

ORIGINAL RESEARCH ARTICLE

A systematic analysis of the global burden of multiple myeloma from 1990 to 2021

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Abstract

Multiple myeloma (MM) is a hematological malignancy characterized by the proliferation of plasma cells in the bone marrow, leading to organ dysfunction. Globally, the incidence of MM has increased substantially in recent decades, necessitating an updated understanding of its global burden and epidemiological trends. This study utilized data from the Global Burden of Disease database to analyze the incidence of MM, deaths, and disability-adjusted life years from 1990 to 2021. Age-standardized rates (ASRs) were used to adjust for variations in age distribution and population size. The estimated annual percentage changes (EAPCs) were used to evaluate temporal trends. Pearson's correlation coefficient was employed to assess the relationship between EAPC values and sociodemographic index (SDI) levels. From 1990 to 2021, the global incident cases increased dramatically from 55.71×10^3 to 148.75×10^3 , with the age-standardized incidence rate rising from 1.47 to 1.74/100,000 population. Deaths also increased significantly from 47.57×10^3 to 116.36×10^3 . High-SDI regions consistently maintained the highest disease burden, while low- to middle-SDI regions demonstrated the most rapid increase in MM incidence. The EAPC of ASRs was negatively correlated with SDI in 2021. The global burden of MM substantially increased from 1990 to 2021, with significant regional and sociodemographic disparities. While high-SDI regions benefited from advances in diagnosis and treatment, low-SDI regions faced mounting challenges that require targeted interventions and coordinated international actions to effectively reduce the global MM burden.

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1. Introduction

Multiple myeloma (MM) is a hematological malignancy characterized by the clonal proliferation of plasma cells in the bone marrow, which produce monoclonal immunoglobulins (M-protein).¹ MM commonly leads to significant organ dysfunction, including hypercalcemia, renal insufficiency, anemia, and bone disease.¹ MM accounts for 10–15% of all hematological malignancies and is the second most common

hematological cancer in high-income countries.² It disproportionately affects older populations, with the median age at diagnosis being 65–75 years.³

Globally, the incidence of MM has risen substantially over the past few decades, increasing by approximately 126% from 1990 to 2016.⁴ Contributing factors include population growth, aging demographics, and rising age-standardized incidence rates (ASIR).⁴ In 2019, there were 155,688 new cases worldwide, with the age-standardized incidence increasing modestly from 1.72 to 100,000 individuals in 1990 to 1.92/100,000 in 2019.⁵ The highest incidence rates were observed in high-income regions, such as Australia, New Zealand, North America, and Northern Europe, while the lowest rates were reported in sub-Saharan Africa, Southeast Asia, and Melanesia.⁶ In the United States (US), the ASIR of MM has increased from 5.5 to 100,000 person-years in the early 1990s to 7.1/100,000 in 2015–2019.⁷ The disease exhibits significant racial and ethnic disparities, with non-Hispanic black individuals experiencing a higher incidence and younger age at diagnosis compared to other populations.⁷

MM remains incurable despite advances in treatment. Novel therapies such as proteasome inhibitors, immunomodulatory drugs, monoclonal antibodies, and autologous stem cell transplantation (ASCT) have improved survival outcomes,⁸ leading to a 5-year survival rate that has increased from 25% in the 1970s to approximately 60% in recent years in the US and Europe.⁹ Nonetheless, most patients relapse, and the disease eventually becomes refractory to available treatments. Patients eligible for ASCT have a median survival of around 10 years, while the median overall survival for ineligible patients is 4–5 years.^{10,11} Advances in immunotherapy, such as bispecific antibodies and chimeric antigen receptor T-cell therapies, hold promise for addressing unmet medical needs, but access to these treatments remains limited globally.

Disparities in MM incidence, management, and outcomes persist, driven by differences in socioeconomic status, race, access to advanced diagnostics, and availability of novel therapies.¹² Lower-income countries face unique challenges, with limited access to emerging treatment modalities, resulting in poorer outcomes and lower survival rates for affected populations.¹² These disparities highlight a need for equitable healthcare strategies in underserved regions to address healthcare inequities. Therefore, this study aims to provide an updated understanding of the global burden of MM from 1990 to 2021, thereby informing future healthcare planning and resource allocation.

2. Data and methods

2.1. Data acquisition and download

The Global Burden of Disease database provides comprehensive statistical data on 369 diseases and injuries across 204 countries and territories. Data on MM, including incident cases, deaths, disability-adjusted life years (DALYs), and corresponding age-standardized rates (ASRs), were obtained from the Global Health Data Exchange platform (<http://ghdx.healthdata.org/gbd-resultstool>). Sociodemographic index (SDI) data were also extracted for correlation analysis. The SDI, which ranges from 0 to 1, assesses the level of social and economic development for each country or region.

2.2. Statistical analysis

To evaluate trends in the burden of MM over time, the estimated annual percentage change (EAPC) was calculated based on the ASRs, using the log-linear regression model shown in Equation 1:

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

where y represents the natural logarithm of the ASR and x is the calendar year. EAPC was computed using Equation (2); EAPC values greater than zero indicate an increasing trend, whereas values less than zero indicate a decreasing trend.

$$\text{EAPC} = 100 \times (10^{\beta} - 1) \quad (2)$$

The correlation between EAPC values and SDI levels was assessed using Pearson's correlation coefficient to examine the association between social development and the burden of MM, with $p < 0.05$ indicating statistical significance.

2.3. Data visualization

All analyses were carried out using R software (version 4.3.2, R Foundation for Statistical Computing, Austria), and data visualization was performed using packages such as ggplot2, maps, RColorBrewer, and dplyr. Visual representations included histograms to display annual trends in MM incidence, deaths, and DALYs from 1990 to 2021, as well as global maps to illustrate the geographical distribution of ASRs for incidence, mortality, and DALYs across 204 countries and territories. Scatterplots combined with regression curves served to analyze and visualize the association between ASRs and SDI values, providing insights into how the burden of MM correlates with levels of social and economic development. In addition, age-specific patterns of MM were depicted using the area under the curve to demonstrate age composition dynamics over the study period.

3. Results

3.1. The incidence of MM and its trend

The global burden of MM demonstrated a substantial increase over the 31-year period from 1990 to 2021 (Table 1 and Figure 1A). The total incident cases increased from 55.71×10^3 (95% uncertainty interval [UI]: 52.02–

59.69) in 1990 to 148.75×10^3 (95% UI: 131.78–162.05) in 2021, with the ASIR rising from 1.47 to 1.74/100,000 population (EAPC = 0.48%, 95% confidence interval [CI]: 0.37–0.60). Gender analysis revealed a higher burden among females compared to males, with females showing a more prominent increase in ASIR from 1.70 to 2.12/100,000 (EAPC = 0.7%, 95% CI: 0.60–0.81), while

Table 1. The incidence and age-standardized incidence rate of multiple myeloma in 1990 and 2021 and their temporal trends from 1990 to 2021

