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A systematic epidemiological trends analysis study in global burden of multiple myeloma and 29 years forecast

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Multiple myeloma is a prevalent hematologic cancer. This investigation analyzes the latest global, regional, and national data from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021. Data on the incidence, prevalence, disability-adjusted life years, and mortality rates of multiple myeloma, including estimates and 95% uncertainty intervals, were sourced from the 2021 Global Burden of Diseases Study. Furthermore, we explored the trends affecting the multiple myeloma burden from 1990 to 2021, breaking it down by demographic, age, and epidemiological factors. By 2021, the global incidence of multiple myeloma involved 148,754.63 reported cases, with confidence intervals ranging from 131,780.43 to 162,049.23. Worldwide, the number of mortality attributed to multiple myeloma reached 116,359.63, with the confidence interval lying between 103,078.62 and 128,470.57, and an age-standardized mortality rate of 1.37 per 100,000 individuals, the confidence interval for which was 1.22 to 1.52. There was a consistent increase in the incidence, prevalence, and disability-adjusted life years associated with multiple myeloma. Most of the disease burdens were seen in high income countries though its incidence is on the rise in low-income countries. Forecast for the years 2022–2050 showed the further increase in the incidence, prevalence, disability-adjusted life years, and age-standardized death rates of multiple myeloma.

Keywords Global burden of Disease Study, Multiple myeloma, Public health, Mortality

Abbreviations

AAPC	Average Annual Percent Change
ASR	Age-standardized Mortality Rate
APC	Annual Percent Change
CI	Confidence Interval
DALYs	Disability-adjusted Life Years
EAPC	Estimated Annual Percentage Changes
GBD	Global Burden of Diseases
MM	Multiple Myeloma
SDI	Socio-demographic Index

Multiple myeloma is a life threatening hematologic neoplasm that mainly arises from the uncontrolled monoclonal growth of plasma cells in the bone marrow[1]. This disease is defined by the excess production of monoclonal immunoglobulins which in turn suppresses the secretion of normal immunoglobulins[2]. In the last few years, there has been a gradual annual rise in the number of multiple myeloma cases, thus becoming a type of hematologic malignancy that affects more than 10% of the patients[3,4], and is estimated to account for 0.9% of all cancer diagnoses worldwide[5]. There are significant progress in the treatment of multiple myeloma with the use of proteasome inhibitors and immunomodulatory drugs as well as the recent approval of new monoclonal antibodies such as daratumumab. Furthermore, investigational treatments including chimeric antigen receptor T-cells that target the B-cell maturation antigen have been reported to produce significant therapeutic effects and have thus greatly impacted the outcomes of patients affected by this disease[6,7]. Although these improvements

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and the use of better autologous hematopoietic stem cell transplantation techniques have been made, multiple myeloma is still a disease that does not have a cure to this date[8,9].

To this end, this analysis leveraged the information from the 2021 iteration of the Global Burden of Diseases study to evaluate the epidemiology of multiple myeloma by different population groups. This study sought to establish the changing patterns and trends in the distribution of this disease so as to provide a strong foundation for the design of prevention and control measures that could reduce the overall impact of this disease on the health of societies across the globe. The latest data available in the Global Burden of Diseases database had brought about important changes in the global burden of multiple myeloma, and the nature of disease epidemiology. In this systematic review, the authors aimed at providing a comprehensive understanding of the current global burden of multiple myeloma based on factors such as age, country, region, gender and income. Further, this study takes its analysis up to the year 2050 in order to try and predict future developments and issues. This comprehensive literature review would help in enhancing the understanding of the existing methods of managing the burden of multiple myeloma and hence support the better strategies of disease prevention and control.

Materials and methods

The data used in this analysis came from the Global Burden of Diseases 2021 database that covered the period from 1990 to 2021 and was stored at The Institute for Health Metrics and Evaluation. The data set covered 204 countries and used sophisticated methods for data analysis like Spatiotemporal Gaussian process regression and Bayesian Meta-Regression with prior distributions to handle the data discrepancies[10,11]. This study identified some important measures of multiple myeloma such as incidence, prevalence, disability-adjusted life years, mortality and socio-demographic index. The socio-demographic index measured factors such as income, education, and fertility rate to divide the countries into five different quintile of sociodemographic with development index.

For this purpose, we applied the estimated annual percentage changes to systematically estimate the overall change in the burden of multiple myeloma. Standardization was a requirement for comparing outcomes across different populations that could be characterized by different age distributions or within the same population where age distribution changed with time. Hence, the estimated annual percentage changes applied to the age-standardized mortality rate was considered a more accurate way of assessing changes in the trends of this disease[12]. A linear regression model was formulated, defined by the equation $y=\alpha+\beta x$, where y represented the natural logarithm of the age-standardized mortality rate, and x was the calendar year. Using this model, the estimated annual percentage changes was calculated by the expression $(\exp(\beta) - 1) * 100\%$, with the 95% confidence interval determined accordingly. When both the estimated annual percentage changes and its lower 95% confidence interval boundary surpass zero, an increasing trend in the age-standardized mortality rate was confirmed. Conversely, if the estimated annual percentage changes and the upper boundary of its 95% confidence interval both fell below zero, a decreasing trend in the age-standardized mortality rate was indicated. If these conditions were not met, the age-standardized mortality rate was considered stable, suggesting no significant changes over the observed period.

To better understand the trends and their changes in the multiple myeloma burden, we used join-point regression analysis in our analysis. This approach divided the overall epidemiological pattern at certain turning points and then gave a segmented picture, by which it was possible to examine the changes in the certain time period. A quantitative assessment of each segment trend was calculated by estimating the annual percent change along with its 95% confidence interval for better accuracy[13]. Furthermore, to estimate the average annual percent change and its 95% confidence interval we employed the powerful Monte Carlo permutation test, with a total of 4,499 records and 1,000 permutations. To prevent spurious results, an appropriate Bonferroni correction was employed to enforce the level of significance across all the analyses conducted in this study[14]. It could be stated that there was an upward trend if annual percent change/average annual percent change was statistically significant and the 95% confidence interval lower bound was also positive. On the other hand, a downward trend was suggested if both annual percent change and the upper limit of its 95% confidence interval were negative to indicate a decrease in the burden in that period.

