

REPORT ON CARDIOVASCULAR DISEASES IN CHINA (2015)

中国心血管病报告2015



National Center for Cardiovascular Diseases, China

国家心血管病中心

中国大百科全书出版社

Encyclopedia of China Publishing House

图书在版编目(CIP)数据

中国心血管病报告. 2015/国家心血管病中心编著. -北京:中国大百科全书出版社, 2016.12
ISBN 978-7-5000-9803-4
I. ①中… II. ①国… III. ①心脏血管疾病-研究报告-中国-2015-英文 IV. ①R54
中国版本图书馆CIP数据核字(2015)第020507号

责任编辑:韩小群

中国大百科全书出版社 出版发行

(北京阜成门北大街17号 邮政编码:100037 电话:010-88390718)
http://www.ecph.com.cn
北京骏驰印刷有限公司印刷(北京市海淀区西北旺屯佃工业园区289号)
新华书店经销
开本:889×1194毫米 1/16印张:12.5 字数:300千字
2016年12月第一次印刷
印数:1-4000册
ISBN 978-7-5000-9803-4
定价:125.00元

本书如有印装质量问题,可与本出版社联系调换。

ISBN 978-7-5000-9803-4
Copyright by Encyclopedia of China Publishing House, Beijing, China, 2016.12
Published by Encyclopedia of China Publishing House
17 Fuchengmen Beidajie, Beijing, China 100037
http://www.ecph.com.cn
Distributed by Xinhua Bookstore
First Edition 2016.12



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Preface

Rapid socioeconomic progress in China has exerted a great impact on lifestyle. An epidemic of cardiovascular diseases (CVD) in China is emerging as a result of lifestyle changes, urbanization and the accelerated process of ageing. The incidence of CVD is continuously increasing and will remain an upward trend in the next decades.

CVD is the leading cause of death for Chinese in both urban and rural area. Nowadays, 44.6% of deaths in rural area and 42.51% of deaths in urban area are caused by CVD. The increasing disease burden of CVD has become a major public health issue. Effective strategies should be enforced urgently for the prevention and treatment of CVD under the supervision of the government. In May 2012, fifteen Ministries, including the Ministry of National Health and Family Planning, jointly issued the Work Plan for Chronic Disease Prevention and Control in China (2012–2015), a guideline for the prevention and control of chronic diseases, especially CVD in China. We should actively follow and implement its recommendations.

Since 2005, the National Center for Cardiovascular Diseases has recruited specialists in cardiology, cardiac surgery, neurology, nephrology, diabetes, epidemiology, community health, health economics and biostatistics and other related fields to compile the annual Report on Cardiovascular Diseases in China. The report aims to provide technical guidance and authoritative evaluations for cardiovascular disease prevention and treatment; provide the technical foundation for government legislation and strategic planning; and to establish a platform for international communication and cooperation.

Note: The term of cardiovascular diseases in this report refers to cardiovascular, cerebrovascular diseases and their related diseases.

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Summary

1. Death from Cardiovascular Diseases

CVD was still the leading cause of death in 2014, higher than deaths caused by tumors or any other diseases. Ever since 2009, the CVD mortality rate in rural areas has exceeded that of urban areas, and consistently remained higher than urban areas. In 2014, the mortality rate of CVD in rural areas was 295.63/100 000, among them, the mortality rate of heart diseases was 143.72/100 000, and the mortality rate of cerebrovascular diseases was 151.91/100 000 (cerebral hemorrhage: 74.51/100 000, cerebral infarction: 45.30/100 000) . Meanwhile, the mortality rates of CVD, heart diseases and cerebrovascular diseases in urban areas were 261.99/100 000, 136.21/100 000 and 125.78/100 000 (with 52.25/100 000 in cerebral hemorrhage, 41.99/100 000 in cerebral infarction) , respectively. CVD-related deaths accounted for 44.60% and 42.51% of all deaths in rural and urban areas, respectively. Two in five deaths are attributed to CVD.

Following the methods of the Global Burden of Disease Study 2013 (GBD 2013) , researchers from China CDC have systematically analyzed all available demographic and epidemiological data sources for China at the provincial level. In 1990, 16 of 33 provinces had lower respiratory infections or preterm birth complications as the leading causes of years of life lost (YLLs) , and 15 provinces had cerebrovascular disease. By 2013, 27 provinces had cerebrovascular disease as the leading cause, 5 had IHD. The age-standardized mortality of CVD in 2013 decreased by 21% compared with 1990. Cerebrovascular disease is the leading cause of death in both men and women in China, with an increase in ischemic stroke (28.8%) and a decrease in hemorrhage stroke (37.7%) . It is notable that, although age-standardized mortality rates of CVD decreases due to population aging in China and other factors, the absolute number of CVD deaths are still rising rapidly by 46% from 1990 to 2013, with IHD and cerebrovascular disease deaths increasing by 90.9% and 47.7%, respectively.

2. Risk Factors of Cardiovascular Diseases

2.1 Hypertension

Hypertension is one of the most common chronic non-infectious diseases and the most important risk factor for cardiovascular diseases. In 2010, hypertension accounted for 2.043 million deaths in China (male 1.15 million, female 0.89 million) , accounted for 24.6% of all deaths in the country. In 2013, hypertension alone accounted for 6.61% of the 3.1869 trillion RMB spent on healthcare in China.

(1) According to data from four national, large-scale surveys focused on hypertension (1958–1959, 1979–1980, 1991, and 2002) , the prevalence of hypertension among subjects aged over 15 has

increased in China (5.1%, 7.7%, 13.6%, and 17.6%, respectively) . On June 30, 2015, the State Council Information Office released the Survey on the Status of Nutrition and Health of the Chinese People in 2012, which showed that 25.2% of adults aged ≥ 18 years old in China have hypertension. Using data from the 2010 National Population Census as a denominator, it is estimated that the total number of people with hypertension in China is approximately 270 million.

(2) High-normal blood pressure: The China Health and Nutrition Survey (CHNS) conducted 7 cross-sectional surveys among adults aged ≥ 18 years old in 9 provinces from 1991 to 2009 (1991, 1993, 1997, 2000, 2004, 2006, and 2009) . The data demonstrated that the prevalence of high-normal blood pressure increased remarkably from 29.4% in 1991 to 38.7% in 2009.

(3) The CHNS on populations aged 18 years or above in 9 provinces from 1991 to 2009 demonstrated that awareness, treatment, and control rates of hypertension exhibited an upward trend, however it is notable that these rates were still relatively low. The awareness, treatment, and control rates of hypertension in 2009 were 26.1%, 22.8%, and 6.1%, respectively.

(4) Risk factors associated with hypertension in the Chinese population include a high sodium and low potassium diet, obesity and overweight, high alcohol consumption, mental stress, family history of hypertension, sedentary lifestyle, old age, high triglyceride, high total cholesterol, and low high-density lipoprotein cholesterol levels. The risk of developing hypertension increased as the number of risk factor for hypertension goes up.

(5) Based on the results of CHNS the prevalence of hypertension among juvenile increased incrementally, from 7.1% in 1991 to 13.8% in 2009, with the average annual growth of 0.47%. Blood pressure levels among children of different genders and ages were all increasing. Analysis from 190 000 Han nationality school-age children (7 to 17 years old) in the National Student Health Study in 2010 found that the prevalence of hypertension in children and adolescents was 14.5% (Boys: 16.1%; Girls: 12.9%) , and that blood pressure levels rose with age.

(6) Overweight/obesity, glucose-lipid metabolism abnormalities, family history of hypertension, low birth weight (< 2.6 kg) , and sleep deprivation are risk factors for hypertension in children and adolescents. A birth weight greater than or equal to 4 kg, poor nutrition in the prenatal and early postnatal periods, suffering from famine at an early stage, and childhood sensitivity to salt are risk factors for developing hypertension in early adulthood.

(7) Children with hypertension were more likely to develop adult hypertension and cardiac remodeling, compared with those who had normal baseline blood pressures (odds ratios: 2.1 for hypertension, 1.5 for cardiac remodeling) . Moreover, the risk of developing hypertension was higher in the older age group compared to the younger age group. The risk of developing cardiac and renal damage among people who had continuously elevated blood pressure from childhood to adulthood was 3 times that of people with normal blood pressures.

2.2 Smoking

(1) China continues to be one of the countries with the highest male smoking rates in the world since 1984. The Global Adult Tobacco Survey (GATS) –China Project in 2010, covering the population of China's 28 provinces, found that the current smoking rate in men ≥ 15 years of age was 52.9%; the current smoking rate in women was found to be 2.4%; the current smoking rates of male medical personnel and teachers between the ages of 15 and 69 had decreased significantly to 40% and 36.5%, respectively; among those who reported to have ever tried smoking, 55.9% of male and 57.0% of female smoked a whole cigarette for the first time before turning 13 years old; 52.7% of current smokers between the ages of 20 and 34 reported that they became daily smokers before the age of 20; Furthermore, there were 738 million Chinese non-smokers exposed to second-hand smoke.

In 2010, investigation of smoking status in China's rural midwestern areas, demonstrated that the overall smoking rate between ages of 18-59 in midwestern residents was 20.9% (44.8% in men, 2.0% in women) . Significant differences in smoking rates were found in populations with different ages, ethnic backgrounds, education levels and occupations. The residents between the ages of 50 and 55 had the highest rate of smoking (30.5%) . The smoking rate of the Han ethnic group was higher than that of any ethnic minority group (27.7% vs. 16.3%) .

Based on the distribution of the employed floating population, the China Non-communicable and Chronic Disease Risk Factor Surveillance in 2012 showed that the current smoking rate was 32.5%, with a significantly higher percentage of men (55.3%) than women (1.9%) . The current smoking rate in men was highest (58.6%) in the floating population working in the construction industry. Among the current smokers, the average number of cigarettes smoked per day was 15.7 (male 15.7 per day; female 10.3 per day) . The percentage of people exposed to second-hand smoking in employed floating population was 68.7% (76.4% in men) , especially high in those working in the construction industry.

A study investigating the smoking status in young Chinese women in 2008 found that the prevalence of ever having smoking was 22%, that the prevalence of currently smoking was 3.2%, and that the prevalence of having an intention to smoke was 2.7%. All three types of smoking prevalence were higher in urban female students than rural female students.

(2) In recent years, the smoking cessation rate has increased slightly in individuals aged 15 years and above, from 9.42% in 1996 to 11.5% in 2002 and 16.9% in 2010. The number of people who have quit smoking has increased by 15 million. In 2010, the GATS-China project showed that 16.1% of current smokers intended to quit smoking within the next 12 months.

(3) The SMHS (Shanghai Men's Health Study) and the SWHS (Shanghai Women's Health Study) demonstrated that cigarette smoking was responsible for 23.9% (95% CI: 19.4–28.3%) and 2.4% (95% CI: 1.6–3.2%) of deaths in men and women, respectively, in Shanghai's citizens of 40–74 years old. Respiratory diseases had the highest PAR in men (37.5%) , followed by cancer (31.3%) , and cardiovascular diseases (CVD) (24.1%) . The top three PARs in women were 1.1% for respiratory diseases, 1.1% for cancer, and 4.0% for CVD.

A multi-center prospective cohort study during 1986 to 2000 with an average of 9.5 years of follow-up showed that the risk for various types of stroke was 1.39 (95% CI 1.15–1.67) in male Chinese current smokers, and the main mediator was the increased risk for ischemic stroke.

2.3 Dyslipidemia

(1) The 2010 Chinese Chronic Disease Survey reported the levels of serum TC and TG among people aged 18 years and older from 31 provinces. Both were found to be significantly higher than in 2002. The average TC levels in men and women were 4.06 mmol/L and 4.03 mmol/L, respectively. The average TG levels in men and women were 1.45 mmol/L and 1.21 mmol/L, respectively. The rates of TC \geq 6.22 mmol/L in men and women were 3.4% and 3.2%, respectively, higher in urban areas than in rural areas, and higher in the eastern than in the central or western regions. The highest prevalence of hypercholesterolemia was found in men aged 45–59 years and women 60 and above. The rates of TG \geq 2.26 mmol/L in men and women were 13.8% and 8.6%, respectively.

In a meta-analysis published in 2014 that included 14 studies from 2003–2013, the estimated prevalence of increased TC, LDL-C and TG, and decreased HDL-C was 7.9%, 7.6%, 13.7% and 11.0%, respectively.

(2) A 2007–2008 Chinese Diabetes and Abnormal Metabolism study examined the prevalence, the rates of awareness, treatment and control for hypercholesterolemia in people over 20 years of age. The prevalence of TC \geq 6.22 mmol/L in men and women was 8.7% and 9.3%, respectively; the awareness rates were 27.6% and 20.7%, respectively; the treatment rates were 21.4% and 14.0%, respectively; the control rates were 18.3% and 11.2%, respectively; and the treatment-control rates were 88.1% and 78.4%, respectively.

(3) In a 2011 survey on dyslipidemia management and the compliance rate to cholesterol-lowering therapies in Chinese patients, 39% of dyslipidemia patients received lipid-lowering therapies, with a majority using statins. The compliance rate for low-density lipoprotein cholesterol (LDL-C) lowering therapies was 25.8%. The compliance rates for patients stratified as at high-risk or extremely high-risk for the cardiovascular disease were 19.9% and 21.1%, respectively. In the 2012 Dyslipidemia International Study-China (DYSIS-China) study, 88.9% of inpatients were treated with statins. Among patients who received lipid-lowering medical therapies, 38.5% failed to reach target levels of LDL-C, and patients with higher risk for cardiovascular disease had a higher non-compliance rates.

2.4 Diabetes

(1) According to the 2010 China Chronic Disease Survey, the estimated prevalence of diabetes was 9.7% in Chinese adults based on the results of fasting blood glucose (FBG) and 2-hour postprandial blood glucose levels. Taking HbA_{1c} level into consideration, the prevalence of diabetes was found to be 11.6%. For both genders, the prevalence of diabetes was higher in urban than in rural areas. It was higher in male than in female who were younger than 60 years old, and higher in female who were over 60 years old instead. The study noted that the prevalence of diabetes increased with both economic development and obesity.

(2) The China Daqing Diabetes Prevention Study followed the subjects for 20 years and found that compared with control participants, the incidence of diabetes among combined lifestyle intervention group was reduced by 51% during 6 years active intervention period, and reduced by 43% over 20 years. The time of diabetes onset in the intervention group was an average of 3.6 years later than the control group. The CVD-related mortality rate and all-cause mortality rate in the lifestyle intervention group were all dramatically lower than those of the control group by 41% and 29% in 23 years.

The Daqing IGT and Diabetes Study compared mortality rate and causes of death among newly diagnosed diabetes (NDD) and normal glucose tolerance (NGT) population. With 23 years of follow-up, there are 56.5% participants with NDD and 20.3% with NGT died. CVD was the predominant cause of the death in whom with diabetes (47.5% in male and 49.7% in female), almost half of which died from stroke. With age standardized, the incidence of all-cause mortality was three times higher in NDD than in NGT. Compared with NGT, the HRs of death from CVD in female with NDM is higher than in male, with HRs of 6.9 in female and 3.5 in male.

(3) The 3B (blood glucose, blood pressure, and blood lipids) Research Study recruited 25 817 type 2 diabetic patients from 104 hospitals. The study showed that 72% DM patients had hypertension and/or dyslipidemia and only 5.6% achieved the target goals for control of blood glucose, blood pressure, and blood lipids.

2.5 Overweight and Obesity

(1) Based on the data of CHNS in 9 China provinces, the prevalence of overweight and obesity presented an upward trend in the past 20 years, the prevalence of overweight+obesity increased from 24.7% in 1991 to 44.0% in 2011.

The 2010 China Chronic Disease Surveillance Program showed that the prevalence of overweight, obesity, and abdominal obesity reached 30.6%, 12.0%, and 40.7% respectively. These numbers were significantly higher than those in 2002. The prevalence of overweight and obese among subjects over 60 years old were 32.1% and 12.4%, respectively, with higher rates in urban areas than in rural areas.

Researchers conducted four cross-sectional health surveys among residents aged 18 to 69 years old in the Guangdong province. Results showed that from 2002 to 2010, the prevalence of overweight and obese had increased from 15.8% to 16.6% without statistical significance; however, the prevalence of abdominal obesity had increased remarkably from 12.9 to 23.7%. This indicates that the type of obesity may have changed in China.

(2) The prevalence of overweight and obesity among children and adolescents is also on the rise. Five national surveys on the health status of Chinese students from 1985 to 2010 showed the prevalence rates of overweight and obesity in 2010 were 8.7 and 38.1 times as high as the rates in 1985 (9.6% vs 1.1%, 5.0% vs 0.1%), respectively.

(3) In 2010, the Chronic Disease Surveillance Program of China conducted a survey which showed that the average time of adult spending on TV was 1.87 hours a day; the risk of being obese was found to increase

by 4% with every hour of TV watching.

(4) Waist–height ratio (WHtR) is an effective parameter for abdominal obesity. The value of 0.50 is used as a cut–off value to diagnose abdominal obesity in Chinese people. The results of CHNS 2009 showed a positive association between abdominal obesity (WHtR \geq 0.50) and the risk of diabetes and other cardiovascular risk factors.

2.6 Physical Inactivity

(1) Results from the 1991–2011 CHNS showed a significant decreasing trend in physical activity among Chinese citizens aged 18–60. The declines were largely driven by reductions in occupational physical activities for both genders. Physical activity levels fell from 382 MET–h/week in 1991 to 264 MET–h/week in 2011 among adult men (a 31% decrease) and from 420 MET–h/week in 1991 to 243 MET–h/week in 2011 among adult women (a 42% decrease). Active physical activity (exercise) remained low – less than 7 MET–h/week for men and 3 MET–h/week for women in 2011. Adolescents aged 11–18 from 10 cities showed that only 19.9% of them reach the recommended level of physical activity, and the proportion of adolescents with lacking physical activity or insufficient physical activity were both about 40%.

The results from China Chronic Disease Monitoring Program in 2010 showed that the proportion of people who participated in regular exercise was only 11.9%, and that this proportion was lowest among younger adults in the 25–44 year age group.

(2) Physical activity level was negatively associated with BMI, waist circumference and body fat. Low physical activity level was associated with a substantial increasing in the risk of type 2 diabetes. Physical inactivity and low physical activity were both associated with higher risks of ischemic heart disease, ischemic stroke, and type 2 diabetes deaths.

2.7 Diet and Nutrition

The CHNS reported that total energy intake decreased in Chinese residence. However, some dietary changes were identified as detrimental to cardiovascular disease prevention, including the decrease in energy contributions from carbohydrates and the increase in energy contributions from fat, as well as the increasing intake of cholesterol. Moreover, fruit and vegetable consumption is still relatively low. Sodium intake decreased significantly and potassium intake increased. Nevertheless, sodium intake remained at a high level of 4.7 g/day (the equivalent of the salt intake of 12.0 g/day), and potassium intake was still below the recommended amount of 2 g/day.

2.8 Metabolic Syndrome (MS)

The 2002 China Health and Nutrition Survey reported that the prevalence of MS in adults above 18–years of age was, respectively, 6.6% and 13.8% based on criteria from the CDS and the NCEP–ATP III.

2.9 Air Pollution

In recent years, numerous studies have concluded that particulate matter (PM) is a risk factor for CVD. $PM_{2.5}$ is identified as a major pathogenic composition in PM, which is more closely related to CVD. Several studies analyzed the relationship between the average daily concentrations of $PM_{2.5}$, SO₂, NO_x and total suspended particle and diseases and death surveillance data. The results indicated that the concentrations of $PM_{2.5}$, SO₂, NO_x and total suspended particle were positively correlated with CVD incidence and mortality. From 2010 to 2012, the mean daily $PM_{2.5}$ concentration was 96.2 $\mu\text{g}/\text{m}^3$ in Beijing and that a 10 $\mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ concentration was associated with a 0.27% (95% CI: 0.21%, 0.33%) increase in IHD morbidity. And a significant hysteresis effect associated with $PM_{2.5}$ and IHD morbidity was also observed. It showed that IHD morbidity would continue to increase one, two and three days after initial exposure to $PM_{2.5}$ air pollution. Additionally, people aged ≥ 65 years were more susceptible to $PM_{2.5}$.

3. Cardiovascular Diseases

3.1 Stroke

(1) According to China Health Statistics Yearbook, cerebrovascular disease mortality rates increased from 2003 to 2014. The mortality rate of cerebrovascular diseases in 2014 was 125.78 per 100 000 for urban residents, and 151.91 per 100 000 in rural areas. Based on the data from the Sixth National Population Census in 2010, it was estimated that 837 300 urban residents and 1 023 400 rural residents died from cerebrovascular diseases in 2014.

(2) A study recruiting the patients admitted to 109 grade III class A hospitals during 2007–2010 with a discharge diagnosis of stroke demonstrated that stroke hospitalizations increased from 79 894 in 2007 to 85 475 in 2010, and in-hospital mortality of stroke decreased from 3.16% in 2007 to 2.30% in 2010. Compared with 2007, the mortality rate decreased for all types of strokes.

(3) Tianjin Brain Study was a population-based stroke surveillance study. The age-standardized incidence of first-ever stroke per 100 000 person-years rapidly increased from 124.5 in 1992–1998 to 190.0 in 1999–2005, and eventually approached 318.2 in 2006–2012. The incidence increased annually by 6.5%, and by 12% among men aged 45–64 years. From 1992 to 2012, the age at first-ever stroke in men decreased by 3.3 years.

(4) China Chronic Disease and Risk Factor Surveillance (CCDRFS) in 2010 found that the age-standardized prevalence of TIA was 2.27%. The prevalence of TIA was higher in women and in subjects who were older, less educated, current smokers, residents in rural or undeveloped areas, or with a history of stroke, hypertension, myocardial infarction, dyslipidemia, or diabetes. Approximately 3.08% of Chinese adults were informed and had knowledge of TIA. Among patients with TIA, only 5.02% received treatment and 4.07% received guideline-recommended therapy.

(5) Non-disabling cerebrovascular events consist of TIA and minor stroke. Clopidogrel in High-risk patients with Acute Non-disabling Cerebrovascular Events (CHANCE) trial conducted by Tian Tan Hospital revealed that the early benefit of clopidogrel-aspirin treatment in reducing the risk of subsequent stroke sustained during 1-year of follow-up. Compared with aspirin alone, cost-effective for early treatment with a 90-day clopidogrel-aspirin was higher for the treatment of nondisabling cerebrovascular events.

(6) Hyperhomocysteinemia (Hcy) in hypertensive patients was significantly associated with the risk of ischemic stroke, while folic acid supplementation for primary hypertension could efficiently down-regulate Hcy levels. The combined application of enalapril and folic acid, in contrast to enalapril alone, significantly reduced the risk of first stroke.

3.2 Coronary Heart Disease

(1) According to data from China Health and Family Planning Commission's Statistical Yearbook, the mortality rate from coronary heart diseases increased from 2002 to 2014. In 2014, the mortality rate from coronary heart diseases was 107.5 per 100 000 in urban areas and 105.37 per 100 000 in rural areas, an increase over 2013. Overall, coronary heart disease mortality is higher in urban than in rural populations, and higher in men than women.

(2) Acute myocardial infarction mortality rate increased from 2002 to 2014. Since 2005, the mortality rate of acute myocardial infarction has increased rapidly. AMI mortality in rural areas actually exceeded that in urban areas in 2007, 2009 and 2011, increased dramatically in 2012, and significantly exceeded that of urban areas in both 2013 and 2014. Mortality from AMI increased with age regardless of gender or urban/rural distinction, and increased most significantly after age 40. The increase approaches an exponential relationship.

(3) Based on data reported via the PCI network of National Health and Family Planning Commission Coronary Heart Disease Interventional Treatment Quality Control Center, the number of PCI cases in China displayed a notably increasing trend. The total number of PCI cases in 2014 was 500 946. The amplitude has slowed down in recent years, 2014 exhibiting the lowest growth rate over the past five years.

(4) The Cardiovascular Disease Key Treatment Technology Clinical Multi-center Research Platform, China Acute Myocardial Infarction (CAMI) study, funded by the 12th National Five-year Science and Technology Support Projects, found that the top three cardiovascular disease risk factors among AMI patients in China are smoking, overweight/obese and hypertension, followed by diabetes and dyslipidemia. Late arrival at hospital was common. Among STEMI patients receiving emergency reperfusion therapy, significant differences existed in time from admission to emergency reperfusion therapy. The median time was 165 minutes from admission to emergency PCI, and 130 minutes from admission to thrombolysis.

3.3 Arrhythmia

(1) According to statistics from the Ministry of Health's online enrollment system, about 53 382

pacemakers were implanted in 2014, an increase of 3.2% when compared to 2013. Among the indications for cardiac pacing, 51.1% were associated with the treatment of sick sinus syndrome (SSS), and 39.8% were related to atrioventricular block, the proportion of dual-chamber pacemakers is nearly 67%, including 2918 pacemakers that are remote monitoring pacemakers.

The number of ICD implantations was 1 959 in 2014, an increase of 2.9% when compared to 2013. The percentage of single-chamber ICD implantations was 67.1%, and the percentage of dual-chamber ICD implantations was 32.9%. The proportion of ICDs for secondary prevention was 52.1%, and for primary prevention was 47.9%. The proportion for primary prevention steadily increased compared to 2012 (42.7%) and 2013 (45%).

The number of CRT implantations was 2 379, an increase of 8.2% when compared to 2013. CRT-D accounted for 55% of implantations and CRT-P for 45%. A study conducted by Fu Wai Hospital analyzed 73 CRT cases of remote monitoring pacemaker in 97 clinical centers in China. The six months follow-up showed that 92.7% of patients experienced abnormal alarm events, 85% of which were related to diseases and 15% were system-related events. It is 3 or 6 months earlier to identify adverse events than clinic visit.

The number of RFCA was 88 200, and the proportion of RFCA cases for atrial fibrillation was 19.7%. Since 2008, China has been building a national online platform for atrial fibrillations statistics to facilitate data collection. Statistics have shown that RFCA therapies for atrial fibrillation have increased steadily. Currently, circumferential pulmonary vein isolation is still the most commonly used technique within RFCA for AF. The total success rate was 77.1%, the recurrence rate was 22.9%, and the complication rate was 5.3%.

(2) Based on a survey conducted in 2004 in 10 different districts, the prevalence rate of AF in people 35–59 years was 0.77% (males 0.78%, females 0.76%). 19% of males and 30.9% of females with AF also had valvular heart diseases. The analysis from a study over 60 years old showed that the baseline prevalence rate of AF was 2.0% for males and 1.6% for females. After 3 years' follow-up, AF prevalence rate was 4.0/1 000 person-years. Only 1% of the AF patients received warfarin anticoagulant treatment. Patients with AF had significantly higher risks of all-cause, cardiovascular mortality, and stroke mortality.

A prospective observational study recruited 2 016 patients (54.8% female) who were admitted to emergency departments due to atrial fibrillation or atrial flutter in twenty representative medical centers. The analysis of the baseline data showed 30.7% were diagnosed with paroxysmal AF, 22.4% with persistent AF, and 46.9% with permanent AF. Only 16.2% of all the patients received more than one anti-thrombotics agent, whereas 68.4% patients received ventricular rate control agents. Among the patients with valvular atrial fibrillation, 41.4% of patients received oral anticoagulant treatment. Only 26.4% of these patients showed international normalized ratio values that were within the target range (2.0–3.0).

(3) The leadless pacemaker implantation, the cardiac contractility modulation, and the station ICD, all are the new technologies in the arrhythmia field. They were all first successfully implanted in Fuwai hospital.

3.4 Heart Failure

(1) In 2000, the prevalence of chronic heart failure in the Chinese population aged 35–74 years was 0.9%,

0.7% in men and 1.0% in women. Prevalence was higher in the north than the south, and higher in urban areas. The prevalence of heart failure increased significantly with age. During the past two to three decades, the main cause for heart failure has shifted from rheumatic valvular heart disease to coronary heart disease.

(2) The preliminary results from the China Heart Failure Registry Study (China-HF) showed that the prevalence of heart failure increased with aging, the average age of patients with heart failure is 66 ± 15 years old. 54.5% of HF patients are males. 84.7% of the patients were at III–IV levels according to the NYHA functional classification criteria. The main comorbidities with heart failure have changed significantly: the proportion with valvular diseases has gradually decreased; coronary artery disease (49.4%), hypertension (54.6%), and chronic kidney disease (29.7%) have become the most common comorbidities. Infection (45.9%) continues to be the primary reason for the onset of heart failure, followed by fatigue or stress (26.0%), and then myocardial ischemia (23.1%). The usage of diuretics in patients during hospitalization has not changed significantly: the usage of digoxin showed a downward trend. The use of angiotensin II receptor antagonist (24.6%), aldosterone receptor antagonist (55.4%) and beta-receptor blocker (50.6%) has increased significantly.

