 1.83), Netherlands (EAPC = 1.83), and Cambodia (EAPC = 1.27), while YLLs rose most steeply in the United Arab Emirates (EAPC = 2.88), Georgia (EAPC = 2.00), and Lesotho (EAPC = 1.81). In contrast, Hungary experienced the largest decreases in both age-standardized death rate (EAPC = –5.47) and DALYs (EAPC = –3.53) during the study period (Fig. 3A–D, Tables S1–2).

Age-specific disparities in LBMD burden among PMW

In 2021, the ASR of all LBMD-related burden indicators, including deaths, DALYs, YLDs, and YLLs, demonstrated a marked increase with advancing age. In terms of the absolute number of cases, LBMD-related deaths were predominantly concentrated among individuals aged 80–94 years, with a peak observed in the 80–84 age group. For DALYs, YLLs, and YLDs, the burden was mainly distributed among those aged 65–89 years, also reaching a maximum in the 80–84 age group. Although the absolute number of cases declined slightly in females aged 95 years and older, the ASRs for all indicators remained substantially elevated in this age group, particularly for deaths and DALYs.

Temporal trends from 1990 to 2021 further revealed that the percentage increase in ASR was most prominent in the 95+ age group across all four measures, suggesting worsening control of LBMD outcomes in the oldest-old population. By contrast, the 55–64 age groups showed the most significant reductions in ASR, especially for deaths and YLLs, implying improved early detection and management among younger PMW. Middle-old age groups (65–84) displayed relatively stable or mildly fluctuating burden rates (Fig. 4E–H).

Table 2 | Cases and ASR of YLDs and YLLs with EAPC for LBMD, globally and by 21 GBD regions