In the detailed analysis of the epidemiological characteristics of multiple myeloma we also aimed at exploring how the incidence of multiple myeloma differs across various age groups, different time periods, and different birth cohorts. In order to better analyze these complex relationships, we employed an enhanced annual percent change model, which included the Intrinsic Estimator method through the use of principal component regression analysis. This advanced statistical methodology enabled a very fine distinction and measurement of the effects in these three temporal domains, which enabled a more accurate measurement of the epidemiological dynamics[15]. The annual percent change model, grounded in the principles of the Poisson distribution, was articulated through the equation[16]: $ln\ (Y_{i,\,j,k}) = \mu+\alpha_i+\beta_j+\gamma_k+\varepsilon_{i,\,j,k}$. Here, $Y_{i,\,j,k}$ represented the incidence or prevalence within the designated demographic segment (i, j, k); μ standed as the model's intercept; α_i, β_j and γ_k respectively denoted the age effect for the i-th age bracket, the period effect for the j-th temporal segment, and the cohort effect for the k-th birth cohort; $\varepsilon_{i,j,k}$ captured any residual deviations within the model. The use of the IE approach in this annual percent change framework enabled one to estimate the coefficients which measured the effects of age, period, and cohort. These coefficients were then exponentiated to give the relative risks, which provided a relative estimate of incidence and prevalence for given age intervals, time intervals, or birth cohorts compared with the overall average across all categories[13].

We embarked on a series of decomposition studies that analyzed the disease burden by gender, while taking into account factors such as fluctuations in population size, variations in age distribution, and shifts in epidemiological patterns[17]. The computation of disability-adjusted life years for various regions was methodically carried out using the following detailed formula: disability-adjusted life $\text{years}_{ay,\,py,\,ey} = \sum_{i=1}^{n} a_{i,\,y} {}^{*} p_y {}^{*} e_{i,\,y}$. Here, disability-adjusted life $\text{years}_{ay,\,py,\,ey}$ symbolized the aggregate disability-adjusted life years for a given year y,

incorporating considerations of age structure, overall population size, and the specific disability-adjusted life years rate for that year. In this formula, $a_{i,y}$ indicated the proportion of the population within each age category i among n total age categories for that year; py signified the total population for that year; $e_{i,y}$ represented the disability-adjusted life years rate applicable to each age category i during that year. We rigorously determined the impact of each demographic factor on the disability-adjusted life years variation between the years 1990 and 2021 by isolating the effect of a single variable change while keeping the others constant, thereby providing a precise measure of how individual factors influenced the overall disease burden over time.

The systematic monitoring of health inequalities was essential for crafting evidence-based health policies that significantly enhanced the effectiveness of targeted interventions aimed at mitigating disparities in health outcomes. In this comprehensive study, we applied two widely recognized measures of inequality: the slope index of inequality and the concentration index, to meticulously analyze the distributional variations in the burden of multiple myeloma across different countries. The slope index of inequality ranked the countries according to their relative sociodemographic status and calculates the differences between the observed and expected disability-adjusted life years rate for all ages through a regression model of the national rates. This relative position was measured by the median point of the socio-demographic index range, which was rather wide and encompasses a rather wide range of population features. For overcoming the possible confounding and to provide a more detailed view of the disparities, a weighted regression model was applied. In addition, the concentration index was estimated using the numerical integration of the area under the Lorenz curve with a lot of precision. This curve was linked with the cumulative disability-adjusted life years and sorts population by their socio-demographic index to present a more detailed picture of the health inequality in relation with the socioeconomic status.

Thus, to support the strategic planning of public health policies and efficient utilization of health care resources, forecasting of the burden of multiple myeloma for the following decades was crucial. This projection was made possible through the use of the Bannual percent change model which was improved through the integration of the Integrated Nested Laplace Approximations. This advanced model was acclaimed for its enhanced precision and wider applicability compared with the annual percent change model and was applied to quantify the global burden of multiple myeloma up to the year 2050[18]. The utilization of Integrated Nested Laplace approximation method within the Bayesian age-period-cohort framework enabled the generation of accurate estimates of marginal posterior densities, thus avoiding the common problems of slow mixing and convergence that are associated with Markov Chain Monte Carlo sampling techniques usually employed in the conventional Bayesian analysis.

For the analysis of this study, various software packages used in order to provide a variety of statistical tests and data visualization tools; these included R version 4.3.1, SPSS version 24.0, Origin 2022, and GraphPad Prism version 10.1.2. This research adhered to the principles for the protection of human subjects enshrined in the Declaration of Helsinki[19] and did not involve any risks or potential harm to the human subjects and had no commercial interest, therefore, making it exempt from institutional review board approval.

Results

Descriptive analysis of multiple myeloma burden at global, regional, and national levels

As of the close of 2021, the global incidence of multiple myeloma reached a total of 148,754.63 documented cases, with statistical confidence intervals spanning from 131,780.43 to 162,049.23. This patient population comprised 716,384.28 male patients (95%confidence interval: 627,210.28 to 812,563.63) and 630,636.26 female patients (95% confidence interval: 551,814.92 to 723,125.83), indicating a significant demographic spread. Notably, the highest frequency of incidence was recorded among individuals aged between 90 and 94 years (Figure S1, Figure S2, Table S1). Over the span from 1990 to 2021, there was a marked increase in both the raw numbers and the crude rates of incidence, prevalence, and disability-adjusted life years across the globe. Despite this general upward trend, the age-standardized mortality rate of incidence, prevalence, and disability-adjusted life years displayed a declining trajectory. The rates among male patients were consistently higher compared to their female counterparts, a disparity highlighted in Figure S3. Comprehensive data detailing the incidence, prevalence, and age-standardized mortality rate of multiple myeloma and disability-adjusted life years for the years 1990 and 2021 were systematically laid out in Tables S2, S3 and S4. On a regional basis, Western Europe exhibited the highest statistics for incidence, prevalence, and disability-adjusted life years of multiple myeloma, while East Asia reported the highest age-standardized mortality rate for these parameters, as documented in Tables S2, S3 and S4. Regarding the socio-demographic index quintile as of 2021, regions classified within the highest socio-demographic index quintile recorded the greatest numbers in terms of incidence, prevalence, and disability-adjusted life years, with these figures escalating alongside increased in income levels. High socio-demographic index nations consistently demonstrated the most elevated age-standardized mortality rate values for incidence, prevalence, and disability-adjusted life years, as detailed across Tables S2, S3 and S4.

