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Global, regional, and national multiple myeloma burden from 1990 to 2021: a systematic analysis for of the Global Burden of Disease Study 2021

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Abstract

Background Multiple myeloma (MM) is the second most common haematological malignancy worldwide. A comprehensive global analysis of MM based on diverse geographic locations and timeframes is lacking. This study aimed to provide the incidence, mortality rate, and disability-adjusted life years (DALYs) of MM, from 1990 to 2021, focusing on the age structure and temporal trends of the disease burden.

Methods This study analysed the most recent MM data (1990 to 2021) from 204 countries and territories obtained from the Global Burden of Disease database. MM incidence, age-standardised mortality rate (ASMR), and DALYs were stratified by age, sex, and region to accurately reflect epidemiological trends and disease burden. The correlation between age-standardised rates and social population index was evaluated. To explore the influencing factors of MM, the annual percentage change (APC) and average APC rate (AAPC), as well as their corresponding 95% confidence intervals (UIs), were calculated.

Results In 2021, there were approximately 35,000 cases of MM worldwide, with the highest numbers in China and Germany, with 47,003 and 32,010 cases, respectively. In 2021, Europe had the highest ASIR and ASPR, while North America had the highest ASMR and DALYs. Globally, age-standardized ASPR, ASMR, and DALYs all increased between 1990 and 2021. From 1990 to 2021, the number of cases, deaths, and disability-adjusted life-years due to MM were higher in males than in females. The higher the sociodemographic index, the higher the ASPR.

Conclusions The global prevalence, ASIR, ASMR and DALYs of MM increased, showing significant regional disparities. These findings underscore the need for prevention in specific populations and emphasise the urgent need for new therapies to reduce ASIR and improve patient prognosis.

Keywords Multiple myeloma, Global Burden of Disease, Epidemiological analysis, Age structure analysis, Joinpoint regression analysis

Background

Multiple myeloma (MM), the second most common haematological cancer, is a clonal plasma cell malignancy characterised by abnormal monoclonal plasma cell proliferation in the bone marrow, which leads to bone marrow failure, osteolysis, renal failure, immune deficiency, and premature death [1–4]. Although still considered a

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single disease, MM is a collection of several plasma cell malignancies with distinct cytogenetic abnormalities [5]. According to the 2016 Global Burden of Disease report, the incidence of MM increased by 126% from 1990 to 2016, and the disease usually occurs in the elderly, with incidence rates of 85% and 60% in people over 55 and over 65 years of age, respectively. [6, 7]. Although bone marrow-clearing chemotherapy and autologous stem cell transplantation improved the median survival time to > 6 years, MM remains largely incurable and imposes a significant financial burden on society and healthcare systems. From 1990 to 2021, the prevalence of MM in China increased significantly by 14.8% (95% UI, 5.3–26.2%), while the age-standardized prevalence increased by 5.8% (95% UI, 1.7–10.8%) [8].

In addition, factors such as a long-term monopoly on anticancer drugs, non-negotiable drug prices between health insurance and pharmaceutical companies, [9] and prohibitions on drug imports have led to persistently high cancer treatment costs. Additionally, increases in laboratory tests and imaging, doctor visits, chemotherapy management, hospital fees, and nursing costs have substantially increased the economic burden [10]. A comprehensive description of the global burden of MM is needed to direct health policy, resource allocation, research, and patient care.

The Global Burden of Disease (GBD) study is a reliable tool for understanding the current assessment of the age-standardised incidence rate (ASIR), age-standardised mortality rate (ASMR), and disability-adjusted life years (DALYs). Therefore, in this study, we aimed to systematically describe the MM disease burden, including the prevalence, ASIR, ASMR, and DALYs, with a focus on age, sex distribution, and temporal trends, using the GBD statistical model. This analysis will help clinicians, epidemiologists, and health policy makers to further optimise the allocation of medical resources and develop more effective public health strategies.

Methods

Data collection and download

In 2021, the GBD (https://ghdx.healthdata.org/gbd-2021/sources) was supported by collaborators from 164 countries using the latest epidemiological data and strengthened standardized methods. Health damages related to 369 diseases and injuries were evaluated in detail, covering 88 risk factors in 204 countries and regions. The global health status and disease burden were evaluated systematically. In this study, we obtained 1990–2021 data (global ASIR, ASMR, DALYs, and ASR of MM) from the GHDx (https://vizhub.healthdata.org/gbdresults/) with an emphasis in morbidity, mortality and DALYs.. In addition, we evaluated MM burden distribution among different age groups, sexes, and social population index. DALYs are composed of years of life lost (YLL) and years lived with disability (YLD). YLL is calculated by multiplying the number of deaths in each age group by the value of years of life lost for that age group. YLD is obtained by multiplying the number of cases by the average years of disability and the severity of the disease. DALYs are the sum of the two [11, 12].

Joinpoint regression analysis

The Joinpoint regression analysis model was used to evaluate the time trend of disease prevalence or death. The model quantitatively describes the important change points of the MM epidemic time-series data globally, nationally, and regionally. The model allowed for annual percentage change (APC) calculation (with 95% confidence intervals [CIs]) to describe the epidemiological trends within the described time range. AAPC or APC > 0 indicates an upward trend, while AAPC or APC < 0 indicates a downward trend, which is only meaningful if the upper and lower limits of their 95% confidence intervals (CIs) have the same sign. Otherwise, the trend is considered to be stable over time [13]. If the AAPC and its 95% CI were higher or lower than zero, it indicated that ASR increased or decreased over time, respectively. When the 95% CI was zero, the ASR did not change significantly. Detailed information is provided in Supplementary Methods.

Age groups

In terms of age, we also categorized patients with MM into 16 age groups: '20–24 years', '25–29 years', '30–34 years', '35–39 years', '40–44 years', '45–49 years', '50–54 years', '55–59 years', '60–64 years', '65–69 years', '70–74 years', '75–79 years', '80–84 years', '85–89 years', '90–94 year', and '95 + years'.

Statistical analysis

The prevalence, ASIR, ASMR, and DALYs were expressed as population projections per 100,000 people, with 95% UI. In addition, we calculated the AAPC of the social population index in 204 countries and used Spearman's correlation analysis to evaluate the relationship between AAPC of social population index and ASR. Statistical significance was set at $p < 0{\cdot}05$. All statistical analyses were performed using R software (version 4·2·2) and the ggplot2 package.

Results

Global, regional, and national MM burden

Globally, the incidence of MM increased from 55,710.10 cases in 1990 to 148,754.63 cases in 2021. The ASIR increased from 1.47 cases per 100,000 in 1990 to 1.74

cases per 100,000 in 2021. In addition, the incidence of MM increased in all five social population index regions, with the high social population index region having the highest number of MM cases at 33,358 (95% UI: 31,615–34,445). In 2021, the ASIR was the highest in the high social population index region (3.16 per 100,000; 95% UI, 2.87–3.34) and lowest in the low social population index region (0.77 per 100,000; 95% UI: 0.51–1.02). Between 1990 and 2021, the highest increase (1.04-fold) in cases was in the middle social population index regions (Table 1).

The global mortality rate for MM also increased during the period 1990–2021. The increasing trend varied by region, with the largest increase in central social population index (0.79 per 100,000; 95% UI: 0.38–1.15), in contrast to high social population index, which showed a decreasing trend (−0·09 per 100,000; 95% UI: −0.14 to −0.05) (Table 2).

The global DALYs for MM also showed an upward trend. Similar to ASMR, the increase was greatest in the medium social population index region (0·79 per 100,000; 95% UI: 0·37–1.16). High social population index agreed that there was a downward trend (−0·15 per 100,000; 95% UI: −0·18–−0·11) (Table 3).

Regionally, MM incidence increased globally, with the largest increase in Asia and the smallest increase in the North American high region. ASIR Europe had the highest MM rate at 3.33 cases per 100,000 (95% UI: 3.06–3.563), followed by North America at 3.10 cases per 100,000 (95% UI: 2.83–3.26). ASIR Asia had the largest increase in 0.70 cases per 100,000 (95% UI: 0.32–1.07), with the largest increase in Europe and the smallest increase in the North American high region. In contrast, ASIR Oceania had the lowest MM rate at 0.36 cases per 100,000 (95% UI: 0.21–0.50), followed by Africa at 0.95 cases per 100,000 (95% UI: 0.61–1.18). The United States of America, China, and India were the three countries that reported the most new cases of MM in 2021, while Mali, the Tokelau Islands, and Niue were the three countries with the fewest reported new MM cases. Monaco, Italy, and Bermuda had the highest ASIRs, whereas Mali, Niger, and Chad had the lowest (Fig. 1).

