#### ORIGINAL RESEARCH

# From Pain to Progress: Comprehensive Analysis of Musculoskeletal Disorders Worldwide

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**Objective:** Comprehensive analyses of the burden of musculoskeletal disorders (MSDs) are crucial for deepening our understanding of their impact on population health and for evaluating progress toward achieving international health goals.

**Study Design:** A comprehensive analysis was performed using data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021.

**Methods:** We gathered data on the number of prevalent cases, incidences, deaths, and disability-adjusted life years (DALYs) for MSDs from 1990 to 2021. Subsequently, crude indicators, age-standardized rates (ASRs) and estimated annual percentage change (EAPC) were calculated for MSDs from 1990 to 2021 at the global, regional, national, age and gender levels. Finally, decomposition analysis, frontier analysis, and EAPC cluster analysis were employed to examine changes in the indicators and the factors influencing them.

**Results:** In 2021, there were 367,193,430 incident cases and 1,686,561,517 prevalent cases of MSDs globally. Between 1990 and 2021, the age-standardized incidence rates (ASIR) declined marginally from 4641.5 to 4351.79 cases per 100,000 population [EAPC: -0.16 (-0.19 to -0.13)], while the age-standardized DALY rates (ASDR) increased from 1886.2 to 1908.87 per 100,000 population [EAPC: 0.09 (0.07 to 0.11)]. The ASRs were markedly elevated in the high SDI regions in comparison to the remaining SDI regions. The EAPC and its phase clustering analyses indicated a notable upward trajectory in the burden of MSDs in the low and middle SDI regions, particularly in Central Asia. The prevalence of MSDs is highest among individuals aged 50–59 years and among women. At the global level, the burden of MSDs is 1.43 to 2.30 times higher for women than for men.

**Conclusion:** From 1990 to 2021, the burden of MSDs has been concentrated in high SDI regions, with a gradual shift towards low and middle SDI regions.

Keywords: musculoskeletal disease, global burden of disease, prevalence, incidence, DALYs, epidemiology

#### Introduction

As the second leading cause of non-fatal disability globally, musculoskeletal disorders (MSDs) are typically characterized by pain, limitations in mobility, dexterity, and overall functioning, as well as reduced work capacity.<sup>1</sup> In the global burden of diseases, injuries, and risk factors (GBD) study, MSDs primarily include rheumatoid arthritis, osteoarthritis, low back pain, neck pain, and gout, with low back pain posing the greatest burden.<sup>2</sup> In the GBD study, low back pain is defined as pain localized in the posterior region of the body, extending from the lower border of the twelfth rib to the subgluteal crease, which may be accompanied by pain in one or both lower limbs.<sup>3</sup> This pain must persist for at least one day, thereby encompassing both non-specific low back pain and low back pain associated with other underlying conditions.<sup>4</sup> An economic survey reveals that healthcare spending in the United States constituted 18% of the overall

3455

economy in 2016, with \$381 billion allocated to healthcare for MSDs and \$134.5 billion specifically for low back pain and neck pain.<sup>5</sup> Additionally, the total cost of lost productivity due to MSDs among the working-age population in the European Union may be as high as 2% of gross domestic product.<sup>6</sup> Therefore, comprehensive estimates of the burden of MSDs are critical for improving our understanding of their impact on population health and for assessing progress towards international health goals.

The GBD study is an ongoing large-scale research endeavor that characterizes global health by estimating key health indicators across time, place, age, and gender.<sup>7</sup> By 2021, the GBD study incorporated data on 371 diseases and injuries, alongside 88 major risk factors, across 204 countries and territories.<sup>8</sup> This provides a reliable evidence base for policymakers, public health experts, and other relevant staff to develop targeted intervention strategies, optimize the allocation of health resources, and promote in-depth research and understanding of major public health issues. Despite several papers in the Lancet documenting the global burden of specific MSDs, a comprehensive study providing an up-to -date overview of the burden and trends of all MSDs up to 2021 is still lacking.<sup>8,9</sup>

Hence, we calculated the prevalence, morbidity, mortality, disability-adjusted life years (DALYs), and corresponding age-standardized ratios (ASRs) for MSDs at the global, national, regional, age, and sex levels, as well as the Estimated Annual Percentage Change (EAPC), for the period from 1990 to 2021.

### Method

### Definition of Musculoskeletal Disorders

The International Classification of Diseases (ICD) codes assigned to MSDs in GBD 2021 are provided in <u>Supplementary</u> <u>Table 1</u>. In summary, the MSDs included in this analysis comprise rheumatoid arthritis, osteoarthritis (including osteoarthritis of the hip, knee, and hand), low back pain, neck pain, and gout.<sup>10</sup>

### Data Sources

The GBD study, conducted by the Institute for Health Metrics and Evaluation (IHME) in collaboration with numerous global partners, serves as a comprehensive measure of the burden of disease, injury, and risk factors. Estimates in the GBD 2021 database are taken from vital registration systems, vital registration samples, cause-of-death autopsies, data from survey records in the Global Health Data Exchange, and GBD's Population Health Data Repository.<sup>8</sup> To date, GBD 2021 includes data on 371 diseases and injuries, along with the corresponding 88 major risk factors, across 204 countries and territories. GBD data is regionally aggregated, lacking information on individual cases, and is based on numbers and rates in a macro-level context.<sup>11</sup> Previous literature provides detailed descriptions of the methods used for estimating both fatal and non-fatal burdens of disease.<sup>8,12</sup> All data utilized in this study were directly obtained from the latest GBD 2021 database. Since the GBD 2021 database is publicly accessible, this study did not require ethical review.

This research utilized the Global Health Data Exchange GBD Results Tool to query relevant data (<u>https://vizhub.</u> <u>healthdata.org/gbd-results/</u>). We selected "Musculoskeletal disorders" as the cause and utilized four indicators for evaluation: "Prevalence", "Incidence", "Deaths", and "Disability-adjusted life years (DALYs)". The retrieved data were subsequently collected and analyzed according to various years, levels of socio-economic development, countries and regions, gender, and different age groups. DALYs represent the total number of years lost due to disease, combining both the number of years of life lost (YLLs) and the number of years lived with disability (YLDs). One DALY can be considered as one healthy year lost due to disability or premature death from a specific cause.<sup>8</sup>

### Statistical Analysis

Four crude indicators, namely the number of prevalence, the number of incidences, the number of deaths and the number of DALYs, are the fundamental indicators of trends in the prevalence of diseases. However, variations in age structure across populations may introduce heterogeneity in the burden of MSDs. Therefore, we collected age-standardized ratios (ASRs), which were calculated by applying different weights to crude indicators based on age composition ratios, ensuring comparability across populations.<sup>8</sup> Finally, we employed age-standardized prevalence rates (ASPR), age-

standardized incidence rates (ASIR), age-standardized mortality rates (ASMR), and age-standardized DALY rates (ASDR) to assess the MSDs burden, thus avoiding potential bias due to demographic differences.

