Heliyon 10 (2024) e32996

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

National and subnational mortality trends of multiple myeloma in China, 2013–2020: Empirical evidence from national mortality

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ARTICLE INFO

Keywords:
Multiple myeloma
Mortality
Epidemiology
China
Strategy

ABSTRACT

The incidence of multiple myeloma (MM) has increased over time in China. Despite this increase, comprehensive and up-to-date statistics on its mortality at national and provincial scales are lacking. To bridge this gap, we used mortality data from the disease surveillance points system operated by the Chinese Center for Disease Control and Prevention. Mortality rates were standardized against the 2010 census population of China (ASMRC) and Segi's world population (ASMRW). Joinpoint regression models were used to analyze temporal trends. Our findings indicated an estimated 14,568 MM-related deaths in China. The observed crude mortality rates ASMRC, and ASMRW were 1.04, 0.80, and 0.62 per 100,000 individuals, respectively. A notable sex-related difference in mortality rates was evident, with male mortalities (8,319) surpassing female mortalities (6,249) by a factor of 1.33. Age-wise, mortality rates tended to increase after 55 years, reaching a maximum in those over 85 years (7.09 per 100,000 individuals). Provincial data revealed that the highest ASMRCs were in Zhejiang, Beijing, and Jiangxi, whereas the lowest were in Tibet, Qinghai, and Hainan. The period from 2013 to 2020 exhibited a significant increase of 58.09 % in MM mortality, with urban and rural areas exhibiting a 44.97 % and 70.94 % increase, respectively. This analysis highlights the growing mortality burden of MM across various demographics and regions, emphasizing the need for tailored disease management and preventive measures.

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https://doi.org/10.1016/j.heliyon.2024.e32996
Received 20 November 2023; Received in revised form 11 June 2024; Accepted 12 June 2024

1. Background

Multiple myeloma (MM) is a malignant plasma cell neoplasm that predominantly affects older individuals. Data from GLOBOCAN 2020 estimate that MM was responsible for approximately 176,404 new cases and 117,077 deaths globally in 2020, accounting for 0.9 % of all newly diagnosed cancer cases and 1.2 % of all cancer-related mortalities worldwide [1]. An investigation of the disease burden across 40 European nations revealed that, in 2018, MM was responsible for approximately 48,300 new diagnoses and 30,900 mortalities. Thus, MM represents 1.2 % of all new cases and 1.6 % of all deaths attributed to the 25 major cancer types, underscoring the significant impact of MM on the region's oncological landscape [2].

Considerable geographical disparities in MM burden have been reported. A previous report indicated that in 2008, the age-adjusted incidence rate of MM was 3.8 per 100,000 individuals in the United States, compared to that of 1.5 per 100,000 individuals in Japan [3]. Projections for 2021 estimated that the United States would witness 34,920 new cases and 12,410 mortalities attributable to MM [4]. In contrast, Korea is expected to report 2,012 new diagnoses and 1,171 deaths related to MM, reflecting the significant variation in the epidemiology of MM across different regions [5].

In China, MM presents a relatively low disease burden, with an analysis conducted in 2016 indicating 16,500 new cases and 10,300 mortalities [6]. Age-standardized incidence and mortality rates have been reported as 1.03 and 0.67 per 100,000 individuals, respectively [6]. Additionally, an annual increase of 4.5 % in the mortality rates of lymphoma and MM was observed from 2004 to 2016 [7]. Despite these reports and statistics, a notable gap remains in obtaining accurate and up-to-date mortality data for MM at both the national and provincial levels within China. Thus, in this study, we aimed to elucidate the epidemiologic spatiotemporal dynamics of MM mortality across China, endeavoring to fill the existing knowledge gap and contribute to a more comprehensive understanding of MM's impact.

Table 1
Mortality rates of multiple myeloma by sex, region and residence in 2020, China.