Additionally, the distribution of incidence, prevalence, and disability-adjusted life years for multiple myeloma showed considerable variability across different countries. Specifically, the United States had the highest reported number of new diagnoses of multiple myeloma, whereas China led in both the prevalence and the total disability-adjusted life years attributed to this condition. Furthermore, Monaco, New Zealand, and again Monaco were identified as having the highest age-standardized mortality rate for incidence, prevalence, and disability-adjusted life years respectively. These findings were detailed in Fig. 1and Tables S5, S6, and S7, providing a clear depiction of the geographical disparities in multiple myeloma burden.

Analysis on multiple myeloma mortality

By the year 2021, the global mortality statistics reported that 116,359.63 individuals (95% confidence interval: 103,078.62 to 128,470.57) had succumbed to multiple myeloma, with an age-standardized mortality rate of 1.37

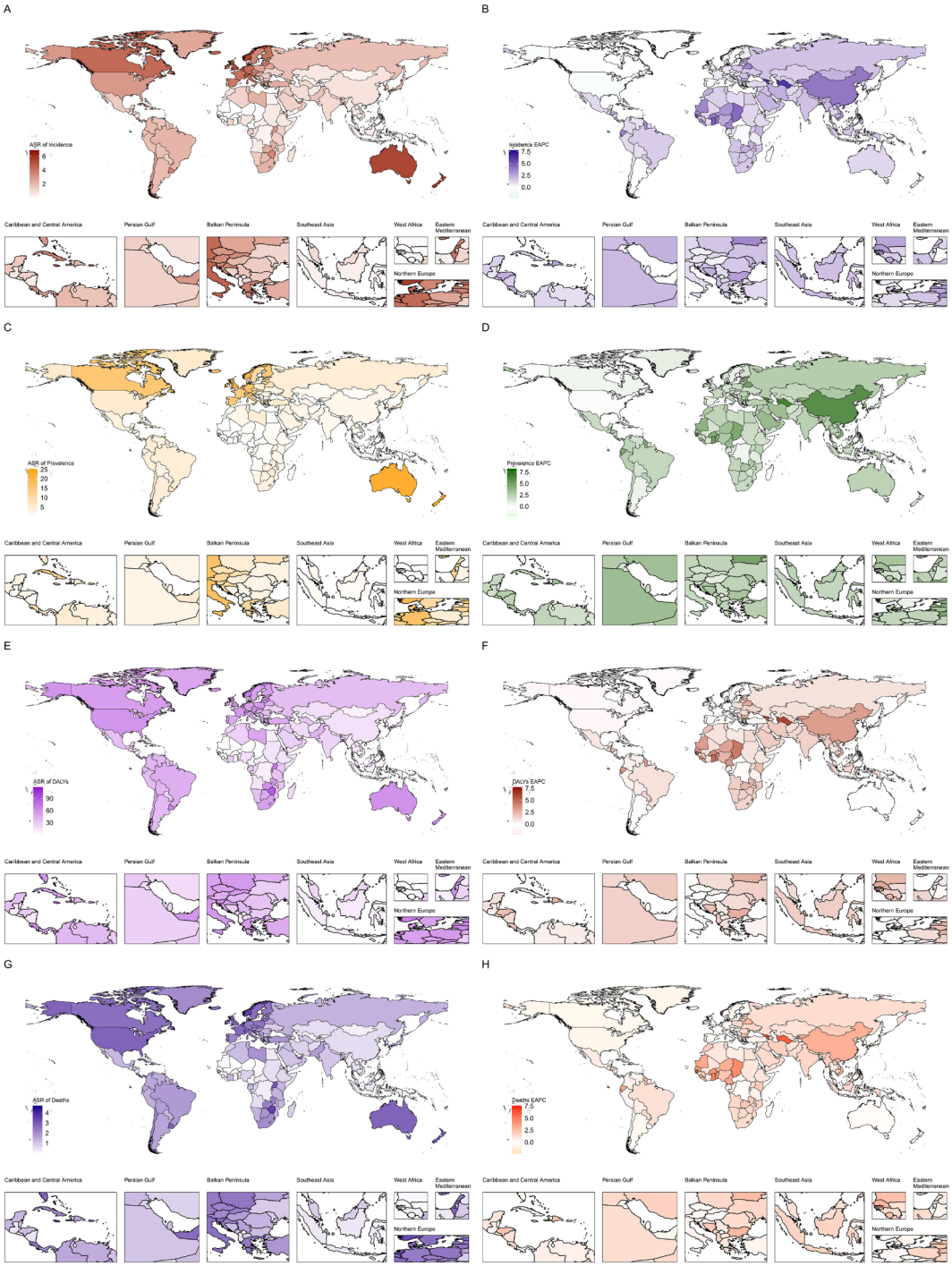

Fig. 1. (**A**) The age-standardized mortality rate of incidence in 2021; (**B**) The trend in age-standardized mortality rate of incidence (estimated annual percentage changes) from 1990 to 2021; (**C**) The age-standardized mortality rate of prevalence in 2021; (**D**) The trend in age-standardized mortality rate of prevalence (estimated annual percentage changes) from 1990 to 2021; (**E**) The age-standardized mortality rate of disability-adjusted life years in 2021; (**F**) The trend in age-standardized mortality rate of disability-adjusted life years (estimated annual percentage changes) from 1990 to 2021; (**G**) The age-standardized mortality rate of mortality in 2021; (**H**) The trend in age-standardized mortality rate of mortality (estimated annual percentage changes) from 1990 to 2021; of multiple myeloma globally.

deaths per 100,000 population (95% confidence interval: 1.22 to 1.52). Over the period from 1990 to 2021, the estimated annual percentage changes for multiple myeloma mortality was calculated at 0.09% (95% confidence interval: -0.01–0.18%), indicating a subtle yet discernible trend in global mortality rates (Table S8, Table S9, Fig. 1).

