

## Cardiovascular Disease Burden Attributable to Diabetes Among Chinese Adults, 1990-2019: Postprint

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### Abstract

**Background** Against the backdrop of deepening global aging, the number of patients with chronic diseases continues to increase, and the phenomenon of multimorbidity is becoming increasingly severe. Cardiovascular disease and type 2 diabetes are generally considered diseases of the elderly; however, with changes in lifestyle pace and dietary behaviors among residents, many diseases are showing a trend toward younger onset. Current studies also indicate that, compared with the general population, patients who develop diabetes at a young age have a relatively increased risk of cardiovascular disease and mortality.

**Objective** To investigate the burden of cardiovascular disease attributable to diabetes among Chinese adults from 1990 to 2019, and to provide evidence for the prevention of comorbidities.

**Methods** Based on data from the Global Burden of Disease Study 2019 (GBD), this study primarily employed indicators such as mortality rate, disability-adjusted life years (DALY) rate, and estimated annual percentage change (EAPC) to assess the burden of cardiovascular disease (including three categories: ischemic heart disease, stroke, and peripheral arterial disease) attributable to diabetes in China. Stratified analyses were conducted by age group (25–49 years, 50–69 years, ≥ 70 years) and sex, and temporal trends in disease burden were analyzed.

**Results** The number of cardiovascular disease deaths attributable to diabetes among Chinese adults aged 25 years and older increased from 298,050 in 1990 to 700,340 in 2019. The age-standardized mortality rate of cardiovascular disease attributable to diabetes increased in males compared with 1990, whereas it decreased in females, with the rate consistently higher in males than in females. In 2019, DALYs attributable to diabetes-related cardiovascular disease

were 13.58585 million person-years. Age-specific mortality and DALY rates increased with age. The decline in the age-standardized DALY rate was more pronounced in females than in males (females: EAPC = -0.32%, 95% CI = -0.49% to -0.11%; males: EAPC = -0.01%, 95% CI = -0.26% to 0.29%). In 2019, mortality and DALY rates for ischemic heart disease and peripheral arterial disease attributable to diabetes increased in most of the three age groups compared with 1990, whereas mortality rates for stroke attributable to diabetes decreased across the three age groups. From 1990 to 2019, the proportion of age-standardized DALY rates attributable to diabetes among the three categories of cardiovascular disease showed fluctuating changes; however, in 2019, the proportions for all three categories were higher than in 1990.

**Conclusion** From 1990 to 2019, the mortality and DALY rates of cardiovascular disease attributable to diabetes among Chinese adults showed an overall upward trend, indicating a substantial risk of diabetes and cardiovascular disease comorbidity in the population. Attention should be paid to screening for cardiovascular disease or individuals at high risk of cardiovascular disease among diabetic patients, with particular focus on males, the elderly, and younger individuals with unhealthy lifestyles, to provide early health interventions and reduce the burden of comorbidities.

## Full Text

### Preamble

#### **Burden of Cardiovascular Diseases Attributable to Diabetes Among Chinese Adults from 1990 to 2019**

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## Abstract

**Background:** Against the backdrop of global aging, the number of patients with chronic diseases is increasing, and multimorbidity is becoming more severe. Traditionally, cardiovascular diseases and type 2 diabetes are mostly considered diseases of the elderly. However, with changes in lifestyle patterns such as the pace of life and diet, many diseases are showing a trend of rejuvenation. Recent studies have also shown that individuals who develop diabetes at a young age have an increased relative risk of developing cardiovascular diseases and higher mortality rates compared to the general population.

**Objective:** To investigate the burden of cardiovascular diseases attributed to diabetes among Chinese adults from 1990 to 2019, so as to provide evidence for comorbidity prevention.

**Methods:** Based on the 2019 Global Burden of Disease (GBD) study data, indicators such as mortality rates, disability-adjusted life years (DALY) rates, and estimated annual percentage change (EAPC) were used to assess the burden of cardiovascular diseases in China (including ischemic heart disease, stroke, and peripheral arterial disease) attributed to diabetes. The analysis was stratified by age group (25-49 years, 50-69 years,  $\geq$  70 years) and gender, and the temporal trends in disease burden were finally analyzed.

