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Comparative diabetes mellitus burden trends across global, Chinese, US, and Indian populations using GBD 2021 database

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Diabetic mellitus (DM) poses a significant challenge and stress to global health, comparing the burden of disease in the world's three most populous countries while projecting changes in trends in age-standardized rate (ASR) -deaths and disability adjusted life years (DALYs) up to 2050. Using GBD2021 data, we examined DM trends in China, US, India and globally for 1990–2021, and projected deaths and DALYs for DM (types 1 and 2) for 2022–2050 using Bayesian age-period-cohort (BAPC) model. It was found that the ASR-DALYs and deaths for T1DM are trending downward globally, while those for T2DM are trending upward. In terms of gender differences, the burden of T1DM by gender was insignificant, whereas the burden of disease was significantly higher in men with T2DM than in women. The burden of disease for T1DM peaks around the ages of 40–44 years, while the burden of disease for T2DM peaks at 65–69 years. Population growth and ageing are major factors influencing the disease burden of diabetes. The projection of ASR-deaths and DALYs globally for 2022–2050 showed a decreasing trend in T1DM and an increasing trend in T2DM (especially in China and India). The increasing burden of T2DM disease globally and in three countries by 2050 should be taken seriously.

Keywords Diabetes mellitus, Disability adjusted life years, Mortality, Global epidemiology, Burden

Diabetes mellitus (DM) is a chronic disease in which the body does not produce enough insulin or fails to respond normally to insulin, resulting in abnormally high blood glucose levels. According to the latest epidemiologic findings[1,2], the global prevalence of type 2 diabetes mellitus (T2DM) increased by more than 1.5% annually from 2000 to 2019, and in 2019 alone, diabetes mellitus caused 2 million deaths worldwide. Long-term chronic elevation of blood glucose can involve microangiopathy (e.g., retinopathy, nephropathy, and neuropathy) and macrovascular disease (e.g., cardiovascular disease), resulting in complications such as blindness, end-stage renal disease, stroke, and heart disease[3,4]. It is evident that DM and its associated complications impose substantial economic and psychological burdens on society and families, emerging as a significant social issue that poses a serious threat to public health globally. In addition, DM presents significant differences in different countries. For example, the prevalence of diabetes is increasing at a faster rate in low- and middle-income countries, while their total health expenditures are more than 300 times lower than those of high-income countries[5,6]. This unequal distribution highlights the urgency of conducting cross-country comparative studies.

The latest 2021 Global Burden of Disease (GBD), Injury, and Risk Factors study, released on May 16, 2024 by the University of Washington's Institute for Health Metric and Evaluation (IHME), comprehensively evaluates the global impact of various health problems over the last three decades, providing information on disease mortality and disability rates, as well as the impact of risk factors on disease. This will help us to understand the major causes of disease deaths and disabilities so that we can target designation and improvement programs.

Although previous GBD studies have provided comprehensive assessments of the burden of disease in diabetes[7], in-depth comparative analyses of major populous countries, as well as in-depth exploration of differentiating characteristics and influencing factors in different socio-cultural contexts, are lacking. This study aims to fill these knowledge gaps and provide a more comprehensive assessment of the burden of DMIn this study,

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China, the United States and India were selected for in-depth comparison, which not only account for nearly 40% of the world's total population, but more importantly, the three countries have different social backgrounds. Comparative analysis of them could reveal the epidemiological characteristics of diabetes in different economic levels, cultural backgrounds, lifestyles and healthcare systems.

The specific aims of this study were: (1) to quantify trends in mortality and disability-adjusted life years (DALYs) for T1 and T2DM globally and in China, the United States, and India from 1990 to 2021; (2) to analyze differences in the burden of DM in 2021 by gender and age group; (3) to identify the main factors influencing changes in the burden of DM (population growth, population ageing and changes in disease epidemiology) and their relative contributions; (4) to assess the extent of diabetes health inequalities in regions with different levels of socio-demographic index (SDI); and (5) to project the global disease burden of DM in 2050 based on 30 years of historical data. This will identify the unique challenges faced by each country, providing valuable insights for the formulation of a global health strategy for the prevention and treatment of DM. Simultaneously, this will help guide the allocation of rehabilitation resources and the development of multidisciplinary models of diabetes care in countries with different social backgrounds and demographic distributions, as well as the precise control and whole-life management of DM.

Methods

Data download

The latest GBD 2021 study provides comprehensive estimates of risk exposure and risk-induced health loss between 1990 and 2021 for 204 countries and regions in the world. We obtained data on the incidence and mortality rates of diabetes mellitus T1DM and T2DM, including age-standardized values, in accordance with the guidelines provided in the GBD 2021 report (http://ghdx.healthdata.org/gbd-results-tool). To further analyze the distribution of diabetes by gender and age, we also acquired detailed demographic information. Additionally, we selected both global data and data from the three most populous countries—China, the United States of America, and India—to examine the trends in DM from 1990 to 2021.

Data analysis

Annual percentage change trends

The Joinpoint regression model is a segmented regression technique that leverages the temporal characteristics of disease distribution. It partitions the study period into distinct intervals using a series of joinpoints, subsequently fitting and optimizing the trend within each interval. This approach allows for a more detailed evaluation of interval-specific disease changes on a global temporal scale. In this study, we employed the Joinpoint regression model to identify inflection points in disease prevalence trends. We calculated the annual percent change (APC) in prevalence rates between these inflection points, as well as the average annual percent change (AAPC) for the entire age cohort. The AAPC, which is the weighted average of the APCs across segmented intervals, encapsulates the overall trend in disease prevalence from 1990 to 2021. If we denote b_i as the slope coefficient for the i^{th} segment with i indexing the segments in the desired range of years, and w_i as the length of each segment in the range of years, then:

$$\mathrm{APC}_i = \{\exp(b_i) - 1\} \times 100$$

$$\mathrm{AAPC} = \left\{\exp\left(\sum w_i b_i \Big/ \sum w_i\right) - 1\right\} \times 100$$

ASR-deaths and ASR- dalys trends

In this study, we further investigated trends in T1DM and T2DM with Age-standardized rate (ASR)-Deaths and ASR- DALYs using age-period-cohort (APC) interaction analysis. With this approach, we simultaneously considered the effects of age, time period, and cohort on the burden of different types of diabetes. By analyzing APC interactions, we gained more insight into the impact of different types of diabetes on changes in disease burden and determined their relative importance in changes in overall burden.

Decomposition analysis

We decomposed the burden of disease into factors such as population age, population size, and epidemiologic change, which was done to gain more insight into how different demographic and disease characteristics contribute to the overall burden of disease. This allowed us to more accurately assess the impact of age structure, demographic changes, and epidemiologic factors on disease burden. In addition, we provided a detailed decomposition of epidemiologic changes to examine the impact of different types of diabetes on changes in disease burden.

Health inequalities analysis

Health Inequality Analysis (HIA) is a statistical method used to assess differences in health status across populations, focusing on understanding the relationship between factors such as socioeconomic status, geographic location, gender and age and their impact on health outcomes. This study revealed the distribution and trends of health inequalities in diabetes between 1990 and 2021 by using the absolute health inequity indicator Slope Inequality Index (SII) and the relative health inequity indicator Concentration Index (CIX), effectively quantifying the impact of socioeconomic factors on health status.

DM burden projections

We used Bayesian age-period-cohort (BAPC) modeling to predict the burden of diabetes globally and in China, India, and the United States from 2022 to 2050. The model not only better addresses noise and uncertainty in the sample, but also can utilize other information known outside the sample to provide more reliable predictions[8].

All data processing in this study was conducted using R.

Results

Global burden of DM

The global impact of DM in 2021 was substantial, with significant variations across countries in terms of mortality and morbidity. As illustrated in Fig. 1A, the absolute number of deaths due to DM showed marked geographical disparities. India bore the heaviest mortality burden, recording 331,308.49 deaths (95% CI: 292,022.58 to 370,529.43). This was followed by China, with 178,475.73 deaths (95% CI: 147,957.14 to 211,654.89), and the United States, reporting 74,017.28 deaths (95% CI: 67,397.27 to 78,431.91). The distribution of DALYs, depicted in Fig. 1B, further emphasizes the health burden of diabetes. Consistent with mortality data, India led with the highest burden of 13,665,849.42 DALYs (95% CI: 11,616,958.07 to 16,073,937.78). China followed closely with 11,713,613.86 DALYs (95% CI: 9,046,221.56 to 15,013,009.95), while the United States ranked third with 5,074,680.65 DALYs (95% CI: 4,019,748.94 to 6,326,281.43). These figures reflect the substantial impact of DM on quality of life and productivity in these nations.

To account for demographic differences and enable more meaningful cross-country comparisons, we analyzed ASR for both deaths and DALYs. Figure 1C illustrated the ASR-Deaths, revealing a nuanced picture of DM mortality risk. India exhibited the highest rate of 31.12 deaths per 100,000 people (95% CI: 27.57 to 34.82), significantly higher than the United States at 12.64 (95% CI: 11.64 to 13.33) and China at 8.98 (95% CI: 7.45 to 10.61). Similarly, Fig. 1D presented the ASR-DALYs, providing insights into the relative burden of diabetes-related disability and premature mortality across populations. India again led with 1,102.82 DALYs per 100,000 people (95% CI: 944.62 to 1,289.58), followed by the United States at 959.49 (95% CI: 764.57 to 1,191.08), and China at 585.43 (95% CI: 448.94 to 754.32). These findings highlight the disproportionate impact of DM on quality of life and years of healthy life lost in India and the United States compared to China, despite China's larger population.