Furthermore, we tracked the trend in ASR over a specified timeframe by calculating the EAPC and utilized a linear regression model to determine the 95% confidence interval (CI) for the EAPC.<sup>13</sup> A linear regression line fitting the natural logarithm of the rate, expressed as  $y = \alpha + \beta x + \varepsilon$ , where x represents the calendar year and  $y = \ln(\text{rate})$ , was employed with the calendar year as the independent variable. The EAPC can then be computed as 100 \* (exp( $\beta$ ) - 1), with its 95% CI calculated using the empirical quantile method. If both the EAPC value and the lower limit of the 95% CI are greater than 0, the ASR for the selected year is considered to have a decreasing trend. Then, we aggregated EAPCs for ASPR, ASIR, ASMR, and ASDR from countries worldwide and conducted comprehensive spatial cluster analyses to visualize and quantify geographic differences and trends in the burden of MSDs.<sup>14</sup>

In addition, this study employs the decomposition analysis proposed by Das Gupta to elucidate the extent to which population age structure, population growth, and changes in epidemiological trends influence the burden of MSDs.<sup>15</sup> The method identifies the specific contribution of each component by decomposing the overall change into multiple components through the application of mathematical decomposition techniques. Finally, we conducted frontier analyses based on four ASRs and sociodemographic index (SDI) with the objective of assessing the unrealized health potential of each country or region at its level of development.<sup>16</sup>

This study was primarily analyzed using the R programming language (version 4.3.2) and several R packages, including ggplot2, dplyr, purrr, tidyr, and ggsci.

### Results

### Global Burden of MSDs

In 2021, the total number of MSDs globally was 1,686,561,517 cases [95% uncertainty interval (UI): 1,599,166,937–1,780,146,354], with an ASPR of 19,832 cases per 100,000 population (95% UI: 18,810–20,938), which represents an increase from 1990 of 3.29%. During 2021, there were 367,193,430 new cases of MSDs (95% UI: 333,085,118–402,083,084), with an ASIR of 4351 cases per 100,000 population (95% UI: 3962–4763), which represents a 6.24% decrease since 1990. Furthermore, MSDs were responsible for 118,499 deaths in 2021 (95% UI: 103,131–128,548), with an ASMR of 1.43 per 100,000 population (95% UI: 1.25–1.56), which represents a 7.22% decrease since 1990. In 2021, the number of DALYs for MSDs reached 16,187,769 (95% UI: 118,018,720–216,145,508) a significant increase of 87.60% compared to 1990. However, the ASDR was only 1908.87 per 100,000 population, an increase of only 1.20% compared to 1990. From 1990 to 2021, the EAPCs for the ASPR, ASIR, ASMR, and ASDR were 0.15 (95% CI: 0.13 to 0.17), -0.16 (95% CI: -0.19 to -0.13), -0.26 (95% CI: -0.36 to -0.17), and 0.09 (95% CI: 0.07 to 0.11), respectively. Despite a downward trend in the ASIR and ASMR of MSDs globally, the ASPR and ASDR are still increasing, indicating that the global burden of MSDs remains significant. All the aforementioned results are detailed in Table 1 and Figure 1.

# Spatial Distribution of the Burden of MSDs

#### Five SDI Regions

As shown in Figure 2 and Table 1, the four crude indicators, ASPR, and ASDR for MSDs increased across all SDI regions from 1990 to 2021. In contrast, the ASIR exhibited a decreasing trend in all SDI regions. Furthermore, ASIR (decreased from 5611 to 5385 cases per 100,000 population), ASPR (increased from 22,490 to 23,724 cases per 100,000 population), and ASDR (increased from 2278 to 2359 cases per 100,000 population) in the high SDI region were significantly higher than those in the remaining SDI regions in all years. In contrast, all MSD indicators are lower in low SDI region. However, the low SDI region experienced the largest increase in the number of incidence cases (128.6%), the number of disease cases (141.2%), and the number of DALYs (140.1%) from 1990 to 2021. In addition, the middle SDI region exhibited the largest increase in ASPR [EAPC: 0.24 (0.22–0.26)] and ASDR [EAPC: 0.18 (0.16–0.21)]. The above phenomenon indicates that the burden of MSDs is concentrated in areas with high SDI, with a lighter burden in middle and low SDI areas. However, there is a tendency for the burden of MSDs to gradually shift to middle and low SDI areas.