Sociodemographic profile	2021		1990–2021		
	Incident cases $\times 10^3$ (95% UI)	ASIR/100,000 (95% UI)	Incident cases $\times 10^3$ (95% UI)	ASIR/100,000 (95% UI)	EAPC (95% CI)
Overall	55.71 (52.02–59.69)	1.47 (1.37–1.57)	148.75 (131.78–162.05)	1.74 (1.54–1.89)	0.48 (0.37–0.60)
Sex					
Male	27.25 (25.20–29.86)	1.30 (1.20–1.43)	66.30 (56.02–75.29)	1.43 (1.21–1.62)	0.20 (0.07–0.33)
Female	28.46 (26.27–31.12)	1.70 (1.57–1.85)	82.45 (71.46–90.74)	2.12 (1.83–2.34)	0.70 (0.60–0.81)
SDI					
High SDI	33.36 (31.61–34.44)	2.98 (2.83–3.08)	68.29 (61.34–72.53)	3.16 (2.87–3.34)	0.15 (–0.02–0.33)
High-middle SDI	12.56 (11.83–13.54)	1.27 (1.20–1.37)	34.79 (30.25–38.63)	1.75 (1.52–1.95)	1.01 (0.89–1.13)
Middle SDI	5.25 (4.56–6.75)	0.51 (0.45–0.66)	28.50 (22.91–33.49)	1.05 (0.84–1.23)	2.15 (1.98–2.33)
Low-middle SDI	3.22 (2.33–4.25)	0.54 (0.39–0.71)	13.20 (11.29–18.48)	0.92 (0.79–1.30)	1.72 (1.64–1.80)
Low SDI	1.24 (0.70–1.75)	0.56 (0.32–0.79)	3.80 (2.52–5.13)	0.77 (0.51–1.02)	0.95 (0.78–1.13)
Region					
Andean Latin America	0.23 (0.17–0.30)	1.15 (0.85–1.46)	1.06 (0.82–1.38)	1.80 (1.40–2.33)	1.59 (1.40–1.78)
Australasia	0.99 (0.92–1.06)	4.16 (3.88–4.46)	2.99 (2.60–3.39)	5.48 (4.77–6.21)	1.03 (0.90–1.17)
Caribbean	0.62 (0.57–0.68)	2.39 (2.20–2.63)	1.71 (1.46–1.96)	3.17 (2.71–3.63)	0.98 (0.86–1.10)
Central Asia	0.14 (0.12–0.15)	0.28 (0.24–0.31)	0.44 (0.39–0.49)	0.50 (0.45–0.56)	2.42 (2.03–2.81)
Central Europe	2.18 (2.05–2.30)	1.44 (1.35–1.51)	4.95 (4.51–5.37)	2.21 (2.01–2.40)	1.36 (1.16–1.56)
Central Latin America	0.92 (0.89–0.95)	1.10 (1.06–1.13)	4.14 (3.70–4.65)	1.63 (1.46–1.83)	1.15 (1.05–1.26)
Central sub-Saharan Africa	0.08 (0.05–0.11)	0.36 (0.25–0.49)	0.24 (0.13–0.35)	0.44 (0.24–0.63)	0.68 (0.40–0.96)
East Asia	1.92 (1.37–3.62)	0.22 (0.15–0.41)	18.19 (11.88–23.58)	0.83 (0.54–1.07)	3.88 (3.25–4.51)
Eastern Europe	2.94 (2.79–3.12)	1.03 (0.97–1.09)	6.17 (5.70–6.69)	1.76 (1.63–1.90)	1.90 (1.64–2.15)
Eastern sub-Saharan Africa	0.64 (0.35–0.92)	0.89 (0.50–1.26)	2.06 (1.25–2.82)	1.24 (0.77–1.68)	1.06 (0.94–1.17)
High-income Asia Pacific	3.97 (3.68–4.20)	1.99 (1.84–2.11)	9.74 (8.16–10.91)	1.93 (1.66–2.16)	–0.04 (–0.22–0.14)
High-income North America	11.85 (11.19–12.24)	3.34 (3.17–3.45)	20.90 (19.02–22.01)	3.10 (2.83–3.26)	–0.39 (–0.54––0.24)
North Africa and the Middle East	1.37 (0.95–1.86)	0.83 (0.58–1.13)	5.84 (4.39–8.00)	1.30 (0.97–1.77)	1.60 (1.51–1.69)
Oceania	0.01 (0.01–0.01)	0.33 (0.21–0.48)	0.03 (0.01–0.04)	0.36 (0.21–0.50)	0.28 (0.24–0.33)
South Asia	3.54 (2.25–4.50)	0.63 (0.40–0.80)	15.91 (12.55–21.56)	1.09 (0.86–1.47)	1.62 (1.46–1.78)
Southeast Asia	0.76 (0.60–1.23)	0.30 (0.24–0.48)	3.51 (2.72–5.68)	0.53 (0.41–0.86)	1.80 (1.75–1.85)
Southern Latin America	1.03 (0.95–1.11)	2.21 (2.06–2.40)	2.03 (1.88–2.19)	2.33 (2.15–2.50)	0.25 (0.08–0.41)
Southern sub-Saharan Africa	0.40 (0.28–0.52)	1.49 (1.01–1.94)	1.35 (0.89–1.64)	2.30 (1.51–2.77)	1.49 (1.36–1.63)
Tropical Latin America	1.20 (1.15–1.25)	1.30 (1.23–1.35)	5.41 (5.05–5.69)	2.10 (1.95–2.21)	1.49 (1.32–1.66)
Western Europe	20.71 (19.52–21.53)	3.54 (3.35–3.68)	41.19 (36.91–44.03)	4.30 (3.91–4.57)	0.64 (0.43–0.86)
Western sub-Saharan Africa	0.22 (0.11–0.30)	0.26 (0.13–0.36)	0.90 (0.37–1.32)	0.48 (0.20–0.69)	2.15 (2.01–2.29)

Abbreviations: ASIR: Age-standardized incidence rate; CI: Confidence interval; EAPC: Estimated annual percentage change; SDI: Sociodemographic index; UI: Uncertainty interval.

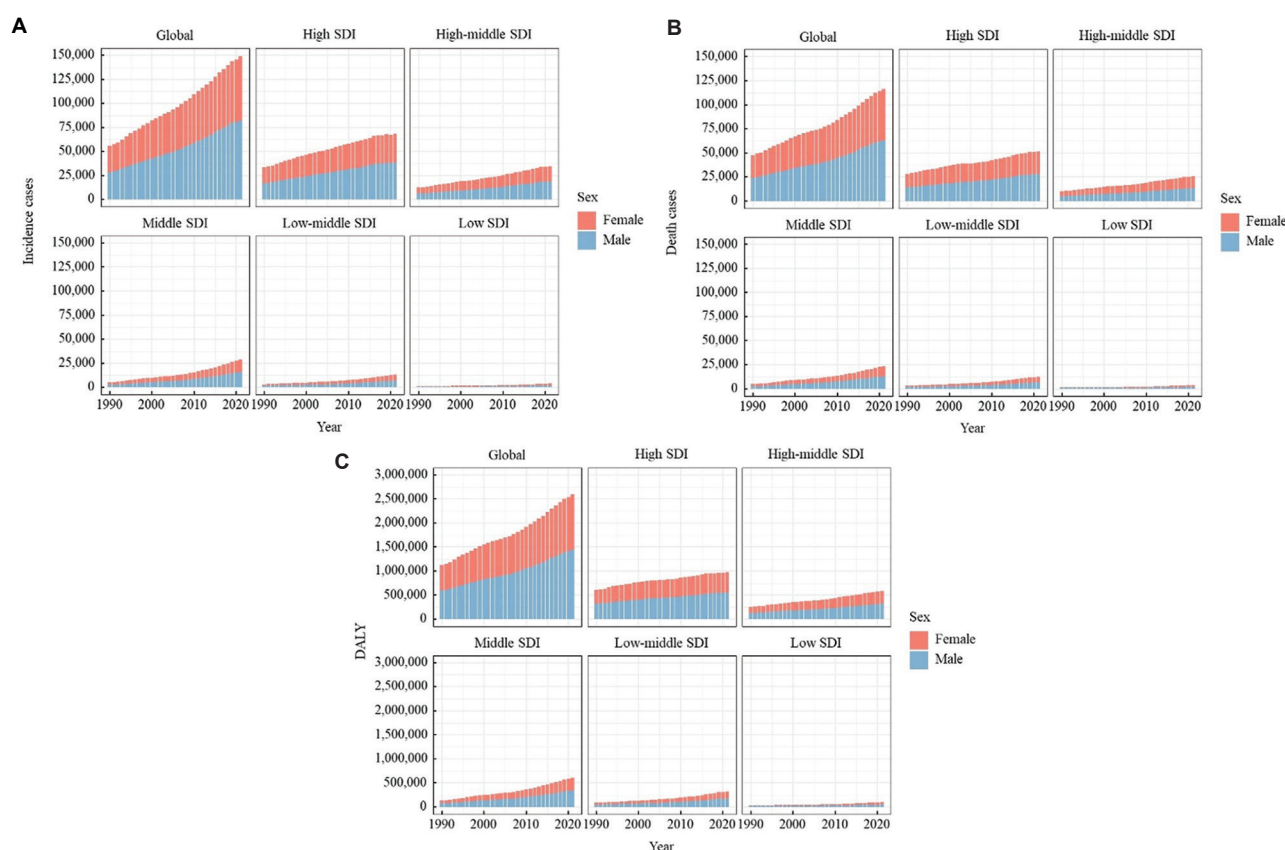


Figure 1. The trends of multiple myeloma's (A) incident cases, (B) death cases, and (C) DALYs from 1990 to 2021. Blue bars represent males and red bars represent females.