**Results:** The number of cardiovascular disease deaths attributable to diabetes increased from 298,050 in 1990 to 700,340 in 2019 among people aged 25 years and older in China. The age-standardized mortality rate for CVD attributed to diabetes increased for males compared to 1990, while it decreased for females, with males consistently having higher rates than females. In 2019, the DALY for CVD attributed to diabetes was 13,585,850 person-years. The age-specific mortality rate and DALY rate increased with age. The downward trend in standardized DALY rate was more pronounced in females (EAPC=-0.32%, 95%CI=-0.49% to -0.11%) than in males (EAPC=-0.01%, 95%CI=-0.26% to 0.29%). The mortality and DALY rates for ischemic heart disease and peripheral arterial disease attributed to diabetes increased in the three age groups from 1990 to 2019, while the mortality rates for stroke attributed to diabetes declined in all three age groups in 2019 compared to 1990. The percentage of standardized DALY rates attributable to diabetes for the 3 cardiovascular diseases in cardiovascular disease fluctuated from 1990 to 2019. However, the percentage of standardized DALY rates for all 3 cardiovascular diseases attributable to diabetes was higher in 2019 than in 1990.

**Conclusion:** From 1990 to 2019, there has been an overall increasing trend in the mortality and DALY rates of cardiovascular diseases attributed to diabetes

among adults in China. The population is at greater risk for comorbidities of diabetes and CVD, emphasizing the need to focus on screening for CVD among individuals with diabetes or those at high risk of developing CVD. Emphasis should be placed on males, the elderly, and younger individuals with unhealthy lifestyle habits for early health interventions to reduce the burden of comorbidities.

**Keywords:** Cardiovascular diseases; Diabetes; Adult; Disease burden; Mortality; Disability-adjusted life years

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## Introduction

The WHO defines “multimorbidity” as an individual simultaneously suffering from two or more chronic conditions [1]. Against the backdrop of deepening global aging, the number of chronic disease patients continues to rise, and the phenomenon of multimorbidity is becoming increasingly severe. Compared with patients with single diseases, multimorbidity not only increases treatment costs but also leads to decreased quality of life and increased psychological stress [2]. Currently, the disease burden caused by multimorbidity has gradually become a focus of public health attention in China, and effective prevention and control of comorbidities can significantly reduce the national health economic burden.

China has the largest number of diabetes patients in the world, accounting for more than one-quarter of the global total, with approximately 140 million patients aged 20-79 years [3]. The vast number of people with prediabetes suggests that prevalence may continue to rise. In 2019, China had nearly 4 million new diabetes cases, and more than 170,000 patients died from diabetes in the same year [4]. The Global Burden of Cardiovascular Disease report shows that China ranks first in the world in cardiovascular disease deaths [5], with cardiovascular disease being the leading cause of death in China—higher than cancer and other diseases—posing a tremendous threat to the health of Chinese residents [6]. Meanwhile, as China’s population aging accelerates, the incidence and mortality of cardiovascular disease continue to rise, and the inflection point for disease burden decline has not yet appeared [7]. Diabetes is a metabolic disease characterized by chronic hyperglycemia, and long-term abnormal glucose metabolism can lead to vascular lesions that subsequently induce cardiovascular disease, making it a risk factor for cardiovascular disease [8].

Traditionally, cardiovascular disease and type 2 diabetes are mostly considered diseases of the elderly. However, with changes in residents’ lifestyles, including pace of life and dietary habits, many diseases are showing a trend toward younger onset. Research indicates that patients who develop diabetes at a young age have a relatively increased risk of cardiovascular disease and mortality compared with the general population [9]. Previous studies on multimorbidity have mostly focused on elderly populations, with very limited data from younger individuals [10]. Therefore, conducting research on the comorbidity of diabetes

and cardiovascular disease in adult populations is essential.

This study is based on data from the 2019 Global Burden of Disease (GBD) study to analyze the disease burden and trends of cardiovascular disease attributable to diabetes in China from 1990 to 2019. By examining this burden, we aim to assess the comorbidity risk of diabetes and cardiovascular disease among Chinese residents, provide prevention and treatment strategies for cardiovascular disease control in China, and offer evidence for reducing the comorbidity burden of diabetes and cardiovascular disease.

