

# Report on cardiovascular health and diseases in China 2021: an updated summary

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**ABSTRACT** In 2019, cardiovascular disease (CVD) accounted for 46.74% and 44.26% of all deaths in rural and urban areas, respectively. Two out of every five deaths were attributed to CVD. It is estimated that approximately 330 million individuals in China are affected by CVD. Among them, there are 13 million cases of stroke, 11.4 million cases of coronary heart disease, 5 million cases of pulmonary heart disease, 8.9 million cases of heart failure, 4.9 million cases of atrial fibrillation, 2.5 million cases of rheumatic heart disease, 2 million cases of congenital heart disease, 45.3 million cases of lower extremity artery disease, and 245 million cases of hypertension. With the dual challenges of population aging and a steady increase in the prevalence of metabolic risk factors, the burden of CVD in China is expected to continue rising. Consequently, new demands arise for CVD prevention, treatment, and the allocation of medical resources. Emphasizing primary prevention to reduce disease prevalence, increasing the allocation of medical resources for CVD emergency and critical care, and providing rehabilitation services and secondary prevention to reduce the risk of recurrence, rehospitalization, and disability among CVD survivors are of paramount importance. Hypertension, dyslipidemia, and diabetes affect millions of individuals in China. Since blood pressure, blood lipids, and blood sugar levels often rise insidiously, vascular disease and serious events such as myocardial infarction and stroke occur by the time they are detected in this population. Therefore, it is crucial to implement strategies and measures to prevent risk factors such as hypertension, dyslipidemia, diabetes, obesity, and smoking. Furthermore, greater efforts should be directed towards assessing cardiovascular health status and conducting research on early pathological changes to enhance prevention, treatment, and understanding of CVD.

To effectively implement the national policy of “focusing on grassroots units and emphasizing prevention” and facilitate the shift of the main battleground for cardiovascular disease (CVD) prevention and treatment from hospitals to communities, the National Center for Cardiovascular Diseases in China annually compiles the “Report on Cardiovascular Health and Diseases in China 2021”. This report provides health administrators and professionals with comprehensive and scientifically supported information. In 2019, CVD accounted for 46.74% and 44.26% of deaths in rural and urban areas, respectively, with 2 out of every 5 deaths attributed to CVD. China is currently confronted with the dual challenge of an aging population and the ongoing prevalence of metabolic risk factors. As a result, the burden of CVD will continue to increase, impacting disease prevention strategies and resource allocation requirements throughout the country.

Primary prevention measures must be employed

to reduce the incidence of CVD, while the allocation of medical resources needs to be increased to address the rising cases of acute and severe cardiovascular conditions. Furthermore, rehabilitation services and secondary prevention strategies should be implemented to mitigate the risks of recurrence, rehospitalization, and disability among a significant number of CVD survivors. In China, the prevalence of hypertension, dyslipidemia, and diabetes has reached alarming levels, necessitating lifelong multi-drug treatments to prevent CVD. It is imperative to conduct more extensive research and develop effective strategies to enhance awareness, treatment, and control rates for these conditions. Additionally, given that these risk factors often progress insidiously, vascular damage and related complications, including myocardial infarction (MI) and stroke, frequently occurred at the time of detection. Despite the high prevalence of subclinical atherosclerotic lesions, the prevention of vascular injury and related treatments have not received sufficient

attention. Accumulating evidence demonstrates that maintaining vascular health is a critical foundation for preventing CVD and degenerative diseases.

Therefore, it is essential to prioritize zero-level prevention strategies by reinforcing the prevention of hypertension, dyslipidemia, diabetes, obesity, smoking, and other risk factors. Simultaneously, there is a pressing need to strengthen the assessment of cardiovascular health status and the prevention and treatment of early pathological changes. By doing so, we can pave the way for substantial advancements in CVD prevention and improve overall cardiovascular health in China.

## CARDIOVASCULAR HEALTH RELATED FACTORS

### Tobacco Use

In 2017, cigarette smoking in China was responsible for 2.6 million deaths, accounting for nearly one-third of global tobacco-related deaths (8.3 million).<sup>[1]</sup> The detrimental health impact of tobacco use in China exceeds the global average. In 2018, the prevalence of secondhand smoke exposure in China was 68.1%, with 35.5% being exposed on a daily basis. Currently, the usage rate of electronic cigarettes stands at 0.9%, while the smoking cessation rate among individuals aged 15 years or older is 20.1%.<sup>[2]</sup>

The China Kadoorie Biobank (CKB) is a large-scale prospective cohort study involving over 500,000 Chinese adults, with an average follow-up period of seven years. Findings from this study revealed that, compared to never-smokers, urban male smokers had a hazard ratio (HR) of 1.63 for mortality from CVD, while rural male smokers had a HR of 1.24. Additionally, female smokers were found to be at an even higher risk of CVD mortality compared to male smokers.<sup>[3]</sup>

### Healthy Diet

Analysis of data from the series of China National Nutrition Surveys (CNNS) spanning 1982-2012 and the China Health and Nutrition Survey (CHNS) conducted between 1989 and 2015 revealed a continuous decline in the consumption of grains and vegetables among the Chinese population, accompanied by a consistent increase in meat consump-

tion, predominantly pork (Figure 1). The consumption of eggs, fish, and dairy products remained relatively low. Additionally, there was a significant increase in the use of cooking oils, while salt consumption showed a decrease; however, both usage levels remained much higher than recommended.

The intake of total energy by Chinese residents has been decreasing, while protein intake has remained stable. Carbohydrate intake as a proportion of energy has considerably decreased, while the contribution of fat has increased (Figure 2), surpassing the recommended levels set by Chinese dietary guidelines (20%-30%). In rural China, the proportion of energy derived from fat has exceeded the recommended upper limit of 30%, while deficiencies in vitamin and mineral nutrient intake persist.

Data from the China National Nutrition and Health Surveillance (CNNHS) conducted from 2015 to 2017, with a sample size of 73,572 individuals aged 2 years and older, revealed the average daily intake per standard person for energy, carbohydrates, protein, and fat to be 2007.4 kcal, 266.7 g, 60.4 g, and 79.1 g, respectively.<sup>[4]</sup> In the China National Nutrition and Health Surveillance of Children and Lactating Mothers conducted in 2016-2017, among 8777 children aged 6-11 years, the average daily intakes of energy, protein, fat, and carbohydrates were 1591.7 kcal, 50.0 g, 69.6 g, and 196.3 g, respectively.<sup>[5]</sup> Among 7265 Chinese individuals aged 12-17 years, the average daily intakes of energy, protein, fat, and carbohydrates were 1995.0 kcal, 61.4 g, 84.5 g, and 253.8 g, respectively. The proportions of total energy derived from carbohydrates, fat, and protein

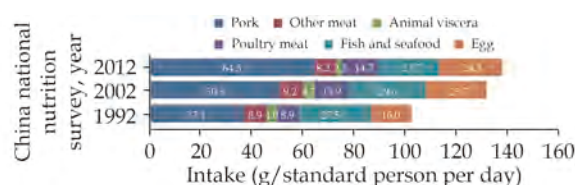


Figure 1 The trend of mean daily food intake by Chinese residents from 1992 to 2012.

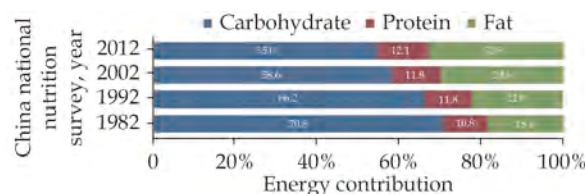


Figure 2 The trend of energy contribution from carbohydrate, protein and fat by Chinese residents from 1982 to 2012.

were 50.6%, 37.1%, and 12.3%, respectively.<sup>[6]</sup>

A study analyzing data from 29,238 Chinese adults participating in the CHNS from 1991 to 2015 demonstrated a shift from traditional dietary patterns to Western dietary patterns.<sup>[7]</sup> The scores for the southern pattern (characterized by high intakes of rice, vegetables, and pork) decreased, while the scores for the modern pattern (characterized by high intakes of fruits, dairy products, cakes, cookies, and pastries) and the meat pattern (characterized by high intakes of organ meats, poultry, and other livestock meat) increased.

In a survey conducted in 2014 involving 27,485 Chinese residents aged 3 years and older from 14 provinces and cities, the daily intake of added sugar from carbonated beverages was found to be 0.5 g, with an energy supply ratio of 0.11%. The mean daily intake of added sugar was 13.4 g, the median was 12.3 g, and the energy supply ratio was 2.69%. Adolescents aged 13–17 years were identified as the group with high consumption of carbonated drinks.<sup>[8]</sup>

The “Nutrition Improvement Program for Rural Compulsory Education” conducted a study on snack consumption among 27,374 primary and middle school students in 2019. The results showed that 14.0% of students from poor rural areas in central and western regions of China consumed snacks two or more times per day. The top three choices of snacks included fruit and vegetables (50.6%), biscuits and bread (50.1%), and puffed food (40.0%).<sup>[9]</sup>

The China National Chronic Non-communicable Disease and Nutrition Surveillance of Adults in 2015 indicated that 36.1% of Chinese residents aged 18–59 years reported eating out in the past week, with 23.9% eating out seven or more times. Males, urban dwellers, individuals with higher education levels, higher family incomes, unmarried individuals, and those with employment were more likely to eat out.<sup>[10]</sup> Compared to the period of 2010–2012, the proportion of people eating out increased by 14.7% among those aged 18–44 years and 9% among those aged 45–59 years.<sup>[11]</sup>

The “China Nutrition and Health Surveillance” project conducted from 2015 to 2017 collected data from 181,795 Chinese individuals aged 18 years or older. The results showed that the drinking rate was 43.7%, and among the drinkers, the average daily alcohol intake was 28.3 g. The rate of dangerous drink-

ing (daily alcohol intake of 41–61 g for males and 21–41 g for females) was 9.4%, and the rate of harmful drinking (daily alcohol intake  $\geq$  61 g for males and  $\geq$  41 g for females) was 13.7%. These rates of drinking, dangerous drinking, and harmful drinking were all higher than those reported in 2010–2013.<sup>[12]</sup>

According to the estimation of the Global Burden of Disease (GBD) in 2017, insufficient intake of dietary fiber was attributed to 170,143 deaths from ischemic heart disease (IHD) in China. Among the five leading risk factors for stroke, three were dietary factors: excessive sodium intake, insufficient fruit intake, and insufficient cereal intake, with population attributable fractions of 38.5%, 24.2%, and 24.1%, respectively.<sup>[13]</sup>

The CKB study analyzed 461,047 adults aged 30–79 years with a median follow-up of 11.2 years and found that unhealthy dietary habits (defined as non-daily consumption of vegetables, fruits, and eggs, and daily or infrequent consumption of red meat) increased the risk of ischemic stroke (HR = 1.23). Excessive alcohol intake (defined as consuming  $\geq$  30 g/day of pure alcohol or having stopped drinking) also increased the risks of both ischemic stroke (HR = 1.21) and hemorrhagic stroke (HR = 1.30).<sup>[14]</sup>

The China Salt Substitute and Stroke Study (SSaSS) is an open-label, cluster-randomized trial involving individuals from 600 villages in rural China. The participants had a history of stroke or were 60 years of age or older with high blood pressure (BP), and the mean follow-up time was 4.74 years. This study demonstrated that compared to those who used regular salt, individuals who used salt substitute had a 14% lower incidence of stroke (events per 1000 person-years: 29.14 vs. 33.65, RR = 0.86). The rate of serious adverse events attributed to hyperkalemia was not significantly higher with the salt substitute than with regular salt.<sup>[15]</sup>

### Physical Activity

Using a multi-stage sample, Chinese School-age Children and Adolescents' Physical Activity and Physical Health research investigated over 120,000 to 130,000 primary and secondary school students from various provinces. The findings indicated that the success rate of physical activity among primary and junior high school students in 2017 was higher compared to 2016, while the compliance rate among



senior high school students did not show a significant change.

In 2016, 85.2% of school students attended at least two physical education classes per week. Additionally, 31.5% of primary and secondary school students engaged in at least five extracurricular physical training sessions per week. The proportions of students spending at least two hours on various screen activities, including watching TV, using mobile phones, or computers, were 8.7%, 11.5%, and 9.0%, respectively. Moreover, these figures increased to 23.7%, 27.7%, and 17.5% during weekends.

According to the National Physical Fitness Monitoring in 2014, the regular exercise rate among Chinese residents was 33.9%. People aged 20–39 years had the lowest rate of regular exercise, except for those over 70 years, while individuals aged 60–69 years had the highest rate.

The CHNS revealed a downward trend in the average total physical activity of adults in China, decreasing from 399 metabolic equivalent (MET)·h/week to 213 MET·h/week between 1991 and 2009. The occupational activity of men in 2011 decreased by 31% compared to 1991, and a similar trend was observed for women. Additionally, CHNS data showed an increase in the average time spent on static behaviors by adults in China, rising from 15.1 h/week in 1991 to 20.0 h/week in 2009. The monitoring report on chronic diseases and their risk factors in China indicated that the duration of amateur static behaviors among adults aged 18 years and above increased from an average of 2.7 h/day in 2010 to 3.3 h/day in 2013. The magnitude of this increase was greater in urban areas compared to rural areas, which showed no significant differences between men and women.

According to the World Health Organization (WHO) report on physical activity data from 168 countries for the years 2001–2016, it was found that meeting the recommended physical activity targets could prevent 13.8% of premature deaths in China among individuals aged 40–74 years.<sup>[16]</sup> This prevention rate is equivalent to avoiding the premature deaths of approximately 1.0165 million people aged 40–74 years each year.

The GBD study conducted in 2016 indicated a decline in the mortality rate of stroke caused by physical inactivity in China from 1990 to 2016. The age-

standardized stroke mortality rate for men decreased from 6.0/100,000 to 1.8/100,000, while for women, it decreased from 3.4/100,000 to 0.6/100,000. The annual net change rates were -1.3% and -2.9% for men and women, respectively.<sup>[17]</sup>

To analyze data from the China-PAR cohort, which included 10,0560 individuals without CVD at baseline and had a median follow-up of 7.3 years,<sup>[18]</sup> it observed that compared to those who did not meet the recommended target for moderate and high-intensity physical activity at baseline, there was a 26% reduction in the risk of CVD (HR = 0.74) among those who met the target. Furthermore, the risk decreased by 38% (HR = 0.62) in individuals who were highly active. Those who maintained an active lifestyle throughout the follow-up period had a 43% lower risk of CVD (HR = 0.57) compared to those who were physically inactive both at baseline and during follow-up.