Characteristics	1990		2021		1990–2021	1990		2021		1990–2021
	YLDs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	YLDs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	EAPC No. (95% CI)	YLLs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	YLLs cases No. (95% CI)	ASR per 100,000 No. (95% CI)	EAPC No. (95% CI)
Global	2136261 (1516091 to 2880897)	623.50 (441.30 to 841.08)	4495820 (3152692 to 6128799)	567.51 (398.07 to 773.51)	−0.36(−0.39 to −0.32)	1512006 (1227605 to 1732919)	450.92 (364.06 to 518.75)	3267682 (2487786 to 3854916)	411.69 (313.77 to 485.32)	−0.21(−0.27 to −0.16)
Andean Latin America	4146 (2970 to 5482)	252.22 (180.24 to 333.75)	13356 (9352 to 18054)	261.01 (182.81 to 352.72)	0.12(0.03 to 0.21)	4636 (3708 to 5581)	286.15 (227.40 to 346.07)	13327 (9783 to 17277)	260.31 (191.15 to 337.40)	−0.32(−0.42 to −0.23)
Australasia	20573 (14132 to 28488)	894.17 (613.21 to 1241.07)	53729 (36735 to 74590)	985.02 (676.22 to 1369.84)	0.53(0.43 to 0.63)	5910 (4709 to 6857)	255.32 (203.05 to 296.62)	17726 (12905 to 21777)	283.60 (210.29 to 345.75)	1.22(0.95 to 1.48)
Caribbean	7863 (5458 to 10643)	363.93 (250.65 to 494.07)	21510 (14527 to 29775)	418.31 (283.71 to 578.33)	0.39(0.3 to 0.49)	8622 (6986 to 10097)	410.01 (326.84 to 484.35)	20701 (15640 to 25537)	390.90 (297.82 to 480.81)	−0.58(−0.78 to −0.39)
Central Asia	14890 (10608 to 20087)	318.84 (226.86 to 430.15)	20790 (14691 to 28267)	276.56 (195.20 to 375.82)	−0.26(−0.34 to −0.17)	7264 (6034 to 8050)	155.60 (128.99 to 172.71)	7969 (6502 to 9119)	106.99 (87.19 to 122.52)	−0.8(−1.1 to −0.5)
Central Europe	133942 (95024 to 180364)	916.17 (647.77 to 1234.66)	146465 (101320 to 202176)	615.58 (426.41 to 851.24)	−1.39(−1.43 to −1.35)	78604 (65952 to 87316)	563.49 (467.14 to 631.13)	54188 (43471 to 62406)	213.73 (172.75 to 245.45)	−3.53(−3.76 to −3.31)
Central Latin America	37765 (27146 to 50090)	580.69 (415.80 to 770.90)	86334 (60757 to 116095)	384.61 (270.56 to 517.07)	−1(−1.17 to −0.83)	26492 (22377 to 29140)	432.71 (361.24 to 480.16)	45617 (36522 to 53462)	204.27 (163.53 to 239.43)	−2.43(−2.64 to −2.23)
Central Sub-Saharan Africa	3988 (2896 to 5272)	256.95 (185.79 to 339.44)	10390 (7538 to 13704)	266.99 (192.76 to 351.94)	0.13(0.08 to 0.19)	11527 (8573 to 15278)	771.87 (566.91 to 1043.54)	29276 (20623 to 40464)	769.52 (535.78 to 1081.80)	−0.01(−0.03 to 0.02)
East Asia	289064 (207696 to 384340)	431.76 (309.35 to 573.93)	867637 (606172 to 1189147)	450.63 (314.27 to 617.66)	−0.21(−0.59 to 0.17)	226375 (176090 to 300725)	381.61 (292.55 to 506.68)	583711 (363216 to 795871)	315.19 (193.11 to 431.64)	−0.34(−0.7 to 0.02)
Eastern Europe	193180 (137265 to 262158)	605.15 (429.42 to 822.16)	199246 (138875 to 276070)	498.94 (347.83 to 691.95)	−0.81(−1.09 to −0.52)	65713 (55702 to 71482)	208.80 (175.84 to 228.15)	65080 (53360 to 74830)	161.80 (132.81 to 186.15)	−1.44(−1.79 to −1.1)
Eastern Sub-Saharan Africa	12919 (9445 to 17020)	259.50 (189.02 to 341.42)	30413 (22110 to 40219)	262.26 (190.03 to 346.53)	0.02(−0.01 to 0.06)	43806 (34391 to 54430)	912.52 (705.88 to 1152.30)	87996 (68933 to 108514)	792.56 (609.07 to 988.71)	−0.59(−0.64 to −0.53)
High-income Asia Pacific	119493 (83356 to 164653)	614.58 (427.95 to 847.51)	254336 (175287 to 353057)	506.71 (350.30 to 705.14)	−0.77(−0.89 to −0.66)	38189 (31417 to 43845)	199.33 (162.60 to 229.75)	67537 (46104 to 84595)	105.26 (75.85 to 129.21)	−2.58(−2.73 to −2.43)
High-income North America	255800 (175684 to 354899)	687.42 (472.03 to 955.67)	581912 (401062 to 813134)	875.36 (604.01 to 1224.04)	0.87(0.79 to 0.94)	78122 (62473 to 87876)	205.19 (165.05 to 229.86)	228108 (175768 to 262942)	318.78 (249.75 to 363.70)	1.67(1.57 to 1.76)
North Africa and Middle East	43982 (31567 to 58187)	357.12 (256.32 to 471.89)	112050 (79442 to 151581)	342.51 (242.57 to 463.17)	−0.11(−0.2 to −0.02)	42237 (33111 to 52713)	368.72 (283.43 to 469.38)	82063 (63231 to 102573)	266.49 (201.89 to 337.00)	−0.93(−0.99 to −0.86)
Oceania	800 (575 to 1065)	451.90 (323.06 to 602.13)	2764 (1993 to 3664)	619.46 (445.60 to 820.33)	0.94(0.86 to 1.03)	654 (426 to 974)	400.38 (262.01 to 599.94)	1665 (1076 to 2441)	382.41 (244.66 to 571.56)	−0.06(−0.15 to 0.04)
South Asia	270413 (192895 to 362057)	741.16 (526.78 to 992.43)	840173 (595504 to 1130345)	753.81 (532.96 to 1013.61)	−0.02(−0.08 to 0.04)	414105 (279103 to 526023)	1142.47 (767.53 to 1463.34)	1201910 (863204 to 1491219)	1079.51 (773.01 to 1351.13)	−0.19(−0.33 to −0.04)
Southeast Asia	78661 (56868 to 104427)	409.85 (295.66 to 543.53)	194850 (139501 to 260921)	369.55 (263.98 to 494.13)	−0.49(−0.54 to −0.44)	118617 (77683 to 152718)	628.87 (396.59 to 827.36)	245282 (166781 to 314469)	473.79 (313.98 to 613.75)	−1.14(−1.29 to −0.99)
Southern Latin America	26047 (18742 to 34780)	598.92 (430.54 to 799.82)	50269 (35325 to 68516)	567.07 (398.53 to 774.35)	−0.1(−0.16 to −0.04)	10978 (9089 to 12525)	261.03 (214.56 to 298.84)	16447 (13034 to 19108)	175.08 (139.73 to 202.72)	−0.73(−0.92 to −0.55)
Southern Sub-Saharan Africa	6251 (4532 to 8239)	261.08 (189.24 to 343.96)	8678 (6261 to 11564)	165.85 (119.40 to 220.87)	−1.62(−1.68 to −1.56)	6112 (4787 to 7703)	259.04 (201.00 to 328.33)	12993 (10621 to 15437)	245.91 (199.35 to 294.58)	−0.22(−0.58 to 0.14)
Tropical Latin America	38967 (27767 to 51665)	525.90 (372.98 to 698.49)	111070 (77829 to 149774)	459.58 (322.18 to 619.67)	−0.46(−0.55 to −0.36)	24353 (20348 to 27052)	345.97 (284.34 to 388.46)	80012 (62272 to 93237)	330.18 (257.69 to 384.15)	0.39(0.06 to 0.72)
Western Europe	560343 (387178 to 768478)	879.77 (605.65 to 1209.30)	850620 (577696 to 1173332)	833.65 (568.42 to 1151.74)	−0.06(−0.12 to 0)	255019 (203524 to 290664)	385.99 (307.49 to 440.58)	315089 (231203 to 376142)	254.39 (192.03 to 298.84)	−1.1(−1.36 to −0.83)
Western Sub-Saharan Africa	17176 (12480 to 22661)	276.64 (200.42 to 364.94)	39228 (28341 to 51999)	292.79 (210.50 to 388.01)	0.2(0.16 to 0.24)	44671 (34447 to 55404)	735.52 (562.16 to 922.25)	90985 (68134 to 115709)	695.73 (520.99 to 884.43)	−0.2(−0.26 to −0.13)

SDI-associated patterns in the global burden of LBMD

Between 1990 and 2021, distinct disparities were observed in the burden of LBMD among PMW across SDI quintiles. Age-standardized trends in deaths, DALYs, YLLs, and YLDs demonstrated a consistent gradient pattern, with higher SDI regions generally showing declining trends, while lower SDI regions experienced increases. Specifically, the EAPC for death rate was highest in low-SDI (EAPC = 0.28) and low-middle-SDI (EAPC = 0.29) regions, in contrast to decreasing trends in high-, high-middle-, and middle-SDI settings. A similar pattern was observed for DALYs and YLLs, where high-SDI regions showed declining rates, while low- and low-middle-SDI regions exhibited mild to moderate increases (Fig. 5A–D).