Region	location	Sex	Crude rate ($1/10^5$)	ASMRC ($1/10^5$)	ASMRW ($1/10^5$)
All	All	Both	1.04	0.80	0.62
		Male	1.17	0.96	0.73
		Female	0.91	0.66	0.52
	Urban	Both	1.13	0.87	0.67
		Male	1.23	1.02	0.78
		Female	1.03	0.74	0.57
	Rural	Both	0.98	0.75	0.59
		Male	1.12	0.92	0.70
		Female	0.83	0.61	0.49
Eastern China	All	Both	1.14	0.84	0.65
		Male	1.26	1.01	0.77
		Female	1.01	0.69	0.55
	Urban	Both	1.18	0.90	0.69
		Male	1.25	1.05	0.79
		Female	1.10	0.77	0.60
	Rural	Both	1.10	0.79	0.62
		Male	1.27	0.99	0.75
		Female	0.92	0.62	0.50
Central China	All	Both	1.00	0.78	0.61
		Male	1.14	0.94	0.73
		Female	0.84	0.63	0.50
	Urban	Both	1.16	0.89	0.68
		Male	1.29	1.05	0.80
		Female	1.03	0.74	0.57
	Rural	Both	0.92	0.72	0.57
		Male	1.07	0.89	0.69
		Female	0.76	0.58	0.47
Western China	All	Both	0.90	0.74	0.57
		Male	0.99	0.86	0.66
		Female	0.81	0.63	0.49
	Urban	Both	0.99	0.78	0.59
		Male	1.10	0.92	0.71
		Female	0.87	0.65	0.48
	Rural	Both	0.84	0.71	0.55
		Male	0.91	0.81	0.62
		Female	0.77	0.62	0.49

Abbreviation: ASMRC, age-standardized mortality rate adjusted by the Chinese standard population; ASMRW, age-standardized mortality rate adjusted by the Segi's population.

