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Global, regional, and national burden of cardiovascular diseases attributable to metabolic risks across all age groups from 1990 to 2021: an analysis of the 2021 global burden of disease study data

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Abstract

Objective The objective is to evaluate the temporal trends in the burden of cardiovascular diseases attributable to metabolic risk factors from 1990 to 2021 and to project the burden over the subsequent 30 years.

Methods A joinpoint regression model was employed to estimate the annual percentage change in cardiovascular disease mortality attributable to metabolic risk factors, utilizing data from the Global Burden of Disease (GBD) 2021. An age-period-cohort analysis was conducted to evaluate the effects of age, period, and cohort. A frontier analysis was employed to investigate the correlation between the prevalence of cardiovascular disease attributable to metabolic risk factors and socio-demographic trends. An autoregressive integrated moving average (ARIMA) model was subsequently constructed to forecast future cardiovascular disease burden.

Results Between 1990 and 2021, the global age-standardized mortality rate (ASMR) of cardiovascular diseases attributable to metabolic factors exhibited a consistent decline (Average Annual Percent Change (AAPC) = -1.28, 95% CI [-1.42, -1.14], $P < 0.01$). However, the absolute number of deaths increased from 8.326 million to 13.595 million. The most substantial reduction in ASMR was observed in the High Socio-Demographic Index (SDI) region (AAPC = -2.98, 95% CI [-3.10, -2.86], $P < 0.01$), whereas the reductions were relatively smaller in the Low-middle SDI and Low SDI regions. The ARIMA model predicts a decline in global cardiovascular disease mortality over the next three decades, with the most pronounced decrease anticipated in the high-middle SDI region and smaller declines expected in the middle SDI and low SDI regions.

Conclusion Notwithstanding a global decline in age-standardized mortality and disability-adjusted life year (DALY) rates, the burden of cardiovascular diseases attributable to metabolic factors remains significant worldwide. Targeted interventions must be implemented without delay, particularly for males and populations in low and middle SDI regions, to mitigate the impact of metabolic factors on public health.

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Keywords Global Burden of Disease, Cardiovascular disease, Autoregressive integrated moving average, Age-standardized mortality rate, Average Annual Percent Change

Introduction

Cardiovascular disease (CVD) represents the most significant cause of mortality and morbidity worldwide, accounting for 32.9% of non-communicable disease-related deaths globally and approximately 18 million deaths annually [1–3]. The number of deaths from CVD increased by approximately 19% between 2010 and 2020 on a global scale. The annual economic burden of cardiovascular disease is considerable, with the economic burden on the European economy exceeding €200 billion per year [4]. The United Nations has established a target of reducing premature mortality from CVD by 25% by 2025, primarily through early detection and enhanced prevention strategies [5]. Metabolic risk factors, insofar as they constitute risk factors for CVD, have emerged as the largest contributors to the CVD burden. This suggests that an in-depth understanding of metabolic risk factors is necessary for subsequent prevention and control efforts [6].

Modifiable risk factors, including human behavior and metabolic risk, represent the primary contributors to the burden of CVD and may be preventable [7–9]. Targeting the reduction of modifiable risk factors represents a powerful and indispensable strategy for preventing poor health outcomes and premature mortality caused by diseases and injuries [10, 11]. Over the past several decades, metabolic risk has been identified as the most critical contributor to cardiovascular disease mortality [12–14]. Despite the pivotal role of metabolic risk in the development of cardiovascular disease, there is a dearth of research globally that examines the burden and classification of cardiovascular disease associated with metabolic risk factors, including high fasting glucose, high low-density cholesterol, high systolic blood pressure, high body mass index, low bone mineral density, and renal insufficiency.

Accordingly, this study employs the most recent data from the GBD 2021 to elucidate the long-term trends in the burden of cardiovascular diseases attributable to metabolic risks over the past 30 years. The study aims to: Characterize the burden of metabolic risks contributing to CVD at both global and regional levels from 1990 to 2021 and examine trends in CVD incidence driven by specific metabolic risk factors globally, including elevated fasting plasma glucose, dyslipidemia, high systolic blood pressure, and increased body mass index. Furthermore, the study aims to elucidate the long-term trends in the burden of cardiovascular diseases attributable to metabolic risks over the past 30 years. In order to achieve this, the following factors will be considered: plasma glucose, dyslipidemia, high systolic blood pressure, increased body mass index, low bone mineral density, and impaired renal function. Finally, the study will endeavor to forecast future trends in CVD mortality attributable to metabolic risk factors from 2022 to 2050.

Materials and methods

Study population and data collection

The Global Burden of Disease Study 2021 employs the latest epidemiological data sources and refined standardization methods to comprehensively assess health impairments in 204 countries and territories, uncovering health damages attributable to 369 diseases and injuries as well as 88 risk factors. The GBD database utilizes sophisticated methods to address missing data and adjust for confounding factors [15]. In this study, we obtained and analyzed GBD study data, encompassing global, regional, and national levels of cardiovascular disease mortality and DALYs attributable to metabolic factors. The Socio-Demographic Index (SDI) serves as a composite measure of educational, economic, and fertility levels, comprising five tiers corresponding to SDI quintiles (i.e., low, low-middle, middle, high-middle, and high). All data from this study are accessible at http://ghdx.healthdata.org/gbd-results-tool. Additionally, the Institutional Review Board of the University of Washington waived the requirement for informed consent for accessing GBD data. This study adheres to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [16].

Statistical analysis

The study design and methodology of the GBD study have been comprehensively detailed in previously published GBD literature. In the present analysis, 95% uncertainty intervals (UIs) were computed for each variable [8, 17]. All rates are expressed per 100,000 population. Statistical analyses were two-tailed, with a *P*-value of < 0.05 considered indicative of statistical significance.

This study utilized the Joinpoint software (version 5.3.0) developed by the U.S. National Cancer Institute to perform Joinpoint regression analysis on trends in the burden of cardiovascular diseases attributable to metabolic risk factors [18]. The Joinpoint regression model identifies multiple"joinpoints"in time-series data, representing significant changes in trends, such as a shift from an increasing trend to a decreasing trend or vice versa. Between each joinpoint, the model applies linear regression to fit the data, segmenting the entire time series into several intervals, each characterized by its own linear trend. Additionally, the study calculated the Average Annual Percent Change (AAPC), which was derived as a weighted average of the slope coefficients from the joinpoint regression model. The weights were proportional to the length of each segment within the interval. The final step involved converting the weighted average of the slope coefficients into an annual percent change. The 95% confidence intervals (CIs) were obtained through the linear regression model. When the AAPC value and its 95% CI were greater than zero, the corresponding age-standardized rate (ASR) was interpreted as exhibiting an increasing trend, whereas a negative AAPC indicated a decreasing trend. If the 95% CI of the AAPC included zero, the ASR was considered stable over time [19].

This study utilized the Age-Period-Cohort (APC) analysis tool developed by the U.S. National Cancer Institute (https://analysistools.nci.nih.gov/apc). This tool implements a set of easily interpretable estimable APC functions and corresponding Wald χ2 tests within R code. Parameter identification employs an intrinsic estimation method capable of analyzing open-ended data to construct regression models for computational analysis [20]. Age groups were categorized into 5-year intervals for this study. To enhance the stability of estimations and facilitate the construction of the age-period-cohort model, the data were grouped into 5-year age intervals and 5-year birth cohorts. The APC analysis tool provided key parameter estimates, including net drift and local drift.Net drift represents the overall linear trend in mortality rates after adjusting for period and cohort effects. It is expressed as the annual percentage change in the logarithm of mortality rates. In contrast, local drift reflects the linear trend in mortality rates for each age group, adjusted for period and cohort effects, and is presented as the annual percentage change in the logarithm of mortality rates for different age groups.

This study employed frontier analysis to further evaluate the relationship between the burden of cardiovascular diseases attributable to metabolic risk factors and sociodemographic development. The frontier represents the lowest achievable burden determined by the level of development and was generated using a nonlinear approach. Non-parametric data envelopment analysis (DEA) was utilized, with methodological details referenced from previous studies [21]. To project the trends in cardiovascular disease mortality attributable to metabolic risks over the next 30 years globally and across the five SDI regions, an autoregressive integrated moving average (ARIMA) model was constructed. ARIMA, a widely used time series analysis method, facilitates forecasting of future values. In the ARIMA modeling process, this study employed the differencing method to stabilize the time series data. The auto.arima() function was subsequently used to identify the optimal model based on the Akaike Information Criterion (AIC) [22]. All statistical analyses and visualizations were conducted using R software (version 4.2.3). A two-tailed *P*-value of <0.05 was considered statistically significant.

Results

The global and regional burden of CVD due to metabolic risks

From 1990 to 2021, the total number of deaths attributable to metabolic factors leading to cardiovascular diseases increased significantly (Tables 1 and 2). Globally, although the ASMR of cardiovascular diseases attributable to metabolic factors declined, the absolute number of deaths steadily rose from 8.33 million (95% UI: 7.43–9.13 million) in 1990 to 13.60 million (95% UI: 12.01–15.14 million) in 2021 (Table 1). Between 1990 and 2021, while the number of deaths decreased in the High SDI region, it increased in the other four SDI regions. Among these, the High SDI region exhibited the most pronounced decline in ASMR, decreasing from 200.80 per 100,000 population (95% UI: 176.84–220.08) in 1990 to 79.08 per 100,000 population (95% UI: 68.06–88.93) in 2021. Notably, the Low-Middle SDI and Low SDI regions showed only minimal declines in ASMR during the same period. Regional data revealed that South Asia, Southeast Asia, and Southern Sub-Saharan Africa experienced increasing ASMR trends, while Central Europe demonstrated the fastest decline, from 408.96 per 100,000 population in 1990 to 213.01 per 100,000 population in 2021. The high-income Asia Pacific region recorded the lowest ASMR at 44.05 per 100,000 population in 2021 (Fig. 1). It is worth noting that although ASMR declined in Eastern Europe and Central Asia, these regions still maintained relatively high levels.