Abbreviations: DALY: Disability-adjusted life year; SDI: Sociodemographic index.

males experienced a more modest increase from 1.30 to 1.43/100,000 (EAPC = 0.2%, 95% CI: 0.07–0.33). When stratified by SDI, regions with high SDI consistently maintained the highest burden of MM, with ASIR increasing from 2.98 to 3.16/100,000 from 1990 to 2021. However, the most rapid increase was observed in low-middle-SDI regions (EAPC = 1.72%, 95% CI: 1.64–1.80), followed by middle-SDI regions (EAPC = 2.15%, 95% CI: 1.98–2.33). Geographical analysis revealed substantial regional variations. Australasia maintained the highest ASIR (5.48/100,000 in 2021), followed by Western Europe (4.30/100,000) and high-income North America (3.10/100,000). The most dramatic increases were observed in East Asia (EAPC = 3.88%, 95% CI: 3.25–4.51), Central Asia (EAPC = 2.42%, 95% CI: 2.03–2.81), and Western sub-Saharan Africa (EAPC = 2.15%, 95% CI: 2.01–2.29). Notably, some high-income regions showed slight decreases in burden, including high-income Asia Pacific (EAPC = –0.04%, 95% CI: –0.22 to 0.14) and high-income North America (EAPC = –0.39%, 95% CI: –0.54 to –0.24). At the country or territory level, the USA had the highest number of cases in both 1990 and 2021 (10,368 in 1990 and

17,693 in 2021) (Figure 2A; Tables S1 and 2). The Bahamas had the highest ASIR in 1990 (ASIR = 5.70), while Monaco had the highest ASIR in 2021 (ASIR = 6.86; Figure 3A, Tables S3 and 4). Georgia had the most rapid increase in ASIR (EAPC = 6.20, 95% CI: 5.45–6.96; Table S5).

3.2. The death of MM and its trend

Globally, deaths attributed to MM increased significantly between 1990 and 2021, rising from 47.57×10^3 cases (95% UI: 44.14–51.42) in 1990 to 116.36×10^3 cases (95% UI: 103.08–128.47) in 2021, reflecting an increase of 144.7% over the 31-year period (Table 2 and Figure 1B). The global age-standardized death rate (ASDR) rose modestly from 1.29 to 100,000 population (95% UI: 1.20–1.39) in 1990 to 1.37/100,000 (95% UI: 1.22–1.52) in 2021, with an estimated EAPC of 0.09 (95% CI: –0.01–0.18). Deaths from MM were slightly higher among females than among males during the entire study period. In 1990, 23.49×10^3 deaths (95% UI: 21.57–25.97) were reported for males, while females accounted for 24.08×10^3 deaths (95% UI: 21.92–26.72). By 2021, deaths had increased to 53.24×10^3 (95% UI: 44.83–60.88) for males and 63.12×10^3 (95% UI: 54.44–

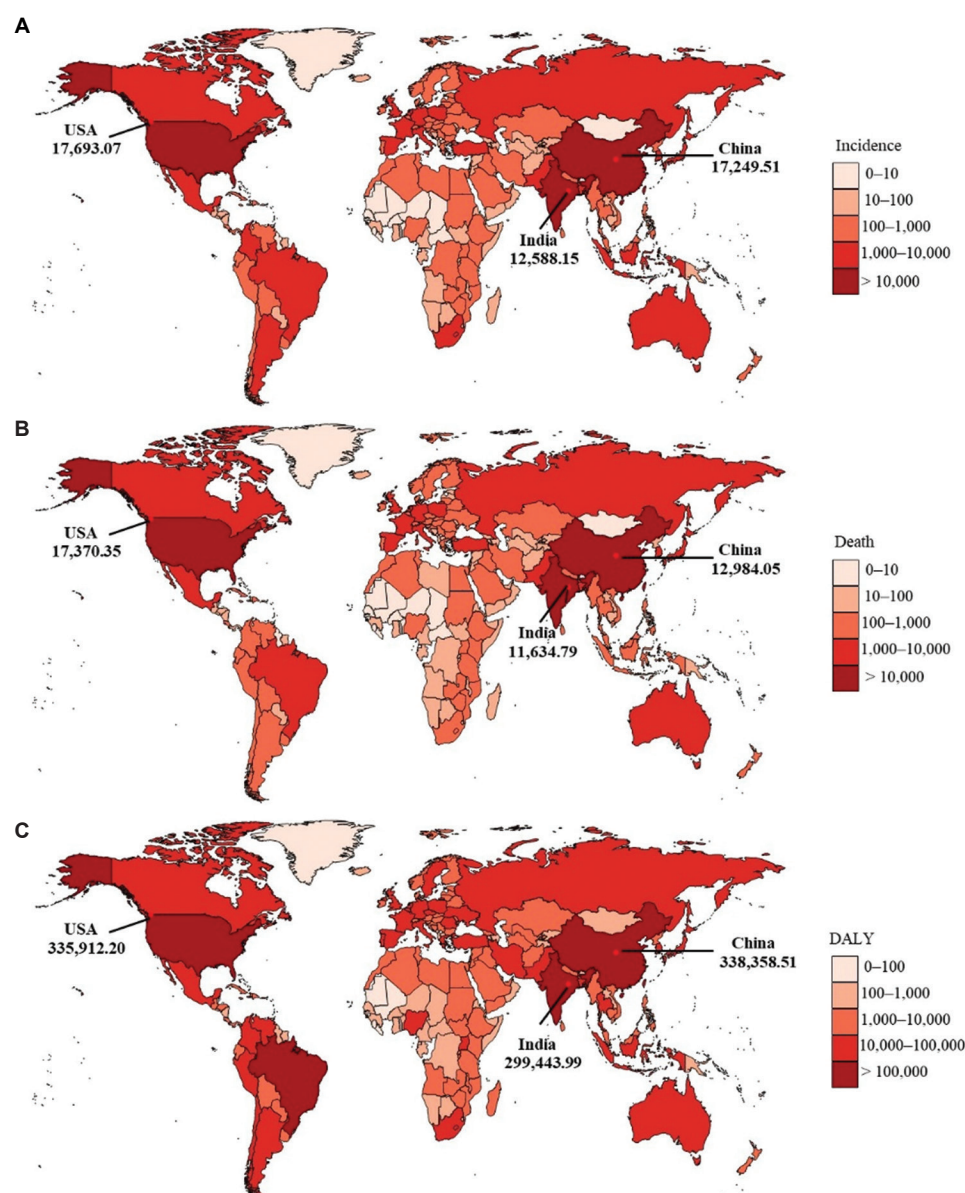


Figure 2. The global disease burden of multiple myeloma in 204 countries or territories: (A) incident cases, (B) death cases, and (C) DALYs
Abbreviation: DALY: Disability-adjusted life year.

70.18) for females. The ASDR among females increased from 1.50 in 1990 to 1.67 in 2021 (EAPC = 0.27, 95% CI: 0.19–0.35), whereas the ASDR for males remained stable, with values of 1.14 in both 1990 and 2021 (EAPC = –0.14, 95% CI: –0.25 to –0.03).