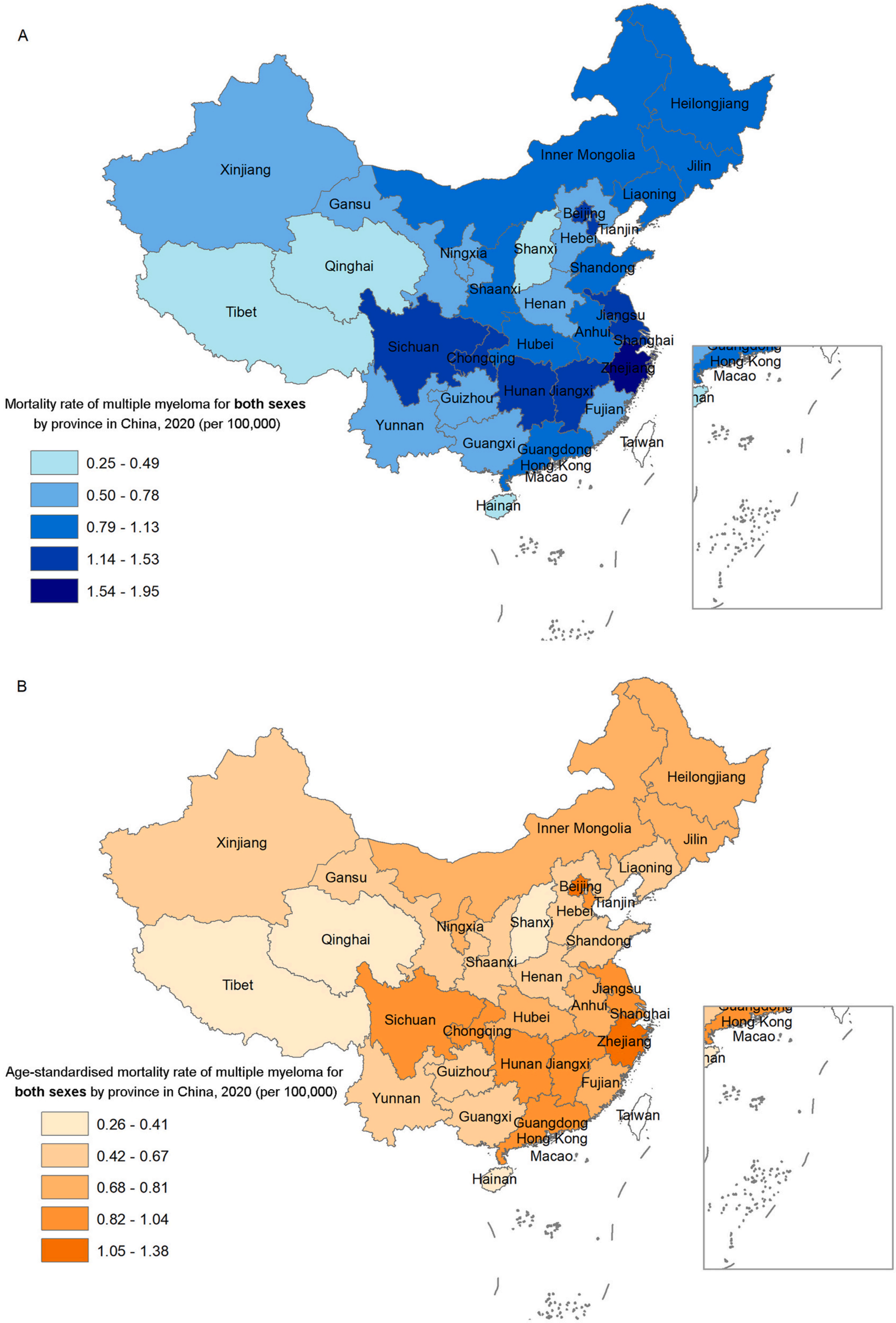

Fig. 1. Mortality rate (panel A) and age-standardised mortality rate (panel B) of multiple myeloma for **both sexes** by province in China, 2020.

2. Methods

Mortality data from 2013 to 2020 were procured from the Chinese Center for Disease Control and Prevention's Disease Surveillance Points system (CDC–DSP). These data were classified according to the International Classification of Diseases-10 under the codes C88–C90.32 (Table SI).

In our analytical framework, we incorporated five pertinent sociodemographic variables: temporal (year), location (urban and rural residence), gender (male and female), age, and regional geography, which were delineated into three broad areas. Age segmentation was meticulously structured into fifteen cohorts, ranging from 0 to 19 years, progressing through two-decade increments up to 20–24 years, 25–29 years, and so forth, culminating in the final age group of individuals aged 85 years and above. This comprehensive approach enabled a detailed exploration of the epidemiological patterns of mortality attributable to MM, underscoring the influence of sociodemographic determinants on disease outcomes.

In this analysis, we employed a suite of summary statistics to quantify the mortality burden of MM, encompassing the crude mortality rate, age-specific mortality rate calculated using population data from the sixth Chinese national census of 2010 (ASMRC), and age-specific mortality rate derived from Segi's world standard population (ASMRW). The crude mortality rate was determined using the annual number of reported deaths per 100,000 individuals. Other relevant metrics were also determined using this methodology. To delve into the epidemiologic details of MM, we analyzed relative mortality rates, scrutinized the variance across age and sex, and identified temporal and spatial trends. The Socio-demographic Index (SDI) is a composite indicator of development status strongly correlated with health outcomes. It is the geometric mean of 0–1 indices of total fertility rate under the age of 25, mean education for those ages 15 and older, and lag distributed income (LDI) per capita. We use SDI to discern geographical disparities at the provincial level, providing a comprehensive perspective to examine the impact of MM across various demographic settings.

Joinpoint regression models are increasingly recognized as potent and dependable methods for delineating temporal trends within surveillance datasets. In our investigation, these models were used to deduce the temporal dynamics of MM incidence from 2013 to 2020. We designated a P-value of less than 0.05 as the threshold for statistical significance. Analyses using joinpoint regression models were conducted using the Joinpoint Regression Program (version 4.9.1.0), while subsequent analytical procedures related to summary statistics were performed using R (version 4.2.1; R Core Team, Vienna, Austria), underscoring our methodological rigor and the integration of sophisticated statistical tools to elucidate the evolving landscape of MM.