In terms of absolute disease burden, low-SDI regions maintained the highest ASR for deaths, DALYs, and YLLs throughout the three-decade observation period. Notably, a peak was recorded between 2013 and 2015, with the highest values reached in 2014: deaths (73.43 per 100,000), DALYs (1482.71 per 100,000), and YLLs (1054.70 per 100,000). This sustained elevation contrasts sharply with the substantially lower ASR observed in high- and high-middle-SDI regions (Fig. 5E–H).

For YLDs, however, a different pattern emerged. Although high- and high-middle-SDI regions experienced decreasing trends in YLDs—especially in high-middle-SDI regions (EAPC = –0.76)—they consistently exhibited higher YLD ASR compared to lower-SDI regions. Throughout the study period, YLDs in high-SDI regions remained above 750 per 100,000 population, more than 1.5 times greater than those in low-SDI settings. This suggests that in higher-SDI regions, while mortality and years of life lost have declined, the non-fatal disability burden associated with LBMD remains substantial.

SDI-Based Inequalities in LBMD Burden Among PMW

Between 1990 and 2021, substantial income-based inequalities in LBMD burden among PMW were identified, both in absolute and relative terms. Absolute inequality, as indicated by the Slope Index of Inequality (SII) derived from weighted regression against SDI rank, showed diverging patterns across burden types (Fig. S1A–D). LBMD-related deaths and YLLs were predominantly concentrated in low-SDI countries. From 1990 to 2021, the SII for deaths was –8 (1990) and –6 (2021), while the SII for YLLs remained consistently large, decreasing slightly from –267 to –230. Conversely, DALYs and YLDs showed an increasing concentration in higher-SDI regions. The SII for DALYs declined from 330 in 1990 to 276 in 2021, and for YLDs remained stable, with values above 500 across both years (537 in 2021), indicating persistent absolute disparities favoring higher-SDI countries.

Relative inequality, as measured by the concentration index, reinforced these findings (Fig. S1E–H). The concentration index for deaths shifted from –0.09 (95% CI: –0.14 to –0.06) in 1990 to –0.11 (95% CI: –0.16 to –0.06) in 2021, and for YLLs from –0.17 (95% CI: –0.22 to –0.12) to –0.19 (95% CI: –0.24 to –0.13), highlighting an increasing concentration of mortality and premature death in lower-SDI settings. In contrast, DALYs remained nearly evenly distributed across the SDI spectrum, with a slight rightward shift in concentration index from 0.03 (1990) to 0.01 (2021). YLDs consistently favored higher-SDI regions, with the concentration index declining only marginally from 0.17 (95% CI: 0.14 to 0.20) to 0.15 (95% CI: 0.12 to 0.19), indicating persistent relative disparities in disability burden (Fig. S1).

Future burden of LBMD

According to projections from the BAPC model, the global burden of LBMD among PMW is expected to continue rising in absolute terms from 2021 to 2045, despite a mild decline in ASR, reflecting a divergence between population aging and disease rate control. Specifically, the number of LBMD-related deaths is projected to surpass 386,000 by 2045, even as the death ASR declines from 28 to 19 per 100,000 population. Similarly, YLDs are expected to exceed 9 million cases globally, with the ASR decreasing to 548 per 100,000 population. DALYs and YLLs will follow the same pattern—continued increases in case numbers accompanied by slight reductions in ASR—suggesting a growing absolute burden due to demographic expansion and life expectancy gains (Fig. S2).

Age-stratified projections further underscore the intensifying burden among the oldest-old. PMW aged ≥85 years will remain the primary contributors to LBMD burden across all metrics, with particularly sharp increases expected in the 95+ age group. By 2045, the YLD ASR in women aged 95 and older is projected to reach 3,336.83 per 100,000 population—twice that of the 90-94 group. For deaths, the ASR among women aged 95+ is projected to be 1.6 times higher than that of those aged 90–94 (Fig. 6). These trends point to a substantial intensification of frailty, comorbidity, and functional loss in the oldest cohorts—indicating that current prevention and treatment strategies may be insufficient to mitigate disability and mortality in this expanding age segment.

Discussion

This study provides the first comprehensive, population-based assessment of the global epidemiological patterns and burden of LBMD among PMW, using data from the GBD 2021 Study. It highlights the substantial impact of regional disparities and socioeconomic development on LBMD outcomes across 204 countries and territories. The main findings are as follows: First, LBMD exhibits a pronounced population clustering effect among PMW. Compared to premenopausal women, PMW had a 15.17-fold higher burden of overall disease mortality, and a 6.29-fold higher burden of YLDs due to LBMD, emphasizing the critical role of the postmenopausal stage in the spectrum of bone metabolic disorders. Second, from 1990 to 2021, although ASR of death, DALYs, YLLs, and YLDs attributable to LBMD in the global PMW population have shown a general decline, the absolute number of affected individuals has continued to rise due to population aging—indicating an expanding demand for bone health services worldwide. Third, significant health improvements have been achieved among women aged 55–74. However, women aged 85 and above have become the core burden group for LBMD. Notably, the risks of death and disability caused by LBMD continue to increase among those aged 90 and older, suggesting that this age group should be prioritized in prevention and control strategies. Fourth, certain countries and regions have shown alarming trends of high and increasing LBMD burden. For example, India has experienced a rapid rise in LBMD-related burden among PMW, likely influenced by multiple factors such as population structure, screening rates, nutritional status, and healthcare resource allocation—requiring further research and targeted policy interventions. Fifth, an observable "high YLDs–low mortality" pattern exists across regions with different SDI levels. In high-SDI regions, elevated YLDs may reflect better recognition and documentation of disease-related functional loss, while early screening and secondary prevention help keep mortality rates low. Conversely, in low-SDI regions, delayed diagnosis and inadequate treatment are associated with significantly higher mortality burdens.