Figure 2 Global Burden of Cardiovascular Diseases Attributable to Metabolic Risks in 2021: Deaths, DALYs, and Age-Standardized Rates. A and C. Age-specific deaths and DALYs: The number of deaths due to cardiovascular diseases attributable to metabolic risks demonstrates a positive correlation with age, with a sharp increase after 60 years, particularly in females. Among those aged 80 and older, the number of deaths significantly exceeds that of males, peaking in the 80–84 age group. Similarly, DALYs increase with age. Males bear a heavier disease burden than females below 80 years, particularly between 60 and 80 years, while females show a higher burden in the 80 +age group. B and D.

Table 1 Cardiovascular disease deaths and age-standardized mortality rates attributable to metabolic risk factors in 1990 and 2021

Location	1990		2021	
	Number of deaths (no. $\times 10^3$) (95% UI)	Age-standardized incidence per 100,000 population (95% UI)	Number of deaths (no. $\times 10^3$) (95% UI)	Age-standardized incidence per 100,000 population (95% UI)
Global	8326.49(7425.09,9132.38)	245.17(216.92, 268.95)	13,594.58(12,010.53,15,134.77)	164.25(145.27,183.25)
Sex				
Male	4048.66(3558.76,4457.21)	270.97(238.64,297.77)	7100.70(6286.84,7957.68)	194.13(171.45,217.36)
Female	4277.83(3774.74,4715.39)	221.70(193.72,244.73)	6493.88(5589.18,7297.31)	138.78(119.58,155.90)
SDI				
High SDI	2212.89(1956.28,2419.16)	200.80(176.84,220.08)	1911.40(1611.15,2168.78)	79.08(68.06,88.93)
High-middle SDI	2561.36(2285.69,2794.59)	306.81(271.67,335.43)	3661.29(3187.74,4147.793)	189.88(165.54,215.11)
Middle SDI	1984.40(1725.51,2223.83)	242.76(211.42,271.99)	4542.34(4002.37,5138.05)	191.15(167.79,216.14)
Low-middle SDI	1147.43(1000.22,1278.82)	222.77(193.72,249.67)	2654.94(2353.24,2924.94)	209.36(186.21,231.01)
Low SDI	407.22(353.19,458.69)	219.74(188.60,249.25)	809.94(705.82,913.42)	195.37(170.05,220.11)
Region				
Central Europe	547.65(497.40,587.24)	408.96(370.86,440.81)	506.73(450.72,558.95)	213.01(190.22,235.01)
Eastern Europe	1060.05(951.61,1144.80)	430.48(384.73,467.75)	1107.99(976.12,1240.92)	310.19(273.57,347.37)
Central Asia	157.74(140.79,171.44)	379.00(339.18,412.79)	219.65(195.19,244.99)	329.05(292.34,367.18)
Caribbean	54.89(48.72,60.44)	231.29(205.58,255.34)	86.22(73.58,100.00)	157.97(134.71,183.36)
Andean Latin America	20.34(17.17,23.45)	110.52(93.96,127.05)	43.55(36.11,52.19)	76.97(63.79,92.12)
Central Latin America	115.08(104.23,124.39)	163.96(147.51,177.74)	288.15(253.86,326.81)	121.13(106.38,137.38)
Tropical Latin America	178.83(158.64,194.43)	227.95(202.36,249.22)	261.19(229.07,287.48)	104.56(91.43,115.30)
North Africa and Middle East	521.28(461.44,575.12)	383.10(335.39,422.97)	1037.46(907.51,1170.25)	278.14(243.46,311.91)
South Asia	917.32(782.66,1036.20)	185.91(158.17,210.99)	2443.76(2145.54,2717.81)	186.52(163.36,207.06)
Southeast Asia	541.81(465.74,612.88)	252.64(216.62,287.50)	1289.30(1133.27,1442.31)	226.49(199.62,253.19)
East Asia	1571.13(1297.50,1832.40)	250.35(206.58,290.47)	3688.58(3037.41,4428.87)	193.40(159.61,232.37)
Oceania	6.31(5.06,7.76)	261.95(213.39,314.50)	15.26(12.31,18.39)	237.97(194.44,284.55)
Central Sub-Saharan Africa	49.27(39.93,58.15)	292.08(240.85,337.62)	103.14(81.89,127.38)	258.38(208.50,317.11)
Eastern Sub-Saharan Africa	120.07(102.24,138.30)	199.66(171.07,231.12)	233.07(200.19,269.64)	172.62(148.12,199.86)
Southern Sub-Saharan Africa	39.94(34.75,45.17)	171.53(148.23,194.82)	95.60(86.02,105.55)	203.22(182.83,223.84)
Western Sub-Saharan Africa	160.08(134.05,184.09)	221.53(185.29,254.53)	321.39(274.72,365.88)	208.19(179.71,234.63)
High-income Asia Pacific	251.14(218.28, 276.83)	142.44(122.61,157.53)	272.01(208.38,318.91)	44.05(35.62,50.60)
Australasia	45.10(39.96,49.41)	199.92(176.66,219.98)	35.77(29.62,40.99)	57.65(48.20,65.64)
Southern Latin America	83.66(72.96,92.19)	198.61(172.99,219.76)	80.01(70.19,88.21)	88.07(77.42,97.11)
High-income North America	682.24(597.89,746.80)	187.80(164.45,205.42)	660.74(557.38,743.31)	93.36(79.47,104.28)
Western Europe	1202.55(1068.50,1313.20)	201.38(178.31,220.21)	805.00(659.53,914.57)	67.84(56.82,76.50)

Age-standardized mortality and DALY rates: Age-standardized mortality rates rise significantly with age, especially after 70 years, for both sexes. Across all age groups, males consistently exhibit higher rates than females. The trends in age-standardized DALY rates align with those of mortality rates, showing a similar age-dependent increase. E and F. Trends from 1990 to 2021 (Deaths, ASMR, DALYs, and ASDR): ASMR and ASDR have shown a consistent decline over the past three decades for both sexes. However, males consistently report higher rates than females annually. Despite these declines, the absolute numbers of deaths and DALYs attributable to metabolic risks have continued to rise, driven by global population growth and aging. Summary: Fig. 2 highlights the age and sex disparities in the burden of cardiovascular diseases attributable to metabolic risks, with males exhibiting higher age-standardized rates across all age groups. Despite global improvements in ASMR and ASDR, the increasing total burden underscores the need for intensified prevention and management strategies

Table 2 Cardiovascular disease deaths and age-standardized mortality rates attributable to specific metabolic risk factors in 1990 and 2021

Location	1990		2021	
	Number of deaths (no. $\times 10^3$) (95% UI)	Age-standardized incidence per 100,000 population (95% UI)	Number of deaths (no. $\times 10^3$) (95% UI)	Age-standardized incidence per 100,000 population (95% UI)
High systolic blood pressure	6419.61(5349.41, 7341.45)	189.42(157.52,217.00)	10,376.44 (8784.05, 12,032.76)	125.33(106.26,145.46)
High fasting plasma glucose	1015.23(881.33, 1167.78)	30.77(26.46,35.41)	2212.98 (1911.64, 2525.67)	26.85(23.14,30.69)
Kidney dysfunction	1312.39(1033.00,1571.48)	40.58(31.93,49.24)	2095.80(1638.36,2562.75)	25.55(19.84,31.36)
High LDL cholesterol	2452.01(1431.74,3504.93)	70.51(39.71,103.61)	3646.00(2129.33,5262.17)	43.67(25.33,63.43)
High body-mass index	836.07(477.90,1316.55)	24.43(13.63,37.3)	1904.24(1072.73,2864.24)	22.77(12.87,34.24)

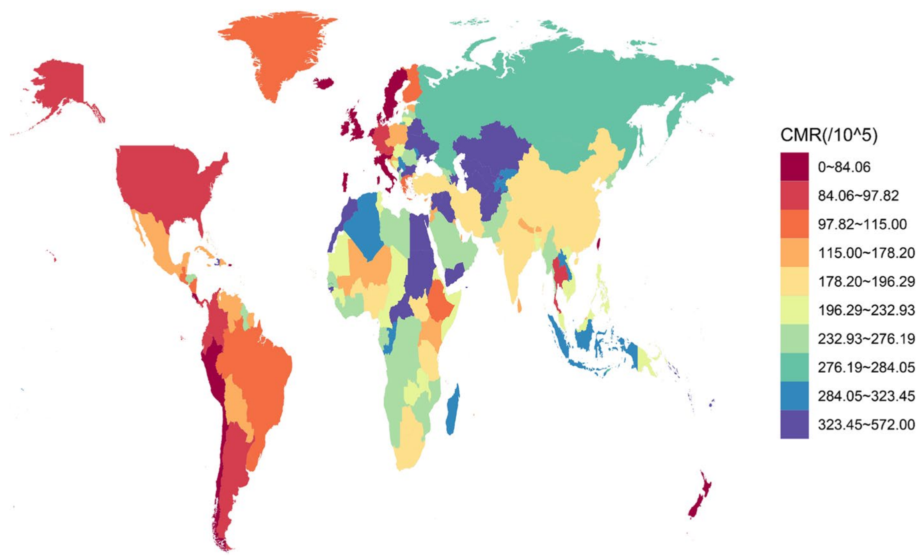

Fig. 1 Age-standardized mortality rates of cardiovascular diseases attributable to metabolic risk factors in 204 countries, 2021

targeting metabolic risks, particularly among aging populations.