Subgroup analysis by SDI revealed stark differences in MM-related deaths and trends. High-SDI regions consistently reported the highest number of deaths, increasing from 28.14×10^3 (95% UI: 26.55–28.97) in 1990 to 51.43×10^3 (95% UI: 45.7–54.8) in 2021. However, this region experienced a decline in ASDR (1990: 2.5; 2021: 2.28,

EAPC = –0.43, 95% CI: –0.54 to –0.32) due to improved healthcare and early detection. Low- to middle-SDI regions showed the highest increase in ASDR (EAPC = 1.53, 95% CI: 1.46–1.61), rising from 0.55 in 1990 to 0.89 in 2021. Similarly, the low-SDI region experienced an increase in ASDR (EAPC = 0.87, 95% CI: 0.7–1.03). Geographically, substantial variability was observed in MM-related deaths and ASDR trends. High-income North America, Western Europe, and East Asia were the top three regions in 2021, with 19.38×10^3 , 15.39×10^3 , and 13.62×10^3 deaths, respectively. These regions collectively accounted for a

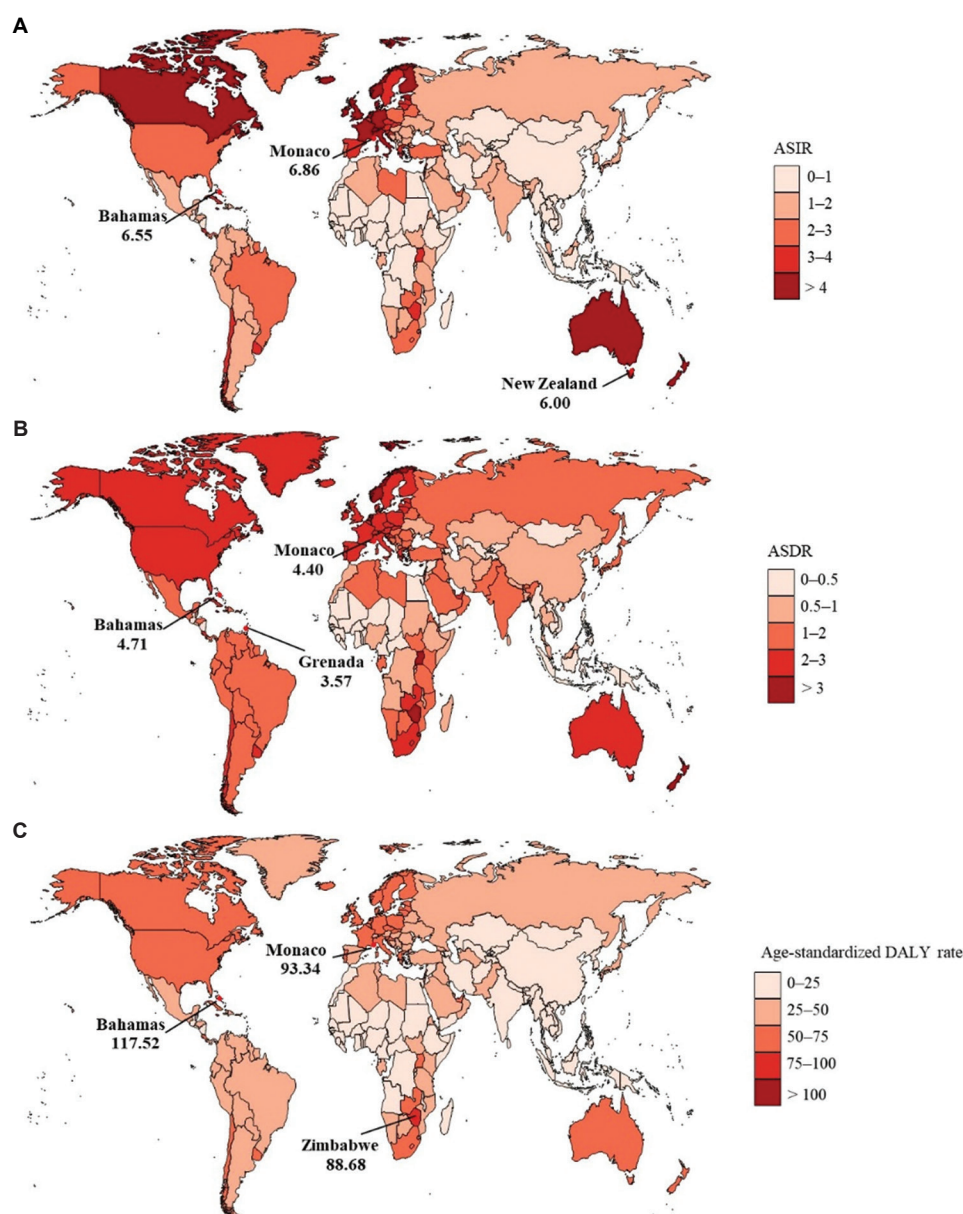


Figure 3. The age-standardized rates of multiple myeloma in 204 countries or territories: (A) ASIR, (B) ASDR, and (C) age-standardized DALY rate
Abbreviations: ASDR: Age-standardized death rate; ASIR: Age-standardized incidence rate; DALY: Disability-adjusted life year.

significant proportion of global MM deaths. Western Europe reported the highest ASDR in 2021 (2.59 per 100,000 population, EAPC = -0.08 , 95% CI: -0.13 – 0.12). East Asia had the highest increase in ASDR (EAPC = 2.99 , 95% CI: 2.31 – 3.68), followed by South Asia (EAPC = 1.41 , 95% CI: 1.26 – 1.55). Andean Latin America and Western sub-Saharan Africa had the lowest MM-related deaths, with fewer than 1,000 deaths annually in both 1990 and 2021. However, Western sub-Saharan Africa experienced a noticeable rise in ASDR (EAPC = 2.01 , 95% CI: 1.89 – 2.13). Subgroup analysis stratified by country or territory

revealed that the USA had the most deaths in both 1990 and 2021 (10,682 cases in 1990 and 17,370 cases in 2021; [Figure 2B](#), Tables S6 and 7). High ASDR was observed in the Bahamas in 1990 and 2017 (ASDR = 4.59 in 1990, 4.71 in 2021; [Figure 3B](#), Tables S8 and 9). Georgia had the most rapid increase in ASDR (EAPC = 6.18 , 95% CI: 5.43 – 6.95 ; Table S10).

3.3. The DALYs of MM and its trend

Globally, the DALY of MM increased significantly from $1,122.52 \times 10^3$ in 1990 to $2,595.59 \times 10^3$ in 2021

Table 2. The death cases and age-standardized death rate of multiple myeloma in 1990 and 2021, and their temporal trends from 1990 to 2021