(3) A domestic study among 3 168 ACS patients showed that 706 (22.3%) had acute heart failure during hospitalization. The study recruited 65 hospitals in 31 provinces in mainland China and Hong Kong from 2006 March through June, of all 3 168 ACS patients, 1 329 patients with acute STEMI, 348 patients with acute NSTEMI, and 1491 patients with unstable angina.

3.5 Pulmonary Disease

(1) Results of a 2007 epidemiological study among people over the age of 40 showed that the prevalence of Chronic Obstructive Pulmonary Disease (COPD) was 8.2% (8.8% in rural areas and 7.8% in urban areas). The COPD prevalence was higher in men (12.4%) than women (5.1%). The estimated number of patients with COPD in China was 43 million. According to statistics released by the National Health and Family Planning Commission in 2008, COPD ranked fourth leading cause of death in urban areas and the third in rural areas. From 1990 to 2008, the COPD mortality rate declined annually.

(2) From 1997 to 2008, a registration study on patients with pulmonary embolism (PE) was conducted in 60 tertiary hospitals involved in the National Cooperative Project for the Prevention and Treatment of Venous Thromboembolism (NCPPT). Among 16 972 182 hospitalized patients, the incidence of PE was 0.1%.

(3) Data from 504 patients with Chronic Thromboembolic Pulmonary Hypertension (CTEPH) admitted at Beijing Anzhen Hospital were collected from 1989 to 2008. For patients with central CTEPH, those who underwent pulmonary thromboendarterectomy demonstrated a higher long-term survival rate (10 year survival rate: 94.6%; 15 years survival rate: 90.96%) than patients treated with the medical regimen (10 year survival rate: 81.4%; 15 years survival rate: 56.43%). For peripheral CTEPH, there was no significant difference between two groups.

3.6 Cardiovascular Surgery

(1) The annual volume of cardiovascular surgery in China has increased over the last decade. However, the growth rate in 2013 was significantly lower than that of previous years. In 2014, 209 765 cardiovascular surgeries were performed in Mainland China. The proportion of cardiopulmonary bypass surgeries among the total performed cardiovascular surgeries has declined since 2007 and reached 75.9% in 2014 (159 108 cases). In Hong Kong (special administrative region, SAR), 1 704 cardiovascular surgeries were performed and 1 534 cases were CPB surgeries in 2014.

In 2014, 82 882 surgeries for congenital heart disease (CHD) were completed in Mainland China and Hong Kong. These surgeries accounted for 39.5% of all aortic surgeries and were the most frequently performed surgery among all categories. Additionally, there were 60 485 cases of valvular surgeries, 41 636 cases of coronary artery bypass grafting, 11 013 cases of aortic surgeries, 370 cases of heart transplantation (including 12 heart–lung transplants), and 711 cases of extracorporeal membrane oxygenation (ECMO) adjuvant treatment.

(2) The monitoring of birth defects has been continuously increased in Mainland China. The incidence of CHD varies in different areas: Ventricular septal defects, atrial septal defects, and patent ductus arteriosus constitute approximately 75% to 80% of all CHD cases. Transcatheter device closure and surgical repair are effective interventions with optimal midterm results for treating perimembranous ventricular septal defect (pmVSD). Application of transcatheter device closure demonstrates relatively low incidence of myocardial injury, slight blood transfusion, fast recovery, short hospital stays, and low medical expenses.

3.7 Chronic Kidney Diseases

(1) A nationwide survey on CKD prevalence was performed from September 2009 to September 2010 by applying stratified multistage sampling with 47 204 adults across 13 provinces, municipalities, and autonomous regions. The results revealed that the overall prevalence of CKD, the adjusted prevalence of estimated GFR (eGFR) <60 ml/min/1.73m², and the urine albumin–creatinine ratio >30 mg/g were [10.8%, 1.7% and 9.4%], respectively. According to this result, the number of patients with CKD was estimated to be approximately 120 million.

(2) A cross–sectional survey using four–stage cluster sampling was employed in the China Health and Retirement Longitudinal Study (CHARLS) during 2011–2012 on 17 708 adults ≥ 45 years of age from 450 villages/communities across 28 provinces. eGFR was calculated using the creatinine–cystatin C (eGFR creat–cys) equation. CKD was defined as a eGFR less than 60 mL/min per 1.73 m². The overall prevalence of CKD was 11.5% in people over 45. Rural populations displayed higher CKD rates than urban populations (13.0% vs 10.0%). The prevalence of CKD also increased with age. 8.7% of the participants aware of having CKD and 4.9% received treatments. The awareness and treatment rates decreased with age.

3.8 Peripheral Vascular Disease

Lower extremity atherosclerotic disease (LEAD) and carotid atherosclerotic disease (CAD) are commonly seen in middle-aged and elderly people. The prevalence of these diseases among those with major risk factors is particularly high and increases with age. 30% of patients with cerebrovascular disease and 25% of patients with ischemic heart disease also had LEAD. The mortality rate among patients with LEAD was much higher than that of same-age patients without LEAD. Results from a 3-year follow-up study comparing the mortality rates of patients with high risk of atherosclerotic diseases categorized by their ABI suggested that all-cause mortality rate doubled in the group with ABI<0.4 compared with that with ABI within 1.0 to 1.4.

A collaborative cross-sectional study involving investigators from China and the United States reported that the ultrasound detection rate of carotid atherosclerotic plaques among patients from 43 to 81 years of age was 60.3% (males 66.7%, females 56.2%), with lesions predominantly located at the carotid sinus. Baseline IMT is an independent predictor of ischemic heart disease in patients without carotid atherosclerotic plaques; in patients with carotid plaques, the risk of ischemic heart disease increased with an increase in overall plaque surface area and number of plaques.

4. Community-based Prevention and Control of CVD

(1) An overview of the community-based prevention and control of CVD

The first hypertension prevention and control center in China, established in 1969 at the Capital Iron and Steel Company by Fuwai Hospital, was a model of functional community-based prevention programme. The risks of stroke can be reduced by 50% through successful control of hypertension. Over the course of more than 40 years, the community-based prevention and control of CVD has gradually developed from spot to larger scale toward the comprehensive prevention and control with the multi-functional cooperation and collaboration under the government and with the large scale participation of the whole society.

(2) A community-based information management model for prevention and control of hypertension in Minhang District, Shanghai

By creating an innovative medical reform model, the Minhang District has achieved an outstanding success in CVD prevention such as hypertension control. Since 2006, the Health Bureau of Minhang District began establishing a regional health information management platform based on the Electronic Health Record (EHR), and continually established a "Trinitarian Management Model on CVD comprehensive prevention and control" in 2007. By circulating information, sharing resources and standardizing hypertension management processes, the district has achieved a scientific and efficient management system for hypertension patients in the community. Currently, more than 200 000 hypertension patients in the Minhang district are managed by the aforesaid system, which is more than twice of that number in 2007. All the hypertension files are managed in the electronic information form, with the standardized management rate of 98%. Compared to that of hypertension patients who were not included in the system, the blood pressure control rate of hypertension patients in the system apparently increased, while stroke and myocardial

infarction incidence rates decreased significantly.

In October 2011, the “Shanghai Institute of Hypertension-Research Base on Community Hypertension Prevention and Control at Xinzhuang Community Health Service Center” was established in the Minhang District. Since 2012, the research base has gradually developed a system and management platform for automatic blood pressure measurement and the direct transmission of results. Through modern communications technology, a fully automated and seamless process from hypertension data acquisition to data collection and transmission and import into the management system and platform can be achieved. This ensures the accuracy, reliability and authenticity of data. Currently, at Xinzhuang community health service centers and all subordinate service sites, automatic blood pressure measurement has been achieved and results are transferred directly to the doctor's workstation and the patient's EHR. Telemetry blood pressure monitors for home have also been configured to each community health service center in Minhang.

5. Medical Treatment and Expenditure of Cardiovascular Diseases

Since 1980, the number of patients with CVD and diabetes discharged from hospitals in China has increased. This rising trend has accelerated, especially since 2000. Correspondingly, the total cost of the hospitalization of patients with CVD also increased rapidly. Since 2004, the average annual rate of increase of the cost has been growing faster than the annual rate of increase of China's GDP. The increase mainly springs from the growing demands of hospitalization and the high proportion of inappropriate prescriptions.

(1) Number of Discharged Patients with CVD and Its Changing Trend

In 2014, the number of discharged patients with CVD reached 17 938 600, accounting for 12.75 % of the total number of discharged patients during the same period. Patients with CVD accounted for 6.63% of total patients, while patients with cerebrovascular disease accounted for 6.12%. Among the discharged patients with CVD, ischemic heart disease (IHD) and cerebral infarction contributed to 36.53% and 29.66% respectively, making up the majority of these patients, while the remaining were patients with hypertension, intracranial hemorrhage, and rheumatic heart diseases. Additionally, in 2013, the number of discharged patients with diabetes was 3 204 400.

From 1980 to 2014, the average annual growth rate of discharged patients with CVD was 10.10%, exceeding that of general discharged patients (6.33%) for the same period. The annual growth rates of all subtypes of CVD in descending order were: cerebral infarction (12.30%), IHD (11.74%), intracranial hemorrhage (9.76%), AMI (8.12%), hypertension (8.06%), hypertension heart disease and kidney disease (5.82%). In addition, from 1980 to 2014, the annual growth rate of discharged patients with diabetes was 14.18%.

(2) Hospitalization Expenses of CVD

For hospitalizations associated with CVD in 2013, the total medical expenses for acute myocardial infarction, intracranial hemorrhage, and cerebral infarction were 13.375 billion, 20.707 billion, and 47.035 billion RMB respectively. The expenses for acute myocardial infarction, intracranial hemorrhage, and cerebral infarction showed an annual increase from 2004 by 32.02%, 18.90% and 24.96%, respectively.

The average individual expenses in 2014 for AMI, intracranial hemorrhage and cerebral infarction were 24 706, 15 929.7, and 8 841.4 RMB, respectively, with average annual growth rates (from 2004) of 8.72%, 6.63% and 2.81%, respectively.



Part 1

Prevalence and Mortality of Cardiovascular Diseases

1.1 Prevalence of Cardiovascular Diseases

According to the Report of Nutrition and Chronic Diseases in China (2015)^[1], which was released by the State Council Information Office of China on June 30th 2015, the prevalence of hypertension among Chinese people ≥ 18 years old was 25.2%. Based on data from the Sixth National Population Census (conducted in 2010), it is estimated that the total number of people with hypertension in China is approximately 270 million.

1.2 Death from Cardiovascular Diseases

1.2.1 Mortality from cardiovascular diseases^[2,3]

CVD was still the leading cause of death in 2014, higher than deaths caused by tumors or any other diseases (Figure 1-2-1 and 1-2-2). Ever since 2009, the CVD mortality rate in rural areas has exceeded that of urban areas, and consistently remained higher than urban areas (Figure 1-2-3).

In 2014, the mortality rate of CVD in rural areas was 295.63/100 000, among them, the mortality rate of heart diseases was 143.72/100 000, and the mortality rate of cerebrovascular diseases was 151.91/100 000 (cerebral hemorrhage: 74.51/100 000, cerebral infarction: 45.30/100 000). Meanwhile, the mortality rates of CVD, heart diseases and cerebrovascular diseases in urban areas were 261.99/100 000, 136.21/100 000 and 125.78/100 000 (with 52.25/100 000 in cerebral hemorrhage, 41.99/100 000 in cerebral infarction), respectively.

[1] Report of Nutrition and Chronic Diseases in China (2015). <http://www.labagd.com/Item/14257.aspx>.

[2] Ministry of Health of the People's Republic of China. Statistics Year Book of Health of the People's Republic of China. 2009–2012. Beijing: Pecking Union Medical College Press.

[3] National Health and Family Planning Commission of the People's Republic of China. 2015 Year Book of Health and Family Planning in the People's Republic of China. Beijing: Pecking Union Medical College Press.

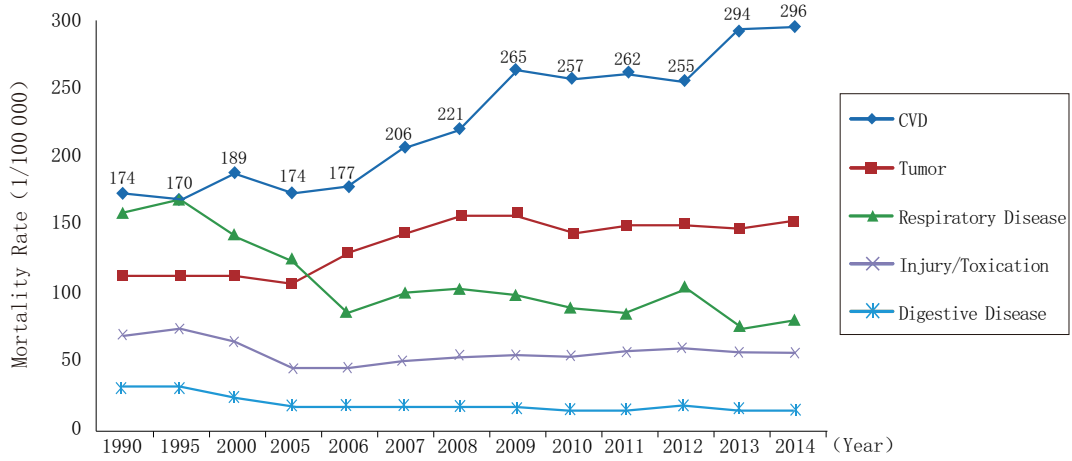


Figure 1-2-1 Mortality Rates of Major Diseases in Rural Chinese Populations (China: 1990–2014)

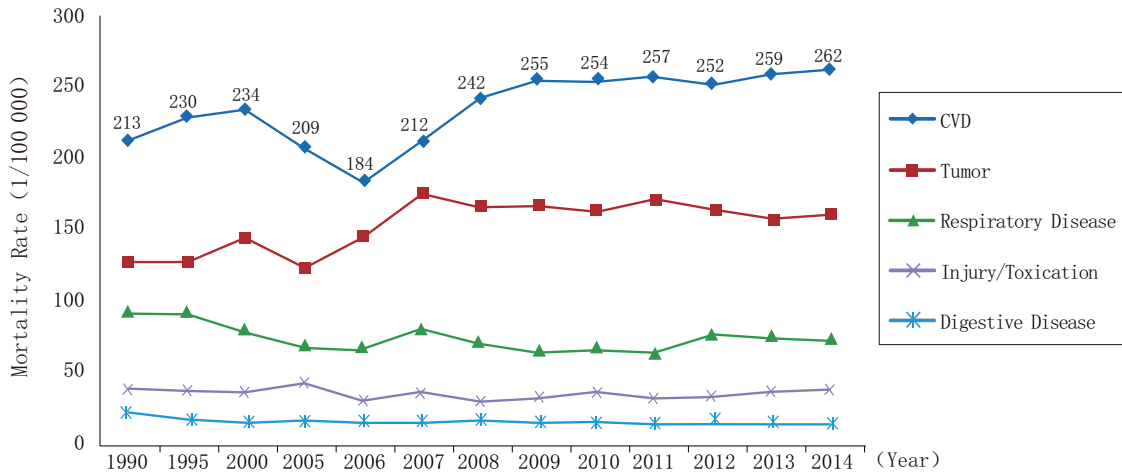


Figure 1-2-2 Mortality Rates of Major Diseases in Urban Chinese Populations (China: 1990–2014)

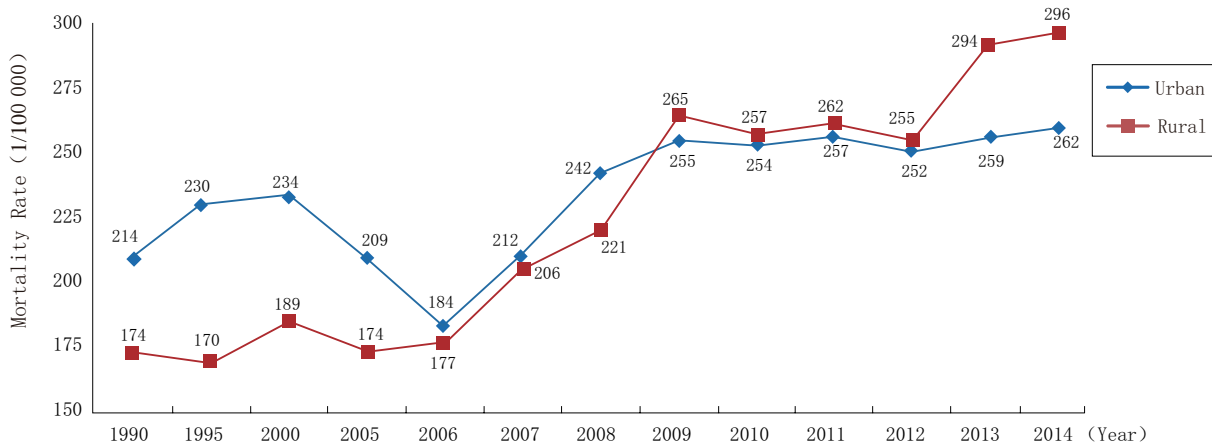


Figure 1-2-3 Mortality Rates of CVD in Urban and Rural Chinese Populations (China: 1990–2014)

1.2.2 Deaths Attributable to Cardiovascular Diseases among All Causes of Death^[1]

CVD is the leading cause of death in both rural and urban populations in China. In 2014, CVD-related deaths accounted for 44.60% and 42.51% of all deaths in rural and urban areas, respectively (Figure 1-2-4 and 1-2-5). Two in five deaths are attributed to CVD.

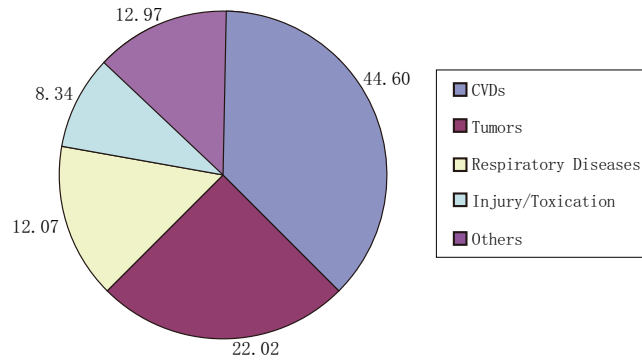


Figure 1-2-4 Major Causes of Death in Rural Population (%) (China: 2014)

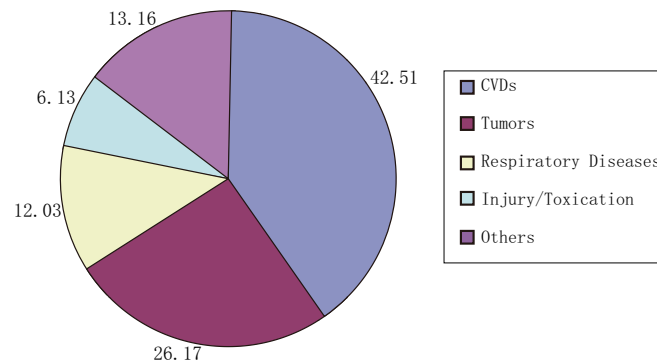


Figure 1-2-5 Major Causes of Death in Urban Population (%) (China: 2014)

1.2.3 Study of Cardiovascular Disease Burden in China^[2]

Following the methods of the Global Burden of Disease Study 2013 (GBD 2013), researchers from China CDC have systematically analyzed all available demographic and epidemiological data sources for China at the provincial level. In 1990, 16 of 33 provinces had lower respiratory infections or preterm birth complications as the leading causes of years of life lost (YLLs). 15 provinces had cerebrovascular disease and two (Hong Kong and Macao) had ischemic heart disease (IHD). By 2013, 27 provinces had cerebrovascular disease as the leading

[1] National Health and Family Planning Commission of the People's Republic of China. 2015 Year Book of Health and Family Planning in the People's Republic of China. 2009-2012 Beijing: Pecking Union Medical College Press.

[2] Zhou MG, Wang HD, Zhu J, et al. Cause-specific mortality for 240 causes in China during 1990-2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. Lancet, Published Online October 26, 2015.

cause, 5 had IHD, and one had lung cancer (Hong Kong). The most common non-communicable diseases, including ischemic heart disease, stroke, chronic obstructive pulmonary disease, and cancers (liver, stomach, and lung), contributed much more to YLLs in 2013 compared with 1990.

The age-standardized mortality of CVD was 389.93/100 000 in 1990 and 307.18/100 000 in 2013, decreasing by 21%. Among all CVD, the mortality of rheumatic heart disease, cerebrovascular disease and hypertensive heart disease has decreased by 71.2%, 20.9% and 41.3%, respectively, while the mortality of IHD and peripheral vascular disease has increased by 2.6% and 91.9%, respectively. Cerebrovascular disease is the leading cause of death in both men and women in China, with an increase in ischemic stroke (28.8%) and a decrease in hemorrhage stroke (37.7%). Mortality rates of IHD has increased in men but decreased in women. Because of improvements in the management and treatment of high blood pressure coupled with improved access to various treatments related to cardiovascular outcomes, this result is not unexpected.

It is notable that, although age-standardized mortality rates of CVD decrease due to population aging in China and other factors, the absolute number of CVD deaths are still rising rapidly by 46% from 1990 to 2013, with IHD and cerebrovascular disease deaths increasing by 90.9% and 47.7%, respectively.

Cerebrovascular disease mortality is inversely related to per capita income, with the highest rates in the poorest provinces (with the exception of Yunnan). Zhejiang Province has the lowest age-standardized mortality of IHD, while the highest mortality of IHD is in Heilongjiang Province. Although the rankings of death causes is not directly related to all-cause mortality, a relatively clear north-to-south gradient exists in IHD mortality, with the mortality in the North obviously higher than that in the South.

Table 1-2-1 Changes of CVD-related Deaths and Age Standardized CVD Mortality (China: 1990 vs. 2013)

	All-age CVD-related Deaths (Num.)			Age-standardized Mortality Rates (1/100 000)		
	1990	2013	Change(%)	1990	2013	Change(%)
Rheumatic Heart Disease	145 306 (115 228-175 059)	72 912 (55 330-90 955)	-49.9 (-57.6-41.6)*	19.77 (15.75-23.84)	5.71 (4.32-7.08)	-71.2 (-75.4-66.6)*
Ischemic Heart Disease	745 373 (663 800-874 909)	1 394 366 (1 061 479-1 563 778)	90.9 (42.7-116.3)*	115.40 (102.60-135.21)	115.89 (88.02-129.32)	2.6 (-23.5-14.9)
Cerebrovascular Disease	1 308 055 (1 191 711-1 436 929)	1 920 888 (1 716 666-2 196 207)	47.7 (30.0-66.2)*	199.66 (182.68-219.55)	157.29 (141.92-180.13)	-20.9 (-29.9-11.5)*
Ischemic Stroke	317 792 (274 000-410 202)	735 976 (554 471-849 199)	143.3 (61.5-183.0)*	51.58 (44.64-66.86)	62.87 (47.07-72.15)	28.8 (-21.1-48.3)
Hemorrhagic Stroke	988 263 (869 269-1 100 203)	1 184 712 (1 024 961-1 462 700)	17.9 (1.8-47.5)*	148.08 (130.44-164.09)	94.42 (81.60-117.82)	-37.7 (-45.7-20.4)*
Hypertensive Heart Disease	211 202 (148 674-253 262)	238 764 (171 628-284 851)	12.4 (-5.6-45.9)	34.67 (24.55-41.32)	20.47 (14.66-24.36)	-41.3 (-50.5-25.4)*
Cardiomyopathy and Myocarditis	9 338 (7 465-16 701)	26 674 (18 939-30 905)	231.3 (24.4-284.7)*	1.06 (0.84-1.91)	2.13 (1.53-2.44)	138.9 (-12.2-171.3)
Atrial Fibrillation and Atrial Flutter	407 (328-479)	1 021 (892-1 229)	148.8 (102.2-228.8)*	0.07 (0.06-0.08)	0.09 (0.08-0.11)	26.4 (2.5-89.0)*
Aortic Aneurysm	5 063 (3 819-6 402)	10 184 (8349-12 210)	100.7 (63.5-161.7)*	0.70 (0.53-0.88)	0.78 (0.64-0.93)	11.5 (-7.8-41.8)
Peripheral Vascular Disease	327 (252-416)	1 209 (1 052-1 425)	276.0 (171.0-403.3)*	0.05 (0.04-0.07)	0.10 (0.09-0.12)	91.9 (39.9-153.3)*
Endocarditis	2 293 (1 592-3 421)	2 901 (2 151-3 560)	29.2 (-18.5-96.0)	0.29 (0.20-0.43)	0.23 (0.17-0.28)	-18.5 (-46.9-22.5)
Other Cardiovascular and Circulatory System Diseases	131 531 (79 721-150 682)	55 051 (46 220-84 473)	-59.9 (-66.3-2.4)	18.27 (10.68-20.96)	4.49 (3.80-6.80)	-76.6 (-80.1-38.3)*
Total	2 556 894 (2 363 658-2 753 189)	3 723 770 (3 345 960-4 017 408)	46.0 (29.9-60.9)*	389.93 (363.14-417.59)	307.18 (278.20-329.23)	-21.0 (-29.2-13.8)*

*: Statistical significance ($p < 0.05$).

Part 2

Risk Factors of Cardiovascular Diseases

2.1 Hypertension

- Disease Burden of Hypertension

Hypertension is one of the most common chronic non-infectious diseases and can cause multiple complications in the heart, brain, and kidney. In 2010, hypertension accounted for 2.043 million deaths in China (male 1.15 million, female 0.89 million), or 24.6% of all deaths in the country^[1]. According to data from 2013, hypertension alone accounted for 6.61% of the 3.1869 trillion RMB spent on healthcare in China^[2].

2.1.1 Primary Hypertension

2.1.1.1 Prevalence of Hypertension

Over the past 50 years, four national, large-scale surveys focused on hypertension have been conducted (from 1958–1959, 1979–1980, in 1991, and in 2002)^[3]. These surveys showed that the prevalence of hypertension among Chinese residents aged over 15 years old has increased in China over the past 50 years (5.1%, 7.7%, 13.6%, and 17.6%, respectively).

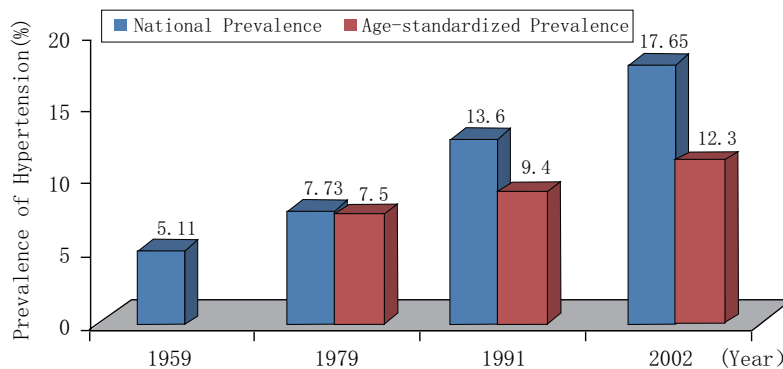


Figure 2–1–1 Prevalence of Hypertension in Chinese Residents over 15 years old in four National Surveys

[1] Liu MB, Li YC, Liu SW, et al. Burden on blood-pressure-related diseases among the Chinese population in 2010. Chinese Journal of Epidemiology, 2014 (6) :65–68.

[2] National Health and Family Planning Commission of the People’s Republic of China. China Health and Family Planning Statistics Yearbook 2015. Peking Union Medical College Press.

[3] Li LM, Rao KQ, Kong LZ, et al. A description on the Chinese national nutrition and health survey in 2002. Chinese Journal of Epidemiology, 2005 (07) :478–484.