Joinpoint Regression Analysis of ASMR

The joinpoint regression analysis of ASMR for cardiovascular diseases attributable to metabolic risks from 1990 to 2021, both globally and across the five Socio-Demographic Index (SDI) regions, is presented in Fig. 3 and Tables 3, 4 and 5. Global Trends: As shown in Fig. 3A, the global ASMR attributable to metabolic risks exhibited a consistent declining trend. According to Tables 3, 4 and 5, the overall Average Annual Percent Change (AAPC) for the global ASMR was − 1.28 (95% CI: − 1.42, − 1.14; $P< 0.01$) during 1990–2021. SDI-Specific Trends: High SDI region: The ASMR declined most rapidly in this region, particularly between 2002 and 2007, with an Annual Percent Change (APC) of − 4.48 (95% CI: − 4.90, − 4.06). The overall AAPC was − 2.98 (95% CI: − 3.10, − 2.86; $P< 0.01$), indicating a substantial reduction in mortality rates. High-middle and Middle SDI regions: Despite some fluctuations, ASMR showed a general downward trend throughout the study period. Low-middle SDI region: For males, ASMR exhibited an increasing trend, with an AAPC of 0.17 (95% CI: 0.11, 0.26; $P< 0.01$). For females, ASMR showed a decreasing trend, with an AAPC of − 0.53 (95% CI: − 0.90, − 0.16; $P< 0.01$). Low SDI region: Although ASMR declined overall, the reduction was minimal, and mortality rates remained high, with an AAPC of − 0.38 (95% CI: − 0.55, − 0.21; $P< 0.01$). Risk Factor-Specific Trends: Globally, ASMR attributable to high systolic blood pressure and high low-density lipoprotein cholesterol (LDL-C) showed a declining trend. However, in middle and low SDI regions, ASMR attributable to high fasting plasma glucose and high body

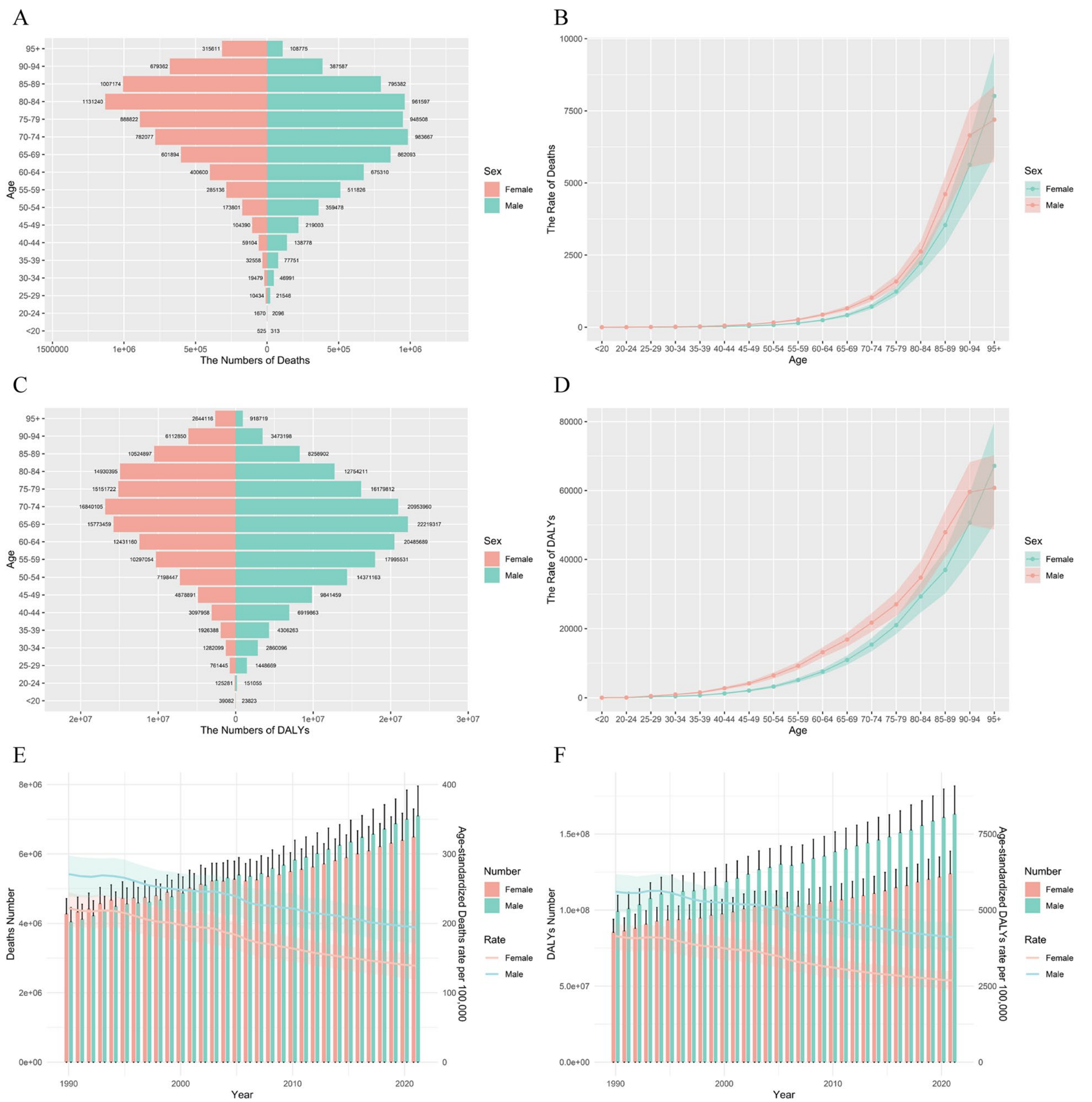

Fig. 2 Global burden of cardiovascular diseases attributable to metabolic risks in 2021. **A** Age-specific number of deaths; **B** Age-standardized mortality rates (ASMR); **C** Age-specific disability-adjusted life years (DALYs); **D** Age-standardized DALY rates; **E** Trends in deaths and ASMR (1990–2021); **F** Trends in DALYs and age-standardized DALY rates (1990–2021). The black bars in Figure E and F represent the 95% confidence intervals (CIs) for the respective data points

mass index (BMI) demonstrated an increasing trend. Particularly in the Low-middle SDI region, males experienced rising ASMR due to high systolic blood pressure, high BMI, high LDL-C, and high fasting plasma glucose, contributing significantly to the cardiovascular disease burden (Table 5). These findings highlight substantial disparities in the trends of ASMR across SDI regions and risk factors. While High SDI regions achieved significant reductions, Low and Low-middle SDI regions face persistent challenges, particularly among males, underscoring the need for targeted interventions to address specific metabolic risks.

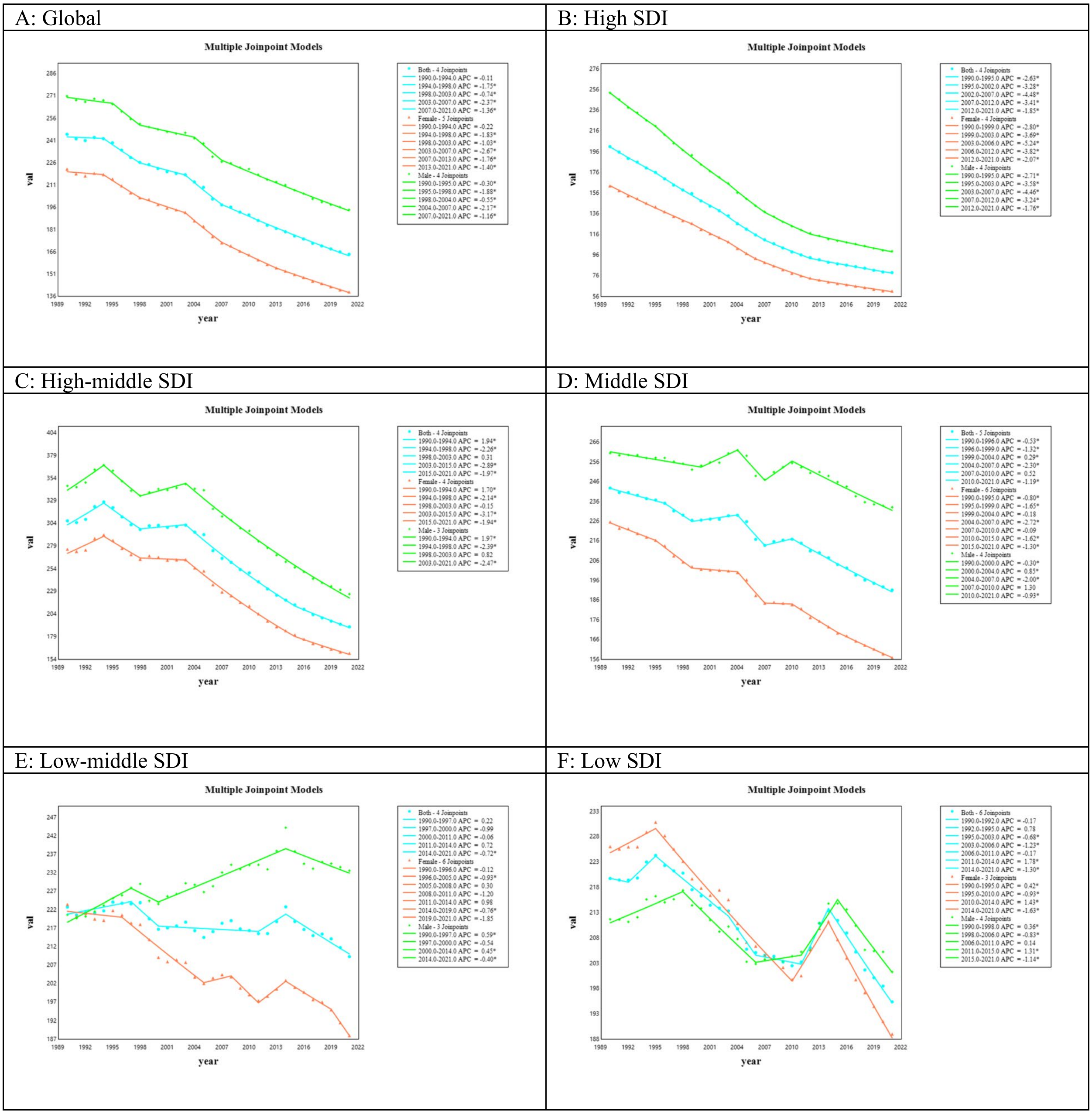

Fig. 3 Joinpoint regression analysis of age-standardized mortality rates (ASMR) for cardiovascular diseases attributable to metabolic risks (1990–2021). **A** Global ASMR; **B** High SDI Region; **C** High-middle SDI Region; **D** Middle SDI Region; **E** Low-middle SDI Region; **F** Low SDI Region