Age and sex differences in MM burden

Globally, both ASIR and ASDR showed a fluctuating trend from 1990 to 2021. Overall, ASIR and ASDR were significantly higher in males than in females. Age-standardised DALYs for both males and females showed a significant upward trend between 1990 and 2021. The age-standardised ASIR and ASMR for males were the highest in the high social population index quintile and lowest in the low social population index quintile in 1990, and a slight difference in age-standardised DALYs was observed between the low and low-middle social population index quintiles. However, between 1990 and 2021, the low-middle social population index quintile increased more significantly than did the low social population index quintile. ASIR and ASDR were generally lower for females than for males, but the trends from 1990 to 2021 were comparable between males and females. For females, the high social population index quintile had the highest age-standardised DALYs in 1990 and 2021. The age-standardised DALYs for women in all quintiles increased from 1990 to 2021.

From 1990 to 2021, the prevalence rates among the age groups remained stable, with the highest rates in the 90–94 age group. In 2021, the highest ASMR was in the high social population index 90–94 age group, and the lowest was in the low social population index 20–24 age group. Globally, DALYs trended upward for both males and females, with the most significant increase in the median social population index quintile. An increase in incidence occurred in both males and females, with a higher increase in males, particularly in the 25–29 age group, in countries with high-middle social population index. The number of deaths was the highest in the 95 + age group. The number of deaths was significantly higher in the high social population index age group. The number of deaths was significantly higher in the low social population index age group. In addition, the number of deaths was higher in males than in females, regardless of age or social population index. The MM ASIR, ASMR, and DALYs increased in all age groups as the population aged (Tables 4, 5, 6 and 7).

Overall time trends in sex and age structure

The MM incidence, ASMR, and DALYs showed significant upward trends from 1990 to 2021 (Fig. 2 Tables 2 and 3). The increasing trend was consistent across sexes, but the degree of increase varied between the sexes. In 1990, ASIR was comparable between sexes; however, in 2021, it increased to 1.70 (1.83–2.34) and 2.12 (1.83–2.34) in males and females, respectively (from 1.30 [1.20–1.43] and 1.43 [1.21–1.91], respectively) (Table 4). ASMR and ASIR trends were broadly similar, with ASMR increasing from 1.50 (1.38–1.66) to 1.67 (1.44–1.86) for males and from 1.14 (1.04–1.26) to 1.14 (0.96–1.31) for females (Table 5). Similarly, DALYs increased from 32.57 (29.55–36.21) in 1990 to 35.83 (30.46–39.98) in 2021 in males and from 22.89 (22.94–28.15) to 25.04 (20.39–29.10) in females (Table 6). The MM burden was significantly higher in males than in females. From the age distribution, it can be seen that ASIR peaked in the 90–94 age group, and both ASMR and DALYs increased with age, with a significantly higher rate of increase in males than in females.

Table 1 ASIR and number of cases of multiple myeloma in different regions in 1990, 2000, 2010 and 2021

	1990		2000			2010			2021		
	ASIR	number of cases	ASIR	number of cases	change	ASIR	number of cases	change	ASIR	number of cases	change
Global	1.47 (1.37 ~ 1.57)	55,710.10 (52,022.49 ~ 59,687.84)	1.72 (1.58 ~ 1.81)	82,252.06 (75,213.73 ~ 86,481.91)	0.17 (00.11 ~ 0.21)	1.75 (1.59 ~ 1.86)	109,379.93 (99,303.26 ~ 116,496.45)	0.02 (0.01 ~ 0.06)	1.74 (1.54 ~ 1.89)	148,754.63 (131,780.43 ~ 162,049.23)	−0.01 (−0.05 ~ 0.05)
SDI											
High SDI	2.98 (2.83 ~ 3.08)	33,358.07 (31,614.85 ~ 34,444.99)	3.47 (3.28 ~ 3.58)	46,634.72 (43,886.04 ~ 48,202.37)	0.16 (0.13 ~ 0.19)	3.49 (3.24 ~ 3.63)	58,416.35 (53,750.75 ~ 60,864.22)	0.01 (−0.02 ~ 0.03)	3.16 (2.87 ~ 3.34)	68,287.53 (61,342.09 ~ 72,525.42)	−0.09 (−0.12 ~ 10.07)
High-middle SDI	1.27 (1.20 ~ 1.37)	12,561.71 (11,834.03 ~ 13,538.50)	1.58 (1.42 ~ 1.67)	18,952.82 (17,005.40 ~ 20,064.58)	0.24 (0.13 ~ 0.31)	1.68 (1.52 ~ 1.79)	25,342.51 (22,842.64 ~ 26,883.36)	0.07 (0.02 ~ 0.12)	1.75 (1.52 ~ 1.95)	34,787.52 (30,245.11 ~ 38,625.23)	0.04 (−0.03 ~ 0.12)
Middle SDI	0.51 (0.45 ~ 0.66)	5,249.24 (4,561.16 ~ 6,753.37)	0.74 (0.57 ~ 0.81)	10,056.35 (7,773.45 ~ 11,067.39)	0.44 (0.19 ~ 0.60)	0.84 (0.69 ~ 0.98)	15,738.87 (12,872.13 ~ 18,287.32)	0.14 (0.07 ~ 0.27)	1.05 (0.84 ~ 1.23)	28,497.75 (22,906.09 ~ 33,491.54)	0.25 (0.13 ~ 0.38)
Low-middle SDI	0.54 (0.39 ~ 0.71)	3,221.81 (2,332.48 ~ 4,254.84)	0.64 (0.50 ~ 0.81)	4,918.66 (3,814.44 ~ 6,243.83)	0.19 (0.10 ~ 0.35)	0.73 (0.61 ~ 0.99)	7,544.96 (6,306.66 ~ 10,224.29)	0.15 (0.04 ~ 0.32)	0.92 (0.79 ~ 1.30)	13,200.85 (11,292.66 ~ 18,482.68)	0.26 (0.12 ~ 0.45)
Low SDI	0.56 (0.32 ~ 0.79)	1,243.33 (695.71 ~ 1,749.92)	0.58 (0.35 ~ 0.82)	1,581.34 (953.39 ~ 2,241.50)	0.03 (−0.06 ~ 0.17)	0.62 (0.41 ~ 0.82)	2,192.32 (1,464.67 ~ 3,007.59)	0.06 (−0.05 ~ 0.29)	0.77 (0.51 ~ 1.02)	3,800.95 (2,523.31 ~ 5,130.65)	0.25 (0.09 ~ 0.49)

Table 2 ASMR and deaths due to multiple myeloma in different regions in 1990, 2000, 2010 and 2021