Four cross-sectional studies have been conducted among adults aged 35–64 years old in Hanzhong rural area of Northwest China in 1982, 1998, 2004, and 2010. The results showed that the prevalence of hypertension increased over the time period (Figure 2–1–2).^[1]

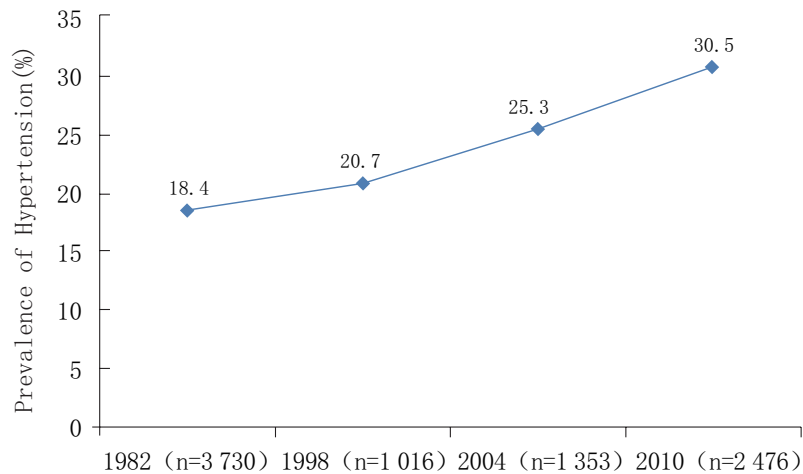


Figure 2–1–2 Trends in Prevalence of Hypertension from 1982–2010 in Rural Area of Northwest China.

According to the Survey on the Status of Nutrition and Health of the Chinese People in 2015^[2], 25.2% of adults aged ≥ 18 years old in China have hypertension. Using data from the 2010 National Population Census as a denominator, it is estimated that the total number of people with hypertension in China is approximately 270 million.

2.1.1.2 Incidence of Hypertension

- Incidence of Hypertension in Rural Areas in Liaoning Province

A population-based sample of 24 360 subjects aged ≥ 35 years and free from hypertension at baseline were followed from 2004–2006 to 2008 in rural areas in Liaoning province^[3], with an average follow-up period of 28 months. The result revealed that 29.6% of the men and 23.4% of the women developed hypertension during the study period, and the age-adjusted incidence rate of hypertension was higher for men than for women (12.75/100 person-years vs 10.04/100 person-years), as shown in Table 2–1–1.

[1] Zhao Y, Yan H, Marshall R J, et al. Trends in population blood pressure and prevalence, awareness, treatment, and control of hypertension among middle-aged and older adults in a rural area of Northwest China from 1982 to 2010. PLoS One, 2013,8 (4) : e61779.

[2] The 2015 Survey Report on the Status of Nutrition and Health of the Chinese People was released. <http://www.labagd.com/Item/14257.aspx>.

[3] Sun Z Q, Zheng L Q, Detrano R, et al. Incidence and predictors of hypertension among rural Chinese adults: results from Liaoning Province[J]. Annals of family medicine, 2010,8 (1) :19–24.

Table 2-1-1 Incidence of Hypertension by Age and Gender in Rural Area of Liaoning Province (1/100 person-years)

Age (Years old)	Male (95%CI)	Female (95%CI)
35-44	9.52 (9.01-10.04)	6.78 (6.36-7.23)
45-54	13.80 (13.08-14.54)	10.74 (10.09-11.42)
55-64	16.27 (15.23-17.35)	14.45 (13.41-15.53)
>65	18.57 (17.05-20.17)	17.95 (16.37-19.61)

Another population-based study^[1] enrolled 10 525 Chinese adults aged 40 years or older who were free from hypertension at baseline. The study found that 28.9% of men and 26.9% of women developed hypertension over the mean 8.2 years of follow-up (Figure 2-1-3).

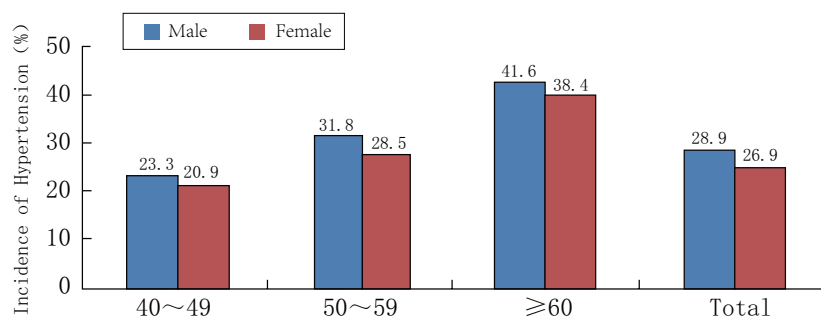


Figure 2-1-3 Cumulative Incidence of Hypertension by Age and Gender

2.1.1.3 Detection Rate of High-normal Blood Pressure

The China Health and Nutrition Survey (CHNS) conducted seven cross-sectional surveys among adults aged ≥ 18 years old in nine provinces from 1991 to 2009 (1991, 1993, 1997, 2000, 2004, 2006, and 2009)^[2]. The data demonstrated that the detection rate of high-normal blood pressure increased from 29.4% in 1991 to 38.7% in 2009 (Table 2-1-2).

Table 2-1-2 Changes in the Detection Rate of High-normal Blood Pressure among Adults (China: 1991-2009)

Age (Years)	1991		1993		1997		2000		2004		2006		2009	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
18-39	4 517	26.8	3 953	31.2	3 788	36.2	3 869	37.3	2 841	41.7	2 551	41.4	2 202	37.8
40-59	2 657	33.6	2 712	37.4	3 192	39.0	3 796	41.5	3 962	42.6	4 175	43.7	3 868	42.8
≥ 60	1 252	30.3	1 240	32.4	1 529	33.0	1 804	34.0	2 044	32.0	2 254	33.8	2 433	33.5

Over the past few years, many regional surveys have been conducted to investigate its detection rates.

[1] Gu D, Wildman RP, Wu X, et al. Incidence and predictors of hypertension over 8 years among Chinese men and women. *J Hypertens*, 2007, 25 (3) : 517-523.

[2] Xi B, Liang Y, Reilly KH, et al. Trends in prevalence, awareness, treatment, and control of hypertension among Chinese adults 1991-2009. *International J of Cardiology*, 2012, 158 (2) : 326-329.

Findings from these surveys, suggest significant differences in the detection rates of high-normal blood pressure across different regions. Some of these studies are summarized in Table 2-1-3.

Table 2-1-3 Detection Rate of High-normal Blood Pressure by Region

Region	Time Period	Age (Years)	Sample Size	Detection Rate (%)	Male/Female (%)
Zhejiang ^[1]	2010	≥18	17 437	34.39	38.57/30.70
Shandong ^[2]	2011	18-69	15 350	37.1	—
Shunde, Guangdong ^[3]	2011-2013	≥35	5 362	38.6	43.5/32.2
Rural Areas in Northeast China ^[4]	2013	≥35	11 576	33.7	35.1/32.5

2.1.1.4 Isolated Systolic Hypertension (ISH)

According to data from a survey^[5] carried out from 2007 to 2010 among 14 618 subjects (≥35 years old) in Xinjiang province, the prevalence of ISH is 11.95%, higher in women than in men (12.92% vs 10.84%). Overall, the prevalence of ISH was found to increase remarkably with age.

Using cluster random sampling, researchers from Xinjiang explored ISH prevalence from January 2010 to December 2012 in 3 416 adults (over 60 years old) from different ethnicity groups^[6]. The findings of this study are shown in Table 2-1-4.

[1] Fei F R, Ye Z, Cong L M, et al. Prevalence and risk factors of pre-hypertension among adults of Zhejiang province. *Zhonghua Liu Xing Bing Xue Za Zhi*,2013,34 (4) :311-315.

[2] Chu J, Wang L, Xu A, et al. [Analysis on prevalence states and associated factors of hypertension and prehypertension among adults in Shandong province]. *Zhonghua Yu Fang Yi Xue Za Zhi*,2014,48 (1) :12-17.

[3] Huang Y, Qiu W, Liu C, et al. Prevalence and risk factors associated with prehypertension in Shunde District, southern China. *BMJ Open*,2014,4 (11) :e6551.

[4] Li Z,Guo X, Zheng L, et al. Prehypertension in rural northeastern China: results from the northeast China rural cardiovascular health study. *J Clin Hypertens (Greenwich)* ,2014,16 (9) :664-670.

[5] Liu F, Ma Y T, Yang Y N, et al. The prevalence of isolated systolic hypertension in adult populations from the Han, Uygur and Kazakh ethnic groups in Xinjiang, China[J]. *Blood Press*, 2014, 23 (3) :154-159.

[6] Yi Liminuer A, Miheireguli A. Prevalence and risk factors of isolated systolic hypertension in elderly people of different nationalities in Urumchi of Xinjiang. *Chinese J of Evidence-Based Cardiovascular Medicine*, 2013,5 (5) : 500-502.

Table 2–1–4 ISH Prevalence among the Elderly by Different Ethnic Groups (%)

Gender	Han (n=1 435)	Urghur (n=1 040)	Kazak (n=482)
Male	165 (23.11)	137 (24.16)	54 (19.71)
Female	232 (32.18)	123 (26.00)	43 (20.67)
Total	397 (27.67)	260 (25.00)	97 (20.13)

2.1.1.5 Awareness, Treatment, and Control Rates of Hypertension

The CHNS^[1] on populations aged 18 years or above in 9 provinces from 1991 to 2009 demonstrated that awareness, treatment, and control rates of hypertension exhibited an upward trend, however it is notable that these rates were still relatively low (Figure 2–1–4).

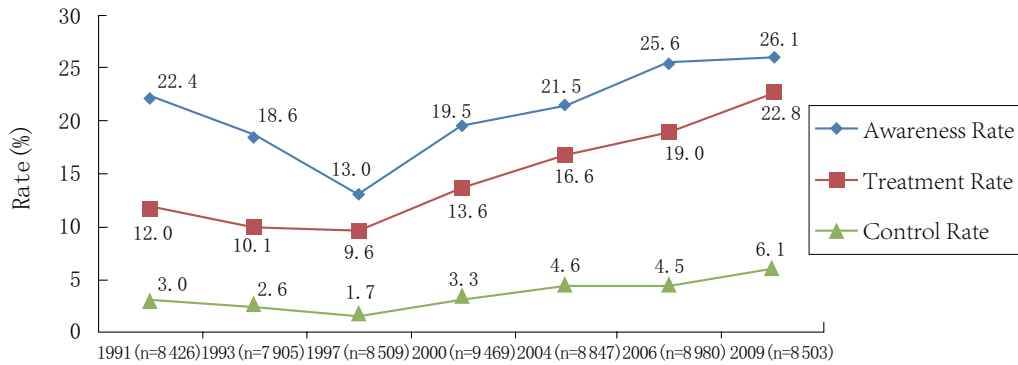


Figure 2–1–4 The Awareness, Treatment, Control, and Treatment Control Rates of Hypertension in 9 Provinces (China: 1991–2009)

2.1.1.6 Risk Factors for Hypertension

- Anxiety and Hypertension

A recent meta-analysis^[2] including results from 13 cross-sectional studies up to November 2014, over 151 389 generalized subjects were analyzed the association between anxiety and hypertension. The results indicated that the risk of hypertension among those with anxiety is 1.18 times (95%CI: 1.02–1.37) higher than those without such a condition. The results of analyzing 80 146 subjects from eight prospective studies demonstrated that anxiety resulted in a 1.55 times greater risk (95%CI: 1.24–1.94) for hypertension compared with people who did not suffer from anxiety.

[1] Xi B, Liang Y, Reilly KH, et al. Trends in prevalence, awareness, treatment, and control of hypertension among Chinese adults 1991-2009. *International Journal of Cardiology*, 2012, 158 (2) : 326-329.

[2] Pan Y, Cai W, Cheng Q, et al. Association between anxiety and hypertension: a systematic review and meta-analysis of epidemiological studies. *Neuropsychiatric Disease and Treatment*, 2015, 11, 1121–30.

• Alcohol and Hypertension

The Kailuan study followed up 32 389 male miner workers for 4 years from June 2006^[1] through 2010, and its findings demonstrated that for different drinking groups, namely no daily alcohol consumption, and alcohol consumption of 1–24g, 25–49g, 50–99g, 100–149g or ≥150g, respectively, the cumulative incidences of hypertension were 25.03%, 28.82%, 30.10%, 37.07%, 40.14%, and 42.49%, respectively. After adjusting for age, physical activity, cigarette smoking, working type, sodium intake, BMI, history of hyperlipidemia, and diabetes the risk of hypertension was found to increase with alcohol consumption.

• Dietary Salt Intake and Hypertension

A survey^[2] was conducted among 19 519 subjects aged 35–91 years old from January to June in 2008. The results indicated that compared with the group whose salt intake is 6–12g/d, the risk of hypertension for the <6g/d group is 0.888 (95%CI: 0.832–0.947) , while the risk for group with >12g/d salt intake is 1.117 (95%CI: 1.1016–1.227) .

• Obesity and Hypertension

A prospective study^[3] followed up 2 115 residents who were free of hypertension at baseline for ten years. The results showed that from 1992 to 2002, the cumulative incidence of hypertension was 34.8%. After adjusting for age, history of smoking, alcohol consumption, and physical activity, the cumulative incidence of hypertension increased along with BMI (Table 2–1–5) .

Table 2–1–5 The Relationship between Baseline BMI and 10–year Cumulative Incidence of Hypertension

BMI (kg/m ²)	Male	Female	Total
	OR (95%CI)	OR (95%CI)	OR (95%CI)
<24	—	—	—
24–<28	1.605 (1.193–2.159)	2.043 (1.561–2.673)	1.849 (1.516–2.256)
>28	3.632 (2.058–6.408)	3.664 (2.419–5.549)	3.569 (2.559–4.977)

A study conducted in Shanghai collected data from 15 158 residents aged 35–74 years old from 2008 to 2011^[4] The analysis showed that the age–adjusted risk of developing hypertension increased as the number of risk factors for hypertension went up (Table 2–1–6) .

[1] Peng M, Wu S, Jiang X, et al. Long-term alcohol consumption is an independent risk factor of hypertension development in northern China: evidence from Kailuan study[J]. J Hypertens,2013,31 (12) :2342–2347.

[2] Survey on prevalence and risk factors for primary hypertension among communities in Changning District, Shanghai. Geriatrics & Health Care, 2012,18 (1) :19–22.

[3] Sun JY, Zhao D, Wang W, et al. Association between body mass index and ten-year-accumulative-risk of hypertension. Chinese Journal of Epidemiology. 2009,30 (5) :435–438.

[4] Wang G, Li LM, Hu YH, et al. Relationship between risk factors for hypertension and the likelihood of developing hypertension among population in Shanghai communities. Chinese Journal of Epidemiology. 2013,34 (4) :307–310.

Table 2-1-6 Association between the Number of Risk Factors and Hypertension Prevalence

No. of Risk Factors	Male			Female		
	Prevalence (%)	OR (95%CI)	P value	Prevalence (%)	OR (95%CI)	P value
0		1.000	—	10.7 (128/1 196)	1.000	—
1	24.8 (294/1186)	3.157 (2.152–4.630)	<0.001	26.9 (784/2 915)	2.917 (2.374–3.585)	<0.001
2	39.2 (707/1804)	6.428 (4.435–9.319)	<0.001	47.4 (1 375/2 900)	6.499 (5.307–7.959)	<0.001
3	52.5 (922/1755)	11.797 (8.135–17.105)	<0.001	69.9 (1 029/1 473)	15.717 (12.609–19.591)	<0.001
4	63.4 (581/916)	19.723 (13.414–29.000)	<0.001	83.1 (222/267)	31.719 (21.744–46.270)	<0.001
>5	73.3 (269/367)	33.051 (21.449–50.930)	<0.001	—	—	—

2.1.2 Secondary Hypertension

Secondary hypertension accounts for 10% of all patients with hypertension, it usually happens among young and middle-aged people. The most common etiologies for secondary hypertension are endocrine system diseases such as renal parenchymal diseases, renal artery stenosis, primary hyperaldosteronism, hypercortisolism, and obstructive sleep apnea hypopnea syndrome (OSAHS)^[1].

One study^[2] analyzed the medical records of 4 642 inpatients with hypertension from 1997 to 2005 in the People's Hospital of Xinjiang Uygur Autonomous Region. The results showed that patients with secondary hypertension accounted for 14.76% of total hypertensives, and that the proportion of secondary hypertension is the highest among the youth (21.9%) and lowest among the elderly (9.85%).

Another study^[3] assessed secondary hypertension etiologies in Guangxi University Affiliated Liuzhou People's Hospital from January 2007 to December 2010. The results showed that among 3 207 inpatients, 351 were diagnosed with secondary hypertension, with a male/female ratio is 0.46/1 (male: 111, female: 240). The main etiology for secondary hypertension was renal hypertension, followed by OSAHS, primary hyperaldosteronism, hyperthyroidism, pheochromocytoma, hypercortisolism, and aortic stenosis.

2.1.3 Hypertension in Children and Adolescents

2.1.3.1 Epidemiological Trends and Distributional Characteristics of Hypertension in Children and Adolescents

(1) Prevalence and trends of hypertension in children and adolescents

[1] Wang JG, Li LH. Hypertension series: the differential diagnosis and treatment for secondary hypertension—continued. Chinese Circulation Journal, 2012,27 (2) :85–86.

[2] Li NF, Wang L, Zhou KM, et al. Analysis of etiology of the patients with hypertension from the People's Hospital of Xinjiang Uygur Autonomous Region. Chinese Journal of Cardiology. 2007,35 (9) :865–868.

[3] Yi QY, Zhang LC. Survey on epidemiology etiology of hypertension in Liuzhou Chinese J of Clinicians (electronic edition), 2011, 5 (20) : 6102–6105.

Analysis from 190 000 Han nationality school-age children (7 to 17 years old) in the National Student Health Study in 2010 found that the prevalence of hypertension in children and adolescents was 14.5% (Boys: 16.1%; Girls: 12.9%) , and blood pressure levels rose with age (Figure 2-1-5)^[1] .

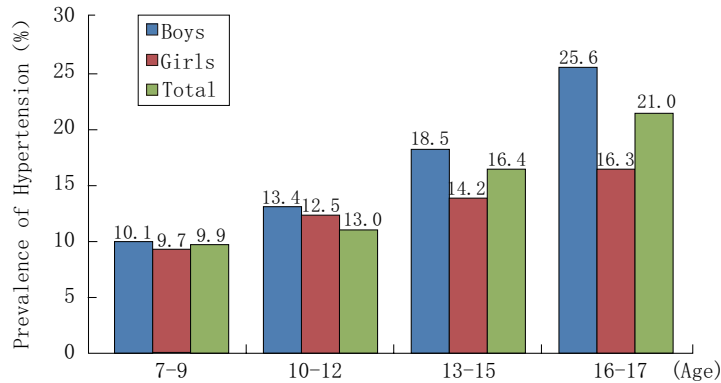


Figure 2-1-5 Prevalence of Hypertension among Different Age Groups of Chinese Children and Adolescents in 2010

The CHNS investigated the trends of blood pressures among children and adolescents from 1991 to 2009^[2,3] . The surveys found that the hypertension prevalence increased incrementally, from 7.1% in 1991 to 13.8% in 2009, with the average annual growth of 0.47% (Figure 2-1-6) .

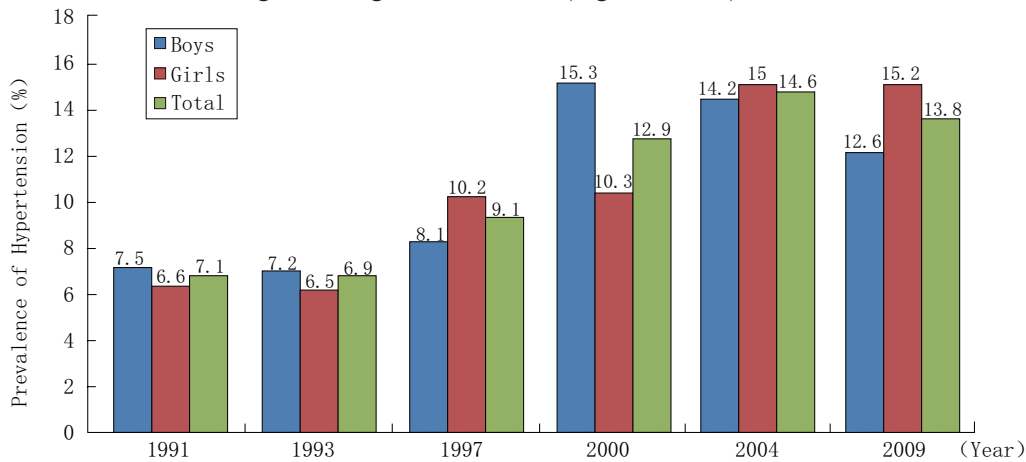


Figure 2-1-6 Trends in Hypertension Prevalence, Ages 6-17 (China: 1991-2009)

Note: Data for 1991-2004 was based on Liang et al.[1] Data for 2009 was based on Xi et al.[2] Both studies used the Chinese Prevention and Treatment Guideline for hypertension (2010 edition) and single time point measurements as the diagnostic criteria of hypertension.

[1] Dong B, Wang HJ, Wang Z, et al. The association of overweight and obesity with blood pressure among Chinese children and adolescents. *Biomedical and Environmental Science*, 2013; 26 (6) : 437-444.

[2] Liang YJ, Xi B, Hu YH, et al. Trends in blood pressure and hypertension among Chinese children and adolescents: China health and nutrition surveys 1991-2004. *Blood Pressure*, 2011, 20 (1) : 45-53.

[3] Xi B, Liang Y, Mi J. Hypertension trends in Chinese children in the national surveys, 1993 to 2009. *International Journal of Cardiology* 2013; 165 (3) : 577-579.

(2) Epidemiological status of juvenile hypertension in different regions.

The prevalence of juvenile hypertension in different regions of Mainland China varied from 3.1% to 23.3%, as shown in Table 2-1-7.

Table 2-1-7 Prevalence of Juvenile Hypertension by Region and Population Characteristics

Survey Region	Survey Period (year)	Ethnic Group	Age (years)	DBP	Sample Size	Prevalence* (%)
Henan ^[1]	2009	Han	6-18	K5	11 571	7.3
Hunan ^[2]	2009	Han	12-17	K4	88 947	3.1
Shanghai ^[3]	2009	Han	7-20	K4	78 114	11.2
Guangxi ^[4]	2009	Han	6-18	K4	7 893	6.6
Xinjiang ^[5]	2009	Kazakh	7-14	K4	2 438	5.6
Shandong ^[6]	2010	Han	7-17	K5	38 860	23.3
Shanxi ^[7]	2010	Han	7-18	K5	66 593	6.2
Beijing ^{[8]†}	2010	Han	3-18	K4	6 692	18.2→5.1→3.1

*: All studies used the diagnostic criteria from Chinese Prevention and Treatment Guideline for Hypertension (2010 edition), using the auscultation method; †: single time point measurements as the diagnostic criteria of hypertension.

2.1.3.2 Risk Factors of Hypertension in Children and Adolescents

(1) Overweight and obesity

A study from Shanghai examined the association between blood pressure and body weight in 78 114 school-aged children (boys: 51.3%)^[3]. The results showed that hypertension prevalence increased with the

[1] Cao JL, Hu YL, Xu F, et al. Epidemiology Study: distribution and trends of hypertension among 11571 students from the primary and middle school. *Guide of China Medicine*, 2011,09 (31): 290-292.

[2] Cao ZQ, Zhu LP, Zhang T, et al. Blood Pressure and Obesity among adolescents: a school-based Population study in China. *American Journal of Hypertension*, 2012, 25 (5): 576-582.

[3] Lu X, Shi P, Luo CY, et al. Prevalence of hypertension in overweight and obese children from a large school-based population in Shanghai, China. *BMC Public Health*, 2013,11;13:24.

[4] Luo JF, Chen SK, Fan X, et al. Prevalence of hypertension and relationship between hypertension and obesity in children and adolescents in Nanning of Guangxi Province. *Chin Journal of Contemporary Pediatric*. 2014,16 (10):1040-1044.

[5] Xu YJ, Li M, Xu PR, et al. Correlation between obesity index and blood pressure in Kazak childhood from Yili, Xinjiang. *Chinese Journal of Epidemiology*, 2012,8 (33): 774-778.

[6] Zhang Y, Sun G, Zhao J, et al. Monitoring of blood pressure among children and adolescents in a coastal province in China: results of a 2010 survey. *Asia-Pacific Journal of Public Health*, 2012. doi: 10.1177/1010539512444777.

[7] Shen CY, Zhang RJ, Chen YL, et al. Prevalence of obesity and hypertension among children and adolescents in Xi'an. *Chinese Journal of School Health*. 2012,05: 588-589.

[8] Meng LH, Liang YJ, Liu JT, et al. Prevalence and risk factors of hypertension based on repeated measurements in Chinese children and adolescents. *Blood Pressure*, 2013, 22 (1): 59-64.

[9] Lu X, Shi P, Luo CY, et al. Prevalence of hypertension in overweight and obese children from a large school-based population in Shanghai, China. *BMC Public Health* 2013; 13: 24. doi: 10.1186/1471-2458-13-24.

increasing BMI, and also with an increasing degree of abdominal obesity (both p-values for trends <0.0001) (Figure 2-1-7).

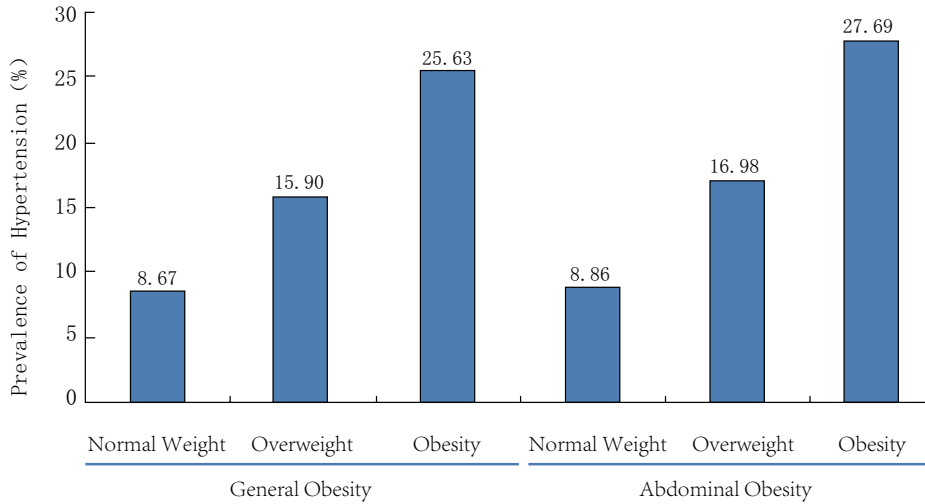


Figure 2-1-7 Hypertension Prevalence by Different Obesity Types

Note: General obesity: evaluated by BMI, the BMI stratification was based on the recommended guidelines set forth by the Working Group on Obesity in China (WGOC). Abdominal obesity: evaluated by waist circumference (WC). Overweight: $WC \geq P_{75} < P_{95}$; Obesity: $WC \geq P_{95}$.

A study in Guangzhou followed up 7 203 children (6-8 years old, boys: 53.0%) for 4 years to explore the relationship between hypertension prevalence and baseline body weight. The results showed that the 4-year cumulative prevalence of hypertension increased with BMI; after adjusting for age, gender, and baseline blood pressure level, hypertension prevalence for children who were overweight or obesity was 1.31 times (95%CI:1.18, 1.46) and 1.82 times (95%CI:1.63, 2.08) higher compared to those with normal body habitus^[1]. Please see Figure 2-1-8 for details.

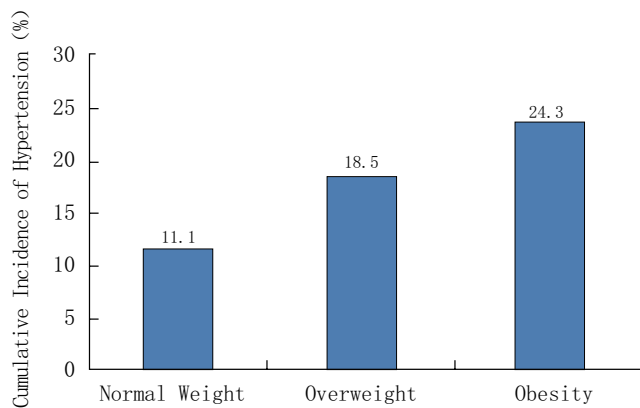


Figure 2-1-8 4-Year Cumulative Incidence of Hypertension for Children by Body Weight at Baseline

[1] Wang J, Zhu Y, Jing J, et al. Relationship of BMI to the incidence of hypertension: a 4 years' cohort study among children in Guangzhou2007-2011.. BMC Public Health, 2015, 15 (1) :782.

