

## Analysis of Cardiovascular Disease Burden Attributable to Metabolic Factors in China, 1990-2021, and Prediction of Burden Trends, 2022-2035: A Postprint

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### Abstract

Background Metabolic factors have become the primary driver of the continuously rising burden of cardiovascular disease (CVD) in China. Objective To evaluate the changing trends in the burden of CVD attributable to metabolic risk factors in China from 1990 to 2021 and to forecast the development trajectory for 2022-2035 using the BAPC model. Methods Based on the GBD 2021 database, the population attributable fraction (PAF) method was employed to quantify the contributions of Level I risk factors and major Level II risk factors (hypertension, air pollution, smoking, high low-density lipoprotein cholesterol, diet-related risks, etc.) to CVD mortality and disability-adjusted life years (DALYs). Joinpoint regression was used to analyze the annual trends in CVD attributable to metabolic factors from 1990 to 2021, and the average annual percentage change (AAPC) of the burden attributable to major metabolic factors was calculated. Finally, the Bayesian age-period-cohort (BAPC) model was integrated to project the burden trends for 2022-2035. Results From 1990 to 2021, the age-standardized DALYs rate for CVD attributable to metabolic factors in China decreased by 4.3% (from 3,927.3/100,000 to 3,756.4/100,000), while the mortality rate increased by 24.9% (from 169.3/100,000 to 211.5/100,000). In 2021, the PAF of metabolic factors for CVD DALYs and mortality was 68.6% and 70.1%, respectively, with hypertension consistently ranking as the leading causative factor, accounting for 53.3% and 55.4% of DALYs and mortality, respectively. Among the four major metabolic factors, the burden associated with high body mass index (BMI) exhibited the most significant growth rate, with its attributable DALYs rate increasing from 281.04/100,000 to 396.09/100,000 (AAPC=1.08%,  $P<0.0001$ ) and mortality rate rising from 13.73/100,000 to 18.80/100,000 (AAPC=1.00%,  $P<0.0001$ ). By contrast, the burden related to

high fasting plasma glucose and high low-density lipoprotein cholesterol showed relatively modest changes, with minimal fluctuations in DALYs and mortality rates during this period, and most AAPC differences were not statistically significant. Sex- and age-stratified analyses revealed that the burden was heaviest among elderly males, with sex disparities widening with advancing age. BAPC model-based projections indicated a continued declining trend in CVD burden through 2035: mortality rates are expected to decrease from 291.97/100,000 in 2022 to 183.33/100,000 in males and from 149.26/100,000 to 103.00/100,000 in females; DALYs rates are projected to decline from 5,296.99/100,000 to 3,274.07/100,000 in males and from 2,863.17/100,000 to 1,814.15/100,000 in females. The projections showed a pronounced inflection point of decline around 2030 for males, whereas females exhibited a sustained and steady downward trend. The mean absolute percentage error (MAPE) for all four indicators was below 2%, indicating high predictive accuracy. Conclusion High BMI and hypertension represent the primary metabolic risk factors, with projections indicating that their attributable burden may continue to rise. Males and elderly populations bear a heavier burden, while BMI-related risks are particularly prominent among young and middle-aged adults. Stratified prevention and control measures should be strengthened.

## Full Text

### Burden of Cardiovascular Diseases Attributable to Metabolic Risk Factors in China, 1990-2021 and Projected Trends from 2022-2035

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## Abstract

**Background:** Metabolic risk factors have become a primary driver of the increasing burden of cardiovascular diseases (CVDs) in China. **Objective:** To assess the temporal trends of CVD burden attributable to metabolic risk factors in China from 1990 to 2021 and project future burden through 2035 using the BAPC model. **Methods:** Based on data from the Global Burden of Disease Study 2021 (GBD 2021), we quantified the contributions of level 1 and major level 2 risk factors (e.g., high blood pressure, air pollution, smoking, high LDL cholesterol, and dietary risks) to CVD mortality and disability-adjusted