Sociodemographic profile	1990		2021		1990–2021
	Death cases×10 ³ (95% UI)	ASDR/100,000 (95% UI)	Death cases×10 ³ (95% UI)	ASDR/100,000 (95% UI)	EAPC (95% CI)
Overall	47.57 (44.14–51.42)	1.29 (1.20–1.39)	116.36 (103.08–128.47)	1.37 (1.22–1.52)	0.09 (–0.01–0.18)
Sex					
Male	23.49 (21.57–25.97)	1.14 (1.04–1.26)	53.24 (44.83–60.88)	1.14 (0.96–1.31)	–0.14 (–0.25–0.03)
Female	24.08 (21.92–26.72)	1.50 (1.38–1.66)	63.12 (54.44–70.18)	1.67 (1.44–1.86)	0.27 (0.19–0.35)
SDI					
High SDI	28.14 (26.55–28.97)	2.50 (2.36–2.57)	51.43 (45.70–54.83)	2.28 (2.05–2.41)	–0.43 (–0.54–0.32)
High-middle SDI	10.13 (9.53–10.99)	1.05 (0.99–1.14)	25.45 (22.13–28.17)	1.28 (1.12–1.43)	0.59 (0.48–0.71)
Middle SDI	4.84 (4.19–6.27)	0.49 (0.43–0.63)	23.40 (18.80–27.50)	0.88 (0.71–1.04)	1.72 (1.54–1.91)
Low-middle SDI	3.16 (2.28–4.16)	0.55 (0.39–0.71)	12.28 (10.53–17.22)	0.89 (0.76–1.24)	1.53 (1.46–1.61)
Low SDI	1.24 (0.69–1.74)	0.58 (0.33–0.81)	3.65 (2.43–4.90)	0.77 (0.52–1.02)	0.87 (0.70–1.03)
Region					
Andean Latin America	0.22 (0.16–0.28)	1.13 (0.83–1.42)	0.88 (0.69–1.15)	1.51 (1.19–1.96)	1.08 (0.91–1.25)
Australasia	0.67 (0.63–0.71)	2.82 (2.65–2.99)	1.66 (1.44–1.85)	2.89 (2.52–3.23)	0.12 (0.01–0.24)
Caribbean	0.47 (0.43–0.52)	1.83 (1.70–2.03)	1.11 (0.96–1.26)	2.05 (1.77–2.33)	0.45 (0.36–0.55)
Central Asia	0.13 (0.11–0.14)	0.26 (0.23–0.29)	0.39 (0.34–0.43)	0.45 (0.41–0.51)	2.28 (1.91–2.64)
Central Europe	2.03 (1.91–2.14)	1.35 (1.27–1.42)	4.42 (4.02–4.79)	1.92 (1.75–2.08)	1.08 (0.91–1.25)
Central Latin America	0.84 (0.82–0.87)	1.03 (0.99–1.06)	3.33 (2.99–3.73)	1.33 (1.19–1.49)	0.73 (0.64–0.82)
Central sub-Saharan Africa	0.08 (0.05–0.11)	0.38 (0.26–0.50)	0.23 (0.12–0.33)	0.44 (0.23–0.63)	0.59 (0.32–0.85)
East Asia	1.76 (1.24–3.36)	0.21 (0.14–0.40)	13.62 (9.02–17.74)	0.63 (0.41–0.81)	2.99 (2.31–3.68)
Eastern Europe	2.46 (2.33–2.59)	0.86 (0.82–0.91)	4.65 (4.30–5.04)	1.31 (1.21–1.42)	1.51 (1.29–1.72)
Eastern sub-Saharan Africa	0.64 (0.35–0.92)	0.92 (0.52–1.31)	1.97 (1.21–2.70)	1.25 (0.78–1.69)	0.96 (0.85–1.07)
High-income Asia Pacific	3.03 (2.84–3.20)	1.54 (1.43–1.63)	6.98 (5.83–7.78)	1.28 (1.09–1.41)	–0.77 (–0.90–0.64)
High-income North America	11.71 (10.99–12.11)	3.25 (3.06–3.36)	19.38 (17.54–20.47)	2.81 (2.56–2.96)	–0.67 (–0.79–0.56)
North Africa and The Middle East	1.29 (0.90–1.75)	0.81 (0.57–1.11)	4.71 (3.54–6.49)	1.10 (0.83–1.51)	1.10 (1.02–1.17)
Oceania	0.01 (0.01–0.01)	0.32 (0.21–0.48)	0.02 (0.01–0.03)	0.34 (0.20–0.49)	0.21 (0.16–0.25)
South Asia	3.48 (2.22–4.42)	0.64 (0.41–0.82)	14.79 (11.66–20.03)	1.04 (0.83–1.41)	1.41 (1.26–1.55)
Southeast Asia	0.70 (0.56–1.15)	0.29 (0.23–0.47)	2.99 (2.31–4.85)	0.46 (0.36–0.75)	1.50 (1.44–1.55)
Southern Latin America	0.96 (0.89–1.03)	2.08 (1.93–2.24)	1.68 (1.54–1.79)	1.89 (1.75–2.02)	–0.22 (–0.38–0.06)
Southern sub-Saharan Africa	0.39 (0.26–0.50)	1.47 (0.99–1.93)	1.24 (0.82–1.49)	2.18 (1.44–2.62)	1.35 (1.19–1.51)
Tropical Latin America	1.10 (1.05–1.14)	1.22 (1.16–1.27)	4.59 (4.25–4.82)	1.80 (1.66–1.89)	1.24 (1.09–1.39)
Western Europe	15.39 (14.49–15.92)	2.58 (2.44–2.66)	26.87 (23.76–28.88)	2.59 (2.33–2.76)	0 (–0.13–0.12)
Western sub-Saharan Africa	0.22 (0.11–0.31)	0.27 (0.14–0.38)	0.86 (0.36–1.24)	0.48 (0.20–0.69)	2.01 (1.89–2.13)

Abbreviations: ASDR: Age-standardized death rate; CI: Confidence interval; EAPC: Estimated annual percentage change; SDI: Sociodemographic index; UI: Uncertainty interval.

(Table 3 and Figure 1C). Compared to females, the male population contributed fewer DALY but exhibited a slight decline in age-standardized DALY rates over the study period. Specifically, for males, the DALY rose from 530.19×10^3 in 1990 to $1,151.27 \times 10^3$ in 2021, with an EAPC of -0.16 (95% CI: -0.26 to -0.05). Among females, the DALY rose more substantially, from 592.33×10^3 in 1990 to

$1,444.32 \times 10^3$ in 2021, accompanied by an increase in the age-standardized DALY rate (EAPC = 0.22 , 95% CI: 0.14 – 0.30). Subgroup analysis stratified by sociodemographic factors indicated that high-SDI regions consistently bore the highest DALY burden, with cases increasing from 609.78×10^3 in 1990 to 976.93×10^3 in 2021. However, the age-standardized DALY rate in these regions modestly

Table 3. The disability-adjusted life years and age-standardized disability-adjusted life years of multiple myeloma in 1990 and 2021, and their temporal trends from 1990 to 2021

Sociodemographic profile	1990		2021		1990–2021
	DALY×10 ³ (95% UI)	Age-standardized DALY rate/100,000 (95% UI)	DALY×10 ³ (95% UI)	Age-standardized DALY rate/100,000 (95% UI)	EAPC (95% CI)
Overall	1,122.52 (1041.4–1,227.73)	28.34 (26.33–30.83)	2,595.59 (2,270.48–2,889.97)	30.00 (26.22–33.37)	0.06 (–0.04–0.15)
Sex					
Male	530.19 (488.24–601.39)	24.89 (22.94–28.15)	1,151.27 (940.29–1,337.06)	25.04 (20.39–29.10)	–0.16 (–0.26–0.05)
Female	592.33 (532.47–665.08)	32.57 (29.55–36.21)	1,444.32 (1,219.07–1,614.79)	35.82 (30.46–39.98)	0.22 (0.14–0.3)
SDI					
High SDI	609.78 (585.95–625.03)	55.37 (53.27–56.75)	976.93 (896.76–1,033.83)	47.33 (44.00–49.82)	–0.64 (–0.76–0.52)
High-middle SDI	254.01 (239.76–277.11)	25.02 (23.59–27.25)	583.31 (504.14–652.35)	29.65 (25.53–33.21)	0.47 (0.37–0.56)
Middle SDI	135.86 (117.17–175.79)	12.23 (10.59–15.76)	609.12 (487.41–714.66)	21.85 (17.50–25.56)	1.68 (1.49–1.87)
Low-middle SDI	87.03 (62.73–115.4)	13.45 (9.70–17.75)	323.36 (274.51–449.77)	21.51 (18.34–29.96)	1.49 (1.42–1.56)
Low SDI	34.29 (18.92–48.49)	14.26 (7.97–20.10)	99.83 (66.16–136.14)	18.43 (12.25–24.91)	0.75 (0.59–0.91)
Region					
Andean Latin America	5.90 (4.32–7.41)	27.75 (20.35–34.85)	22.22 (17.27–29.04)	36.98 (28.79–48.20)	1.04 (0.86–1.22)
Australasia	14.96 (14.1–15.75)	63.56 (59.99–66.95)	32.24 (28.60–35.87)	60.65 (54.09–67.37)	–0.08 (–0.17–0.01)
Caribbean	11.31 (10.45–12.75)	43.02 (39.75–48.42)	26.90 (23.07–30.71)	49.86 (42.79–56.92)	0.52 (0.42–0.62)
Central Asia	4.07 (3.53–4.56)	7.81 (6.78–8.78)	11.94 (10.64–13.42)	13.06 (11.63–14.64)	2.06 (1.73–2.40)
Central Europe	50.82 (47.92–53.41)	33.22 (31.32–34.95)	95.12 (86.99–103.20)	43.87 (40.13–47.69)	0.83 (0.66–1.00)
Central Latin America	23.53 (22.81–24.15)	26.40 (25.60–27.11)	88.78 (79.14–99.66)	34.39 (30.68–38.61)	0.73 (0.64–0.83)
Central sub-Saharan Africa	2.30 (1.51–3.14)	9.38 (6.27–12.67)	6.65 (3.62–9.69)	10.89 (5.93–15.83)	0.58 (0.32–0.84)
East Asia	51.85 (37.02–98.33)	5.36 (3.80–10.25)	354.33 (228.71–464.09)	16.31 (10.44–21.37)	3.03 (2.38–3.67)
Eastern Europe	69.12 (65.36–72.84)	24.23 (22.90–25.55)	118.76 (109.04–128.80)	34.51 (31.74–37.42)	1.19 (1.01–1.37)
Eastern sub-Saharan Africa	17.75 (9.54–25.62)	22.37 (12.26–32.03)	55.54 (33.19–77.26)	30.11 (18.31–41.16)	0.94 (0.83–1.05)
High-income Asia Pacific	69.22 (65.58–72.65)	33.90 (32.00–35.60)	118.27 (101.40–130.30)	25.57 (22.47–27.98)	–1.05 (–1.19–0.90)
High-income North America	252.72 (242.62–259.51)	73.46 (70.75–75.37)	374.04 (348.99–390.78)	57.28 (53.8–59.76)	–1.04 (–1.16–0.92)
North Africa and the Middle East	35.66 (24.58–48.76)	19.80 (13.69–26.95)	124.88 (93.51–171.85)	26.02 (19.48–35.88)	0.96 (0.89–1.04)
Oceania	0.25 (0.15–0.37)	7.76 (4.81–11.52)	0.70 (0.38–1.01)	8.43 (4.77–12.16)	0.29 (0.24–0.34)
South Asia	97.1 (61.06–123.44)	15.82 (10.10–20.14)	383.53 (302.58–511.79)	24.96 (19.65–33.42)	1.32 (1.17–1.46)
Southeast Asia	19.91 (15.81–32.18)	7.24 (5.76–11.77)	80.58 (62.89–128.42)	11.53 (8.96–18.56)	1.42 (1.36–1.48)
Southern Latin America	23.13 (21.63–24.93)	49.35 (46.14–53.18)	37.8 (35.38–40.29)	43.97 (41.24–46.90)	–0.31 (–0.47–0.15)
Southern sub-Saharan Africa	10.83 (7.51–13.64)	37.35 (25.56–47.90)	34.72 (23.14–42.58)	55.55 (36.80–67.46)	1.38 (1.22–1.53)
Tropical Latin America	30.47 (29.4–31.53)	31.23 (30.02–32.36)	113.48 (107.33–118.28)	43.43 (41.00–45.28)	0.98 (0.82–1.14)
Western Europe	326.02 (311.08–336.76)	57.28 (54.88–59.05)	492.17 (447.36–523.56)	53.56 (49.55–56.61)	–0.25 (–0.39–0.11)
Western sub-Saharan Africa	5.62 (2.90–7.82)	6.23 (3.22–8.66)	22.96 (9.46–33.91)	11.10 (4.68–16.12)	2.04 (1.91–2.18)