(2) Abnormal Glucose and Lipid Metabolism

A juvenile hypertension survey among 8 898 children (aged 7–13 years) across 6 cities in 2009 reported that after adjusting for factors such as age, gender, and BMI, for children in the hypertriglyceridemia, hyperglycemia, metabolic syndrome, and high homeostatic model assessment–insulin resistance (HOMA–IR) index groups, the risk of developing hypertension was 1.4 times (95%CI: 1.0–2.0), 1.5 times (95%CI: 0.9–2.5), 2.8 times (95%CI: 1.5–5.4), and 1.6 times (95%CI: 1.4–2.0) higher than among normal children, respectively^[1].

(3) Nutritional Status in Early Stages of Life and Factors that Affect Growth

Relationships between low birth weight and hypertension From 1992 to 2000, 81 538 (37.3% boys) children between the ages of 6 to 18 underwent a health examination in Taiwan; their birth weights were obtained from the Taiwan Birth Registry. Wei JN et al analyzed the data and found that, after adjusting for other factors, low birth weight infants (<2600g) were at higher risk (1.16 times) for juvenile hypertension than normal birth weight infants (3000g–3542g; 95% CI: 1.04–1.29)^[2].

In another study, 628 individuals (41–47 years old, 49.2% boys) who were born in the Peking Union Medical College Hospital between 1948 and 1954 were enrolled and followed^[3,4]. The study found that, after adjusting for factors such as mothers' age at delivery, gestational weeks, and BMI in adulthood, blood pressure in adulthood was negatively correlated with a person's birth weight and the Ponderal Index (PI=birth weight/birth height³, kg / m³; P <0.05). For each one–kilogram increase in birth weight, the SBP and DBP decreased by 3.0 mmHg and 1.9 mmHg, respectively. Furthermore, those classified as low birth weight infants (PI <24kg / m³) and obese adults (BMI ≥P75) showed the highest prevalence (34.4%) of hypertension (defined as SBP ≥160mmHg or DBP ≥95mmHg or according to past municipal hospital diagnosis of hypertension) at adulthood. Additionally, no patient was diagnosed with hypertension among the group with PI ≥28kg / m³ and thin in adulthood (BMI <P25). These findings indicate that low birth weight and obesity in adulthood are two independent risk factors for hypertension, and that the interaction between these two risk factors significantly increases the risk of developing hypertension.

Relationship between exposure to unhealthy environments during early stages of life and hypertension in adulthood. The 2002 China Health and Nutrition Survey investigated the effects of early exposure to the Great Famine (1959–1961) on risk of hypertension in adulthood among 7 874 participants (aged 38–50 years old)^[5]. In areas that suffered serious famine, after adjusting for age, gender, social status, lifestyle, diet, history of hypertension, and other factors, the early exposure groups were 1.74–2.22 times more likely to

[1] Xu H, Hu X, Zhang Q, et al. The Association of Hypertension with Obesity and Metabolic Abnormalities among Chinese Children. *International Journal of Hypertension*, 2011; 2011: 987159. doi: 10.4061/2011/987159.

[2] Wei JN, Li HY, Sung FC. Birth weight correlates differently with cardiovascular risk factors in youth. *Obesity (Silver Spring)*, 2007;15 (6) :1609-1616.

[3] Mi J, Zhang KL. Association between born emaciation and hypertension in adulthood. *J of China Public Health*, 1998,04:34-35.

[4] Mi J, Law C, Zhang KL, et al. Effects of infant birthweight and maternal body mass index in pregnancy on components of the insulin resistance syndrome in China. *Ann Intern Med*, 2000; 132 (4) :253-260.

[5] Li Y, Jaddoe VW, Qi L, et al. Exposure to the Chinese famine in early life and the risk of hypertension in adulthood. *Journal of hypertension*, 2011;29 (6) :1085-1092.

develop adult hypertension compared with the control groups (Figure 2-1-9).

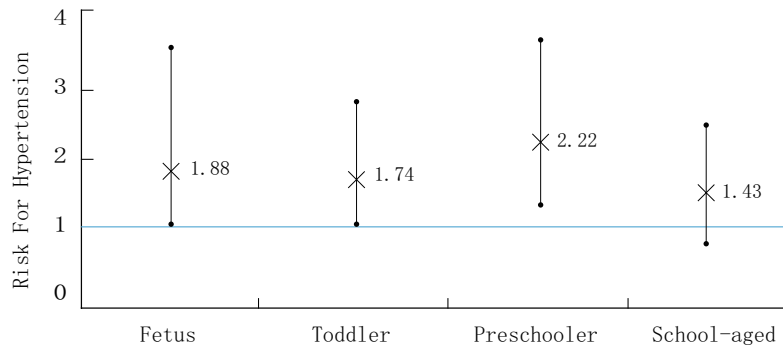


Figure 2-1-9 Adulthood Hypertension Prevalence Based on Exposure to the Great Famine During Early Stages of Life

Note: (1) The diagnostic criteria were based on recommendations from the US JNC6 guidelines; (2) The Great Famine period was from 1959 to 1961; (3) The control group includes those born between Oct 1, 1962, and Sept 30, 1964. The fetal exposure group includes those born between Oct 1, 1959, and Sept 30, 1961. The toddler exposure group includes those born between Oct 1, 1956, and Sept 30, 1958. The preschooler exposure group includes those born between Oct 1, 1954, and Sept 30, 1956. The school-aged exposure group includes those born between Oct 1, 1952, and Sept 30, 1954.

(4) Salt Sensitivity

In Hanzhong city, Shanxi province, a cohort study randomly selected 310 children (age 6–15 years, boys: 56.5%) to test their salt-sensitivity and followed them up for 18 years^[1]. The results found that among salt-sensitive children, their SBP and DBP in early adulthood (age 24–33 years) appeared higher than their non-salt-sensitive counterparts ($p < 0.05$). Furthermore, compared with the non-salt-sensitive children, they had a 1.34-times higher rate of developing hypertension (RR = 2.34, 95% CI: 1.04 – 5.25).

(5) Sleep

Blood pressure and sleep data were collected from 123 919 (42.4% male) teenage pubescent students (male: 11–17 years old, female: 9–17 years old; puberty was defined as having had their first spermatorrhea/menarche, which was obtained from a survey questionnaire) who participated in the 2010 National Student Physical Fitness and Health Survey^[2]. The results showed that before puberty, the prevalence of hypertension was higher in teenagers who had insufficient sleep than in those who had sufficient sleep, with the difference being statistically significant ($P < 0.01$) (Figure 2-1-10).

[1] Mu J, Zheng S, Lian Q, et al. Evolution of blood pressure from adolescents to youth in salt sensitivities: an 18-year follow-up study in Hanzhong children cohort. *Nutrition Journal* 2012; 11:70.

[2] Dong B, Wang HJ, Ma J. Association between sleep duration and puberty blood pressure among students aged 9 to 17 years in China. *Chinese Journal of Preventive Medicine*, 2013, 47 (8) : 718-725.

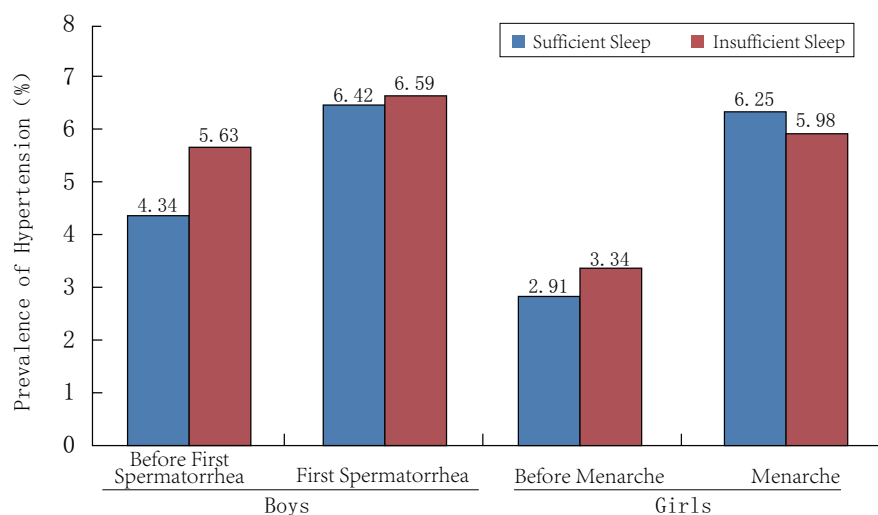


Figure 2-1-10 Hypertension Prevalence by Sleep Time among Teenagers

Notes: (1) Hypertension was defined according to the 95th percentile SBP/DBP values of students (both rural and urban, boys and girls) from the 2010 National Student Physical Fitness and Health Survey; (2) sufficient sleep: sleep time ≥ 9 h for students aged 7–12 years old, ≥ 8 h for students aged 13–15 years old, ≥ 7 h for students aged 16–18 years old. Individuals not meeting these conditions were placed in the insufficient sleep group.

2.1.3.3 Prediction of Adult Hypertension and Organ Damage Based on Childhood Blood Pressure Levels

Analysis of data from the Beijing Child Blood–Pressure Study (BBS), which included 1 259 children (6–18 years old) who were followed–up for 24 years, discovered that after controlling for age, gender, adult height, BMI and other factors, children who were diagnosed with hypertension (SBP/DBP $> P_{95}$) were more likely to develop adult hypertension and cardiac remodeling, compared with those who had normal baseline blood pressures (odds ratios: 2.1 for hypertension, 1.05 for cardiac remodeling). Moreover, the risk of developing hypertension was higher in the older age group compared to the younger age group (Table 2–1–8)^[1].

Table 2–1–8 Effects of Juvenile Hypertension on Adulthood Hypertension and Cardiac Remodeling (%)

Adulthood	Younger Age Group (6–12 Years Old)			Older Age Group (13–18 Years Old)		
	Normal BP	HTN	OR (95%CI)	Normal BP	HTN	OR (95%CI)
HTN	8.6	18.9	1.9 (1.1–3.5)	11.6	24.0	2.5 (1.4–4.4)
Cardiac Remodeling	40.1	50.7	1.4 (0.9–2.0)	40.4	57.4	1.6 (1.1–2.4)

Notes: (1) Juvenile Hypertension was defined according to the 80th percentile SBP/DBP values in the baseline population; (2) adulthood hypertension was defined as SBP/DBP $\geq 140/90$ mmHg; (3) cardiac remodeling was defined as meeting at least one of the following criteria: carotid–femoral pulse wave velocity (cfPWV) $\geq P_{80}$, carotid intima–media thickness test (cIMT) $\geq P_{80}$ or with plaque, left ventricular mass index (LVMI) $\geq P_{80}$.

[1] Liang Y, Hou D, Shan X, et al. Cardiovascular remodeling relates to elevated childhood blood pressure: Beijing Blood Pressure Cohort Study. International Journal of Cardiology. 2014;177 (3) :836-839.

The Hanzhong Children Hypertension Cohort study revealed that the brachial artery flow-mediated dilation measurements (FMD) among adults in the juvenile hypertension group (0.103 ± -0.004 mm) were lower than those in their counterparts in the cohort with normal blood pressure (0.117 ± 0.05 mm). This difference was statistically significant ($p < 0.05$). The former group's arterial elasticity index (C2) (12.93 ± 3.31 ml/mmHg \times 10) was also significantly less than that in the latter group (15.21 ± 4.11 ml/mmHg \times 10) ($p < 0.01$)^[1].

2.1.3.4 Evaluation for Secondary Hypertension in Children and Adolescents

Currently, surveys of juvenile secondary hypertension in China are mainly from hospitals. The Beijing Children's Hospital and the First Affiliated Hospital of Jilin University conducted retrospective analyses on hospitalized children (2003–2007, 2002–2012, respectively) with the diagnosis of 'hypertension'.^[2,3] The studies showed that more than half of the hypertensive patients enrolled were secondary hypertension. The average age of the children with secondary hypertension was lower than that of children with primary hypertension (Table 2-1-9). Renal hypertension is the leading cause of secondary hypertension. Meanwhile, drug-related hypertension has become the second most common cause of secondary hypertension, accounting for 18.3% of all cases (Table 2-1-10).

Table 2-1-9 Hypertension Type and Average Age of Admitted Children

Survey Region	HTN Type (n, %)		Age (x \pm s, y)	
	Primary HTN	Secondary HTN	Primary HTN	Secondary HTN
Beijing	146 (48.0)	158 (52.0)	12.3 \pm 3.1	9.1 \pm 4.6
Jilin	50 (24.6)	153 (75.4)	11.8 \pm 3.2	10.2 \pm 4.0

Table 2-1-10 Breakdown of Secondary HTN Etiology

Ranking	Beijing Children's Hospital (%)	First Affiliated Hospital of Jilin University (%)
1	Renal disease (39.9)	Renal disease (49.0)
2	Endocrinal disease (29.8)	Drug-related HTN (18.3)
3	Cardiovascular disease (13.9)	Cardiovascular disease (16.3)
4	Central nervous disease (8.2)	Endocrinal disease (5.2)
5	Others (stress, infection, congenital abnormalities) (8.2)	Central nervous disease (4.6)
6	—	Others (6.5)

[1] Mou JJ, Liu ZQ. Risk factors for juvenile hypertension in Shanxi children hypertension cohort. Chinese Journal of Cardiology. 2008,36 (suppl.) 115-116.

[2] Liu C, Du ZD, Li X, et al. Etiology and Differential Diagnosis of Admitted Children with Hypertension. J of Capital Medical University, 2010, 31 (2): 187-191.

[3] Zhang DL, Zhai SB, Wang JH, et al. Analysis of 203 hypertensive children. Chinese J of Laboratory Diagnosis, 2013, 12: 2238-2240.

2.2 Smoking

2.2.1 Prevalence of Smoking

2.2.1.1 Current Status of Smoking

China continues to be one of the countries with the highest male smoking rates in the world since 1984 (Table 2-2-1). The percentage of men who reported smoking was as high as 60% between 1996 and 2010. The Global Adult Tobacco Survey (GATS) –China Project in 2010, covering the population of China’s 28 provinces, found that the current smoking rate in men 15 years of age or higher was 52.9%; the current smoking rate in women was found to be 2.4% (Table 2-2-1, Figure 2-2-1, Figure 2-2-2). After normalizing the current smoking rate by age using 2010 census data, the normalized smoking rate fell by an average of 0.87% per year from 1996 to 2002 and by an average of 0.08% per year from 2002 to 2010. (Figure 2-2-3).^[1,2,3,4]

Table 2-2-1 Smoking Rates in Four National Smoking Surveys among Chinese Aged over 15

Survey Time	Sample Size	Age (year)	Male Smoking Rate (%)	Female Smoking Rate (%)	Total (%)
1984	519 600	15–	61.0	7.0	33.9
1996	122 700	15–69	66.9	4.2	37.6
2002	16 056	15–69	66.0	3.1	35.8
2010	13 354	15–69	52.9	2.4	28.1

Note: The definition of smoking differed in the four surveys

The National smoking sampling survey in 1984 defined a smoker as a current smoker who smoked more than 1 cigarette per day and had been smoking continuously for more than 1 year.

The National epidemiological survey of smoking behavior in 1996 defined a smoker as a current smoker who had been smoking for more than 6 months, continuously or accumulatively.

The 2002 Smoking and passive smoking survey in Chinese population defined a current smoker as a smoker who had smoked 100 cigarettes or more, continuously or cumulatively.

The 2010 Global Adult Tobacco Survey (GATS) –China Project defined the smoking rate as the prevalence rate of current smokers.

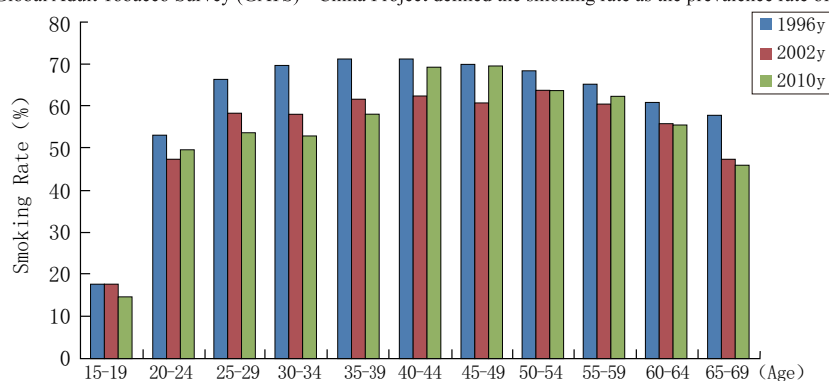


Figure 2-2-1 Current Smoking Rate in Men Over 15-year Old by Age in 1996, 2002, 2010

[1] Yang GH. Smoking and passive smoking in Chinese population, 2002. Chinese J of Epidemiology, 2005,26 (2) :77-83.

[2] Yang GH, Fan LX, Tan J, et al. Smoking in China: Findings of the 1996 National Prevalence Survey. JAMA. 1999,282 (13) : 1247-1253.

[3] Yang GH. Global Adult Tobacco Survey (GATS) -China Report, 2010. Beijing: Three-Gorgas Press, 2011.11.

[4] Yang GH, Li Q, Jason Hsia. Prevalence of smoking in China in 2010. N Engl J Med. 2011, 364 (25) : 2469-2470.

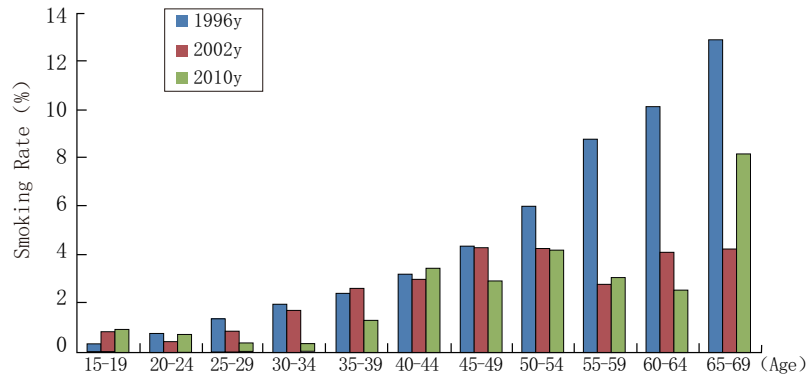


Figure 2-2-2 Current Smoking Rate in Women over 15-year Old

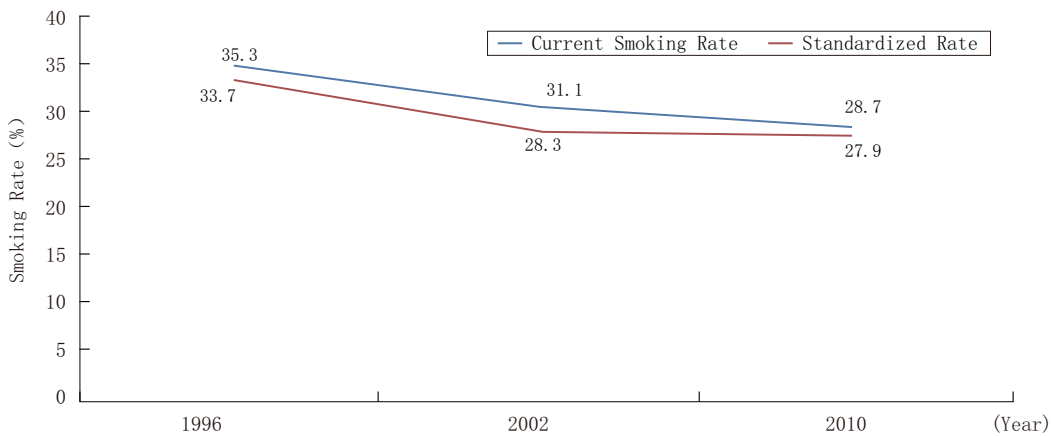


Figure 2-2-3 Trend of Current Smoking Rate in Population between the Ages of 15 and 69

- Smoking status in residents in midwestern rural areas^[1]

In 2010, the National Tobacco Control Office utilized a multi-stage stratified random sampling method to investigate the status of smoking, passive smoking and smoking cessation in residents in China's rural midwestern areas. 5 486 residents between 15 and 69 years of age from 16 counties and 84 administrative villages in Shanxi province, Gansu province, Qinghai province and Xinjiang were enrolled. The study demonstrated that the overall smoking rate in midwestern residents was 20.9% (44.8% in men, 2.0% in women) . Significant differences in smoking rates were found in populations with different ages, ethnic backgrounds, education levels and occupations ($p < 0.001$) . The residents between the ages of 50 and 55 had the highest rate of smoking (30.5%) . The smoking rate of the Han ethnic group was higher than that of any ethnic minority group (27.7% vs. 16.3%) . People who had graduated from high schools and technical secondary schools had the highest smoking rates (28.2%) . The smoking rate was higher in rural residents working in animal husbandry and non-agricultural labor than that of those engaged in agricultural labor

[1] Xiao L, Jiang H, Li Q, et al. Survey on status of smoking, passive smoking and quitting smoking in rural areas of the midwestern provinces in China. Chinese J of Epidemiology, 2013,34 (2) : 676-680.

(33.3%, 40.0% and 24.6%, respectively) .

- Smoking status in the Chinese employed floating population aged 18–59 in 2012^[1]

Based on the distribution of the employed floating population between the ages of 18 and 59, the China Non-communicable and Chronic Disease Risk Factor Surveillance in 2012 surveyed 170 Disease Surveillance Points (DSPs) using a multi-stage stratified equal-sized cluster sampling method that stratified by six occupational groups. Cigarette smoking information was collected through face-to-face interviews. 48 699 subjects were enrolled. Among subjects, the current smoking rate was 32.5% (95% CI: 32.0%–33.0%) , with a significantly higher percentage of men (55.3%) than women (1.9%) (Figure 2–2–4) . The current smoking rate in men was highest (58.6%) in the floating population working in the construction industry (Figure 2–2–5) . Among the current smokers, the average number of cigarettes smoked per day was 15.7 (male 15.7 per day; female 10.3 per day) . The daily consumption of cigarettes in current male smokers increased with age and decreased with an increase in educational attainment. The highest daily consumption of cigarettes was found in the floating population working in the construction industry, which was 18.2 per day. 47.1% of smokers smoked more than 20 cigarettes per day, with a higher percentage in men (47.6%) than women (21.9%) . The number of smokers who smoked 20 cigarettes or more per day increased with age but decreased with educational attainment. The smoking rate was the highest in the construction industry (60.4%) . The rate of smokers attempting to quit smoking was quite low, and the percentage of those who quit successfully was even lower. Among the current smokers, the percentage of smokers attempting to quit was 10.3% (10.1% in men, 14.8% in women) . The rate of smokers attempting to quit among the current smokers increased with age, but there was no significant difference in the percentage of smokers attempting to quit between different educational levels or occupations. The percentage of smokers who had successfully quit smoking was 6.1% (6.1% in males, 7.2% in females) . The rate of success increased with age.

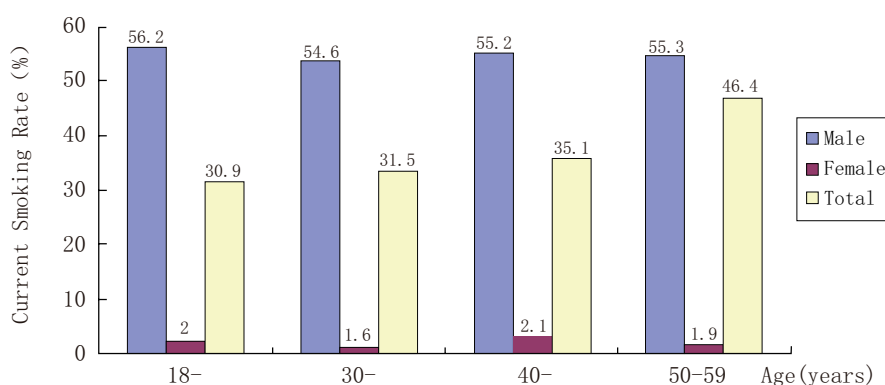


Figure 2–2–4 The Currently Smoking Rate in Chinese Employed Floating Population Aged 18–59

* Current smoking rate means the proportion of smokers in study period.

[1] Huang ZJ, Wang LM, Zhang M, et al. Smoking behavior among the Chinese employed floating population aged 18-59 in 2012. Chinese Journal of Epidemiology, 2014 35 (11) :1192-1197.

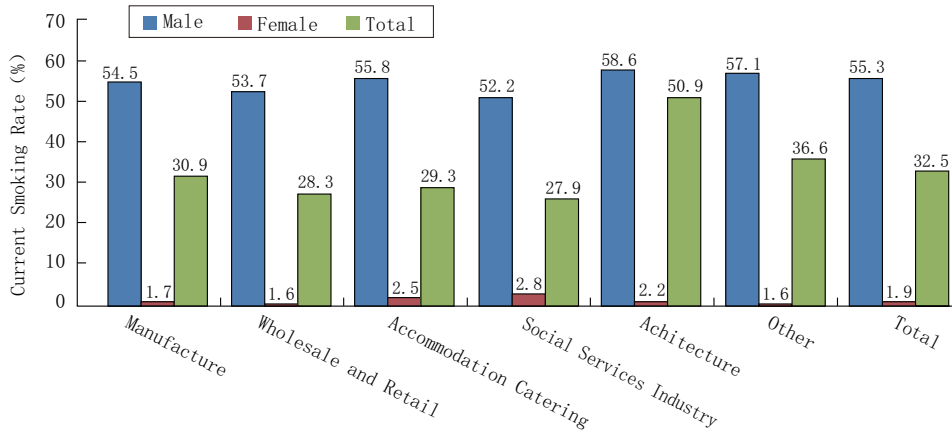


Figure 2-2-5 The Current Smoking Rate by Occupational Groups in the Floating Population Aged 18-59

- The smoking status in Chinese male doctors and teachers between 2002 and 2010

The smoking rates of male Chinese doctors and teachers both exceeded 50% in 1996 and 2002.^[1,2] The GATS study in 2010 demonstrated that the current smoking rates of male medical personnel and teachers between the ages of 15 and 69 had decreased significantly to 40% and 36.5%, respectively^[3] However, China remains one of the countries with the highest smoking rates in male doctors around the world.^[4,5,6]

- The smoking status in Chinese youth

A national survey in 2005 found that the smoking rate was 22.4% in male young adults and 3.9% in female young adults. Additionally, the smoking rates of male students were found to increase significantly with age.^[7] In 2012, 11 593 students from six universities in Guangzhou were selected and investigated by stratified cluster random sampling. This investigation showed that the current smoking rate among undergraduates was 6.1% (11.5% in men and 1.4% in women).^[8] Another meta-analysis of the smoking status in adolescents aged 12-17 years (middle/high school students) studied the smoking prevalence among the Chinese adolescents during the 1981-2010. It demonstrated that the prevalence of ever having smoking stayed in a narrow range (39.04%-46.03%) in that 20-year period for young men, while progressively

[1] Yang GH. Smoking and passive smoking in Chinese population, 2002. Chinese J of Epidemiology, 2005,26 (2) :77-83.

[2] Yang GH, Fan LH, Tan J, et al. Smoking in China: Findings of the 1996 national prevalence survey. JAMA. 1999,282 (13) :1247-1253.

[3] Yang GH. Global Adult Tobacco Survey (GATS) -China Report, 2010. Beijing: Three-Gorgas Press, 2011.11.

[4] Yang GH. Smoking and passive smoking in Chinese, 2002.Chinese J of Epidemiology. 2005, 26 (2) 77-83.

[5] Yang GH. Global Adult Tobacco Survey (GATS) -China Report, 2010. Beijing: Three-Gorgas Press, 2011.11.

[6] Yang GH, Li Q, Jason Hsia. Prevalence of smoking in China in 2010. N Engl J Med,2011,364;25:2469-2470.

[7] Ji CY. Health status and risky behaviors an integrated survey report of Chinese adolescent, 2005. Beijing: Peking University Medical Press, 2007.