The results of the CKB cohort study, involving over 487,000 individuals without CVD at baseline and with an average follow-up of 7.5 years, revealed a significant negative association between total physical activity and CVD mortality. The highest quintile of physical activity ( $\geq 33.8$  MET h/day) had a 41% lower risk of CVD mortality (HR = 0.59) compared to the lowest activity group ( $\leq 9.1$  MET h/day).<sup>[19]</sup> Moreover, for every 4 MET·h/day increase in physical activity, the risk of CVD mortality decreased by 12%. Increasing either occupational or non-occupational activity was associated with a reduced risk of CVD mortality.

In the long-term follow-up study conducted by the Shanghai Health Study, involving over 120,000 adults, it was found that participants engaged in moderate-intensity leisure-time physical activities (such as Tai Chi, dancing, fitness walking, etc.) had a 14% lower risk of CVD mortality (HR = 0.86) compared to those who did not participate in any leisure-time physical activities. Notably, even if the minimum recommended dose of physical activity (7.5 MET·h/week) was not achieved, there was still a significant reduction in the risk of CVD mortality, and a dose-response relationship was observed.<sup>[20]</sup>

According to the GBD study in 2013, the medical expenses resulting from insufficient physical activity in China totaled nearly \$4.86 billion, which accounted for 10% of the global total. These costs in-





cluded \$1.78 billion in indirect costs and \$3.08 billion in direct costs. Among the expenditures, household expenditures accounted for 33.90%, government expenditures accounted for 55.80%, and third-party expenditures accounted for 10.30%.

A comprehensive analysis of data from the China Chronic Diseases and Risk Factors Surveillance (2007) and the National Health Service Surveys (2003) revealed that in 2007, the proportion of Chinese residents who suffered from coronary artery disease (CAD), stroke, hypertension, cancer, and type 2 diabetes directly attributable to insufficient physical activity (not meeting the WHO recommended standards) were 12.3%, 15.7%, 8.5%, 11.3%, and 13.5%, respectively. Additionally, being overweight or obese due to physical inactivity can further exacerbate the risk of these conditions. In 2007, the economic burden caused by physical inactivity amounted to \$6.7 billion, accounting for 15.2% of the total economic expenditure on major chronic diseases that year. Furthermore, the direct medical expenditure alone exceeded 15.0% of the total direct economic burden of China's major non-communicable diseases.

### Healthy Weight

In 2013, the prevalence of overweight and obesity among children under six years old in China was 8.4% and 3.1%, respectively. These rates had increased by 1.9% and 0.4%, respectively, compared to 2002. Among Chinese residents aged  $\geq 18$  years in 2012, the rates of overweight and obesity were 30.1% and 11.9%, respectively. These rates had grown by 7.3% and 4.8%, respectively, compared to 2002, with higher growth rates observed in rural areas compared to urban areas.<sup>[21]</sup> From 2014 to 2018, the China Patient-centered Evaluative Assessment of Cardiac Events (China PEACE) study, which included 2.7 million people aged 35–75 years, revealed that the age-standardized rate of abdominal obesity (defined as waist circumference  $\geq 85$  cm for women and  $\geq 90$  cm for men) was 32.7% for women and 36.6% for men. It is estimated that one in three people nationwide has abdominal obesity.<sup>[22]</sup>

It is speculated that by 2030, the rates of overweight and obesity among Chinese adults (based on Chinese standards), children and adolescents aged 7–17 years (based on Chinese standards), and children  $\leq 6$  years (based on the WHO diagnostic criteria)

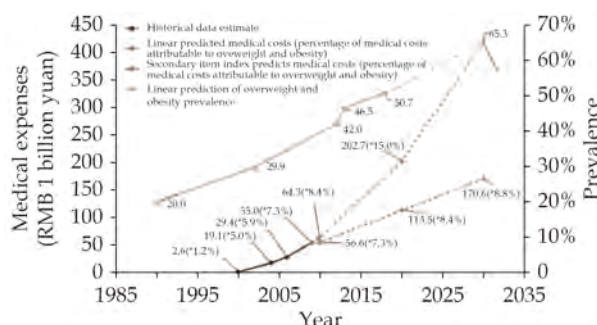
could reach 65.3%, 31.8%, and 15.6%, respectively. Additionally, the number of individuals affected by overweight and obesity may reach 789.95 million, 58.92 million, and 18.19 million, respectively.<sup>[23]</sup>

According to the GBD study in 2019, the number of CVD deaths attributed to high body mass index (BMI) in China was 549,500, with an age-standardized CVD mortality rate attributed to high BMI of 38.64 per 100,000 population. High BMI accounted for 11.98% of CVD deaths. The direct medical costs associated with overweight and obesity in China range between \$8.4 billion and \$23.9 billion, while the indirect medical costs amount to \$62.6 billion.<sup>[24]</sup> Based on observed trends in overweight and obesity rates and costs from the CHNS, it is estimated that the medical costs attributed to overweight and obesity in 2030 could reach 418 RMB billion, without considering the long-term growth in healthcare service costs (Figure 3).<sup>[23]</sup>

### Healthy Psychology

Based on a meta-analysis of 23 hospital-based studies, the prevalence of depression among Chinese hospitalized patients with CAD was found to be 51%. Within this population, 0.5%–25.4% of patients were diagnosed with major depression. Another study conducted among community-based CAD patients reported a prevalence of depression ranging from 34.6% to 45.8%, with 3.1% to 11.2% being diagnosed with major depressive disorder.

The INTERHEART study found that the prevalence of depression in Chinese patients with acute MI (AMI) was 21.7%, significantly higher than in the control group (10.4%). Although the prevalence



**Figure 3** Estimated prevalence of overweight and obesity and medical costs due to overweight and obesity in Chinese adults ( $\geq 18$  years old) in 2030. \*: Accounting for the total medical expenses

of depression in China is lower than that in 51 other countries and regions worldwide, the correlation between depression and AMI is higher than that in other countries (China: OR = 2.27; other countries: OR = 1.37).

An analysis conducted by the CKB involving 486,541 Chinese residents aged 30–79 years found the prevalence of major depressive disorder to be 0.6%. Major depressive disorder was identified as one of the risk factors for heart disease, with a HR of 1.32. Notably, the risk was significantly higher among urban residents (HR = 1.72).

Furthermore, an analysis conducted by the Shanghai Mental Health Center, which involved 3273 depressed patients from 32 hospitals in China, indicated that approximately 31.3% of depressed patients experienced circulatory disorders as their first-episode symptom. Other manifestations included insomnia, gastrointestinal disorders, trunk pain, paresthesia, neurological disorders, loss of libido, body pain, etc.<sup>[25]</sup>

## CARDIOVASCULAR RISK FACTORS

### Hypertension

A nationwide sampling survey conducted in 1958–1959, 1979–1980, 1991, and 2002 assessed the prevalence of hypertension among residents aged  $\geq 15$  years, revealing a continuous upward trend in hypertension rates (Table 1). The survey reported prevalence rates of 5.1%, 7.7%, 13.6%, and 17.6% for the respective time periods. These findings highlight a significant increase in the prevalence of hypertension over time.

The China Hypertension Survey (CHS)<sup>[26]</sup> conducted between 2012 and 2015 provided further insights into the prevalence of hypertension among Chinese residents aged  $\geq 18$  years. The survey revealed a prevalence rate of 27.9%, with a weighted rate of 23.2%. These estimates suggest that approximately 245 million adults in China have hypertension. Additionally, the detection rate of high-normal BP was reported as 39.1%, with a weighted rate of 41.3%. These figures indicate that there are approximately 435 million individuals nationwide with high-normal BP.

In 2018, a nationwide surveillance of chronic diseases and risk factors was conducted in 298 counties (districts) across 31 provinces, autonomous regions, and municipalities directly under the central government.<sup>[27]</sup> The findings revealed a hypertension prevalence of 27.5%.

The CHNS conducted a prospective cohort survey involving 12,952 Chinese adults aged  $> 18$  years.<sup>[28]</sup> The study reported an age-standardized incidence of hypertension, which increased from 40.8 per 1000 person-years in 1993–1997 to 48.6 per 1000 person-years in 2011–2015. Over the course of multiple cross-sectional surveys conducted between 1991 and 2011, involving adults  $\geq 18$  years from 8 provinces (increased to 9 in 1997 and 12 in 2011), the age-standardized detection rate of high-normal BP values showed an upward trend, rising from 23.9% in 1991 to 33.6% in 2011.

The CHS study<sup>[26]</sup> examined the awareness rate, treatment rate, and control rate (weighted rate) of hypertension among Chinese adults aged  $\geq 18$  years, with results showing an overall increase with age.

Table 1 National sampling survey on the prevalence of hypertension.

Study	Year	Age	Sampling method	Sample size	Prevalence(%)
Key Project of Chinese Academy of Medical Sciences-Hypertension Research	1958-1959	$\geq 15$	Non-random sampling	739,204	5.1
National Hypertension Sampling Survey	1979-1980	$\geq 15$	Random sampling	4,012,128	7.7
National Hypertension Sampling Survey	1991	$\geq 15$	Stratified random sampling	950,356	13.6
China Health and Nutrition Survey	2002	$\geq 18$	Multi-stage cluster random sampling	272,023	18.8
Survey on Nutrition and Chronic Disease Status of Chinese Residents	2012	$\geq 18$	Multi-stage stratified random sampling	/	25.2
China Hypertension Survey	2012-2015	$\geq 18$	Multi-stage stratified random sampling	451,755	27.9 (weighted rate 23.2)
Chronic Disease and Risk Factor surveillance in China	2018	$\geq 18$	Multi-stage stratified cluster random sampling	179,873	27.5 (weighted rate)



The treatment and control rates exhibited an initial increase followed by a decrease (Figure 4). In 2015, the awareness rate, treatment rate, and control rate of hypertension among Chinese adults aged  $\geq 18$  years were reported as 51.6%, 45.8%, and 16.8%, respectively; which represented significant improvements compared to previous surveys.<sup>[26]</sup> Table 2 provides an overview of the research on hypertension awareness, treatment, and control rates in China over the years.

A 5-year follow-up study involving 12,497 adults from 2005 to 2010 revealed that, after adjusting for other risk factors, the risk of hypertension among male drinkers was 1.236 times that of non-drinkers, and 1.409 times that of women.

A national survey of 8 provinces from 2007 to 2010, a cross-sectional study of 28 provinces from 2011 to 2012, and the China Health and Retirement Longitudinal Survey, all suggest that air pollution can increase the risk of hypertension. The CHS showed that systolic BP and diastolic BP decreased by 0.74 mmHg (1 mmHg = 0.133 kPa) and 0.60 mmHg, respectively, for every 10 °C increase in ambient temperature.

A meta-analysis of 41 clinical studies examining the relationship between hypertension and depression showed that the prevalence of depression among hypertensive patients in China was 28.5%.

A multicenter randomized controlled study published in the *"New England Journal of Medicine"* demonstrated that during a median follow-up of 3.34 years involving 8511 elderly hypertensive patients, the rate of primary outcome events in the intensive treatment group (47 out of 4243 patients, 3.5%) was significantly lower compared to the standard-care

group (196 out of 4268 patients, 4.6%) (RR = 0.74), with an absolute difference of 1.1%.<sup>[29]</sup>

Another study indicated that compared to standard hypertension control (BP target reduction to 140/90 mmHg), intensive hypertension control (BP target reduction to 133/76 mmHg) could potentially prevent 2.209 million CAD events, 4.409 million stroke events, and 75,100 CVD deaths among Chinese hypertensive patients within 10 years.<sup>[30]</sup> Intensive hypertension control was associated with a 13% reduction in stroke events, and in men and women, 17% and 11% of CAD events were avoided, respectively, compared to standard hypertension control.

According to the 2015–2025 China CVD policy model, treating patients with stage 1 and stage 2 hypertension, with and without CVD, compared to no treatment, could lead to a reduction of 803,000 CVD events each year (including 690,000 strokes and 113,000 cases of MI), and gain 1.2 million quality-adjusted life-years (QALY).

If China adopts the 2017 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the diagnosis and treatment of hypertension in adults and achieves current rates of hypertension treatment, it is estimated to reduce lifetime CVD treatment costs by \$3.77 billion, while preventing 1.41 million life-years lost due to disability.<sup>[31]</sup>

A community multicenter prospective cohort study assessed the long-term antihypertensive efficacy, cost-effectiveness, and cardiovascular outcomes of generic antihypertensive drugs compared to brand-name drugs using propensity score matching and cost-effectiveness analysis.<sup>[32]</sup> The findings showed that the average annual cost per patient in the generic drug group was significantly lower than in the brand-name drug group (\$220.4 and \$472.7, respectively). Using the generic drug resulted in an average savings of \$252.3 per patient per year, while the reduction in systolic BP was similar in both groups ( $7.1 \pm 1.0$  mmHg and  $7.9 \pm 1.0$  mmHg, respectively). The cost-effectiveness ratio, which represents the average annual cost of a 1 mmHg reduction in systolic BP at follow-up, was 31.0 for the generic group and 59.8 for the brand-name group. Compared to generic drug treatment, the cost of the original brand-name drug increased by \$315.4 for each additional 1

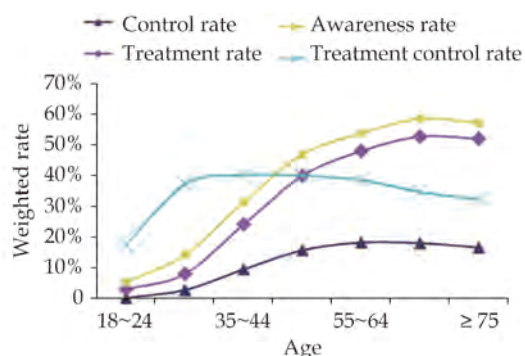


Figure 4 The awareness rate, treatment rate, control rate and treatment control rate of hypertension in different age groups in China Hypertension Survey (CHS).