Distribution of DM subtypes

In the GBD database, DM is categorized into type 1 and type 2. According to data from 1990, T2DM accounted for 94.1% of deaths (632,321.96 cases, 95% UI: 596,870.01 to 662,081.61) worldwide, while type 1 diabetes mellitus (T1DM) accounted for only 5.9% (39,699.81 cases, 95% UI: 35,362.41 to 45,496.36). DALYs due to diabetes in the same year showed a similar distribution, with 90.6% for T2DM and 9.4% for T1DM (2,573,014.44 cases, 95% UI: 2,269,184.53 to 2,927,132.41). By 2021, the global distribution of DM deaths changes slightly compared with 1990, with T2DM increasing to 97.1% (75,340,873.71 cases, 95% UI: 63,483,094.23 to 90,254,281.75) and T1DM decreasing to 2.9% (3,597,713.34 cases, 95% UI: 3,037,759.10 to 4,249,993.60). Similarly, the distribution

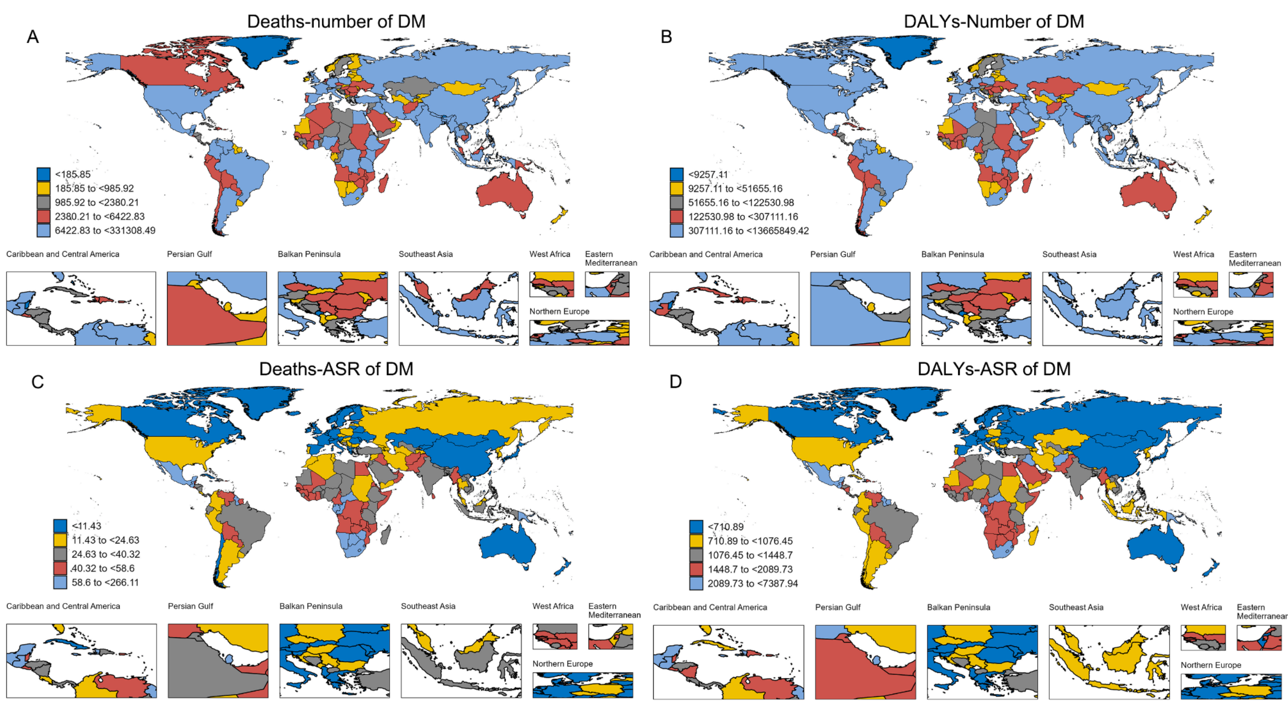

Fig. 1. Global distribution of DM burden in 2021. (**A**) Deaths-Number of DM. (**B**) DALYs-Number of DM. (**C**) Deaths-ASR of DM. (**D**) DALYs-ASR of DM.

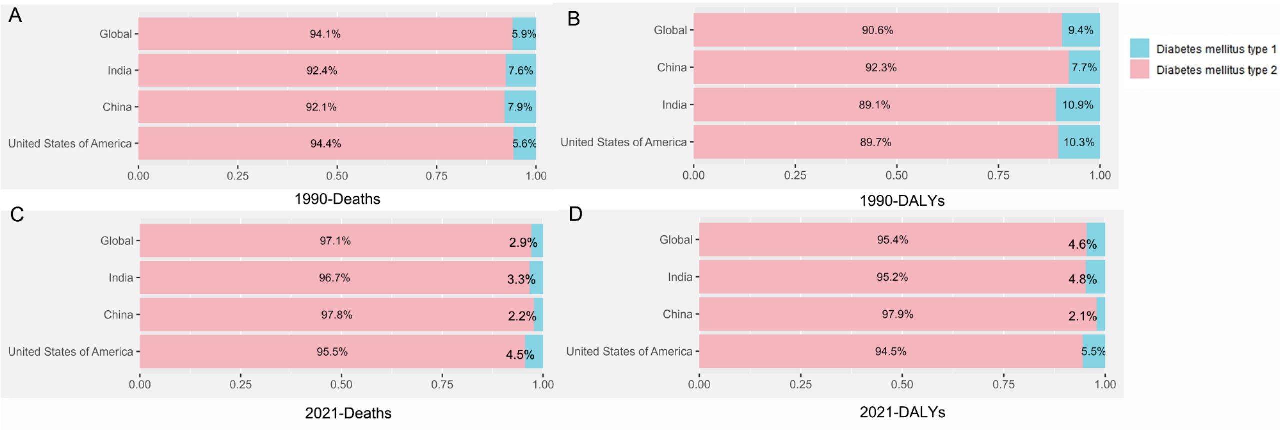

Fig. 2. Distribution of different DM types. (**A**) Distribution of DM Deaths in 1990. (**B**) Distribution of DM DALYs in 1990. (**C**) Distribution of DM Deaths in 2021. (**D**) Distribution of DM DALYs in 2021.

Location	Case	DALYs		Deaths	
		AAPC (95% CI)	*P* value	AAPC (95% CI)	*P* value
Global	T1DM	-0.41(-0.48 to 0.34)	< 0.001	-1.1(-1.2 to -1.01)	< 0.001
	T2DM	1.16(1.09 to 1.22)	< 0.001	0.31(0.21 to 0.42)	< 0.001
China	T1DM	-2.56(-2.74 to -2.38)	< 0.001	-2.62(-2.94 to -2.29)	< 0.001
	T2DM	0.88(0.77 to 0.99)	< 0.001	-0.16(-0.34 to 0.02)	0.074
India	T1DM	-0.71(-0.9 to 0.52)	< 0.001	-0.86(-1.15 to -0.57)	< 0.001
	T2DM	1.28(1.06 to 1.51)	< 0.001	1.07(0.35 to 1.8)	0.003
United States of America	T1DM	0.17(-0.03 to 0.36)	0.095	-0.39(-0.7 to -0.08)	0.013
	T2DM	1.53(1.41 to 1.66)	< 0.001	-0.62(-0.89 to -0.35)	< 0.001

Table 1. The AAPC of dalys and deaths due to T1DM and T2DM in global, China, India, and the united States from 1990 to 2021.

of DALYs changed in 2021, with T2DM increasing to 95.4% (1,608,123.22 cases, 95% UI: 1,493,437.70 to 1,708,293.64) and T1DM decreasing to 4.6% (48,511.30 cases, 95% UI: 43,623.65 to 53,957.72, Fig. 2).

Additionally, we conducted an analysis of the proportion of diabetes subtypes contributing to DALYs and deaths in China, India, and the United States in both 1990 and 2021. In China, the proportion of T2DM increased from 92.1% in 1990 to 97.8% in 2021 for deaths, and from 92.3 to 97.9% for DALYs. Conversely, the proportion of T1DM decreased from 7.9 to 2.2% for deaths, and from 7.7 to 2.1% for DALYs. Similar trends were observed in India, where between 1990 and 2021, deaths from T2DM increased from 92.4 to 96.7%, DALYs from 89.1 to 95.2%. And T1DM deaths declined from 7.6 to 3.3%, and DALYs decreased from 10.9 to 4.8%. The United States showed a less pronounced shift, with T2DM increasing from 94.4% in 1990 to 95.5% in 2021 for deaths, and from 89.7 to 94.5% for DALYs. T1DM decreased from 5.6 to 4.5% for deaths, and from 10.3 to 5.5% for DALYs.

To elucidate the temporal trends in DM burden, we conducted an AAPC analysis for both T1DM and T2DM from 1990 to 2021. A consistent decreasing trend was observed for both DALYs (AAPC: -0.41, 95% CI: -0.48 to -0.34, $p < 0.001$) and deaths (AAPC: -1.1, 95% CI: -1.2 to -1.01, $p < 0.001$) of T1DM in global. In contrast, T2DM showed an increasing trend in both DALYs (AAPC: 1.16, 95% CI: 1.09 to 1.22, $p < 0.001$) and deaths (AAPC: 0.31, 95% CI: 0.21 to 0.42, $p < 0.001$).