	1990		2000			2010			2021		
	ASMR	number of cases	ASMR	number of cases	change	ASMR	number of cases	change	ASMR	number of cases	change
Global SDI	1.29 (1.20 ~ 1.39)	47,568.96 (44,137.51 ~ 51,416.50)	1.44 (1.30 ~ 1.53)	67,089.63 (60,409.60 ~ 71,010.86)	0.11 (0.05 ~ 0.15)	1.38 (1.24 ~ 1.48)	84,398.84 (75,918.25 ~ 91,116.43)	−0.04 (−0.07 ~ 0.00)	1.37 (1.22 ~ 1.52)	116,359.63 (103,078.62 ~ 128,470.57)	0.00 (−0.04 ~ 0.05)
High SDI	2.50 (2.36 ~ 2.57)	28,142.69 (26,550.76 ~ 28,971.06)	2.69 (2.51 ~ 2.79)	36,811.02 (34,246.23 ~ 38,177.84)	0.08 (0.05 ~ 0.10)	2.45 (2.25 ~ 2.56)	42,448.34 (38,708.54 ~ 44,478.41)	−0.09 (−0.11 ~ −0.08)	2.28 (2.05 ~ 2.41)	51,434.7 7(45,704.74 ~ 54,830.47)	−0.07 (−0.1. ~ −0.05)
High-middle SDI	1.05 (0.99 ~ 1.14)	10,133.47 (9,534.96 ~ 10,990.15)	1.26 (1.12 ~ 1.34)	14,820.31 (13,130.17 ~ 15,760.93)	0.19 (−0.08 ~ 0.26)	1.27 (1.13 ~ 1.35)	18,902.06 (16,903.50 ~ 20,090.46)	0.01 (−0.03 ~ 0.07)	1.28 (1.12 ~ 1.43)	25,451.41 (22,131.83 ~ 28,174.45)	0.01 (−0.05 ~ 0.08)
Middle SDI	0.49 (0.43 ~ 0.63)	4,837.77 (4,187.44 ~ 6,267.88)	0.69 (0.53 ~ 0.76)	9,030.03 (6,918.37 ~ 9,934.63)	0.39 (0.15 ~ 0.55)	0.75 (0.61 ~ 0.87)	13,580.11 (11,082.47 ~ 15,795.84)	0.09 (0.02 ~ 0.22)	0.88 (0.71 ~ 1.04)	23,404.7 7(18,799.77 ~ 27,500.91)	0/18 (0.07 ~ 0.29)
Low-middle SDI	0.55 (0.39 ~ 0.71)	3,155.97 (2,278.87 ~ 4,161.56)	0.64 (0.50 ~ 0.82)	4,772.51 (3,712.55 ~ 6,097.24)	0.17 (0.09 ~ 0.34)	0.72 (0.60 ~ 0.97)	7,204.84 (6,022.30 ~ 9,756.16)	0.13 (0.01 ~ 0.30)	0.89 (0.76 ~ 1.24)	12,282.85 (10,526.79 ~ 17,215.46)	0.23 (0.09 ~ 0.41)
Low SDI	0.58 (0.33 ~ 0.81)	1,235.17 (688.66 ~ 1,741.47)	0.60 (0.36 ~ 0.84)	1,569.75 (948.02 ~ 2,221.25)	0.03 (−0.06 ~ 0.17)	0.63 (0.42 ~ 0.86)	2,153.44 (1,439.97 ~ 2,954.36)	0.05 (−0.06 ~ 0.27)	0.77 (0.52 ~ 1.02)	3,648.51 (2,427.37 ~ 4,903.81)	0.22 (0.07 ~ 0.46)

Table 3 DALYs and number of multiple myeloma in different regions in 1990, 2000, 2010 and 2021

	1990		2000			2010			2021		
	DALYs	case	DALYs	case	change	DALYs	case	change	DALYs	case	change
Global SDI	28.34 (26.33 ~ 30.83)	1,122,517.31 (1,041,399.48 ~ 1,227,728.68)	31.35 (27.98 ~ 33.26)	1,552,974.93 (1,383,285.29 ~ 1,647,480.04)	0.11 (0.04 ~ 0.15)	29.90 (26.76 ~ 32.39)	1,917,585.51 (1,714,313.94 ~ 2,079,643.34)	−0.05 (−0.07 ~ 0.00)	30.00 (26.22 ~ 33.37)	2,595,594.99 (2,270,483.60 ~ 2,889,968.19)	0.00 (−0.05 ~ 0.07)
High SDI	55.37 (53.27 ~ 56.75)	609,781.35 (585,948.41 ~ 625,027.66)	58.56 (55.97 ~ 60.33)	770,379.04 (735,433.47 ~ 794,804.57)	0.06 (0.03 ~ 0.08)	52.74 (49.65 ~ 54.69)	858,003.43 (803,574.43 ~ 892,161.76)	−0.10 (−0.11 ~ −0.09)	47.33 (44.00 ~ 49.82)	976,932.53 (896,756.87 ~ 1,033,833.12)	−0.10 (−0.13 ~ −0.08)
High-middle SDI	25.02 (23.59 ~ 27.25)	254,005.86 (239,764.50 ~ 277,110.15)	29.13 (25.49 ~ 30.95)	358,299.96 (313,630.56 ~ 380,366.34)	0.16 (0.04 ~ 0.24)	29.00 (25.61 ~ 31.00)	440,865.56 (389,355.12 ~ 471,489.07)	0.02 (−0.05 ~ 0.10)	29.65 (25.53 ~ 33.21)	583,311.88 (504,141.16 ~ 652,354.98)	0.00 (−0.05 ~ 0.06)
Middle SDI	12.23 (10.59 ~ 15.76)	135,857.94 (117,165.68 ~ 175,791.40)	17.12 (13.09 ~ 18.85)	249,194.61 (188,820.09 ~ 274,606.69)	0.08 (0.01 ~ 0.21)	18.46 (14.97 ~ 21.39)	364,824.39 (294,478.36 ~ 423,493.90)	0.40 (0.13 ~ 0.57)	21.85 (17.50 ~ 25.56)	609,118.62 (487,413.38 ~ 714,664.77)	0.18 (0.08 ~ 0.30)
Low-middle SDI	13.45 (9.70 ~ 17.75)	87,031.83 (62,726.59 ~ 115,403.00)	15.70 (12.18 ~ 19.94)	129,666.29 (100,181.14 ~ 165,385.41)	0.17 (0.08 ~ 0.33)	17.62 (14.72 ~ 23.88)	192,541.87 (160,786.89 ~ 259,672.81)	0.12 (0.01 ~ 0.30)	21.51 (18.34 ~ 29.96)	323,359.00 (274,506.55 ~ 449,769.08)	0.22 (0.08 ~ 0.41)
Low SDI	14.26 (7.97 ~ 20.10)	34,292.99 (18,917.44 ~ 48,485.48)	14.61 (8.81 ~ 20.73)	43,402.30 (25,903.24 ~ 61,828.46)	0.04 (−0.08 ~ 0.27)	15.20 (10.11 ~ 20.85)	58,828.98 (38,808.04 ~ 80,724.37)	0.03 (−0.07 ~ 0.17)	18.43 (12.25 ~ 24.91)	99,828.04 (66,163.61 ~ 136,137.06)	0.21 (0.06 ~ 0.45)