Impact of age, period, and cohort on cardiovascular disease mortality attributable to metabolic risks

The APC model was utilized to examine the effects of age, period, and cohort on mortality from cardiovascular diseases attributable to metabolic risks. These effects represent different dimensions of influence: Age effect: Reflects changes due to biological and social aging processes, such as the increased risk of cardiovascular diseases with age, which is a critical determinant of disease incidence. Period effect: Denotes changes resulting from factors that impact all age groups simultaneously, such as advancements in healthcare or economic recessions. Cohort effect: Indicates variations in disease rates across different generations due to differential exposure to risk factors. Findings from Fig. 4: A. Relationship Between Mortality and Age: Mortality rates increased with age across all SDI regions, as shown in Fig. 4A. The smallest increase in mortality with age was observed in the High

Table 3 AAPC in ASMR for cardiovascular diseases attributable to metabolic risks (1990–2021)

	Global		High SDI		High-middle SDI		Middle SDI		Low-middle SDI		Low SDI	
	Both	**P**	**Both**	**P**	**Both**	**P**	**Both**	**P**	**Both**	**P**	**Both**	**P**
Metabolic risks	− 1.28(− 1.42,− 1.14)	< 0.01	− 2.98(− 3.10,− 2.86)	< 0.01	− 1.51(− 1.78,− 1.23)	< 0.01	− 0.78(− 0.93,− 0.64)	< 0.01	− 0.16(− 0.39,0.07)	0.17	− 0.38(− 0.55,− 0.21)	< 0.01
High systolic blood pressure	− 1.33(− 1.49,− 1.17)	< 0.01	− 3.19(− 3.32,− 3.06)	< 0.01	− 1.53(− 1.79,− 1.26)	< 0.01	− 0.80(− 0.95,− 0.66)	< 0.01	− 0.15(− 0.39,0.09)	0.21	− 0.42(− 0.58,− 0.26)	< 0.01
High fasting plasma glucose	− 0.41(− 0.54,− 0.27)	< 0.01	− 1.90(− 1.98,− 1.83)	< 0.01	− 0.60(− 0.90,− 0.30)	< 0.01	0.10(− 0.08,0.29)	0.28	0.92(0.64,1.20)	< 0.01	0.56(0.35,0.77)	< 0.01
Kidney dysfunction	− 1.49(− 1.71,− 1.27)	< 0.01	− 3.32(− 3.39,− 3.25)	< 0.01	− 1.78(− 2.09,− 1.47)	< 0.01	− 0.88(− 1.06,− 0.70)	< 0.01	− 0.23(− 0.51,0.06)	0.12	− 0.38(− 0.61,− 0.15)	< 0.01
High LDL cholesterol	− 1.51(− 1.68,− 1.34)	< 0.01	− 3.53(− 3.67,− 3.39)	< 0.01	− 1.66(− 1.99,− 1.35)	< 0.01	− 0.41(− 0.57,− 0.24)	< 0.01	− 0.08(− 0.18,0.01)	0.11	− 0.16(− 0.35,0.02)	0.08
High body-mass index	− 0.21(− 0.37,− 0.05)	0.01	− 1.46(− 1.64,− 1.29)	< 0.01	− 0.48(− 0.85,− 0.11)	0.01	0.60(0.48,0.72)	< 0.01	1.17(1.11,1.24)	< 0.01	0.90(0.84,0.97)	< 0.01

Table 4 AAPC in ASMR for cardiovascular diseases attributable to metabolic risks among females (1990–2021)

	Global		High SDI		High-middle SDI		Middle SDI		Low-middle SDI		Low SDI	
	Female	**P**	**Female**	**P**	**Female**	**P**	**Female**	**P**	**Female**	**P**	**Female**	**P**
Metabolic risks	− 1.48(− 1.62, − 1.34)	< 0.01	− 3.14(− 3.30, − 2.98)	< 0.01	− 1.70(− 1.97, − 1.42)	< 0.01	− 1.16(− 1.29, − 1.03)	< 0.01	− 0.53(− 0.90, − 0.16)	< 0.01	− 0.57(− 0.70, − 0.44)	< 0.01
High systolic blood pressure	− 1.52(− 1.65, − 1.38)	< 0.01	− 3.32(− 3.49, − 3.14)	< 0.01	− 1.75(− 2.02, − 1.48)	< 0.01	− 1.18(− 1.31, − 1.05)	< 0.01	− 0.53(− 0.84, − 0.22)	< 0.01	− 0.61(− 0.73, − 0.48)	< 0.01
High fasting plasma glucose	− 0.61(− 0.71, − 0.52)	< 0.01	− 2.14(− 2.22, − 2.06)	< 0.01	− 0.78(− 1.10, − 0.47)	< 0.01	− 0.21(− 0.40, − 0.03)	0.02	0.66(0.29,1.03)	< 0.01	0.36(0.19,0.53)	< 0.01
Kidney dysfunction	− 1.71(− 1.90, − 1.52)	< 0.01	− 3.12(− 3.20, − 3.04)	< 0.01	− 1.92(− 2.24, − 1.60)	< 0.01	− 1.28(− 1.46, − 1.09)	< 0.01	− 0.53(− 0.91, − 0.16)	< 0.01	− 0.65(− 0.82, − 0.48)	< 0.01
High LDL cholesterol	− 1.75(− 1.94, − 1.57)	< 0.01	− 3.73(− 3.90, − 3.55)	< 0.01	− 1.84(− 2.15, − 1.53)	< 0.01	− 0.75(− 0.91, − 0.59)	< 0.01	− 0.47(− 0.64, − 0.29)	< 0.01	− 0.49(− 0.63, − 0.35)	< 0.01
High body-mass index	− 0.37(− 0.55, − 0.19)	< 0.01	− 1.60(− 1.72, − 1.49)	< 0.01	− 0.58(− 0.97, − 0.19)	< 0.01	0.23(0.08,0.37)	< 0.01	0.61(0.50,0.72)	< 0.01	0.50(0.45,0.56)	< 0.01

Table 5 AAPC in ASMR for cardiovascular diseases attributable to metabolic risks among males (1990–2021)

	Global		High SDI		High-middle SDI		Middle SDI		Low-middle SDI		Low SDI	
	Male	**P**	**Male**	**P**	**Male**	**P**	**Male**	**P**	**Male**	**P**	**Male**	**P**
Metabolic risks	− 1.07(− 1.22, − 0.92)	< 0.01	− 2.97(− 3.09, − 2.86)	< 0.01	− 1.38(− 1.65, − 1.10)	< 0.01	− 0.39(− 0.62, − 0.16)	< 0.01	0.17(0.11,0.26)	0.17	− 0.15(− 0.31, − 0.01)	0.06
High systolic blood pressure	− 1.11(− 1.26, − 0.95)	< 0.01	− 3.21(− 3.38, − 3.03)	< 0.01	− 1.31(− 1.57, − 1.06)	< 0.01	− 0.40(− 0.64, − 0.16)	< 0.01	0.20(0.13,0.26)	< 0.01	− 0.18(− 0.30, − 0.06)	< 0.01
High fasting plasma glucose	− 0.30(− 0.41, − 0.19)	< 0.01	− 1.91(− 1.99, − 1.83)	< 0.01	− 0.55(− 0.90, − 0.19)	< 0.01	0.36(0.13,0.58)	< 0.01	1.15(1.02,1.28)	< 0.01	0.72(0.48,0.95)	< 0.01
Kidney dysfunction	− 1.23(− 1.42, − 1.04)	< 0.01	− 3.06(− 3.17, − 2.94)	< 0.01	− 1.67(− 1.93, − 1.42)	< 0.01	− 0.48(− 0.70, − 0.26)	< 0.01	0.14(− 0.26,0.54)	0.50	− 0.16(− 0.45,0.13)	0.27
High LDL cholesterol	− 1.33(− 1.50, − 1.16)	< 0.01	− 3.50(− 3.61, − 3.40)	< 0.01	− 1.59(− 1.94, − 1.24)	< 0.01	− 0.08(− 0.35,0.19)	0.57	0.30(0.13,0.47)	< 0.01	0.14(− 0.02,0.29)	0.09
High body-mass index	0.04(− 0.11,0.18)	0.6	− 1.43(− 1.60, − 1.26)	< 0.01	− 0.27(− 0.54,0.01)	< 0.01	1.07(0.93,1.20)	< 0.01	1.90(1.83,1.96)	< 0.01	1.56(1.46,1.66)	< 0.01