In China, we observed a marked decline in the burden of T1DM over the study period (Table 1). The AAPC for T1DM-related DALYs was −2.56 (95% CI: -2.74 to -2.38, $p < 0.001$), while the AAPC for T1DM-related deaths was −2.62 (95% CI: -2.94 to -2.29, $p < 0.001$). We observed a slight but significant increase in T2DM-related DALYs (AAPC: 0.88, 95% CI: 0.77 to 0.99, $p < 0.001$), indicating a growing disease burden. However, T2DM-related deaths showed a non-significant decrease (AAPC: -0.16, 95% CI: -0.34 to 0.02, $p = 0.074$). India demonstrated a different pattern compared to China. While T1DM burden also decreased in India, the decline was less pronounced. The AAPC for T1DM-related DALYs was −0.71 (95% CI: -0.91 to -0.52, $p < 0.001$), and for T1DM-related deaths, it was −0.86 (95% CI: -1.15 to -0.57, $p < 0.001$). The AAPC for T2DM-related DALYs was 1.28 (95% CI: 1.06 to 1.51, $p < 0.001$), and for T2DM-related deaths, it was 1.07 (95% CI: 0.35 to 1.8, $p = 0.003$). The United States exhibited a unique and complex pattern of diabetes trends. For T1DM, we observed a non-significant increase in DALYs (AAPC: 0.17, 95% CI: -0.03 to 0.36, $p = 0.095$) coupled with a significant decrease in deaths (AAPC: -0.39, 95% CI: -0.7 to -0.08, $p = 0.013$). We found a significant increase in T2DM-related DALYs (AAPC: 1.53, 95% CI: 1.41 to 1.66, $p < 0.001$), indicating a rising disease burden.

Joinpoint regression analysis of T1DM and T2DM trends

We employed Joinpoint regression analysis to identify significant changes in the temporal trends of T1DM and T2DM burden. This statistical method allows for precise quantification of disease trend changes, identification of turning points, and calculation of the AAPC over the entire study period (Fig. 3). The ASR-Deaths for T1DM exhibited a significant decreasing trend globally, with an AAPC of -1.1. The rates decreased steadily from 1995 onwards, with the most significant decrease being observed between 2003 and 2011 (APC = -2.05). The ASR-DALYs related to T1DM showed a similar pattern to ASR-Deaths (AAPC = -1.04). Global rates decreased steadily, with the most significant decrease occurring between 2004 and 2012 (APC = -1.03). Global ASR-Deaths of T2DM increased until 2003, then declined slightly (AAPC = -1.1). DALYs for T2DM increased across all regions, but with varying magnitudes (AAPC = 1.16).

Specifically, China showed remarkable progress in managing T1DM, achieving the largest overall reduction in ASR-Deaths (AAPC = -2.62), with a particularly rapid reduction occurring between 2004 and 2007 (APC = -6.88). For the T1DM ASR-DALYs, China demonstrated the most significant overall improvement (AAPC = -1.86), especially from 2003 to 2006 (APC = -5.05). For T2DM, China presented a mixed picture. While the ASR-Deaths showed a slight decreasing trend (AAPC: -0.2), the ASR-DALYs exhibited a minor increase (AAPC: 0.9). India's T1DM trends, while positive, were less pronounced compared to China. Both ASR-Deaths and ASR-DALYs for T1DM showed decreasing trends (AAPC: -0.86 and − 0.71, respectively), indicating gradual improvements in T1DM outcomes. However, India faced significant challenges with T2DM, with significant increases in ASR-Deaths and ASR-DALYs (AAPC: 1.07 and 1.28, respectively), particularly for ASR-DALYs in the 2005–2014 timeframe (APC = 2.64). The United States presented a unique and complex pattern of diabetes trends. For T1DM, there was a slight decrease in the death rate (AAPC: -0.39), but a marginal increase in ASR-DALYs (AAPC: 0.17). Contrary to global trends, the T2DM ASR-Deaths showed a decreasing trend (AAPC: -0.62). However, the United States experienced a significant increase in ASR-DALYs (AAPC: 1.53), which was the highest of the four countries analyzed.

Age and gender distribution of DM burden

This study presented a comprehensive analysis of the disparities in diabetes burden, quantified through DALYs and deaths, across age groups and genders. Our findings revealed a distinctive age-related distribution of T1DM burden globally. The impact of T1DM, as measured by both DALYs and deaths, demonstrated a peak in younger age groups, with the highest burden observed in the 40–44 years age bracket (Fig. 4A-B). Following this peak, there was a gradual decline in burden with increasing age. Gender disparities in T1DM burden were notable, with males generally experiencing a higher burden compared to females across most age groups. In contrast to T1DM, T2DM exhibited a markedly different age-related pattern (Fig. 4C-D). Globally, both DALYs and deaths attributable to T2DM showed a consistent increase with age, reaching a peak in the 65–69 years age group, followed by a gradual decline in older age groups. Gender differences in T2DM burden were apparent. While the age-related trend was similar for both genders, females tend to reach peak burden slightly later than males, typically in the 70–74 years age group. Moreover, the magnitude of T2DM burden, in terms of both DALYs and

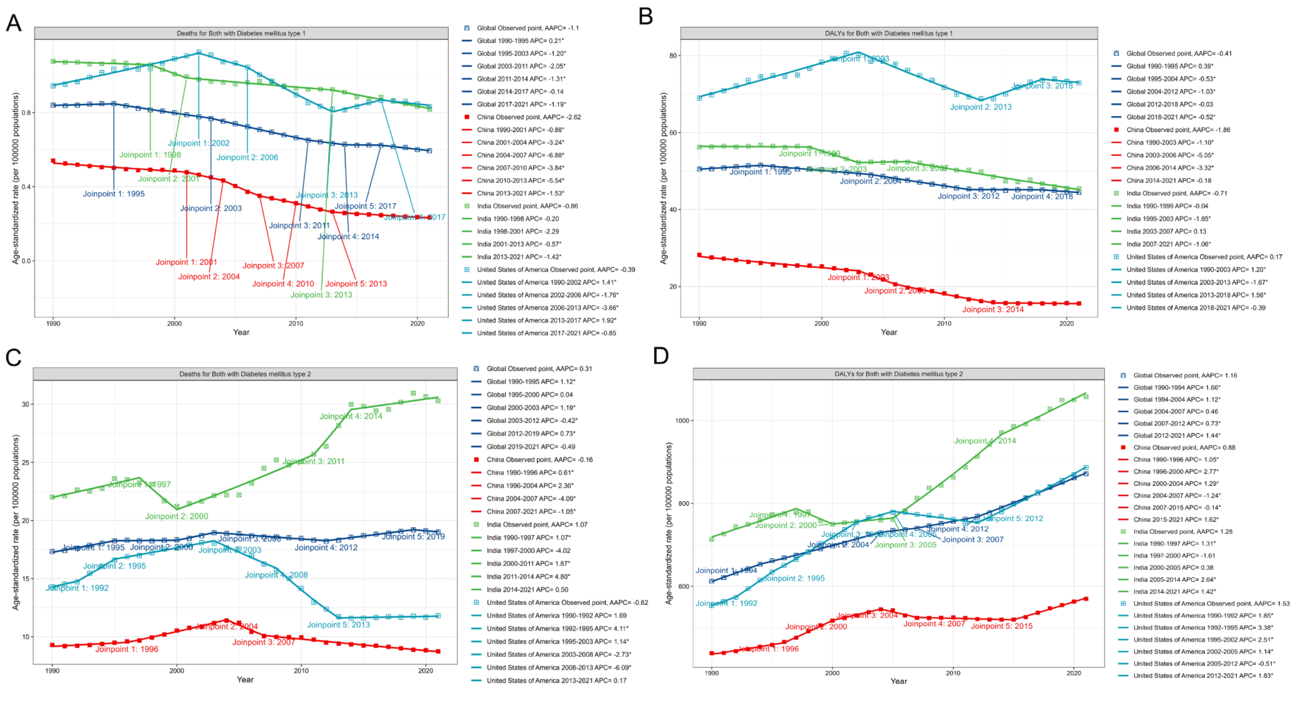

Fig. 3. Joinpoint regression analysis of T1DM and T2DM Trends. (**A**) ASR-Deaths in T1DM. (**B**) ASR-DALYs in T1DM. (**C**) ASR-Deaths in T2DM. (**D**) ASR-DALYs in T2DM.