Table 2 Hypertension awareness, treatment, and control rates in different studies.

Study	Year	Age	Sampling method	Sample size	Awareness rate (%)	Treatment rate (%)	Control rate (%)
National Hypertension Sample Survey	1991	≥ 15	Multistage random sampling	950,356	27.0	12.0	3.0
China Health and Nutrition Survey	2002	≥ 18	Multistage stratified cluster random sampling	272,023	30.2	24.7	6.1
Survey on Nutrition and Chronic Disease Status of China Residents	2012	≥ 18	Multistage stratified random sampling	/	46.5	41.1	13.8
Monitoring of Nutrition and Health Status of Chinese Residents	2010-2012	≥ 18	Multistage stratified cluster random sampling	120,428	46.5	41.1	14.6
Survey on Prevalence Awareness Treatment and Control Rate of Hypertension in China's Working Population	2012-2013	18-60	Multistage cluster sampling	37,856	57.6 (Standardized rate 47.8)	30.5 (Standardized rate 20.6)	11.2 (Standardized rate 8.5)
Chinese Hypertension Survey	2012-2015	≥ 18	Multistage stratified cluster random sampling	451,755	51.6 (Weighted rate 46.9)	45.8 (Weighted rate 40.7)	16.8 (Weighted rate 15.3)
Surveillance of Chronic Diseases and Risk Factors in China	2013-2014	≥ 18	Multistage stratified random sampling	174,621	31.9	26.4	9.7
Early Screening and Comprehensive Intervention Program for High-risk Groups of Cardiovascular Disease	2014	35-75	Multistage stratified random sampling	640,539	46.5 (Standardized rate)	38.1 (Standardized rate)	11.1 (Standardized rate)
Surveillance of Chronic Diseases and Risk Factors in China	2018	≥ 18	Multistage stratified cluster random sampling	179,873	41.0 (Weighted rate)	34.9 (Weighted rate)	11.0 (Weighted rate)





mmHg reduction in systolic BP.

The China Child and Adolescent Cardiovascular Health (CCACH) project conducted from 2012 to 2015 surveyed 44,396 children aged 6–17 years in 6 cities across the country. The survey employed a screening strategy of three time points on different days to investigate the prevalence of childhood hypertension.<sup>[33]</sup> Although there was a difference in the prevalence of hypertension at a single time point screened using the latest standards in China and the United States (17.1% vs. 15.4%), the prevalence decreased by 79% after 3 consecutive BP measurements on different days, and the final prevalence of hypertension was similar (3.7% vs. 3.3%).

In a randomized controlled study on nutrition and exercise intervention for hypertension prevention conducted in 30 primary schools across five cities, 15 schools were assigned as the control group (3333 participants), and the other 15 schools were assigned as the intervention group (3431 participants). The intervention group implemented a population-based nutrition promotion strategy (including nutrition courses, distribution of nutrition brochures, and guidance on meal preparation in school cafeterias) and exercise promotion (at least 20 min of moderate-to-high-intensity physical activity per day). After one year, compared to the control group, children in the intervention group experienced a 0.9 mmHg reduction in systolic BP and a 1.8% reduction in the incidence of hypertension.<sup>[34]</sup>

### Dyslipidemia

The 2015 China Adult Chronic Disease and Nutrition Surveillance project conducted a survey on 179,728 residents aged  $\geq 18$  years, revealing that the levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), and triglycerides (TG) in Chinese residents were higher compared to those in 2002 (Figure 5).<sup>[35]</sup>

Analysis conducted by the NCD Risk Factors Collaborative Group revealed that in 1980, the average non-HDL-C level among Chinese residents was one of the lowest globally. However, by 2018, it had reached or surpassed the non-HDL-C levels observed in many high-income Western countries, reaching as high as 4 mmol/L.<sup>[36]</sup>

The Beijing Child and Adolescent Metabolic Syn-



**Figure 5** Thirteen-year changes in blood lipid levels in Chinese adults aged  $\geq 18$  years. HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TG: total triglycerides.

drome (BCAMS) study examined 1660 and 1649 children and adolescents aged 6–18 years in Beijing in 2004 and 2014, respectively. The results demonstrated a significant increase in TC, LDL-C, non-HDL-C, and TG levels in 2014 compared to 10 years earlier (Figure 6).

Four large-scale epidemiological surveys conducted by CHNS in 2002, the 2010 China National Survey of Chronic Kidney Disease,<sup>[37]</sup> the 2011 CHNS,<sup>[38]</sup> and the 2012 Nutrition and Chronic Disease Surveillance of Chinese Residents indicated a substantial rise in the prevalence of dyslipidemia (defined as the presence of any type of dyslipidemia, including TC  $\geq 6.22$  mmol/L, LDL-C  $\geq 4.14$  mmol/L, HDL-C  $< 1.04$  mmol/L, TG  $\geq 2.26$  mmol/L) among Chinese individuals aged  $\geq 18$  years, from 18.6% in 2002 to 40.4% in 2012.

A CHS survey conducted from 2012 to 2015 involving 29,678 Chinese residents aged  $\geq 35$  years revealed an overall prevalence of dyslipidemia of 34.7%.<sup>[39]</sup> The 2014 the China National Stroke Screening and Prevention Project (CNSSPP) indicated that the age- and sex-standardized prevalence of dyslipidemia among Chinese residents aged  $\geq 40$  years was 43.0%.<sup>[40]</sup> Data from the fourth China Chronic Disease and Risk Factor Surveillance project<sup>[41]</sup>



**Figure 6** 10-year changes in blood lipid levels in children and adolescents aged 6–18 in Beijing. HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TG: total triglycerides.

and the 2015 China Adult Chronic Disease and Nutrition Surveillance project<sup>[35]</sup> from 2013 to 2014 demonstrated that the main types of dyslipidemia observed in Chinese residents were low HDL-C and high TG.

A study conducted from 2012 to 2013 investigated 16,434 children and adolescents aged 6–17 years from 93 primary and secondary schools across 7 provinces, autonomous regions, and municipalities in China. The overall detection rate of dyslipidemia was 28.5% (with the cut-off point for dyslipidemia in children defined as TC > 5.18 mmol/L, LDL-C ≥ 3.37 mmol/L, HDL-C < 1.03 mmol/L, and TG > 1.7 mmol/L).<sup>[42]</sup>

According to the CHS survey conducted from 2012 to 2015, the awareness rate of dyslipidemia among Chinese adults aged ≥ 35 years was 16.1%. The treatment rate was 7.8%, and the control rate was 4.0%.<sup>[39]</sup>

The fourth China Chronic Disease and Risk Factor Surveillance project survey, which included 163,641 residents, revealed that among the 15,382 individuals in the high-risk group (9.4% of the total population), the prevalence of LDL-C ≥ 2.6 mmol/L was as high as 74.5%. Among the 2945 cases in the extremely high-risk group (1.8% of the total population), the prevalence of LDL-C ≥ 1.8 mmol/L was as high as 93.2%.<sup>[41]</sup>

The analysis of the Dyslipidemia International Study-China (DYSIS-China), which involved 25,317 patients aged ≥ 45 years who had been treated with lipid-lowering drugs for at least 3 months,<sup>[43]</sup> showed that the LDL-C treatment control rate for individuals at high risk of atherosclerotic cardiovascular disease (ASCVD) was 44.1%, while for those at extremely high risk of ASCVD, it was 26.9%.

The Improving Care for Cardiovascular Disease in China (CCC) project enrolled 6523 patients with acute coronary syndrome (ACS) who had a documented history of MI or coronary revascularization in 150 tertiary hospitals across the country from November 2014 to June 2017. The results revealed that the statin treatment rate at admission was 50.8%, and the LDL-C control rate was 36.1% (LDL-C < 1.8 mmol/L). However, in patients aged ≥ 75 years at admission, the statin treatment rate was lower, at only 33.9%, and the control rate was also lower, at only 24.7% (LDL-C < 1.8 mmol/L).<sup>[44,45]</sup>

The GBD 2017 data demonstrated that 81.76% of

deaths attributed to high LDL-C were due to IHD, and 18.24% were due to ischemic stroke. The population attributable fractions of high LDL-C to IHD death and ischemic stroke was 40.30% and 18.49%, respectively. The mortality rate attributable to high LDL-C was 61.08 per 100,000 population, and high LDL-C accounted for 18.1621 million disability-adjusted life-years (DALY), of which IHD attributable DALY was 13.9415 million person-years, representing 76.76% of the total. The DALY rate was 1285.83 per 100,000 population.<sup>[46]</sup>

The Kailuan Prospective Cohort study followed 51,407 individuals for an average of 6.84 years and found that the cumulative exposure time to elevated LDL-C (≥ 3.4 mmol/L) and the cumulative exposure value of LDL-C measured multiple times significantly increased the risk of new-onset AMI. These findings suggest that the cardiovascular harm associated with LDL-C exhibits a “cumulative exposure” effect, which is independent of single LDL-C measurement.<sup>[47]</sup>

The CKB study demonstrated a positive correlation between LDL-C levels and ischemic stroke,<sup>[48]</sup> while a significant negative correlation with cerebral hemorrhage was observed (every 1 mmol/L reduction in LDL-C was associated with a 15% reduction in the relative risk of ischemic stroke, whereas the relative risk of hemorrhage increased by 16%). This correlation was further supported by Mendelian randomization analysis, which showed that a 1 mmol/L decrease in LDL-C level associated with genetic risk score corresponded to a 25% decrease in the relative risk of ischemic stroke and a 13% increase in the relative risk of hemorrhage. HDL-C levels were inversely associated with the risk of ischemic stroke (LDL-C and HDL-C independently associated with ischemic stroke) but not with cerebral hemorrhage. Additionally, TG levels showed a weak positive association with ischemic stroke and a negative association with intracerebral hemorrhage.

In a multi-provincial cohort study in China, 21,265 adults (aged 35–64 years) without ASCVD were included. Participants were classified based on the 10-year ASCVD risk assessment outlined in the “Guidelines for the Prevention and Treatment of Dyslipidemia in Chinese Adults (Revised 2016)”. The results indicated that low-dose statin intervention can reduce the 10-year incidence of ASCVD by 4.1%,



9.7%, and 15.5% in the low-, intermediate-, and high-risk groups, respectively. Furthermore, reducing statin prices to the level set by the central government's centralized procurement policy in 2019 can significantly decrease the incremental cost-effectiveness ratio for various risk groups, thus improving the cost-effectiveness of statins for primary prevention of ASCVD.<sup>[49]</sup>

## Diabetes

Multiple prevalence surveys on diabetes were conducted in China from 1980 to 2017 (Figure 7). In 1980, a study involving 300,000 individuals reported a diabetes prevalence of 0.67%. Between 2015 and 2017, a cross-sectional survey was conducted among 75,880 adults aged 18 years and above in 31 provinces, autonomous regions, and municipalities of China. This survey directly assessed the prevalence of diabetes in Chinese adults based on the diagnostic criteria set by the WHO. The results showed a prevalence of 11.2% (95% CI: 10.5%–11.9%), and the detection rate of prediabetes was 35.2% (95% CI: 33.5%–37.0%). Using the diagnostic criteria of the American Diabetes Association (ADA), the prevalence of diabetes was 12.8% (95% CI: 12.0%–13.6%). Furthermore, the prevalence of previously confirmed diabetes was 6.0% (95% CI: 5.4%–6.7%), and the prevalence of newly diagnosed diabetes was 6.8% (95% CI: 6.1%–7.4%). It is estimated that the total number of adults with diabetes in mainland China is 129.8 million (70.04 million males and 59.4 million females).<sup>[50]</sup>

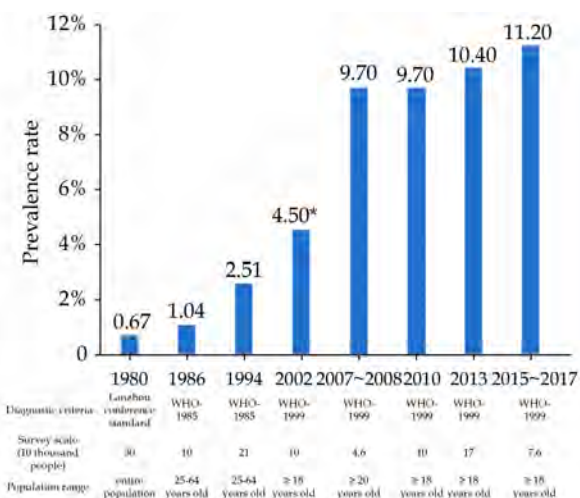


Figure 7 The prevalence of diabetes mellitus in China. Note: \*: Prevalence of diabetes in the urban population

Based on the Diabetes Surveillance System of Zhejiang Province, data from 879,769 newly diagnosed patients with type 2 diabetes, between January 1, 2007, and December 31, 2017, were analyzed. The results revealed that the age-standardized total incidence of type 2 diabetes was 281.73 per 100,000 person-years (95% CI: 281.26–282.20). The standardized annual incidence increased from 164.85 per 100,000 person-years in 2007 to 268.65 per 100,000 person-years in 2017. The average annual increase was 4.01 percent, with a faster increase observed among men, young people, and individuals living in rural areas.<sup>[51]</sup>

The Daqing Diabetes Prevention Study in China enrolled 577 adults with impaired glucose tolerance diagnosed through glucose tolerance tests from 33 clinics. Participants were randomly assigned to a control group or to one of three lifestyle interventions (diet, exercise, or diet plus exercise). The intensive lifestyle intervention lasted from 1986 to 1992. Over 30 years of follow-up, compared to the control group, the intervention group experienced a median delay of 3.96 years in the onset of diabetes, a 39% lower risk of diabetes, a 26% lower risk of cardiovascular events, a 35% lower risk of composite microvascular events, a 33% lower risk of cardiovascular death, and a 26% lower risk of all-cause death. The incidence of stroke and severe retinopathy in the intervention group was also significantly lower than that in the control group, and the average life expectancy in the intervention group was 1.44 years longer than that in the control group.<sup>[52]</sup>

Mathematical models estimated that nationwide lifestyle interventions for individuals with prediabetes had a high effective potency ratio. The cumulative incidence rate of diabetes was reduced by 9.53%, average life expectancy increased by 0.82 years, QALY increased by 0.52, average total cost reduced by \$700, and the incremental cost-effectiveness ratio was -\$1339 per QALY.<sup>[53]</sup>

## Chronic Kidney Disease

A total of 47,204 participants aged over 18 years were enrolled in the national prevalence study of chronic kidney disease (CKD), conducted in 13 provinces, autonomous regions, and municipalities from September 2009 to September 2010. The res-

ults showed that the overall prevalence of CKD was 10.8%, indicating that there were approximately 120 million CKD patients in China. The prevalence of renal dysfunction [estimated glomerular filtration rate (eGFR) < 60 mL/min per 1.73 m<sup>2</sup>] was 1.7%, and the prevalence of albuminuria (urinary albumin to creatinine ratio > 30 mg/g) was 9.4%.