Within different socio-demographic index levels, the highest age-standardized mortality rate were observed in countries with high socio-demographic index, while the most significant estimated annual percentage changes was noted in countries with a middle socio-demographic index. Regionally, Western Europe reported the highest numbers and the top age-standardized mortality rate values, whereas East Asia recorded the greatest estimated annual percentage changes. At the national level, the United States reported the highest number of cases. Zimbabwe registered the highest age-standardized mortality rate, and Georgia exhibited the most pronounced estimated annual percentage changes (Table S9).

Data revealed that the age bracket of 70–74 years recorded the highest mortality globally for both sexes. This pattern prevailed across regions with varying socio-demographic index levels. Specifically, the principal age at death in territories with high-middle and low-middle socio-demographic index was similarly recorded in the 70–74 year range. In stark contrast, the peak mortality age ascended to 80–84 years within high socio-demographic index locales, reflecting advanced healthcare outcomes. Conversely, in regions with middle and low socio-demographic index standings, the maximum death age descended to 65–69 years, underscoring different health resource allocations and disease management efficiencies. Moreover, in regions marked by elevated mortality rates, such as Western Europe, South Asia, affluent parts of North America, and Western Sub-Saharan Africa, female multiple myeloma patients typically had a lower age at death compared to their male counterparts, as illustrated in Fig. 2.

Overall trends in multiple myeloma burden using broad estimation method

Over the period from 1990 to 2021, a detailed analysis of the age-standardized mortality rate revealed notable increased in the incidence, prevalence, and disability-adjusted life years related to multiple myeloma. Specifically, there was a 0.48% rise in incidence (95% confidence interval confidence interval: 0.37–0.6%), a 1.24% increase in prevalence (95% confidence interval: 1.03–1.46%), and a 0.06% growth in disability-adjusted life years (95% confidence interval: -0.04–0.15%), as documented in Tables S2, S3 and S4. The regional assessment indicated that East Asia experienced the most significant escalations in age-standardized mortality rate across these metrics, with incidence climbing by 3.88% (95% confidence interval: 3.25–4.51%), prevalence by 5.63% (95% confidence interval: 5.08–6.18%), and disability-adjusted life years by 3.03% (95% confidence interval: 2.38–3.67%), as shown in the respective tables. At a country-specific level, the distribution and trends in multiple myeloma disease burden exhibited substantial variations among 204 countries and territories, as depicted in Fig. 1. The highest estimated annual percentage changes in incidence were recorded in Georgia, while Turkmenistan observed the highest estimated annual percentage changes for both prevalence and disability-adjusted life years, as listed in Supplementary Tables S5, S6, and S9. Additionally, middle socio-demographic index countries demonstrated the highest estimated annual percentage changes in incidence, prevalence, and disability-adjusted life years across all measured indices, according to data from Tables S2, S3 and S4.

Local trends in multiple myeloma burden using join-point regression analysis

Figure S4 illustrated the outcomes of the join-point regression analysis concerning the burden of multiple myeloma over the period from 1990 to 2021. During these years, incidences, prevalence, and disability-adjusted life years of multiple myeloma consistently exhibited a significant ascending pattern. Notably, the most rapid increases were observed between 1992 and 1995, 1992 and 1997, and again between 1992 and 1995, with each metric displaying five join-points as per Table S10.

In terms of age-standardized mortality rate, there was an overall trend of growth in the incidence, prevalence, and disability-adjusted life years of multiple myeloma. The age-standardized mortality rate for incidence specifically showed a slow increase during the periods 1990–1992 and 2006–2017, surged markedly from 1992 to 1995 and 1995–2000, before experiencing a deceleration from 2000 to 2006 and 2017–2021. Prevalence rates followed a similar upward trajectory, with modest rises from 1990 to 1992 and 1998–2017, a sharp increase from 1992 to 1998, and a tapering growth from 2017 to 2021. disability-adjusted life years experienced growth phases from 1990 to 1992, 1992–1995, 1995–2000, and 2008–2018, and then started to show a decline from 2000 to 2008 and 2018–2021, as detailed in Table S6.

Age-period-cohort analysis on multiple myeloma incidence and prevalence

Figure S5, along with supplementary Figures S6 and S7, delineates the findings from an age-period-cohort analysis focusing on the incidence and prevalence of multiple myeloma, with additional breakdowns by gender. Post-adjustment for period and cohort variables, the impact of age on multiple myeloma risk was profoundly significant in determining the patterns of both incidence and prevalence. Specifically, the relative risks for both metrics increased initially, reaching a zenith in individuals within the 85–89 age group, and subsequently demonstrated a decline, as thoroughly documented in Table S11. This peak risk at age 85–89 was consistent across both male and female cohorts, corroborated by data in Table S12. Furthermore, the analysis highlighted substantial period effects on multiple myeloma risk after accounting for age and cohort variations. These effects showed increasing trends in risk for both incidence and prevalence, with the relative risks escalating by factors of 1.537 and 1.541, respectively, from the period extending from 1992 to 2017, culminating in the highest risk observed in the 2017 period, as detailed in Table S11. Subgroup analysis stratified by gender revealed that males consistently exhibited higher risks than females for both incidence and prevalence in the periods of 2002, 2007, 2012, and 2017, as recorded in Table S12. Isolating the effects of age and period further, the analysis underscored the influence of birth cohorts on multiple myeloma risk. It was noted that earlier cohorts faced significantly higher risks for both incidence and prevalence compared to later cohorts, with relative risks decreasing steadily from cohorts beginning in 1897 up to those in 2017, indicating a notable trend across the decades.