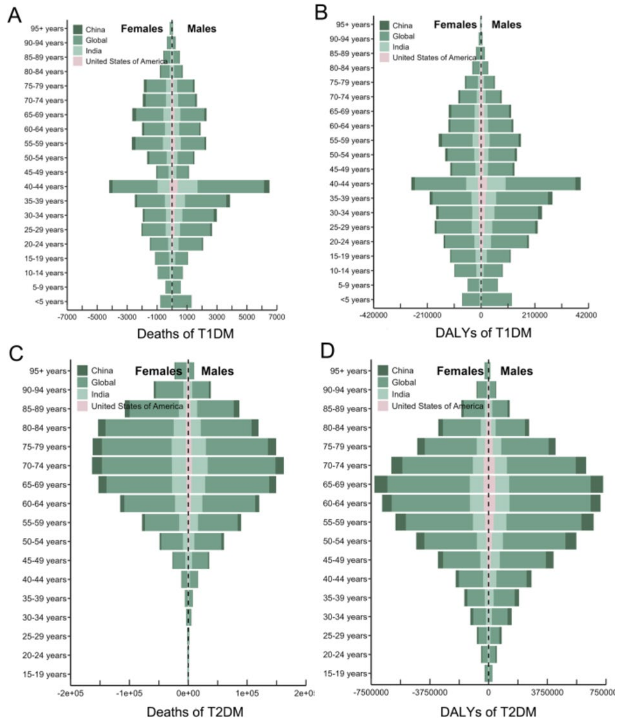

Fig. 4. Distribution of deaths due to T1DM and T2DM (stratified by sex and age) worldwide, in the United States, China, and India in 2021. (**A**) Deaths caused by T1DM. (**B**) DALYs caused by T1DM. (**C**) Deaths caused by T2DM. (**D**) DALYs caused by T2DM.

deaths, was generally lower in females compared to males, with this disparity being particularly pronounced in middle-age groups.

In terms of age distribution, all three countries closely mirrored the global trend for T1DM, with peak burden occurring around the 40–44 years age group. However, notable variations in the magnitude of burden were observed across countries. In particular, India demonstrated a higher T1DM burden in younger age groups compared to China and the United States. For T2DM, the age distribution patterns in China, the United States, and India generally aligned with the global trend. All three countries exhibited peak T2DM burden in the 65–74 years age range, with a slight delay in peak age for females compared to males.

Age-period-cohort analysis

Our age-cohort analyses showed a general decline in T1DM deaths with decreasing cohort age. This trend was particularly evident worldwide and in China. However, the United States and India were an exception, with an upward trend in Deaths-ASR within the same age cohort. For DALYs-ASR, we observed an arching pattern, with the burden peaking in different regions for different cohorts. Globally and in China, shifts in each age cohort were associated with linear downward trends. The pattern was more complex in India and the United States, where there were clear fluctuations between upward and downward trends in different cohorts (Fig. 5A).

The age-period analysis indicated that T1DM Deaths-ASR increased with age across all studied regions and periods. However, the rate of increase and absolute values varied among regions, with the United States consistently showing higher overall rates. DALYs-ASR exhibited an arch-shaped pattern across all regions, peaking in the middle-age range (approximately 40–44 years). While global and Chinese data showed a gradual decrease in peak DALYs-ASR over time, the United States demonstrated a slight increase in recent periods. India's pattern was less distinct, showing fluctuations across periods (Fig. 5B).

Within the same period, T1DM Deaths-ASR gradually decreased with cohort progression across all regions. However, within-cohort trends varied by region: increasing in the United States, relatively stable globally and in India, and decreasing in China. DALYs-ASR showed an arch-shaped variation within period curves as cohorts progressed, particularly evident in global and US data. The relationship between DALYs-ASR and period within cohorts was complex, with some cohorts experiencing increases and others decreases. China generally showed a decreasing trend across periods for most cohorts, while India and the US exhibited more varied patterns (Fig. 5C).

For T2DM, a decrease in cohort age was associated with a consistent decrease in Deaths-ASR globally, in China, in the United States and in India. However, there were large differences within the age group > 85 years, as evidenced by a mountainous trend in Deaths-ASR in the US and China, and a decreasing trend followed by a sharp increase in India. Overall mortality was consistently higher in the United States, especially in the older age groups (Fig. 6A). DALYs-ASR also increased with age, but more gradually compared to Deaths-ASR. Globally, this increase was steady across all age groups. China uniquely showed a slight decline in the oldest age groups

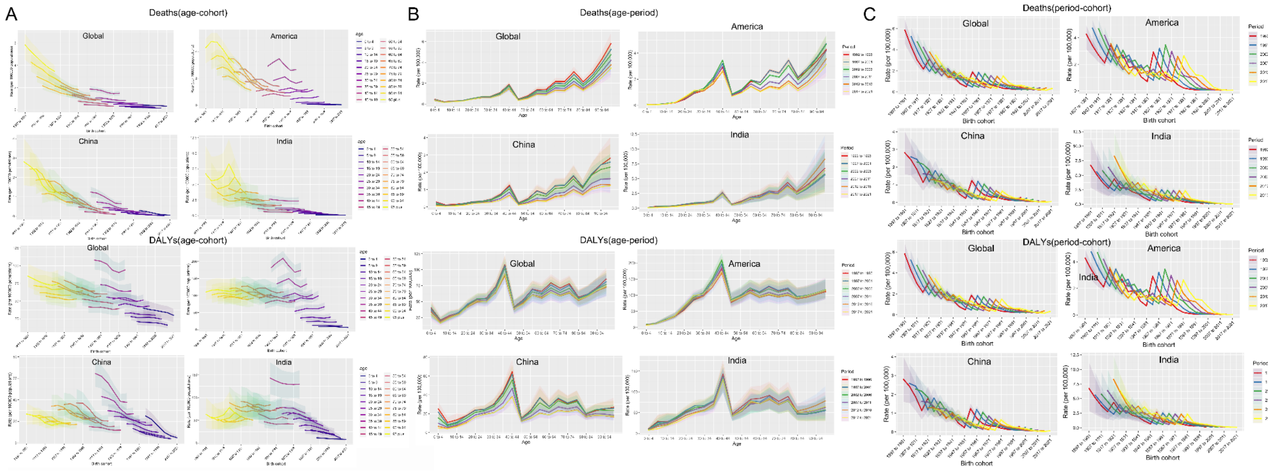

Fig. 5. The APC analyzes T1DM outcomes in deaths and DALYs. (**A**) Age-cohort analysis. (**B**) Age-period analysis. (**C**) Period-cohort analysis.

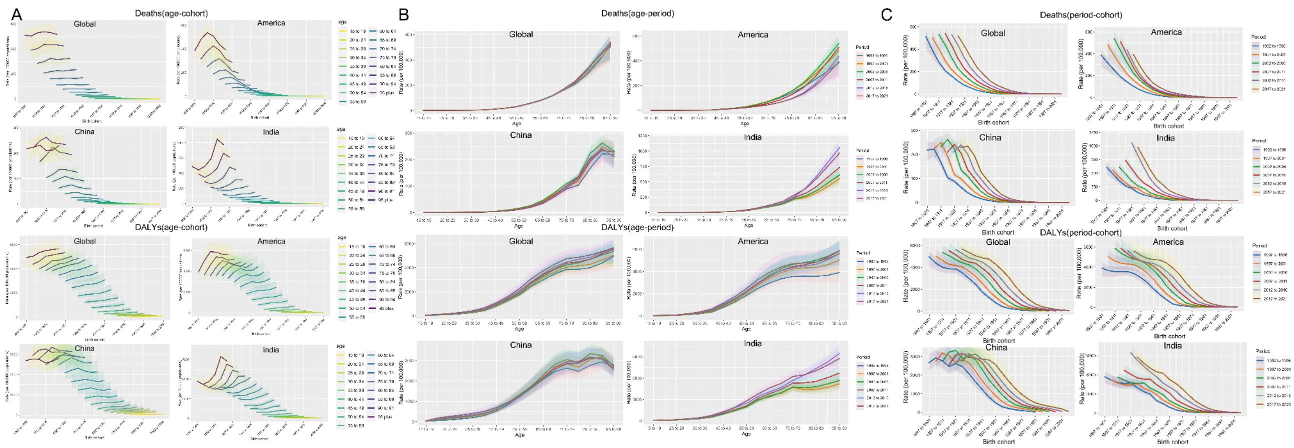

Fig. 6. The APC analyzes T2DM outcomes in deaths and DALYs. (**A**) Age-cohort analysis. (**B**) Age-period analysis. (**C**) Period-cohort analysis.

after peaking around 75–79 years. The United States maintained higher DALYs-ASR across all age groups and periods, while India demonstrated steady increases with age but at lower overall rates (Fig. 6B).

Within periods, T2DM Deaths-ASR gradually decreased with cohort progression across all regions. However, within cohorts, T2DM Deaths-ASR generally increased over time, indicating an overall rise in T2DM mortality. This trend was most prominent in the United States and least pronounced in China. DALYs-ASR showed a generally decreasing trend with cohort progression within periods. Within cohorts, DALYs-ASR tended to increase over time, particularly in global and US data. China exhibited a more complex pattern, suggesting intricate interactions between cohort and period effects. India showed lower overall rates, but maintained the general trend of declining rates for younger cohorts and increasing rates across periods (Fig. 6C).

Decomposition analysis

To elucidate the underlying factors contributing to changes in diabetes-related mortality and morbidity from 1990 to 2019, we conducted a comprehensive decomposition analysis. This analysis quantified the relative contributions of population ageing, population growth, and epidemiological changes in both T1DM and T2DM.

Our results revealed a substantia global increase of 919,068.36 DM-related deaths during this period (Fig. 7A). Population growth emerged as the main driver, accounting for 53.6% of this increase, followed closely by population ageing at 36.51%. Changes in T2DM epidemiology resulted in a 11.24% increase in death, while changes in T1DM epidemiology were slightly less pronounced, resulting in a 1.34% decrease in mortality. In terms of the global burden of disease, we observed an increase of 46,458,258.51 DALYs attributable to DM (Fig. 7B). The pattern of factor contributing to DALYs was somewhat different from that for deaths. While population growth remained the dominant factor, explaining 46.37% of the increase, epidemiological changes in T2DM played a more significant role, accounting for 31.48% of the increase in DALYs.