In the China Health and Retirement Longitudinal Survey study conducted in 2015–2016, 6706 participants aged 60 years and older were included. The total prevalence of reduced renal function (eGFR < 60 mL/min per 1.73 m<sup>2</sup>) was 10.3%. With increasing age, the prevalence rate of reduced renal function increased continuously (60–64 years: 3.3%; 65–69 years: 6.4%; 70–74 years: 11.4%; 75–79 years: 22.2%; > 80 years: 33.9%).<sup>[54]</sup>

According to the 2016 annual report of China Kidney Disease Network (CK-NET), patients with CKD accounted for 4.86% of the total inpatients in that year. The prevalence of CKD was 13.90% in patients with diabetes, 11.41% in patients with hypertension, and 7.96% in patients with CVD. Among hospitalized CKD patients, 18.82% had CAD, 16.91% had heart failure (HF), 13.22% had stroke, and 4.01% had atrial fibrillation (AF).<sup>[55]</sup>

In 2016, the per capita hospitalization expenditure for CKD patients was 15,405 RMB (IQR: 8435–29,542 RMB), which was higher than the 11,182 RMB (IQR: 5916–18,922 RMB) for patients without CKD. The average cost was 89,257 RMB for hemodialysis patients and 79,653 RMB for peritoneal dialysis patients.<sup>[55]</sup>

## Metabolic Syndrome

In the survey of the nutrition and health status of Chinese residents conducted from 2010 to 2012,<sup>[56]</sup> researchers included 98,042 subjects older than 18 years from 31 provinces, autonomous regions, and municipalities directly under the central government. They found that the prevalence of metabolic syndrome was 24.2% based on the revised National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) standard.

In the same survey, researchers also included 16,872 children and adolescents aged 10–17 years. The results showed that the prevalence of metabolic syndrome was 2.4% based on the diagnostic criteria proposed by the Society of Pediatrics, Chinese

Medical Association. Using the Cook criteria, the prevalence of metabolic syndrome was 4.3%.

## Air Pollution

Ambient air pollution and indoor air pollution are the third and 13<sup>th</sup> risk factors affecting DALY in China. Compared with 1990, the total number of deaths related to indoor air pollution decreased by 72.7%, and DALY loss decreased by 80.2% in 2019.

From 2000 to 2016 in China, the number of excess mortality cases attributed to long-term exposure to PM<sub>2.5</sub> exceeded 30 million, with annual numbers ranging from 1.5 million to 2.2 million.<sup>[57]</sup>

A nationwide study evaluated the long-term exposure to PM<sub>2.5</sub> and its associated disease burden. The results showed that from 2000 to 2016 in China, the number of deaths attributable to PM<sub>2.5</sub> pollution reached 30.08 million. Since 2013, there has been a gradual decrease in the total number of deaths caused by PM<sub>2.5</sub> exposure.<sup>[57]</sup>

From 2013 to 2015 in China, a series of studies based on daily air pollution data and cause of mortality in 272 cities were conducted. These studies found that as exposure concentrations to PM<sub>2.5</sub>, coarse particles (diameter: 2.5–10.0 μm), ozone (O<sub>3</sub>), sulfur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>), and carbon monoxide (CO) increased, the risk of mortality from CVD also increased. The increase in exposure concentrations to air pollutants was also associated with an increased risk of mortality from CAD and hypertension.<sup>[58–61]</sup>

A prospective cohort study based on 226,000 urban residents in China showed that compared with residents who always use clean fuel for cooking, residents who use solid fuel had a 19% higher risk of all-cause mortality, a 24% higher risk of CVD mortality, and a 43% higher risk of respiratory disease mortality. Additionally, the use of kitchen ventilation reduced the risk of all-cause mortality by 19% and CVD mortality by 25%.<sup>[62]</sup>

## COMMUNITY PREVENTION AND TREATMENT OF CVD

The National Demonstration Area for Comprehensive Prevention and Control of Chronic Diseases, referred to as the “Demonstration Area”, is an innovative project aimed at implementing the





concept of “Healthy China” and promoting health policies. By 2020, a total of 488 national-level demonstration areas had been established in 31 provinces, autonomous regions, and municipalities directly under the central government in mainland China, covering 17.1% of the country’s counties, cities, and districts.<sup>[63]</sup> This has surpassed the mid-term target set in China’s Medium-to-Long Term Plan for the Prevention and Treatment of Chronic Diseases (2017–2025), which aimed for a 15% coverage of demonstration areas by 2020.

In Tianjin’s Demonstration Area, while implementing the “Three Reductions and Three Health” healthy lifestyle initiative, various innovative models were explored, such as community hypertension management and the establishment of medical alliances. From 2008 to 2018, the average life expectancy in the demonstration area increased from 81.48 years to 82.38 years. The average life expectancy for males increased from 79.66 years to 80.31 years, while for females, it increased from 83.44 years to 84.51 years. However, there was no upward trend in the average life expectancy for males in the non-demonstration areas. The crude mortality and standardized mortality rates for AMI in the demonstration area showed a downward trend, with annual percentage changes greater than those in the non-demonstration area (crude mortality: -5.36% vs. -4.02%; standardized mortality: -6.27% vs. -5.41%).

Through the continuous construction and improvement of the chronic disease surveillance system in Chongqing and Guiyang, the probability of premature death from major chronic diseases in the demonstration area was analyzed. The results showed a significant downward trend in the probability of premature death from major chronic diseases in the demonstration area, decreasing from 17.21% in 2012 to 15.38% in 2017. This probability was consistently lower than that in the non-demonstration area, which showed no significant annual changes (16.79% in 2012 and 17.05% in 2017). In Guiyang, the analysis indicated that in 2018, the probability of premature death from major chronic diseases in the demonstration areas (including 2 national and 3 provincial demonstration areas) was 15.95%. The probability of premature death from CVD was 7.48%, meaning that the overall probability of death due to CVD for a person aged 30 years, who was expected to survive

until aged 69 years, was 7.48% based on the probability of CVD death for each age group between 30 and 69 years.

## CARDIOVASCULAR DISEASE

### Epidemiological Trend

The prevalence of CVD in China is increasing. It is estimated that there are 330 million individuals with CVD, including 13 million stroke cases, 11.4 million cases of CAD, 8.9 million cases of HF, 5 million cases of pulmonary heart disease, 4.9 million cases of AF, 2.5 million cases of rheumatic heart disease (RHD), 2 million cases of congenital heart disease (CHD), 45.3 million cases of lower extremity arterial disease, and 245 million cases of hypertension.

Since 2009, the rural CVD mortality rate has surpassed and remained higher than the urban rate (Figure 8A). CVD is the leading cause of disease-related deaths among both urban and rural residents.<sup>[64]</sup> In 2019, CVD accounted for 46.74% of deaths in rural areas and 44.26% of deaths in urban areas (Figure 8B). Two out of every five deaths are attributed to CVD. In the same year, the CVD mortality rate in rural areas was 323.29/100,000, with heart disease accounting for 164.66/100,000 and cerebrovascular disease accounting for 158.63/100,000 (Figure 9A). The CVD mortality rate in urban areas was 277.92/100,000, with heart disease accounting for 148.51/100,000 and cerebrovascular disease accounting for 129.41/100,000 (Figure 9B).

### Coronary Artery Disease

According to the China Health Statistics Yearbook 2020,<sup>[64]</sup> the mortality rate of coronary artery disease (CAD) among urban residents in China was 121.59/100,000 in 2019, while in rural areas, it was 130.14/100,000. The mortality rate of CAD has shown an upward trend since 2012 and significantly increased in rural areas, surpassing the urban rate by 2016 (Figure 10A).

The mortality rate of AMI generally increased from 2002 to 2018 but slightly decreased in 2019. Starting from 2005, there was a rapid upward trend in the AMI mortality rate. The AMI mortality rate in rural areas not only exceeded that in urban areas in



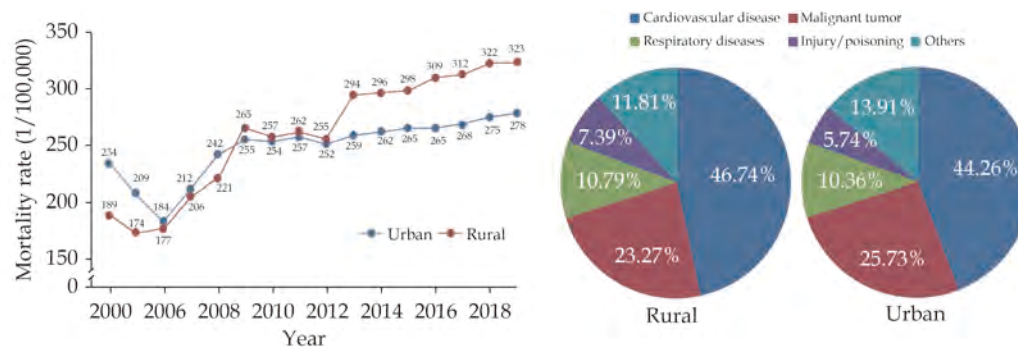


Figure 8 Changes in cardiovascular mortality rates of urban and rural residents in China, 2000 to 2019 (A) and constituent ratios of major causes of death of urban and rural residents in China, 2019 (B).

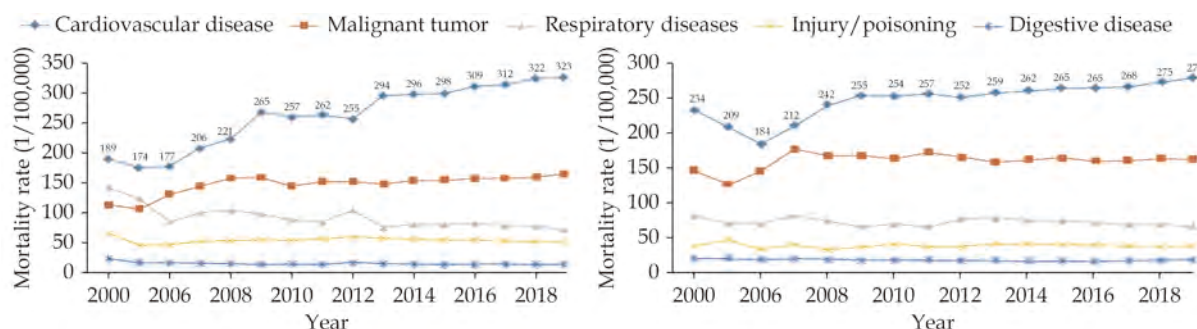


Figure 9 Mortality of major diseases in rural (A) and urban (B) residents in China from 2000 to 2019.

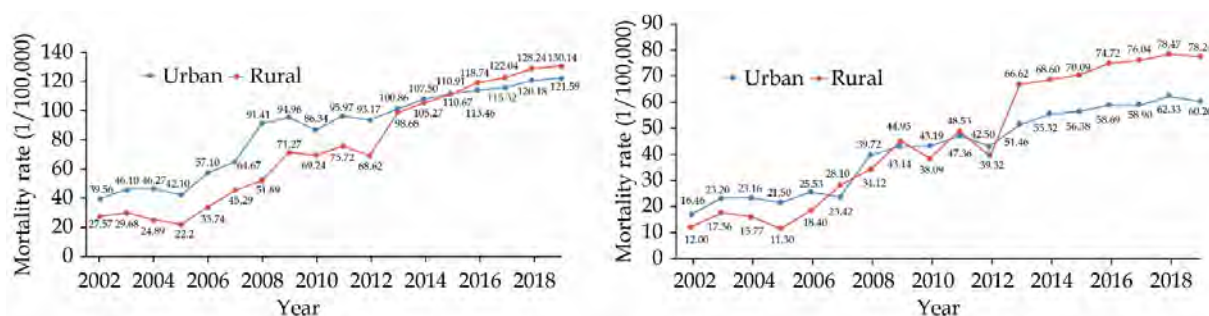


Figure 10 Trends of CAD mortality (A) and acute myocardial infarction mortality (B) in urban and rural China from 2002 to 2019.

2007, 2009, and 2010 but also significantly increased since 2012 and remained higher than that in urban areas since 2013 (Figure 10B).

According to the fifth China Health Service Survey in 2013, the prevalence of CAD was 10.2% in the population aged  $\geq 15$  years and 27.8% in the population aged over 60 years in the Chinese mainland. The overall prevalence increased compared with the fourth survey in 2008 (7.7%). In 2013, the number of people aged  $\geq 15$  years with CAD in mainland China was 11.4 million, an increase of about 1.08 million over the number of people with CAD at all ages in the fourth National Health Service Survey in 2008.

China PEACE analyzed 13,815 inpatient medical

records from 162 randomly selected secondary and tertiary hospitals in 31 provinces, autonomous regions and municipalities in mainland China. The study found that the number of patients hospitalized for ST-segment elevation MI (STEMI) per 100,000 people in China increased annually from 2001 to 2011. When estimated based on the natural population, STEMI hospitalization rates rose from 3.7/100,000 in 2001 to 8.1/100,000 in 2006 and 15.8/100,000 in 2011. Studies have also revealed significant geographical variations in the medical processes and outcomes of AMI patients in China, which persist across the four time points of 2001, 2006, 2011, and 2015.<sup>[65]</sup>

Analysis of the Chinese Acute Myocardial Infarc-

tion Registry<sup>[66]</sup> study revealed significant differences in the treatment and outcomes of STEMI patients across different levels of hospitals in China. Compared to provincial hospitals, district and county hospitals had a lower proportion of STEMI patients receiving reperfusion therapy and a higher proportion of in-hospital deaths.