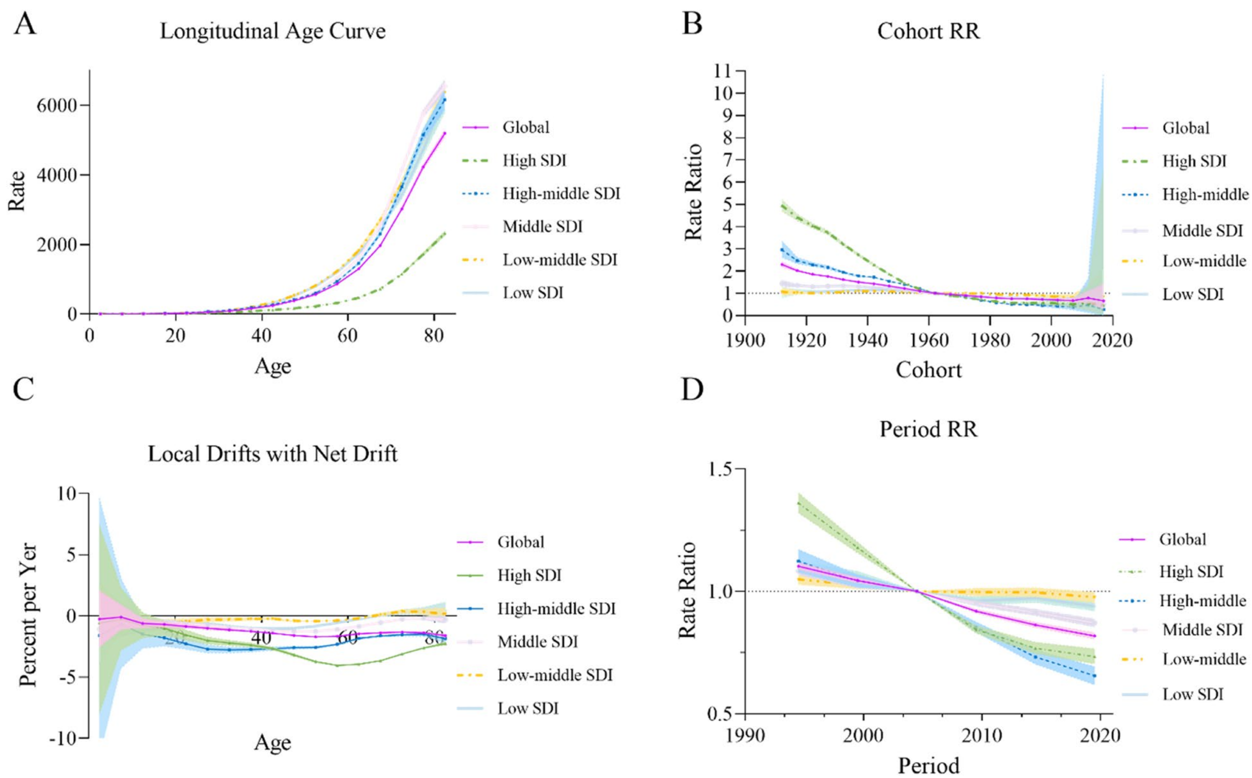

Fig. 4 Age-Period-Cohort (APC) model analysis for cardiovascular disease mortality attributable to metabolic risks. **A** Longitudinal Age Curve (Age Effect); **B** Cohort Relative Mortality (Cohort Effect); **C** Local Drifts with Net Drift (Temporal Trends); **D** Period Effect on Mortality (Period Effect)

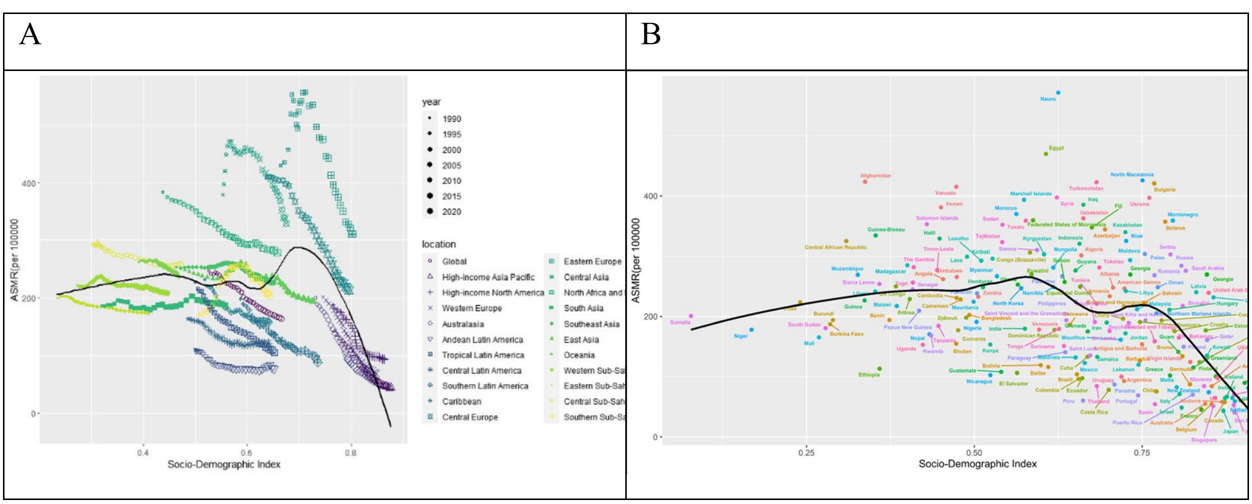

Fig. 5 Relationship between cardiovascular disease burden attributable to metabolic risks and socio-demographic index (SDI). **A** Global and 21 Regions: ASMR vs. SDI Relationship (1990–2021); **B** Global and 204 Countries: ASMR vs. SDI Relationship (2021)

SDI region, reflecting better prevention and management of metabolic risk factors in older populations. B. Relationship Between Mortality and Birth Cohort: Using the 1962–1967 birth cohort as the reference (set to 1), Fig. 4B shows that mortality generally decreased with more recent birth cohorts. High SDI regions exhibited the most pronounced decline in mortality rates across cohorts, while Low-middle SDI and Low SDI regions showed only modest reductions, suggesting persistent intergenerational disparities in exposure to metabolic

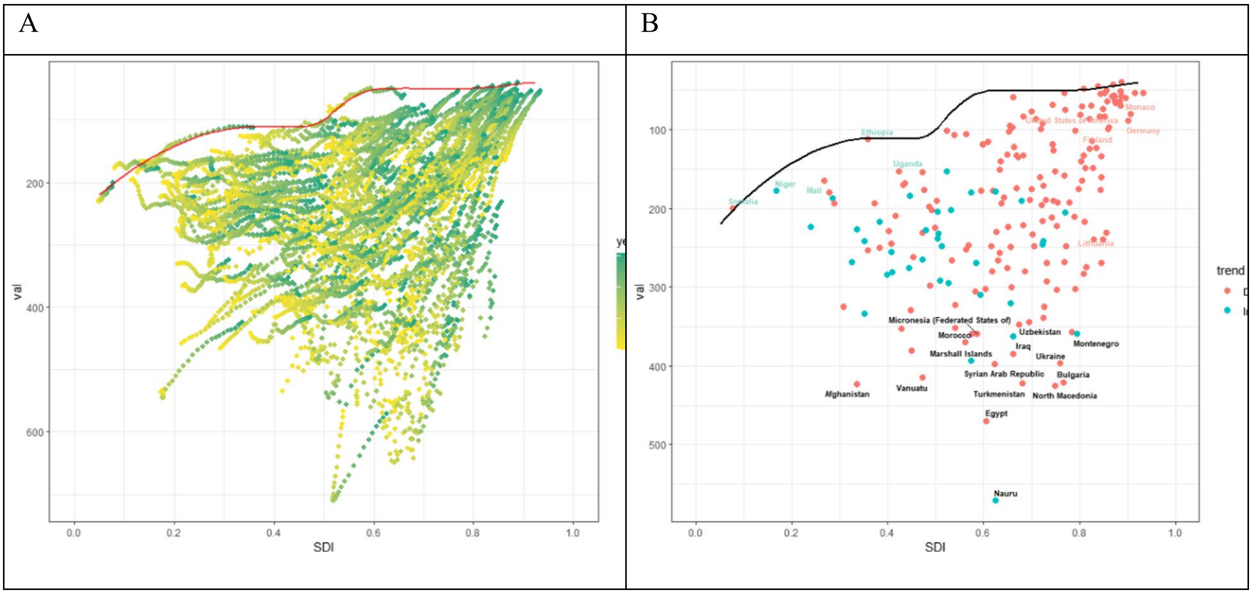

Fig. 6 Frontier analysis of the relationship between socio-demographic index (SDI) and Age-Standardized Mortality Rate (ASMR). **A** SDI and ASMR Trends (1990–2021); **B** 2021 Frontier Analysis for SDI and ASMR

risks. C. Temporal Trends in Age-Specific Mortality: Using the APC model, Fig. 4C estimated the APC in mortality for specific age groups, highlighting the influence of cohort effects. The global Net Drift (overall trend) was less than 0, with statistically significant *P*-values (< 0.05), indicating a decline in mortality over time. Across all age groups, mortality decreased annually in High SDI and High-middle SDI regions. However, in Low-middle SDI and Low SDI regions, mortality among individuals aged 67.5 years and above increased annually, underscoring the disproportionate burden in older populations in these regions. D. Relationship Between Mortality and Period: Using 2002–2017 as the reference period (set to 1), Fig. 4D demonstrates that mortality generally declined over time across most SDI regions. The High-middle SDI region experienced the steepest decline, while Low-middle SDI and Low SDI regions showed minimal reductions, reflecting stagnation in mortality improvements during recent years. The APC analysis reveals significant temporal and intergenerational trends in cardiovascular disease mortality attributable to metabolic risks. While global mortality has declined over time, substantial disparities remain across SDI regions. High and High-middle SDI regions benefit from consistent reductions in mortality across all age groups, driven by healthcare advancements and reduced cohort-specific exposure to metabolic risks. In contrast, older populations in Low-middle SDI and Low SDI regions face rising mortality rates, emphasizing the need for targeted interventions to address age-specific and cohort-specific metabolic risk burdens in these regions.