Osteoporosis is highly prevalent in aging women and is closely linked to the postmenopausal hormonal transition[12,19]. Although multiple risk factors—such as aging, genetics, lifestyle, and comorbidities—contribute to the pathogenesis of osteoporosis, estrogen deficiency remains the dominant driver in PMW[19]. The North American Menopause Society underscores this by identifying menopause-related hypoestrogenism as the most critical factor precipitating rapid bone loss in this population[20]. Supporting this, data from Cauley et al. show that women with serum estradiol (E2) levels below 5 pg/mL have a 2.5-fold increased risk of vertebral and hip fractures, confirming the direct link between estrogen depletion and skeletal fragility[21]. The clinical imperative for studying LBMD in PMW is rooted in the profound physiological consequences of estrogen deficiency on bone metabolism[22]. Estrogen plays a central role in regulating bone remodeling by maintaining the balance between osteoblastic bone formation and osteoclastic bone resorption. During menopause, the sharp decline in circulating estrogen—particularly E2—leads to an upregulation of basic multicellular unit (BMU) activity, increased osteoblast apoptosis, and prolonged osteoclast lifespan[23]. These changes

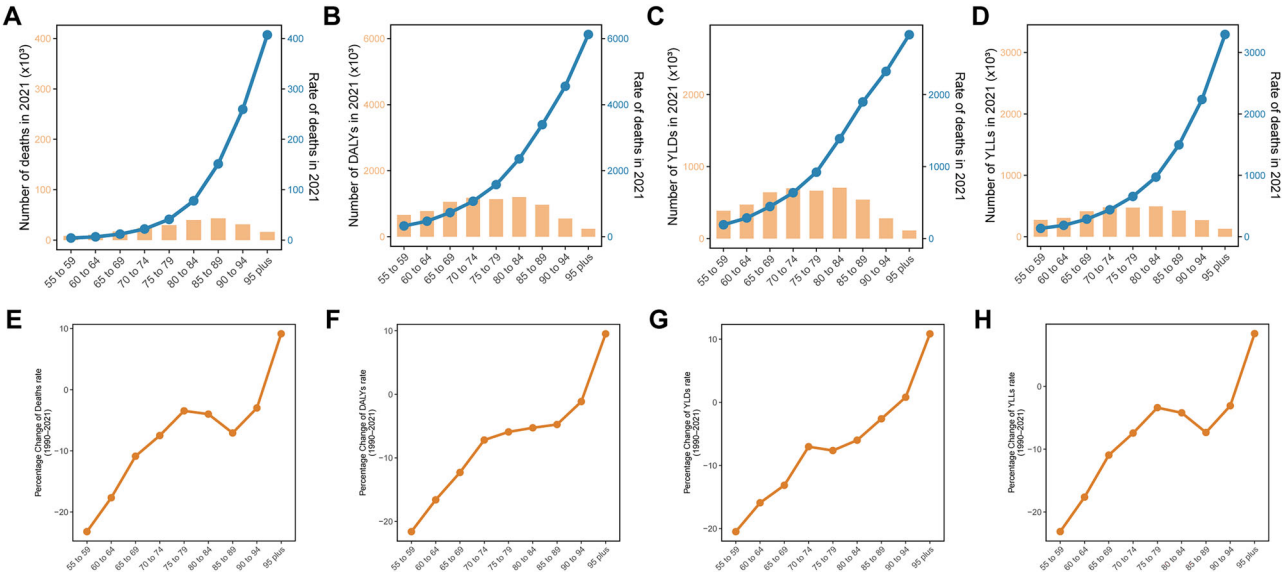

Fig. 4 | Age-specific burden and temporal changes in LBMD-related outcomes among PMW. A–D Number of cases (bars, left axis) and rate (lines, right axis) of LBMD-related deaths (**A**), DALYs (**B**), YLDs (**C**), and YLLs (**D**) across age groups of PMW in 2021. The *x*-axis represents age groups in 5-year intervals from 55–59 to 95+ years. **E–H** Percentage change in rates of deaths (**E**), DALYs (**F**), YLDs (**G**), and YLLs (**H**) from 1990 to 2021 across age groups, showing the differential trends in disease burden over time. The *x*-axis represents age groups in 5-year intervals from 55–59 to 95+ years.