life years (DALYs) using the population attributable fraction (PAF) method. Joinpoint regression was applied to estimate the average annual percent change (AAPC) of CVD burden attributable to metabolic factors from 1990 to 2021. A Bayesian age-period-cohort (BAPC) model was used to project future burden trends from 2022 to 2035. **Results:** From 1990 to 2021, the age-standardized DALY rate of CVDs attributable to metabolic factors declined by 4.3% (3,927.3 per 100,000 to 3,756.4 per 100,000), while the mortality rate increased by 24.9% (169.3 per 100,000 to 211.5 per 100,000). In 2021, metabolic factors accounted for 68.6% of CVD-related DALYs and 70.1% of CVD deaths. Elevated systolic blood pressure remained the leading risk factor, contributing 53.3% and 55.4% to DALYs and deaths, respectively. Among the four main metabolic risks, high body mass index (BMI) showed the most significant increase, with the attributable DALY rate rising from 281.04 to 396.09 per 100,000 (AAPC=1.08%,  $P<0.0001$ ), and the mortality rate increasing from 13.73 per 100,000 to 18.80 per 100,000 (AAPC=1.00%,  $P<0.0001$ ). In contrast, the burden associated with high fasting plasma glucose and high LDL cholesterol changed minimally, with most AAPCs showing no statistical significance. Age- and sex-stratified analyses indicated the heaviest burden among older males, with widening gender differences at older ages. Projections based on the BAPC model suggest a continued decline in CVD burden by 2035: for males, the mortality rate is projected to decrease from 291.97 per 100,000 to 183.33 per 100,000 and the DALY rate from 5,296.99 per 100,000 to 3,274.07 per 100,000; for females, mortality is projected to decline from 149.26 to 103.00 per 100,000 and DALYs from 2,863.17 per 100,000 to 1,814.15 per 100,000. A clear downward inflection point is expected around 2030 in males, while a steady decline is projected for females. All model predictions had mean absolute percentage errors (MAPE) below 2%, indicating high predictive accuracy. **Conclusion:** High BMI and high blood pressure remain the predominant metabolic risk factors for CVDs in China. The projected burden attributable to these risks is expected to continue rising, with males and older adults experiencing a higher burden. Younger adults are increasingly affected by BMI-related risks, highlighting the need for targeted, stratified prevention strategies.

**Keywords:** Cardiovascular disease; Metabolic risk factors; Global Burden of Disease; DALYs; Mortality; Projection

## Introduction

Cardiovascular disease (CVD) has remained the leading cause of death globally and among Chinese residents for many consecutive years, posing a substantial threat to population health and socioeconomic development. According to the latest Global Burden of Disease (GBD) data, CVD caused 19.8 million deaths worldwide in 2021, accounting for 32% of all deaths, with China recording the highest number of CVD deaths globally and bearing a particularly pronounced disease burden. With China's rapid economic development and population aging, the prevalence and mortality of CVD have continued to rise, placing

heavy pressure on the healthcare system and society.

Among the numerous CVD risk factors, the role of metabolic risk factors has become increasingly prominent. Metabolic abnormalities such as hypertension, hyperglycemia, elevated low-density lipoprotein cholesterol, and high BMI have emerged as the primary drivers of the sustained increase in CVD burden among Chinese residents, with attributable risks far exceeding those of traditional behavioral and environmental factors. Although China's chronic disease prevention and control system has been continuously improving, the CVD burden associated with metabolic risk factors remains severe. The GBD 2021 systematically integrates multi-source health data and applies population attributable fraction (PAF) and disability-adjusted life years (DALYs) metrics to achieve standardized, comparable dynamic assessments of major diseases and risk factors at global, regional, and national levels. Recent studies based on the GBD database have revealed the overall trends and regional distribution characteristics of CVD burden in China and globally. However, systematic analyses of the structural changes in burden attributable to multiple metabolic risk factors, sex and age differences, and future burden projections remain lacking.

Therefore, this study, based on the GBD 2021 database, systematically evaluates the CVD burden attributable to major metabolic risk factors in China from 1990 to 2021 and employs a Bayesian age-period-cohort (BAPC) model to project burden levels through 2035, aiming to provide scientific evidence for optimizing chronic disease prevention strategies and targeting interventions for priority populations.

## Methods

### Data Sources

This study utilized data from the GBD 2021 database (<https://vizhub.healthdata.org/gbd-results/>), which systematically assessed 371 diseases and injuries and 88 risk factors across 204 countries and territories, covering incidence, prevalence, mortality, and other indicators. We extracted data on deaths, mortality rates, DALY rates, age-standardized mortality rates (ASMR), and age-standardized DALY rates (ASDR) for CVD attributable to metabolic factors in China from 1990 to 2021, as well as burden attribution metrics for each metabolic risk factor (high systolic blood pressure [hypertension], high fasting plasma glucose, high low-density lipoprotein cholesterol, and high BMI). GBD classifies CVD diagnoses according to the International Classification of Diseases, 10th Revision (ICD-10) standards.