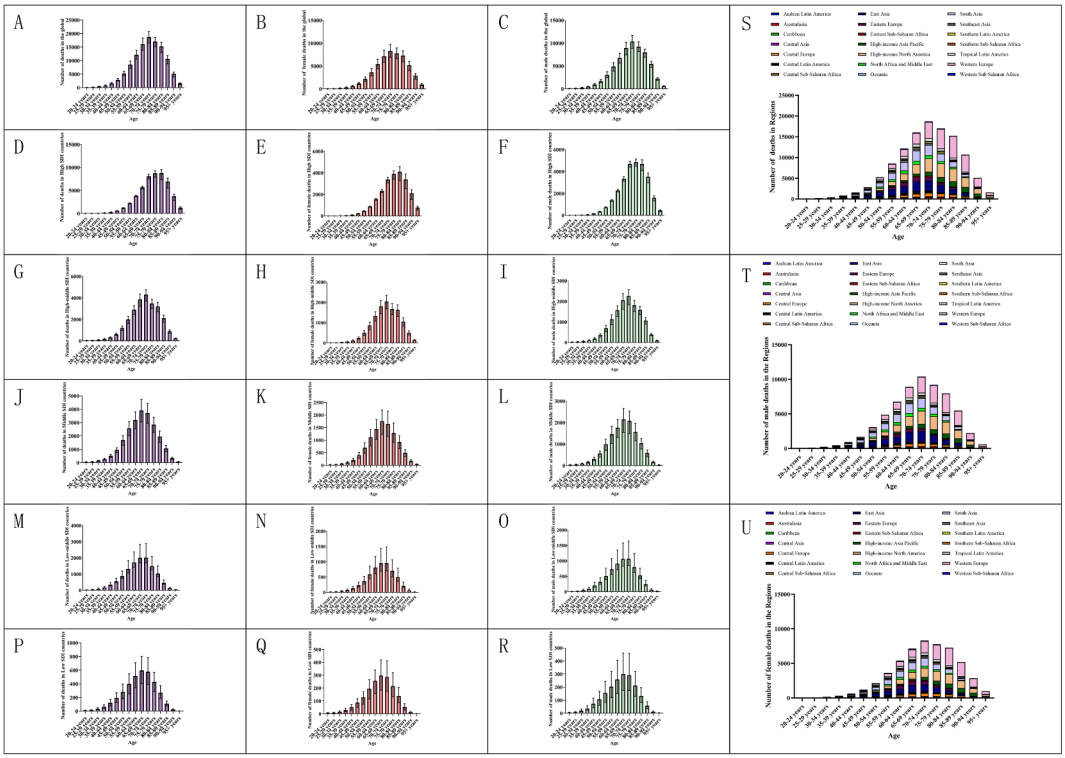

Fig. 2. (**A**) The number of deaths of multiple myeloma worldwide in 2021; (**B**) The number of female deaths of multiple myeloma worldwide in 2021; (**C**) The number of male deaths of multiple myeloma worldwide in 2021; (**D**) The number of deaths of multiple myeloma in High socio-demographic index countries worldwide in 2021; (**E**) The number of female deaths of multiple myeloma in High socio-demographic index countries worldwide in 2021; (**F**) The number of male deaths of multiple myeloma in High socio-demographic index countries worldwide in 2021; (**G**) The number of deaths of multiple myeloma in High-middle socio-demographic index countries worldwide in 2021; (**H**) The number of female deaths of multiple myeloma in High-middle socio-demographic index countries worldwide in 2021; (**I**) The number of male deaths of multiple myeloma in High-middle socio-demographic index countries worldwide in 2021; (**J**) The number of deaths of multiple myeloma in Middle socio-demographic index countries worldwide in 2021; (**K**) The number of female deaths of multiple myeloma in Middle socio-demographic index countries worldwide in 2021; (**L**) The number of male deaths of multiple myeloma in Middle socio-demographic index countries worldwide in 2021; (**M**) The number of deaths of multiple myeloma in Low-middle socio-demographic index countries worldwide in 2021; (**N**) The number of female deaths of multiple myeloma in Low-middle socio-demographic index countries worldwide in 2021; (**O**) The number of male deaths of multiple myeloma in Low-middle socio-demographic index countries worldwide in 2021; (**P**) The number of deaths of multiple myeloma in Low socio-demographic index countries worldwide in 2021; (**Q**) The number of female deaths of multiple myeloma in Low socio-demographic index countries worldwide in 2021; (**R**) The number of male deaths of multiple myeloma in Low socio-demographic index countries worldwide in 2021; (**S**) The number of deaths of multiple myeloma in regions worldwide in 2021; (**T**) The number of female deaths of multiple myeloma in regions worldwide in 2021; (**U**) The number of male deaths of multiple myeloma in regions worldwide in 2021.

Decomposition analysis on multiple myeloma disability-adjusted life years

Figure 3 revealed a substantial increase in the global burden of multiple myeloma as measured by disability-adjusted life years over the past 32 years, with countries classified under the Middle socio-demographic index experiencing the most significant rises. An in-depth analysis of the factors driving this increase indicated that aging accounts for 29.95% of the global upsurge in disability-adjusted life years, population growth contributes 63.44%, and epidemiological changes were responsible for 6.61%, as detailed in Table S13. Furthermore, a gender-specific analysis showed that the disease burden was considerably higher among men than women. The impact of population growth was particularly pronounced on women's disability-adjusted life years. Countries with a Low socio-demographic index were predominantly affected by demographic factors, while those in the High socio-demographic index bracket were more influenced by aging and epidemiological shifts, highlighting differing vulnerabilities based on socio-economic environments.