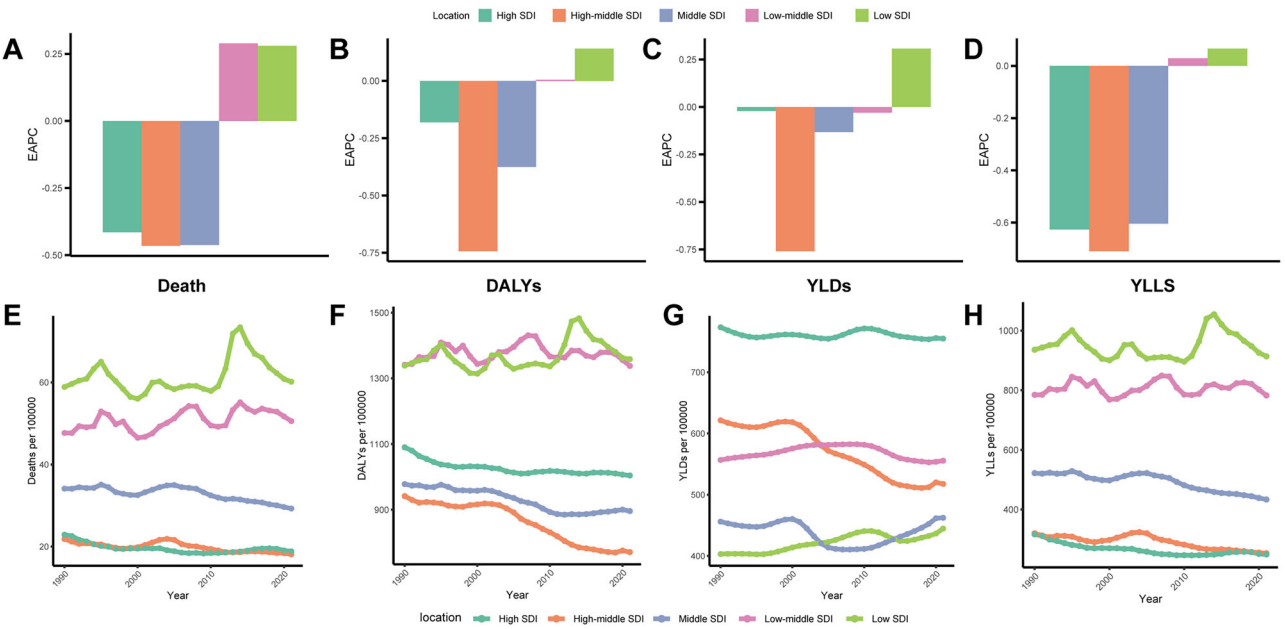

Fig. 5 | Trends in LBMD burden among PMW across SDI regions from 1990 to 2021. A–D EAPC of deaths (**A**), DALYs (**B**), YLDs (**C**), and YLLs (D) due to LBMD among PMW across five SDI regions (high, high-middle, middle, low-middle, and low SDI) between 1990 and 2021. **E–H** Temporal trends in ASR for deaths (**E**), DALYs (**F**), YLDs (**G**), and YLLs (**H**) from 1990 to 2021, stratified by SDI region. Each line represents a specific SDI category, demonstrating how the LBMD burden has evolved over time in different socioeconomic contexts.

result in a net loss of bone mass and microarchitectural deterioration, hallmark features of postmenopausal osteoporosis[24,25]. Furthermore, the prolonged BMU cycle exacerbates the imbalance, wherein bone resorption exceeds formation, leaving newly formed bone insufficient to compensate for structural voids. These findings underscore the need to complement molecular insights with large-scale epidemiological studies to assess the real-world burden of disease, better inform clinical risk models, and guide resource allocation and prevention strategies for aging female populations.

According to data from the United Nations Department of Economic and Social Affairs, the global PMW population increased from 360 million in 1990 to 790 million in 2019, representing a 117% rise[26]. The proportion of PMW in the total female population also grew from 13.7% to 20%, indicating a rapidly expanding group under global aging trends. Alarmingly, although PMW account for only one-fifth of the female population, the health burden from LBMD is disproportionately high. Our analysis shows that PMW bear more than 80% of the total LBMD-related disease burden among women, with over 90% of female deaths from LBMD occurring in