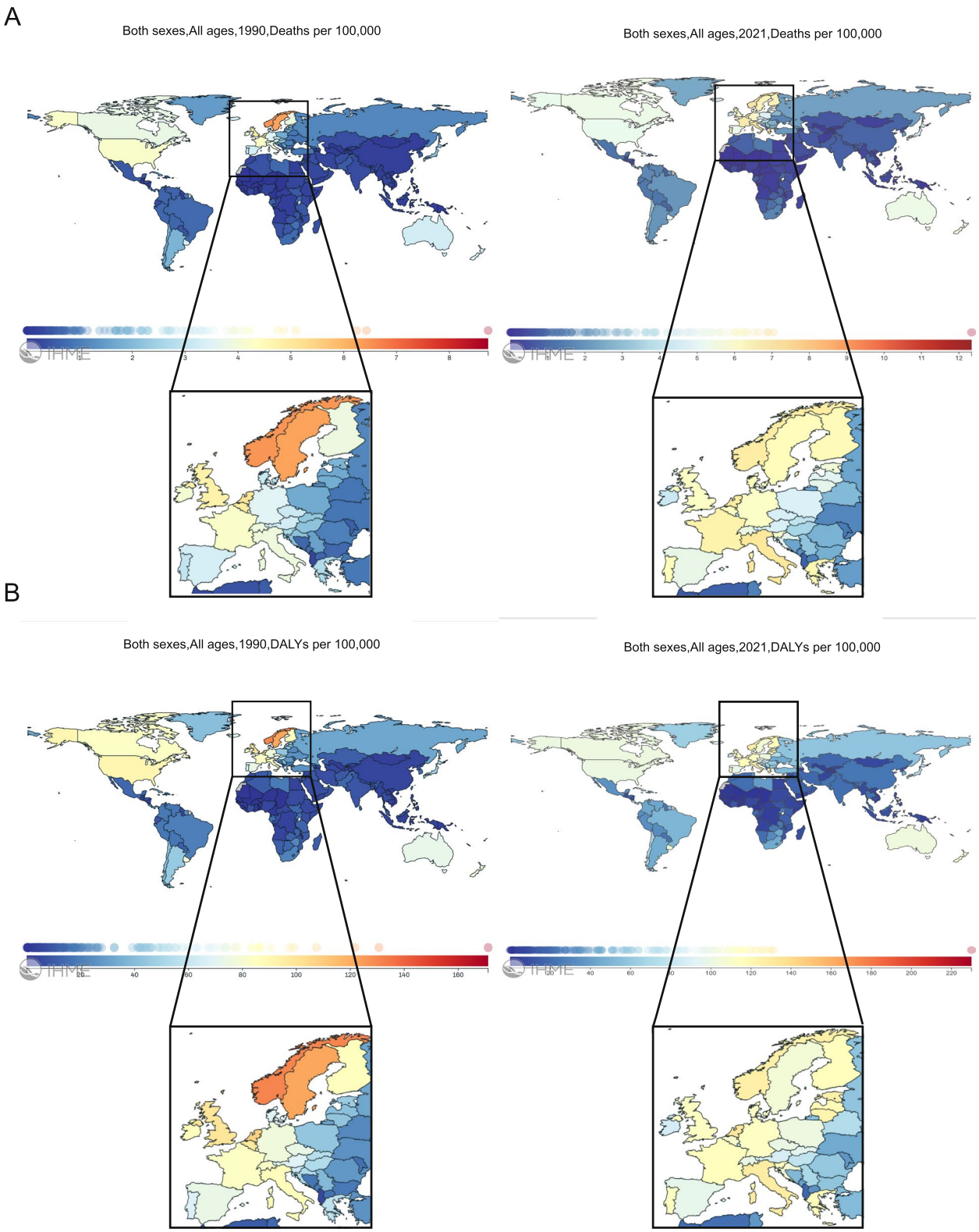

Fig.1 Global distribution of mortality (**A**) and disability-adjusted life years (DALYs) (**B**) for multiple myeloma (MM) in 1990 and 2021

Table 4 ASIR of multiple myeloma in different regions and genders in 1990, 2000, 2010 and 2021

ASIR	1990			2000			2010			2021		
	Both	Male	Female	Both	Male	Female	Both	Male	Female	Both	Male	Female
Global SDI	1.47 (1.37 ~ 1.57)	1.70 (1.57 ~ 1.85)	1.30 (1.20 ~ 1.43)	1.72 (1.58 ~ 1.81)	1.99 (1.79 ~ 2.11)	1.51 (1.37 ~ 1.62)	1.75 (1.59 ~ 1.86)	2.08 (1.85 ~ 2.23)	1.48 (1.31 ~ 1.64)	1.74 (1.54 ~ 1.89)	2.12 (1.83 ~ 2.34)	1.43 (1.21 ~ 1.62)
High SDI	2.98 (2.83 ~ 3.08)	3.68 (3.3.56 ~ 3.78)	2.50 (2.32 ~ 2.61)	3.47 (3.28 ~ 3.58)	4.24 (4.05 ~ 4.38)	2.91 (2.69 ~ 2.91)	3.49 (3.24 ~ 3.63)	4.31 (4.06 ~ 4.47)	2.85 (2.58 ~ 3.00)	3.16 (2.87 ~ 3.34)	3.99 (3.70 ~ 4.23)	2.47 (2.17 ~ 2.66)
High-middle SDI	1.27 (1.20 ~ 1.37)	1.50 (1.40 ~ 1.65)	1.12 (1.03 ~ 1.24)	1.58 (1.42 ~ 1.67)	1.87 (1.65 ~ 2.00)	1.38 (1.24 ~ 1.48)	1.68 (1.52 ~ 1.79)	2.04 (1.80 ~ 2.19)	1.43 (1.24 ~ 1.56)	1.75 (1.52 ~ 1.95)	2.14 (1.77 ~ 2.42)	1.46 (1.21 ~ 1.66)
Middle SDI	0.51 (0.45 ~ 0.66)	0.57 (0.44 ~ 0.78)	0.46 (0.39 ~ 0.65)	0.74 (0.57 ~ 0.81)	0.83 (0.60 ~ 0.94)	0.66 (0.51 ~ 0.76)	0.84 (0.69 ~ 0.98)	0.97 (0.73 ~ 1.15)	0.73 (0.56 ~ 0.90)	1.05 (0.84 ~ 1.23)	1.24 (0.90 ~ 1.50)	0.88 (0.54 ~ 1.09)
Low-middle SDI	0.54 (0.39 ~ 0.71)	0.59 (0.36 ~ 0.87)	0.49 (0.33 ~ 0.71)	0.64 (0.50 ~ 0.81)	0.70 (0.47 ~ 0.98)	0.58 (0.42 ~ 0.81)	0.73 (0.61 ~ 0.99)	0.82 (0.64 ~ 1.18)	0.66 (0.52 ~ 0.91)	0.92 (0.79 ~ 1.30)	1.04 (0.82 ~ 1.53)	0.82 (0.62 ~ 1.19)
Low SDI	0.56 (0.32 ~ 0.79)	0.60 (0.27 ~ 0.95)	0.52 (0.28 ~ 0.85)	0.58 (0.35 ~ 0.82)	0.62 (0.29 ~ 0.97)	0.54 (0.31 ~ 0.85)	0.62 (0.41 ~ 0.82)	0.65 (0.36 ~ 0.98)	0.58 (0.36 ~ 0.80)	0.77 (0.51 ~ 1.02)	0.80 (0.50 ~ 1.19)	0.73 (0.47 ~ 0.99)

Table 5 ASMR of multiple myeloma in different regions and genders in 1990, 2000, 2010 and 2021

ASMR	1990			2000			2010			2021		
	Both	Male	Female	Both	Male	Female	Both	Male	Female	Both	Male	Female
Global SDI	1.29 (1.20 ~ 1.39)	1.50 (1.38 ~ 1.66)	1.14 (1.04 ~ 1.26)	1.44 (1.30 ~ 1.53)	1.66 (1.48 ~ 1.78)	1.27 (1.14 ~ 1.37)	1.38 (1.24 ~ 1.48)	1.64 (1.44 ~ 1.78)	1.18 (1.03 ~ 1.32)	1.37 (1.22 ~ 1.52)	1.67 (1.44 ~ 1.86)	1.14 (0.96 ~ 1.31)
High SDI	2.50 (2.36 ~ 2.57)	3.12 (3.01 ~ 3.20)	2.09 (1.93 ~ 2.18)	2.69 (2.51 ~ 2.79)	3.30 (3.14 ~ 3.40)	2.27 (2.08 ~ 2.38)	2.45 (2.25 ~ 2.56)	3.05 (2.86 ~ 3.16)	2.01 (1.81 ~ 2.13)	2.28 (2.05 ~ 2.41)	2.87 (2.64 ~ 3.03)	1.82 (1.59 ~ 1.95)
High-middle SDI	1.05 (0.99 ~ 1.14)	1.27 (1.17 ~ 1.40)	0.92 (0.85 ~ 1.02)	1.26 (1.12 ~ 1.34)	1.50 (1.311 ~ 1.63)	1.10 (0.98 ~ 1.18)	1.27 (1.13 ~ 1.35)	1.55 (1.34 ~ 1.67)	1.09 (0.95 ~ 1.18)	1.28 (1.12 ~ 1.43)	1.57 (1.31 ~ 1.78)	1.08 (0.89 ~ 1.24)
Middle SDI	0.49 (0.43 ~ 0.63)	0.56 (0.43 ~ 0.76)	0.44 (0.36 ~ 0.61)	0.69 (0.53 ~ 0.76)	0.78 (0.57 ~ 0.89)	0.61 (0.46 ~ 0.70)	0.75 (0.61 ~ 0.87)	0.87 (0.65 ~ 1.04)	0.64 (0.49 ~ 0.79)	0.88 (0.71 ~ 1.04)	1.05 (0.77 ~ 1.26)	0.74 (0.53 ~ 0.92)
Low-middle SDI	0.55 (0.39 ~ 0.71)	0.60 (0.37 ~ 0.88)	0.50 (0.34 ~ 0.72)	0.64 (0.50 ~ 0.82)	0.71 (0.47 ~ 0.99)	0.57 (0.41 ~ 0.81)	0.72 (0.60 ~ 0.97)	0.81 (0.63 ~ 1.17)	0.64 (0.50 ~ 0.90)	0.89 (0.76 ~ 1.24)	1.01 (0.81 ~ 1.49)	0.78 (0.59 ~ 1.13)
Low SDI	0.58 (0.33 ~ 0.81)	0.63 (0.28 ~ 0.98)	0.54 (0.29 ~ 0.87)	0.60 (0.36 ~ 0.84)	0.64 (0.31 ~ 1.00)	0.56 (0.31 ~ 0.87)	0.63 (0.42 ~ 0.86)	0.66 (0.37 ~ 1.00)	0.59 (0.37 ~ 0.81)	0.77 (0.52 ~ 1.02)	0.81 (0.50 ~ 1.20)	0.73 (0.47 ~ 0.98)