## Methods

### 1.1 Data Sources

This study utilized data from GBD 2019, which comprehensively assessed the disease burden of 369 diseases or injuries and 87 risk factors across multiple countries from 1990 to 2019, grouped by region, year, gender, and age. We extracted data on the burden of cardiovascular disease attributable to diabetes among Chinese adults aged 25 years and older from 1990 to 2019.

### 1.2 Indicator Extraction

When diabetes is considered a risk factor for various other diseases, GBD uses high fasting plasma glucose (applicable only to adults over 25 years) as a risk factor to more broadly estimate the disease burden caused by diabetes as a risk factor [11]. Therefore, this study used high fasting plasma glucose as the risk factor to link and conduct attribution analysis of the disease burden of diabetes and cardiovascular disease caused by diabetes. We extracted data from 1990 to 2019 on the burden of cardiovascular disease attributable to diabetes in China, including ischemic heart disease, stroke, and peripheral arterial disease (with ICD-10 codes I20-I25, I60-I69, and I70-I79, respectively). The main evaluation indicators included mortality rate, DALY rate, and estimated annual percentage change (EAPC). Age groups were extracted as 25-49 years, 50-69 years, and ≥70 years. To exclude differences caused by age structure when comparing disease burden across age groups, we standardized the crude mortality and crude DALY rates for each age group using the world standard population structure [12].

### 1.3 Statistical Methods

We used Excel 2003 to organize and analyze the relevant data, describing the distribution of mortality rates, DALY rates, and their 95% uncertainty intervals (UI) for cardiovascular disease attributable to diabetes from 1990 to 2019 by year, gender, and age. R 4.1.2 statistical software was used to calculate the EAPC and its 95% confidence interval (CI) for mortality and DALY rates from 1990 to 2019, and the ggplot2 package was used for visualization.

## Results

### 2.1 Overview of Disease Burden from Cardiovascular Disease Attributable to Diabetes in 1990 and 2019

**2.1.1 Mortality** From 1990 to 2019, the number of deaths from cardiovascular disease attributable to diabetes among Chinese adults aged 25 years and older increased from 298,050 to 700,340, with the crude mortality rate rising from 49.55/100,000 to 67.30/100,000 (EAPC=0.36%, 95%CI=0.06%-0.75%). In 2019, there were 294,970 female deaths and 405,370 male deaths. The age-standardized mortality rate was lower in females than in males (31.24/100,000 vs. 55.85/100,000). From 1990 to 2019, the crude mortality rate for males increased more significantly than for females (EAPC=0.63%, 95%CI=0.22%-0.53%). After standardization, the mortality trend for males remained stable (EAPC=0.05%, 95%CI=-0.23%-0.37%), while for females it showed a decreasing trend (EAPC=-0.27%, 95%CI=-0.48%-0.01%). In 2019, except for the crude mortality rate in the 50-69 age group, all other age groups showed increased crude mortality rates compared with 1990 .

**2.1.2 Disability-Adjusted Life Years (DALY)** In 2019, the DALY for cardiovascular disease attributable to diabetes among Chinese adults aged 25 years and older was 13,585,850 person-years, including 8,190,540 person-years for males and 5,395,310 person-years for females. The total age-standardized DALY rate was 714.60/100,000, with males having a higher rate than females (932.96/100,000 vs. 534.32/100,000). The declining trend in age-standardized DALY rate was more pronounced in females (EAPC=-0.32%, 95%CI=-0.49%-0.11%) than in males (EAPC=-0.01%, 95%CI=-0.26%-0.29%). In 2019, except for the crude DALY rate in the 25-49 age group, all other age groups showed decreased crude DALY rates compared with 1990 .

### 2.2 Changes and Trends in Disease Burden of Three Types of Cardiovascular Disease Attributable to Diabetes by Gender and Age

In 2019, among Chinese patients with cardiovascular disease attributable to diabetes, the age-standardized mortality rates for ischemic heart disease, peripheral arterial disease, and stroke were 28.26/100,000, 0.04/100,000, and 27.55/100,000 for males, respectively, and 16.43/100,000, 0.02/100,000, and 14.78/100,000 for females, respectively. For all three types of cardiovascular disease, age-standardized mortality rates were higher in males than in females, and in both genders, the rates from highest to lowest were ischemic heart disease, stroke, and peripheral arterial disease .