3. Results

3.1. *Expected deaths and mortality rate in 2020*

An estimated 14,568 deaths were attributed to multiple MM. As shown in Table I, the crude mortality rate along with the ASMRC and ASMRW were 1.04, 0.80, and 0.62 per 100,000 individuals, respectively. Notably, mortality rates were higher in urban than in rural settings. Furthermore, Eastern and Central China exhibited marginally higher mortality rates than Western China, as detailed in Table 1, illustrating a subtle spatial variation in MM mortality rates across China.

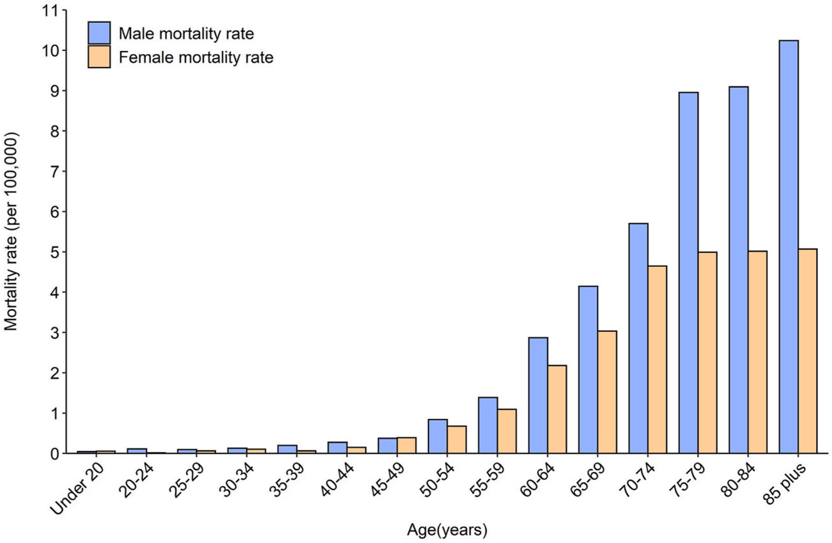

Fig. 2. Mortality rates of multiple myeloma by age groups and sex in 2020.

3.2. Mortality rates stratified by age and sex in 2020

As depicted in Fig. 1, mortality rate remained notably low (<1.00 per 100,000 individuals) in individuals less than 55 years. Subsequent to this age threshold, there was a progressive increase in mortality rates with an increase in age, culminating in a peak rate of 7.09 per 100,000 individuals in individuals aged above 85 years (Table SII).

The age-standardized mortality rate per 100,000 individuals was 0.96 for males and 0.66 for females. Males consistently exhibited elevated mortality rates compared to females across both urban and rural settings, as detailed in Table 1. This disparity extended across nearly all age groups, with the divergence amplifying by approximately 1.5-2-fold in individuals aged above 75 years (Fig. 2). An in-depth analysis of the geographical distribution of MM mortality rates by sex revealed a parallel pattern between males and females across the provinces. Notably, Beijing, Tianjin, Shanghai, Jiangsu, Zhejiang, Sichuan, and Chongqing had higher crude mortality rates. However, when examining age-standardized mortality rates, Zhejiang and Jiangxi emerged with elevated figures (Figs. S1 and S2).

3.3. Mortality rates stratified by province in 2020

Results revealed that provinces characterized by high SDIs exhibited age-standardized mortality rates that surpassed those in provinces with low SDIs (Fig. S3).