Abbreviations: DALYs: Disability-adjusted life years; CI: Confidence interval; EAPC: Estimated annual percentage change; SDI: Sociodemographic index; UI: Uncertainty interval.

decreased (EAPC = –0.64, 95% CI: –0.76 to –0.52). In contrast, low-SDI regions experienced rapid growth in DALYs (from 34.29 × 10³ in 1990 to 99.83 × 10³ in 2021), as well as an increase in age-standardized DALY rate

(EAPC = 0.75, 95% CI: 0.59–0.91). Similarly, the rates of increase in the middle- and low-middle-SDI regions were noteworthy, with EAPCs of 1.68 (95% CI: 1.49–1.86) and 1.49 (95% CI: 1.42–1.56), respectively.

Geographically, high-income North America and Western Europe had the highest age-standardized DALY rates in 2021, with 57.28/100,000 and 53.56/100,000, respectively. However, both regions experienced a slight reduction in age-standardized DALY rates during the study period (EAPC = -0.36 , 95% CI: -0.45 to -0.28 for high-income North America; EAPC = -0.25 , 95% CI: -0.39 to -0.11 for Western Europe). Conversely, Western sub-Saharan Africa exhibited the fastest increase in the age-standardized DALY rate, with an EAPC of 2.04 (95% CI: 1.91–2.18). At the country or territory level, the USA recorded the highest DALY in 1990 (DALY = 229849), and China had the highest DALY in 2021 (DALY = 338,358; Figure 2C, Tables S11 and 12). The Bahamas exhibited the highest age-standardized DALY in 1990 and 2021 (117.1 in 1990; 117.5 in 2021, ranking first; Figure 3C, Tables S13 and 14). Turkmenistan exhibited the most rapid increase in the age-standardized DALY rate over the past 31 years (EAPC = 6.04, 95% CI: 5.45–6.64; Table S15).

3.4. The association between the SDI and the incidence and mortality rates of MM

The correlation coefficient between ASIR in 1990 and the corresponding EAPC value was examined. The results revealed a negative correlation between the EAPC of ASIR and the ASIR in 1990 (correlation coefficient = -0.45 , $p < 0.0001$), indicating that regions with a higher baseline

incidence in 1990 showed a slower growth in ASIR over time (Figure 4A). The correlation between SDI and the EAPC values for ASIR, ASDR, and age-standardized DALY rate in 2021 was assessed in 204 countries or territories. The results indicate that the EAPC of ASIR was weakly negatively correlated with SDI (correlation coefficient = -0.19 , $p < 0.01$; Figure 4B), suggesting a slower growth in ASIR in regions with higher SDI. In addition, the EAPC of ASDR showed a negative correlation with SDI (correlation coefficient = -0.31 , $p < 0.0001$; Figure 4C), indicating that regions with higher SDI experienced a greater decline in mortality rates for MM. Similarly, a negative correlation was also observed between the EAPC of the age-standardized DALY rate and SDI (correlation coefficient = -0.34 , $p < 0.0001$; Figure 4D).

We then analyzed the correlation between the SDI and the ASIR, ASDR, and age-standardized DALY rates of MM across 18 global regions from 1990 to 2021. The results revealed that all ASRs exhibited a significant positive correlation with SDI (correlation coefficient of ASIR = 0.70, of ASDR = 0.69, of age-standardized DALY rate = 0.68, all $p < 0.0001$; Figure 5A–C).

3.5. The incidence and age structure of MM

The incidence and ASIR of MM were analyzed across five age groups (under 5 years, 5–14 years, 15–49 years,

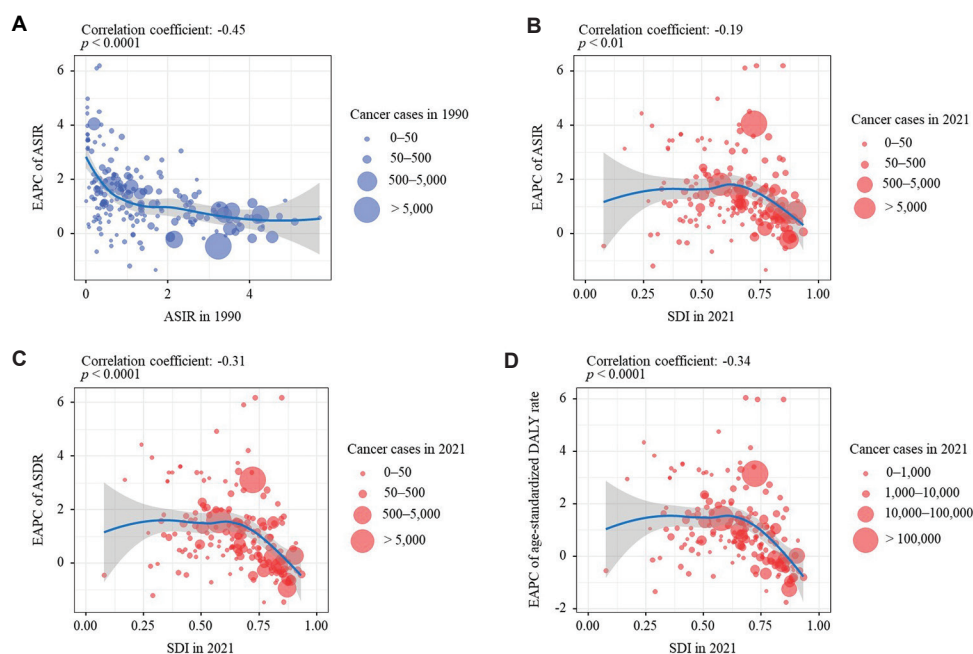


Figure 4. Correlation analyses between the (A) EAPC of ASIR and ASIR in 1990, (B) between EAPC of ASIR and SDI in 2021, (C) between EAPC of ASDR and SDI in 2021, and (D) between EAPC of age-standardized DALY rate and SDI in 2021 across 204 countries or territories. The size of the circle represents the quantity of multiple myeloma patients in one country or territory.