	Prevalence					Incie	dence	DALYs				
	Counts		ASR (per 100,000)		Counts		ASR (per 100,000)		Counts		ASR (per 100,000)	
	2021 (millions)	Percentage change*	2021 (thousands)	EAPC	2021 (millions)	Percentage change*	2021 (thousands)	EAPC	2021 (millions)	Percentage change*	2021 (thousands)	EAPC
Global	1686.5 (1599.1–1780.1)	95.0%	19.8 (18.8–20.9)	0.15 (0.13–0.17)	367.1 (333.0–402.0)	70.5%	4.4 (4.0–4.7)	-0.16 (-0.19 to -0.13)	161.9 (118.0–216.1)	87.6%	1.9 (1.4–2.5)	0.09 (0.07–0.11
High SDI	363.8 (348.4–379.2)	59.7%	23.7 (22.7–24.8)	0.19 (0.19–0.2)	78.4 (71.4–85.0)	40.9%	5.4 (4.9–5.9)	-0.09 (-0.11 to -0.06)	35.4 (26.0–47.3)	54.4%	2.3 (1.7–3.1)	0.14 (0.13–0.14
High-middle SDI	337.1 (319.2–355.5)	71.8%	19.2 (18.1–20.3)	0.14 (0.11–0.17)	75.7 (68.2–83.0)	46.5%	4.5 (4.1–4.9)	-0.21 (-0.25 to -0.17)	31.5 (22.9–42.5)	62.5%	1.8 (1.3–2.4)	0.05 (0.02–0.09
Middle SDI	524.5 (495.5–554.8)	120.1%	19.1 (18.1–20.2)	0.24 (0.22–0.26)	108.3 (98.4–119.0)	88.5%	4.0 (3.6–4.4)	-0.06 (-0.1 to -0.02)	49.3 (36.0–66.3)	109.0%	1.8 (1.3–2.4)	0.18 (0.16–0.21
Low-middle SDI	332.0 (312.5–353.1)	122.9%	19.6 (18.5–20.7)	0.19 (0.16–0.22)	72.0 (64.9–79.4)	99.6%	4.2 (3.8–4.6)	-0.09 (-0.14 to -0.04)	32.7 (24.1–43.2)	119.3%	1.9 (1.4–2.5)	0.18 (0.14–0.22
Low SDI	27.8 ( 19.3–136.3)	141.2%	17.8 (16.8–18.8)	0.1 (0.08–0.12)	32.3 (29.1–35.8)	128.6%	4.2 (3.8–4.6)	-0.11 (-0.14 to -0.09)	12.7 (9.3–16.8)	140.1%	1.7 (1.2–2.2)	0.09 (0.05–0.12
Asia	975.6 (1033.4–922.4)	114.2%	19.0 (18.0–20.2)	0.22 (0.19–0.26)	200.8 (220.2–182.3)	82.4%	4.0 (3.6–4.3)	-0.15 (-0.2 to -0.1)	92.1 (123.3–67.2)	103.8%	1.8 (1.3–2.4)	0.15 (0.11–0.19)
High-income North America	134.4 (129.9–139.0)	68.8%	27.6 (26.6–28.5)	0.3 l (0.29–0.32)	27.2 (25.1–29.2)	46.3%	5.8 (5.4–6.2)	-0.01 (-0.07 to 0.04)	13.2 (9.8–17.4)	63.9%	2.8 (2.0–3.6)	0.26 (0.24–0.27
Central Europe	35.6 (33.4–37.7)	22.5%	21.2 (19.9–22.6)	0.11 (0.1–0.11)	8.8 (7.9–9.8)	12.4%	6.3 (5.7–7.0)	-0.03 (-0.03- to -0.02)	3.5 (2,579,533– 4,810,324)	18.2%	2.2 (1.6–2.9)	0.06 (0.06–0.07
Southeast Asia	24.7 ( 17.4–132.6)	132.5%	17.2 (16.3–18.3)	0.24 (0.24–0.24)	26.1 (23.7–28.9)	109.1%	3.6 (3.3–4.0)	0.05 (0.04–0.06)	11.8 (8.6–15.9)	123.1%	1.6 (1.2–2.2)	0.2 (0.2–0.21)
Oceania	1.7 (1.6–1.8)	152.8%	16.9 (16.0–18.0)	0.1 (0.09–0.11)	0.4 (0.4–0.5)	142.0%	3.8 (3.5–4.2)	0.02 (0.01–0.04)	0.1 (0.1–0.2)	148.3%	1.5 (1.1–2.1)	0.08 (0.07–0.08
Minimal Health System	32.4 (30.0–34.7)	145.3%	16.8 (15.8–17.8)	0.06 (0.05–0.07)	9.1 (8.2–10.1)	143.9%	4.3 (3.9–4.7)	-0.03 (-0.05 to -0.01)	3.3 (2.4–4.3)	147.5%	1.6 (1.2–2.1)	0.06 (0.05–0.06
Central Asia	16.8 (15.6–17.9)	79.6%	18.3 (17.2–19.5)	0.21 (0.19–0.22)	4.7 (4.2–5.2)	67.5%	5.0 (4.5–5.5)	0.03 (0.02–0.04)	1.6 (1.2–2.2)	77.2%	1.8 (1.3–2.4)	0.21 (0.19–0.22
China	342.1 (322.5–361.0)	100.5%	17.4 (16.4–18.4)	0.21 (0.16–0.26)	68.6 (62.0–75.0)	63.4%	3.6 (3.3–4.0)	-0.18 (-0.26-0.11)	30.4 (21,752,735– 41,618,819)	82.9%	1.6 (1.1–2.1)	0.08 (0.02–0.14

Zhou et al

Tokelau	0.00026 (0.00025– 0.00028)	14.9%	18.4 (17.3–19.4)	0.23 (0.22–0.24)	0.000056 (0.000051– 0.000061)	7.7%	4.0 (3.6–4.3)	0.05 (0.04–0.07)	0.000024 (0.000017– 0.000032)	14.3%	1.7 (1.2–2.2)	0.18 (0.18–0.19)
Eritrea	0.6 (0.6–0.7)	159.1%	15.0 (13.9–16.1)	0.32 (0.31–0.32)	0.2 (0.2–0.2)	132.2%	3.9 (3.5–4.3)	0.05 (0.04–0.06)	0.06 (0.04–0.08)	157.3%	1.4 (1.0–1.9)	0.36 (0.35–0.37)
United States of America	121.6 (117.6–125.7)	68.5%	27.9 (26.9–28.8)	0.33 (0.31–0.35)	24.8 (22.9–26.7)	45.7%	5.9 (5.5–6.3)	0 (-0.06-0.06)	12.0 (8.9–15.8)	63.8%	2.8 (2.1–3.6)	0.28 (0.26–0.29)
Hungary	3.2 (3.0–3.4)	15.0%	22.3 (20.9–23.8)	0.1 (0.1–0.11)	0.9 (0.8–1.0)	6.2%	6.5 (5.8–7.2)	-0.03 (-0.03-0.02)	0.3 (0.2–0.4)	13.2%	2.3 (1.7–3.1)	0.11 (0.1–0.12)
Myanmar	8.7 (8.2–9.3)	106.4%	16.0 (15.1–17.1)	0.34 (0.32–0.35)	1.8 (1.6–2.0)	84.2%	3.2 (2.9–3.6)	0.06 (0.05–0.08)	0.8 (0.6–1.1)	95.2%	1.5 (1.1–2.0)	0.24 (0.23–0.26)

Notes: \*: Percentage change from 1990 to 2019.

Abbreviations: DALYs, disability-adjusted life years; ASRs, age-standardized rates; EAPCs, estimated annual percentage change.