[8] Xu XH, Chen JW, Sun A, et al. Analysis of tobacco-related knowledge, attitude and related factors among college students in Guangzhou city. Chinese Journal of Preventive Medicine. 2013, 47 (12) :1128-1131.

increasing from 2.47% in 1981–1985 to 19.72% in 2001–2005 for women (Figure 2–2–6) . The current smoking rates (within a 30–day period) in young men declined from 1981–1985 to 1996–2000, and it increased again afterwards; in young women, the rates were found to have continuously increased (Figure 2–2–7) . This study indicated a high rate of male smoking and the rapid growth of female smoking in China.^[1]

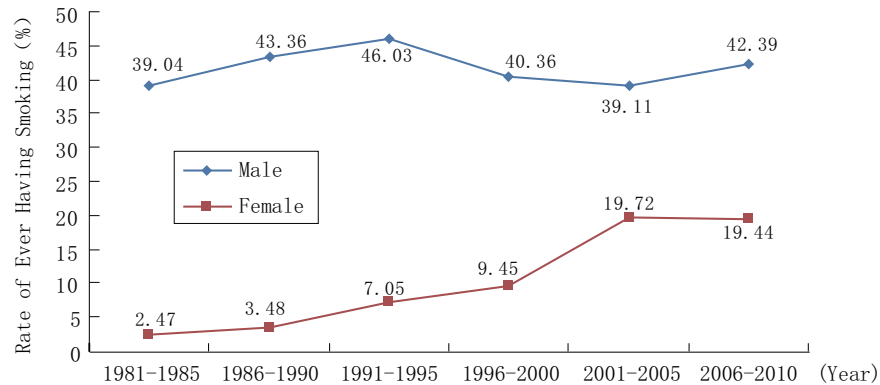


Figure 2–2–6 The Prevalence of Ever Having Smoking in Adolescents Aged 12–17 Years in China

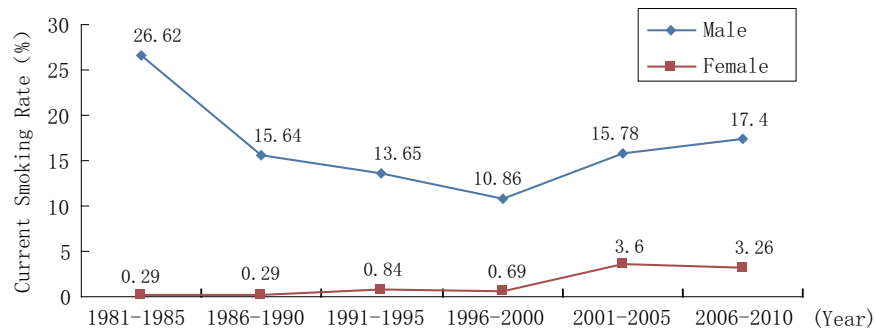


Figure 2–2–7 Current Smoking Rates in Adolescents Aged 12–17 Years in China

In China, smoking has become more and more common in adolescents. According to GATS in 2010^[2], among those who reported to have ever tried smoking, 55.9% of male and 57.0% of female smoked a whole cigarette for the first time before turning 13 years old. Furthermore, 52.7% of current smokers between the ages of 20 and 34 reported that they became daily smokers before the age of 20.

- The smoking status in young Chinese women^[3]

A first study investigating the smoking status in young Chinese women was conducted on 11 095 individuals aged 14–24 years, attending high school or college in 6 provinces in 2008. It showed that the prevalence of ever having smoking was 22%, that the prevalence of currently smoking was 3.2%, and that

[1] Han J, Che XG. A Meta-Analysis of Cigarette Smoking Prevalence among Adolescents in China: 1981-2010. *Int. J Environ. Res. Public Health*,2015,12,4617-4630.

[2] Yang GH. *Global Adult Tobacco Survey (GATS) -China Report, 2010*. Beijing: Three-Gorgas Press, 2011.11.

[3] Michael GH, Ma SJ, Zia W,et al. Smoking among rural and urban young women in China. *Tobacco Control*, 2010,19:13-18.

the prevalence of having an intention to smoke was 2.7%. All three types of smoking prevalence were higher in rural female students than urban female students (Table 2-2-2).

Table 2-2-2 The Smoking Status of Young Women, China, 2008

	Total	Urban Female Students	Rural Female Students	P Value
Mean Age First Puff	12.7±4.3	12.3±4.3	13.0±4.3	
Smoking Behavior				
Ever-smoker	20.1%	19.0%	22.0%	<0.01
Established Smoking	1.7%	0.9%	2.4%	<0.01
Current Smoking	3.2%	1.9%	4.2%	<0.01
Intention to Smoke	2.7%	1.7%	3.5%	<0.01
Never-smoker	79.3%	81.0%	78.0%	<0.01

2.2.1.2 The Status of Second-hand Smoking

Second-Hand Smoking (SHS), refers to non-smokers who have been exposed to tobacco smog from smokers at home or at work. In 2002, the prevalence of passive smoking in non-smokers was up to 51.9%, which represented 540 million passive smokers. The GATS in 2010 adapted a different definition of SHS and showed a high SHS prevalence (Figure 2-2-8). According to the GATS data, there were 738 million Chinese non-smokers exposed to second-hand smoke in 2010.^[1]

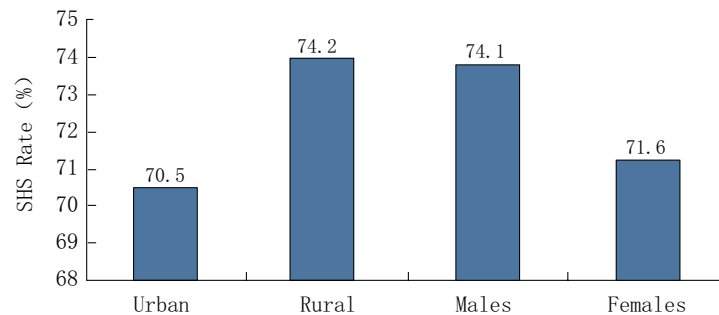


Figure 2-2-8 The Rate of Exposure to Second-hand Smoking by Region and Gender in 2010

Note: The GATS in 2010 asked the question “In general, how many days per week are you exposed to second-hand smoking?” and defined second-hand smokers as those who had been exposed to tobacco smog directly from the lit ends of cigarettes or who had breathed in the smog of smokers for at least one day per week.

- The SHS status in the children and adults in rural areas^[2]

2008 China National Rural Household Survey (NRHS) included a total of 5 442 non-smokers (including

[1] Yang GH. Global Adult Tobacco Survey (GATS) -China Report, 2010. Beijing: Three-Gorgas Press, 2011.11.

[2] Yao T, Sung HY, Mao Z, et al. Secondhand smoke exposure at home in rural China. Cancer Causes Control, 2012,23 (01) :109-115.

1 456 children and 3 986 adults) living in the rural areas of six Chinese provinces (Qinghai–northwest, Anhui–east, Hubei–middle, Yunnan–west, Jiangsu–east, and Chongqing–southwest) . This study revealed that the rates of SHS at home for the non–smoking children and adults was 68.0% and 59.3%, respectively. A multi–factor regression analysis showed that children living in the households with low educational level and low income parents have a high rate of SHS. There is also a high rate of SHS in the households of single female at the age of 19–34, with low educational level and low income. In addition, the children and female in the Qinghai province had the highest SHS rate.

- The SHS status in the employed floating population aged 18–59 in 2012^[1]

Using the data from the China Non–communicable and Chronic Disease Risk Factor Surveillance in 2012 and the specialized survey for the floating population, the status of SHS in the employed floating population was investigated. The results indicated that the percentage of people exposed to second–hand smoking in this population was 68.7%. There were significant difference between people with different education levels and occupations ($P < 0.0001$) . Smoking was very common in the male employed floating population and the rate of SHS was as high as 76.4%. Those working in the construction industry have the highest rate of SHS (Figure 2–2–9, Figure 2–2–10) .

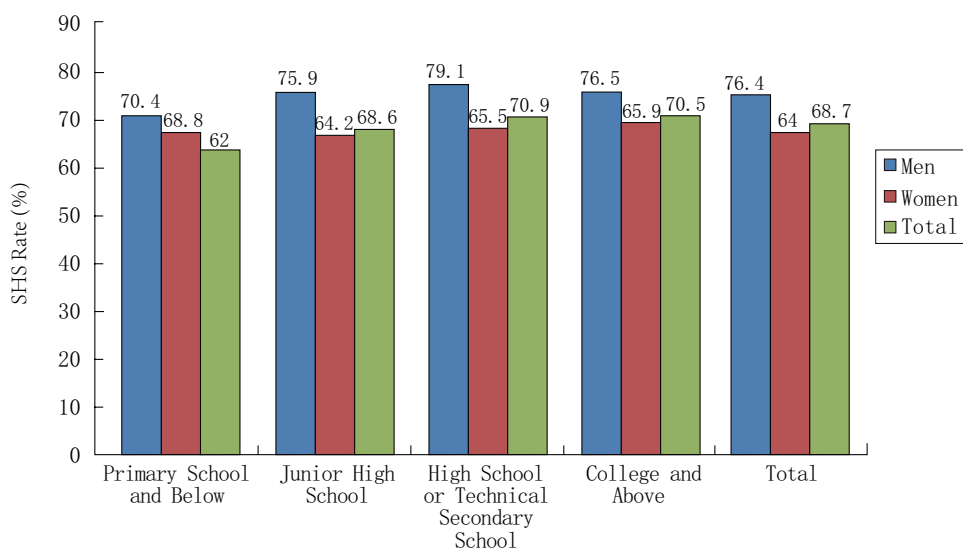


Figure 2–2–9 The Rates of Non–smokers Exposed to Second–hand Smoking at Different Education Levels in the Employed Floating Population Aged 18–59 Years

[1] Huang ZJ, Wang LM, Zhang M, et al. Smoking behavior among the Chinese employed floating population aged 18–59 in 2012. Chinese Journal of Epidemiology, 2014 35 (11) :1192–1197.

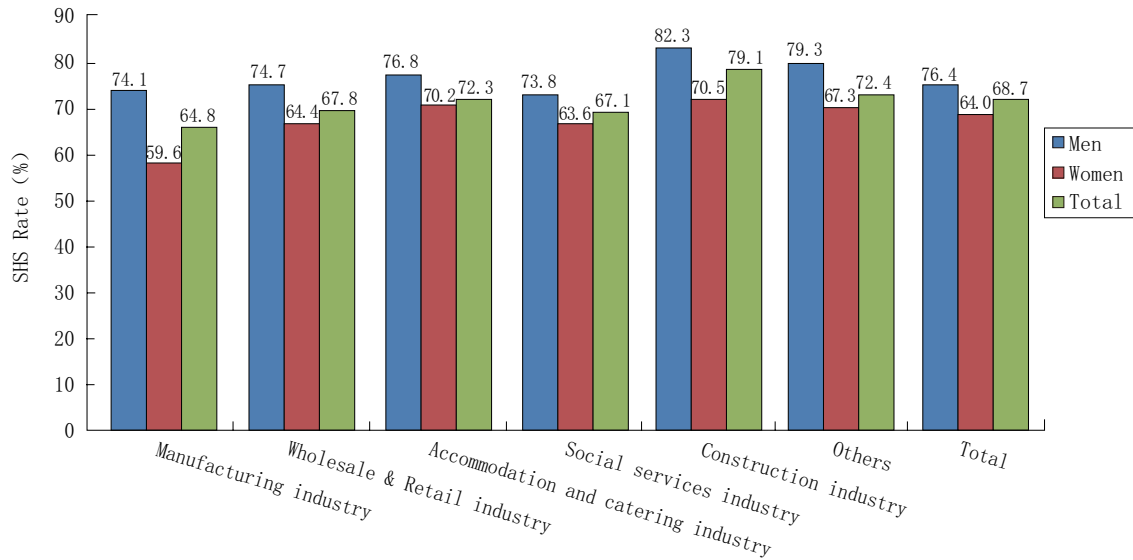


Figure 2-2-10 The Rates of Non-smokers Exposed to Second-hand Smoking in Different Occupations in the Employed Floating Population Aged 18-59 Years

2.2.2 Smoking Cessation

In recent years, the smoking cessation rate has increased slightly in individuals aged 15 years and above, from 9.42% in 1996 to 11.5% in 2002 and 16.9% in 2010. The number of people who have quit smoking has increased by 15 million. In 2010, the GATS-China project showed that 16.1% of current smokers intended to quit smoking within the next 12 months.^[1] Since 2002, there has been no significant change in the proportion of smokers who have no intention to stop smoking (44% in 2002, vs. 44.9% in 2010). The relapse rates have also not improved and actually increased from 10.5% in 1996 to 32.5% in 2002 and 33.1% in 2010.^[2,3,4] In 2010, the rate of smoking cessation was low (1.9%) in rural residents aged 15-69 years in four midwestern Chinese provinces^[5] A multicenter prospective study in a Chinese population showed that the rate of smoking cessation was quite low: over an average 9.5-year follow-up period, the rate was 7.2% in men and 1.5% in women.^[6]

[1] Yang GH. Global Adult Tobacco Survey (GATS) -China Report, 2010. Beijing: Three-Gorgas Press, 2011.11.

[2] Yang GH. Smoking and passive smoking in Chinese population, 2002. Chinese J of Epidemiology, 2005,26 (2) :77-83.

[3] Yang GH, Fan LX, Tan J, et al. Smoking in China: Findings of the 1996 national prevalence survey. JAMA. 1999,282 (13) : 1247-1253.

[4] Yang GH. Global Adult Tobacco Survey (GATS) -China Report, 2010. Beijing: Three-Gorgas Press, 2011.11.

[5] Xiao L, Jiang Y, Li Q, et al. Survey on status of smoking, passive smoking and smoking cessation in rural areas of the midwestern provinces in China. Chinese J of Epidemiology, 2013,34 (2) :676-680.

[6] L.A. Tse, X.H. Fang, w.Z. Wang, etc. Incidence of ischemic and heamorrhagic stroke the association with smoking and smoking cessation: A 10-year multicenter prospective study in China. Public Health. 2012,126: 960-966.

Smoking Control

• Beijing Smoking Control Regulation^[1]

The Beijing Smoking Control Regulation has been in effect since June 1st 2015. It is consistent with international standards and is the most stringent legislation for smoking control in China. It clearly states that all indoor smoking is banned; that no advertisement, promotions or sponsorships from tobacco companies are allowed; and that the enforcement abilities of the personnel in charge of smoking control are to be strengthened. This regulation rules that smoking behavior is prohibited in all indoor public areas and workplaces, as well as on public transportation. Smoking is also prohibited in outdoor areas located near nurseries, primary and secondary schools, cultural relics, stadiums, and children's hospitals. Violators will be fined up to 200 RMB for individuals, and 10 000 RMB for organizations.

A survey showed that 96% of city residents supported the comprehensive ban of indoor smoking in public places. The implementation of this smoking control regulation will greatly promote the progress of tobacco control in the city of Beijing, and is expected to serve as a model for other cities. The effects of this regulation will be evaluated after it has been implemented for some time.

2.2.3 Hazards of Smoking and Passive Smoking

(1) A prospective study demonstrated that smoking and passive smoking are major preventable risk factors for mortality in China. The relative risk (RR) of death and the population attributable risk (PAR) of death in the Chinese population were 1.23 (95% CI: 1.18–1.27) and 7.9%, respectively. For men, the RR was 1.18 (1.13–1.23) and the PAR was 10.0%; for women, the RR was 1.27 (1.19–1.34) and the PAR was 3.5%.^[2]

(2) The population attributable risks (PAR) of smoking for all-cause death, cancers and other chronic diseases in residents aged 40–74 years in the urban area of Shanghai, China.^[3]

The SMHS (Shanghai Men's Health Study) and the SWHS (Shanghai Women's Health Study) conducted baseline surveys in 61 480 men aged 40–74 years from 2002 to 2006, and 74 941 female aged 40–74 years from 1997 to 2000. Study response rates were 74.0% and 92.3%, respectively. A Cox proportional hazards regression model was used to estimate the mortality of RRs. The rate of smoking exposure and the predicted RRs were used to estimate PARs and its 95% confidence intervals (95% CIs) (Table 2–2–3). Cigarette smoking was responsible for 23.9% (95% CI: 19.4–28.3%) and 2.4% (95% CI: 1.6–3.2%) of deaths in men and women, respectively. Respiratory diseases had the highest PAR in men (37.5%), followed by cancer (31.3%), and cardiovascular diseases (CVD) (24.1%). The top three PARs in women were 1.1% for respiratory diseases, 1.1% for cancer, and 4.0% for CVD (Table 2–2–4). In conclusion, in the urban area of Shanghai, 23.9% of deaths in men and 2.4% of deaths in women could be prevented if smoking is banned. Effective smoking control programs should be strongly advocated to reduce the burden of smoking related death.

[1] http://www.sc.xinhuanet.com/content/2015-05/31/c_1115462765.htm.

[2] Gu D, Kelly TN, Wu X, et al. Mortality attributable to smoking in China. *N Engl J Med*. 2009;360 (2) :150-159.

[3] Wang YY, Zhang W, Li HL, et al. Population attributable risks of cigarette smoking for deaths of all causes, all cancers and other chronic diseases among adults aged 40-74 years in urban Shanghai, China. *Chin J Cancer Res*, 2015, 27 (1) :59-65.

Table 2-2-3 Association between Smoking and All-cause Death, General Cancer, Lung Cancer, CVD, or Respiratory Diseases in SMHS and SWHS

Gender	Cause of Death	RR1 (95%CI) *	RR2 (95%CI) **
Male	All-cause Death	1.76 (1.64 - 1.90)	1.54 (1.43 - 1.67)
	General Cancer	2.02 (1.79 - 2.28)	1.77 (1.56 - 2.01)
	Lung Cancer	5.50 (4.09 - 7.40)	4.43 (3.27 - 6.01)
	CVD	1.75 (1.55 - 1.98)	1.56 (1.37 - 1.78)
	Respiratory Diseases	2.52 (1.87 - 3.40)	2.05 (1.50 - 2.80)
	Diabetes	1.54 (1.09 - 2.19)	1.40 (0.97 - 2.02)
Female	All-cause Death	1.61 (1.44 - 1.79)	1.45 (1.30 - 1.62)
	Cancer	1.30 (1.06 - 1.58)	1.24 (1.02 - 1.52)
	Lung Cancer	2.69 (1.96 - 3.68)	2.54 (1.83 - 3.52)
	CVD	1.87 (1.57 - 2.22)	1.67 (1.41 - 1.99)
	Respiratory Diseases	3.93 (2.63 - 5.86)	3.10 (2.05 - 4.68)
	Diabetes	1.38 (0.91 - 2.10)	1.15 (0.75 - 1.75)

*, adjusted by age; **, adjusted by age, BMI, educational level, household annual per capita income, ever-drinking behavior, routine physical exercise within the past 5 years.

Table 2-2-4 The PAR (%) for all-cause Death, General Cancer, Lung Cancer, CVD, or Respiratory Diseases in the Smoking Population of SMHS and SWHS

Gender	Cause of death	PAR1 (95%CI)	PAR2 (95%CI)
Male	All-cause Death	0.295 (0.259 - 0.330)	0.239 (0.194 - 0.283)
	General Cancer	0.366 (0.311 - 0.419)	0.313 (0.246 - 0.377)
	Lung Cancer	0.723 (0.644 - 0.786)	0.684 (0.582 - 0.765)
	CVD	0.288 (0.228 - 0.347)	0.241 (0.167 - 0.312)
	Respiratory Diseases	0.444 (0.314 - 0.557)	0.375 (0.215 - 0.516)
	Diabetes	0.210 (0.023 - 0.382)	0.170 (-0.032 - 0.359)
Female	All-cause Death	0.030 (0.022 - 0.038)	0.024 (0.016 - 0.032)
	General Cancer	0.014 (0.003 - 0.024)	0.011 (0.000 - 0.023)
	Lung Cancer	0.068 (0.035 - 0.100)	0.065 (0.024 - 0.107)
	CVD	0.048 (0.032 - 0.064)	0.040 (0.024 - 0.056)
	Respiratory Diseases	0.024 (-0.006 - 0.054)	0.011 (-0.019 - 0.042)
	Diabetes	0.140 (0.075 - 0.205)	0.127 (0.061 - 0.193)

Note: PAR1: adjusted by age; PAR2: adjusted by age, BMI, educational level, household annual per capita income, ever-drinking behavior, routine physical exercise within the past 5 years.

• Smoking increased risk for ischemic and hemorrhagic stroke^[1]

A multi-center prospective cohort study during 1986 to 2000 investigated 26 607 subjects with an average of 9.5 years of follow-up. The data showed that the risk for various types of stroke was 1.39 (95% CI 1.15-1.67) in male Chinese current smokers, and the main mediator was the increased risk for ischemic

[1] Kelly TN, Gu D, Chen J, et al. Cigarette Smoking and Risk of Stroke in the Chinese Adult Population. *Stroke*. 2008, 39 (6) : 1688-1693.

stroke[HR 1.49 (95% CI 1.17–1.90)]. In the male smokers who smoked more than 15 cigarettes per day and had a history of smoking for more than 25 years, the risk for general stroke as well as ischemic stroke both significantly increased.

2.3 Dyslipidemia

2.3.1 Blood Lipid Levels and the Prevalence of Dyslipidemia in Adults

An international collaborative study conducted in the 1980's and 1990's showed^[1,2] that the levels of serum TC and LDL-C were significantly lower in the Chinese population compared to Western populations. Another domestic multi-center study^[3,4] demonstrated that the level of TC and the prevalence of hypercholesterolemia in adults were significantly different across different regions. In the past 30 years, the blood lipid levels and the prevalence of dyslipidemia have gradually increased in the Chinese population. Prevalence of dyslipidemia is higher in more economically developed regions and also in middle-aged and elderly individuals.^[5,6,7]

The 2002 Chinese Residents Nutrition and Health Survey (CNHS)^[8] and the 2010 Chinese chronic disease surveillance study^[9] reported the average levels of TC, TG and HDL-C in Chinese individuals aged 18 years and above from 31 provinces. Compared to the data from 2002, the average TC and TG levels in both men and women increased significantly in 2010 (Table 2-3-1) .

[1] Tao SC, Li YH, Xiao ZK et al. Serum lipids and their correlates in Chinese urban and rural populations of Beijing and Guangzhou. *Inter J Epidemiol*,1992,21 (5) :893-903.

[2] The WHO MONICA Project. Geographical variation in the major risk factors of coronary heart disease in men and women aged 35-64 years. *World Health Statistics*,1988,41 (3/4) :115-140.

[3] Wu ZS, Yao CH, Zhao D, et al. Multi provincial monitoring of trends and determinants in cardiovascular diseases (Sino-MONICA project) . *Chinese J of Cardiology*, 1997,25 (4) :255-259.

[4] Zhou BF, Zhang HY, Wu YF, et al. Ecological analysis of the association between incidence and risk factors of coronary heart disease and stroke in Chinese population. *CVD Prevention*,1998,1 (3) :207-216.

[5] The Collaborative Study Group on Trends of Cardiovascular Diseases in China and Preventive Strategy. Current status of major cardiovascular risk factors in Chinese population and their trend in the past two decades. *Chinese J of Cardiology*, 2001,29 (2) :74-79.

[6] He J, Gu D, Reynolds K et al. Serum total and lipoprotein cholesterol levels and awareness, treatment, and control of hypercholesterolemia in China. *Circulation*,2004,110 (4) :405-411.

[7] Yang WY, Xiao JZ, Yang ZJ, et al. Serum lipids and lipoproteins in Chinese men and women. *Circulation*,2012,125: 2212-2221.

[8] Zhang J, Man QQ, Wang CR, et al. Level and distribution characteristics of blood lipid among Chinese aged more than 18. *Chinese J of Preventive Medicine*, 2005,39 (5) :302-305.

[9] Li JH, Mi SQ, Li YC, et al. The levels and distribution of serum lipids in Chinese adults, 2010. *Chinese J of Preventive Medicine*, 2014,46 (7) :607-612.

Table 2-3-1 Mean Lipid Levels in Chinese People Aged 18 Years and above from 31 Provinces

Year	Study	Population	Sample size	Gender	Blood lipid level (mmol/L)		
					TC	HDL-C	TG
2002	CNHS	urban/rural	49 252	Men	3.81	1.26	1.13
				Women	3.82	1.33	1.05
2010	Chinese Non-communicable/Chronic Disease Survey	161 surveillance centers, urban/rural	90 395	Men	4.06	-	1.45
				Women	4.03	-	1.21

Note: The numbers in this table were calculated using compound weighing.

The international collaborative study on cardiovascular diseases in Asia (InterAsia)^[1] in 2000–2001 and the Chinese Diabetes Mellitus and Metabolic Disorder Study (CNDMDS)^[2] in 2007–2008 investigated the average blood lipid levels among the populations in several regions in China and the results are shown in Table 2-3-2.

Table 2-3-2 Average Blood Lipid Levels in Certain Regions of China*

Year	Study	Population	Sample Size	Gender	Blood Lipid Level (mmol/L)			
					TC	LDL-C	HDL-C	TG
2000–2001	InterASIA	10 provinces and cities, urban/rural areas, 35–74 y	15 540	Men	4.76	2.80	1.32	1.46
				Women	4.86	2.86	1.36	1.43
2007–2008	CNDMDS	14 provinces and cities, urban/rural areas, >20 y	46 239	Men	4.70	2.68	1.25	1.71
				Women	4.73	2.69	1.35	1.42

*: Standardized by age.

The CNHS survey reported the prevalence of TC ≥ 5.20 mmol/L in the Chinese population aged 18 years and older: 6.6% in men and 7.1% in women; 9.2% in urban areas and 5.7% in rural areas. The prevalence of TG ≥ 1.70 mmol/L was 14.5% in men and 9.9% in women; 14.2% in urban areas and 9.9% in rural areas. The 2010 Chinese Chronic Disease Surveillance Study^[3] showed that the prevalence of increased TC (TC ≥ 6.22 mmol/L) was higher in urban areas than in rural areas, and higher in the east than in the middle and western regions of the country. The highest prevalence was found in men aged 45–59 years and women 60 and above. The prevalence of increased TG (TG ≥ 2.26 mmol/L) was significantly higher in men. (Table 2-3-3)

[1] He J, Gu D, Reynolds K et al. Serum total and lipoprotein cholesterol levels and awareness, treatment, and control of hypercholesterolemia in China. *Circulation*, 2004, 110 (4) :405-411.

[2] Yang WY, Xiao JZ, Yang ZJ, et al. Serum lipids and lipoproteins in Chinese men and women. *Circulation*, 2012, 125: 2212-2221.

[3] Li JH, Wang LM, Li YC, et al. Epidemiologic characteristics of dyslipidemia in Chinese adults in 2010. *Chinese J of Preventive Medicine*, 2012, 46 (5) :414-418.

Table 2-3-3 Prevalence of Increased TC and TG in Different Genders, Regions and Age Groups (China: 2010) (%)

		TC ≥ 6.22 mmol/L		TG ≥ 2.26 mmol/L	
		Men	Women	Men	Women
Total		3.4	3.2	13.8	8.6
	Urban	4.1	4.3	15.7	8.5
	Rural	3.0	2.7	13.0	8.7
Urban/rural Areas	East	4.2	4.3	13.8	8.1
	Central	2.5	2.2	14.1	9.3
	West	3.4	2.8	13.6	8.6
Geography Age Groups	18-44	3.0	1.3	14.1	5.8
	45-59	4.5	5.0	16.1	12.2
	≥ 60	2.9	6.9	8.7	12.9

Note: The numbers in this table were calculated using compound weighing.

The 2000-2001 InterAsia study^[1] and the 2007-2008 CNDMDS study^[2] investigated the prevalence of dyslipidemia in the populations of certain regions (Table 2-3-4). A meta-analysis in 2014^[3], which included 14 studies from 2003-2013, estimated the prevalence of increased TC, increased LDL-C, increased TG, and decreased HDL-C in the population aged 18 years and above (also shown in Table 2-3-4). CNDMDS demonstrated that the prevalence of increased TC increased with age. The prevalence of increased TC (≥ 6.22 mmol/L) was greater in women aged 50 years or older than in men (Figure 2-3-1). The prevalence of dyslipidemia among different ethnic groups in Liaoning's rural area and Xinjiang is shown in Table 2-3-5.

Table 2-3-4 Prevalence of Dyslipidemia in Certain Regions of China (%)

Study	Population	Sample Size	Prevalence Rate of Dyslipidemia (%)		
			Category	Male	Female
InterASIA*	10 provinces and cities, urban/rural area, 35-74 y	15 540	Borderline high TC	23.5	24.1
			High TC	7.9	10.2
			Borderline high LDL-C	16.4	17.5
			High LDL-C		
			Moderately high LDL-C	4.9	5.4
			Severely high LDL-C	2.3	3.2
			Low HDL-C	22.1	16.2

[1] He J, Gu D, Reynolds K et al. Serum total and lipoprotein cholesterol levels and awareness, treatment, and control of hypercholesterolemia in China. *Circulation*, 2004, 110 (4): 405-411.

[2] Yang WY, Xiao JZ, Yang ZJ, et al. Serum lipids and lipoproteins in Chinese men and women. *Circulation*, 2012, 125: 2212-2221.