### Study Population

The study population comprised the entire Chinese population from 1990 to 2021, stratified by sex and age groups [15–49 years (young and middle-aged), 50–69 years (middle-aged and elderly), and ≥ 70 years (elderly)]. The analysis

included three groups: the total population, males, and females, focusing on the changing trends of metabolic risk factors' impact on CVD deaths and DALYs across different populations. To simulate future disease burden trends, we constructed a BAPC model based on observed data from 1990-2021 to project age-standardized CVD mortality and DALY rates in China from 2022 to 2035. Projection results were stratified by sex, with analytical methods consistent with historical trend analyses.

## Research Methods

This study employed the population attributable fraction (PAF) method to quantify the contribution of major metabolic risk factors to CVD burden. PAF is calculated based on risk factor exposure levels and relative risk (RR) to assess the proportion of CVD attributable to each factor, providing clear guidance for public health interventions. Separate models were constructed for the four major metabolic factors, with Joinpoint regression analysis applied to their standardized mortality and DALY rates to determine trend significance by comparing average annual percentage changes (AAPC). The Joinpoint regression model, developed by the U.S. National Cancer Institute (NCI), was used to analyze the annual percentage change (APC), AAPC, and 95% confidence intervals (CI) of age-standardized CVD mortality and DALY rates attributable to metabolic factors from 1990 to 2021.

For predictive analysis, the BAPC model was employed to model and estimate age-standardized CVD mortality and DALY rates from 2022 to 2035. Implemented using the BAPC and INLA packages in R software, the model captures long-term trends and calculates prediction error metrics such as mean absolute percentage error (MAPE) and root mean square error (RMSE) to evaluate model fit and predictive accuracy.

## Results

### Trends in CVD Burden Attributable to Metabolic Risk Factors in China, 1990-2021

From 1990 to 2021, trends in CVD mortality and DALY rates attributable to metabolic risk factors in China showed significant fluctuations occurring at similar time points [Figure 1: see original paper]. Between 1998 and 2004, the total population experienced the largest mortality increase (APC=4.60, 95%CI=2.02-4.82), reflecting a sharp rise in CVD burden during this period. From 2004 to 2007, mortality briefly declined (APC=-1.08, 95%CI=-1.47 to -0.53), showing a negative growth trend. Subsequently, mortality rose again from 2010 to 2021, with a significant increase from 2018 to 2021 (APC=2.61, 95%CI=1.69-3.79).

Trends in CVD burden for female and male populations were generally similar to the total population, but male mortality showed greater increases during 1990-1998 (APC=1.99, 95%CI=1.70-2.23) and 2010-2021 (APC=1.72,

95%CI=1.56-1.86). For DALY rates, the largest change occurred during 1998-2004 (APC=3.73, 95%CI=3.57-3.87). From 2004 to 2007, DALY rates showed negative growth (APC=-0.84, 95%CI=-1.13 to -0.53), indicating weakened influence of metabolic risk factors during this period.

The total population AAPC was 1.59 (95%CI=1.55-1.64), with female and male AAPCs of 1.14 (95%CI=1.10-1.18) and 1.90 (95%CI=1.86-1.94), respectively, all statistically significant ( $P<0.0001$ ) [TABLE:1, TABLE:2].

### **Comparison of CVD Attributable Fractions from Metabolic and Other Major Risk Factors in China, 2021**

In 2021, metabolic risk factors accounted for 68.6% (95%CI=60.6%-75.1%) of CVD DALYs and 70.1% (95%CI=62.4%-76.6%) of CVD deaths, significantly higher than behavioral risk factors (DALYs PAF=46.8%, death PAF=43.5%) and environmental/occupational risk factors (DALYs PAF=39.0%, death PAF=40.6%) .

Among specific risk factors, high systolic blood pressure (hypertension) ranked first for both DALYs and deaths, with PAFs of 53.3% (95%CI=43.4%-62.0%) and 55.4% (95%CI=45.7%-64.1%), respectively. High low-density lipoprotein cholesterol (DALYs PAF=18.0%, death PAF=16.1%) and high fasting plasma glucose (DALYs PAF=9.8%, death PAF=10.5%) also contributed more than most behavioral and environmental risks. Non-metabolic factors such as air pollution, smoking, and diet-related risks showed DALYs PAFs of 28.0%, 22.4%, and 29.3%, and death PAFs of 28.6%, 18.7%, and 27.7%, respectively.