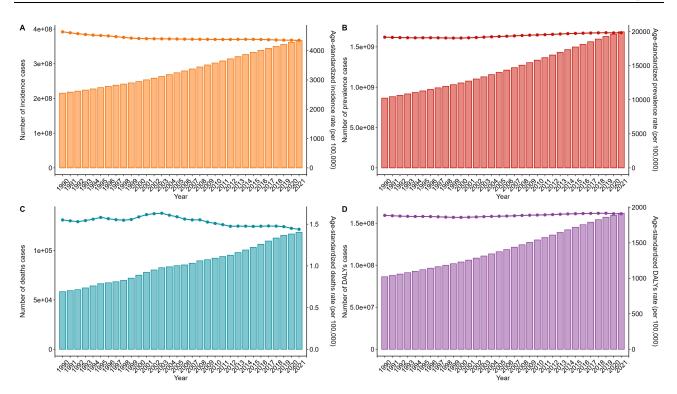


Figure I The global prevalence, incidence, death, DALYs and ASRs for musculoskeletal disorders between the years 1990 and 2021. (A): incidence and ASIR; (B): prevalence and ASPR; (C): death and ASMR; (D): DALYs and ASDR.

#### 54 GBD Regions

As shown in <u>Supplementary Table 2</u> and Figure 3, in 2021, Asia had the highest number of disease cases (975,630,015 cases, 95% UI: 922,460,302–1,033,352,246), incidence cases (200,837,175 cases, 95% UI: 182,344,-612–220,226,486), deaths (67,282 cases, 95% UI: 54,450–75,821), and DALYs (92,056,204, 95% UI: 67,236,-357–123,282,406). High-income North America recorded the highest ASPR with 27,620 cases per 100,000 people and the highest ASDR with 2762 years per 100,000 people in 2021; Central Europe recorded the highest ASIR in 2021, with 6315 cases per 100,000 population. In addition, in high-income North America, the EAPC was higher for both the ASPR (27.6, 95% CI: 26.6–28.5) and the ASDR (0.26, 95% CI: 0.24–0.27).

In contrast, Oceania had the lowest number of disease cases (1,729,824 cases, 95% UI: 1,615,429-1,849,544), incidence cases (415,703 cases, 95% UI: 374,296-460,315), deaths (38 cases, 95% UI: 14-63), DALYs (163,786, 95% UI: 119,667-219,915), ASMR (0.34 cases per 100,000 population, 95% UI: 0.15-0.54), and ASDR (1543 per 100,000 population, 95% UI: 1121-2072) in 2021. In addition, the Minimal Health System region had the lowest ASPR (16,792 cases per 100,000 population, 95% UI: 15,765-17,835), while Southeast Asia had the lowest ASIR (3603 cases per 100,000 population, 95% UI: 3274-3956).

By clustering the EAPCs corresponding to the ASPR, ASIR, ASMR, and ASDR across the 54 GBD regions, we identified distinct trends. As illustrated in Figure 4, the burden of MSDs in Central Asia exhibited a significant increasing trend [EAPC for ASPR: 0.21 (0.19–0.22); EAPC for ASIR: 0.03 (0.02–0.04); EAPC for ASMR: 6.14 (4.91–7.39); EAPC for ASDR: 0.21 (0.19–0.22)], whereas regions such as Tropical Latin America, Central Africa, and Sub-Saharan Africa demonstrated a significant decrease in disease burden.

#### 204 Countries and Regions

Figure 5 and Table 1 show that in 2021, China had the highest number of MSDs (342,123,786 cases, 95% UI: 322,541,-900.2–361,025,855.3), incidence cases (68,646,957 cases, 95% UI: 61,976,491.3–74,990,168.2), and DALYs (30,419,426, 95% UI: 21,752,735.4–41,618,818.7). The United States of America had the highest ASPR (27,919 cases per 100,000 people, 95% UI: 26,947.1–28,824.7) and ASDR (2791 cases per 100,000 people, 95% UI: 2052.2–3646.5) in 2021. In addition, the

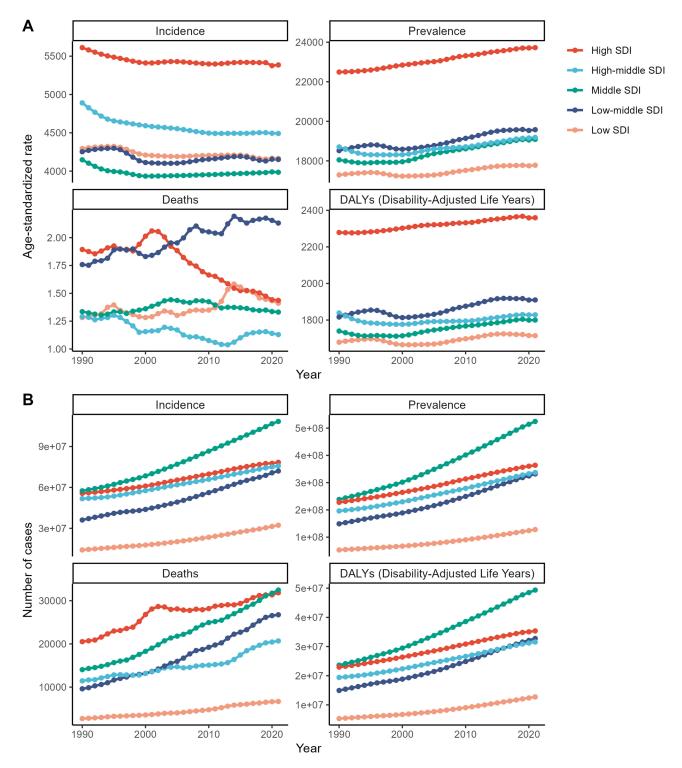


Figure 2 The number of prevalence, incidence, death, DALYs, and ASRs for musculoskeletal disorders in five SDI regions from 1990 to 2021. (A): ASIR, ASPR, ASMR and ASDR; (B): the number of incidences, prevalences, deaths and DALYs.

top three highest ASIR were all in Central Europe, with Hungary in first place (6517 cases per 100,000, 95% UI: 5871.3–7216.4), followed by Poland (6515 cases per 100,000, 95% UI: 5870.6–7224.9), and then the Czech Republic (6341 cases per 100,000, 95% UI: 5686.8–7058.8). In contrast, Tokelau had the lowest number of prevalent MSD cases (260 cases, 95% UI: 250–280), morbidity cases (56 cases, 95% UI: 51–61), and DALYs (24 cases, 95% UI: 17–32). MSDs were lowest in Eritrea for both the ASPR (15,036 cases per 100,000 population, 95% UI: 13,858.0–16,129.3) and the ASDR