Table 6 DALYs of multiple myeloma in different regions and genders in 1990, 2000, 2010 and 2021

DALYs	1990			2000	2000		2010			2021		
	Both	Male	Female	Both	Male	Female	Both	Male	Female	Both	Male	Female
Global SDI	28.34 (26.33 ~ 30.83)	32.57 (29.55 ~ 36.21)	24.89 (22.94 ~ 28.15)	31.35 (27.98 ~ 33.26)	35.93 (31.51 ~ 38.68)	27.51 (24.44 ~ 29.56)	29.90 (26.76 ~ 32.39)	35.20 (30.81 ~ 38.90)	25.38 (22.23 ~ 28.54)	30.00 (26.22 ~ 33.37)	35.82 (30.46 ~ 39.98)	25.04 (20.39 ~ 29.10)
High SDI	55.37 (53.27 ~ 56.75)	67.87 (66.08 ~ 69.33)	46.01 (43.43 ~ 47.61)	58.56 (55.97 ~ 60.33)	70.65 (68.06 ~ 72.58)	49.13 (46.35 ~ 50.96)	52.74 (49.65 ~ 54.69)	64.66 (61.40 ~ 66.71)	42.91 (39.68 ~ 44.85)	47.33 (44.00 ~ 49.82)	58.80 (55.02 ~ 61,79)	37.50 (34.21 ~ 39.87)
High-middle SDI	25.02 (23.59 ~ 27.25)	29.20 (27.02 ~ 32.38)	22.01 (20.46 ~ 24.84)	29.13 (25.49 ~ 30.95)	33.81 (29.19 ~ 36.69)	25.64 (22.53 ~ 27.48)	29.00 (25.61 ~ 31.00)	34.43 (29.45 ~ 37.35)	24.74 (21.17 ~ 26.84)	29.65 (25.53 ~ 33.21)	35.33 (28.21 ~ 40.40)	25.02 (19.74 ~ 28.99)
Middle SDI	12.23 (10.59 ~ 15.76)	13.63 (10.51 ~ 18.63)	10.96 (8.97 ~ 15.59)	17.12 (13.09 ~ 18.85)	19.20 (13.96 ~ 21.78)	15.20 (11.20 ~ 17.44)	18.46 (14.97 ~ 21.39)	21.36 (15.85 ~ 25.18)	15.79 (11.99 ~ 19.66)	21.85 (17.50 ~ 25.56)	25.71 (18.67 ~ 30.88)	18.36 (13.11 ~ 22.84)
Low-middle SDI	13.45 (9.70 ~ 17.75)	14.71 (9.06 ~ 21.85)	12.17 (8.21 ~ 18.09)	15.70 (12.18 ~ 19.94)	17.40 (11.65 ~ 24.08)	14.00 (10.07 ~ 19.95)	17.62 (14.72 ~ 23.88)	19.77 (15.48 ~ 28.79)	15.57 (12.16 ~ 21.73)	21.51 (18.34 ~ 29.96)	24.32 (19.55 ~ 35.70)	18.94 (14.27 ~ 27.43)
Low SDI	14.26 (7.97 ~ 20.10)	15.38 (6.90 ~ 24.31)	13.11 (6.90 ~ 21.88)	14.61 (8.81 ~ 20.73)	15.64 (7.46 ~ 24.69)	13.58 (7.60 ~ 21.89)	15.20 (10.11 ~ 20.85)	16.11 (9.07 ~ 24.57)	14.30 (8.86 ~ 19.61)	18.43 (12.25 ~ 24.91)	19.35 (11.96 ~ 29.21)	17.56 (11.03 ~ 23.27)

Table 7 Age-specific ASMR, ASIR and DALYs for MM, 1990 and 2021

Age (years)	ASMR (95%UI)		Change	ASIR (95%UI)		Change	DALYs (95%UI)		Change
	1990	2021		1990	2021		1990	2021	
Over all	1.29 (1.20–1.39)	1.37 (1.22–1.52)	0.06 (−0.03–0.16)	1.04 (0.98–1.12)	1.89 (1.67–2.05)	0.18 (0.08–0.28)	21.05 (19.53–23.02)	32.89 (28.77–36.62)	0.06 (−0.04–0.16)
20–24	0.02 (0.01–0.02)	0.02 (0.02–0.03)	0.56 (−0.06–1.14)	0.02 (0.01–0.02)	0.03 (0.02–0.04)	0.87 (0.13–1.60)	1.04 (0.83–1.42)	1.62 (1.09–1.99)	0.56 (−0.06–1.14)
25–29	0.02 (0.02–0.03)	0.04 (0.02–0.04)	0.66 (0.16–1.12)	0.03 (0.02–0.03)	0.05 (0.04–0.07)	0.94 (0.36–1.48)	1.35 (1.09–1.67)	2.24 (1.53–2.69)	0.66 (0.16–1.12)
30–34	0.05 (0.04–0.06)	0.07 (0.05–0.09)	0.49 (0.15–0.82)	0.06 (0.05–0.08)	0.11 (0.08–0.13)	0.71 (0.31–1.08)	2.76 (2.27–3.39)	4.12 (3.03–4.98)	0.50 (0.16–0.83)
35–39	0.11 (0.09–0.12)	0.14 (0.11–0.17)	0.34 (0.11–0.60)	0.16 (0.14–0.18)	0.24 (0.19–0.19)	0.53 (0.26–0.81)	5.70 (4.93–6.66)	7.69 (5.97–9.38)	0.35 (0.11–0.60)
40–44	0.26 (0.23–0.30)	0.31 (0.25–0.38)	0.19 (0.01–0.39)	0.38 (0.34–0.43)	0.51 (0.40–0.61)	0.33 (0.14–0.53)	12.78 (11.18–14.53)	15.26 (12.02–18.54)	0.19 (0.01–0.39)
45–49	0.58 (0.52–0.65)	0.61 (0.51–0.72)	0.05 (−0.08–0.21)	0.84 (0.76–0.92)	0.99 (0.84–1.14)	0.19 (0.05–0.36)	25.26 (22.54–28.21)	26.77 (22.36–31.27)	0.06 (−0.08–0.22)
50–54	1.17 (1.06–1.31)	1.18 (0.98–1.37)	0.00 (−0.13–0.15)	1.70 (1.56–1.86)	1.95 (1.65–2.21)	0.14 (0.00–0.29)	45.75 (41.50–51.34)	46.23 (38.56–53.85)	0.01 (−0.12–0.15)
55–59	2.12 (1.94–2.35)	2.15 (1.82–2.48)	0.02 (−0.11–0.15)	2.89 (2.66–3.20)	3.33 (2.86–3.77)	0.15 (0.01–0.30)	72.56 (66.12–80.24)	74.22 (62.53–85.46)	0.02 (−0.10–0.16)
60–64	3.78 (3.50–4.13)	3.80 (3.31–4.33)	0.01 (−0.10–0.12)	4.90 (4.58–5.33)	5.54 (4.88–6.20)	0.13 (0.02–0.26)	111.55 (103.29–121.94)	113.10 (98.10–128.71)	0.01 (−0.09–0.13)
65–69	6.02 (5.62–6.53)	5.82 (5.01–6.64)	−0.03 (−0.14–0.07)	7.35 (6.86–7.92)	7.92 (6.88–8.81)	0.08 (0.65–0.96)	149.84 (139.84–163.53)	146.11 (126.07–166.57)	−0.02 (−0.13–0.08)
70–74	8.61 (8.06–9.41)	9.09 (8.03–10.08)	0.06 (−0.03–0.15)	9.77 (9.17–10.53)	11.64 (10.42–12.81)	0.19 (0.09–0.30)	176.79 (165.71–192.88)	188.43 (166.52–209.37)	0.07 (−0.02–0.16)
75–79	12.32 (11.55–13.10)	12.89 (11.49–14.12)	0.05 (−0.05–0.13)	13.26 (12.46–14.12)	15.50 (13.85–16.95)	0.17 (0.07–0.26)	202.34 (189.50–215.01)	213.93 (190.23–234.97)	0.06 (−0.03–0.14)
80–84	16.15 (14.40–17.28)	17.43 (14.82–19.16)	0.08 (0.00–0.15)	15.93 (14.01–17.05)	19.03 (15.89–20.83)	0.80 (0.65–0.0.96)	208.40 (186.28–223.15)	226.71 (193.13–248.72)	0.09 (0.01–0.16)
85–89	20.03 (17.24–21.76)	23.37 (25.98–19.23)	0.17 (0.09–0.25)	18.07 (15.46–19.75)	23.56 (19.22–26.41)	0.30 (0.20–0.40)	204.96 (176.40–222.78)	240.83 (198.43–267.98)	0.17 (0.09–0.25)
90–94	22.99 (18.75–25.39)	28.48 (22.14–32.07)	0.24 (0.17–0.30)	18.70 (15.12–20.71)	26.27 (20.54–29.86)	0.40 (0.31–0.50)	203.55 (165.74–224.98)	254.69 (199.38–287.41)	0.25 (0.18–0.31)
95 +	21.56 (16.51–24.22)	28.94 (21.08–33.26)	0.34 (0.26–0.40)	13.83 (10.59–15.55)	19.13 (13.89–21.98)	0.38 (0.30–0.45)	178.29 (136.93–200.81)	236.72 (172.96–272.34)	0.33 (0.25–0.38)