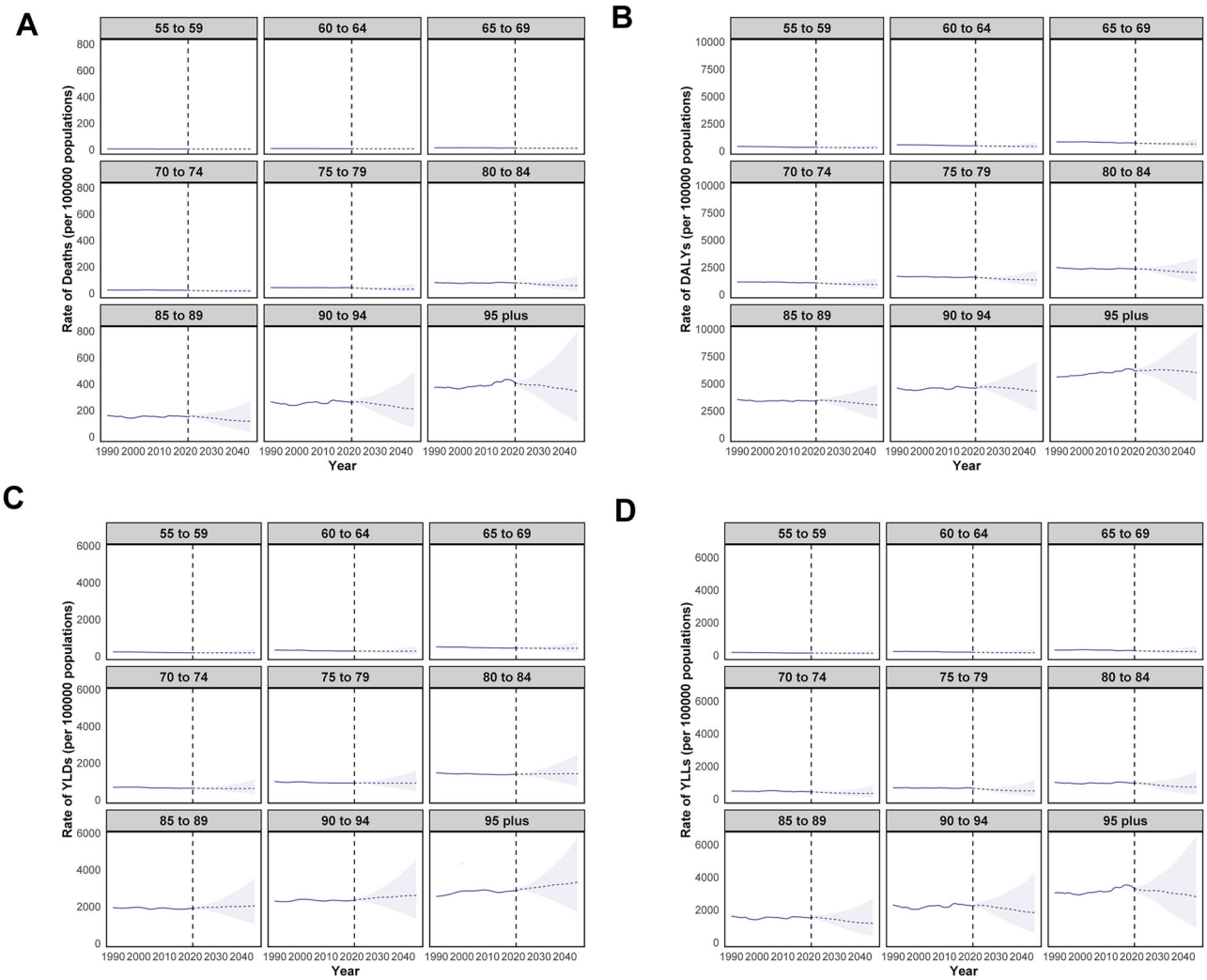

Fig. 6 | Projected trends in LBMD burden rates among PMW by age group, 1990–2045. A–D Historical and projected trends in rates of deaths (**A**), DALYs (**B**), YLDs (**C**), and YLLs (**D**) due to LBMD across nine postmenopausal age groups from 1990 to 2045. The dashed vertical line at 2021 separates observed data (1990–2021) from forecasted data (2022–2045). Solid lines represent mean estimates, with shaded areas indicating 95% uncertainty intervals.

this group. Even more concerning is that the mortality risk from LBMD among PMW is more than 15 times that of premenopausal women, reaffirming the central importance of this population in bone health management. This trend is also supported by epidemiological evidence. For instance, a study in the UK reported that approximately 50% of women aged over 50 will suffer from osteoporotic fractures in their lifetime—twice the incidence seen in men of the same age group[27]. This illustrates both the severity and specificity of postmenopausal osteoporosis at the population level.

The stark contrast between high- and low-SDI regions further highlights the role of social determinants in LBMD prevention and control. The highest concentration of deaths and DALYs from LBMD occurs in low-SDI regions, particularly sub-Saharan Africa and South Asia, consistent with widespread shortages of DXA screening, calcium/vitamin D supplementation programs, and access to osteoporosis medications[28–30]. For example, a Canadian study found that women in the lowest income quintile were twice as likely to qualify for osteoporosis treatment based on fracture risk assessment using the FRAX® tool with bone mineral density, compared to those in the highest income group[31]. This diagnostic gap contributes to a higher proportion of late-stage cases, with major disabling outcomes such as fractures often becoming irreversible. The rising mortality rate in low-SDI areas (EAPC = 0.28) likely reflects systemic failures in post-fracture care. Studies from Nigeria have reported 1-year mortality rates of 22.5% following hip fractures, attributed to limited surgical resources, inadequate rehabilitation services, and the absence of secondary prevention programs[32]. In contrast, high-SDI countries in Western Europe to USA have significantly reduced LBMD mortality by implementing fracture liaison services (FLS), which improve bisphosphonate adherence and reduce secondary fracture risk by approximately 37.2%[33].

South Asia has become the "epicenter" of LBMD-related deaths, reporting 70,968 such deaths in 2021. The underlying causes are multifaceted, including accelerated population aging, widespread vitamin D deficiency (60–80% among Indian PMW), and cultural constraints on physical activity. South Asia accounts for 26% of the global female population but contributes to 32% of LBMD deaths—an imbalance that likely stems from overlapping structural factors: (1) Nutritional deficiencies, particularly in vitamin D and calcium, influenced by poor dietary diversity and sun exposure restrictions (e.g., the "purdah" system)[34,35]; (2) Fragmented medical infrastructure focusing more on fracture treatment than prevention[36]; (3) Rapid PMW population growth (India will have more than 401 million PMW by 2026), outpacing healthcare system preparedness[37]; (4) High out-of-pocket expenditures in several South Asian countries, limiting access to early diagnosis. In India, for example, the age-standardized death rate from LBMD reached 2100.67 per 100,000 in 2021, illustrating the amplified health burden under constrained resources. In contrast, the significant reduction in LBMD mortality in Central European countries

reflects the effectiveness of national prevention strategies. Hungary's nationwide LBMD program, which subsidized DXA screening for women aged 50 and above and mandated fracture registries, reduced hip fracture incidence by 28% between 2010 and 2020. Similarly, the Netherlands implemented mandatory vitamin D fortification in margarine and promoted fall-prevention programs in elderly care institutions, successfully slowing the growth of DALYs despite increasing population aging[38,39].