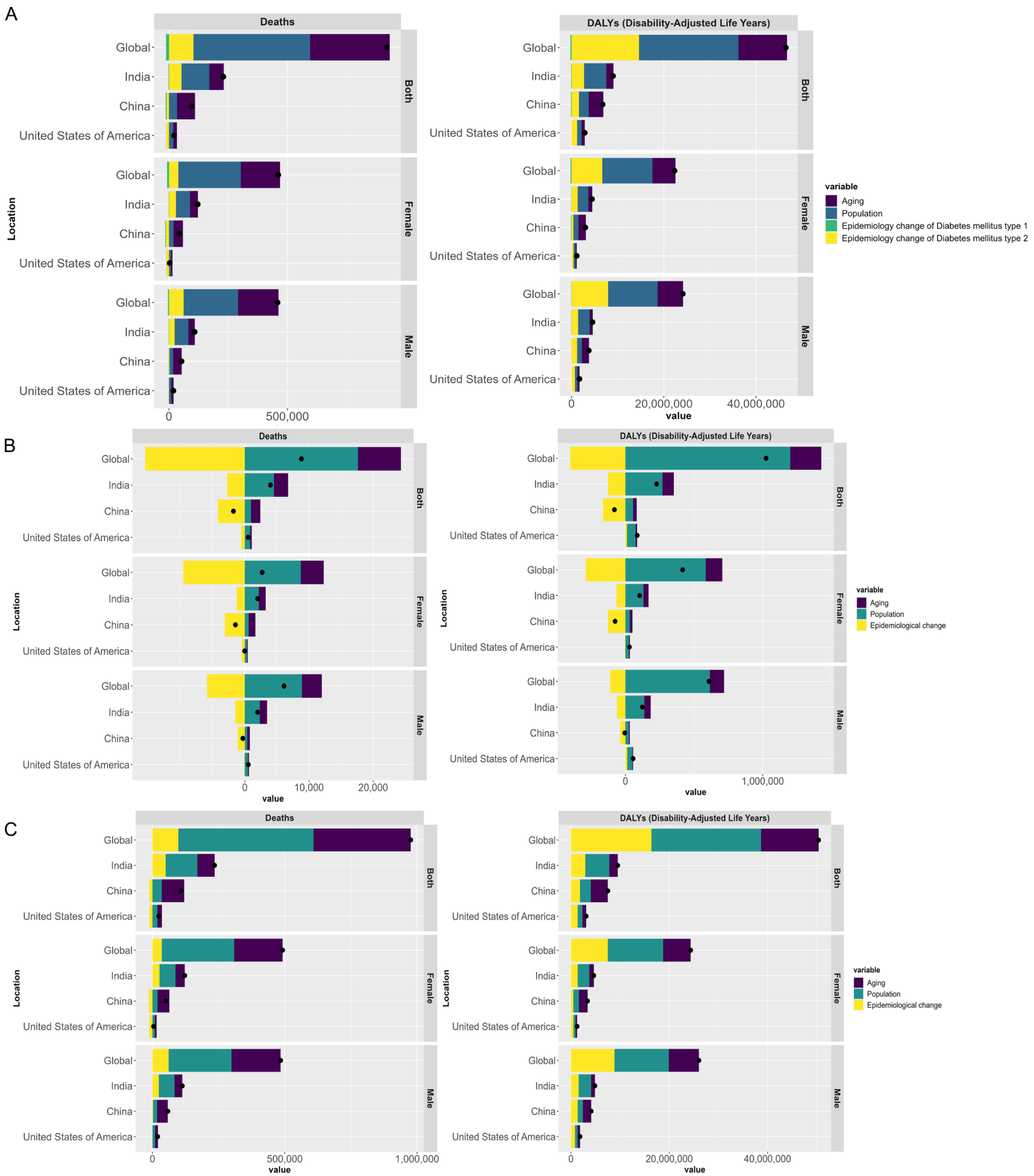

Fig. 7. Decomposition analysis results of DM-related deaths and DALYs. (**A**) Different decomposition factors for DM Globally, in India, China, and the United States, by gender. (**B**) Different decomposition factors for T1DM. (**C**) Different decomposition factors for T2DM.

In China, population ageing emerged as the predominant factor influencing both deaths and DALYs, accounting for 78.4% and 46.46% of the increases, respectively. Interestingly, epidemiological changes in both T1DM and T2DM had negative impacts on death rates in China. However, for DALYs, epidemiological changes in T2DM had a positive impact. The United States presented a unique pattern where both ageing and population growth had substantial positive impacts on deaths, while epidemiological changes in both T1DM and T2DM showed negative impacts. For DALYs in the United State, T2DM epidemiological changes emerged as the primary driver, followed by population growth and ageing, indicating a growing burden of T2DM-related

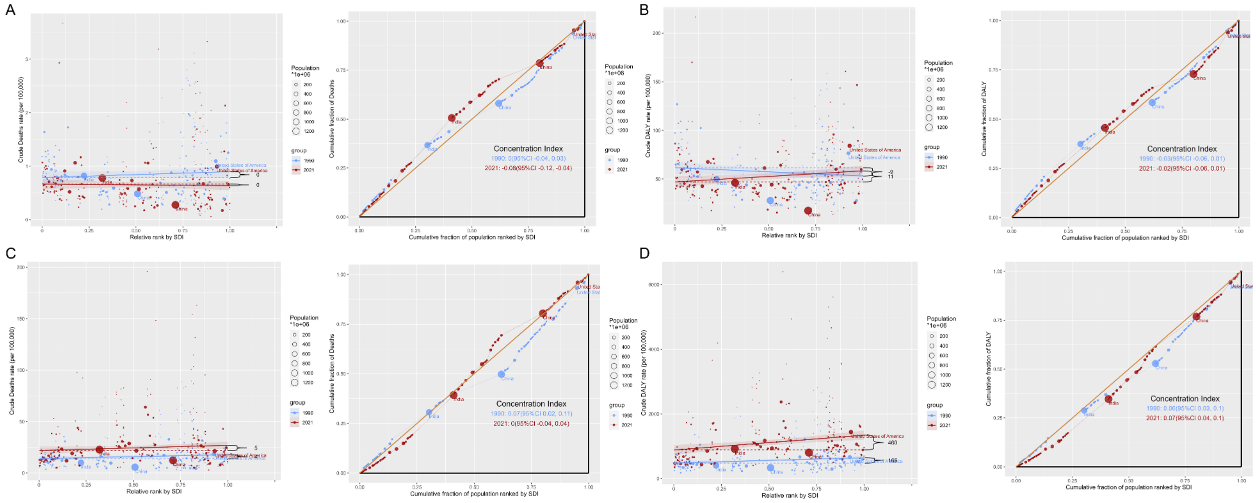

Fig. 8. Visualization of SII and CIX results of deaths and DALYs related to T1DM and T2DM. (**A**) The SII and CIX analysis of Deaths for T1DM. (**B**) The SII and CIX analysis of DALYs for T1DM. (**C**) The SII and CIX analysis of Deaths for T2DM. (**D**) The SII and CIX analysis of DALYs for T2DM.

complications and disability. In India, population growth was the dominant factor for both deaths and DALYs. Epidemiological changes in T2DM also played a significant role, particularly in DALYs. Ageing had a moderate impact on both outcomes, while T1DM epidemiological changes had minimal negative impacts (Fig. 7C-F).

Health inequality analysis for T1DM and T2DM

To clarify the socioeconomic disparities in the burden of DM, we performed an exhaustive health inequality analysis for T1DM and T2DM. Our study employed the SII and CIX methodologies to examine crude Death rates and DALY rates across different levels of the Socio-Demographic Index (SDI) from 1990 to 2021.

The SII analysis for T1DM crude Death rates revealed a slight narrowing of the gap between the highest (SDI = 1) and lowest (SDI = 0) SDI regions (Fig. 8A). The gap decreased from approximately 1 death per 100,000 in 1990 to about 0.8 deaths per 100,000 in 2021. Notably, the United States consistently showed higher rates than expected for its SDI level in both years, while India had lower rates than expected. China's position shifted from lower-than-expected rates in 1990 to rates closer to the expected level for its SDI in 2021. The CIX for T1DM deaths underwent a significant shift, moving from 0 (95% CI: -0.04 to 0.03) in 1990 to -0.08 (95% CI: -0.12 to -0.04) in 2021. This transition indicates a growing burden in lower SDI regions over time, representing a reversal of the socioeconomic gradient in T1DM mortality. For T1DM DALYs, the SII increased from approximately 9 DALYs per 100,000 in 1990 to about 11 DALYs per 100,000 in 2021 (Fig. 8B). Similar to the death rates, the United States consistently exhibited higher DALY rates than expected, while China and India showed lower-than-expected rates for their respective SDI levels. The CIX for T1DM DALYs remained relatively stable, changing only slightly from − 0.03 (95% CI: -0.06 to 0.01) in 1990 to -0.02 (95% CI: -0.06 to 0.01) in 2021. This suggests that the socioeconomic distribution of T1DM DALYs did not significantly change over the study period, with a slight tend towards a higher burden in lower SDI regions.