Overall, from 1990 to 2021, ASMR, incidence, and DALYs increased across all age groups, but the degree of change varied in each age group. A high increase was seen in the 20–44 age group, while the 50–84 age group exhibited a lower increase. This suggests that the MM disease burden has increased in the younger population, while MM in middle-aged and older age groups have been effectively prevented and controlled (Table 7).

Differences in disease burden in different SDI regions

Joinpoint regression analyses for ASIR of different social population index regions revealed a significant upward trend in the MM-associated ASIR from 1990 to 2021. Although all the social population index regions showed an increasing trend, the degree of change varied. The largest change occurred in the middle social population index (4·43%; 95% UI: 4·33–4·54%, $P<0·001$), whereas the smallest change occurred in the low social population index (1·02%; 95% UI: 0·90–1·13%, $P<0·001$) (Table 8 and Fig. 3A), Regression analysis of ASMR for different social population index regions found that from 1990 to 2021, MM-related ASRM showed a significant upward trend. The magnitude of the increase varied among groups, with the greatest change occurring in the middle

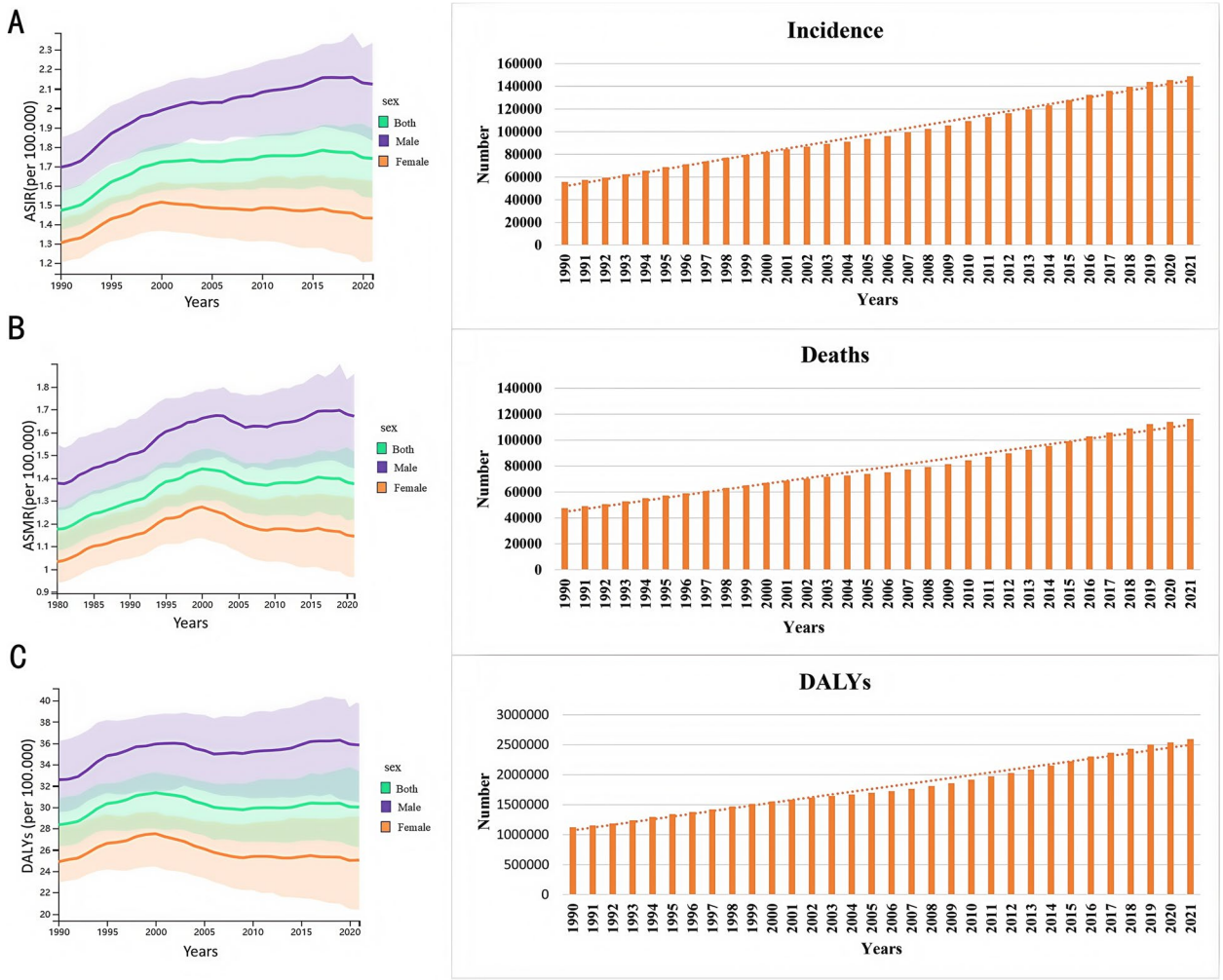

Fig.2 Changes in age-standardised incidence rate (ASIR) (**A**), age-standardised mortality rate (ASMR) (**B**) and DALYs (**C**) and the numbers of them for MM: 1990–2021

social population index (1·91%; 95% UI: 1,77–2,05%, $P<0·001$), and the smallest was in the high social population index region (0.55%; 95% UI: 0.43–0.66%, $P<0.001$). (Table 9 and Fig. 3B). An analysis of DALYs also shows that middle social population index regions had the largest increase (1.90%; 95% UI: 1.78–2.03%, $P<0.001$), while high social population index regions showed a downward trend (–0.51%; 95% UI: –0.63––0.39, $P<0.001$). (Table 10 and Fig. 3C)The data show that MM is better controlled in the High area and less well controlled in the middle social population index area.

Discussion

This study provides an in-depth analysis of the global burden of MM from 1990 to 2021, focusing on regional, gender and age differences, which will be useful in guiding public health policy and resource allocation. Meanwhile MM is a serious public health concern worldwide and imposes a significant financial burden. Data on the global burden of MM that would inform health policies, resource allocation, and treatment strategies is lacking. Therefore, in this study, we analyzed the burden of MM, from 1990 to 2021, across 204 countries, 16 age groups, and both sexes. Of note is the innovative time-trend assessment of the MM burden, which has significant implications for changes in key years.