The highest crude mortality rates were recorded in Zhejiang (1.95 per 100,000 individuals), Shanghai (1.53 per 100,000

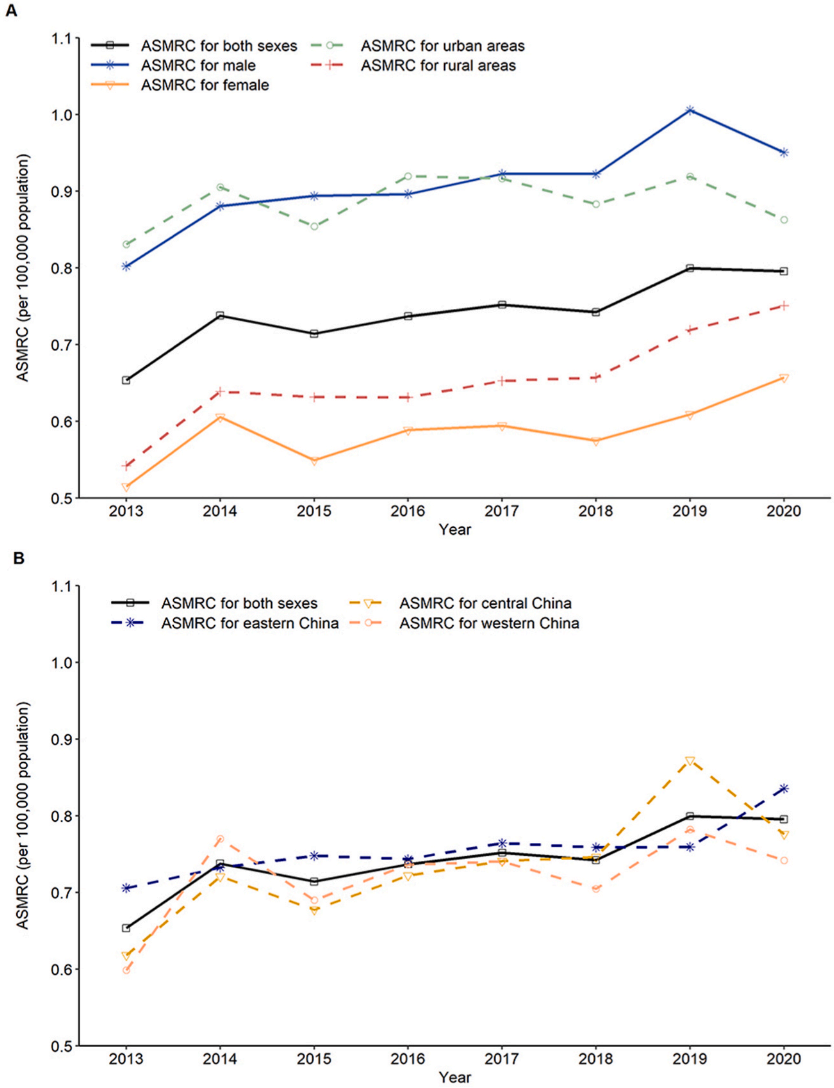

Fig. 3. Trends in ASMRC of multiple myeloma by sex, residence and region in China, 2013 to 2020. Panel A shows the trends in ASMRC of multiple myeloma by sex and residence. Panel B shows the trends in ASMRC of multiple myeloma by region.

individuals), and Beijing (1.49 per 100,000 individuals). In contrast, the lowest crude mortality rates were found in Tibet (0.25 per 100,000 individuals), Qinghai (0.26 per 100,000 individuals), and Hainan (0.33 per 100,000 individuals; Fig. 1A).

Similarly, the highest ASMRC values were recorded in Zhejiang (1.38 per 100,000 individuals), Beijing (1.16 per 100,000 individuals), and Jiangxi (1.04 per 100,000 individuals). Conversely, the lowest ASMRC values were recorded in Tibet (0.26 per 100,000 individuals), Qinghai (0.29 per 100,000 individuals), and Hainan (0.32 per 100,000 individuals; Fig. 1B).