The Clinical Pathways for Acute Coronary Syndromes in China (CPACS)<sup>[67]</sup> included 15,140 ACS patients from 70 hospitals in 17 provinces, autonomous regions and municipalities in mainland China. The results showed a decreasing trend in the application rate of standardized secondary prevention drugs in ACS patients after discharge. The application rate was 86% at discharge, but dropped to 68% after one year and 59.7% after two years.

A study involving 3387 patients with AMI within 24 h of onset from 53 hospitals across different regions of China<sup>[68]</sup> reported a 30-day rehospitalization rate of 6.3%, with nearly 50% of rehospitalizations occurring within 5 days after discharge. Among these rehospitalizations, 77.7% were due to cardiovascular events, including angina pectoris (31.2%), HF (16.7%), and AMI (13.0%).

The China-PEACE study<sup>[69]</sup> demonstrated a high recurrence rate of early MI in Chinese AMI patients after discharge, with a one-year recurrence rate of 2.5%, of which 35.7% occurred within 30 days after discharge. Patients with recurrent MI had a 25.42 times higher one-year mortality rate, and those with early recurrent MI had the highest one-year mortality rate (53.5%).

The Chinese Acute Myocardial Infarction Registry study analyzed 80 hospitals that admitted  $\geq 50$  STEMI patients and were capable of emergency percutaneous coronary intervention from 2013 to 2016.<sup>[70]</sup> A total of 29,581 consecutive STEMI patients were admitted to these hospitals, and the in-hospital mortality rate was 6.3%. Based on the Chinese guidelines for the diagnosis and treatment of STEMI and the American quality standard for MI, the opportunity-based composite score (OBCS) showed that the in-hospital mortality rates of STEMI patients in hospitals with lower OBCS ( $< 71.1\%$ ), middle OBCS (71.1%–76.5%), and higher OBCS ( $> 76.5\%$ ) were 7.2%, 6.6%, and 5.4%, respectively.

According to the Hospital Quality Monitoring System (HQMS), 10,259,521 cases of CVD were treated in 1910 tertiary public hospitals (79.5% of

the total number of tertiary public hospitals in China) and 2124 secondary public hospitals (35.9% of the total number of secondary public hospitals). Based on the initial data extracted from relevant inpatients' medical records (excluding military and Traditional Chinese Medicine hospitals), the number of patients who underwent percutaneous coronary intervention in China in 2020 was 1,014,266.<sup>[71]</sup>

Data from the Chinese Cardiac Surgery Registry (CCSR) study,<sup>[72]</sup> which involved 87 heart centers in China, demonstrated that 56,776 patients underwent coronary artery bypass grafting from 2013 to 2016, with an overall in-hospital mortality rate of 2.1% after coronary artery bypass grafting.

A multicenter cross-sectional study conducted at nine locations in China from 2017 to 2019, involving over 6000 patients undergoing coronary angiography or CT angiography, revealed an association between facial features and an increased risk of CAD. The research team developed and validated a deep learning algorithm for detecting CAD based on facial photos, which shows potential for assisting in CAD identification and could be promising for outpatient CAD probabilistic assessment or community CAD screening.<sup>[73]</sup>

## Cerebrovascular Diseases

Stroke was the leading cause of death in China in 2019, with 2,189,175 cases, representing a 12.4% increase compared to 2009. In the same year, there were 3,935,182 new stroke cases in China, bringing the total number of stroke patients to 28,760,186. Stroke also ranked first in terms of DALY in 2019, with a total of 45,949,134 DALY and an age-standardized DALY rate of 2412.52/100,000.<sup>[74]</sup>

In 2019, the crude mortality rate of cerebrovascular diseases among Chinese residents was 149.56/100,000, accounting for 22.17% of all deaths. Among all causes of death, cerebrovascular diseases ranked third after malignant tumors (162.46/100,000) and heart diseases (160.26/100,000).

The crude mortality rate of cerebrovascular diseases in urban residents was 129.41/100,000, accounting for 20.61% of total deaths in urban areas. In rural areas, the rate was 158.63/100,000, accounting for 22.94% of total deaths. The crude mortality rate of cerebrovascular diseases in Chinese residents is higher in males than in females and higher in rural areas than in urban areas.<sup>[64]</sup>



From 2003 to 2019, the crude mortality rate of cerebrovascular diseases in the rural population was consistently higher than that in urban residents each year. Between 2006 and 2009, the crude mortality rate of cerebrovascular diseases increased by 1.41-fold in urban residents and 1.44-fold in rural areas. From 2009 to 2012, the crude mortality rate of cerebrovascular diseases showed a downward trend year by year, but experienced a slight increase from 2013 to 2019, particularly significant in rural areas (Figure 11).

From 1997 to 2015, an analysis of 15,917 residents conducted by CHNS revealed that the age-standardized incidence of stroke was 4.17/1000 person-years in the northern region and 1.95/1000 person-years in the southern region, showing a statistically significant north-to-south gradient difference. This difference was primarily observed in rural areas rather than urban areas. Hierarchical model analysis

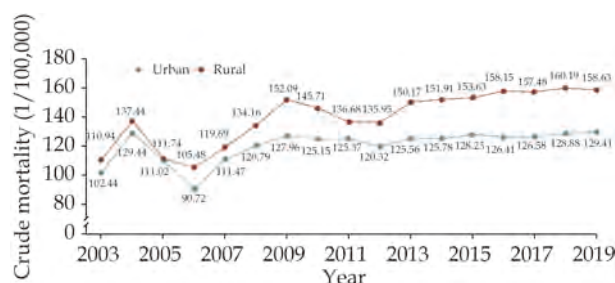


Figure 11 Trends of crude mortality from cerebrovascular disease in urban and rural residents in China from 2003 to 2019.

is suggested that the regional disparity could be attributed to variations in hypertension prevalence.<sup>[75]</sup>

In the national epidemiological study of transient ischemic attack (TIA) conducted in 2013, a face-to-face survey was carried out in 178,059 households across 155 disease surveillance sites. Among the 595,711 participants, the weighted incidence of TIA was 23.9/100,000, with a rate of 21.3/100,000 in males and 26.6/100,000 in females. It was estimated that there are approximately 310,000 new TIA cases in China each year.<sup>[76]</sup>

The epidemiological survey in 2013 revealed that the prevalence of stroke in China was 1596.0/100,000, with an age-standardized prevalence of 1114.8/100,000. The prevalence was higher in rural areas (1291.1/100,000) than in urban areas (814.4/100,000). Among the different regions, central China had the highest prevalence of stroke (1549.5/100,000), followed by northeast China (1450.3/100,000) and North China (1416.5/100,000), while South China had the lowest prevalence (624.5/100,000).<sup>[77]</sup>

According to the 2019 cerebrovascular disease surveillance platform, a total of 291,632 inpatients with acute ischemic stroke were enrolled from 31 provinces in China. The intravenous thrombolysis rate using human recombinant tissue plasminogen activator was 30.4%, and the in-hospital mortality rate was 0.4% among patients who arrived at the hospital within 4.5 h of symptom onset (Table 3).

Table 3 Medical quality indicators for inpatients with acute ischemic stroke in 2019.

Medical quality indicator	N (%)
Process indicators	
Rate of intravenous thrombolysis with RT-PA in patients admitted to hospital within 4.5 h after onset	22,400 (30.4%)
Prophylaxis rate of deep vein thrombosis in patients unable to walk within 48 h after admission <sup>#</sup>	9,266 (12.0%)
Dysphagia screening rate	231,089 (80.7%)
Rehabilitation assessment rate	212,028 (74.0%)
Rate of antithrombotic therapy at discharge	251,035 (88.7%)
Rate of anticoagulant therapy in patients with atrial fibrillation at discharge	9,166 (45.9%)
Rate of statin therapy in patients with non-cardiogenic cerebral infarction at discharge	248,258 (90.7%)
Rate of antihypertensive therapy in patients with hypertension at discharge	143,232 (64.9%)
Rate of hypoglycemic drug treatment in patients with diabetes at discharge	63,678 (78.4%)
Outcome indicators	
In-hospital mortality rate	1,066 (0.4%)

RT-PA: Human recombinant tissue plasminogen activator. <sup>#</sup>Defined as the number of patients who received deep vein thrombosis prophylaxis (anticoagulant drugs and/or intermittent inflatable compression) as a proportion of hospitalized patients unable to walk within 48 h of admission.





## Arrhythmias

According to statistics from the National Health Commission's online registration system and data reported by provincial quality control centers, there were 86,181 cases of pacemaker implantation in China in 2020. Dual-chamber pacemakers accounted for 73% of these cases. The nationwide incidence of pacemaker implantation decreased by 4.8% in 2020 compared to 2019, primarily due to the impact of the COVID-19 epidemic. The main indications for pacemaker implantation included sick sinus syndrome (55.0%), atrioventricular block (41.5%), and others (3.5%). Clinical studies exploring the feasibility, safety, and efficacy of His bundle-Purkinje pacing (including His bundle or left bundle branch pacing) in patients with bradyarrhythmias have been rapidly advancing.<sup>[78]</sup> The technology of left bundle branch pacing originated from China, and since 2019, over 70 related articles have been published in international CVD journals.

According to the results of the CHS conducted from 2012 to 2015,<sup>[79]</sup> the prevalence of AF in Chinese adults over 35 years was 0.7%, with 34% of them being newly diagnosed and unaware of their condition. The prevalence of AF was higher in rural areas compared to urban areas (0.75% vs. 0.63%).

Based on the China National Stroke Screening Survey (CNSSS), which included 1,252,703 Chinese adults over 40 years during 2013 and 2014, 12% of patients with ischemic stroke were found to have AF as a complication, suggesting a potential coexistence of ischemic stroke and AF in over 2.15 million patients. Among those with ischemic stroke and AF, only 2.2% were receiving anticoagulant therapy, with warfarin accounting for 98.2% of the prescribed medications.<sup>[80]</sup>

The China Atrial Fibrillation Registry study included 7977 patients with nonvalvular AF in 32 hospitals between 2011 and 2014, and found that there were 36.5% and 28.5% of patients receiving oral anticoagulants in those with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores  $\geq 2$  and of 1, respectively. Among those with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 0, there were also 21.4% patients had taken oral anticoagulants. Oral anticoagulants prescription was higher in tertiary hospitals (9.6% – 68.4%), compared to non-tertiary hospitals (4.0% – 28.2%).

According to statistics from the National Atrial Fibrillation Registry network, the proportion of radiofrequency catheter ablation for AF has been increasing. In 2017, 2018, 2019, and 2020, it accounted for 27.3%, 31.9%, 33.0%, and 32.2% of overall radiofrequency catheter ablation cases, respectively. Currently, circumferential pulmonary vein electrical isolation remains the predominant method of AF radiofrequency catheter ablation, representing 60.2% of all ablation cases. The incidence of perioperative ischemic stroke and hemorrhagic stroke was 0.4% and 0.1%, respectively.<sup>[81]</sup>

Radiofrequency catheter ablation has been widely adopted in over 600 hospitals in China. Data from the National Health Commission's online registration system demonstrate a significant increase in the number of radiofrequency catheter ablation procedures since 2010, with an annual growth rate of 13.2%–17.5%. However, due to the COVID-19 epidemic, the number of radiofrequency ablation procedures in 2020 was significantly lower than in previous years, totaling 102,864 cases. In 2020, catheter ablation for supraventricular tachycardia and AF accounted for 40.7% and 32.2% of all catheter ablation cases, respectively; which was similar to the distribution in 2019.

In a prospective study involving 678,718 participants, it was found that between July 2005 and June 2006, there were 2983 deaths, including 284 cases (9.5%) of sudden cardiac death (SCD). The incidence of SCD was 41.8 per 100,000 person-years, with higher rates in men (44.6 per 100,000) than in women (39.0 per 100,000). It is estimated that there are nearly 500,000 cases of SCD in China each year.

According to statistics from the National Health Commission's online registration system and data reported by provincial quality control centers, the number of implantable cardioverter defibrillator (ICD) cases in 2020 slightly decreased compared to 2019 (4800 cases vs. 5031 cases) due to the COVID-19 outbreak. Single-chamber ICD implantation accounted for 50% of all ICD cases in 2020, with 53% for primary prevention and 47% for secondary prevention.

Regarding long QT syndrome (LQTS), a previous study including 230 LQTS patients from 10 hospitals in China found that the proportions of LQT types 1 (KCNQ1 mutation), 2 (KCNH2 mutation),



and 3 (SCN5A mutation) were 37%, 48%, and 2%, respectively; representing the three main types of LQTS.

According to research conducted by the National Ion Channel Diseases Registry Center and the International Project Collaborative Group, the average onset age of LQTS probands is  $17.3 \pm 14.2$  years. Overall, 60% of LQTS patients experience onset before the age of 20 years, and 76% of them are women. LQTS in children is highly malignant and often presents as complex arrhythmias, with a detection rate of pathogenic or possibly pathogenic variants reaching 71%.<sup>[82]</sup> In Southwest China, 33.7% of patients with unexplained sudden death were found to harbor LQTS-associated mutations (KCNQ1 and KCNH2).<sup>[83]</sup>

Results from previous health checkup studies focused on workers aged 20–50 years showed that early repolarization is more common in males and individuals with moderate or higher labor intensity, with a detection rate of 2.73%–3.99%. An electrocardiogram (ECG) screening analysis of 13,405 high school or college students found an early repolarization detection rate of 1%, which was more common in males. Early repolarization is most frequently observed in the inferior leads, followed by a combination of the inferior and lateral leads. The main ECG morphology associated with early repolarization is slurring and notching. During a follow-up period of 12 to 36 months, no cardiovascular events or arrhythmias (including SCD) were observed. Another ECG study involving 1215 college athletes revealed that 35.9% of participants exhibited early repolarization, with a higher prevalence among males. Similarly, most cases of the early repolarization ECG pattern presented as notching and were observed in the inferior leads.