The results of SII analysis for T2DM showed a significant increase inequality in crude death rates. The disparity between the highest (SDI = 1) and lowest (SDI = 0) SDI regions widened from approximately 5 deaths per 100,000 individuals in 1990 to 10 deaths per 100,000 in 2021 (Fig. 8C). Notably, high SDI regions consistently had higher death rates. India and China maintained lower-than-anticipated crude death rates for their SDI levels, whereas the United States consistently showed higher than expected rates. The CIX for T2DM deaths demonstrated a trend towards a more equitable distribution across SDI levels, with a decrease from 0.07 (95% CI: 0.02, 0.11) in 1990 to 0 (95% CI: -0.04, 0.04) in 2021. This suggests a shift towards a more balanced distribution of the T2DM mortality burden across socioeconomic levels. With regard to the burden disease attributable to T2DM, there was a notable increase in the gap between the most and least developed regions. The difference between the highest and lowest SDI regions grew from 165 DALYs per 100,000 in 1990 to 460 DALYs per 100,000 in 2021 (Fig. 8D). The pattern of country-specific deviations mirrored that observed in mortality rates, with India and China exhibiting lower-than-expected DALY rates and the United States showing higher-than-expected rates. The CIX for T2DM DALYs demonstrated a slightly increase from 0.06 (95% CI: 0.03, 0.1) in 1990 to 0.07 (95% CI: 0.04, 0.1) in 2021, indicating a persistent and slightly growing burden in higher SDI regions.

Future projections of DM burden

Based on the results of the global DM disease burden from 1980 to 2021, the BAPC model was used to predict the changes in DM disease burden from 2022 to 2050 globally and in China, the United States, and India (Fig. 9). The BAPC model projections indicated a continuing decline in the global burden of T1DM. The ASR for both Deaths and DALYs was expected to decrease steadily, albeit gradually. In stark contrast to T1DM, T2DM projections revealed a concerning upward trajectory. The model forecasts increased in both ASR-Deaths and

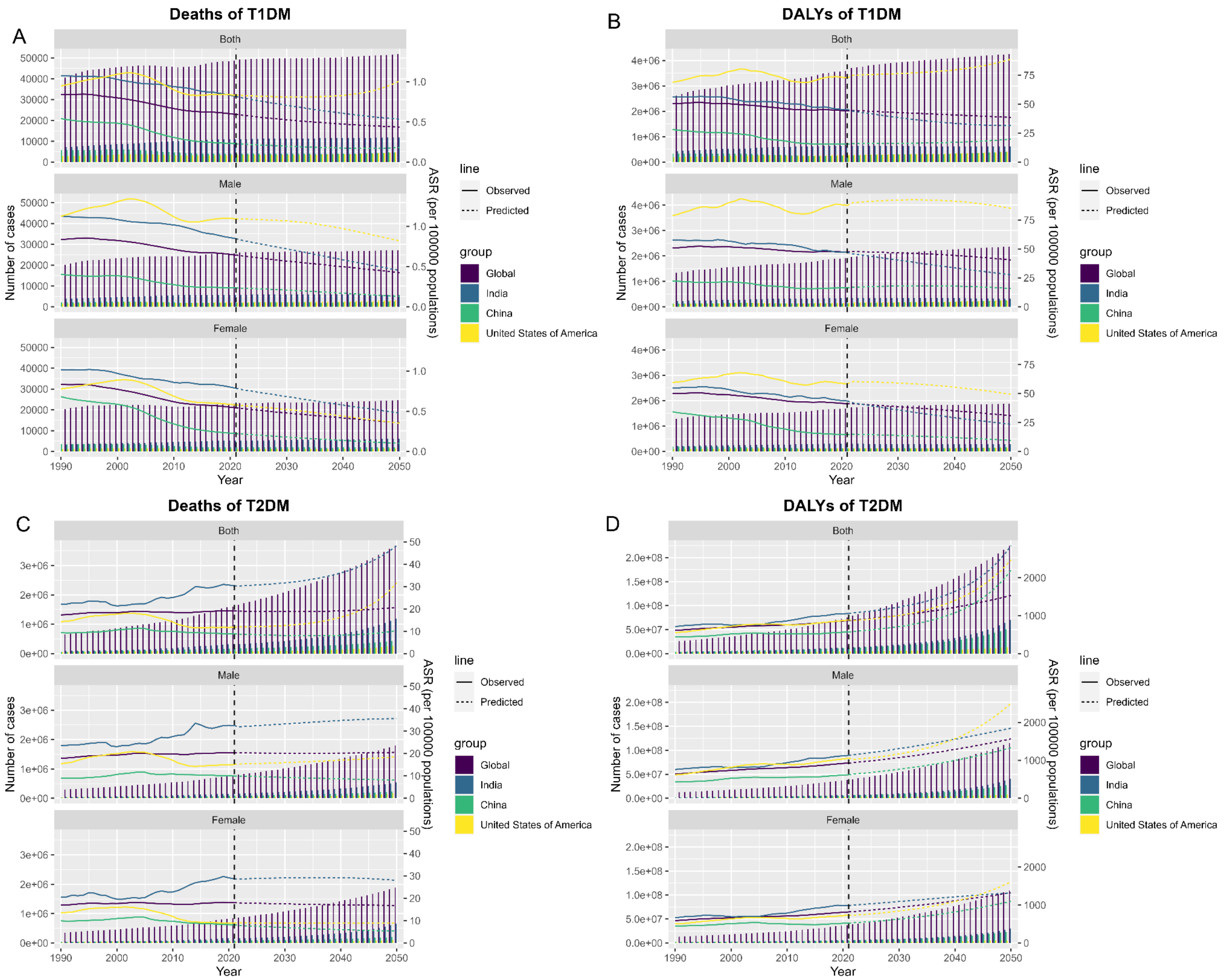

Fig. 9. Predictions of DM burden using the BAPC forecasting model for global, China, United States, and India (up to 2050). (**A**) BAPC model predicted T1DM ASR-Deaths. (**B**) BAPC model predicted T1DM ASR-DALYs. (**C**) BAPC model predicted T2DM ASR-Deaths. (**D**) BAPC model predicted T2DM ASR-DALYs.)

ASR-DALYs globally, indicating a growing burden of T2DM on population health. By 2050, the number of globally T1DM deaths would be 51,837 cases (6.7% increase from 2021), and the number of T2DM deaths would reach 3,676,447 cases (128.6% increase from 2021).

Of the countries analyzed, the United States had the least optimistic projections for T1DM. The model predicted significantly higher ASR-deaths and ASR-DALYs for T1DM than for the global and the other two countries, especially for males. In the case of T2DM, while the burden of disease in the United States was projected to remain on an upward trend, it was relatively modest compared to other regions. Between 1990 and 2021, the burden of disease for T1DM in China showed a sharp downward trend, and these would be expected to continue to improve by 2050. China's ASR-DALYs for T2DM were projected to be on the rise, especially with a sharp increase after 2037, which required our attention. India's projections presented a complex picture. For T1DM, a downward trend in ASR-deaths and DALYs was projected for India. T2DM in India had the most worrisome projections, with the most rapid increase in disease burden and substantial increases in both ASR-deaths and ASR-DALYs, which were significantly higher than globally and in the other two countries. Among the regions analyzed, rates of ASR-deaths and ASR-DALYs were consistently higher in males with T1DM compared to females. Although the gender gap in T2DM was less pronounced than in T1DM, the number of male deaths was still expected to be slightly higher than that of females in most regions.

Age-specific projections of diabetes burden

This investigation employed a BAPC forecasting model to conduct predictive analyses for age-specific cohorts affected by T1DM and T2DM. The analysis focused on the 35–54 age group for T1DM and the 60–84 age group for T2DM, projecting trends up to 2050. Analyses of T1DM patients in the 35–54 age group revealed disparate patterns across regions with regard to ASR and absolute numbers (Fig. 10A, B). A decline was observed in both deaths-ASR and DALYs-ASR on a global scale. This decline was more pronounced in females than in males in