Abbreviations: ASDR: Age-standardized death rate; ASIR: Age-standardized incidence rate; DALY: Disability-adjusted life year; EAPC: Estimated annual percentage change; SDI: Sociodemographic index.

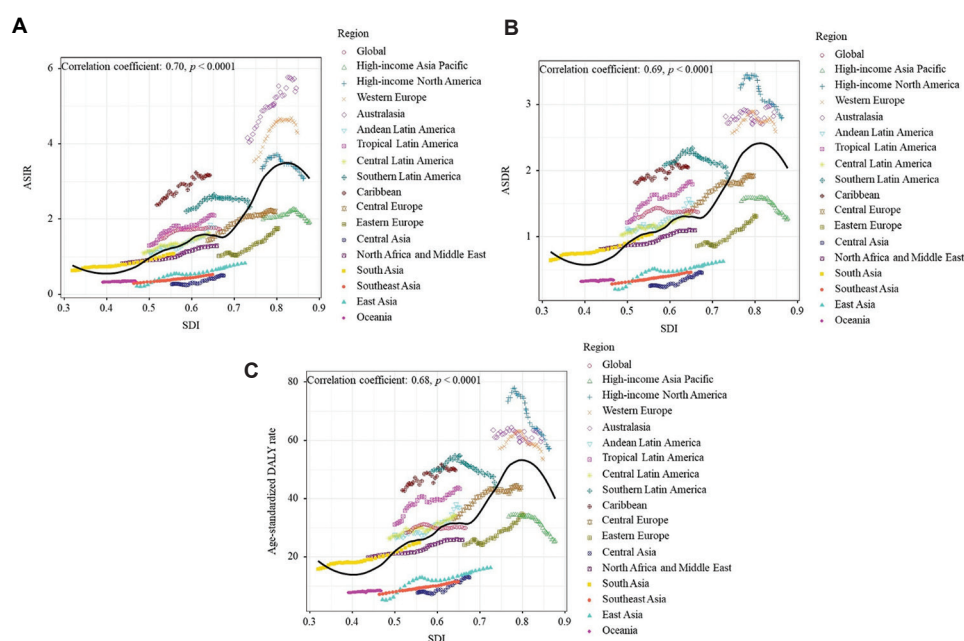


Figure 5. Trends and correlation analyses (A) between ASIR and SDI, (B) between ASDR and SDI, and (C) between age-standardized DALY rate and SDI from 1990 to 2021 across 18 regions

Abbreviations: ASDR: Age-standardized death rate; ASIR: Age-standardized incidence rate; DALY: Disability-adjusted life year; SDI: Sociodemographic index.

50–69 years, and 70 years or older) globally and in regions grouped by SDI. Our results showed that most MM cases worldwide occurred in populations aged 50 years or older. In 2021, approximately 96.8% of MM cases in high-SDI regions were among patients aged 50 years or older, whereas in low-SDI regions, the proportion was about 85.5% (Figure 6A). Among all age groups, patients aged 70 years or older had the highest incidence and ASIR; the trend was more pronounced in high-SDI regions, with the incidence rate increasing significantly from 1990 to 2021. Conversely, low-SDI regions displayed relatively low ASIR across all age groups despite a slight upward trend over the same period (Figure 6B). The younger age groups (under 5 years and 5–14 years) maintained consistently low incidences and ASIRs globally and across all SDI regions. Overall, the burden of MM incidence is concentrated in older populations, with significant regional disparities.

4. Discussion

The heterogeneous distribution of healthcare resources and demographic structure contributes to substantial variability in MM burden globally,^{4,13,14} adding complexity to its prevention and control strategies. In the current study, we comprehensively analyzed the temporal trends in MM incidence, mortality, and DALYs at global, regional, and national levels from 1990 to 2021. Overall, both the incidence and mortality of MM increased substantially

over the study period. However, temporal trends in MM burden demonstrated significant variation across regions and countries, largely corresponding to the SDI levels. Consequently, understanding the diverse patterns and drivers of MM burden is critical for developing tailored prevention, diagnosis, and treatment strategies globally.

One of the most significant findings in this study is the substantial increase in MM incidence over the past three decades. The global incident cases nearly tripled, accompanied by a moderate growth in the ASIR. This pattern aligns with previous studies on MM, which attribute the rising incidence to multiple factors, including demographic shifts, improvements in diagnostic techniques, and possibly increasing exposure to risk factors, such as obesity, genetic predisposition, and environmental toxins.^{15–17} The global aging population is likely the dominant driver of increased MM incidence, as the disease predominantly affects individuals aged 50 years and older.¹⁸ In this study, more than 96% of MM cases in high-SDI regions and 85% in low-SDI regions occurred among individuals over 50 years old in 2021. These findings support previous research suggesting that aging is a key risk factor for MM due to the gradual accumulation of genetic and epigenetic alterations, increased production of reactive oxygen species, diminished DNA repair capacity, and elevated susceptibility to malignant transformation in B cells over time.¹⁹ Importantly, while the younger