Compared with 1990, the crude mortality rate for ischemic heart disease attributable to diabetes among Chinese adults aged 25 years and older in 2019 decreased only in the 50-69 age group, while it increased in both the 25-49 and 70+ age groups; this pattern remained consistent after standardization. The crude DALY rate for ischemic heart disease in 2019 increased in the 25-49 and

\$ \$70 age groups compared with 1990, while it decreased in the 50-69 age group; this pattern also remained consistent after standardization. The 2019 burden of ischemic heart disease attributable to diabetes showed an upward trend in mortality and DALY rates in both the 25-49 and \$ \$70 age groups compared with 1990, with a more pronounced trend in the \$ \$70 age group (EAPC for mortality and DALY rates in the 25-49 group: 0.38% and 0.36%, respectively; in the \$ \$70 group: 0.60% and 0.42%, respectively) .

For peripheral arterial disease attributable to diabetes, the mortality rate in 2019 increased compared with 1990 in the 25-49 and \$ \$70 age groups, with a more pronounced increase in the 25-49 age group (EAPC=0.89%, 95%CI=0.24%-1.75% for 25-49; EAPC=0.56%, 95%CI=0.11%-0.95% for \$ \$70). The DALY rate for peripheral arterial disease in the 25-49 age group also increased in 2019 compared with 1990 (EAPC=0.86%, 95%CI=0.24%-1.70%) .

For stroke attributable to diabetes among Chinese adults aged 25 years and older, the crude mortality rate in 2019 decreased across all three age groups compared with 1990, and this pattern remained consistent after standardization. The crude DALY rate for stroke in 2019 also decreased across all three age groups compared with 1990, with consistent results after standardization. The crude mortality rate for stroke attributable to diabetes in 2019 showed a relatively stable trend compared with 1990, with a decreasing trend in the 50-69 age group (EAPC=-0.48%, 95%CI=-0.60%-0.31%). The crude DALY rate for stroke in the 50-69 age group also showed a decreasing trend (EAPC=-0.44%, 95%CI=-0.57%-0.27%) .

In 2019, the age-standardized DALY rates for ischemic heart disease, peripheral arterial disease, and stroke attributable to diabetes were 434.88/100,000, 1.37/100,000, and 496.71/100,000 for males, respectively, and 239.41/100,000, 2.45/100,000, and 292.46/100,000 for females, respectively .

### **2.3 Changes in the Proportion of Age-Standardized DALY Rates for Three Types of Cardiovascular Disease Attributable to Diabetes from 1990 to 2019**

Based on GBD 2019 data, this study compared the disease burden and trends of cardiovascular disease (ischemic heart disease, peripheral arterial disease, and stroke) attributable to diabetes among Chinese adults aged 25 years and older in 1990 and 2019. The results showed that the proportion of age-standardized DALY rates attributable to diabetes for the three types of cardiovascular disease generally increased from 1990 to 2019, with differences between genders. Studies have shown that patients with type 2 diabetes have a higher risk of cardiovascular disease compared with non-diabetic individuals [13], and cardiovascular disease accounts for 20.1% of total deaths in non-diabetic patients but 47.2% in diabetic patients [14], suggesting that diabetes combined with cardiovascular disease may increase the disease burden.

Analysis of trends in the proportion of age-standardized DALY rates for ischemic heart disease, stroke, and peripheral arterial disease attributable to diabetes revealed that the maximum proportion for all three cardiovascular diseases occurred in 2005 for both genders [Figure 1: see original paper]. Before 2005, the proportion of age-standardized DALY rates for the three cardiovascular diseases increased over time in males, while in females it showed volatility with both increases and decreases. After 2005, the proportion of age-standardized DALY rates for the three cardiovascular diseases showed volatility in males, while in females it showed an increasing trend. Although the proportion of DALY rates for cardiovascular disease attributable to diabetes showed some decline after the peak in 2005, this may be related to improvements in cardiovascular disease treatment levels in China. In addition, in 2005 the former Ministry of Health issued the “National Health Education and Health Promotion Work Plan,” which called for establishing and improving a health education and health promotion system adapted to social development and implementing various forms of health education and health promotion activities in communities targeting key populations to enhance health awareness and self-care capacity [21]. Such health education and promotion activities may have improved population health literacy to some extent, thereby promoting changes in risk behaviors and potentially reducing disease burden.