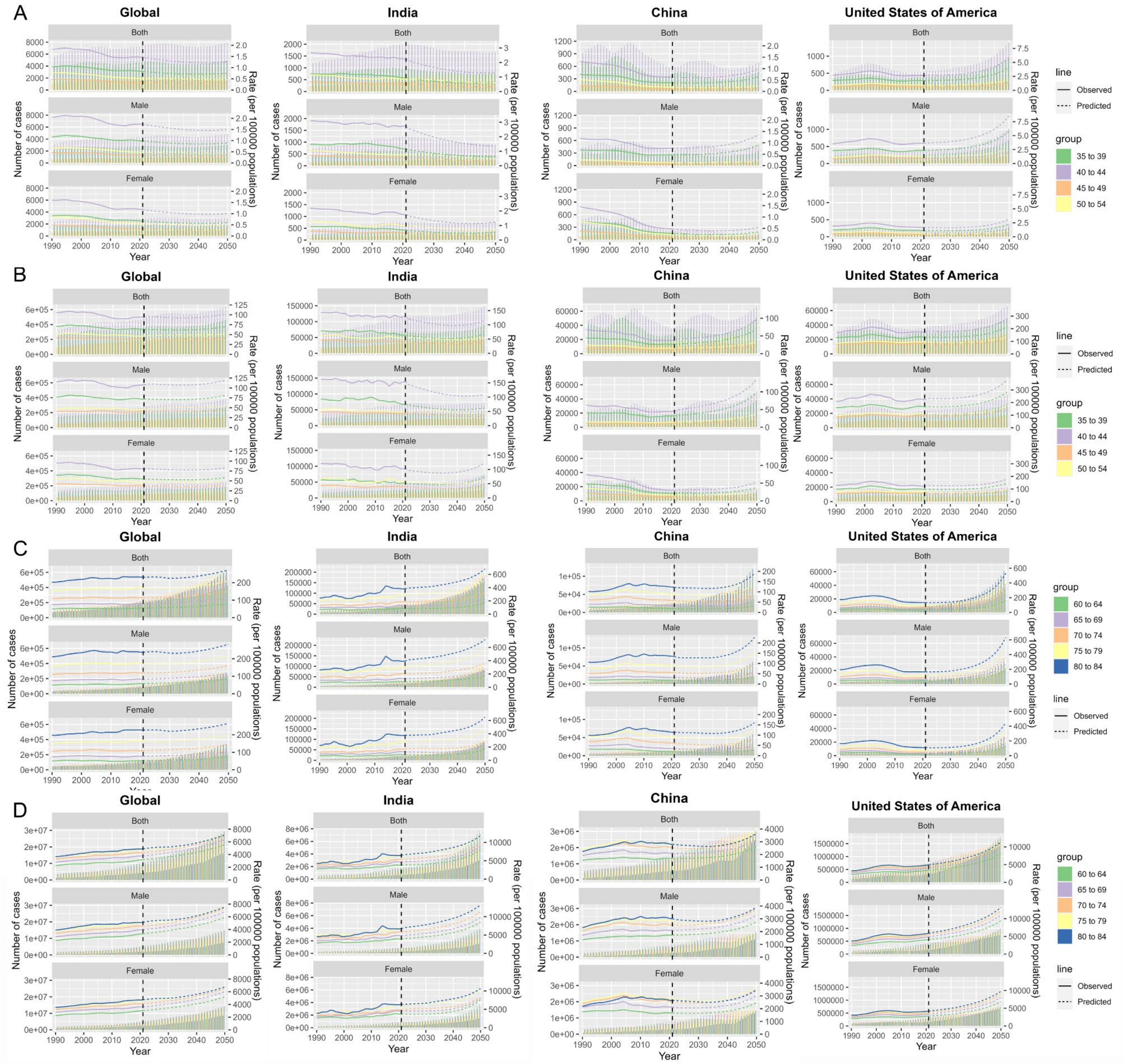

Fig. 10. Prediction of Deaths-ASR and DALYs-ASR for specific age-cohorts affected by DM globally, in China, the US, and India. (**A**) Predictions of T1DM-related Deaths-ASR in the 35–54 age group for global, US, China, and India. (**B**) Predictions of T1DM-related DALYs-ASR in the 35–54 age group for global, US, China, and India. (**C**) Predictions of T2DM-related Deaths-ASR in the 60–84 age group for global, US, China, and India. (**D**) Predictions of T2DM-related DALYs-ASR in the 60–84 age group for global, US, China, and India.

terms of DALYs. However, this global trend was not reflected uniformly across all regions under study. In the United States, contrary to the global pattern, both Deaths-ASR and DALYs-ASR exhibited an upward trajectory. This increase was particularly evident among males, suggesting a growing burden of T1DM in this demographic within the U.S. China, on the other hand, demonstrated a steep decline in both Deaths-ASR and DALYs-ASR up to 2021. However, our projections indicate a slight increase or stabilization for both genders beyond 2021, marking a potential shift in the country's T1DM burden. India's projections aligned more closely with the global trend, showing a gradual decline in both Deaths-ASR and DALYs-ASR, which is expected to continue into the future. When examining the relationship between ASR and absolute numbers, we uncovered several divergent trends.

Globally, while death numbers showed an overall decreasing trend, DALYs numbers slightly increased, likely attributable to population growth. The United States stood out with projections indicating increases in both ASR and absolute numbers for deaths and DALYs, with a more pronounced rise among males. China's projections revealed a complex pattern. Following an initial decline, absolute DALYs numbers are expected to increase, particularly in the 40–44 and 45–49 age groups. Conversely, death numbers in China showed a steep decline, which is projected to stabilize in the future. India presented another nuanced scenario where, despite declining ASR, absolute death numbers are projected to increase, particularly in the 40–44 and 45–49 age groups. Indian DALYs exhibited a complex pattern with a slight increase in absolute numbers despite declining ASR, especially noticeable in the 40–44 age group.

Analysis of T2DM in the 60–84 age group revealed varying trends across different regions (Fig. 10C, D). Globally, both Deaths-ASR and DALYs-ASR demonstrated a relatively stable trend with a slight increase projected for both genders. However, this global trend was not uniformly reflected in the country analyses. In the United States, we observed a declining trend in both Deaths-ASR and DALYs-ASR until 2021. However, our projections indicate a reversal of this trend beyond 2021, with an upward trajectory that is particularly pronounced among males. This shift suggests a potential resurgence of T2DM burden in the elderly U.S. population in the coming years. China's projections for T2DM revealed a more complex pattern. Deaths-ASR showed a stable trend up to 2021, followed by a projected slight increase for both genders. The DALYs-ASR in China demonstrated a stable trend up to 2021, after which we project a slight decrease followed by an increase for both genders. This non-linear pattern highlights the dynamic nature of T2DM burden in China's elderly population. India's projections for T2DM in the elderly population were particularly concerning. Both deaths-ASR and DALYs-ASR were on an upward trend, which was expected to continue. Notably, this increase was expected to be faster in men, indicating a growing gender gap in the burden of T2DM in India's older population.

Discussion

This study provided an in-depth analysis of the global burden of DM, which showed complex trends from 1990 to 2021. Global DALYs and mortality for T1DM have shown a decreasing trend, whereas T2DM has shown an increasing trend. This is consistent with the International Diabetes Federation (IDF) report, which states that DM has become one of the major public health challenges worldwide[5]. The difference may reflect different etiological characteristics and the effectiveness of management strategies. Previous studies have found similar trends, particularly for T1DM in children[9–11]. For T2DM, studies have demonstrated a global trend of increasing incidence, especially in low- and middle-income countries[12,13]. This suggests that T2DM should be a priority for future prevention and control strategies worldwide. In contrast to previous studies[7,14,15], this study concentrated on the three most populous countries in the world: China, India and the United States. India bore the heaviest burden of deaths, with about 331,308 deaths due to diabetes, followed by China (178,476) and the United States (74,017). In terms of DALYs, India also ranked first (13,665,849), followed by China (11,713,61) and the United States (5,074,68). These three countries shared about one-third of the global burden of diabetes, highlighting the severe impact of the disease on these populous countries and the need for special attention from global health authorities.

Country-level analyses revealed a more complex picture. China has made remarkable progress in the management of T1DM, with significant reductions in both DALYs and mortality (AAPC of -2.6 for both). Meanwhile, China had a slight decrease in T2DM mortality (AAPC: -0.16) but an increasing trend in DALYs (AAPC: 0.88). This may be related to China's comprehensive public health policy and the gradual improvement of its healthcare system[16,17]. For example, China's health insurance coverage rate increased from 29.7% in 2003 to 95.7% in 2011, while remaining stable at over 95% since 2013[18]. This has greatly reduced deaths and complications resulting from untimely treatment of illnesses due to low income or poverty. Certainly, Chinese traditional medicine also plays a great role, and studies have proved that TCM therapies can be effective for both T1DM and T2DM[19–23]. The trend for T1DM in India was also decreasing, but at a lower rate (AAPC of -0.71 for DALYs and − 0.86 for mortality). The largest increases in the burden of T2DM were observed in India, with AAPCs of 1.28 and 1.07 for DALYs and mortality, respectively. The continued increase in the burden of diabetes in India is associated with rapid urbanization and lifestyle changes[24]. In addition, Indian scholars have found that increasing age, family history of diabetes, lack of physical activity and abdominal obesity are the most common risk factors for T2DM in women[25]. The United States showed a unique pattern, with a slight increase in DALYs (AAPC: 0.17, 1.53) and a decrease in mortality (AAPC: -0.39, -0.62) for both T1DM and T2DM. The unique pattern in the United States may relate to its complex health care system, social determinants and lifestyle[26,27]. The study found that, despite the provision of health care, the U.S. population with diabetes also suffers from poor outcomes due to social determinants such as economic instability, food insecurity, education and literacy, access to quality health care, neighborhoods and built environments, and social and community environments[27]. A systematic evaluation and meta-analysis showed that lifestyle interventions can reduce the overall risk of T2DM by 0.53, as well as reduce the risk of cardiovascular and microvascular complications[28]. The AAPC for DALYs of T2DM was positive in all three countries, suggesting that T2DM can lead to an increased economic burden of disease in these countries. In addition, T2DM was a major contributor to the DM disease burden. Previous studies have identified obesity, dietary risks, tobacco, physical inactivity and air pollution as major risk factors for the development of T2DM[7,29,30]. Therefore, more attention needs to be paid to preventing T2DM in the first place by intervening on risk factors in advance.