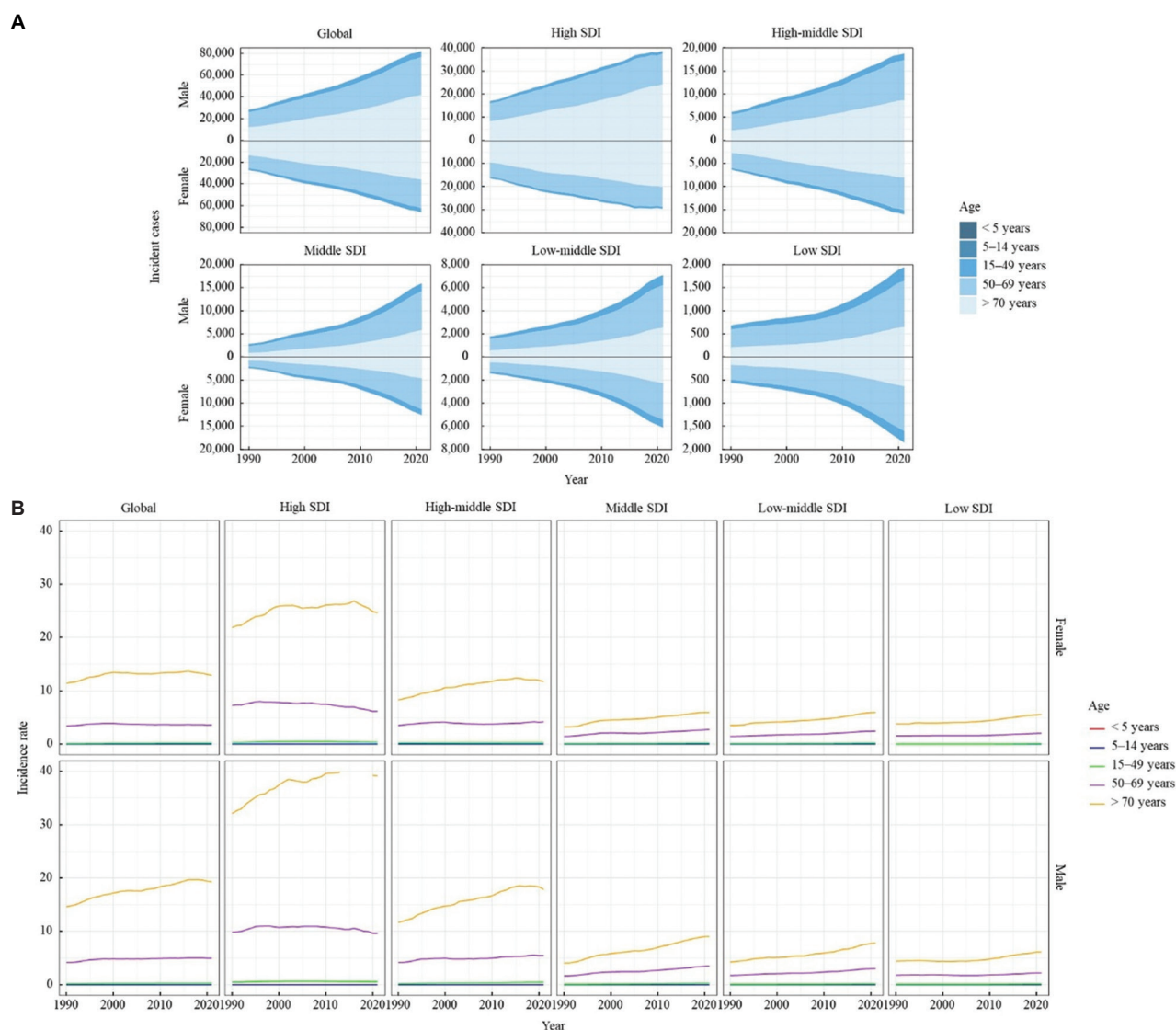


Figure 6. The incident cases and corresponding ASIR of MM in different age groups from 1990 to 2021. (A) The incident cases of MM in five different age groups around the globe and various regions. (B) The ASIR of MM in five different age groups around the globe and various regions. Abbreviations: ASIR: Age-standardized incidence rate; MM: Multiple myeloma; SDI: Sociodemographic index.

age groups (under 50 years) had stable incidence rates, the relatively low burden in these populations suggests minimal epidemiological changes, emphasizing the need for regionally tailored MM interventions for older age cohorts.

Another contributing factor to the rising burden of MM is improved diagnostic infrastructure, particularly in high- and middle-SDI regions. Advances in imaging modalities (e.g., positron emission tomography-computed tomography), the increased availability of sensitive diagnostic techniques (such as the serum-free light chain assay), and the wider application of bone marrow biopsy have potentially contributed to the identification of

previously undetected cases.²⁰ However, disparities persist, as low-SDI regions continue to experience diagnostic challenges due to a lack of healthcare access and resource limitations. This scenario may underestimate the MM burden in these regions and obscure the understanding of true incidence trends. Future efforts should focus on enhancing diagnostic capabilities in lower-resourced settings, complemented by education campaigns to raise awareness of MM symptoms among healthcare providers and the public.

While deaths from MM have risen globally in absolute terms, ASDR increased only minimally between 1990 and 2021. Declining mortality trends in high-SDI regions,

as observed in this study, likely reflect the significant impact of advances in MM treatment, earlier diagnosis, and improved supportive care.²¹ However, many low- and middle-SDI regions experienced a marked increase in mortality rates, illustrating stark inequities in healthcare access, treatment availability, and disease outcomes. In high-income countries, the introduction of novel therapeutic agents, such as immunomodulatory drugs, proteasome inhibitors, monoclonal antibodies, and ASCT, was transformative in lengthening survival in MM patients.^{20,22} Studies have shown that median survival in MM improved from under 3 years in the early 2000s to more than 6–8 years with the implementation of modern therapeutic regimens, particularly in patients eligible for stem cell transplantation.²³ Furthermore, supportive care advancements with the use of bone-strengthening agents, such as bisphosphonates, infection prevention, and personalized treatment plans, improved patient quality of life and longevity.^{24,25}

Conversely, regions with limited access to modern therapies displayed significantly poorer outcomes. In low-SDI regions, persistent constraints in healthcare infrastructure, the lack of access to expensive novel therapies, and delayed or inaccurate diagnosis potentially explain the rapid rise in ASDR and deaths attributed to MM.^{26–28} Challenges in managing comorbidities and complications, including infections, renal failure, and fractures, further exacerbate MM outcomes in these settings.²⁹ Addressing these gaps requires policies focused on improving the affordability and distribution of MM therapies, paired with global health initiatives to strengthen cancer care infrastructures in low-resource settings.

The study revealed significant regional disparities in MM burden, with high-SDI regions displaying the highest ASIR and ASDR values but also showing evidence of stabilization or decline in mortality burdens. In high-income North America and Western Europe, ASDR decreased despite the high absolute number of deaths, highlighting the effectiveness of well-developed healthcare systems in sustaining advanced cancer care and achieving earlier diagnosis. In contrast, low- and low- to middle-SDI regions experienced the sharpest upward trajectory in ASDR and age-standardized DALY rates, reflecting underlying inequities in healthcare delivery systems and access to life-saving interventions. These patterns demonstrate a global epidemiological paradox.³⁰ Higher ASIR observed in high-SDI regions may, in part, reflect better surveillance programs and more structured registries rather than a true increase in disease frequency. Meanwhile, lower recorded ASIR values in low-SDI regions do not necessarily equate to a lower disease burden

but may instead indicate underreporting and diagnostic gaps. Differences in cancer reporting systems, registries, and surveillance capabilities between developed and developing nations underscore the need for strengthened global health data systems to comprehensively monitor MM trends worldwide.

In addition, variations in MM mortality and ASIR correlating with SDI underscore the interplay between socioeconomic determinants and MM outcomes. Improved SDI is often associated with better cancer prognosis due to increased public health awareness, access to routine screening, and health-seeking behavior.^{31–33} As demonstrated by this study, lower SDI regions reported slower diagnostic advancement and higher mortality growth, which may perpetuate an ongoing cycle of inequity.

The findings of this study highlight the urgent need for coordinated global action to address the rising burden of MM. Disparities across regions emphasize the need to prioritize access to MM diagnostics and therapeutics in low-resource regions. Leveraging international collaborations to negotiate the affordability of novel treatments or incorporating MM management into larger cancer care frameworks may mitigate treatment gaps in such regions. Support for education and training of healthcare workers in MM-specific diagnosis and treatment approaches is also critical. Although MM lacks established primary prevention, screening programs initiated in populations with high-risk genetic backgrounds (e.g., African Americans) or precursor conditions (monoclonal gammopathy of undetermined significance [MGUS]) may be useful in high-burden populations.^{34–36} Increasing population-level awareness campaigns for early presentation may offer an opportunity for timely interventions. MM should be integrated into global efforts to address non-communicable diseases, particularly cancer, with funding allocations supporting MM-specific research, capacity-building initiatives, and international collaborations to standardize care guidelines. Further studies are needed to clarify the roles of risk factors, such as environmental toxins and obesity, across regions. Longitudinal studies on the progression of MGUS into MM and its implications for initiating preventive treatment are critical to improving survival outcomes.

This study provides the most comprehensive view of global MM trends to date, yet limitations such as regional variability in data quality, potential underreporting in resource-limited areas, and lack of granular data on treatment outcomes should be acknowledged. Future iterations of these analyses should integrate real-world treatment outcomes and biomarker-based studies to

further refine the understanding of MM incidence and mortality trends.

5. Conclusion

The global burden of MM has demonstrated consistent increases in incidence, mortality, and DALY from 1990 to 2021, with striking regional and sociodemographic disparities magnifying the challenges faced by low-SDI regions. While advancements in MM diagnosis and treatment in high-SDI regions represent a major success, the rapid increases in burden within low-SDI regions require immediate and targeted attention. Reducing the global MM burden will require coordinated international actions, innovative healthcare policies, and strengthened regional cancer care infrastructure, particularly in resource-limited settings.

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Conflict of interest

The authors declare they have no competing interests.

Author contributions

Conceptualization: Xuena Wang, Qi Mei

Formal analysis: All authors

Methodology: All authors

Writing—original draft: All authors

Writing—review & editing: Xuan Su, Xuena Wang

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Data related to MM, including incident cases, deaths, DALYs, and corresponding ASRs, were obtained from the Global Health Data Exchange platform (<http://ghdx.healthdata.org/gbd-resultstool>).

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