### Valvular Heart Disease

In a previous national survey that included 34,994 Chinese individuals aged 35 years or older, conducted using stratified multistage random sampling, it was observed that 1309 individuals were diagnosed with valvular heart disease (VHD) through echocardiography between October 2012 and December 2015. The weighted prevalence of VHD was found to be 3.8%, suggesting that there are approximately 25 million patients with VHD in China.<sup>[84]</sup>

RHD is the primary cause of VHD in China, although the prevalence of degenerative valve disease has been significantly increasing in recent years. The main etiologies of VHD in China include RHD (55.1%) and degenerative valve disease (21.3%) (Figure 12).

In a retrospective study conducted at Zhongshan Hospital of Fudan University, Shanghai, China, 3673 patients with bicuspid aortic valve were identified among 325,910 individuals who underwent transthoracic echocardiography from January 2011 to December 2015. The study revealed a male predominance of 69.1%, with 58.4% of patients having overt aortic valve dysfunction, 52.5% experiencing ascending aortic dilatation, and 19.2% displaying aortic root dilatation.<sup>[85]</sup>

### Congenital Heart Diseases

CHD are the most common birth defects in many areas of China, with a prevalence that varies between 2.9‰ and 16‰ among different territorial regions.

A meta-analysis focused on the birth prevalence and spatial distribution of CHD in China,<sup>[86]</sup> including 617 studies involving 76,961,354 births from 1980 to 2019. The results showed that the detection rate of neonatal CHD in China has continued to increase, from 0.201‰ in 1980–1984 to 4.905‰ in 2015–2019. The national birth prevalence of CHD gradually increased from the western region to the eastern region but decreased from the southern to the northern region.

A survey conducted in 12 hospitals in eastern China and 6 hospitals in western China from Au-

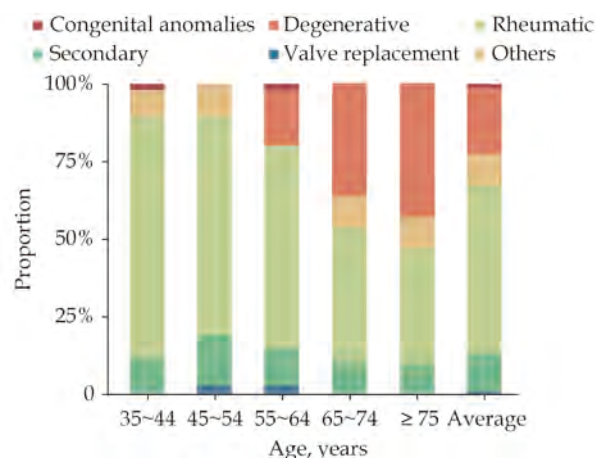


Figure 12 Proportion of the etiology for valvular heart disease among age stratifications.

gust 2011 to November 2012,<sup>[87]</sup> involving 122,765 neonates, showed that the detection rate of CHD in Chinese neonates was 8.98‰. The prevalence of CHD in female births (11.11‰) was higher than in male births (7.15‰).

According to the China Health Statistics Yearbook 2020,<sup>[64]</sup> the mortality rate of CHD in Chinese urban and rural areas was 0.76/100,000 and 0.91/100,000, respectively, in 2019.

Based on data from the Chinese Society of Extracorporeal Circulation from 714 Chinese hospitals (including Hong Kong, China),<sup>[88]</sup> a total of 62,704 CHD operations were conducted in 2020, accounting for 28.2% of all heart and aorta surgeries. The proportion of CHD surgeries showed a downward trend, becoming the second most common disease in cardiovascular surgery departments for the first time (Figure 13). This decline may be attributed to a decrease in the number of births and annual birth rate, as well as the increased popularity of prenatal diagnosis and screening. In 2020, there were 37,665 heart surgeries performed on patients under 18 years, accounting for 60.1% of all CHD surgeries. Compared with 2019, there was a 6.5% decrease in heart surgery among patients under 18 years in 2020, indicating an increasing trend in the number of CHD surgeries in adult patients.

According to data from the National Health Commission's Congenital Heart Disease Interventional Therapy Network Reporting System and the Military Congenital Heart Disease Interventional Ther-

apy Network Reporting System, there were a total of 39,027 cases of interventional therapy for CHD in mainland China in 2019. The number of intervention therapy cases in local hospitals on the mainland reached 34,758 in 2019, representing a 5.45% increase compared to 2018. The interventional procedures for CHD had a relatively high success rate of 98.41%, with a serious complication rate of 0.12% and a mortality rate of 0.01%. Overall, the number of interventional therapies for CHD in Chinese local hospitals has shown a slow upward trend. In 2019, there were 313 local hospitals and 483 physicians in mainland China qualified to perform CHD interventional procedures.

### Cardiomyopathy

From October 2001 to February 2002, a stratified cluster sampling survey was conducted across nine provinces in China, including 8080 individuals (4064 male and 4016 female). The survey observed a crude prevalence of 0.16% for hypertrophic cardiomyopathy (HCM), with a higher prevalence in males (0.22%) than females (0.10%). After adjusting for age and sex, the prevalence was estimated to be 80/100,000, suggesting that there are more than ten thousand adult patients with HCM in China. The study also revealed that the prevalence of dilated cardiomyopathy (DCM) in China during the same period was 19/100,000. Another study, involving 49,751 Chinese participants from 120 villages in seven provinces, aimed to investigate the prevalence of DCM in northern China areas without epidemics of Keshan disease. The results showed that six patients were diagnosed with DCM from July 2011 to December 2011, indicating an estimated prevalence of 12/10,000.

An analysis conducted by the Chinese Society of Cardiology, which included 10,714 patients with HF from 42 hospitals, revealed that the prevalence of DCM was 6.4%, 7.4%, and 7.6% in the 1980s, 1990s, and 2000s, respectively.

From July 2006 to December 2018, the clinical data of hospitalized children treated in 33 Pediatric Departments in China were retrospectively analyzed by the Subspecialty Group of Cardiology of the Society of Pediatrics in the Chinese Medical Association.<sup>[89]</sup> The study included a total of 4981 hospitalized children with cardiomyopathy, accounting

■ Surgery for congenital heart diseases ■ Surgery for valvular heart diseases  
■ Coronary artery bypass grafting ■ Surgery for large vessels ■ Others

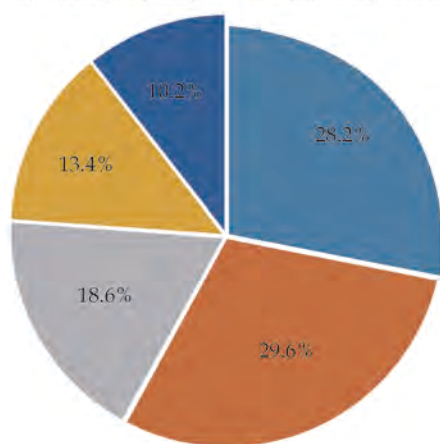


Figure 13 Proportions of heart and large vessels surgery in 714 Chinese hospitals in 2020.



for 0.079% (4981/6,319,678 cases) of pediatric hospitalized children. DCM was the most common type of cardiomyopathy ( $n = 1641$ , 32.95%), followed by endocardial fibroelastosis ( $n = 1283$ , 25.76%) and left ventricular noncompaction ( $n = 635$ , 12.75%). The total number of hospitalized children with cardiomyopathy showed an increasing trend annually (Figure 14).

In an analysis that included 529 Chinese patients with HCM, variants were identified in 43.9% of the patients, predominantly located in *MYH7* and *MYBPC3* genes. Another study conducted by Fuwai Hospital of the Chinese Academy of Medical Sciences (Beijing, China) found that common variants could also contribute to the development of HCM.<sup>[90]</sup> This study also suggested the existence of non-Mendelian inheritance of HCM and provided important insights into the ethnic differences in the genetic architecture of HCM.<sup>[90]</sup>

Arrhythmogenic cardiomyopathy (ACM) is mainly caused by desmosomal genetic variants. Results from a previous Chinese study showed that a pathogenic desmosomal variant was identified in 63.3% of ACM patients, with *PKP2* being the most common variant.<sup>[91]</sup> The homozygous founder variant of *DSG2* (p.Phe531Cys) was found to be a predisposing factor for ACM in China, with a high frequency of 8.47% among Chinese ACM patients and a high penetrance rate.<sup>[92]</sup> The homozygous variant c.245G > A/p.G82D in *PNPLA2* is associated with the phenotypic manifestations in Chinese patients with ACM.<sup>[93]</sup>

Regarding noncompaction cardiomyopathy (NC-

CM), a prior Chinese study retrospectively reviewed fetuses with a prenatal diagnosis of NCCM between October 2010 and December 2019. Out of 49,898 participants, 37 fetuses were identified with NCCM, indicating an incidence of 0.07% in the fetal population. Among the 20 fetuses undergoing copy number variation sequencing and whole-exome sequencing, 47% had positive genetic results, with non-sarcomere gene mutations accounting for the majority. No mutations were identified in the three most common sarcomere genes (*MYH7*, *TTN*, and *MYBPC3*) in pediatric and adult patients.<sup>[94]</sup>

### Heart Failure

The survey of 15,518 participants covering 10 provinces, 20 cities and counties in China showed that the prevalence of chronic HF in patients aged 35–74 years was 0.9% in 2000, suggesting that there are approximately 4 million patients with chronic HF in China.

The CHS of 22,158 participants revealed that 1.3% (estimated 13.7 million) of the Chinese population aged  $\geq 35$  years had HF,<sup>[95]</sup> with 1.4% of participants exhibiting left ventricular systolic dysfunction (left ventricular ejection fraction < 50%), and 2.7% classified as having moderate or severe diastolic dysfunction.

The China Heart Failure (China-HF) Registry, which enrolled 13,687 patients with HF from 132 hospitals between January 2012 and September 2015,<sup>[96]</sup> reported an in-hospital mortality rate of 4.1%. The 2020 China Heart Failure Medical Quality Control Report<sup>[97]</sup> analyzed 33,413 cases of HF patients recorded in 113 hospitals across the country from January 2017 to October 2020, revealing an in-hospital mortality rate of 2.8%.

A five-year follow-up of 3335 patients diagnosed with acute HF admitted in emergency departments of 14 hospitals in Beijing between January 1, 2011 and September 23, 2012 showed a five-year all-cause mortality rate at 55.4%, a CVD mortality rate at 49.6%, and a median survival time at 34 months.<sup>[98]</sup>

According to the 2020 China Heart Failure Medical Quality Control Report,<sup>[97]</sup> the average age of HF patients was  $67 \pm 14$  years, and 60.8% of them were males. The proportion of HF patients with valvular disease has been decreasing over the years, while hypertension (56.3%) and CAD (48.3%) have em-

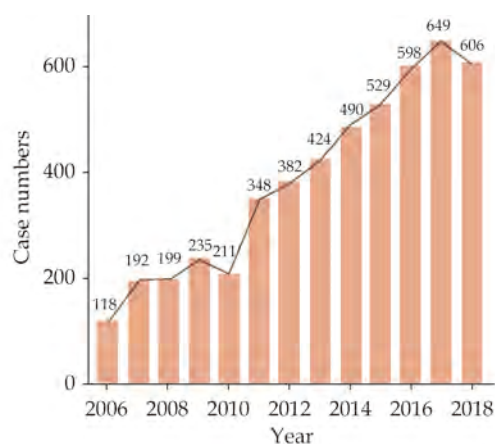


Figure 14 The number of hospitalized children with cardiomyopathy in 33 hospitals in China from 2006 to 2018.



erged as the main causes of HF in China. Infection was identified as the primary trigger for HF exacerbations, followed by myocardial ischemia and exertion. The proportions of HF with reduced ejection fraction, HF with mid-range ejection fraction, and HF with preserved ejection fraction were 40.2%, 21.8%, and 38.0%, respectively.

The overall diuretic usage rate among hospitalized HF patients in China did not show significant changes, whereas the usage rate of digoxin, influenced by international clinical studies, exhibited a downward trend. Conversely, the usage rates of aldosterone receptor antagonists and beta-receptor blockers increased. The overall utilization of renin-angiotensin system blockers is on the rise, while the usage of angiotensin receptor/neprilysin inhibitors, angiotensin-converting enzyme inhibitors, and angiotensin II receptor antagonists decreased (Table 4).<sup>[9]</sup>

According to the statistics from the National Health Commission's online registration data and the data reported by the provincial quality control centers, the number of cardiac resynchronization therapy (CRT) implants in 2020 was 3869, reflecting a 13.9% decrease from 2019. The proportion of CRT-D (cardiac resynchronization therapy defibrillator) implantation has been increasing over the years because patients who meet the indications for cardiac resynchronization therapy pacemaker (CRT-P) are

also eligible for CRT-D. A study involving 454 CRT-P/D patients across 22 centers from 2013 to 2015 found that 52.2% of them opted for CRT-D treatment. Furthermore, in 2019, the proportion of CRT-D implants among all CRT cases further increased to 64%. Notably, hospitals with more than 40 cases per year had a higher proportion of CRT-D implants, while areas with lower GDP levels had an even lower proportion of CRT-D implants.

To date, a total of 16 hospitals in China have performed nearly 100 cases of left ventricular assist device (LVAD) implantation. Among them, the National Medical Products Administration (NMPA) approved three clinical trial studies to assess the safety and efficacy of implantable LVADs for the treatment of end-stage HF.

The first study, named EVAHEART I, led by Fuwai Hospital of the Chinese Academy of Medical Sciences and produced by Chongqing Yongrenxin, completed a total of 17 cases of EVAHEART I implantation from January 2018 to January 2021, with no perioperative deaths reported. During long-term follow-up, 15 patients survived with the artificial heart for a considerable duration ranging from 350 to 1100 days, except for two patients who underwent heart transplantation at 156 days and 1035 days after surgery.

The second study, a clinical trial on the safety and

Table 4 Use of the drug in patients with heart failure.