Relationship between cardiovascular disease burden attributable to metabolic risks and socio-demographic index (SDI)

Figure 5A Trends in ASMR and SDI (1990–2021). During 1990–2021, a parabolic relationship was observed between ASMR and SDI across the 21 GBD regions and globally. Between 1990 and 1998, the global ASMR attributable to metabolic risks exceeded expected levels based on SDI but fell below expectations from 1999 onward. Regions such as Eastern Europe, Central Europe, the Caribbean, North Africa, and the Middle East consistently exhibited ASMR above expected levels throughout the study period. Conversely, regions like Australasia, High-income North America, and Western Europe exceeded expectations only in recent years. In regions with SDI >0.7, the decline in ASMR over time was pronounced, reflecting significant improvements in cardiovascular health management. For regions with SDI <0.5, ASMR reductions were relatively modest, indicating slower progress in mitigating cardiovascular disease burden in low-SDI settings. Figure 5B: Relationship Between ASMR and SDI in 204 Countries (2021). A negative correlation was evident between ASMR and SDI, with higher SDI countries generally experiencing lower ASMR. Nauru showed a disproportionately high ASMR attributable to metabolic risks, significantly exceeding expectations based

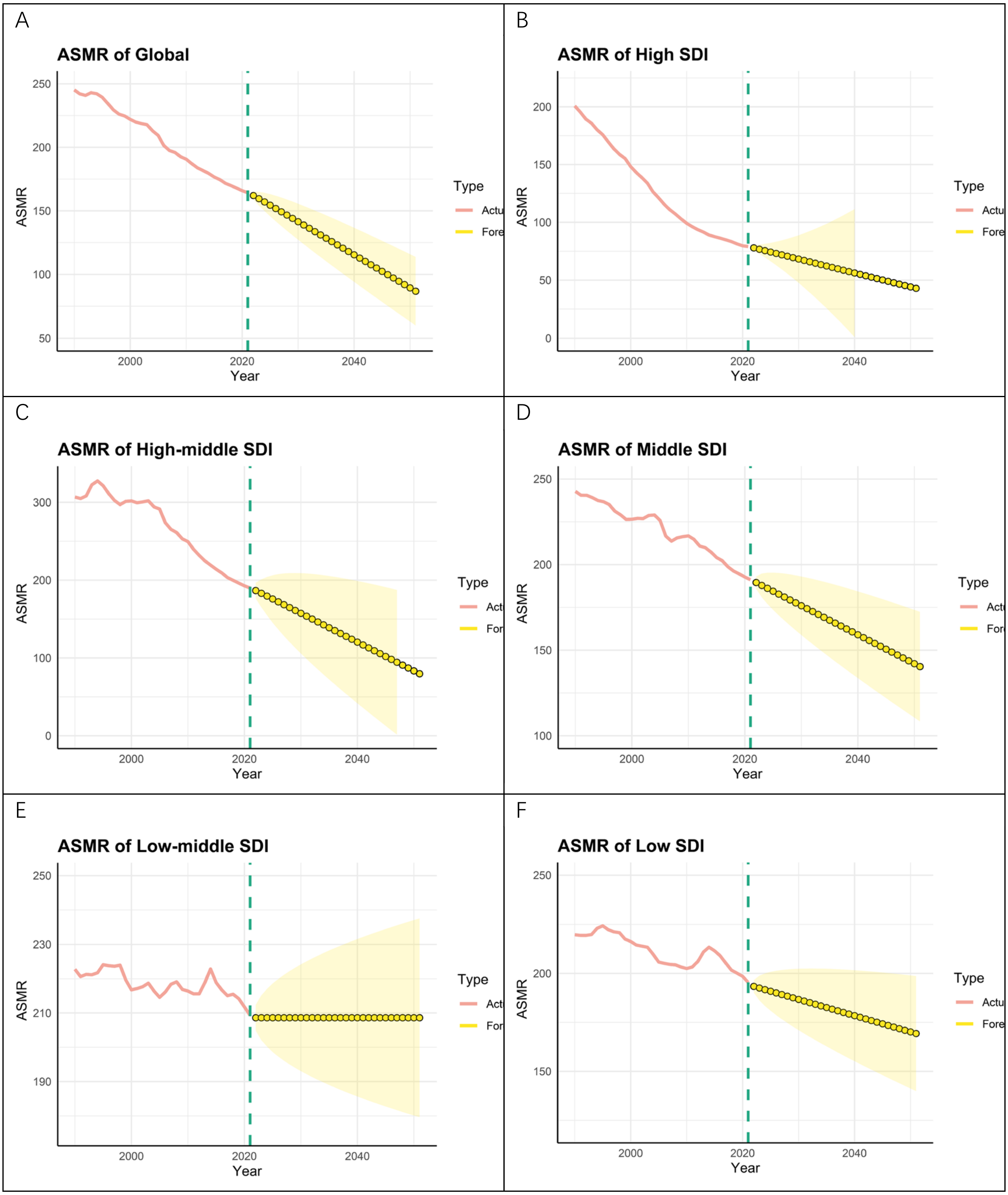

Fig. 7 Forecasted trends in cardiovascular disease mortality attributable to metabolic risks over the next 30 Years (Global and Five SDI Regions)

on its SDI level. Notably, some low-SDI regions, such as Ethiopia and Mali, maintained ASMR levels below expected values, suggesting effective management of metabolic risks despite limited resources. These findings highlight the strong association between SDI and ASMR for cardiovascular diseases attributable to metabolic risks. While higher-SDI regions demonstrate substantial reductions in ASMR, disparities persist, with several lower-SDI regions continuing to face significant challenges. Nonetheless, certain low-SDI regions outperform expectations, underscoring the potential for effective interventions even in resource-limited settings.

Frontier analysis: evaluating the relationship between disease burden and sociodemographic development

Frontier analysis is a critical quantitative tool that uses techniques such as Data Envelopment Analysis (DEA) and Locally Estimated Scatterplot Smoothing (LOESS) to evaluate and optimize health system performance. It is particularly useful in analyzing the relationship between disease burden and sociodemographic development by identifying"frontiers"or optimal benchmarks of performance. Findings from Fig. 6 A. Frontier Analysis of SDI and ASMR (1990–2021): Visualization: The red solid line represents the frontier (optimal practice boundary). Points represent individual countries or regions, with color gradients indicating progression over time (from lighter shades in 1990 to darker shades in 2021). Insights: As SDI increases, ASMR decreases, indicating that higher sociodemographic development correlates with lower cardiovascular disease burden attributable to metabolic risks. Countries with lower SDI levels exhibit greater potential for improvement in ASMR, suggesting that targeted interventions could significantly reduce their disease burden. B. 2021 SDI and ASMR Frontier Analysis: Visualization: Each point represents a specific country or region in 2021. The black solid line delineates the frontier. The top 15 countries with the largest effective differences (deviation from the frontier) are marked in black. Examples of countries with low SDI (< 0.5) and low effective differences (e.g., Somalia, Niger, Mali, Ethiopia, and Uganda) are marked in blue. Examples of countries with high SDI and relatively high effective differences (e.g., America, Monaco, Germany, Finland, and Lithuania) are marked in red. Red points indicate countries where ASMR has decreased from 1990 to 2021, while blue points indicate countries where ASMR has increased. Insights: Effective differences generally decline as SDI increases, highlighting the potential for substantial burden reductions in lower-SDI countries. Frontier countries (marked in blue) demonstrate effective management of metabolic risks relative to their development level, offering models for replication in similar settings. High-SDI countries with substantial effective differences (marked in red) indicate areas where improvements in metabolic risk management could further optimize outcomes. Frontier analysis underscores the significant relationship between sociodemographic development and cardiovascular disease burden attributable to metabolic risks. It highlights disparities in performance and identifies opportunities for improvement, particularly in lower-SDI countries with a high potential for burden reduction. At the same time, even high-SDI countries can benefit from targeted interventions to bridge gaps between current outcomes and optimal benchmarks.

ARIMA model: predicting cardiovascular disease mortality attributable to metabolic risks

The ARIMA model is a widely used time-series analysis method for forecasting future trends. By integrating autoregression (AR), differencing (I), and moving average (MA) components, ARIMA effectively captures trends and seasonality in data. The model is denoted as ARIMA (p, d, q): p (Autoregressive order): Indicates the number of prior observations used to predict the current value. d (Differencing order): Specifies how many differencing operations are needed to make the data stationary by eliminating trends or seasonality. q (Moving average order): Represents the number of prior error terms used in predicting the current value. Findings from Fig. 7 A. Global Trend (1990–2051): The red line shows the observed trend in mortality rates from 1990 to 2021, while the yellow dashed line and shaded region represent the predicted trend and 95% confidence intervals (CI) for the next 30 years. Globally, cardiovascular disease mortality attributable to metabolic risks is projected to continue declining over the next three decades.

B–F. Trends Across SDI Regions (1990–2051): High-middle SDI Region (Fig. 7C): This region is expected to experience the most significant decline in mortality rates, reflecting advancements in healthcare and effective management of metabolic risks. Middle and Low SDI Regions (Fig. 7D and F): Mortality rates in these regions are projected to decline at a slower pace, indicating persistent challenges in addressing metabolic risks. Low-middle SDI Region (Fig. 7E): Unlike other regions, this region is predicted to show almost no decline in mortality rates over the next 30 years, highlighting a critical need for targeted interventions and resource allocation. The ARIMA model provides valuable insights into future trends in cardiovascular disease mortality attributable to metabolic risks. While global mortality rates are expected to decline, disparities across SDI regions remain stark. The most significant progress is anticipated in high-middle SDI regions, whereas low-middle SDI regions face considerable barriers, with virtually no projected improvement. These findings underscore the importance of tailored strategies to accelerate progress in regions with slower reductions in mortality.

Discussion

This study investigated the trends in the global burden of cardiovascular diseases attributable to metabolic risks over the past three decades, focusing on mortality, DALYs, and age-standardized rates across different SDI regions. Key Findings: Global Decline in ASMR: From 1990 to 2021, the global ASMR attributable to metabolic risks decreased significantly (AAPC $= -1.28$, 95% CI: -1.42, -1.14, $P < 0.01$), while the absolute number of deaths increased from 8.33 million to 13.60 million. The simultaneous rise in deaths despite declining ASMR can be attributed to population growth, aging, and changes in mortality proportions, underscoring the persistent burden of cardiovascular diseases due to metabolic factors.

Age and Gender Disparities in Cardiovascular Disease Mortality Attributable to Metabolic Risks. Overall Trends in Mortality and DALY Rates: Both male and female ASMR and DALY rates have shown a general decline over the study period. Males consistently exhibit higher ASMR and DALY rates compared to females, which may be attributable to gender-based genetic and biological differences [7]. Despite the decline in ASMR and DALY rates, the absolute number of deaths and DALYs continue to rise due to global population growth and aging. Age is a critical factor, as ASMR increases significantly with advancing age for both sexes, highlighting the need for age-specific prevention strategies. Males show persistently higher ASMR and DALY rates compared to females across all SDI regions. The disparity is particularly pronounced in middle and low SDI regions, where male ASMR showed an increasing trend during 1990–2014 (APC $=0.32$, 95% CI: 0.27, 0.37, $P < 0.05$). Contributing factors include greater gender differences in lifestyle behaviors such as physical activity and smoking in lower SDI regions, compared to more uniform patterns in high SDI regions. These findings suggest the need for targeted prevention strategies aimed at reducing the cardiovascular disease burden among men and older populations. Gender-specific interventions, such as promoting healthier lifestyles and addressing behavioral risks (e.g., smoking cessation and physical activity promotion), could play a significant role in mitigating disparities [23–25]. Further research is required to explore additional factors driving gender disparities, particularly in low and middle-SDI regions, where social, cultural, and economic influences may exacerbate the burden of metabolic risks among men. Tailored interventions that address these region-specific and gender-specific differences could help close the gap in cardiovascular health outcomes. By focusing on age- and gender-specific prevention and treatment strategies, policymakers and healthcare providers can make significant strides in reducing the global cardiovascular disease burden attributable to metabolic risks.