In 2021, the global incidence of MM was 119,679, bringing the total number of cases to 131,040·71 The observed increase was the highest in high social population index countries and may reflect population migration and birth rate trends; however, these factors require further investigation. While haematopoietic stem cell technology and new drug development have increased the survival rate [14, 15], these observations emphasis the need to continuously evaluate and improve prevention and control strategies according to the current

Table 8 AAPC and APC for ASIR of multiple myeloma, 1990–2021

ASIR	Period	APC (95%UI, $P<0.001$)	AAPC (95%UI, $P<0.001$)
Global	1990–1992	0.96* (0.13–1.89)	0.55 (0.43–0.66)
	1992–1995	2.60*(1.78–3.43)	
	1995–2000	1.30* (1.05–1.55)	
	200–2006	−0.03 (1.05–0.16)	
	2006–2017	0.28* (0.21–0.36)	
	2017–2021	−0.53* (−0.90- −0.16)	
High SDI	1990–1992	1.15* (0.12–2.20)	1.66 (−0.05–0.39)
	1992–1995	2.64* (1.61–3.68)	
	1995–2001	1.00* (0.76–1.24)	
	2001–2010	−0.07 (−0.20–0.07)	
	2010–2013	−0.74 (−2.11–0.64)	
	2013–2016	0.05 (−1.44–1.56)	
	2016–2021	−1.63* (−2.00- −1.25)	
High-middle SDI	1990–1992	2.71* (1.40–4.04)	2.70 (2.51–2.880)
	1992–1995	4.05* (2.77–5.35)	
	1995–1999	3.26* (2.57–3.97)	
	1999–2006	2.24* (1.99–2.50)	
	2006–2015	2.71* (2.53–2.90)	
	2015–2021	2.14* (1.77–2.51)	
Middle SDI	1990–1992	3.43* (2.35–4.52)	4.44 (4.33–4.54)
	1992–1998	6.97* (6.76–7.19)	
	1998–2007	2.78* (2.68–2.88)	
	2007–2019	4.77* (4.70–4.83)	
	2019–2021	3.49* (2.47–4.53)	
Low-middle	1990–1992	1.42* (0.25–2.60)	1.76 (1.63–1.89)
	1992–1997	2.28* (1.92 –2.63)	
	1997–2006	1.04* (0.93 –1.16)	
	2006–2013	1.93* (1.75 –2.11)	
	2013–2019	2.72* (2.48 –2.96)	
	2019–2021	0.61 (−0.46–1.70)	
Low SDI	1990–1994	0.82* (0.56- 1.08)	1.02 (0.90–1.13)
	1994–2005	−0.05 (−0.11 −0.01)	
	2005–2008	0.95* (0.20–1.70)	
	2008–2012	1.85* (1.50 –2.20)	
	2021–2015	2.67* (2.02 –3.34)	
	2015–2019	2.00* (1.68 –2.32)	
	2019–2021	1.33* (0.67 –1.99)	

* Indicate that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level

population dynamics. With scientific and technological advancements, industrialization and increased healthcare resources in high social population index regions. Significant advances have been made in the treatment of MM, improving the prognosis and quality of life for patients., while other regions are still growing [16, 17]. The updated IMWG criteria improve MM prognosis and provides scientific guidelines for myeloma treatment worldwide. Our study provides a global picture of the disease burden and its trends in patients with MM, which helps identify susceptible populations that can be regularly screened to minimize disease progression. Additionally, the life expectancy of patients with MM has rapidly increased worldwide, especially in high social population index regions.

The Joinpoint regression analysis revealed that ASIR, ASMR, and DALYs increased yearly from 1990 to 2021, but the degree of increase varied in different social population index regions. DALYs were associated with the most significant difference: in the high social population

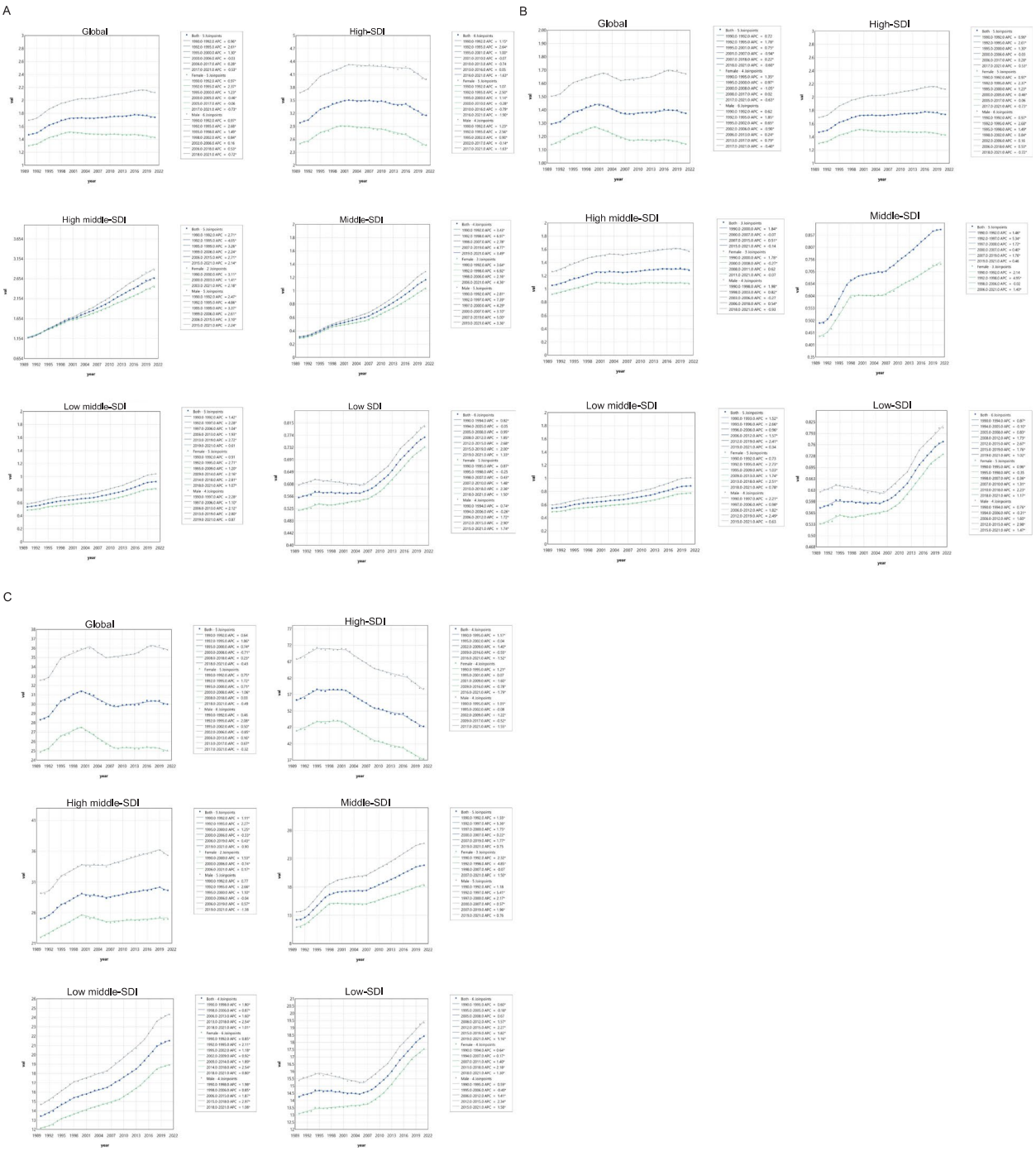

Fig.3 AAPC in ASIR (**A**), ASMR (**B**) and DALYs (**C**) for MM in different social population index regions, 1990–2021

index region, DALYs levelled off between 2002 and 2009, increased between 2009 and 2017, and then leveled off after 2017. During which global policies and MM management were strengthened. Currently, the MM treatment process typically includes induction therapy, consolidation therapy, and maintenance/extended therapy. The specific drugs and regimens used in each phase of treatment may vary depending on the patient's age, overall functional status, health and disease characteristics, and ability to receive high-dose chemotherapy and hematopoietic stem cell transplantation (HSCT) [18]. Meanwhile, the development of immunomodulatory