Sources of research	Year	Number	Therapeutic drug use rate (%)								Calcium antagonists
			Nitrates	Diuretic	Digitalis	ARB	ACEI	ARN	MRA	β-blocker	
42 hospitals in China	1980	1756	44.7	73.7	51.7	0.4	14.0	-	10.0	8.5	6.1
	1990	2181	36.0	70.2	45.5	1.4	26.4	-	8.4	9.5	16.4
	2000	6777	53.0	48.6	40.3	4.5	40.4	-	20.0	19.0	10.5
Hubei	2000-2010	16,681	-	69.1	46.2	18.7	51.6	-	-	46.6	-
10 hospitals	2005-2009	2154	53.2	74.4	57.6	66.0	-	74.6	68.3	46.1	-
Kunmin	2008-2012	2106	-	84.8	28.2	82.8	-	76.6	72.2	-	-
Xinjiang Uygur Autonomous Region	2011-2012	5357	-	45.5	26.8	72.8	-	46.6	66.8	-	-
The China-HF Registry	2012-2015	13,687	41.4	72.2	-	28.8 <sup>a</sup>	71.7 <sup>b</sup>	-	74.1 <sup>b</sup>	70.0 <sup>b</sup>	-
						51.3 <sup>c</sup>	49.4 <sup>c</sup>		48.7 <sup>c</sup>	52.2 <sup>c</sup>	
Heart Failure Quality Control Report	2007-2020	33,413	-	75.0	29.3	44.0	36.9	87.8	82.2	-	-

<sup>a</sup>Intravenous medication during hospitalization; <sup>b</sup>discharge oral medication in HFrEF patients; <sup>c</sup>discharge oral medication in HFpEF patients. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor antagonist; ARNI: angiotensin receptor/neprilysin inhibitor; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; MRA: mineralocorticoid receptor antagonist.

efficacy of CH-VAD implantable LVADs, was conducted under the leadership of Fuwai Hospital of the Chinese Academy of Medical Sciences and produced by Suzhou Tongxin. From January 2019 to December 2020, a total of 33 cases of CH-VAD LVAD implantation were performed in five centers. Among them, three cases resulted in perioperative deaths, while the remaining 30 cases exhibited recovery to NYHA grade I and II within one month after surgery. Long-term follow-up showed that one patient had the device removed 166 days after cardiac function restoration, one patient received a heart transplant and had the device removed 190 days after surgery, and the remaining 28 patients survived with the device for durations ranging from 360 to 1600 days.

The third study, a clinical trial on the safety and efficacy of the “rocket heart” for the treatment of end-stage HF, was produced by Aerospace Taixin. Fifty cases have been enrolled, but specific data is yet to be released.

According to data from the China Heart Transplant Registration System, as of 2020, a total of 56 medical institutions in China possess heart transplant qualifications. From 2015 to 2020, the annual number of heart transplant surgeries performed and reported by transplant centers in China was as follows: 279, 368, 446, 490, 679, and 557 cases, respectively. Over a span of six years, a total of 2819 cases were completed and reported (excluding data from Hong Kong Special Administrative Region, Macao Special Administrative Region, and Taiwan Region of China). In 2020, non-ischemic cardiomyopathy accounted for 74.4% of heart transplant recipients in China, with non-ischemic cardiomyopathy comprising 84.9% of pediatric heart transplant recipients. The in-hospital survival rate for Chinese heart transplant recipients in 2020 was 88.5%, and the causes of early death were predominantly multiple organ failure and transplant HF, accounting for more than 60% of cases. From 2015 to 2020, the one-year survival rate after heart transplantation in China was 85.3%, and the three-year survival rate after surgery was 80.4%. Specifically, the one-year survival rate for adult heart transplant recipients was 85.3%, and the three-year survival rate was 80.4%. For pediatric heart transplant recipients, the one-year and three-year survival rates were 91.0% and 84.0%, respectively.

## Pulmonary Vascular Disease and Venous Thromboembolic Disease

### *Pulmonary hypertension*

A national multicenter study conducted from May 2007 to October 2010 included 551 patients with confirmed adult pulmonary hypertension (PH). Of these, 487 patients (88.4%) had arterial PH (PAH), and 64 patients (11.6%) had chronic thromboembolic PH. Among the PAH cases, 273 cases (56.1%) were related to CAD, 64 cases (13.1%) were associated with connective tissue disease, and 150 cases (30.8%) were idiopathic PAH (IPAH).

Data from the National Systemic Lupus Erythematosus Multicenter Collaboration (CSTAR) in 2014 showed that the prevalence rate of PAH, defined as the presence of resting pulmonary artery systolic pressure  $\geq 40$  mmHg measured by echocardiography, was 3.8% (74 out of 1934).<sup>[99]</sup>

Before 2006, there were no targeted drugs available for PAH treatment in China. The 1-year, 3-year, and 5-year survival rates for IPAH and familial PAH were 68.0%, 38.9%, and 20.8%, respectively. After the introduction of targeted drugs, the survival outcomes for IPAH significantly improved, with 1-year and 3-year survival rates of 92.1% and 75.1%, respectively.<sup>[100]</sup>

### *Pulmonary thromboembolism and deep venous thrombosis*

Between 1997 and 2008, a total of 18,206 cases of pulmonary embolism were diagnosed among 16,972,182 inpatients in over 60 third-class hospitals in China, accounting for 0.11% of all inpatients. The fatality rate of pulmonary embolism in China decreased significantly from 25.1% in 1997 to 8.7% in 2008.

A study analyzing hospitalization rates and fatality rates of venous thromboembolism (VTE) in China included 105,723 VTE patients from 90 hospitals on the mainland between January 2007 and December 2016. Among these, 43,589 cases (41.2%) were pulmonary embolism with deep venous thrombosis (DVT), and 62,134 cases (58.7%) were simple DVT. After adjusting for age and sex, the hospitalization rate increased from 3.2 per million in 2007 to 17.5 per 100,000 in 2016. The hospital mortality rate decreased from 4.7% in 2007 to 2.1% in



2016 (Figure 15), and the length of hospital stay decreased from 14 days to 11 days.<sup>[101]</sup>

The China Pulmonary Thromboembolism Registry Study (CURES)<sup>[102]</sup> included 7438 adult hospitalized patients with acute symptomatic pulmonary embolism from medical institutions in 31 provinces, autonomous regions, and municipalities directly under the central government between 2009 and 2015. The study found that 4.2% of patients were at high risk (hemodynamic instability), 67.1% were at medium risk [simplified Pulmonary Embolism Severity Index (sPESI)  $\geq 1$ ], and 28.7% were at low risk (sPESI = 0). CT pulmonary angiography was the most commonly used diagnostic method (87.6%), and anticoagulant therapy was the most frequently employed initial treatment (83.7%). The proportion of initial systemic thrombolytic therapy decreased from 14.8% to 5.0%, and the mortality rate of acute pulmonary embolism decreased from 3.1% to 1.3%.

The Dissolve-2 study,<sup>[103]</sup> which investigated the risk characteristics of VTE in Chinese inpatients, enrolled 13,609 patients who underwent medical or surgical emergency hospitalization for  $\geq 72$  h in 60 tertiary Grade A hospitals in China from March to September 2016. Among these, 6623 patients (48.7%) were in internal medicine, and 6986 patients (51.3%) were in surgery. Risk stratification was performed according to the 9<sup>th</sup> edition of the CHEST guidelines. The results showed that 63.4% of medical patients were classified as low risk, and 36.6% were high risk. In surgical patients, 13.9% were low risk, 32.7% were medium risk, and 53.4% were high risk. The main risk factors for VTE in surgical inpatients were open surgery (52.6%), while acute infection was the primary risk factor in medical inpatients

(42.2%). Among all patients, 14.3% received any VTE preventive measures (19.0% in surgery and 9.3% in internal medicine), and 10.3% received VTE preventive measures recommended in the 9<sup>th</sup> edition of the CHEST guidelines (11.8% in surgery and 6.0% in internal medicine).

## Aortic and Peripheral Artery Disease

### Aortic disease

Based on 2011 Chinese Health Insurance data, the estimated annual incidence of acute aortic dissection in mainland China was approximately 2.8 per 100,000, with a higher incidence in men compared to women (3.7 per 100,000 vs. 1.5 per 100,000).<sup>[104]</sup>

Findings from the Registry of Aortic Dissection in China (Sino-RAD) study revealed that the average age of patients with aortic dissection in China was 51.8 years, which is about 10 years younger than in Europe and the United States. In terms of treatment, for type A aortic dissection, the open surgery rate was 89.6%, drug treatment rate was 7.8%, endovascular treatment rate was 1.6%, hybridization treatment rate was 1.3%, and in-hospital mortality rate was 5.5%. In contrast, for type B aortic dissection, the rates were 21.3% for drug therapy alone with a mortality rate of 9.8%, 4.4% for surgical therapy with a mortality rate of 8.0%, and 69.6% for endovascular therapy with a mortality rate of 2.5%.

The duration of hospitalization and associated costs vary among different types of patients undergoing thoracic aortic surgery. According to HQMS data, the average hospital stay for thoracic endovascular aortic repair in China in 2020 was 15.9 days,

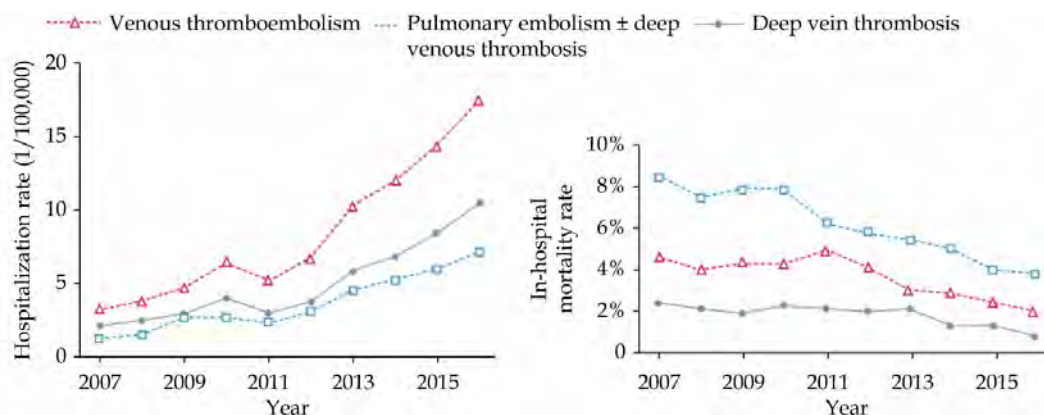


Figure 15 2007-2016 hospitalization rate of venous thromboembolism (A) and hospitalization mortality (B) in China.



with an average cost of 157,500 RMB. The average hospital stay for simple aortic valve prosthesis with ascending aortic replacement (Bentall surgery) was 23.4 days, with an average cost of 211,600 RMB. For total aortic arch prosthesis replacement, the average hospitalization period was 23.2 days, with an average cost of 274,100 RMB.

Screening of 5402 individuals aged 40 years and older with relevant risk factors in three cities and two rural communities in central China revealed a prevalence of 0.33% for abdominal aortic aneurysm. The prevalence of abdominal aortic aneurysm was higher in individuals aged 55–75 years compared to other age groups (0.51% vs. 0.11%).<sup>[105]</sup> In a cross-sectional survey of 3560 individuals aged over 60 years in four cities in Liaoning Province who underwent abdominal aortic ultrasound screening, the positive detection rate for abdominal aortic aneurysms was 0.9%.<sup>[106]</sup>

A meta-analysis on the growth rate of abdominal aortic aneurysms in the Chinese population<sup>[107]</sup> demonstrated an annual growth rate ranging from 0.18 cm to 0.75 cm, with larger aneurysms exhibiting faster growth rates.

According to HQMS data, the average hospitalization period for patients undergoing abdominal aortic prosthetic vascular replacement in China in 2020 was 22 days, with an average cost of 123,000 RMB. For endovascular aneurysm repair, the average hospital stay in 2020 was 14 days, with an average cost of 178,400 RMB.

### Peripheral arterial disease

**Lower extremity arterial disease** A stratified random sample survey conducted in mainland China indicated that the prevalence of lower extremity artery disease in the general population aged 35 years and older was 6.6%. This estimate suggests that there are approximately 45.3 million patients with lower extremity artery disease in China.<sup>[108]</sup> Among these patients, 1.9% received revascularization, amounting to an estimated 860,000 cases.

**Carotid atherosclerotic disease** An analysis of carotid ultrasound findings from 106,918 community residents aged 40 years and older, conducted by the China National Stroke Prevention Project (CSPP) in 2018, revealed a prevalence of moderate and higher carotid stenosis of 0.5%.<sup>[109]</sup>

According to the China Stroke Prevention and Control Report 2019, there were 4910 reported cases of carotid endarterectomy in 2018, with a rate of serious complications at 2.79%. Additionally, 15,801 cases of carotid artery stenting were performed in 2018, with a rate of serious complications at 1.92%.<sup>[110]</sup>

**Renal artery stenosis** A single-center study spanning 18 years and involving a total of 2905 patients with renal artery stenosis (RAS)<sup>[111]</sup> found that the etiologies of RAS included atherosclerosis (82.4%), Takayasu arteritis (11.9%), fibromuscular dysplasia (4.3%), and other causes (1.4%). Atherosclerosis increased from 50% between 1999 and 2000 to 85% in 2016. Non-atherosclerotic etiologies were more common in patients aged 40 years or younger.