Subtype-Specific Metabolic Risk

High systolic blood pressure (SBP) remains the leading metabolic risk factor contributing to the global burden of CVD across all SDI regions [26]. The ASMR due to high SBP has shown a consistent decline globally, with an AAPC of -1.33 (95% CI: -1.42, -1.14, $P < 0.05$). The age-standardized DALYs rate attributable to high SBP decreased from 3668.45 in 1990 to 2513.43 in 2021. These reductions highlight the significant global progress in managing high SBP over the past decades. In 2020, the International Society of Hypertension (ISH) introduced global practice guidelines for managing hypertension in adults aged 18 and older [27]. These guidelines were developed through a comprehensive review of existing evidence and are tailored for practical use across diverse healthcare settings. Notably, the guidelines emphasize applicability in both resource-rich and resource-limited environments, providing evidence-based, adaptable care standards to reduce the burden of hypertension worldwide. The sustained global efforts in SBP management, supported by guidelines such as those from the ISH, have significantly contributed to the decline in the CVD burden associated with high SBP. Expanding these initiatives, particularly in low- and middle-income countries, where access to care may be limited, will be critical in further reducing the global impact of high SBP on cardiovascular health. This success underscores the importance of international collaborations, evidence-based guidelines, and targeted interventions in addressing high-priority metabolic risks like elevated systolic blood pressure.

Impact of High BMI on Cardiovascular Disease Burden Across SDI Regions. Diverging Trends Across SDI Regions

High BMI-related CVD burden is decreasing in High SDI and High-middle SDI regions, reflecting increased attention to weight management and preventive healthcare in developed countries. In contrast, Middle SDI, Low-middle SDI, and Low SDI regions exhibit significant increases in the CVD burden attributable to high BMI, highlighting growing public health challenges in these settings. Advancements in High-SDI Regions: Developed countries have adopted comprehensive approaches to weight management, including behavioral interventions, pharmacological treatments, and surgical options, as emphasized in CVD prevention guidelines [28]. These efforts underscore the importance of promoting healthy weight and mitigating obesity-related risks to reduce the overall CVD burden. Challenges in Low- and Middle-SDI Regions: The use of weight-loss medications remains limited due to restricted availability, safety concerns, and public skepticism toward their efficacy [29]. Many cardiovascular specialists in developing countries fail to prioritize weight management for CVD prevention and treatment, indicating a gap in clinical practice and public health education. Public Health Implications of Obesity: Obesity is a critical and widespread public health issue, particularly in low-resource settings. Addressing obesity through effective strategies represents one of the most cost-effective approaches for preventing early-onset CVD, particularly among younger populations. These strategies include: Lifestyle Modifications: Promoting healthy dietary habits, such as reducing the intake of processed foods, salt, and sugar-sweetened beverages, while encouraging the consumption of fruits, vegetables, whole grains, and lean protein sources. Increased Physical Activity: Implementing tailored and structured programs, including aerobic exercise and strength training, has been shown to be effective for weight management when customized to individual needs.Behavioral Support: Interventions such as cognitive-behavioral therapy (CBT), community support groups, and other structured behavioral therapy approaches can assist in achieving and maintaining long-term weight loss.Policy Measures: Public health strategies, such as imposing taxes on sugar-sweetened beverages, introducing nutrition labeling, and improving access to healthy foods in underdeveloped areas, can facilitate healthier choices on a broader scale. Pharmacological Interventions: For individuals who fail to achieve significant weight loss through non-pharmacological means, medical interventions such as pharmacotherapy or bariatric surgery may be considered under the guidance of healthcare professionals.

For Low- and Middle-SDI Regions

Increase accessibility and affordability of safe and effective weight management interventions, including pharmacological and surgical options. Promote community-based programs to encourage healthy lifestyles, including balanced diets and regular physical activity. Enhance awareness among healthcare providers about the importance of weight management in preventing and managing CVD, especially for high-risk patients. For High-SDI Regions: Continue to prioritize weight management programs, emphasizing sustainable behavioral and lifestyle modifications. Share best practices with lower-SDI regions to help address disparities in obesity management and reduce the global burden of CVD. The increasing burden of high BMI-related cardiovascular diseases in low- and middle-SDI regions underscores the urgent need for effective public health strategies. While high-SDI regions demonstrate the benefits of prioritizing weight management, addressing barriers to care and raising awareness in low-resource settings are crucial steps to combat the growing obesity epidemic and its impact on global cardiovascular health [26].

Impact of Elevated Fasting Plasma Glucose on Cardiovascular Disease Burden in Low- and Middle-SDI Regions. Rising Trends in Low-SDI and Low-Middle SDI Regions: The CVD burden attributable to elevated fasting plasma glucose (FPG) is increasing in Low-middle SDI and Low SDI regions, contrasting with declining trends in high-SDI countries. Declining Burden in High-SDI Regions: Developed countries have successfully reduced the CVD burden associated with high FPG due to effective diabetes management programs, improved healthcare access, and widespread public health initiatives [30]. Challenges in Developing Countries: A large-scale study spanning 49 developing countries revealed that glycemic control among patients with type 2 diabetes is suboptimal, reflecting gaps in diabetes care and self-management practices [31]. Limited access to healthcare services, inadequate diabetes education, and insufficient resources hinder progress in controlling high FPG-related risks. Enhance Healthcare Accessibility and Quality: Strengthen healthcare infrastructure to improve access to diagnostic tools, medications, and follow-up care for diabetes management in resource-limited settings. Train healthcare providers in evidence-based guidelines for managing diabetes and associated cardiovascular risks. Promote Self-Management and Patient Education: Increase efforts to educate patients on the importance of blood glucose monitoring, medication adherence, and lifestyle modifications. Develop culturally sensitive educational programs tailored to local contexts, emphasizing the role of diet and exercise in managing diabetes. Expand Public Health Campaigns: Launch national campaigns to raise awareness about diabetes prevention, early detection, and the link between elevated FPG and cardiovascular diseases. Engage communities through outreach initiatives to empower individuals with knowledge and tools for effective diabetes management. Leverage International Guidelines: Utilize the 2022 consensus report by the American Diabetes Association and the European Association for the Study of Diabetes, which provides comprehensive guidance on managing diabetes and preventing CVD in high-risk populations [30]. The increasing burden of elevated fasting plasma glucose on cardiovascular health in low-SDI and low-middle SDI regions demands urgent action. Enhancing healthcare accessibility, improving medical education, and promoting public awareness are critical for reversing these trends. Leveraging international best practices while addressing local challenges can pave the way for improved diabetes care and cardiovascular outcomes in developing countries.

The study identifies a nonlinear yet overall negative correlation between a country's Socio-Demographic Index (SDI) and the CVD burden attributable to metabolic risks. Higher SDI countries generally exhibit lower ASMR, reflecting advanced healthcare systems and better management of metabolic risk factors. Nauru demonstrates an ASMR significantly exceeding expectations, highlighting unmet needs in addressing metabolic risks despite its development level. Conversely, low-SDI regions such as Ethiopia and Mali achieve ASMR below predicted levels, showcasing effective health interventions and risk management in resource-constrained environments. The global pattern of CVD burden does not adequately represent country-specific contexts, underlining the importance of national-level data in shaping health policy and interventions. Evaluating health system performance solely based on observed burden is insufficient. Instead, comparing actual burden with expected burden, adjusted for development level, provides a clearer picture of preventable causes and areas for improvement. Countries exceeding expected burdens (e.g., Nauru) require urgent investigation to address gaps in healthcare delivery and metabolic risk management. Frontier countries (e.g., Ethiopia, Mali) can serve as models for effective health interventions in similar low-resource settings. Health-related decision-making should prioritize country-specific patterns rather than relying solely on global averages. Tailored strategies that account for local contexts are essential for effective burden reduction. Investigate factors contributing to disproportionately high burdens in certain countries (e.g., Nauru) to identify preventable causes and implement targeted interventions. Address systemic barriers in healthcare access, resource allocation, and public health strategies. Study successful approaches in low-SDI frontier countries (e.g., Ethiopia, Mali) to identify scalable interventions and best practices for other resource-limited settings. Encourage the use of country-level data to inform health policies and prioritize interventions tailored to national contexts, especially in countries with high preventable burdens. This study underscores the importance of comparing actual and expected CVD burdens to evaluate health system performance effectively. While higher SDI generally correlates with lower burdens, outliers in both directions provide critical insights into effective practices and areas requiring immediate attention. Decision-making should be grounded in national-level data to address disparities and optimize outcomes.

According to ARIMA model predictions, over the next three decades (2022–2051), CVD mortality attributable to metabolic risk factors is projected to decline steadily. This finding aligns with prior research reporting global trends, where advancements in medical technologies, improved management of metabolic risk factors, and public health measures targeting lifestyle modifications have collectively contributed to significant reductions in CVD mortality rates [6, 32]. Notably, the enhanced screening and control of hypertension, diabetes, and dyslipidemia in high-income regions have likely been key drivers of this decline [33]. However, the ARIMA model also highlights that, despite declining mortality rates, the absolute number of deaths remains alarmingly high due to population growth and aging, consistent with other time-series studies on global CVD trends [34].