Table 9 AAPC and APC for ASMR of multiple myeloma, 1990–2021

Location	Period	APC (95%UI,$P<0.001$)	AAPC (95%UI,$P<0.001$)
Global	1990–1992	0.72 (−0.06–1.51)	0.20* (0.09–0.31)
	1992–1995	1.78* (1.00–2.57)	
	1995–2001	0.75* (0.57–0.92)	
	2001–2007	−0.94* (−1.11- −0.76)	
	2007–2018	0.22* (0.15–0.29)	
	2018–2021	−0.60* (−1.14- −0.06)	
High SDI	1990–1992	0.96* (0.13–1.80)	0.55* (0.43–0.66)
	1992–1995	2.60* (1.78–3.43)	
	1995–2000	1.30* (1.05–1.55)	
	2000–2006	−0.03 (−0.21–0.16)	
	2006–2017	0.28* (0.21–0.36)	
	2017–2021	−0.53 (−0.90- −0.16)	
High-middle SDI	1990–2000	1.84* (1.72–1.96)	0.68* (0.57–0.79)
	2000–2007	−0.07 (−0.33–0.20)	
	2007–2015	0.51* (0.28–0.75)	
	2015–2021	−0.14 (−0.50–0.23)	
Middle SDI	1990–1992	1.46* (0.36–2.57)	1.91* (1.77–2.05)
	1992–1997	5.34* (5.02–5.66)	
	1997–2000	1.72* (0.79–2.65)	
	2000–2007	0.40* (0.24–0.55)	
	2007–2019	1.76* (1.70–1.82)	
	2019–2021	0.46* (−0.56–1.49)	
Low-middle	1990–1993	1.52* (1.02–2.03)	1.58* (1.46–1.71)
	1993–1996	2.66* (1.68–3.64)	
	1996–2006	0.96* (0.88–1.04)	
	2006–2012	1.57* (1.36–1.77)	
	2012–2019	2.41* (2.25–2.56)	
	2019–2021	0.34 (−0.57–1.27)	
Low SDI	1990–1994	0.87* (0.59–1.16)	0.93* (0.80–1.05)
	1994–2005	−0.10* (−0.17- −0.04)	
	2005–2008	0.83* (0.01–1.65)	
	2008–2012	1.73* (1.35–2.11)	
	2012–2015	2.67* (1.96–3.39)	
	2015–2019	1.76* (1.42–2.10)	
	2019–2021	1.02* (0.31–1.74)	

drugs, proteasome inhibitors and monoclonal antibodies over the past 20 years has significantly changed the treatment paradigm for newly diagnosed multiple myeloma [19]. Effective diagnosis and treatment of MM and its complications may be directly responsible for the slowed growth of DALYs.

The significant sex differences in patients with MM may be related to genetic, social, cultural, and biological factors. A higher burden of disease is observed in men than in women. The main reason is that they may have healthier attitudes and behaviors and are more likely to adopt behaviors that are good for muscle health after improved treatment. Male patients may also have comorbidities at the time of diagnosis and Male patients may have more complications at the time of MM diagnosis, which potentially contributes to their lower survival rates [20]. MM prevalence is particularly high among first-degree relatives [21, 22].

As with other GBD studies, this study has some limitations. First, the GBD database relies on disease registries, death reports, and literature data from countries around the world, but many low- and middle-income countries lack well-established cancer registries, resulting in incomplete data on incidence and mortality of multiple

Table 10 AAPC and APC for DALYs of multiple myeloma, 1990–2021

Location	Period	APC (95%UI,$P < 0.001$)	AAPC (95%UI,$P < 0.001$)
Global	1990–1992	0.64 (−0.15–1.43)	0.18* (0.08–0.29)
	1992–1995	1.86* (1.12–2.61)	
	1995–2000	0.74*(0.50–0.98)	
	2000–2008	−0.71*(−0.82- −0.60)	
	2008–2018	0.23*(0.14–0.31)	
	2018–2021	−0.43(−0.99–0.13)	
High SDI	1990–1995	1.17*(0.93–1.42)	−0.51(−0.63- −0.39)
	1995–2002	−0.04(−0.24–0.17)	
	2002–2009	−1.40*(−1.64- −1.16)	
	2009–2016	−0.55*(−0.84- −0.26)	
	2016–2021	−1.52*(−1.95- −1.08)	
High-middle SDI	1990–1992	1.11* (0.37–1.86)	0.55*(0.42–0.67
	1992–1995	2.27*(1.54–3.00)	
	1995–2000	1.25*(1.00–1.51)	
	2000–2006	−0.33*(−0.52- −0.14)	
	2006–2019	0.43*(0.38–0.49)	
	2019–2021	−0.90(−2.14–0.37)	
Middle SDI	1990–1992	1.55*(0.57–2.53)	1.90*(1.78–2.03)
	1992–1997	5.36*(5.07–5.64)	
	1997–2000	1.75*(0.93–2.59)	
	2000–2007	0.22*(0.09–0.36)	
	2007–2019	1.77*(1.71–1.83)	
	2019–2021	0.75(−0.16–1.67)	
Low-middle SDI	1990–1998	1.80*(1.68–1.91)	1.55*(1.47–1.64)
	1998–2006	0.87* (0.74–0.99)	
	2006–2013	1.60*(1.44–1.76)	
	2013–2018	2.54*(2.22–2.86)	
	2018–2021	1.01*(0.50–1.52)	
Low SDI	1990–1995	0.60*(0.40–0.81)	0.83*(0.70–0.96)
	1995–2005	−0.18* (−0.26- −0.10)	
	2005–2008	0.67(−0.15–1.49)	
	2008–2012	1.57*(1.18–1.95)	
	2012–2015	2.27*(1.54–3.02)	
	2015–2019	1.82*(1.47–2.18)	
	2019–2021	1.16* (0.42–1.90)	

myeloma (especially underreporting or misdiagnosis of early-stage cases), which affects the accuracy and comparability of the data. Second, the GBD database uses Bayesian modeling to fill in missing data, but estimates for rare diseases (e.g., MM) may be subject to greater uncertainty due to insufficient sample sizes, especially when subgroup analyses (e.g., by age, sex, and region) are performed with wide confidence intervals. Third, MM exists in different molecular subtypes (e.g., IgG-type, light-chain type), which have significant differences in clinical progression and prognosis, but the GBD does not provide subtype-level analysis of disease burden. Fourth, indicators such as the standardized mortality ratio and mortality rate are only used to make reasonable comparisons of morbidity and mortality rates between different populations or regions, and do not reflect the true level. DALYs also have many shortcomings. For example, the current calculation of DALYs focuses on the loss of healthy life years due to premature death and disability, but does not take into account the burden of disease on individuals, families, and society. Fifth,GBD and Joinpoint are promarily used to describe trends and do not directly explain the causes of change (e.g., the impact of advances in treatment,aging or environmental factors).

Nonetheless, this study provides a comprehensive view of the global, regional, and national MM burden from 1990 to 2021 and these findings provide valuable epidemiological information for the development of innovative treatments, while emphasizing the need for continuous improvement. There are significant differences in the burden of MM worldwide, and concerted global efforts are needed to strengthen medical care and cooperation between different regions, improve diagnosis and treatment of MM, and reduce the disease burden on patients, society and countries. Further research is needed to determine the reasons for the observed differences in disease burden.

Conclusions

This study provides a new basis for long-term trends in global MM morbidity and mortality. Although MM is more common in high SDI, it is a global disease. From 1990–2021, there are a large number of MM cases worldwide, mainlyconcentrated in high SDI areas,among men,and among older patients. Over the past tree decades, the global burden of MM has generally been on the rise and there is a significant gender difference in the burden of MM, with a higher burden in males than in females.Age is also an important factor, with elderly people at higher risk. Therefore, there is a need for increased knowledge and education and targeted interventions to reduce the burden of MM.

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
XN designed the study. D XX, B TR, N SM and G LL extracted, collected, and analysed the data. D XX and C ST drafted the manuscript. D XX and XN verified data. D XX, B TR, C ST, N SM, G LL and XN reviewed the results and revised the manuscript. XN supervised the study. The corresponding author attests that all listed authors meet the authorship criteria and that no others meeting the criteria have been omitted.

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Data availability
The data sources and codes used in the Global Burden of Diseases, Injuries, and Risk Factors Study 2021 are publicly available on the Internet (http://ghdx.healthdata.org/gbd-results-tool).

Declarations

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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