**Subclavian artery stenosis** An inter-arm systolic pressure difference of  $\geq 15$  mmHg is a strong predictor of  $> 50\%$  subclavian artery stenosis and can be utilized for epidemiological screening and diagnosis of subclavian artery stenosis. A study involving a cohort of 3133 elderly individuals with a mean age of 69 years from a community in Shanghai reported a prevalence of inter-arm systolic pressure difference  $\geq 15$  mmHg at 1.7%. A single-center study examining patients hospitalized with subclavian artery stenosis revealed that atherosclerosis accounted for 95.9% of cases in patients over 40 years of age, while Takayasu arteritis accounted for 90.5% of cases in patients aged 40 years or younger.<sup>[112]</sup>

### Oncological Cardiology

A large cohort study involving 710,000 patients found that 18% of cancer patients had concomitant CVD risk factors or existing CVD. Among these, 13% had at least one CVD risk factor, and 5% had a diagnosed CVD. After adjusting for age, sex, tumor stage, and treatment received, the study revealed that oncology patients with coexisting HF had the worst prognosis, with a 79% increased risk of all-cause mortality. This was followed by cancer patients with a history of MI, who had a 50% increased risk of all-cause mortality.<sup>[113]</sup>

## REHABILITATION OF CVD

### Cardiac Rehabilitation

In 2016, a survey assessing the status of cardiac





rehabilitation in hospitals across China<sup>[114]</sup> included 124 Class 3 Grade A hospitals in seven regions of the mainland China. The results indicated that only 30 hospitals (24%) provided cardiac rehabilitation services, resulting in an average of 2.2 hospitals per 100 million population capable of offering cardiac rehabilitation. Among the 13 hospitals that completed 36 surveys and provided cardiac rehabilitation, 3 (23%) offered in-hospital Phase I rehabilitation, 3 (23%) provided Phase II rehabilitation, and 7 (54%) offered both Phase I and Phase II rehabilitation.

### Stroke Rehabilitation

In 2016, there was a significant increase in the number of rehabilitation hospitals and rehabilitation beds in China compared to previous years.<sup>[115]</sup> The National Medical Quality Management and Control Information System Sampling Survey conducted in 2018 included data from 7544 hospitals in 32 provinces, autonomous regions, and municipalities, including Xinjiang Production and Construction Corps. The results revealed that 2147 hospitals were equipped with rehabilitation medical wards, resulting in a ward allocation rate of 28.46%. The average number of beds in the 1897 rehabilitation wards included in the statistics was 41.17. In 2018, the average number of discharged patients in the rehabilitation medicine department of general hospitals in China was 753.25, including 241.56 stroke patients. The rate of early rehabilitation (within 24–48 h of hospitalization) in neurology wards was 11.79%, and the rate of early rehabilitation for acute ischemic stroke was 25.25%.<sup>[116]</sup>

A survey conducted in 2009 indicated that there were 16,000 rehabilitation doctors, 14,000 therapists, and 12,000 nurses in China. By 2018, the number of rehabilitation doctors and nurses had increased to 38,000 and 15,000, respectively. Approximately 70% of rehabilitation therapists graduated from rehabilitation majors, while around 15% graduated from traditional Chinese medicine programs.<sup>[115,116]</sup>

In 2018, the per capita hospitalization cost of patients in the rehabilitation medicine department was 11,222 RMB. Among this, the drug cost was 2286 RMB, accounting for 20.37% of the total. The cost of rehabilitation was 5567 RMB, with treatment costs comprising 49.61%.<sup>[116]</sup> The Department of Rehabil-

itation Medicine at Peking University Third Hospital, Beijing, China conducted a statistical analysis on 1,552,248 samples from 462 tertiary hospitals with rehabilitation medicine wards. The results indicated that the average length of stay in the Department of Rehabilitation Medicine from 2013 to 2018 was 21.53 days, and the average daily hospitalization cost was 810 RMB. The proportion of rehabilitation-related expenses (rehabilitation fees and physical therapy fees) increased each year, while the proportion of medication-related expenses (western medicine fees, traditional Chinese medicine fees, and Chinese herbal medicine fees in discharge fees) decreased over time.<sup>[117]</sup>

## CARDIOVASCULAR BASIC RESEARCH AND DEVICE DEVELOPMENT

### Cardiovascular Basic Research

Since 2005, high-level basic research on cardiovascular topics in mainland China has emerged, with the most influential studies being published mainly in *Circulation* and *Circulation Research*. In recent years, there has been a rapid increase in high-level cardiovascular basic research in China, as evidenced by data obtained from journals such as *Cell*, *Nature Medicine*, *Circulation*, *Journal of the American College of Cardiology*, *European Heart Journal*, *Circulation Research*, and *Nature Communications* (Figure 16).

From 2020 to 2021, 48 basic research papers of which the corresponding authors and lead authors are from mainland China were published, exploring cardiac and vascular anatomy, development, function, and pathogenesis. These studies covered

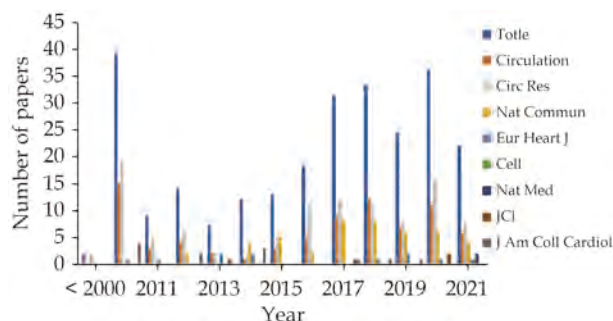


Figure 16 Papers of cardiovascular basic research published by Chinese who is the the lead author or corresponding author from 2000 to 2021.

various myocardial diseases (such as IHD, cardiomyopathy, myocarditis, HF, etc.), heart rhythm abnormalities, atherosclerosis, and growth and development. Hot research topics included heart protection and regeneration, single-cell sequencing technology, gene therapy, and machine learning.

### Research and Development Product of Cardiovascular Medical Device

From September 1, 2020, to August 31, 2021, the NMPA approved 68 medical devices to enter the review pathway for innovative medical devices. Among these, 31 (45.6%) were cardiovascular-related products, indicating that cardiovascular innovation plays a leading role in the field of medical device innovation in China. Furthermore, 58 (85.3%) of the approved products were domestically developed originals. During the same period, a total of 15 medical devices were approved to enter the priority review pathway for medical devices, with 2 of them being cardiovascular-related products.

From September 1, 2020, to August 31, 2021, the NMPA approved 142 products to obtain registration certificates for medical devices in the cardiovascular field. Among them, 101 products were domestically developed originals, and 11 products went through the national innovative medical device review pathway. Comparing this data with the period from September 1, 2019 to August 31, 2020 (141 registration certificates and 96 domestic original products, with 5 passing the national innovative medical device evaluation procedure), we observe a faster evaluation process by the NMPA for licensing cardiovascular devices, as well as a significant increase in approved innovative medical facilities overall. China is experiencing rapid development in the industrialization of cardiovascular devices. Out of the 101 domestic original products, there were 90 intervention products, 4 imaging products, 3 blood flow measurement systems, 2 open surgery products, 1 active surgery product, and 1 artificial intelligence software.

## MEDICAL EXPENSES FOR CVD

### Total Number of Discharged Patients and Changing Trends

In 2019, the number of discharged patients with

cardiovascular and cerebrovascular diseases in Chinese hospitals was 26.8441 million (Figure 17), accounting for 14.03% of the total number of all discharged patients during the same period. Among them, there were 14.3488 million patients with CVD and 12.4953 million patients with cerebrovascular disease, accounting for 7.50% and 6.53% of the total number of discharged patients, respectively.

The main diseases from which the discharged CVD patients suffered were IHD and cerebral infarction. There were 8.9348 million IHD patients and 8.276 million cerebral infarction patients, accounting for 36.92% and 34.20% of the total number of discharged patients, respectively. Additionally, the number of discharged patients with diabetes was 4.6127 million in 2019 (Figure 18).

From 1980 to 2019, the average growth rate of the number of discharged CVD patients in China was 9.59% per year, which was faster than the growth rate of all discharged patients (6.33%). The diseases ranked based on the average growth rate of the number of discharged CVD patients were HF (20.66%), angina pectoris (13.02%), cerebral infarction (11.91%), pulmonary embolism (11.45%), IHD (11.04%), AMI (10.94%), cerebral hemorrhage (8.84%), hypertension (7.04%), arrhythmia (6.15%), hypertensive he-

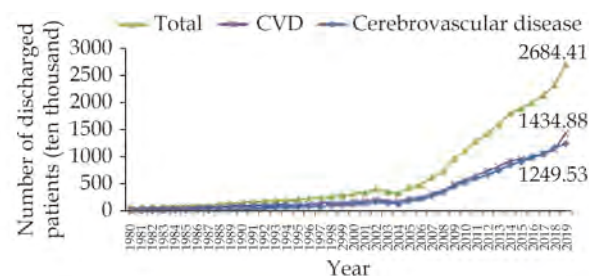


Figure 17 Changing trend of the number of discharged patients with CVD in China from 1980 to 2019. CVD: cardiovascular disease.

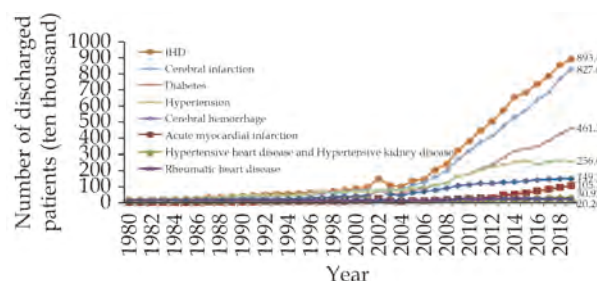


Figure 18 Changing trend of the number of discharged patients with various major cardiovascular diseases and diabetes in China from 1980 to 2019. IHD: ischemic heart disease.

art disease and hypertensive kidney disease (5.95%), chronic RHD (0.70%), and acute rheumatic fever (-11.98%). The average growth rate of the number of discharged patients with diabetes was 13.31% per year.

### Hospitalization Expenses

In 2019, the total hospitalization expenses of inpatients with cardiovascular and cerebrovascular diseases in China amounted to 313.366 billion RMB. The total hospital cost for CVD was 177.338 billion RMB, including 125.625 billion RMB for IHD (which comprised 42.784 billion RMB for angina pectoris and 32.118 billion RMB for AMI), 18.099 billion RMB for arrhythmia, 16.721 billion RMB for hypertension (including 2.761 billion RMB for hypertensive heart disease and hypertensive kidney disease), 13.064 billion RMB for HF, 1.930 billion RMB for RHD, 1.809 billion RMB for pulmonary embolism, and 90 million RMB for acute rheumatic fever. The total hospital cost for cerebrovascular disease was 136.028 billion RMB, including 81.197 billion RMB for cerebral infarction and 29.633 billion RMB for cerebral hemorrhage (Figure 19). Additionally, the total hospital cost for diabetes was 36.592 billion RMB.

Since 2004, the average annual growth rate of total hospitalization expenses for AMI, cerebral infarction, and cerebral hemorrhage has been 25.99%, 18.82%, and 13.51%, respectively; after excluding the influence of price factors (Figure 20). In 2019, compared to 2018, the total hospitalization expenses increased by 9.55% for IHD (14.41% for angina pectoris), -2.03% for hypertension (7.91% for hypertensive heart disease and hypertensive kidney disease), 11.53% for pulmonary embolism, 15.59% for arrhythmia, 24.04% for HF, -0.18% for chronic RHD,

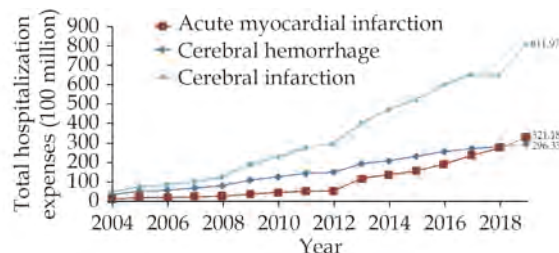


Figure 19 Changing trend of the total hospitalization expenses for acute myocardial infarction, cerebral hemorrhage and cerebral infarction from 2004 to 2019 (current year's prices).

-9.46% for acute rheumatic fever, and 7.72% for diabetes.

The average hospitalization cost per occurrence was 14,060.20 RMB for IHD (15,486.51 RMB for angina pectoris and 30,368.54 RMB for AMI), 9811.18 RMB for cerebral infarction, 19,843.37 RMB for cerebral hemorrhage (Figure 21), 6514.19 RMB for hypertension (8929.68 RMB for hypertensive heart disease and hypertensive kidney disease), 17,169.01 RMB for pulmonary embolism, 16,028.28 RMB for arrhythmia, 9368.51 RMB for HF, 9525.63 RMB for chronic RHD, 5780.11 RMB for acute rheumatic fever, and 7932.88 RMB for diabetes, respectively.

Since 2004, the average annual growth rate of the average hospitalization expenses per occurrence for AMI, cerebral infarction, and cerebral hemorrhage has been 5.86%, 1.29%, and 4.59%, respectively. In 2019, compared to 2018, the average hospitalization expenses per occurrence increased by 4.94% for IHD (1.23% for angina pectoris), 0.62% for hypertension (1.62% for hypertensive heart disease and hypertensive kidney disease), 0.07% for pulmonary embolism, 8.89% for arrhythmia, 2.80% for HF, 1.53% for chronic RHD, 2.87% for acute rheumatic fever, and -0.35% for diabetes.

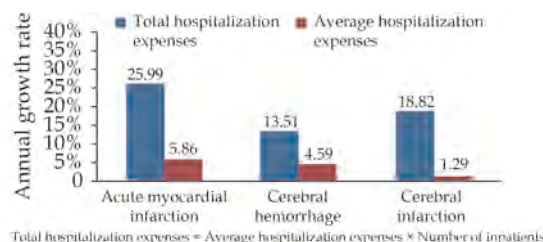


Figure 20 The average growth rate per year of the total hospitalization expenses, as well as the average hospitalization expenses per time, for acute myocardial infarction, cerebral hemorrhage and cerebral infarction from 2004 to 2019.

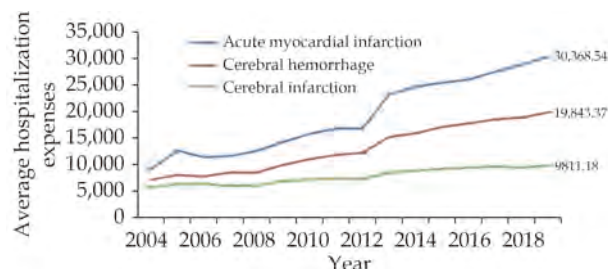


Figure 21 Changing trend of the average hospitalization expenses per time for acute myocardial infarction, cerebral hemorrhage and cerebral infarction from 2004 to 2019 (current year's prices).





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## CONFLICT OF INTEREST

None

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