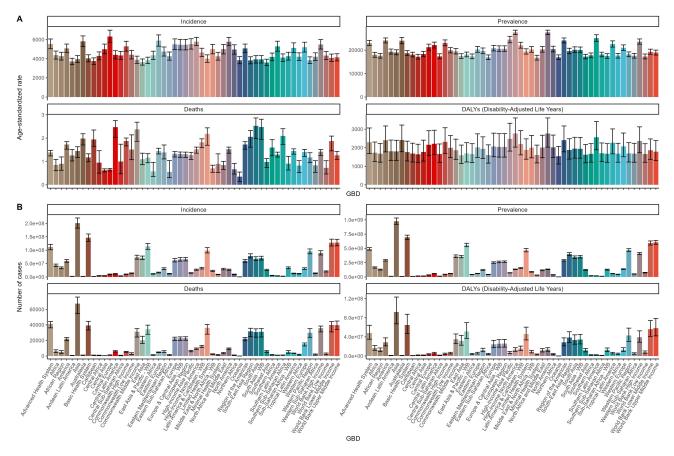


Figure 3 The number of prevalence, incidence, death, DALYs, and ASRs for musculoskeletal disorders in 54 GBD regions in 2021. (A): ASIR, ASPR, ASMR and ASDR; (B): the number of incidences, prevalences, deaths and DALYs.

(1394 cases per 100,000 population, 95% UI: 992.9–1883.8). In addition, the ASIR was lowest in Myanmar, with 3248 cases per 100,000 population (95% UI: 2954.9–3562.5).

As shown in <u>Supplementary Table 2</u> and Figure 6, Qatar experienced the largest increase in the number of MSD cases (729%), incidence cases (836%), and DALYs (826%) from 1990 to 2021, followed by the United Arab Emirates in second place (819%, 682%, and 774%), and Jordan in third place (412%, 346%, and 388%). In contrast, Georgia had the smallest increase in the number of MSDs cases (-16%), incidence cases (-21%), and DALYs (-20%), followed by Latvia (-4%, -14%, and -6%), and thirdly Bulgaria (-1%, -9%, and -6%).

As shown in <u>Supplementary Table 2</u> and Figure 7, from 1990 to 2021, the EAPC was highest for ASPR in Pakistan (0.45, 95% CI: 0.42–0.49), ASIR in Sweden (0.47, 95% CI: 0.34–0.61), ASMR in Georgia (9.97, 95% CI: 8.03–11.95), and ASDR in Taiwan Province of China (0.57, 95% CI: 0.52–0.63). In contrast, the minimum values of EAPC for ASPR were -0.25 (95% CI: -0.32 to -0.19) and for ASDR were -0.34 (95% CI: -0.43 to -0.26), both observed in Burundi. In addition, the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.35, 95% CI: -0.41 to -0.29), and the minimum values of EAPC for ASIR were in Denmark (-0.30).

#### Population Distribution of the Burden of MSDs

As shown in <u>Supplementary Table 2</u> and Figure 8, with the exception of the ASMR, the four crude indicators of MSDs, as well as the ASPR, ASIR, and ASDR in 2021, exhibited an increasing and then decreasing trend with the age of the population. MSDs manifested the highest number of prevalence cases (182,480,403, 95% UI: 199,784,-273–165,987,655) and DALYs (16,683,547, 95% UI: 11,397,152–23,549,503) among individuals aged 55–59 years. Moreover, the highest number of incidence cases (37,340,151, 95% UI: 29,002,083–47,084,774) was noted among those aged 50–54 years. However, after adjusting for age standardization, the ASPR (62,129 cases

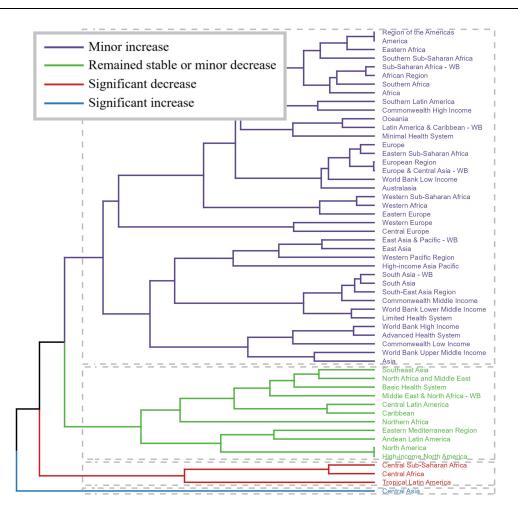


Figure 4 A cluster analysis of EAPCs of ASRs in 54 GBD regions from 1990 to 2021.

per 100,000 population, 95% UI: 57,304.5-66,801.8), ASIR (11,671 cases per 100,000 population, 95% UI: 9127.4-14,640.8), and ASDR (5451 cases per 100,000 population, 95% UI: 3916.6-7683.5) were highest in individuals aged 75-85 years. Additionally, ASMR shows an exponential increase with the age of the population.

Figure 9 shows a clear surge in the number of prevalent cases of MSDs, the number of incidences, and the number of DALYs for individuals in the 50–54 and 55–59 age groups around the year 2000. Furthermore, between 1990 and 2021, the highest levels of ASIR, ASPR, and ASDR were consistently found among individuals aged 75 to 85. Figure 10 shows that between 1990 and 2021, female MSDs exhibited significantly higher values in all four crude indicators and four ASRs compared to males. Moreover, the gap between females and males in the four crude indicators widened progressively over the years. In 2021, all of the indicators associated with MSDs are 1.43 to 2.30 times higher for women than for men globally.