### **Trends in Disease Burden from Four Major Metabolic Factors in CVD, 1990-2021**

Among metabolic risk factors, high systolic blood pressure (hypertension) caused the highest CVD burden. In 1990 and 2021, the corresponding DALY rates were 3,695.71 and 2,728.48 per 100,000, and mortality rates were 201.79 and 155.21 per 100,000, respectively. The AAPCs for standardized DALY and mortality rates were -0.06% (95%CI=-0.34% to 0.21%,  $P=0.6539$ ) and 0.11% (95%CI=-0.25% to 0.48%,  $P=0.5395$ ), with no statistically significant changes ( $P>0.05$ ).

The burden associated with high BMI increased rapidly. Its DALY rate rose from 281.04 per 100,000 in 1990 to 396.09 per 100,000 in 2021 (AAPC=1.08%, 95%CI=0.89%-1.27%,  $P<0.0001$ ), while mortality increased from 13.73 to 18.80 per 100,000 (AAPC=1.00%, 95%CI=0.77%-1.22%,  $P<0.0001$ ), with statistically significant changes. High fasting plasma glucose DALY rates decreased from 521.36 to 500.31 per 100,000 (AAPC=-0.99%, 95%CI=-1.13% to -0.86%,  $P<0.0001$ ), while mortality remained essentially unchanged (29.37 to 29.28 per 100,000). High low-density lipoprotein cholesterol-related DALY rates decreased from 953.85 to 920.69 per 100,000, with mortality slightly increasing (43.10 to

44.97 per 100,000), though changes were not statistically significant ( $P>0.05$ ) [TABLE:4, TABLE:5].

### **CVD Burden Attributable to Metabolic Risk Factors by Sex and Age Group, 1990-2021**

Analyses of CVD mortality and DALY rates attributable to metabolic factors by age and sex showed that both metrics increased with age and were consistently higher in males than females. In 2021, mortality among men aged 70+ years was 7,538.3 per 100,000 compared to 5,516.8 per 100,000 for women, while DALY rates were 57,642.6 and 42,911.7 per 100,000, respectively. The 15-49 age group had the lowest burden, with male mortality of 15.4 per 100,000 and female mortality of 11.1 per 100,000, and DALY rates of 1,237.4 and 925.8 per 100,000, respectively. Burdens in both the 50-69 and 70+ age groups exceeded those in the 15-49 group and increased with age. Male burden exceeded female burden across all age strata, with gender differences most pronounced in the 70+ age group. From 1990 to 2021, CVD mortality and DALY rates attributable to metabolic factors generally showed an “increase then decrease” pattern across age groups, with the 70+ age group consistently bearing the highest burden and the 15-49 age group the lowest [Figure 2: see original paper].

### **Projected CVD Burden Attributable to Metabolic Risks in China, 2022-2035**

BAPC model projections for CVD mortality and DALY rates attributable to metabolic risks show that male mortality will decrease from 291.97 per 100,000 in 2022 to 183.33 per 100,000 by 2035, with a slight decline to 294.49 per 100,000 by 2025, then dropping to 272.34 per 100,000 by 2030 before the more substantial decrease. The curve bends downward from 2025, with the main trend line and prediction intervals indicating accelerated decline and expanding uncertainty. Female mortality shows a more linear decreasing trend, declining steadily from 149.26 per 100,000 in 2022 to 128.20 per 100,000 by 2030 and further to 103.00 per 100,000 by 2035, with relatively stable annual declines and narrow prediction intervals indicating high concentration.

Male DALY rates will be 5,296.99 per 100,000 in 2022, slightly decreasing to 5,273.63 per 100,000 by 2025, then accelerating downward to 4,580.42 per 100,000 by 2030 and 3,274.07 per 100,000 by 2035, with a clear inflection point after 2025. Female DALY rates will decrease from 2,863.17 per 100,000 in 2022 to 2,469.02 per 100,000 by 2030 and 1,814.15 per 100,000 by 2035, with relatively stable annual declines and narrow prediction intervals indicating stable trends and low uncertainty [Figure 3: see original paper].

Male indicators show a clear downward turning point around 2030, while female indicators demonstrate continuous, balanced declines. Uncertainty prediction bands expand after 2030, more significantly in males, suggesting greater influence of potential factors in male projections.

Model prediction accuracy assessment shows MAPE values below 2% for all indicators: mortality predictions had MAPEs of 1.54% for males and 1.59% for females, while DALY rate predictions had MAPEs of 0.98% for males and 1.02% for females. These small overall errors indicate good model fit and predictive stability .