3.4. Changes in mortality rates

Over 13 years (2008–2020), a significant upward trajectory in MM mortality rate was observed. The crude mortality rate escalated from 0.69 per 100,000 individuals in 2008 to 1.04 per 100,000 individuals in 2020, accompanied by an AAPC of 5.3 % with a 95 % confidence interval of 3.9%–6.8 %, underscoring the statistical significance of this increase ($P < 0.001$) as detailed in Table SIII. Upon further disaggregation by residence (urban vs. rural) and geographical region (eastern, central, and western China), similar upward trends were observed. Both residential and regional analyses over the same period revealed a consistent increase in crude mortality rates, marked by a positive AAPC as shown in Tables SIV and SV. Between 2013 and 2020, the ASMRC value for MM increased by 58.09 %, with a more pronounced increase observed in rural areas (70.94 %) than in urban areas (44.97 %), as depicted in Fig. 3A. This trend was consistently evident across the eastern, central, and western regions of China (Fig. 3B). Further, this change was attributed to a combination of three primary factors: population growth (5.13 %), population aging (23.55 %), and age-specific mortality rate increase (29.41 %), as shown in Table II.

4. Discussion

This study provides an updated evaluation of the mortality burden of MM in China. Given the CDC–DSP's coverage of 24.3 % of the total national population, it is possible to determine the mortality characteristics of MM based on age, sex and geography and explore the trends of mortality over time.

Population aging is an important reason for the rising burden of MM because older individuals have a higher disease burden than younger individuals [8]. A study forecasted that new MM cases in patients aged 64–84 will double in the United States (from 12,700 in 2011–2013 to 24,400 in 2032–2034), indicating that approximately three-quarters of new MM cases will be diagnosed in this age group in 2032–2034 [9]. Similarly, a large-scale study involving 56,010 patients with MM in England showed that the proportions of patients aged <64, 65–74, and 75–90 years were 29 %, 30 %, and 41 %, respectively [10]. Moreover, increasing age is correlated with poorer prognosis, attributed to factors such as diminished performance status, comorbidities, and therapy-induced toxicities [11,12]. A study involving 3,807 patients with MM aged 65 years found that mortality was related to frailty [13]. The median overall survival rates were 38.4, 27.1, 15.6, 8.4,and 9.5 months for non-frail, mildly, moderately, and severely frail patients, respectively. Additionally, moderately and severely frail patients had a 2-fold higher risk of death than non-frail patients. A study that included Swedish cancer

Table 2
Decomposition of changes in multiple myeloma deaths from 2013 to 2020 by sex and residence.

	Both sexes	Male	Female
All			
Observed number of people in 2013	2221	1330	891
Number expected with 2020 population, 2013 population age structure, and 2013 deaths	2335	1393	940
Number expected with 2020 population, 2020 population age structure, and 2013 deaths	2858	1688	1164
Observed number of people in 2020	3511	2002	1509
Percentage change from 2013 due to population growth	5.13	4.73	5.54
Percentage change from 2013 due to population ageing	23.55	22.17	25.09
Percentage change from 2013 due to change in age-specific mortality rate	29.41	23.60	38.77
Observed percentage change from 2013 to 2020	58.09	50.51	69.40
Urban areas			
Observed number of people in 2013	1099	648	451
Number expected with 2020 population, 2013 population age structure, and 2013 deaths	1233	728	506
Number expected with 2020 population, 2020 population age structure, and 2013 deaths	1522	894	627
Observed number of people in 2020	1593	884	709
Percentage change from 2013 due to population growth	12.23	12.31	12.15
Percentage change from 2013 due to population ageing	26.27	25.66	26.80
Percentage change from 2013 due to change in age-specific mortality rate	6.48	−1.47	18.17
Observed percentage change from 2013 to 2020	44.97	36.50	57.12
Rural areas			
Observed number of people in 2013	1122	682	440
Number expected with 2020 population, 2013 population age structure, and 2013 deaths	1129	682	446
Number expected with 2020 population, 2020 population age structure, and 2013 deaths	1364	812	548
Observed number of people in 2020	1918	1118	801
Percentage change from 2013 due to population growth	0.56	−0.12	1.28
Percentage change from 2013 due to population ageing	21.02	19.18	23.33
Percentage change from 2013 due to change in age-specific mortality rate	49.36	44.76	57.39
Observed percentage change from 2013 to 2020	70.94	63.82	82.00

data from 1967 to 2016 demonstrated that the estimated annual percent change in MM mortality in men and women decreased by 95 % and 109 % in the age groups of 0–69 years, by 53 % and 37 % in the age groups of 70–79 years, and by 52 % and 13 % in the age group of 80–85 years and above, respectively [14]. In the present study, significantly higher mortality rates of MM were observed in patients aged >55 years, with a peak occurring after 85 years. These findings underscore the marked age-associated mortality trend and highlight the importance of age-specific strategies for disease management and prevention, particularly in older individuals.