Notably, while the overall burden of LBMD among PMW is declining globally, women aged 85 and older are experiencing a reversed trend. GBD data show that in 2021, both mortality rates and YLDs related to LBMD among women aged 90 and above reached historic highs, with a sharper increase than in any other age group. However, this group remains largely underserved in current bone health strategies. Studies report that the 1-year mortality rate following a first hip fracture among women aged 80+ can reach 30%, significantly higher than in the 65–79 age group. Despite this, diagnostic and treatment rates for osteoporosis in this cohort remain notably low. For example, a retrospective Japanese cohort study on denosumab treatment found that patients aged 80 years and above had significantly lower continuation rates than those aged below 80. The continuation rate declined from 85.3% at 12 months to 69.3% at 60 months[40]. Barriers include multimorbidity, which complicates prescribing decisions due to drug interactions and side effects; renal function decline limiting the use of common osteoporosis drugs; age limits in clinical trials (often capped at 80), leading to a lack of evidence-based guidance; and societal misconceptions that "aggressive prevention" is unnecessary in this age group. These attitudes often overlook the profound impacts of fractures on independence and quality of life. Current bone health interventions primarily target those aged 65–79, while the 85+ group faces marked deficits in drug accessibility, rehabilitation support, and family care. An age-sensitive management system is urgently needed. Integrating bone health assessments into multimorbidity management, improving community-based care networks, and promoting age-friendly home environments and muscle-strengthening programs can help build a sustainable, low-burden intervention system tailored to this group—essential for addressing the "third wave" of fracture burden driven by demographic shifts.

While forecasts suggest that by 2045, the global age-standardized death rate from LBMD may decline to 19 per 100,000, this statistic masks structural vulnerabilities. PMW aged 80 and above are expected to bear the greatest future burden, and health systems must prioritize geriatric fracture care accordingly. Japan's "Orange Plan," which combines community fitness[41], home safety renovation, and pharmacist-led medication reviews, led to a 45% reduction in YLLs between 1990 and 2021. This low-cost, community-centered model shows high adaptability for high-burden regions such as South Asia. Nevertheless, widespread implementation faces challenges, including weak infrastructure, fragmented service delivery, and age-related cultural attitudes. Capacity-building through community health worker training, integration with family-based care, and low-cost environmental modifications can improve feasibility—provided resource constraints and data gaps are addressed through phased pilots and policy integration.

To address the growing burden of postmenopausal LBMD, a comprehensive and multifaceted prevention strategy is essential. The increasing global prevalence of LBMD, particularly among women aged 85 and older, necessitates both individual-level interventions and systemic public health strategies. At the individual level, early identification through periodic fracture risk assessments, using tools such as FRAX® with or without BMD input, is crucial, especially in resource-limited settings. Nutritional optimization—ensuring adequate calcium and vitamin D intake—alongside regular weight-bearing exercises and muscle-strengthening activities, has proven effective in reducing fracture risk, improving balance, and preventing falls. Smoking cessation, alcohol moderation, and home safety modifications should be part of routine counseling for PMW to further minimize risk. On the pharmacological front, bisphosphonates and denosumab remain first-line treatments for high-risk individuals, while emerging anabolic agents such as romosozumab have shown promise in enhancing bone formation and structural integrity. For women in the early stages of menopause with low fracture risk but significant symptoms, hormone therapy (HT) and estrogen therapy (ET) can provide effective prevention, offering benefits that outweigh potential risks when appropriately used. Public health strategies must also tackle the disparities in LBMD outcomes across different socioeconomic strata. In low- and middle-income countries, increasing access to affordable DXA screenings, subsidizing calcium/vitamin D supplementation, and deploying trained community health workers will be key to improving early detection and treatment adherence. Programs like Japan's "Orange Plan," Hungary's subsidized DXA program, and Korea's integration of osteoporosis care into primary health services provide scalable and cost-effective models for intervention. National FLS, when incorporated into hospital discharge and outpatient systems, have been shown to reduce secondary fractures by over 35%, demonstrating the importance of a holistic approach to osteoporosis care. Digital health platforms and mobile-based educational tools present new opportunities to enhance awareness and improve compliance, particularly in regions with low health literacy. Ultimately, addressing LBMD in PMW requires a life-cycle approach, starting from peak bone mass optimization in early adulthood to promoting active aging strategies for the elderly. A multilevel approach, combining clinical interventions, community-based programs, and policy initiatives, is crucial to mitigating the future fracture epidemic, reducing long-term disability, and enhancing quality of life for aging women worldwide.

This study reveals LBMD as a biosocial disease shaped not only by menopausal biology but also by persistent inequalities in healthcare systems. Although ASRs have declined, the absolute burden among PMW continues to rise—particularly in low-SDI regions and among the oldest-old, where access to timely diagnosis and treatment remains limited. Addressing this challenge requires a shift in perspective: from seeing LBMD as an inevitable sign of aging to treating it as a preventable, manageable condition through integrated, life-course-based strategies. Crucially, LBMD is not merely a marker of biological aging—it is a lens through which we must confront the deeper inequities embedded in global aging and gendered health systems. Ensuring equitable access to bone health interventions is not only a clinical necessity but a moral imperative in the era of demographic transition.

Methods

Data source

This study utilizes data from the GBD 2021 results (available at https://vizhub.healthdata.org/gbd-results/), offering a comprehensive assessment of the burden of 371 diseases and injuries at global, regional, and national levels. GBD 2021 estimates cover 204 countries and territories across 21 regions. LBMD, as defined by the World Health Organization (WHO), is a skeletal disease marked by reduced bone density and microarchitectural deterioration, leading to increased fracture risk[42].