#### **Decomposition Analysis**

The decomposition analysis revealed that from 1990 to 2021, there were globally 738,903,045 new cases of disease (an 85.41% increase), 135,055,774 new morbidities (a 62.71% increase), 51,781 new deaths (an 88.69% increase), and 68,028,817 new DALYs (a 78.84% increase). As shown in Figure 11 and <u>Supplementary Table 3</u>, the global increase in MSDs indicators and in the five SDI regions is primarily attributed to population growth. However, the rise in mortality rates in the high-middle SDI region (76.23%) and the high SDI region (106.53%) is predominantly driven by population ageing. Globally, the burden of disease, morbidity, mortality, and DALYs for MSDs has increased by 63.49%, 80.81%, 60.42%, and 67.45%, respectively, over the past 30 years due to population growth. In addition, population growth had the most significant impact on the increase in prevalence (89.31%), incidence (103.00%), mortality (89.31%), and DALY (96.42%) of MSDs in the low SDI region. In contrast, the impact of epidemiological changes on morbidity (-13.62%, -11.65%, and

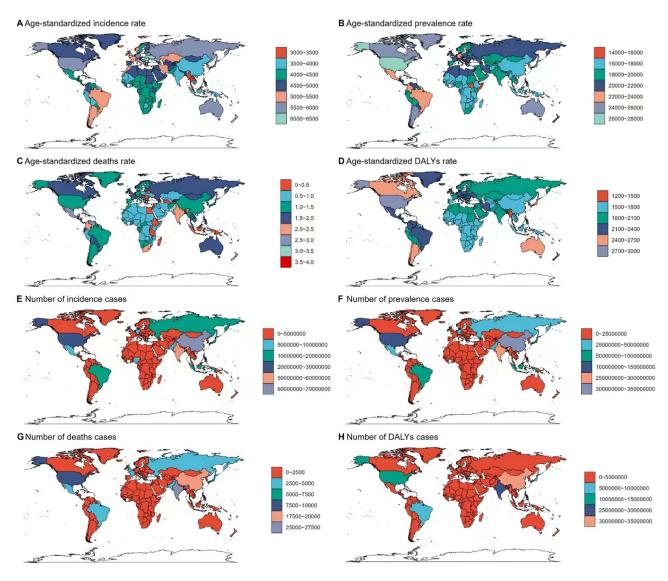


Figure 5 The number of prevalence, incidence, deaths, DALYs and ASRs for musculoskeletal disorders in 204 countries and regions in 2021. (A): ASIR; (B): ASPR; (C): ASMR; (D): ASDR; (E): number of incidences; (F): number of prevalences; (G): number of deaths; (H): number of DALYs.

-4.63%) and mortality (-13.89%, -66.66%, and -22.36%) was negative for the globe, the high SDI region, and the highmiddle SDI region. However, these differences were insufficient to offset the overall upward trend. The decomposition analysis of MSDs indicates that population growth and ageing are the primary drivers of change in most regional indicators.

#### Frontier Analysis

Frontier analysis entails identifying the lowest achievable age-standardized burden of disease across various SDI levels by establishing an optimal "frontier" or boundary. Effective difference quantified as the absolute distance of countries or regions from the frontier, serving as a measure of the unrealized health potential specific to each country or region at its corresponding level of development. As depicted in Figure 12 and <u>Supplementary Table 4</u>, the top five countries with the largest effective differences in the ASIR are Hungary, Czechia, Ukraine, Romania, and Albania (Range: 3021.1–3348.9). Conversely, the top five countries with the smallest effective differences in the ASIR were Mali, Timor-Leste, Seychelles, Malaysia, and Burkina Faso (Range: 100.8–311.9). Furthermore, the top 5 countries with the largest effective differences in ASPR are the United States, Japan, Greenland, Brunei Darussalam, and Brazil (Range: 8962.5–14,221.9). The five countries with the smallest effective differences in ASPR are Somalia, Niger, Rwanda, Cambodia, and Papua New Guinea (range: 118.58–2760.06).

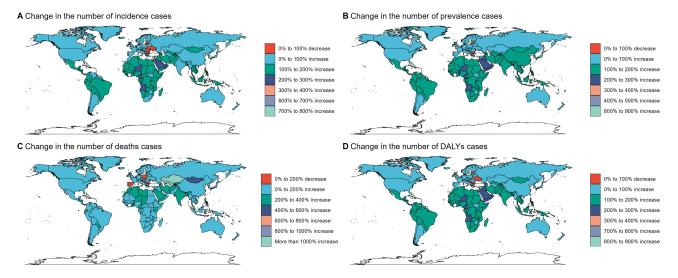


Figure 6 The changes in prevalence cases, incidence cases, death cases and DALYs for musculoskeletal disorders in 204 countries from 1990 to 2021. (A): change in the number of incidences; (B): change in the number of prevalences; (C): change in the number of deaths; (D): change in the number of DALYs.

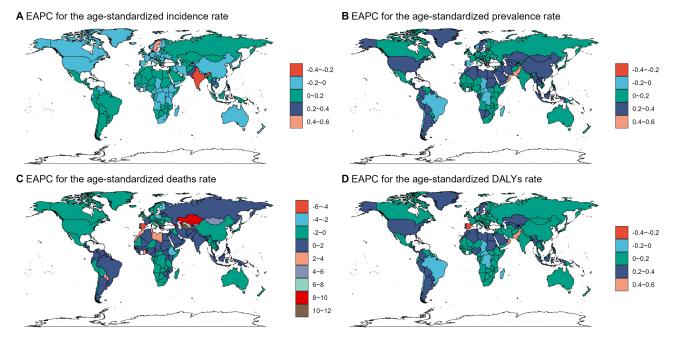


Figure 7 The EAPC for ASPR, ASIR, ASIR, ASDR in 204 countries and regions for musculoskeletal disorders from 1990 to 2021. (A): EAPC for ASIR; (B): EAPC for ASPR; (C): EAPC for ASMR; (D): EAPC for ASPR.

# Discussion

In the GBD 2021 database study, we integrated decomposition and frontier analyses to examine the temporal, spatial, age, and gender distribution of the global burden of MSDs from 1990 to 2021, as well as to analyze trends. The number of cases of MSDs, morbidity, mortality, and DALYs has increased significantly over the past three decades. As the second leading cause of non-fatal disability, MSDs affect nearly 1.68 billion people worldwide, representing 21.38% of the population.<sup>17</sup> Nevertheless, the ASIR and ASMR exhibited a downward trend between 1990 and 2021, with a mere 3.29% increase in the ASPR and 1.20% in the ASDR. Although this seems inconsistent with the rise in the four crude indicators for MSDs, it is important to note that these crude indicators are affected by population growth and ageing. These factors are typically associated with increasing trends in disease burden. Therefore, these findings should be interpreted with caution. Moreover, the results are strikingly similar to those observed in 2017.<sup>18</sup> Similarly, decomposition analyses have affirmed that social