Cross-country inequality analysis

Figure 4 illustrated a significant and expanding disparity in the burden of multiple myeloma associated with different levels of the socio-demographic index over time. This analysis revealed that the distribution of disability-adjusted life years was increasingly concentrated in nations with higher sociodemographic development. In

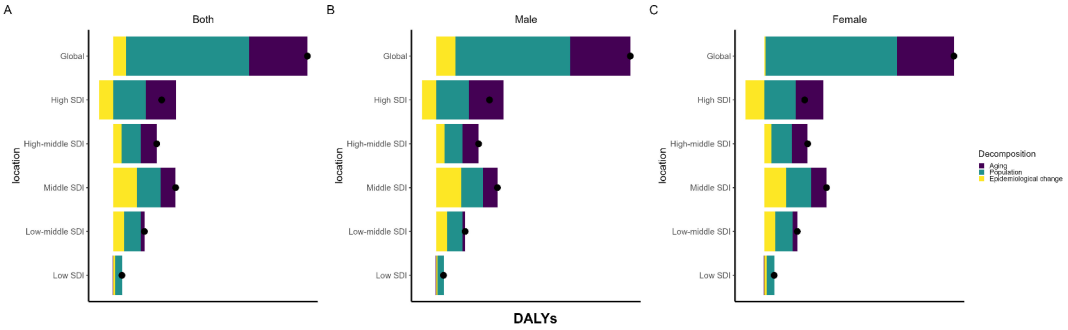

Fig. 3. Changes in disability-adjusted life years of multiple myeloma according to aging, population growth and epidemiological change from 1990 to 2021 at global level by socio-demographic index quintile and by subgroups of sexes. The black dot denotes the overall value of the change resulting from all three components. For each component, the magnitude of a positive value suggests a corresponding increase in multiple myeloma disability-adjusted life years attributed to the component; the magnitude of a negative value suggests a corresponding decrease in multiple myeloma disability-adjusted life years attributed to the component.

1990, the slope index of inequality indicated a substantial excess of 47.22 disability-adjusted life years per 100,000 people between the highest and lowest socio-demographic index countries (95% confidence interval: 38.27 to 56.16). This gap widened significantly by 2021, with the excess increasing to 86.69 disability-adjusted life years per 100,000 people (95% confidence interval: 75.20 to 98.17). Moreover, the concentration index, which measured the relative inequality across countries, showed a decrease from 0.53 (95% confidence interval: 0.45 to 0.60) in 1990 to 0.38 (95% confidence interval: 0.33 to 0.43) in 2021, indicating a less equitable distribution of multiple myeloma burden across nations with varying socio-demographic index levels. The observed trends suggested an intensifying concentration of health disparities in higher socio-demographic index regions, reflecting broader global health inequities.

Predictive analysis on multiple myeloma burden to 2050

Figure 5 presented projections for the numbers and age-standardized mortality rate of incidence, prevalence, disability-adjusted life years, and deaths from multiple myeloma extending up to the year 2050. The forecast showed that both the absolute case numbers and the age-standardized mortality rate for these metrics would experience a consistent annual rise through the forecast period. The specific figures for these projections, encompassing case numbers and age-standardized mortality rate for incidence, prevalence, disability-adjusted life years, and mortality rates, were meticulously catalogued in Table S14.

Discussion

This investigation updated the statistics on multiple myeloma from 1990 to 2021, assessing incidence, prevalence, disability-adjusted life years, and mortality rates across various global, regional, economic, and national contexts. It also introduced a robust evaluation methodology that integrates trend analysis, decomposition analysis, inequality analysis, and predictive modeling to offer a comprehensive view of multiple myeloma's impact. By the close of 2021, the total number of multiple myeloma cases globally was estimated at 148,754.63 (95% confidence interval: 131,780.43 to 162,049.23), with males comprising 716,384.28 of these cases (95% confidence interval: 627,210.28 to 812,563.63) and females accounting for 630,636.26 (95% confidence interval: 551,814.92 to 723,125.83). The incidence rate in males was significantly higher than in females, approximately 1.5 times greater[20–22], a disparity that may be influenced by gender-specific health risk behaviors such as smoking and alcohol consumption, genetic susceptibility as well as a higher prevalence of obesity among males. However, the direct correlation of these risk factors with multiple myeloma remained unconfirmed. Notably, the United States and China, being the largest and second largest economies respectively, were experiencing the most substantial burdens of multiple myeloma worldwide[23]. In China, the rates of increase in incidence, prevalence, and disability-adjusted life years remained high, indicative of an ongoing health challenge, whereas these rates were observed to be declining in the United States, suggesting effective interventions or changes in population health dynamics.

The mortality rate of multiple myeloma, notably high, had consistently raised concerns regarding healthcare outcomes[24]. In regions with higher economic status, the incidence and corresponding mortality figures were significantly elevated, with Western Europe, a cluster of developed nations, experiencing the highest fatalities. The examination methods in the economically developed areas were more advanced and the diagnosis rate is higher. In addition, the lifestyle, work pressure, industrial environmental pollution, genetic susceptibility and other adverse conditions in economically developed areas would greatly increase its morbidity and mortality. This statistic should be of concern especially in the light of inequalities in the availability of health care across the globe. In the same manner, the estimated annual percentage changes of multiple myeloma mortality rates in East Asia remained the highest across the globe, with Turkmenistan being the main reason for this. This case points to the importance of the need to build up the health care system and implement interventions to combat this disease in Turkmenistan.