We extracted data on the annual incidence, death, and DALY for LBMD from 1990 to 2021. Bayesian meta-regression disease modeling (DisMod-MR, version 2.1) was used for data analysis. This framework generates internally consistent estimates of disease prevalence, incidence, remission, and death, stratified by sex, region, year, and age group, and supports ASR analyses using linear regression models[43]. DALYs, the primary metric in our study, represent the sum of YLLs and YLDs, offering a comprehensive measure of health losses due to premature death and reduced quality of life. YLDs are calculated using disease prevalence and associated disability weights, while YLLs are based on death counts and life expectancy data, estimated via demographic data and survival models. DisMod-MR enables consistent estimation of these metrics, accounting for factors such as sex, age group, region, and year[43]. Additionally, the SDI, a composite measure of social development, was incorporated. The SDI, calculated as the geometric mean of fertility rates, education levels, and per capita income, is categorized into five levels: low, low-middle, middle, high-middle, and high. This classification helps analyze the impact of socioeconomic development on health outcomes across regions.

Statistics

All rate data are reported per 100,000 population with 95% confidence intervals (CI), derived by drawing 1000 samples from the posterior distribution and calculating the 25th and 95th ordered values. DALYs rates are presented as estimates per 100,000 population, while case counts represent the absolute burden of LBMD among PMW; both metrics include 95% CI. All data analyses and visualizations were performed using R software, with two-sided p-values less than 0.05 considered statistically significant.

EAPC

Temporal trends in age-standardized incidence and DALY rates for LBMD were assessed using the EAPC method. ASR is calculated to adjust for population age structure, enabling cross-temporal comparisons. EAPC, derived from a log-linear regression model, quantifies the annual rate of change in ASR. The model is expressed as (1):

$$y = \alpha + \beta x + \epsilon \quad (1)$$

where y is the natural logarithm of ASR, x denotes calendar year, α is the intercept, β represents the slope coefficient, and ε is the error term. The EAPC is calculated as (2):

$$\mathrm{EAPC} = 100 \times \left(e^{\beta} - 1\right) \quad (2)$$

Trends were categorized as follows based on 95% CI: increasing if the EAPC and its lower CI limit were both positive, decreasing if the EAPC and its upper CI limit were both negative, and stable if the 95% CIs included zero. All analyses were conducted in R (version 4.3.1) using the ggplot2 package for visualization, with graphical outputs refined in Adobe Illustrator 2024 (version 28) to ensure clarity and reproducibility[44].

Cross-country inequality analysis

We quantified absolute and relative inequalities in LBMD burden among PMW using the WHO-recommended SII and Concentration Index. SII for incidence, death, and DALYs was derived via weighted regression models based on a relative socioeconomic position scale, defined by cumulative population percentiles ranked by per capita GDP. The Concentration Index was calculated by integrating the area between the Lorenz curve of the LBMD burden and the line of equality, linked to income distribution. To assess temporal trends (1990–2021), we analyzed data from 204 countries/territories using robust regression (rlm) to minimize bias from outliers and heterogeneity. Sensitivity analyses confirmed the superiority of rlm over linear regression (lm) in handling skewed data. For DALYs-based inequality, the Concentration Index was further calculated by aligning cumulative DALY proportions with population distributions ranked by SDI. Global burden metrics (deaths, DALYs, YLLs, YLDs) were systematically evaluated for LBMD among PMW. This dual approach (SII/ Concentration Index) provided robust estimates of both absolute and relative health inequalities, supporting comparative analyses across populations and time periods[45].

BAPC model projection

In this study, we utilized the BAPC model to forecast the global trends in LBMD death and disease burden among PMW. The BAPC model, which has been widely applied in epidemiological forecasting, was chosen for its ability to estimate age-specific rates while accounting for temporal effects and cohort effects. This approach allows for more accurate predictions by considering age-related trends, period-specific variations, and cohort-specific influences. The model was implemented in a Bayesian framework, using a Markov Chain Monte Carlo (MCMC) algorithm to estimate the posterior distributions of parameters. This allowed us to incorporate uncertainty in the model's predictions and generate 95% CI for all outcomes. Specifically, we used data from the GBD study, which provides comprehensive estimates of death and DALYs for LBMD on a global scale. The data were age-standardized to account for differences in population structures over time, and the model was fitted separately for each region and sex. The model incorporated data from 1990 to 2021 and projected future trends up to 2045. Sensitivity analyses were conducted to assess the robustness of the model, particularly in regions with limited data availability. In addition to estimating the overall global burden, we also assessed regional variations and incorporated potential socio-economic factors that may influence trends in LBMD death and disease burden. The results of the BAPC model were presented as point estimates along with the 95% credible intervals, providing a range of uncertainty for the predicted values[46].

Data availability

The data analyzed is publicly provided by the Institute for Health Metrics and Evaluation (http://www.healthdata.org/; http://ghdx.healthdata.org/gbd-results-tool).

Code availability

Some or all data, models, or code generated or used during the study are available from the corresponding author by request.

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Author contributions

J.Y.T., S.K.Z., and B.S.Y. conceived and designed the study. H.F.L., S.B.C., and M.L.S. contributed to drafting the manuscript and collecting GBD data. H.F.L., S.B.C., M.L.S., and J.L.X. conducted age standardization of the data, EAPC analysis, and health inequality analysis of the GBD data. J.Y.T., B.S.Y., H.F.L., S.B.C., C.X.Z., and J.L.X. participated in the discussion of the manuscript and the verification and confirmation of the study conclusions. Final approval of manuscript: all authors.

Competing interests

The authors declare no competing interests.

Additional information

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