[3] Huang YX, Gao L, Xie XP, et al. Epidemiology of dyslipidemia in Chinese adults: meta-analysis of prevalence, awareness, treatment, and control. *Population Health Metrics* 2014, 12:28.

Table 2-3-4 Prevalence of Dyslipidemia in Certain Regions of China (%) (Continued)

Study	Population	Sample Size	Prevalence Rate of Dyslipidemia (%)		
			Category	Male	Female
CNDMDS*	14 provinces and cities, urban/rural area, over 20 y	46 239	Borderline high TC	22.6	22.4
			High TC	8.7	9.3
			Borderline high LDL-C	13.6	14.2
			High LDL-C	3.5	3.5
			Severely high LDL-C	3.1	3.0
			Low HDL-C	27.1	17.5
Meta-analysis**	9 studies, over 18 y	143 350	High TC	7.9 (4.6 – 13.2)	
			High TG	13.7 (10.7 – 17.4)	
	5 studies, over 18 y	130 826	Low HDL-C	11.0 (6.9 – 16.9)	
			High LDL-C	7.6 (2.1 – 24.3)	

*: Borderline high TC (5.18–6.21mmol/L), High TC (≥ 6.22 mmol/L), Borderline high LDL-C (3.37–4.13mmol/L), High LDL-C (4.14–4.91mmol/L), Severely High LDL-C (≥ 4.92 mmol/L).

**: High TG (≥ 2.26 mmol/L), Low HDL-C (≤ 1.04 mmol/L).

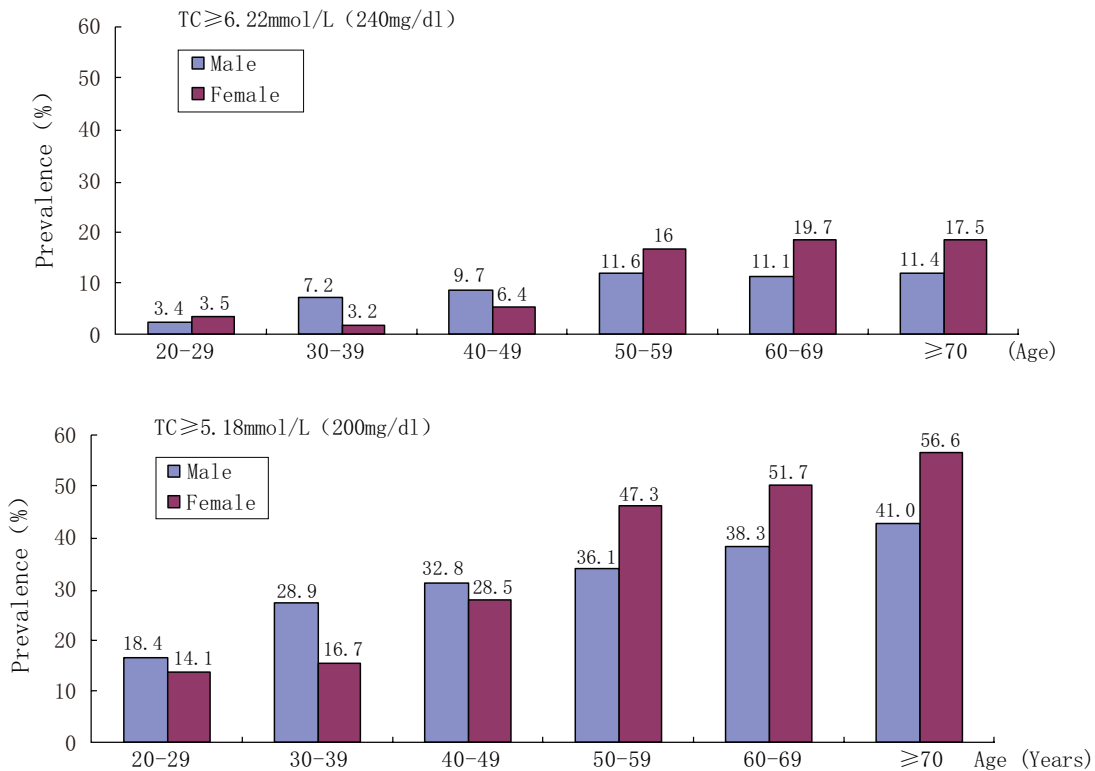


Figure 2-3-1 Prevalence of High TC in CNDMS among Different Genders and Age Groups

Table 2-3-5 Prevalence of Dyslipidemia among Different Ethnic Groups in Liaoning Rural Areas and Xinjiang

Year	Study	Population	Sample Size	Prevalence of Dyslipidemia (%)			
				Category*	Men	Women	
2013 ^[1]	Cross-sectional	Rural areas in Liaoning province, over 35y	11 956	Borderline high TC	30.9	31.8	
				High TC	14.3	18.2	
				Borderline high LDL-C	16.8	19.2	
				Moderately high LDL-C	4.6	6.5	
				Severely high LDL-C	1.6	2.3	
				Low HDL-C	17.3	10.8	
				Borderline high TG	12.9	13.8	
				Borderline high TG	15.3	15.7	
				Severely high TG	2.3	1.5	
2009-2010 ^[2]	Cross-sectional	Over 18y	Wei 3 625 Ha 4 148 Han 3 733	Category**,#	Wei	Ha	Han
				High TC	5.2	6.9	6.0
				High TG	9.3	9.3	17.3
				Low HDL-C	33.6	20.8	11.1
				High LDL-C	2.4	2.9	2.0

*: Borderline high TC (5.18-6.21mmol/L), High TC (>6.22mmol/L), Borderline high LDL-C (3.37-4.13mmol/L), High LDL-C (4.14-4.91mmol/L), Severely High LDL-C (>4.92mmol/L).

** : High TG (>2.26mmol/L), Low HDL-C (< 1.04mmol/L).

: Standardized by age.

In 1983-1984, 1998, 2004 and 2011, multiple cross-sectional sampling surveys^[3] were conducted in Guangzhou Shipyard and Panyu District in people between 35 and 65 years of age. The level of serum TC and the prevalence of increased TC are shown in Table 2-3-6.

Table 2-3-6 Trends in TC Levels and The Prevalence of High TC among Rural and Urban Residents in Guangzhou

Year	Male			Female		
	Sample Size	TC ($\bar{x}\pm S$)	TC>6.22 (%)	Sample Size	TC ($\bar{x}\pm S$)	TC>6.22 (%)
Urban Residents						
1983-1984	1 171	4.75±0.03	4.44	1 074	5.03±0.03	5.75
1998	564	5.06±0.04	9.45	349	5.10±0.05	11.24
2004	638	5.04±0.04	11.31	627	5.07±0.04	11.87
2011	492	5.14±0.04	13.19	516	5.19±0.04	16.68
Rural Residents						
1983-1984	1 091	4.11±0.03	1.13	1 212	4.10±0.02	1.06
1998	307	4.81±0.05	6.21	373	4.62±0.04	3.80
2004	383	4.71±0.04	6.56	411	4.66±0.04	3.49

Note: Standardized by age.

[1] Sun GZ, Li Z, Guo L, et al. High prevalence of dyslipidemia and associated risk factors among rural Chinese adults. *Lipids in Health and Disease* 2014, 13:189.

[2] Guo SX, Ma RL, Guo H, et al. Epidemiological analysis of dyslipidemia in adults of three ethnicities in Xinjiang, China. *Genetics and Molecular Research*, 2014, 13 (2) : 2385-2393.

[3] Mai JZ, Gao XM, Wu Y, et al. Long term trends of blood lipid and glucose change in Guangzhou urban and rural natural population. *Chinese J of Cardiovascular disease*, 2014, 42 (6) :515-519.

A multi-provincial cohort study^[1] showed changes in the baseline levels of serum TC and the prevalence of hypercholesterolemia in 5 740 people aged 35–64 years from 1992 to 2007. The level of TC in women was found to have increased rapidly after menopause. Over the course of 15 years, the average TC level in women increased from 4.63 mmol/L to 5.43 mmol/L, an increase of 0.80mmol/L; the average TC level in men increased from 4.65 mmol/L to 4.96 mmol/L, an increase of 0.31mmol/L. The prevalence of hypercholesterolemia (TC \geq 6.22mmol/L) increased from 4.9% to 20.0% in women, and from 5.1% to 8.5% in men.

2.3.2 Prevalence of Dyslipidemia among Children and Adolescents

The 2002 China National Nutrition and Health Survey^[2] found that the prevalence of high cholesterol (TC \geq 220mg/dl or 5.72mmol/L) was 0.8% (1.4% in urban areas, 0.6% in rural areas) among the children and adolescents (aged 3–17.9 years) and that the prevalence of high triglycerides (TG \geq 150 mg / dl or 1.70 mmol/L) was 2.8% (2.5% in urban areas, 2.9% in rural areas) .

Surveys in Beijing, Guangzhou and other areas between 1987 and 2007 showed that the prevalence of high TC and TG among the children and adolescents ranged from 0.8%–2.1% and 2.2%–9.5%, respectively^[3,4] According to a meta-analysis report^[6], the prevalence of high TC and TG among children and adolescents aged 2–18 years was found to be elevated in the period of 2006–2011, compared with the period of 2001–2005 (Table 2–3–7) . Additionally, a 2007 survey among children and adolescents in Beijing^[7] demonstrated that the prevalence of dyslipidemia in obese children (TC \geq 5.20 mmol/L or TG \geq 1.70 mmol/L) significantly exceeded that of non-obese children (Figure 2–3–2) .

[1] Wang W, Liu J, Wang M, et al. Serum total cholesterol change from 1992 to 2007 in the general population from Chinese multi-provincial cohort study. *Chinese J of Cardiovascular disease*, 2014,42 (3) :1-6.

[2] Zhao WH, Zhang J, Li Y. Report of Chinese nutrition and health status: blood lipid. 2002.

[3] Li JZ, Niu QT, Li PY, et al. Study of blood lipid and lipoprotein among infants and adolescents. *Peking Medicine*,1987,9 (6) :346-349.

[4] Ma WJ, Xu YJ, Fu CX, et al. A cross sectional survey on serum lipid level and its influencing factors in children aged 3-14 years in Guangdong province, *Chinese J of Cardiology*,2005,33 (10) :950-955.

[5] Liu Y, Mi J, Du JB, et al. A survey on dyslipidemia of 6-18-year old children in Beijing area. *Chinese J of Practical Pediatrics*. 2007;22 (2) :101-102.

[6] Ding WQ, Dong HB, Mi J, et al. Prevalence of dyslipidemia in Chinese children and adolescents: a Meta-analysis. *Chinese J of Epidemiology*,2015,36 (1) :71-77.

[7] Yan H, Mi J, Liu Y, et al. Screening for dyslipidemia based on family history and obesity in children. *J of Peking university (health science)* , 2007;39 (6) :591-594.

Table 2-3-7 Prevalence of Dyslipidemia (%) in Children and Adolescents from Different Districts during Different Periods

District	Publish Year	Age (y)	Sample Size	Increased TC*	Increased TG**
Beijing City ^[1]	1987	7-19	1 201	1.3	4.2
Guangdong Province ^{#[2]}	2005	3-14	6 188	2.1	2.2
Beijing City ^{#[3]}	2007	6-18	City 9 978	1.6	9.5
			Suburb 9 523	0.8	8.1
Meta-analysis ^{***[4]}	2001-2005	2-18	62 824	2.2	4.1
	2006-2011	2-18	30 762	4.7	11.6
	2001-2011	2-6	TC: 2 871 TG: 5 294	5.5	2.9
		7-18	TC: 12 677 TG: 40 176	6.2	11.0

*: High TC: TC ≥ 200 mg/dl (5.17mmol/L) ; **: High TG: TG ≥ 150 mg/dl (1.70mmol/L) ; ***:Studies included in the meta-analysis needed to have clear criteria for dyslipidemia, but a consistent definition was not necessary. #: Fasting peripheral blood test.

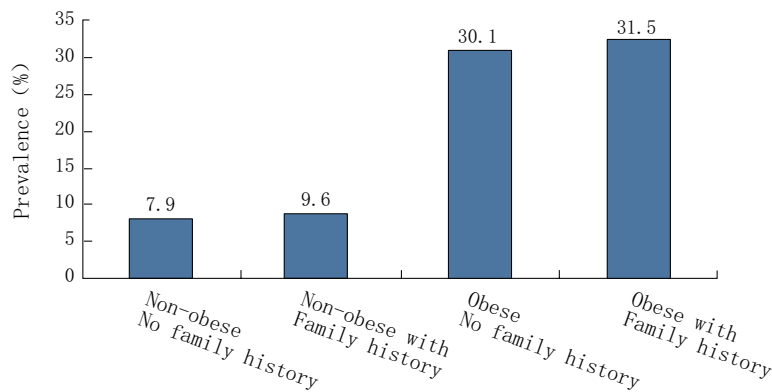


Figure 2-3-2 Prevalence of Dyslipidemia in Children by Obesity and Family History

2.3.3 The Correlation between Dyslipidemia and Cardiovascular Diseases

Dyslipidemia is one of the most important risk factors for cardiovascular diseases in the Chinese population. Multiple prospective cohort studies in China have shown that elevated blood TC and LDL-C or decreased HDL-C can increase the risk of cardiovascular diseases. Additionally, other studies have proven that the increase in non-HDL-C, VLDL-C, and TG may also be predictors for cardiovascular diseases. (Table 2-3-8)

[1] Li JZ, Niu QT, Li PY, et al. Study of blood lipid and lipoprotein among infants and adolescents. Peking Medicine, 1987,9(6):346-349.

[2] Ma WJ, Xu YJ, Fu CX, et al. A cross sectional survey on serum lipid level and its influencing factors in children aged 3-14 years in Guangdong province, Chinese J of Cardiology, 2005,33(10):950-955.

[3] Liu Y, Mi J, Du JB, et al. A survey on dyslipidemia of 6-18-year old children in Beijing area. Chinese J of Practical Pediatrics, 2007;22(2):101-102

[4] Yan H, Mi J, Liu Y, et al. Screening for dyslipidemia based on family history and obesity in children. J of Peking university (health science), 2007;39(6):591-594.

Table 2-3-8 Blood Lipid Levels and the Risk of Cardiovascular Disease in Chinese Cohort Studies (RR, 95%CI)

Study	Sample Size	Follow-up (y)	Endpoint	Blood Lipid Level (mmol/L)				
				TC<5.18	5.18-5.67	5.70-6.19	>6.22	
Sino-USA collaborative study on epidemiology of cardiovascular diseases ^[1]	11 155	Baseline in 1983-1984, follow-up to 2000	Ischemic cardiovascular disease	1	1.2 (0.9-1.6)	1.7 (1.2-2.3)	1.7 (1.2-2.3)	
Cohort study on cardiovascular diseases in multiple cities ^[2]	29 564	Baseline in 1992, follow-up to 2000	Ischemic cardiovascular disease	1	1.3 (1.0-1.6)	1.3 (1.0-1.8)	1.6 (1.2-2.1)	
Collaborative epidemiological research among multiple centers in China ^[3]	17 330	Baseline in 1992-1994, follow-up to 2000	Ischemic cardiovascular disease	1	2.0 (1.5-3.7)			
Cohort study on male employees of the Capital Iron and Steel Company ^[4]	5 137	Baseline in 1974, 1979 and 1980, follow-up to 2001	Myocardial infarction	TC <4.7	TC 4.7-5.1	TC 5.2-5.6	TC 5.7-6.1	TC >6.2
				1	1.70 (1.03-2.82)	1.95 (1.14-3.32)	2.76 (1.54-4.95)	3.69 (2.18-6.24)
Cohort study on male employees of the Capital Iron and Steel Company ^[4]	1 464 patients of hypertension	—	Myocardial infarction	TC <5.17	6.17-5.68	5.69-6.20	6.21-6.71	>6.72
				1	1.2 (0.6-2.7)	2.4 (1.0-5.5)	3.4 (1.4-8.0)	4.0 (1.7-9.0)
Cohort study on cardiovascular diseases in multiple cities ^[5]	29 564	Baseline in 1992, follow-up to 2000	Ischemic cardiovascular disease	1	1.3 (1.0-1.6)	1.4 (1.0-2.0)	2.0 (1.4-2.9)	
Long term follow-up of cohort study on the elderly population ^[6]	1 211	Baseline in 1986-1987, follow-up to 2000	Coronary heart disease	LDL-C <3.37	3.37-4.12	4.14-4.90	LDL >4.92	
				1	1.55 (1.32-1.81)	1	0.89 (0.57-0.82)	
Prospective Collaborative cohort study (the China Cardiovascular Health Study and the China Multicenter Collaborative Study of Cardiovascular Epidemiology) ^[1]	27 020	follow-up to 2007-2008	LDL-C <2.59	2.59-3.37	3.37-4.14	>4.14		
			Coronary heart disease	1	1.04 (0.85-1.27)	1.33 (1.07-1.66)	2.03 (1.58-2.01)	
			Cerebrovascular stroke	1	1.13 (0.79-1.61)	1.65 (1.13-2.41)	3.12 (2.07-4.69)	
		Baseline in 1998, follow-up to 2007-2008	Cerebrovascular stroke	1	1.05 (0.82-1.36)	1.29 (0.91-1.71)	1.67 (1.19-2.35)	

- [1] Wu YF, Zhao D, Zhou BF, et al. Cutoffs and stratification of dyslipidemia in Chinese adults. *Chinese J of Cardiology*, 2007; 35 (5) 428-433.
- [2] Zhou BF. Prospective study for characters of risk factors of cardiovascular diseases in Chinese population. *Chinese J of Epidemiology*, 2005,26 (1) : 58-61
- [3] Yue H, Gu D, Wu Y, et al. A 20-year prospective study on risk factor of myocardial infarction of 5137 men in Capital Steel and Iron Company. *Chinese J of Preventive Medicine*, 2004, 38 (1) : 43-46.
- [4] Li JX, Cao J, Lu XF, Chen SF, et al. The Effect of Total Cholesterol on Myocardial Infarction in Chinese Male Hypertension Population. *Biomedical and Environmental Sciences*, 2010,23 (1) :37-41.
- [5] Li J, Chen M, Wang Yu, et al. A long-term follow-up study of serum lipids and cardiovascular disease in the elderly. *Chinese J of Cardiology*, 2002; 30 (11) : 647-650.
- [6] Gu X, Yang X, Li Y, et al. Usefulness of Low-Density Lipoprotein Cholesterol and Non-High-Density Lipoprotein Cholesterol as Predictors of Cardiovascular Disease in Chinese. *Am J Cardiol*, 2015, 116 (7) : 1063-1070.

Table 2-3-8 Blood Lipid Levels and the Risk of Cardiovascular Disease
In Chinese Cohort Studies (RR, 95%CI)

(Continued)

Study	Sample Size	Follow-up (y)	Endpoint	Blood Lipid Level (mmol/L)			
				HDL-C > 1.0	HDL-C < 1.0	—	—
Prospective cohort study on cardiovascular diseases in multiple cities ^[1]	30 378	Baseline in 1992, follow-up to 2002	Acute coronary event	1	1.39 (1.00-1.92)	—	—
			Ischemic stroke	1	1.45 (1.15-1.83)	—	—
Prospective cohort study on cardiovascular diseases in multiple cities ^[2]	30 378	Baseline in 1992, follow-up to 2004	Acute coronary event	TG < 0.81	TG 0.81-1.14	TG 1.15-1.59	TG > 1.60
				1	1.18 (0.74-1.87)	1.81 (1.18-2.78)	1.58 (1.03-2.45)
Sino-USA Collaborative study on epidemiology of cardiovascular diseases ^[3]	10 222	Baseline in 1983-1984, follow-up to 2000	Ischemic cardiovascular disease	Non-HDL-C < 3.88	Non-HDL-C 3.88-4.38	Non-HDL-C 4.39-4.90	Non-HDL-C > 4.91
				1	1.44 (1.07-1.94)	1.81 (1.26-2.60)	1.53 (1.06-2.22)
Prospective cohort study on cardiovascular diseases in multiple cities ^[4]	29 937	Baseline in 1992, follow-up to 2004	Acute coronary event	1	1.24 (0.91-1.70)	1.78 (1.26-2.53)	2.23 (1.48-3.35)
			Ischemic stroke	1	1.34 (1.07-1.68)	1.38 (1.04-1.83)	1.38 (0.97-1.94)
Prospective Collaborative cohort study (the China Cardiovascular Health Study and the China Multicenter Collaborative Study of Cardiovascular Epidemiology) ^[5]	27 020	Baseline in 2001, follow-up to 2007-2008	Cardiovascular disease	1	1.12 (0.92-1.36)	1.30 (1.04-1.62)	1.93 (1.50-2.47)
			Coronary heart disease	1	1.40 (1.00-1.98)	1.58 (1.07-2.33)	2.80 (1.86-4.21)
		Baseline in 1998, follow-up to 2007-2008	Cerebrovascular stroke	1	1.03 (0.80-1.32)	1.27 (0.96-1.69)	1.57 (1.12-2.20)

2.3.4 Prevention and Control of Dyslipidemia in China

The rates of dyslipidemia awareness and treatment among citizens remain generally low, though in-hospital dyslipidemia management and control have improved.

[1] Wang W, Zhao D, Sun GY, et al. Risk factors comparison in Chinese patients developing acute coronary syndrome, ischemic or hemorrhagic stroke: A multi-provincial study. *Chinese J of Cardiology*, 2006, 34 (12) : 1133-1137.

[2] Wang M, Zhao D, Wang W, et al. Serum triglyceride is an independent risk factor for acute coronary heart disease events in 35-64 years old Chinese-Chinese provincial cohort study. *Chinese J of Cardiology*, 2008, 36 (10) : 940-943.

[3] Li Y, Chen ZH, Zhou BF, et al. The predictive effects of lipids and lipoproteins on the incidence of ischemic cardiovascular disease in middle-aged Chinese population. *Chinese J of Cardiology*, 2004, 32 (7) : 643-647.

[4] Ren J, Zhao D, Liu J, et al. Correlation between non-HDL-C level and risk of cardiovascular disease. *Chinese J of Cardiology*, 2010, 38 (10) : 934-938.

[5] Gu X, Yang X, Li Y, et al. Usefulness of Low-Density Lipoprotein Cholesterol and Non-High-Density Lipoprotein Cholesterol as Predictors of Cardiovascular Disease in Chinese. *Am J Cardiol*, 2015, 116 (7) : 1063-1070.

(1) Community Surveys

Data from the 2002 China Community Nutrition and Health Survey^[1] showed that the awareness rate among the adults (≥ 18 years old) with dyslipidemia (meeting at least one of the following criteria: TC ≥ 5.72 mmol/L and/or TC ≥ 1.70 mmol/L and/or HDL-C < 0.91 mmol/L) was only 3.2: 3.4% in men, 2.7% in women, 7.0% in urban areas, and 1.5% in rural areas. The rate of ever having taken a blood lipid examination was 6.4%: 6.9% in men, 6.0% in women, 16.5% in urban areas, and 2.2% in rural areas. The InterAsia^[2] and CNDMDS studies^[3] investigated the rates of awareness, treatment and control for hypercholesterolemia in the Chinese population as shown in Table 2-3-9.

Table 2-3-9 Rates of Awareness, Treatment, and Control for Hypercholesterolemia in Chinese Population from Certain Regions (%)

Year	Study	Population		Male		Female	
				TC ≥ 6.22	TC ≥ 5.18	TC ≥ 6.22	TC ≥ 5.18
2000-2001	InterASIA	35-74y; 15 540	Awareness	21.3	8.8	18.1	7.5
			Treatment	14.0	3.5	11.6	3.4
			Control	11.3	1.9	9.5	1.5
2007-2008	CNDMDS	$> 20y$; 46 239	Awareness	27.6	12.8	20.7	9.3
			Treatment	21.4	6.1	14.0	4.1
			Control	18.3	3.3	11.2	2.2
			Treatment-control rate	88.1	52.1	78.4	55.4

The China non-communicable disease surveillance program^[4] surveyed 98 658 people aged 18 years or older from 162 centers across 31 provinces in 2010. The rates of awareness, treatment and control for dyslipidemia in populations with different glycaemic levels are shown in Table 2-3-10.

Table 2-3-10 Rates of Awareness, Treatment, and Control for Dyslipidemia among People by Glycemic Levels (%)

	Glycemic Levels			
	Normal	Pre-diabetes	Newly-diagnosed Diabetes	Previously-Diagnosed Diabetes
Prevalence	47.2 (46.5,47.9)	51.5 (50.9,52.1)	63.2 (61.8,64.5)	70.0 (68.2,71.7) *
Awareness	5.4 (5.0,5.8)	8.3 (7.9,8.7)	12.8 (11.7,13.9)	33.9 (31.8,36.1) *
Treatment	2.3 (2.0,2.5)	3.7 (3.5,4.0)	5.4 (4.6,6.2)	18.9 (17.2,20.7) *
Control	20.1 (15.8,25.2)	15.6 (13.1,18.5)	9.5 (6.4,13.8)	15.9 (12.3,20.3)

Notes: Post-consumption of lipid-lowering drugs, or abnormal lipid levels (TC ≥ 6.22 mmol/L or TG ≥ 1.70 mmol/L or HDL-C < 1.04 mmol/L or high); Data in the table is shown by percentage after weighing (95% CIs); * Compared with Newly-diagnosed diabetes P < 0.0001

- [1] Zhang WH, Zhang J, Li Y. Survey Report on the Status of Nutrition and Health of the Chinese People: Series Four. 2002, Blood lipid.
- [2] He J, Gu D, Reynolds K, et al. Serum total and lipoprotein cholesterol levels and awareness, treatment, and control of hypercholesterolemia in China. *Circulation*, 2004, 110 (4) : 405-411.
- [3] Yang WY, Xiao JZ, Yang ZJ, et al. Serum lipids and lipoproteins and Chinese men and women. *Circulation*, 2012, 125: 2212-2221.
- [4] Wang TG, Xu Y, Xu M, et al. Awareness, treatment and control of cardiometabolic disorders in Chinese adults with diabetes: a national representative population study. *Cardiovascular Diabetology*, 2015, 14 (1) :1-10.

(2) Inpatient Studies

Several multi-center clinical studies for the control of dyslipidemia have been conducted since 2000 and the results are shown in Table 2-3-11.

Table 2-3-11 Rates of Treatment and Control for Hypercholesterolemia In Chinese Inpatients (%)

Year	Study	Sites	Population Features	Sample Size	Dyslipidemia Control Status		
					Statin Treatment Rate	Rate of Reaching LDL-C Target	
2000	Study of current status on clinical control of hypercholesterolemia in China ^[1]	More than 20 tertiary and secondary hospitals in > 10 cities	Dyslipidemia	2 136	—	26.5 [*]	—
2006	Study of current status on clinical control of hypercholesterolemia in China ^[2]	52 centers in 6 provinces and cities	CHD (high risk, very high risk)	2 237	—	34 ^{**}	50 ^{***}
2008	The China Cholesterol Education Program (CCEP) ^[3]	49 hospitals	ACS	4 778	82.2	36.2 ^{**}	42.2 ^{***+} , 10.9 ^{***++}
2009	Clinical Pathways for Acute Coronary Syndromes in China (CPACS study) ^[4]	6 tertiary hospitals in Beijing	Type 2 diabetes mellitus	2 901	80.4% (discharge), 65.8% (follow-up in 6m), 59.4% (follow-up in 12m)	—	—
2009	Management status of type 2 diabetes mellitus ^[5]	6 large centers of cardiovascular diseases	CHD (in-patient and out patient)	1 151	—	34.0 (#)	—
2010	Survey of achieving recommended lipid goals in Chinese patients with coronary artery disease ^[6]			2 436	96.7	67 (<100mg/dl)	38 (<70mg/dl)

[1] The current status on clinical control of hypercholesterolemia in China collaborative research group. A multi-center study of current status on clinical control of hypercholesterolemia in China: success rate and related factors. *Chinese J of Cardiology*, 2002, 30 (2): 109-104.

[2] The collaborative research group for the second multi-center survey of clinical management of Dyslipidemia in China. The second multi-center survey of dyslipidemia management in China: goal attainment rate and related factors, *Chinese J of Cardiology*, 2007, 35 (5): 420-427.

[3] Hu DY, Li J, Li XK for CCEP. Investigation of blood lipid levels and Statin Interventions in outpatients with coronary heart disease in China—The China Cholesterol Education Program (CCEP). *Circ*. 2008, 72:2040-2045.