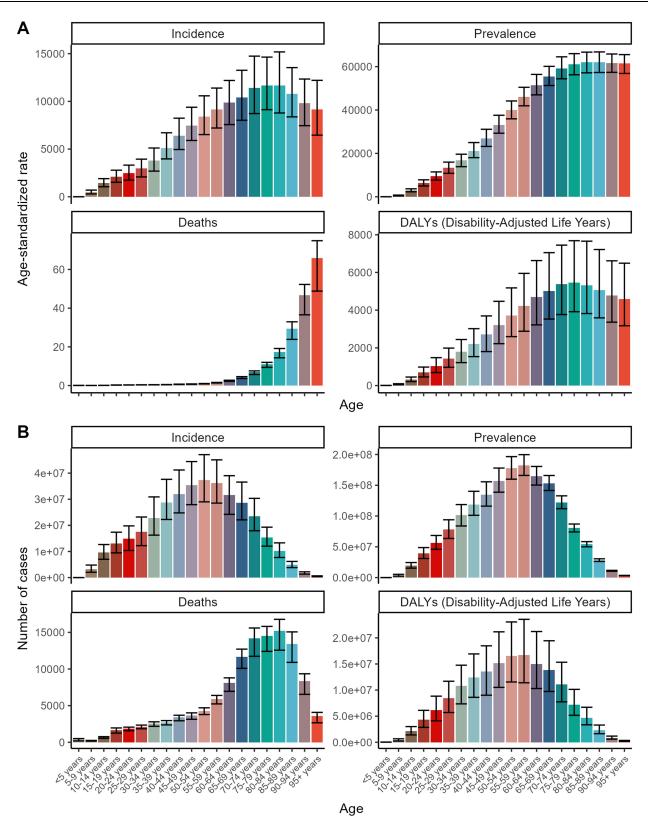


Figure 8 The number of prevalence, incidence, death, DALYs, and ASRs for musculoskeletal disorders in different age groups in 2021. (A): ASIR, ASPR, ASMR and ASDR; (B): the number of incidences, prevalences, deaths and DALYs.

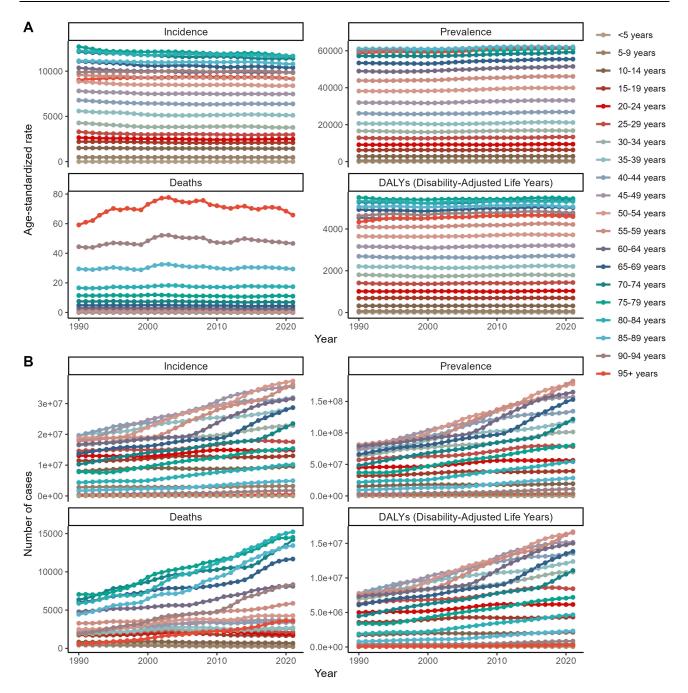


Figure 9 The number of prevalence, incidence, death, DALYs, and ASRs for musculoskeletal disorders in different age groups from 1990 to 2021. (A): ASIR, ASPR, ASMR and ASDR; (B): the number of incidences, prevalences, deaths and DALYs.

ageing and population expansion predominantly underpin the rise in crude indicators across most regions, while conversely, epidemiological changes exert a limiting influence.

Regional analyses indicate that the burden of MSDs is predominantly concentrated in high SDI regions, with a gradual shift towards middle and low-middle SDI regions. Retrospective studies have demonstrated that individuals residing in high SDI areas are more likely to have an elevated body mass index (BMI), which has been identified as a significant risk factor for osteoarthritis, low back pain, gout, and various other MSDs.<sup>19,20</sup> Analyzing the BMI of 128.9 million children and adolescents, the NCD Risk Factor Collaboration revealed that although many high SDI regions exhibit elevated BMI levels among youth, the upward trend has stabilized. However, accelerated increases are observed in certain parts of Asia.<sup>21</sup> This not only elucidates the reasons behind the disproportionate prevalence of MSDs

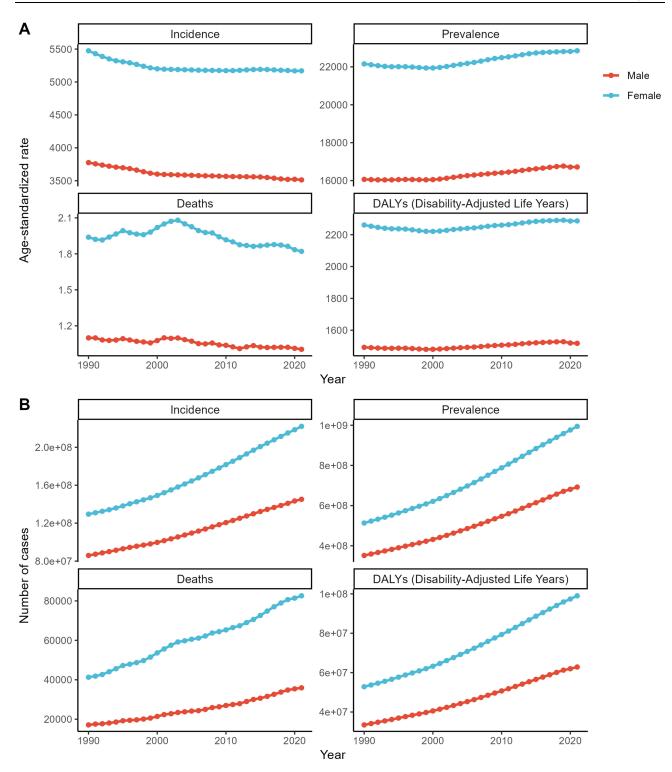


Figure 10 The number of prevalence, incidence, death, DALYs, and ASRs for musculoskeletal disorders in different sexes from 1990 to 2021. (A): ASIR, ASPR, ASMR and ASDR; (B): the number of incidences, prevalences, deaths and DALYs.