In addition to age, many other risk factors for MM have been explored. A pooled analysis of an Asian cohort of 805,309 participants evaluated the risk factors for MM and found that MM mortality was associated with body mass index (BMI) rather than smoking or alcohol consumption [15]. In this study, the risk of MM mortality increased 1.17-fold in those with a BMI of 25.0–29.9 kg/m^2 and increased 1.61-fold in those with a BMI of ≥30 kg/m^2 compared with those with a BMI of 18.5–24.9 kg/m^2. In contrast, the prevalence of obesity in adults doubled in China (8.34 % in 1997 vs. 17.74 % in 2011), with an increase in central obesity from 6.52 % in 1997 to 16.79 % in 2011 [16]. Factors such as the proliferation of fast–food establishments and adoption of a Western lifestyle have been suggested as factors contributing to the burgeoning obesity rates [17]. Thus, the association between MM and other risk factors such as occupational exposure and dietary structure should be explored in future studies [18,19]. Together, these insights support the formulation of a systemic model to assess the MM mortality risk encompassing a broad spectrum of risk factors.

Geographical disparities play a pivotal role in determining the mortality burden in patients with MM. Research conducted in the United States from to 2012–2016 revealed that the mortality rates of MM in metropolitan areas (4.79 per 100,000 individuals) were comparable to those in non-metropolitan regions (4.82 per 100,000 individuals) [20]. In contrast, in China, more developed provinces such as Zhejiang have reported the highest MM mortality rates, whereas less developed regions such as Hainan have reported the lowest mortality rates [6]. Furthermore, urban locales demonstrated elevated mortality rates compared to their rural counterparts [7]. These geographical disparities in China necessitate a deeper investigation to discern the underlying causes and factors. For instance, the SDI may have a significant influence on MM mortality. Consistent with prior studies, Zhejiang, a province with a high SDI, recorded the highest ASMRC, in stark contrast to Tibet, where a low SDI corresponds with a mortality rate nearly five times lower than that of Zhejiang. Moreover, developed provinces or urban areas, characterized by a higher proportion of elderly individuals and more pronounced aging trends, could inherently increase MM incidence and mortality rates. Additionally, these areas might report elevated mortality rates due to superior medical resources and higher patient density, which might not accurately reflect the actual disease burden. Therefore, a mere comparison of numerical data without consideration of these complex factors could result in misunderstandings. Finally, the varied pattern of MM mortality at the provincial level might also be associated with disparities in medical insurance coverage. Less developed regions and rural areas often have lower medical insurance coverage, leading to many patients being unable to afford the costs of diagnosis and treatment, which could cause MM to remain undiagnosed.

Despite the classification of MM as an incurable disease, advancements in modern therapeutic approaches have notably enhanced survival outcomes [21–23]. A population-based study showed that the annual percent change in mortality rates of MM was −2.5 % after 2005 in Japan and −2.0 % after 2002 in the United States, consistent with the introduction of novel agents in both countries [24]. Furthermore, an investigation involving 10,524 patients with MM in Norway demonstrated significant improvements in the 5- and 10-year relative survival rates, increasing from 36 % to 18 % during 1982–1987 to 67 % and 44 % during 2013–2017, respectively [25]. This improvement in the survival rates was predominantly observed in younger patients. In Spain, research indicates that the 5-year age-standardized net survival for individuals aged 15−49 years increased from 32.4 % in 1994–2001 to 78.5 % in 2010–2016, whereas for those aged 50−69 years, it increased from 27.5 % to 58.5 %, and for those aged 70 years and above, it marginally increased from 24.8 % to 26.3 % [26]. A comparable trend was reported in a study conducted in the United Kingdom [10]. Consequently, owing to ongoing improvements in therapeutic approaches, the annual mortality rate for MM might demonstrate a declining trend. Nonetheless, the degree of these survival gains seems to be associated with the age at diagnosis, warranting further investigation into the underlying causes in future research efforts.