[4] Bi YF, Gao RL, Patel A et al. Evidence-based medication use among Chinese patients with acute coronary syndromes at the time of hospital discharge and 1 year after hospitalization: Results from the Clinical Pathways for Acute Coronary Syndromes in China (CPACS) study. *Am Heart J*. 2009, 157:509-516.

[5] Li MZ, Ji LN, Meng ZL, et al. Management status of type 2 diabetes mellitus in tertiary hospitals in Beijing: gap between guideline and reality. *Chin Med J*. 2012; 125 (23): 4185-9.

[6] Guo YL, Liu J, Li JJ, et al. A multi-center survey of achieving recommended lipid goals in Chinese patients with coronary artery disease in real world cardiovascular practice. *Int J Cardio*, 2011, 153 (2) 211-212.

Table 2-3-11 Rates of Treatment and Control for Hypercholesterolemia in Chinese Inpatients (%)

(Continued)

Year	Study	Sites	Population Features	Sample Size	Dyslipidemia Control Status		
					Statin Treatment Rate	Rate of Reaching LDL-C Target	
2011	Management and attainment of cholesterol targets for patients with dyslipidemia in China. (The Reality China survey) ^[1]	84 hospitals in 19 provinces	Dyslipidemia	12 040	39% (blood-lipid lowering therapy, 94.5% with statins)	25.8** (all)	19.9*** (high risk), 21.1*** (very high risk)
2007 - 2009	Use of secondary preventive medications in patients with atherosclerotic disease in urban China ^[2]	51 hospitals in 14 cities	Atherosclerosis	16 860	47	—	—
2012	Dyslipidemia International Study-China ^[3] (DYSIS-China)	122 centers	Dyslipidemia with metabolism syndrome	25 317	88.9	46.9 (LDL-C ⁺)	52.2 (LDL-C ⁺⁺)
			Dyslipidemia without metabolism			68.6 (LDL-C ⁺)	67.1 (LDL-C ⁺⁺)
2001 - 2011	PEACE-Retrospective Acute Myocardial Infarction Study ^[4]	162 centers	ST-segment elevated	1 995 (2001)	29.7 (27.5 - 31.9) #	—	—
			myocardial infarction	3 626 (2006)	75.2 (73.8 - 76.6) #	—	—
			(in-hospital patients)	6 643 (2011)	92.0 (91.4 - 92.7) #	—	—
2006 - 2012	China, BRIG ^[5]	31 provinces (65 hospitals) in 2006	Acute coronary syndrome	3 124 (2006)	69.8	—	—
		21 provinces (34 hospitals) in 2012	(in-hospital patients)	3 124 (2012)	90.0	—	—

*: According to the criteria of 《2007 Prevention and treatment suggestion on dyslipidemia》.

**： According to the criteria of American NCEP ATP III in 2004.

***: According to the criteria of 《2007 Prevention and treatment suggestion on dyslipidemia for Chinese adults》.

#: According to the criteria of 《2007 Chinese Guideline on type 2 diabetes mellitus》 (CGT2D). Weighted rates.

+： LDL-C target 2.59mmol/L

++： LDL-C target 1.82mmol/L

[1] Gao F, Zhou YJ, Hu da Y, et al. Contemporary management and attainment of cholesterol targets for patients with dyslipidemia in China. PLoS One. 2013; 8 (4) : e47681.

[2] Li J, Chen YP, Li X, et al. Use of secondary preventive medications in patients with atherosclerotic disease in urban China: a cross-sectional study of 16 860 patients Chin Med J. 2012,125 (24) :4361-4367.

[3] Wang F, Ye P, Hu DY et al. Lipid-lowering therapy and lipid goal attainment in patients with metabolic syndrome in China: Subgroup analysis of the Dyslipidemia International Study-China (DYSIS-China). Atherosclerosis, 2014,237: 99-105.

[4] Li J, Li X, Wang Q, et al. ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. Lancet, 2015;385 (9966) :441-51.

[5] Liu J, Zhao D, Liu J, et al. Changes in the diagnosis and treatment of hospitalized patients with acute coronary syndrome from 2006 to 2012 in China. Chinese J of Cardiology, 2014,42 (11) :957-962.

2.4 Diabetes

2.4.1 The Prevalence of Diabetes

The 2010 China Chronic Disease Survey, published in September 2013, revealed the prevalence rates of diabetes^[1]. The study collected data from 162 local disease control centers of 31 administrative regions during 2010, with a sample size of 98 658 people aged 18 years and older. HbA1c, fasting blood glucose (FBG), and 2-hour postprandial blood glucose levels were measured for all subjects. Diabetes was defined as (1) self-reported diabetes with a confirmed diagnosis by a medical professional; (2) an FBG level equal to or greater than 126 mg/dl; (3) a 2-hour postprandial blood glucose level equal to or greater than 200 mg/dl; or (4) an HbA1c level equal to or greater than 6.5%.

According to the previous diagnosis, fasting blood glucose (FBG) and 2-hour postprandial blood glucose levels, the estimated prevalence rate of diabetes was 9.7% in Chinese adults, which was the same as Yang, Wenying's report (9.7%) in 2010^[2]. Taking HbA1c level into consideration, the prevalence rate of diabetes was found to be 11.6%. For both genders, the prevalence rate of diabetes was higher in urban than in rural areas (Table 2-4-1). The rate was higher in male than female who were younger than 60 years old, and higher in female who were over 60 years old instead. The study noted that the prevalence rate of diabetes was higher in persons living in economically developed regions and among obesity people.

Table 2-4-1 Prevalence of Diabetes In Chinese Adults

	Prevalence Rate (%*,95%CI)								
	Total	FBG>126 mg/dL	2HPBS>200g/dl	HbA1c>6.5%	FBG>126 mg/dL and/or 2HPBS >200mg/dl	FBG>126 mg/dL and/or HbA1c>6.5%	2HPBS>200mg/dl and/or HbA1c>6.5%	FBG>126, 2HPBS>200mg/dl and/or HbA1c>6.5%	Previously diagnosed with diabetes
Overall	11.6 (11.3-11.8)	4.5 (4.4-4.7)	3.5 (3.4-3.7)	4.6 (4.4-4.7)	6.2 (6.0-6.4)	6.9 (6.7-7.2)	6.2 (6.0-6.4)	8.1 (7.9-8.3)	3.5 (3.4-3.6)
Gender									
Male	12.1 (11.7-12.5)	5.0 (4.7-5.2)	3.8 (3.5-4.0)	4.6 (4.4-4.9)	6.6 (6.4-6.9)	7.3 (7.0-7.6)	6.4 (6.1-6.7)	8.5 (8.2-8.8)	3.6 (3.4-3.8)
Female	11.0 (10.7-11.4)	4.0 (3.8-4.3)	3.3 (3.1-3.5)	4.5 (4.3-4.7)	5.7 (5.4-6.0)	6.6 (6.3-6.9)	6.0 (5.7-6.2)	7.7 (7.4-8.0)	3.4 (3.2-3.5)
Region									
Urban	14.3 (13.9-14.8)	5.0 (4.8-5.3)	4.1 (3.8-4.3)	5.3 (5.0-5.5)	6.8 (6.5-7.1)	7.7 (7.3-8.0)	7.0 (6.7-7.3)	8.8 (8.5-9.1)	5.6 (5.3-5.8)
Rural	10.3 (10.0-10.6)	4.3 (4.1-4.5)	3.3 (3.1-3.5)	4.3 (4.0-4.5)	5.9 (5.7-6.2)	6.6 (6.4-6.9)	5.8 (5.6-6.1)	7.8 (7.5-8.1)	2.5 (2.4-2.7)

Note: HbA1c, glycosylated hemoglobin; unit conversion: Glucose unit conversion 1mg/dL=0.0555mmol/L; the values in a are weighted averages in percentages.

[1] Xu Y, Wang L, He J, et al. Prevalence and Control of Diabetes in Chinese Adults. JAMA, 2013,310 (9) : 948-958.

[2] Yang WY, Lu JM, Weng JP, et al. Prevalence of diabetes among men and women in China. N Eng J Med, 2010,362 (12) :1090-1101.

2.4.2 Prevention of Diabetes

The China Daqing Diabetes Prevention Study is the earliest and longest-running study in the world with adopting lifestyle interventions to prevent diabetes. The study followed the subjects for 20 years and the incidence of diabetes was reduced by 51% during in the past 6 years. Additionally, it also induced a positive active in the period of lifestyle intervention. Moreover, with the 20-year follow-up, the morbidity rates of diabetes were 80% for the intervention groups, but 93% for the control group. Interestingly, the morbidity rate of the intervention group was lower than the control group by 43% (HRR 0.57, 95% CI 0.41–0.81) and the time of diabetes onset of the intervention group was an average of 3.6 years later than the control group (when adjusted for age and random group factors)^[1]. Healthy lifestyles interventions also decreased the risk of developing severe retinopathy (laser treatment and blindness) by 47%^[2].

Six years of healthy lifestyles intervention were identified to have significantly reduced the CVD-related mortality rate for the 20-year follow-up^[3]. The CVD-related mortality rate, all-cause mortality rate, and risk of developing diabetes in the intervention group were all dramatically lower than the values of the control group by 41% (11.9% vs 19.6%), 29% (28.1% vs 38.4%), and 45% (72.6% vs 89.9%), respectively. The study showed that healthy lifestyle interventions not only reduce the long-term risk of developing diabetes, but also reduce life-threatening illnesses consequences and deaths attributable to CVD.

The Daqing IGT and Diabetes Study compared mortality rate and causes of death among 690 people with newly diagnosed diabetes (NDD) and 519 with normal glucose tolerance (NGT) who were identified as a result of screening 110 660 adults aged 25–74 years for diabetes in 1986^[4]. With 23 years of follow-up, there are 338 (56.5%) participants with NDD and 100 (20.3%) with NGT died. CVD was the predominant cause of the death in whom with diabetes (47.5% in male and 49.7% in female), almost half of which died from stroke (52.3% in male and 42.3% in female). With age-standardized, the incidence of all-cause mortality was three times higher in NDD than whom are NGT with the incidences (per 1 000 person-years) of 36.9 (95% CI 31.5–42.3) vs. 13.3 (10.2–16.5) in male ($P < 0.0001$) and 27.1 (22.9–31.4) vs. 9.2 (7.8–10.6) in female ($P < 0.0001$). When it compared with patients with NGT, the HRs of death from CVD in female with NDD is higher than in male, with HRs of 6.9 in female (95% CI 3.3–14.2) and 3.5 in male (95% CI 2.3–5.3) (Figure 2-4-1).

[1] Li GW, Zhang P, Wang J, et al. Long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet*.2008,371:1783-89.

[2] Gong Q, Gregg EW, Wang J, et al. Long-term effects of a randomised trial of a 6-year lifestyle intervention in impaired glucose tolerance on diabetes-related microvascular complications: the China Da Qing Diabetes Prevention Outcome Study. *Diabetologia*, 2011,54 (2) :300-307.

[3] Li GW, Zhang P, Wang JP, et al. Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study. *Lancet Diabetes Endocrinol*.2014,2 (6) :474-480.

[4] An YL, Zhang P, Wang JP, et al. Cardiovascular and All-Cause Mortality Over a 23-Year Period Among Chinese With Newly Diagnosed Diabetes in the Da Qing IGT and Diabetes Study. *Diabetes Care*, 2015, 38 (7) :1365-1371.

Moreover, the study revealed that the CVD mortality rates in the male and female with NDD (17.5[13.8–21.2] vs. 13.5[1.5–16.5]/1 000 person–years) did not show dramatic difference. Significantly higher mortality rate attributable to renal diseases and infections were also found in the NDD group.

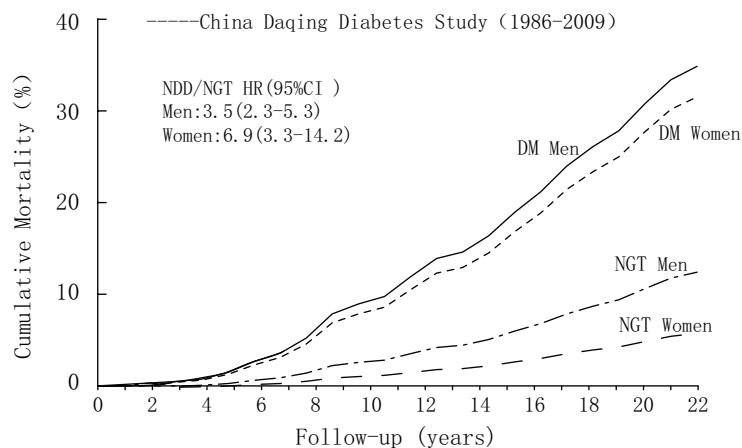


Figure 2-4-1 Daqing Diabetes Prevention Study: Age-adjusted Cumulative Incidence and Age-adjusted HRs of Death from CVD in Male and Female with NGT and NDD over The 23 Years of Follow-up (1986–2009)

2.4.3 The Management of Diabetes

The 3B (blood glucose, blood pressure, and blood lipids) Research Study^[1] was a multi-center cross-sectional observational study, in which 25 817 type 2 diabetic patients from 104 hospitals were recruited, with an average age of 62.6 years. 47% of the patients were male, and 72% reported comorbid hypertension, dyslipidemia, or both. The average HbA1c level was 7.6%. Patients with concurrent type 2 diabetes, hypertension, and dyslipidemia were 6 times more likely to report a prior history of cardiovascular disease compared with those with type 2 diabetes alone. The control rates of blood glucose (HbA1c<7%), blood pressure (systolic blood pressure <130 mm Hg, diastolic blood pressure <80 mm Hg) , and blood lipid levels (TC<4.5 mmol/L) were 47.7%, 28.4% and 36.1%, respectively. However, only 5.6% of the patients had all three values under control. The unhealthy living habit was strongly associated with cardiovascular risk factors.

The China National Chronic Kidney Disease Work Group investigated 46 683 people for four cardiovascular risk factors: hypertension, diabetes, dyslipidemia and overweight status. The study also aimed to discern the relationship between unhealthy lifestyles (drinking, physical inactivity, long-term use of nonsteroidal anti-inflammatory drugs and the improved score of DASH (Dietary Approaches to Stop Hypertension) diet) and the presence of such cardiovascular risk factors^[2]. The study results showed that only

[1] Ji L, Hu D, Pan C, et al. Primacy of the 3B Approach to Control Risk Factors for Cardiovascular Disease among Type 2 Diabetes. *Am J Med.* 2013,126 (10) :925e11–22.

[2] Gao B, Zhang L, Wang H. Clustering of Major Cardiovascular Risk Factors and the Association with Unhealthy Lifestyles in the Chinese Adult Population. *PLoS One.* 2013,8 (6) :e66780.

31.1% of participants didn't have above cardiovascular risk factors and that 20 292 participants (43.5%) had all four cardiovascular risk factors. The adjusted combined rate of the cardiovascular risk factors was 36.2%, and was higher for male than female (37.9% vs. 34.5%) . Habitual alcohol consumption, physical inactivity and long-term use of nonsteroidal anti-inflammatory drugs were positively correlated to the aggregation of cardiovascular risk factors, with odds ratios of 1.60 for frequently alcohol use (95% CI: 1.40–1.85) , 1.20 for physical inactivity (95% CI: 1.11–1.30) , and 2.17 for the drug use (95% CI: 1.84–2.55) . The study also showed that unhealthy lifestyles in populations with poor socioeconomic status are more prominent. Improved blood pressure and diet control were negatively associated with the aggregation of cardiovascular risk factors, with an odds ratio of 0.73 (95% CI, 0.67–0.78) .

2.5 Overweight and Obesity

2.5.1 The Current Epidemiological Features of Obesity and Overweight in China

With China economic development and changes in lifestyle, the prevalence of overweight (BMI: 24.0–27.9kg/m²) and obesity (BMI ≥28.0kg/m²) has shown continuous growth over the past 30 years. According to the 2002 China Health and Nutrition Survey (CHNS) , 200 million people were diagnosed as being overweight (prevalence rate 17.6%) and 60 million people were diagnosed with obesity (prevalence rate 5.6%) in 2002.^[1]

Following the long-term monitoring of the diet and health statuses of people in 9 Chinese provinces, a number of cross-sectional studies (at least 5 000 subjects in each study) showed that in the past 20 years, the prevalence rate of overweight or obesity increased.^[2] In 2011, the prevalence of overweight and obesity (BMI ≥24.0kg/m²) reached 44.0% (Figure 2–5–1) . The prevalence of abdominal obesity in 2009 was 45.3% (defined as waist circumference ≥85cm for males, ≥80cm for females) (Figure 2–5–2) .

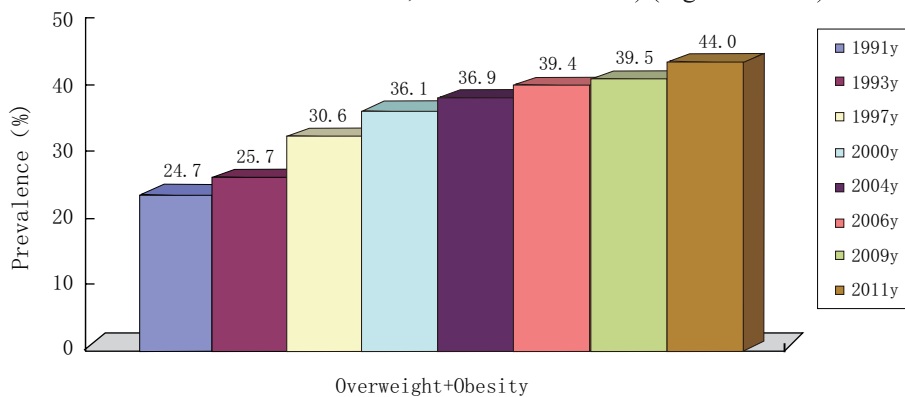


Figure 2–5–1 Trend of the Prevalence of Overweight and Obesity in China (9 Provinces and Cities)

[1] Ma GS, Li YP, Wu YF, et al. The prevalence of body weight and obesity and its change among Chinese people during 1992 to 2002. Chin J Prev Med. 2005;39 (5) :311-315.

[2] Gordon Larsen P, Wang H, Popkin B M. Overweight dynamics in Chinese children and adults. Obesity Reviews, 2014, 15 (S1) : 37-48.

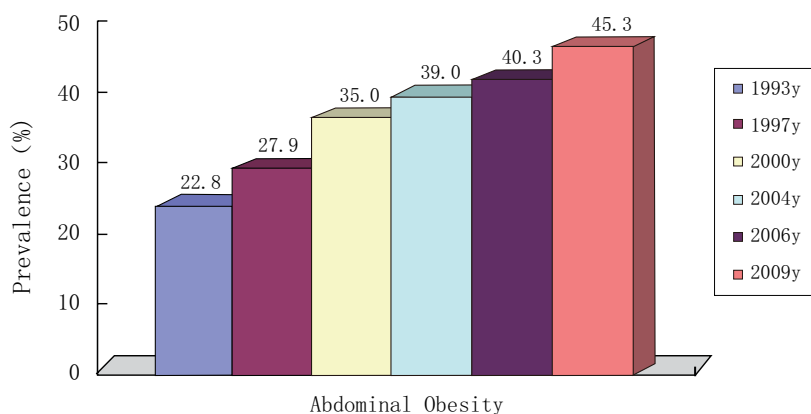


Figure 2-5-2 Trend of Abdominal Obesity Prevalence among Adults in China 9 (Provinces and Cities)

The Chronic Disease and Risk Factors Surveillance Program of Shanghai conducted surveys among residents (older than 15) in 2007 and 2010^[1]. The prevalence rates of both overweight and obesity were on an upward trend, as shown in Table 2-5-1.

Table 2-5-1 Prevalence and Change of Overweight and Obesity among Residents over 15 Years Old in Shanghai in 2007 and 2010

Year	N	Overweight	Obesity	Overweight+Obesity
2007	17 174	29.0	8.1	37.1
2010	15 663	31.3*	8.6*	39.9*
% change		7.9	6.2	7.5

*: compared with 2007, $p < 0.05$.

In 2010, the Chronic Disease Surveillance Program of China conducted surveys among approximately 100 000 residents (older than 18) at 162 monitoring sites in 31 provinces, municipalities or autonomous regions using cluster random sampling. The results showed that the prevalence of overweight, obesity, and abdominal obesity reached 30.6%, 12.0%, and 40.7% respectively in China (Figure 2-5-3)^[2,3]. These numbers were significantly higher than those of 2002.

[1] Xu JY, Yao HH, Yan QH, et al. The present status and development trend of overweight and obesity in residents (≥ 15 years old) of Shanghai. Chinese Journal of Prevention and Control of Chronic Diseases, 2014,22 (2) :170-173.

[2] Li XY, Jiang Y, Hu N, et al. Prevalence and characteristic of overweight and obesity among adults in China, 2010. Chin J Prev Med. 2012;46 (8) :683-686.

[3] Jiang Y, Zhang M, Li YC, et al. Prevalence of abdominal obesity and distribution of waistline among Chinese adults in 2010. Chin J Prev Contr Chron Non-commun Dis. 2013,21 (3) :288-291.

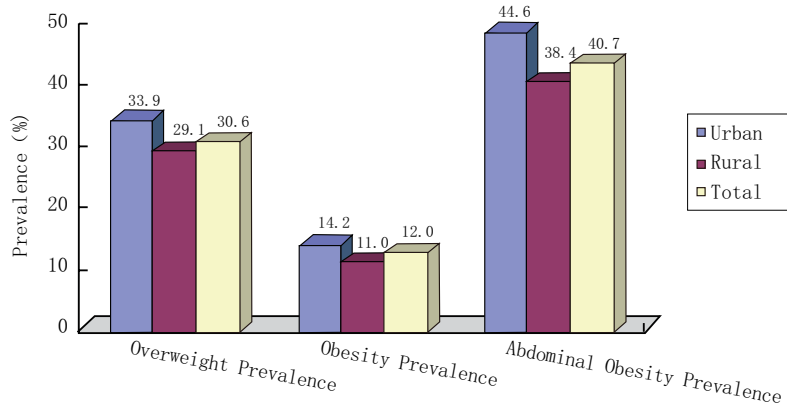


Figure 2-5-3 Prevalences of Overweight and Obesity in 2010

Researchers conducted four cross-sectional health surveys among residents aged 18 to 69 years old in Guangdong province^[1]. The number of participants included in the present analysis for surveys conducted in 2002, 2004, 2007 and 2010 were 13 058, 7 646, 6 441 and 8 575, respectively. Results showed that from 2002 to 2010, the prevalence of overweight and obesity had increased from 15.8% to 16.6% without statistical significance ($P>0.05$); however, the prevalence of abdominal obesity had increased remarkably from 12.9 to 23.7% (Table 2-5-2). This indicates that the type of obesity may have changed in China.

Table 2-5-2 Temporal Trends in Prevalence of Overweight and Obesity among Adults (aged 18-69) in Guangdong Province

	Year				Change from 2002 to 2010	P for trend
	2002	2004	2007	2010		
BMI (kg/m ²)	21.7	21.7	21.9	22.3	0.6	0.062
Overweight+Obesity (%)	15.8	13.7	13.1	16.6	0.8	0.82
Waist Circumference (cm)	73.7	75.8	76.9	78.4	4.7	<0.001
Abdominal Obesity (%)	12.9	20.1	21.3	23.7	10.8	<0.001

Researchers explored the overweight and obesity rates among 19 882 adults 60 years or older from the Chronic Disease Surveillance Program of China in 2010^[2]. Data showed that nearly half of the people over 60 years old were overweight. The prevalence of overweight and obese adults over 60 years old were 32.1% and 12.4%, respectively, with higher rates in urban areas than in rural areas (Table 2-5-3).

[1] Lao X Q, Ma W J, Sobko T, et al. Overall obesity is leveling-off while abdominal obesity continues to rise in a Chinese population experiencing rapid economic development: analysis of serial cross-sectional health survey data 2002-2010. *International Journal of Obesity*, 2015,39 (2) :288-294.

[2] Zhang M, Jiang Y, Li YC et al. Prevalence of overweight and obesity among Chinese elderly aged 60 and above in 2010. *Chinese Journal of epidemiology*, 2014,35 (4) :365-369.

Table 2-5-3 Prevalence of Overweight and Obesity among Adults over 60 Years Old in 2010

Region	Overweight		Obesity	
	N	Prevalence (%)	N	Prevalence (%)
Urban	3 252	38.3	1 449	16.5
Rural	3 419	29.1*	1 296	10.3*
Total	6 671	32.1	2 745	12.4

Notes:*compared with urban, P<0.05.

Prevalence rates of obesity and overweight among children and adolescents are also concerning. Five national surveys focused on the health status of Chinese students from 1985 to 2010. More than 200 000 students aged 7–18 years old were monitored in each study. The results showed an increasing trend in the prevalence rates of both overweight and obesity^[1] (Figure 2-5-4). The prevalence rates of overweight and obesity in 2010 were 8.7 and 38.1 times as high as the rates in 1985, respectively.

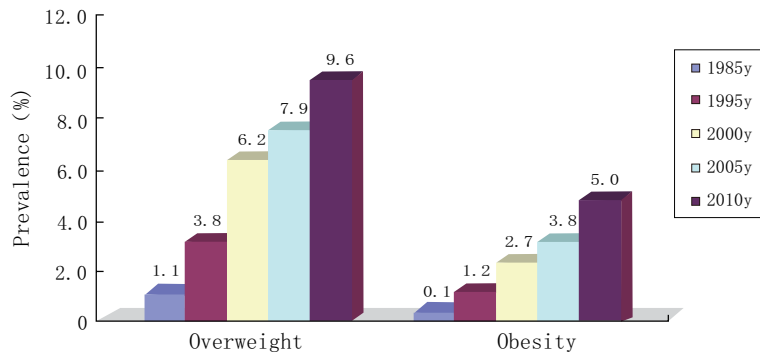


Figure 2-5-4 Temporal Trends in The Prevalence of Overweight and Obese Adolescents in China

In Guangzhou, two cross-sectional surveys were conducted among 28 000 and 38 000 students aged 7–18 years old in 2007 and 2011, respectively^[2]. The results showed a similar overweight prevalence, but a significantly increase in the prevalence of obesity (from 5.96% in 2007 to 6.56% in 2011, P<0.05), as shown in Figure 2-5-5.

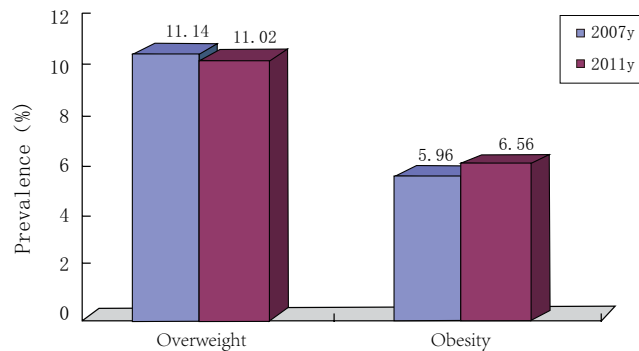


Figure 2-5-5 Temporal Trends of Overweight and Obesity Prevalence among Children Aged 7-18 in Guangzhou

[1] Ma J, Cai XH, Wang HJ, et al. The trend analysis of overweight and obesity in Chinese students during 1985-2010. Chin J Prev Med. 2012;46 (9) :776-780.

[2] Liu BY, Jing J, Mai JC, et al. Secular trends of overweight and obesity prevalence between 2007 and 2011 in children and adolescents in Guangzhou. Chin J Prev Med. 2014,48 (4) :312-317.

Survey was conducted among 3 000 residents aged 18 years or older in Hong Kong from 2009 to 2010, collecting data pertaining to lifestyle such as TV viewing time and physical activity performed. After adjusting for certain factors, the risk of being obese (BMI $\geq 25\text{kg/m}^2$) was found to increase by 10% with every hour of TV watched. This relationship was more significant among people under 45 years old^[1] (Table 2-5-4).

Table 2-5-4 The Risk of being Obese as a Result of Hours of TV Watching in Hong Kong Adults

	N	OR (95% CI)	P
Total*	2 772	1.10 (1.05-1.15)	<0.001
Age group (Year) **			
18-34	659	1.38 (1.19-1.61)	<0.001
35-44	379	1.15 (1.04-1.28)	<0.01
45-54	712	1.06 (0.95-1.18)	0.32
55-64	631	1.10 (0.99-1.23)	0.07
>65	391	0.98 (0.88-1.08)	0.66

*: Gender, age, occupation, marital status, education attainment, alcohol use, and high-intensity level of physical activity were adjusted for in the logistic regression analysis

** : Gender, occupation, marital status, education attainment, alcohol use, and high-intensity level of physical activity were adjusted for in the age-subgroup analysis

In 2010, the Chronic Disease Surveillance Program of China conducted a survey among 45 006 men and 53 392 women that explored the relationship between TV watching time and obesity^[2]. Results showed that adults spent average 1.87 hours on watching TV a day. After adjusting for certain factors by multivariate logistic regression, the risk of being obese was found to increase by 4% with every hour of TV watching (Table 2-5-5). Among people over 45 years old, such a relationship was more significant than the relationship reported in the Hong Kong study.