in high-SDI regions but also aligns with the findings of the EAPC cluster analysis, which highlighted a notable upward trend in the burden of MSDs in Central Asia. Furthermore, as developing countries, Central Asian countries have a markedly higher prevalence of vitamin D deficiency in children, ranging from 38.1% to 78.7%, which increases their susceptibility to MSDs, including non-specific muscle pain, reduced muscle strength and low bone density.<sup>22,23</sup>

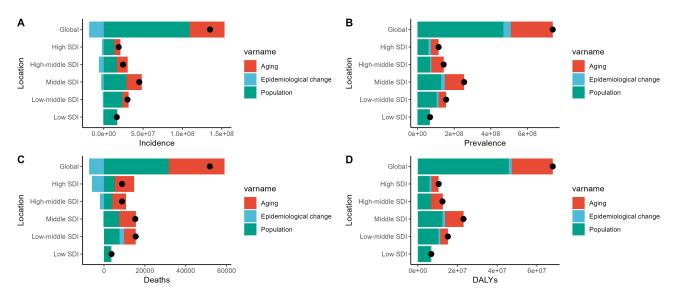


Figure 11 Decomposition analysis of the prevalence, incidence, death and DALYs associated with musculoskeletal diseases from 1990 to 2021. (A): the number of incidences; (B): the number of prevalences; (C): the number of deaths; (D): the number of DALYs.

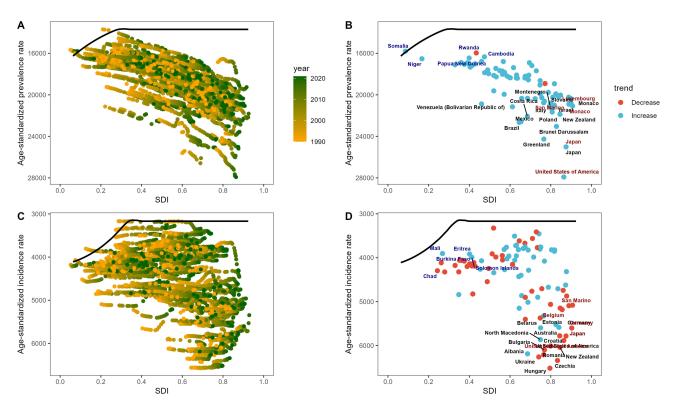


Figure 12 Frontier analysis of ASIR and ASPR in musculoskeletal diseases from 1990 to 2021. (A) and (B): ASPR; (C) and (D): ASIR.

As the country with the highest number of cases of MSDs, morbidity, and DALYs in the world, China is confronted with significant challenges. On one hand, the prevalence of vitamin D deficiency in Chinese children is alarmingly high, with up to 50% having serum 25-hydroxyvitamin D levels  $< 12.5 \text{ nmol/L}^{23}$  On the other hand, China is undergoing a nutritional transition, marked by a shift from malnutrition to a rapid rise in obesity. A review of relevant surveys indicates that the prevalence of adult obesity in China increased by a factor of 2.61 between 2004 and 2018.<sup>24</sup> With the implementation of the "Healthy China 2030" plan, there will be greater awareness of the importance of MSDs, creating favorable conditions for the early identification and treatment of MSDs.<sup>25</sup> Following age-standardized

adjustment, the burden of MSDs is most significant in the United States of America and certain countries in Central Europe, a finding consistent with the 2017 findings.<sup>18</sup> Additionally, Pakistan, Sweden, Georgia, and Taiwan Province of China exhibited the highest EAPCs for ASRs. This suggests that the future burden of MSDs in these regions will continue to escalate, necessitating proactive measures by these regions and their respective ministries to address this emerging challenge.

In age-period-cohort analyses, the global burden of MSDs is most pronounced among individuals aged 50–59 years. Moreover, all indicators of MSDs were significantly higher in women than in men, aligning with previous studies.<sup>18</sup> This disparity is largely attributable to the gender segregation within the labor force and the enduring gender imbalance in domestic work.<sup>26</sup> Frontier analyses suggest that the United States, Japan, and other advanced countries have greater potential for improvement in reducing the burden of MSDs. In 2018, an article in the Lancet highlighted the need to address the growing global burden of lower back pain and outlined a range of actions needed to address this challenge.<sup>27</sup> However, the article did not address all MSDs. Furthermore, only half of the countries in the Organization for Economic Co-operation and Development explicitly prioritize musculoskeletal health and pain, indicating inadequate attention to MSDs in many regions globally.<sup>28</sup> Therefore, pertinent global health agencies, such as the World Health Organization, should raise awareness about MSDs and advocate for enhanced early prevention and treatment of these conditions across all countries and regions.

To the best of our knowledge, this study represents the latest report on the global burden of MSDs spanning from 1990 to 2021. Nevertheless, this report has certain limitations. Firstly, the estimates remain constrained by the availability and comprehensiveness of the data sources. The absence of robust civil registration and vital statistics systems in numerous low-income and middle-income countries, which are essential for the generation of reliable data, introduces significant uncertainty into all population estimates. Secondly, owing to the diverse array of statistical modeling techniques employed by the GBD collaborators, particularly at the national level, the data derived from the GBD heavily relies on modeled data, given the scarcity of raw data. The data, which are based on estimates derived from statistical modelling methods, are susceptible to significant uncertainties that can affect the precision of assessments concerning age, period, and birth cohort effects. Thirdly, As the GBD 2021 database does not encompass osteoporosis and sarcopenia among its musculoskeletal disease classifications, these conditions are consequently omitted from this paper, thereby diminishing the comprehensiveness and accuracy of the analysis regarding the burden of musculoskeletal diseases.

### Conclusion

By analyzing the GBD 2021 database, we discovered that the global burden of MSDs is substantial. This burden is predominantly concentrated in developed countries, particularly the United States, with a smaller portion found in developing countries, notably China. Additionally, the analysis indicates that the burden of MSDs is expected to shift towards middle-low SDI regions, specifically Central Asia, in the future.

# Disclaimer

The funding sources had no role in the study design, data analysis, interpretation, or decision to submit for publication.

### **Data Sharing Statement**

Data are available upon reasonable request.

# **Ethics Approval**

This study does not contain personal or medical information about identifiable living individuals, and animal subjects were not involved.

Written informed consents from participants were not applicable in this study.

The institutional review board of the Zhejiang provincial people's hospital determined that the study did not need ethics approval because it used publicly available data. This study followed the Guidelines for Accurate and Transparent Health Estimates Reporting Guidelines for cross-sectional studies.

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### **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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### Disclosure

The authors declare that they have no conflict of interest.

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