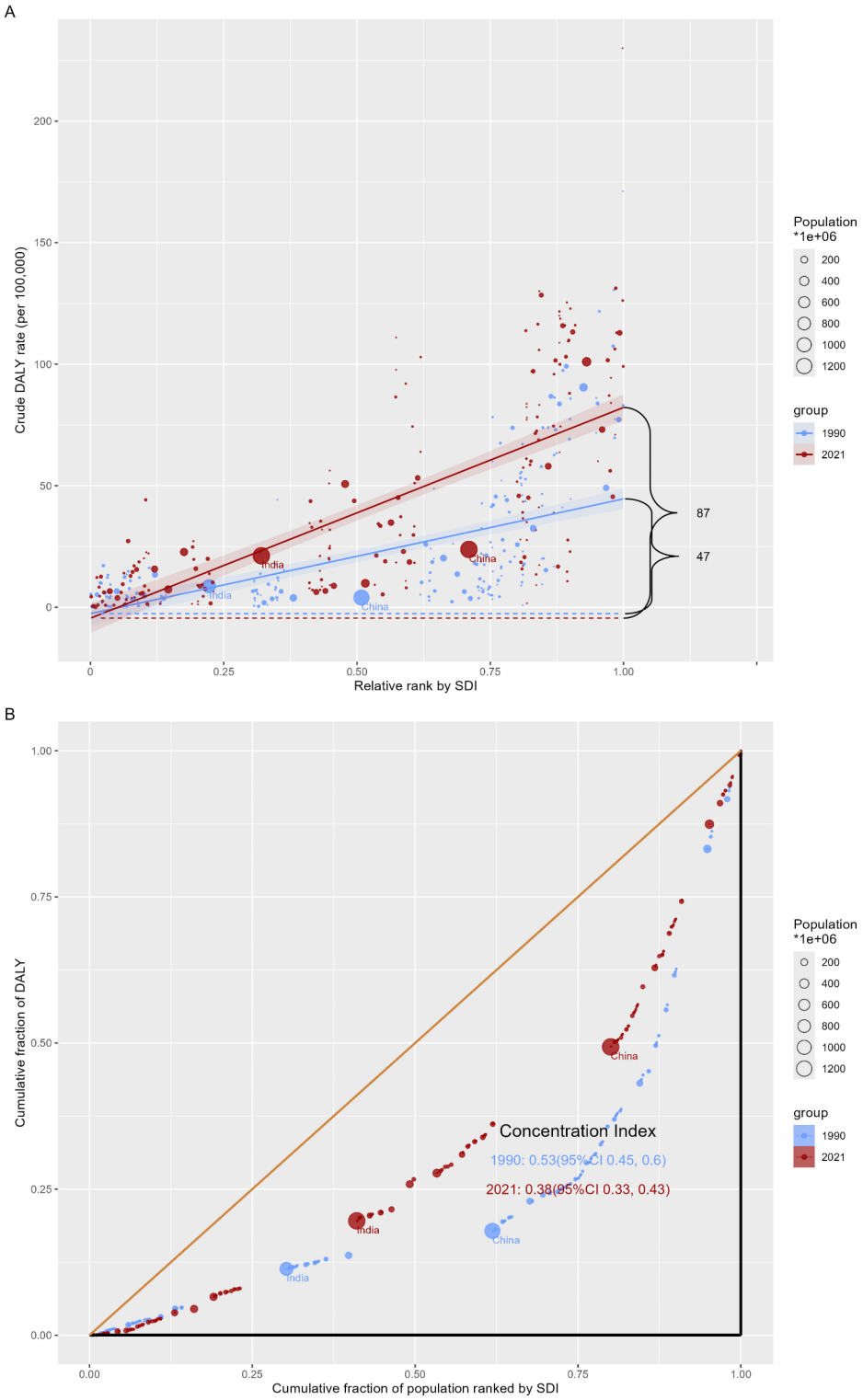

Fig. 4. Socio-demographic index-related health inequality regression (**A**) and concentration (**B**) curves for the disability-adjusted life years of VID globally, 1990 and 2021.

The current research also showed that the death rate among male patients with multiple myeloma was higher than that of female patients, which was in conformity with the trends of gender differences in the onset of the disease. The study further showed that the mortality rates for both males and females was generally highest in the 70–74 age group which was relatively younger than the age group most likely to develop multiple myeloma. Also, a clear pattern was observed that the mean age of death of multiple myeloma patients was reducing with the diminishing of socio-economic status. In high income countries, multiple myeloma patients especially males