In middle-to-high SDI regions (Fig. 7C), CVD mortality rates are projected to decrease substantially, which is consistent with prior studies attributing this decline to robust healthcare infrastructure, increased metabolic risk screening, and the effective implementation of national health policies [35, 36]. For instance, studies from regions like Eastern Europe and East Asia have demonstrated significant improvements in CVD outcomes following strategies such as salt reduction initiatives, smoking cessation programs, and the widespread use of statins and antihypertensive medications [37]. The ARIMA predictions further underscore the effectiveness of continued investment in health interventions aimed at addressing metabolic risk factors [38]. In middle-to-low SDI regions (Fig. 7D and F), the model predicts that the rate of decline in CVD mortality will be significantly slower compared to high-income regions. This aligns with existing literature, which identifies severe social, economic, and infrastructural barriers that hinder the effective prevention and management of metabolic risks in these areas. Limited access to medications, insufficient awareness of risk factors, and underdeveloped healthcare systems contribute to stagnated progress [37]. For example, evidence from sub-Saharan Africa indicates that a large proportion of individuals with hypertension and diabetes remain undiagnosed or untreated, further exacerbating CVD-related mortality [37, 38]. Particularly concerning are the projections for certain middle-to-low SDI regions (Fig. 7E), where negligible reductions in CVD mortality are expected over the next three decades. This highlights grave inequalities in the accessibility and effectiveness of healthcare services. Studies conducted in parts of South Asia and Latin America reveal that resource allocation challenges, diagnostic delays, and poor treatment adherence are key drivers of the high CVD burden [2, 38]. Our findings emphasize the urgent need for targeted, long-term public health interventions to prevent and manage metabolic disorders in these vulnerable populations.

The results of the ARIMA analysis, which demonstrate a global decline in age-standardized mortality rates (ASMR) alongside a widening gap between higher and lower SDI regions, support conclusions from previous studies on CVD trends. For example, the 2019 Global Burden of Disease Study similarly concluded that progress has been uneven, particularly in resource-limited settings. Collectively, these studies underline the need for sustained international efforts to address the socioeconomic determinants of health, including improving education about metabolic risk factors, ensuring affordability of medications, and strengthening primary healthcare systems [39].

Insights from Frontier Analysis

Countries such as Somalia, Niger, Mali, Ethiopia, and Uganda have achieved relatively low ASMR attributable to metabolic risks, despite their limited resources. These nations demonstrate effective strategies for managing CVD burden, providing valuable models for other low-resource countries with high CVD burdens. Conversely, countries like Egypt, Afghanistan, and Vanuatu exhibit rising ASMR due to metabolic risks, far exceeding expected levels based on their SDI. These trends indicate systemic healthcare challenges and require immediate attention. Exploring the success factors of low-SDI frontier countries can help identify scalable interventions, such as community-based programs, innovative resource utilization, and robust public health campaigns. Countries with disproportionately high ASMR (e.g., Egypt, Afghanistan, Vanuatu) highlight critical gaps in healthcare systems, requiring tailored solutions to address unique challenges. Factors such as limited healthcare access, inadequate public health education, and poor management of metabolic risks may be driving these trends. The rising ASMR in high-burden countries necessitates international collaboration to mitigate disparities in health outcomes, focusing on resource allocation, capacity-building, and knowledge transfer. Conduct indepth studies to identify key drivers of success in low-SDI frontier countries, including cultural, policy, and systemic factors. Disseminate these findings to other resource-constrained nations for potential adoption and adaptation. Develop customized action plans for high-burden outliers, addressing specific barriers to effective CVD management and prevention. Invest in strengthening healthcare infrastructure, enhancing provider training, and implementing evidence-based public health initiatives. Mobilize global resources to support countries with rising ASMR, ensuring equitable healthcare access and addressing socioeconomic determinants of health. Facilitate knowledge-sharing networks to spread best practices from frontier countries to those lagging. Low-SDI frontier countries offer critical insights into achieving positive health outcomes despite limited resources, serving as models for others. However, the alarming trends in nations with rising ASMR underscore the urgency of addressing systemic inequities and healthcare deficiencies. International focus and collaboration are essential to bridging these gaps and ensuring more equitable cardiovascular health outcomes globally.

This study utilized the 2021 GBD database, which is widely employed for analyzing health burdens at global, regional, and national levels. Recently, several studies based on the same database have been published, providing relevant analyses on the burden of cardiovascular diseases and metabolic risk factors across different populations [40–46]. While the aforementioned studies are also based on the GBD database, their objectives, methodologies, and focal points differ from those of the present study. The unique contribution of this study lies in its comprehensive analysis of the cardiovascular disease burden across all age groups, augmented by the incorporation of Joinpoint regression, APC analysis, and ARIMA modeling, which provide a broader perspective on historical trends and future projections. In defining the study population, our analysis spans all age groups and includes a detailed methodological description of data stratification by five-year age intervals, as outlined in the methods section. This study offers age-stratified data analysis, which is particularly critical for understanding the impact of metabolic risk factors on the cardiovascular disease burden across different age groups.

The study by Chen et al. analyzed the global burden of cardiovascular diseases attributable to metabolic risk factors across 204 countries and territories from 1990 to 2021 [46]. While we acknowledge that the use of the same database may introduce a degree of data overlap, the two studies differ significantly in their research objectives, analytical approaches, and presentation of results. This study integrates multiple quantitative analytical methods, including Joinpoint regression, ARIMA modeling, and APC analysis, to provide a more comprehensive understanding of trends in cardiovascular disease burden. Additionally, it offers predictive insights to guide global and regional health policy formulation over the next three decades. By addressing the potential overlap and delineating the differences between the two studies, this work further highlights its academic value and practical significance. In contrast to Zhou XD et al. [44], which focuses on adolescents and young adults aged 15–39, our study encompasses all age groups, highlighting the unique burden across diverse age strata. Similarly, while Zhang J et al. [43] predominantly investigate the burden and trends of metabolism-related ischemic stroke, our analysis thoroughly assesses the broader impact of metabolic risk factors on the full spectrum of cardiovascular diseases. Additionally, Liang J et al. [40] specifically address the effects of metabolic risk factors on atrial fibrillation, whereas our study expands its scope to provide a comprehensive examination of the cardiovascular disease burden. We recognize the possible issues regarding data overlap given the shared use of the GBD database. Nonetheless, our study is distinct in analytical scope and methodological approach. By integrating Joinpoint regression, APC analysis, and advanced ARIMA modeling, we further elucidate trends and anticipate future trajectories of the cardiovascular disease burden, thereby contributing a unique perspective to global public health research. The synthesis of these sophisticated methodologies with the comprehensive GBD dataset significantly enhances the originality and relevance of our findings. Our study delivers crucial insights into historical trends and future patterns of cardiovascular disease burden, supplying an essential evidence base for the development of targeted health interventions in regions with varying SDI levels and specific metabolic risk factors.

Study limitations

Data Quality and Availability

The accuracy of the estimates may vary due to differences in the quality and availability of data across countries and regions. In low- and middle-income countries, the lack of reliable epidemiological data and underreporting of cardiovascular disease cases could lead to an underestimation of the true burden. Modeling Assumptions in GBD Methodology: The GBD methodology relies on various assumptions and modeling techniques to estimate disease burden. These assumptions may introduce uncertainties in the estimates, particularly when extrapolating data to regions with sparse or inconsistent reporting. Implications for Future Research: Strengthen data collection and surveillance systems in low- and middle-income countries to improve the accuracy of disease burden estimates. Conduct sensitivity analyses to assess the robustness of estimates and identify areas where data improvements are most needed. Although the ARIMA model is powerful, it has certain limitations: Assumption of Linear Patterns: The ARIMA model assumes that past trends (e.g., autoregressive components) and seasonal behaviors can adequately predict future patterns. However, unexpected nonlinear changes—such as the effects of new interventions, pandemics, or economic shifts—may compromise the accuracy of its predictions. Dependence on Stationarity: To generate meaningful outputs, ARIMA requires data to be stationary, necessitating differencing (I) to eliminate trends or seasonality. This preprocessing step may over-simplify some of the complex dynamics inherent in real-world circumstances. Lack of Causal Interpretation: While ARIMA identifies temporal trends, it does not evaluate causal relationships between variables, limiting its utility in identifying the underlying drivers of the observed patterns. Despite these limitations, ARIMA remains a robust and effective tool for forecasting epidemiological trends when applied with careful interpretation and an acknowledgment of its constraints.

Conclusion

In conclusion, despite the decline in age-standardized prevalence, the absolute burden of cardiovascular disease due to metabolic factors remains relatively high, with large variations between regions, countries, and SDI areas. Between 2020 and 2050, global standardized mortality rates are expected to decrease. However, low- and middle-SDI regions are projected to see only minimal improvements, underscoring the persistence of regional inequities. In low-SDI regions, population growth and aging are the primary drivers of this high absolute burden.

To address these challenges, tailored strategies should be prioritized in resource-limited settings. Efforts must focus on expanding access to essential healthcare services, strengthening healthcare infrastructure, and improving care quality through evidence-based practices. Community-based programs that encourage healthier dietary habits, increased physical activity, and reduced use of tobacco and alcohol are vital. Additionally, tackling the underlying social determinants of health and addressing socioeconomic disparities is essential to fostering equitable conditions for disease prevention and management.

Scaling up the most cost-effective prevention and management strategies in high-burden regions is critical. Policies should be adapted to local contexts while drawing on successful examples from similar settings. Collaborative efforts to reinforce healthcare systems, promote healthy lifestyles, and bridge gaps in healthcare access can substantially reduce the global burden of CVD attributable to metabolic risks, particularly in low-resource environments.

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Authors' contributions

ZXY and SMQ conceived and designed this manuscript. ZXY. JZM and LX analyzed and interpreted the data of this study. ZXY wrote the original draft. SFF and TJW reviewed and edited the manuscript. All authors contributed to drafting and revising the article approved the final version to be published.

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Data availability
This study employed publicly available data sets for analysis. The data can be accessed here: https://vizhub.healthdata.org/gbd-results/. Should further information regarding the data presented in this study be required, the corresponding author may be contacted.

Declarations

Ethics approval and consent to participate
The GBD data are de-identified and publicly accessible, exempting the study from institutional ethics board review.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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