The study stratified the number of DALYs and deaths associated with T1 and T2 diabetes globally, in China, the United States and India in 2021 by gender and age. The results showed that the gender burden of T1DM was not significant, whereas males with T2DM had a significantly higher disease burden than females. These findings have also been confirmed in previous studies[31,32]. Gender differences in T2DM may be closely related to genetics, culture, lifestyle, environment, socioeconomic status, and psychological factors, among which hormones, smoking, parental history of diabetes and body mass index (BMI) may be the main factors causing gender differences in T2DM[33–36]. For example, T2DM is more common in males with a low BMI, while females commonly have a high BMI. In addition, higher household income is positively associated with the prevalence and incidence of diabetes in both genders, with the relationship being stronger for males than for females[37]. In terms of age groups, the disease burden for T1DM reached its peak at around 40–44 years of age, whereas for

T2DM it peaked at 65–69 years of age and then gradually declined. The age peak for T1DM in the three countries is globally consistent, while the burden of T2DM peaks at 65–74 years. Previous studies by Jiang[38] have confirmed a significant increase in the global burden of diabetes in adults ≥ 70 years of age, which is closely related to the continued ageing of the population. India showed a higher prevalence of T1DM in younger age groups, which may be related to earlier diagnosis of T1DM and increased survival rates due to poverty reduction, improved communication and technology, increased awareness among healthcare workers and more trained specialists[39].

Age-period-cohort analysis provided a comprehensive overview of trends in the burden of DM globally, as well as in China, the United States and India. The analysis showed a general decline trend of Deaths in T1 and T2DM across age cohorts. The peak of DALYs for T1DM occurred at 40–44 years of age globally and in the three countries. It was notable that the DALYs of T1DM in the United States have shown an upward trend in recent periods. This was also similar to the results of cost assessments of T1DM healthcare in the United States, where the healthcare burden resulting from complications may increase as people with T1DM live longer[40,41]. Mortality rates of T2DM also increased with age, particularly after age 60, reflecting the combined effects of demographic changes, medical interventions, and socioeconomic factors on the burden of DM[42,43]. Furthermore, considering the COVID-19 pandemic, these projections might be conservative and the actual situation might be more severe than predicted[44–46].

A decomposition analysis of the key factors influencing the disease burden of DM globally, in China, the United States, and India. It found that population growth was the main driver, contributing 53.6%of the increase in Deaths and 46.37% of the increase in DALYs globally. Population ageing was the second most important factor, while changes in the epidemiology of T2DM also played an important role, particularly in the increase in DALYs. This is consistent with the findings of Bommer, who also emphasized the importance of these factors in driving the increased economic burden of DM[47]. Country-level analyses revealed different patterns. In China, population ageing was the dominant factor, while in the United States, epidemiological changes in T2DM had the greatest impact on the increase in DALYs[48]. In India, population growth was the dominant factor of T2DM, followed by changes in the epidemiology, which has also been confirmed in previous studies[49,50]. These findings emphasized the need for country-specific strategies and targeted interventions to address the increasing burden of DM.

The health inequality analysis conducted in this study, combined with research on the burden of DM globally and in China, the United States and India, reveal noteworthy trends in Deaths and DALYS in regions with different socio-demographic characteristics[51]. The results of the SII suggest that the gap in crude deaths rate for T1DM in the period 1990–2021 between regions with high SDI and low SDI is narrowing, while the burden of DALYs is slightly increasing in lower SDI regions. However, deaths rate declined between all three countries, but were significantly lower than expected in China and slightly higher than expected in India and the United States by 2021. Notably, the US was the only one of the three countries with elevated DALYs for T1DM in 2021. Smoking, poor diet and lack of physical activity are not only risk factors for T2DM, but may also have an impact on the prognosis of T1DM[52,53]. In contrast, the gap in T2DM crude deaths rate and DALYs widened significantly between regions with high SDI and low SDI, with all three countries experiencing significant increase. These findings emphasized the complex interplay of socioeconomic factors and healthcare systems in influencing DM outcomes. Similarly, the CIX results highlighted differences in the distribution of diabetes-related Deaths and DALYs across SDI levels. Negative values indicated that mortality and DALYs are concentrated in areas with lower SDI levels, suggesting a disproportionate burden in regions of lower socioeconomic conditions, consistent with previous research[12]. These findings pointed to the importance of targeted interventions to address health inequalities in diabetes, particularly in areas with low SDI levels, and the need for strategies aimed at improving access to healthcare and addressing the social determinants of health.

This study projected the development of ASR associated with the disease burden of different types of DM across the entire age range and age-specific groups by 2050 globally, in China, the United States, and India. From 1990 to 2021, there was an overall declining trend in ASR associated with T1DM in these regions, with the overall levels in India and the US above the global average. In contrast, ASR associated with T2DM showed an overall increasing trend, with India above the global average. However, the trend of ASR associated with T1DM disease burden showed an increase only in India during the projection period, with it being more pronounced in males. This suggested that the downward trend in ASR for T1DM was more pronounced, whereas T2DM was on an upward trend in all the regions studied, which emphasized the need to strengthen prevention and management strategies for T2DM, especially in India. It has been pointed out that low level of awareness, lack of trained medical and paramedical staff and unaffordability of medicines and services are the challenges and difficulties faced by India in DM management[49]. Moreover, the study showed that in rural Tamil Nadu, 66% of the study participants had no knowledge of diabetes[54]. This highlights the need for India to strengthen specialized training for primary healthcare workers and expand public awareness campaigns on diabetes symptoms, complications, and self-management in rural areas[55].

This study focused on predicting the development of ASR in relation to the disease burden of T1DM (35–54 years) and T2DM (60–84 years). The results showed a gradual decrease in the disease burden of T1DM in the global 35–54 age group and a progressive increase in the disease burden of T2DM in the 60–84 age group. There were significant differences between countries, with the burden of T1DM in the United States bucking the global trend and showing a gradual increase, particularly in men. There have been reports of a linear increase in the prevalence of T1DM in the United States over the next 30 years, with the prevalence projected to triple by 2050[56,57]. In contrast, India showed a decreasing trend in the burden of T1DM. In China, the overall burden of T1DM was slightly elevated, with a predominantly elevated burden in men. In the T2DM age group, the US showed a sharp increase in burden after 2030, while China and India showed slightly increasing trends. Bommer's study predicted a significant increase in the global cost of diabetes in 2030[47], which may be closely related to the growth of the disease in T2DM.

Strength and limitations

This study was the first to systematically compare the differences in the burden of DM among the world's three most populous countries (China, India, and the United States), revealing the heterogeneity of their disease profiles and providing direct evidence for the development of country-specific strategies. Meanwhile, based on GBD data from 1990 to 2021, we observe the long-term trend changes of T1DM and T2DM, especially the impact of macro factors such as aging and population growth on the disease burden. Finally, based on the characteristics and influencing factors of different disease burdens in each country, it will help to plan medical resources and preventive and control measures in advance, and optimize the allocation of resources.

Our study has limitations. First, the reliability of GBD data depends on the quality and availability of vital registration systems in each country. However, in regions where data sources were not available, GBD estimates relied on modelling processes, predictive covariates and time trends obtained from neighboring countries, which may have biased the results. Second, the age threshold for T2DM was set at 15 years, and children and adolescents under 15 years of age were not included in the analyses due to insufficient data, but this had little impact on the findings. Finally, there was a lack of purposive analyses of specific populations (e.g., adolescent T2DM, gestational diabetes), which will guide future research.

Conclusion

Overall, our findings emphasized the continuing relevance of DM as an important global public health problem. T1DM showed a declining trend in ASR-Deaths and ASR-DALYs globally, whereas the burden of T2DM increased significantly, with a significant gender difference (higher burden in males). The burden of disease for T1DM peaks at 40–44 years of age, whereas the burden of disease for T2DM peaks at 65–69 years of age. Population growth and ageing were the main factors driving the burden of DM, with India and China being particularly affected by population growth, and China with the highest proportion of ageing contribution. China was effective in T1DM management (ASR-deaths AAPC=-2.62). T2DM ASR-deaths declined but ASR-DALYs rose in the US (AAPC = 1.53), reflecting the challenge of managing complications. HIA revealed that the burden of T2DM is increasing in low-income areas and that intervention strategies need to be tailored to address socioeconomic disparities. By 2050, the burden of T2DM is projected to continue to increase, particularly in developing countries.

These findings have important implications for public health policy development, indicating the need to (1) strengthen the level of medical practitioners, as well as raise the level of public awareness of DM and its complications; (2) prevent and intervene in advance with risk factors for diabetes, such as lifestyle interventions and early diagnostic screenings; (3) differentiated screening and preventive strategies should be formulated for different genders and age groups; (4) address the population aging and socioeconomic disparities, improve equity in the distribution of healthcare resources, and focus on regions with lower levels of socioeconomic development. These interventions will help to further reduce the global burden of DM.

Data availability

The data used in the analyses are publicly available and can be viewed at the Global Health Data GBD 2021 website (http://ghdx.healthdata.org/gbd-results-tool).

Received: 11 February 2025; Accepted: 26 March 2025
Published online: 08 April 2025

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Author contributions
MJ made contributions to the conception of this study. CY and GW analyzed the data and wrote the main manuscript. ZH, XL, MS was responsible for acquisition of data. BH, SS, LW and WW helped with the analysis of the data and revised the manuscript. All authors contributed to the article and approved.

Funding
This research was funded by Basic Chinese Medicine Evidence-based Capacity Building Project (No.2019XZZX-JB004) of Traditional Chinese Medicine and Clinical Collaboration Capacity Building Project of Chinese and Western Medicine for Major Difficult Diseases (State Administration of Traditional Chinese Medicine and Medical Affairs [2018] No. 3) of State Administration of Traditional Chinese Medicine, National Health and Family Planning Commission, and the Health Bureau of the Logistics and Security Department of the Central Military Commission.

Declarations

Competing interests
The authors declare no competing interests.

Ethics statement
This research does not contain any studies involving human or animal participants.

Additional information
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