Similar to that of other major cancers, the disease burden of MM differs between Eastern and Western countries. For example, the Global Burden of Disease Study (GBD) 2019 showed an approximately 6-fold difference in the incidence and mortality rates between the United States and China [27]. The age-standardized incidence and mortality rates per 100,000 individuals were 1.32 and 0.94 in China and 8.25 and 5.47 in the United States, respectively, in 2019. In the present study, the ASMRW of MM was 0.62 per 100,000 individuals in China in 2020, which was similar to that in the statistics of GLOBOCAN 2020 (0.69 per 100,000 individuals), however, lower than that reported by GBD 2019 [6,27]. Consequently, these observations suggest a pressing need for refining the methodologies employed in the evaluation of disease burden, particularly for conditions such as MM, which are characterized by relatively low mortality rates.

The findings of this study have a few interpretative limitations. Firstly, there is a potential underestimation of cancer mortality across provinces due to underreporting, compounded by estimations derived from a 24 % surveillance population. To mitigate this underreporting bias, we provided adjusted mortality rates based on periodic underreporting surveys. Additionally, the lack of distribution of data on cancer staging and classification, treatment status, and risk factors such as BMI, smoking, and occupational exposures prevents an adequate discussion and explanation of cross-regional differences in mortality.

5. Conclusions

In the present study, using nationally representative datasets, we delineated the mortality characteristics attributable to MM in China. Older individuals had a higher mortality burden of MM than younger individuals, whereas males had a higher mortality burden than females. Geographical differences were observed across the provinces. Notably, the ASMRC of MM showed an upward trend, with an increase of 58.09 % from 2013 to 2020. Together, these insights hold potential value for informing and tailoring disease control and prevention strategies to address the multifaceted impact of MM.

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. The Ethical Review Board of National Center for Chronic and Noncommunicable Disease Control and Prevention, Beijing, China (Project No. 2022–19) approved the study protocol, and the requirement for informed consent was waived owing to the retrospective nature of the study.

Consent for publication

Not applicable.

Funding

The current study was supported by the grants from National Natural Science Foundation of China (No. 81974361, 82272768) and Beijing Xisike Clinical Oncology Research Foundation (Grant No. Y-HS202202-0104, Y-Young 2023-0286).

Data availability statement

The data that support the findings of this study are available from the Chinese Center for Disease Control and Prevention, but restrictions apply to the availability of these data, which were used under license for the current study, and, thus, are not publicly available. However, data are available from the authors upon reasonable request and with permission of the Chinese Center for Disease Control and Prevention.

CRediT authorship contribution statement

Xiaosheng Ding: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Xiaoyan Li:** Methodology, Investigation, Formal analysis, Data curation. **Peng Yin:** Validation, Supervision, Software. **Lijun Wang:** Validation, Resources, Project administration. **Jinlei Qi:** Writing – review & editing, Supervision, Conceptualization. **Weiping Liu:** Writing – review & editing, Validation, Supervision, Funding acquisition, Conceptualization.

Declaration of generative AI and AI-assisted technologies in the writing process

The authors declare that generative artificial intelligence (AI) and AI-assisted technologies were not used in the writing process or any other process during the preparation of this manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors thank all of the persons who contributed to the data collection, analysis, vetting, and critical interpretation of the present study.

Abbreviations

ASMRC	age-standardized mortality rate of China
ASMRW	age-standardized mortality rate of Segi's population
BMI	body mass index
CDC–DSP	Chinese Center for Disease Control and Prevention–Disease Surveillance Points system
GBD	Global Burden of Disease Study
MM	multiple myeloma
SDI	socio-demographic index

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32996.

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