Currently, China is facing the dual pressures of population aging and the continued prevalence of metabolic risk factors [22], and therefore should continue to pay attention to the disease burden of cardiovascular disease caused by diabetes and the comorbidity issue between the two conditions.

Although China has been at the world-leading level in many cardiovascular disease treatment technologies in the past 30 years, changes in dietary structure and reduced physical activity among young people may have had negative effects on disease occurrence and development. Previous studies have found that patients diagnosed with type 2 diabetes before age 45 have the highest relative risk for cardiovascular disease and all-cause mortality compared with age- and sex-matched controls [23]. Another study showed that young-onset type 2 diabetes is associated with an increased risk of premature death from cardiovascular disease [9].

## Discussion

This study demonstrates that compared with 1990, the burden of cardiovascular disease attributable to diabetes among Chinese adults aged 25 years and older increased significantly in 2019, with overall upward trends in mortality and DALY rates. The risk of comorbidity between diabetes and the three types of cardiovascular disease is substantial. Therefore, we recommend that relevant departments and units strictly implement health education policies, improve health literacy among patients with type 2 diabetes, and increase emphasis on cardiovascular disease screening among diabetic patients to achieve early detection, diagnosis, and treatment of cardiovascular disease. Simultaneously,

younger patients with type 2 diabetes should be encouraged to make stricter lifestyle changes, including regular physical activity, healthy dietary patterns, and weight loss.

Stratified analysis by gender showed that the overall burden of cardiovascular disease attributable to diabetes was higher in males than in females, which may be because males are more affected by changes in fasting plasma glucose than females. A Chinese study found that higher visit-to-visit fasting blood glucose variability was associated with increased lifetime risk of cardiovascular disease in males but no significant association was found in females. Due to the protective effects of estrogen, females may be more adaptable to fasting glucose variability than males, which may reduce the risk of cardiovascular disease caused by glucose fluctuations [20].

This study has several limitations. First, due to limitations of GBD 2019 data, this study used high fasting plasma glucose as a proxy for diabetes in the attribution analysis (this indicator includes the disease burden of both diabetes and milder hyperglycemic states). Second, because cardiovascular diseases attributable to high fasting plasma glucose in the GBD data only include ischemic heart disease, peripheral arterial disease, and stroke, other cardiovascular diseases were not analyzed. Third, this study covers a large time span, primarily comparing disease burden between 1990 and 2019; future research could expand the time points to enrich the temporal trend analysis. Fourth, due to lack of detailed data sources, we could not analyze the disease burden across different regions within China, and therefore could not reflect regional differences in disease burden.

## Conclusion

In summary, compared with 1990, the mortality and DALY rates of cardiovascular disease attributable to diabetes among Chinese adults aged 25 years and older showed an overall upward trend in 2019. The risk of comorbidity between diabetes and cardiovascular disease is substantial. Attention should be paid to screening for cardiovascular disease among individuals with diabetes or those at high risk, with particular focus on males, the elderly, and younger individuals with unhealthy lifestyle habits for early health interventions to reduce the burden of comorbidities.

## Author Contributions

LIANG Dong, OU Yangjiang, LIN Xiuquan, ZHAO Yang, YANG Chenglin, and LIN Xiaoru conceived, designed, and discussed the study and analyzed its feasibility. YANG Chenglin and LIN Xiaoru collected the data. YANG Chenglin and LIN Xiaoru organized the data. YANG Chenglin and LIN Xiaoru performed the statistical analysis and interpreted the results. YANG Chenglin and LIN Xiaoru wrote the initial draft. OU Yangjiang and LIN Xiuquan provided revisions and edited the manuscript. LIANG Dong, OU Yangjiang, LIN Xiuquan,

and ZHAO Yang were responsible for quality control and final review of the article and overall responsibility for the work.

## Conflict of Interest

This article has no conflict of interest.

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