## Discussion

This study, based on GBD 2021 data, found that hypertension is the primary metabolic risk factor for CVD burden in China, with high BMI showing particularly significant burden growth. Projections suggest that without effective interventions, CVD-related deaths and DALYs will remain high before 2035. Males and older adults bear a heavier burden, while risk is rising rapidly among young and middle-aged adults. Enhanced screening of high-risk populations, metabolic indicator monitoring, and multi-level interventions are needed to advance CVD prevention and enable more precise strategies.

Among the four major metabolic risk factors evaluated, high systolic blood pressure (hypertension) consistently ranks as the leading contributor to CVD burden, with its contribution to mortality and DALY rates remaining dominant over time. Although the absolute burden level associated with high BMI is relatively lower, its growth rate is the most significant, reflecting the rapid accumulation of obesity-related risks in the Chinese population. In contrast, the burden attributable to high fasting plasma glucose and high low-density lipoprotein cholesterol remains relatively stable with limited changes. Sex- and age-stratified results show that CVD burden attributable to metabolic factors is consistently higher in males than females and increases significantly with age, with men aged 70+ being the most heavily burdened group requiring priority intervention. Additionally, despite relatively low burden levels in the 15-49 age group, an upward trend is gradually emerging, indicating a younger onset of metabolic abnormalities and underscoring the importance of early prevention.

BAPC model projections indicate that assuming current risk exposure levels remain unchanged, CVD mortality and DALY rates are expected to decline slowly from 2022 to 2035; however, the magnitude of decrease is limited. Combined with the Joinpoint model analysis showing continued growth in high BMI-related burden, this risk may continue to increase. Overall, the contribution of metabolic factors to CVD will remain high.

Our findings demonstrate that high BMI and hypertension constitute the core metabolic risk factors for CVD burden in China. Obesity can activate the sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS) through leptin, induce insulin resistance, chronic inflammation (elevated interleukin-6 and C-reactive protein), oxidative stress, and endothelial dysfunction, accompanied by microvascular rarefaction and autonomic dysregulation, leading to increased vascular resistance and atherosclerosis. Meanwhile, hypertension causes structural damage through long-term elevated blood pressure,

including left ventricular remodeling, arterial stiffness, and neurohormonal abnormalities (angiotensin II, endothelin), substantially increasing risks of heart failure, stroke, and coronary heart disease. In response, China's "Healthy China 2030" strategy has incorporated hypertension and obesity control as national priorities through community screening, family doctor contract services, dual monitoring of weight and blood pressure, and comprehensive interventions including low-salt diet and exercise education. The WHO also recommends promoting low-salt healthy diets, encouraging physical activity, managing body weight, and implementing screening and interventions for high-risk populations.

As an important driver of CVD, metabolic syndrome interventions should focus on life-course management and high-risk stratification. Expert consensus emphasizes that for populations with metabolic abnormalities but without organic disease, intervention should start earlier through community-based integrated pathways for screening, assessment, and follow-up. Specific measures should include promoting healthy lifestyles (weight control, sodium restriction, increased physical activity, improved sleep quality) and strengthening metabolic indicator management through regular monitoring of BMI, blood pressure, glucose, and lipids. High-risk populations should receive tiered interventions: primary prevention focusing on lifestyle modification, secondary prevention initiating pharmacological treatment on top of metabolic abnormality management, and tertiary prevention requiring chronic disease follow-up and multidisciplinary joint management. International evidence shows that glucagon-like peptide-1 (GLP-1) receptor agonists such as semaglutide can reduce major cardiovascular event risk in high-BMI populations with elevated CVD risk, providing new options for individualized intervention. In summary, metabolic syndrome prevention and control should not be limited to single indicator management but should implement systematic strategies with tiered classification, comprehensive intervention, and focused monitoring to effectively curb early-onset and progressive CVD risk.

This study has several limitations. First, GBD data are model-based and lack original metabolic exposure monitoring data for some regions, potentially affecting accuracy of regional or specific population burden assessments. Second, the BAPC model assumes stable trends and cannot reflect disruptions from sudden public health interventions, drug popularization, or technological advances, limiting predictive adaptability. Third, this study did not incorporate interactions with behavioral and environmental risk factors, failing to comprehensively evaluate synergistic effects among multiple risks. Future research should integrate real-world data to construct multi-dimensional prediction models covering metabolic, behavioral, and environmental factors to improve accuracy of CVD burden assessment and public health intervention targeting.

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**Data Availability:** The datasets analyzed during the current study are available in the GBD 2021 repository (<https://vizhub.healthdata.org/gbd-results/>).

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