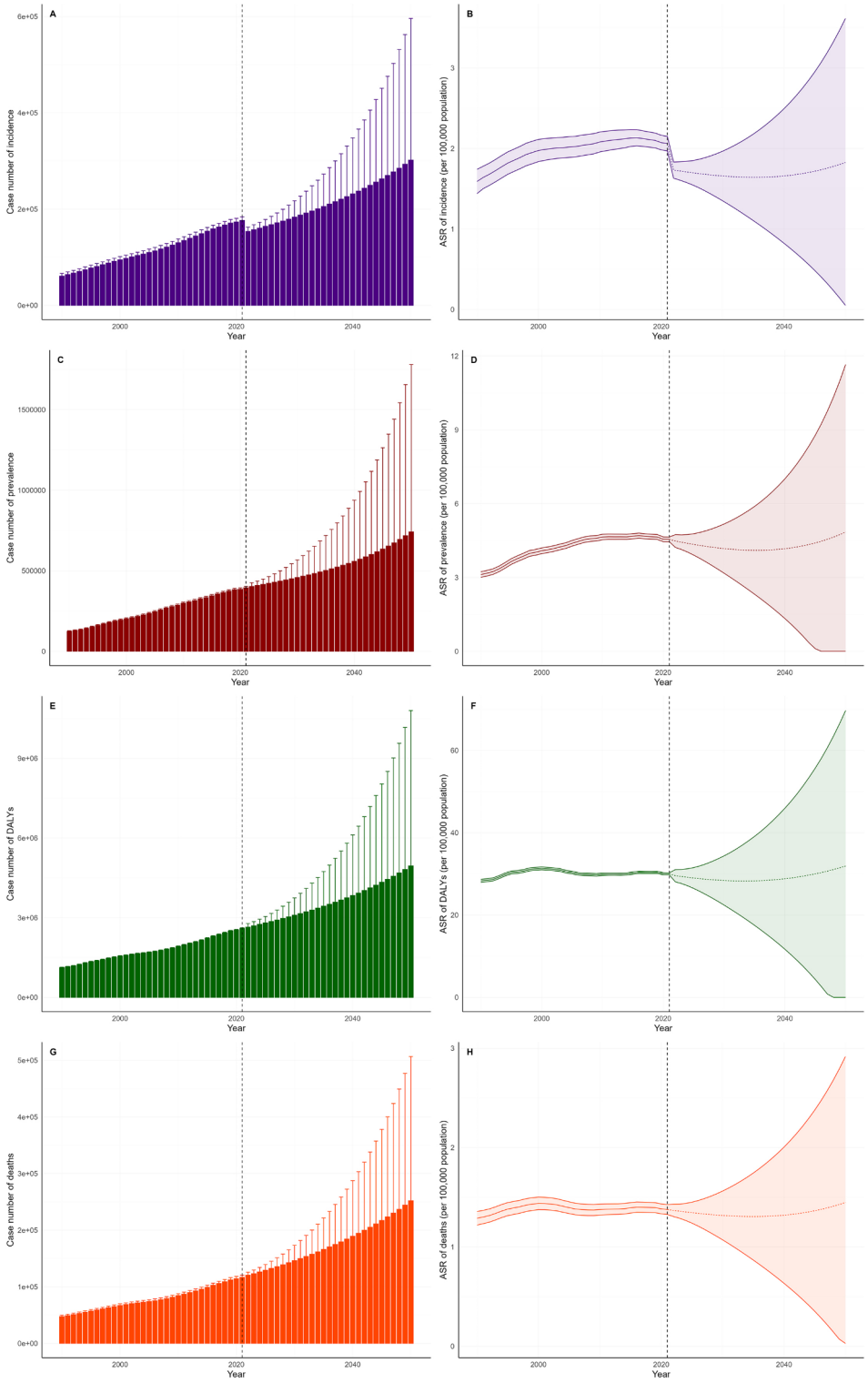

Fig. 5. (**A**) The predicted case number of incidence to 2050; (**B**) The predicted age-standardized mortality rate of incidence from 2050; (**C**) The predicted case amount of prevalence to 2050; (**D**) The predicted age-standardized mortality rate of prevalence to 2050; (**E**) The predicted case number of disability-adjusted life years to 2050; (**F**) The predicted age-standardized mortality rate of disability-adjusted life years to 2050; (**G**) The predicted case number of Deaths to 2050; (**H**) The predicted age-standardized mortality rate of Deaths to 2050 of multiple myeloma worldwide.

had a shorter life expectancy than their female counterparts which underlined the fact that men were at higher risk in regions where the disease burden was high.

Decomposition analysis revealed that population growth was the major determinant of increased multiple myeloma burden. The trends depicted by this pattern indicate that multiple myeloma was more likely to occur in crowded areas and regions with high socio-demographic index including the western Europe.

A comprehensive analysis of disparities across countries revealed that nations with a high socio-demographic index encounter a disproportionate share of the burden associated with multiple myeloma. In the year 2021, the global statistics for multiple myeloma included 148,754.63 newly diagnosed cases, 394,481.73 existing cases, and a total of 2,595,594.99 disability-adjusted life years. The highest number of these cases was recorded in Western Europe, whereas the highest age-standardized mortality rate were observed in Australasia. These findings emphasize that the impact of multiple myeloma was notably concentrated in regions with advanced economies. It is critical to address not only the regions currently facing the highest disease burdens but also those where significant increases were documented over the past few decades. Between 1990 and 2021, East Asia saw the most substantial rise in incidence, prevalence, and disability-adjusted life years related to multiple myeloma, drawing significant attention to this region, particularly Turkmenistan, which accounted for a considerable proportion of these increases. Nationally, the United States reported the highest number of new cases, while China had the largest counts of both prevalent cases and disability-adjusted life years, illustrating the influence of population size on MM's burden. India, with the world's largest population, also showed high figures in incidence, prevalence, and disability-adjusted life years, indicating a significant burden of MM[25,26]. Notably, even though high-income countries historically seen higher incidence rates of multiple myeloma, their age-standardized mortality rate were declined over recent decades, whereas middle socio-demographic index countries experienced the highest growth in multiple myeloma's estimated annual percentage changes in recent years. This trend suggested that high-income countries were making strides in managing multiple myeloma effectively, whereas low-income countries continued to face challenges in disease control. Therefore, there was a compelling need for wealthier nations to provide support to their lower-income counterparts in managing and controlling multiple myeloma effectively. It is critical that global health policymakers came up with specific and flexible policies to help strengthen the delivery of primary care, and health management policies should be tailored to the handling capacity of different regions.

It is important to note that the forecasts suggested that the number, age-standardized mortality rate, disability-adjusted life years, and mortality for multiple myeloma will keep on increasing every year from 2022 to 2050. These trends underscored the need for further steps on the international level in the fight against multiple myeloma. Today's data repositories did not have distinct classifications for the different phases of multiple myeloma including MGUS, Smultiple myeloma, and amultiple myeloma[27]. This lack of a detailed classification system was an indication of the fact that there were demands to enhance the data collection and classification systems to enable research and treatment planning.

Conclusion

The data also showed that the incidence, prevalence, and disability-adjusted life years of multiple myeloma were increasing over the past 32 years with the number of cases reported each year and mortality rates still high. Interestingly, mortality and morbidity rates were generally higher among men than women. As seen in the above analysis, the burden of multiple myeloma was still mostly borne by high-income countries but the effect of multiple myeloma was also being felt in low-income countries. The anticipation for the years 2022 to 2050 showed that the incidence, prevalence, disability-adjusted life years, and age-standardized mortality rate of multiple myeloma would continue to rise. These statistics highlighted the major problems in the prevention and treatment of multiple myeloma, which was characterized by an expanding patient load, uneven geographical distribution, and high death rates. These were very important in the formulation and implementation of policies especially in the area of health and in the distribution of resources in the health care systems. This is why it is crucial that the global health policymakers came up with specific and flexible policies that could help in the enhancement of the delivery of the primary health care and came up with ways of addressing the different health care needed that are present in different countries.

Data availability

This article uses the GBD, Injuries, and Risk Factors Study 2021 public database and all primary data are available. Data can be downloaded free of charge from the GBD Open database: https://vizhub.healthdata.org/gbd-results/ .

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Author contributions

Qianru Hou designed the analytical strategies, performed data analyses and wrote the manuscript. Xinyang Li, Di Fu and Huanxin Ma performed data analyses. Aijun Liao conceived the research and wrote the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

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Additional information

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