Table 2-5-5 The Risk of being Obese as a Result of Hours of TV Watched

Model	N	OR	95%CI	P value
Total				
Hours of TV watching (h)	98 398	1.04	1.01-1.07	<0.01
Age group*				
18-34y	21 847	1.03	0.98-1.09	0.28
35-44y	23 216	0.99	0.93-1.04	0.59
45-54y	22 791	1.05	1.01-1.09	0.01
55-64y	18 323	1.10	1.06-1.15	<0.001
>65y	12 221	1.12	1.07-1.18	<0.001

*: Gender, urbanization, smoking, alcohol, marital status, education level, and physical activity were adjusted for in the age-subgroup analysis. Age was also adjusted for in the whole sample analysis.

[1] Xie YJ, Stewart SM, Lam TH, et al. Television viewing time in Hong Kong adult population: associations with body mass index and obesity. PLoS One, 2014,9 (1) :e85440.

[2] Deng Q, Wang LM, Chen XR, et al. Television viewing time of Chinese adults: associations with body mass index and obesity. Chinese Journal of the Frontiers of Medical Science. 2015, (1) :46-50.

2.5.2 Disease Risks Associated with Overweight and Obesity

A prospective study was conducted among over 27 000 Chinese adults (aged 35–74 years old) who were free of diabetes mellitus (DM) at baseline, with a mean follow-up of 8.0 years. Results showed the age-standardized incidence of DM was 9.6/1000 person-years and 9.2/1000 person-years in men and women, respectively. There was a significant positive correlation between baseline waist circumference (WC) and the new onset of DM (Table 2–5–6).^[1]

Table 2–5–6 Hazard Ratios and Age-standardized Incidence for Type 2 DM by WC

WC (cm)	Age-standardized Incidence (Per 1 000 Person-years)	HR (95%CI)
Men		
<90	7.0	1.0
90–94	17.2	2.1 (1.7–2.7)
95–99	24.4	2.7 (2.0–3.7)
≥100	29.0	3.3 (2.4–4.6)
P for trend		<0.001
Women		
<80	5.3	1.0
80–84	10.4	1.8 (1.4–2.3)
85–89	15.3	2.6 (2.0–3.3)
≥90	26.0	3.4 (2.7–4.3)
P for trend		<0.001

Note: Adjusted for geographic region (north vs south), urbanization, education level, cigarette smoking, alcohol consumption, work-related physical activity, family history of diabetes and CVDs.

Waist-height ratio (WHR) is an effective parameter for abdominal obesity, which is hardly affected by gender, height, race and other factors. The value of 0.50 is an internationally used cut-off value to diagnose abdominal obesity, namely “the waist circumference should not be more than half of the height”. This cut-off has also been validated among the Chinese population by several Chinese studies^[2,3,4]. The result of CHNS 2009 showed a positive association between abdominal obesity (WHR ≥ 0.50) and the prevalence of cardiovascular risk factors (Table 2–5–7).^[5]

[1] Xue H, Wang C, Li Y, et al. Incidence of type 2 diabetes and number of events attributable to abdominal obesity in China: A cohort study. *Journal of diabetes*. 2015.

[2] Zhao LC, Li Y, Peng YG, et al. The cut-off value of waist-to-height ratio in detecting central obesity in Chinese adult population. *Chin J Prev Med*. 2012;07:481-485.

[3] He Y, Zhai F, Ma G, et al. Abdominal obesity and the prevalence of diabetes and intermediate hyperglycaemia in Chinese adults. *Public health nutrition*. 2009, 12 (08) : 1078-1084.

[4] Guangdong Provincial Co-operation Group for Diabetes Epidemiological Study. Waist / Height ratio: an effective index for abdominal obesity predicting diabetes and hypertension. *Chinese Journal of Endocrinology and Metabolism*. 2004;20 (3) :272-275.

[5] Adair LS, Gordon-Larsen P, Du SF, et al. The emergence of cardiometabolic disease risk in Chinese children and adults: consequences of changes in diet, physical activity and obesity. *Obesity Reviews*. 2014, 15 (S1) : 49-59.

Table 2-5-7 Association between Abdominal Obesity (WHR>0.50) and Cardiovascular Risk Factors

Risk Factors	OR (95%CI)	
	Men	Women
Hypertension	1.47 (1.24-1.73)	1.79 (1.50-2.13)
Abnormal HbA1c	2.17 (1.52-3.10)	2.25 (1.55-3.28)
High CRP	1.43 (1.12-1.83)	1.64 (1.27-2.11)
High LDL-C	1.54 (1.28-1.85)	1.24 (1.04-1.47)
Low HDL-C	1.76 (1.48-2.08)	1.58 (1.33-1.88)
High TG	2.46 (2.05-2.95)	1.79 (1.48-2.15)

Note: Logistic regression adjusted for age, education level, urbanization, household income and living conditions.

Studies have shown that prevalence rates of overweight and obesity are increasing in China. One of the most important tasks for cardiovascular diseases control and prevention is to halt the epidemic of obesity and other chronic disease risk factors. The “Chronic Disease Prevention and Control Work Plan (2012–2015)” and the “Nationwide Fitness Program (2011–2015)” should be actively implemented and more national efforts should be made to prevent chronic diseases and to promote health, which will in return reverse the increasing trend of obesity.

2.6 Physical Inactivity

2.6.1 The Status, Trends, and Influence Factors of Physical Activity

One cross-sectional study analyzed more than 460 000 adults (aged 34–74) who were enrolled from 10 regions across China from 2004 to 2008.^[1] The mean total physical activity of 21.7 MET-h/day, was derived mainly from occupational activities (62%) and housework (26%), with little from physical exercise (4%). Different kinds of physical activity levels are shown in Table 2-6-1.

Table 2-6-1 Levels of Physical Activity by Gender among Adults (aged 35–74 years) In 10 Regions Across China (MET-h/day)

Type of Physical Activity	Male (n=188 647)	Female (n=277 958)	Total (n=466 605)
Occupational activity	17.3±14.9	10.9±12.5	13.5±13.9
Housework	2.9±2.8	7.7±3.9	5.7±4.2
Physical exercise	0.8±2.2	0.8±2.2	0.8±2.2
Overall	22.8±15.1	20.9±12.8	21.7±13.8

Results from the 1991–2011 CHNS showed a significant decrease in the trend of the amount of physical activity among Chinese citizens aged 18–60 in different 9 provinces. The declines were largely driven by

[1] Du HD Li LM, Whitlock G, et al. Patterns and socio-demographic correlates of domain-specific physical activities and their associations with adiposity in the China Kadoorie Biobank Study. BMC Public Health. 2014, 14 (826) .

reductions in occupational physical activities for both genders. Physical activity levels fell from 382 MET-h/week in 1991 to 264 MET-h/week in 2011 among adult men (a 31% decrease) and from 420 MET-h/week in 1991 to 243 MET-h/week in 2011 among adult women (a 42% decrease). Active physical activity (exercise) remained low – less than 7 MET-h/week for men and 3 MET-h/week for women in 2011.^[1]

A study conducted among 9 901 adolescents aged 11–18 from 10 cities showed that only 19.9% of them reached the recommended level of physical activity. The proportion of adolescents lacking in physical activity and the proportion of adolescents with insufficient physical activity were both about 40%^[2]. (Table 2–6–2).

Table 2–6–2 Physical Activity Levels among Adolescents aged 11–18 Years in 10 Cities (China)

Level of physical activity	Male (N=5 057)		Female (N=4 844)		Total (N=9 901)	
	N	%	N	%	N	%
None	1 605	31.7	2 345	48.4	3 950	39.9
Insufficient	2 185	43.2	1 794	37.0	3 979	40.2
Sufficient	1 267	25.1	705	14.6	1 972	19.9

Note: Estimation of PA was based on the self-reported number of days in a typical week in which respondents performed >60 min MVPA (moderates to vigorous physical activity). “none” (MVPA on 0 days), “insufficient” (MVPA on 1–4 days), and “Sufficient” (MVPA on >5 days).

2.6.2 Physical Inactivity and Cardiovascular Diseases

The China Multicenter Collaborative Study of Cardiovascular Epidemiology (China MUCA) and the China Cardiovascular Health Study analyzed data from 6 348 citizens aged 35 to 74 years old who were free of MI, stroke and diabetes at baseline, with an average follow-up period of 7.9 years. The study found that the baseline physical activity level was negatively associated with type 2 diabetes. Higher physical activity level was associated with a substantial reduction in the risk of type 2 diabetes (Table 2–6–3).^[3]

Table 2–6–3 Relative Risk for Type 2 Diabetes by Physical Activity Levels

	Physical Activity Level at Baseline (PAL)			
	1.00–1.39	1.40–1.59	1.60–1.89	>1.89
Incidence (1/1000 person-year)	11.45	8.55	9.85	8.54
RR*	1.00	0.92 (0.69–1.22)	0.67 (0.50–0.89)	0.59 (0.45–0.77)

Note: Cox regression adjusted for age, sex, geographic region, educational level, smoking, alcohol consumption, and family history of diabetes.
*: p for trend <0.0001.

[1] Ng S W, Howard A G, Wang H J, et al. The physical activity transition among adults in China: 1991–2011. *Obesity Reviews*. 2014, 15 (S1) : 27-36.

[2] Chen Y, Zheng Z, Yi J, et al. Associations between physical inactivity and sedentary behaviors among adolescents in 10 cities in China. *BMC public health*. 2014, 14 (1) : 744.

[3] Fan S, Chen J, Huang J, et al. Physical activity level and incident type 2 diabetes among Chinese adults. *Med Sci Sports Exerc*. 2015, 47 (4) :751-756.

Data from the Chronic Diseases and Risk Factors Surveillance Survey and the death registry system in Jiangxi province from 2007 to 2010 showed that comparing to sufficient physical activity, physical inactivity and low physical activity were both associated with higher risks of death from ischemic heart disease, ischemic stroke, and type 2 diabetes (Table 2–6–4) . If the proportion of insufficient physical activity was reduced by 50% or 30%, 3 678 or 2 090 deaths would have been avoided, and life expectancy would have increased by 0.40 or 0.23 years respectively.^[1]

Table 2–6–4 RR (95% CI) for CVD and Diabetes Deaths by Physical Activity Level

Physical Activity Level	Age Group	Outcomes		
		Ischemic Heart Disease	Ischemic Stroke	Type 2 Diabetes
Physical Inactivity	18 – 44	1.71 (1.58 – 1.85)	1.53 (1.31 – 1.79)	1.45 (1.37 – 1.54)
	45 – 69	1.71 (1.58 – 1.85)	1.53 (1.31 – 1.79)	1.45 (1.37 – 1.54)
	70 – 79	1.50 (1.38 – 1.61)	1.38 (1.18 – 1.60)	1.32 (1.25 – 1.45)
	>80	1.30 (1.21 – 1.41)	1.24 (1.06 – 1.33)	1.20 (1.14 – 1.28)
Low Physical Activity	18 – 44	1.44 (1.28 – 1.62)	1.10 (0.89 – 1.37)	1.24 (1.11 – 1.39)
	45 – 69	1.44 (1.28 – 1.62)	1.10 (0.89 – 1.37)	1.24 (1.11 – 1.39)
	70 – 79	1.31 (1.17 – 1.48)	1.08 (0.87 – 1.33)	1.18 (1.04 – 1.32)
	>80	1.20 (1.07 – 1.35)	1.05 (0.85 – 1.30)	1.11 (0.99 – 1.25)

Note: compared with sufficient physical activity.

The studies above show that the physical activity level of Chinese residents has significantly decreased, especially in occupational activities. Active physical exercise is an effective way to increase the amount of physical activity; however, the proportion of active physical exercise remains low. To improve this situation, action is needed throughout society to implement the “Nationwide Fitness Program (2011–2015)” developed by the National Health and Family Planning Commission, which aims to promote sports nationwide, invoking the residents' enthusiasm to exercise and improving conditions and facilities for physical exercise. This in turn will curb the prevalence of chronic diseases and promote the health conditions of residents.

2.7 Diet and Nutrition

2.7.1 Current Status and Trends of Nutrition and Health

The 2002 National Nutrition and Health Survey reports that dietary patterns in China have significantly changed. Some dietary changes were identified as detrimental to cardiovascular disease prevention, including the decrease in whole-grain food intake, the increase in fat intake, the decrease in energy contributions from

[1] Xu G, Sui X, Liu S, et al. Effects of Insufficient Physical Activity on Mortality and Life Expectancy in Jiangxi Province of China, 2007-2010. *PLoS one*. 2014, 9 (10) : e109826.

carbohydrates and the increase in energy contributions from fat^[1]. Moreover, fruit and vegetable consumption is still relatively low among Chinese population. Although the salt intake level has somewhat decreased, it still exceeds the recommended standard level significantly (the average intake of salt among Chinese population was about 15.9g/d according to the 2002 National Nutrition and Health Survey).

The CHNS has completed repeated investigations on the trends of nutrient intake of the same individuals in 9 provinces. The reports found that energy contributions from fat consumption have increased, exceeding the recommended contribution of 20%–30% of an average diet by far. The energy contribution from carbohydrates, meanwhile, has decreased to lower than the recommended level (55%–65%)(Table 2–7–1).^[2,3]

Table 2–7–1 Change in Proportion of Calories from Fat (>30%) and Carbohydrates (<55%) in 9 Provinces and Cities (China: 1989–2009)

Calorie Source	Survey Year							
	1989	1991	1993	1997	2000	2004	2006	2009
Aged 18–49								
Fat Calories >30%	35.8	30.3	28.9	32.7	42.2	40.6	51.5	55.0
Carbohydrate Calories <55%	30.4	26.2	25.9	27.3	34.8	35.1	48.3	53.1
Aged 6–17								
Fat Calories >30%	25.4	24.8	25.1	30.2	42.7	41.6	51.5	58.1
Carbohydrate Calories <55%	19.1	19.1	21	23.7	34.1	32.9	47.1	55.1

The CHNS also conducted 7 cross-sectional studies from 1989 to 2006 to investigate the changes in primary dietary patterns among people aged 18 to 59.^[4] The studies showed the following trends: decrease in whole-grain intake; increase in meat, poultry, and dietary oil intake; decrease in vegetable intake; and increase in fruit intake (Table 2–7–2). Similarly, among people aged 6–17, meat and fruit consumption increased and vegetable consumption decreased^[5,6]. With the exception of the trend in fruit consumption, other trends in dietary pattern changes from the CHNS were essentially the same to the results of the other three national nutrition surveys from 1982 to 2002.

[1] Zhai FY, Yan XG. Survey Report on the Status of Nutrition and Health of the Chinese People in 2002: Series Two, Status of Diet and Nutrients consumption. Beijing: People's Medical Publishing House, 2006. 7.

[2] Zhang B, Wang HJ, Du WM, et al. The trends of nutrients consumption of Chinese residents in nine Provinces from 1989 to 2009 (II): The general consumption trend of Chinese adults aged 18-49 years, *Acta Nutrimenta Sinica*, 2011, 33 (3): 237-242.

[3] Zhang B, Wang HJ, Su C, et al. Trend of energy consumption among Chinese children and adolescents in nine provinces from 1989 to 2009. *Chinese J of Preventive Medicine*, 2012; 46 (12): 1064 – 1068.

[4] Zhang B, Wang H, Du WM, et al. Food consumption trend of Chinese adults in nine provinces (autonomous region) from 1989 to 2006. *Chinese Journal of Preventive Medicine*, 2011, 45 (4): 330-334.

[5] Wang HB, Zhang B, Wang HJ, et al. Trend in meat consumption patterns among Chinese children in nine provinces (autonomous region) aged 6 to 17 years between 1991 and 2011. *Chin J Prev Med*. 2013,47 (9):826-831.

[6] Wang ZH, Zhang B, Wang HJ, et al. Trend in vegetable and fruit consumption among Chinese children and adolescents aged 6 to 17 years from 1991 to 2009 and related socio-demographic factors. *Chin J Epidemiol*. 2013,34 (9):863-868.

Table 2-7-2 Dietary Changes (g/day) among Resident Aged 18-59 in 9 Provinces and Cities (China: 1989-2006)

Food Type	Survey Year						
	1989	1991	1993	1997	2000	2004	2006
Male							
Whole Grain	552.8	537.0	529.2	535.8	477.9	490.7	466.3
Meat	97.0	102.9	113.4	114.2	125.2	131.1	141.5
Eggs	11.4	16.3	15.9	24.0	27.3	26.8	32.0
Dietary Oil	31.5	36.8	33.9	42.1	44.5	40.6	46.5
Vegetable	401.6	365.2	389.2	356.6	363.4	383.7	374.5
Fruit	124.6	92.9	126.4	145.9	137.4	133.8	229.1
Female							
Whole Grain	505.7	490.1	478.9	460.1	404.6	417.5	392.6
Meat	80.2	83.4	91.6	98.4	106.6	110.4	118.4
Eggs	10.8	14.7	14.0	23.2	25.8	25.1	29.9
Dietary Oil	29.5	32.8	30.2	37.1	38.7	36.0	39.5
Vegetable	385.3	338.37	363.5	336.5	337.1	354.7	346.4
Fruit	120.5	97.6	122.0	156.0	131.9	146.1	228.0

The CHNS analyzed the patterns and trends of dietary sodium and potassium intake among individuals aged 20-60 years old from 1991 to 2009^[7]. Results showed that sodium intake decreased significantly and potassium intake increased (P for both trends < 0.001), as seen in Table 2-7-3. Nevertheless, sodium intake remained at a high level of 4.7 g/day (the equivalent of the salt intake of 12.0 g/day), and potassium intake was still below the recommended amount of 2 g/day.

Table 2-7-3 Average Sodium Intake and Potassium Intake (g/day) among Individuals Aged 20-60 Years from 1991-2009 (\pm)

	Survey Year						
	1991	1993	1997	2000	2004	2006	2009
dietary Sodium	6.6 \pm 3.4	6.6 \pm 3.4	6.2 \pm 3.5	6.0 \pm 3.2	5.2 \pm 2.7	5.0 \pm 2.8	4.7 \pm 2.6
dietary Potassium	1.5 \pm 0.5	1.6 \pm 0.6	1.8 \pm 0.6	1.8 \pm 0.7	1.8 \pm 0.7	1.8 \pm 0.7	1.8 \pm 0.7

[7] Du S, Neiman A, Batis C, et al. Understanding the patterns and trends of sodium intake, potassium intake, and sodium to potassium ratio and their effect on hypertension in China. *Am J Clin Nutr*, 2014, 99 (2) : 334-343.

A survey was conducted among about 97 000 residences aged over 18 years old from 162 sites from the national disease surveillance system. Results showed that 60% of adults knew of the health benefits of reducing salt intake, and about 40% of them had actually taken actions. Both situations were better in urban areas than in rural areas (Table 2-7-4)^[1]. The increasing awareness rate and behavior changing rate were consistent with the sodium intake reduction observed in CHNS.

Table 2-7-4 Awareness and Behavior of Salt Reduction In China

	No. of Individuals	Awareness (%)	Behavior (%)
Urban	38 642	77.1*	56.5*
Rural	58 274	56.3	35.6
Total	96 916	62.9	42.2

Note: compared with rural, *: P<0.01.

2.7.2 Effects of Diet on CVD and Associated Risk Factors

134 000 participants (aged 40–74) were enrolled in two population-based prospective studies, the Shanghai Men’s Health Study (SMHS) and the Shanghai Women’s Health Study (SWHS), with average follow-up of 6.5 years and 12.0 years, respectively^[2]. Decreased risks for total mortality, cancer mortality, and diabetes mortality, as well as cardiovascular disease in men were observed in association with a higher adherence rate (CHFP score) (Table 2-7-5).

Table 2-7-5 RRs (95% CIs) for Cause-specific Mortality by Quartiles of Dietary Recommendation Adherence Scores

	Quartile of Dietary Recommendation Adherence Scores				P. Trend
	1	2	3	4	
Male (n=61 239)					
Total Mortality	1.00	0.78 (0.71–0.86)	0.77 (0.69–0.85)	0.67 (0.60–0.75)	<0.005
CVD Mortality	1.00	0.73 (0.62–0.87)	0.68 (0.57–0.81)	0.54 (0.45–0.66)	<0.005
Cancer Mortality	1.00	0.82 (0.71–0.96)	0.88 (0.75–1.02)	0.83 (0.70–0.97)	0.02
Diabetes Mortality	1.00	0.83 (0.52–1.32)	0.53 (0.30–0.96)	0.58 (0.31–1.10)	0.02
Female (n=73 216)					
Total Mortality	1.00	0.99 (0.92–1.07)	0.95 (0.88–1.04)	0.87 (0.80–0.95)	0.004
CVD Mortality	1.00	0.94 (0.82–1.08)	0.88 (0.76–1.03)	0.88 (0.75–1.03)	0.06
Cancer Mortality	1.00	1.02 (0.90–1.15)	0.99 (0.87–1.12)	0.89 (0.77–1.02)	0.11
Diabetes Mortality	1.00	0.91 (0.68–1.20)	0.90 (0.65–1.23)	0.73 (0.51–1.05)	0.11

Note: Cox proportional hazards model was adjusted for age; education; income; smoking; alcohol consumption; multi-vitamin use; menopausal status and hormone therapy (for women only); physical activity; BMI; waist-to-hip ratio; history of cardiovascular disease, diabetes, or hypertension; and total energy intake.

[1] Xu JW, Yan LX, Chen XR, et al. Investigation on knowledge, attitude and behavior of salt reduction in Chinese adults (2010). Chinese Journal of Preventive Medicine, 2014, 48 (5) :350-354.

[2] Yu D, Zhang X, Xiang Y B, et al. Adherence to dietary guidelines and mortality: a report from prospective cohort studies of 134,000 Chinese adults in urban Shanghai. Am J Clin Nutr, 2014, 100 (2) : 693-700.

Another prospective population-based study showed that during a mean follow-up of 9.8 years in women and 5.4 years in men, women in the highest quartile of total fruit and vegetable intake (median: 814 g/d) had a hazard ratio (HR) for CHD of 0.62 (38% lower than the mean ratio) compared with those in the lowest quartile (median: 274 g/d, P for trend=0.04). A similar association was discovered for fruit and vegetable intake in men but there was no statistical significance. (Table 2-7-6)^[1]

Table 2-7-6 RR of Incident Coronary Heart Disease by Fruit and Vegetable Intake

	Quartile				P. Trend
	Q1	Q2	Q3	Q4	
Female (n=67 211)					
Median Intake (g/d)	274	432	581	814	
No. of Cases	60	35	29	24	
RR	1.00	0.74 (0.48-1.12)	0.68 (0.43-1.07)	0.62 (0.38-1.02)	0.04
Male (n=55474)					
Median Intake (g/d)	242	379	507	722	
No. of Cases	65	51	47	54	
RR	1.00	0.80 (0.55-1.16)	0.75 (0.51-1.10)	0.85 (0.58-1.25)	0.45

Note: Cox model was adjusted by birth cohort (5-year intervals) and adjusted for baseline age, BMI, income, education, smoking, alcohol drinking, physical activity, use of aspirin, vitamin E and multi-vitamin supplements, (in women only: menopause and hormone replacement therapy), total energy and intakes of red meat and fish/shellfish.

By conducting a prospective observational study among individuals without hypertension at baseline, the CHNS found that high sodium intake and low potassium intake have significant associations with a high risk of incident hypertension (Table 2-7-7)^[2].

Table 2-7-7 RRs (95% CI) for Incident Hypertension by Quintiles of Sodium Intake and Potassium Intake (g/day)

	Quintiles of Intake				
	1	2	3	4	5
Sodium Intake	<3.2	3.2-4.3	4.4-5.5	5.6-7.5	>7.6
RR	1.00	0.99 (0.84-1.18)	1.20 (1.01-1.42)	1.37 (1.16-1.62)	1.84 (1.56-2.16)
Potassium Intake	<1.2	1.2-1.4	1.5-1.7	1.8-2.1	>2.2
RR	1.00	0.83 (0.71-0.97)	0.94 (0.80-1.10)	0.74 (0.63-0.87)	0.66 (0.56-0.78)

Note: Model were adjusted for energy intake, age, sex, education, income, region, BMI, physical activity, smoking status, and alcohol consumption. Additionally, RRs were adjusted for sodium intake.

A meta-analysis of six randomized controlled trials (5 from China) was conducted to evaluate the effect

[1] Yu D, Zhang X, Gao YT, et al. Fruit and vegetable intake and risk of CHD: results from prospective cohort studies of Chinese adults in Shanghai. *Br J Nutr*, 2014, 111 (2) :353-362.

[2] Du S, Neiman A, Batis C, et al. Understanding the patterns and trends of sodium intake, potassium intake, and sodium to potassium ratio and their effect on hypertension in China. *Am J Clin Nutr*, 2014, 99 (2) : 334-343.

of long term low-sodium salt intake on lowering blood pressure. Pooled analysis results showed that low-sodium salt intake had a significant effect on SBP (mean difference: -4.9 mm Hg, $P < 0.001$) and DBP (mean difference: -1.5 mm Hg, $P = 0.013$)^[1].

Evidence from previous studies showed that since the 1980s, dietary patterns have been changing significantly in China. Although the salt intake has decreased (but still remains twice as much as the recommended amount), and the fruit consumption has increased, other dietary changes that are detrimental to the prevention and control of chronic diseases still persist, and even show worsening trends (e.g. imbalance of energy contributions, decrease in vegetable intake, etc.). To prevent chronic diseases, including cardiovascular diseases, the government, health departments, and the public should take this issue seriously and work together to promote dietary guidelines and optimize residents' dietary patterns.

2.8 Metabolic Syndrome (MS)

To date, the reported and commonly referred guidelines of criteria for MS diagnosis include the China Diabetes Society (CDS) for MS, the Joint Committee for Developing Chinese Guidelines on Prevention & Treatment of Dyslipidemia in Adults (GCDCJ), the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III), and the guidelines from the International Diabetes Federation (IDF).

2.8.1 Prevalence of Metabolic Syndrome

2.8.1.1 Prevalence of Metabolic Syndrome in Adults from Different Regions

The 2002 China Health and Nutrition Survey reported that the prevalence of MS in adults above 18 years of age was 6.6% and 13.8%, respectively, based on criteria from the CDS and the NCEP-ATP III (Table 2-8-1). The prevalence of MS in different regions, the different characteristics in populations and the different standard definitions of MS are listed in Table 2-8-1. Subjects at Karamay, Xinjiang included populations of Han, Uyghurs and Kazakhs, in which the prevalence of MS (GCDCJ standard) was 38.8%, 42.9% and 46.7%, respectively. There was no statistical significance among three ethnic populations ($P > 0.05$).

[1] Peng Y G, Li W, Wen X X, et al. Effects of salt substitutes on blood pressure: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*, 2014, 100 (6) : 1448-1454.

Table 2-8-1 Prevalence of MS in Different Regions (%)

Region	Year	Age	Population	Sample	Prevalence (%)				
					NCEP	CDS	GCDCJ	IDF	ATP III
Nantong ^[1]	2007-2008	18-74	Peasant	20 502				21.1	
Xinjiang ^[2]	2007-2010	>35	Community Resident	3 821			39.3		
Northeast ^[3]	2009-2010	18-74	Community Resident	15 477	27.4				
Jiangsu ^[4]	2010	>18	Community Resident	8 400		18.4	22.8	29.5	37.3
Chongqing ^[5]	2011-2012	>35	Community Resident	5 384				20.28	
Gansu ^[6]	2012-2013	18-96	Community Resident	6 609		13.42			30.43
Dongguan ^[7]		>18	Perimenopausal Andpostmenopausal Women	3 391		23.5			

2.8.1.2 Prevalence of MS in Children and Adolescents

Study was conducted via stratified sampling among 2 125 children with ages ranging from 10 to 15 years in Zhejiang province. Prevalence of MS was 2.0% according to the criteria from the Chinese Children MS Standard and Prevention Advice (2012) (MS-CHN2012) Standard.^[9]

For middle-school adolescents in northeast China, the prevalence of MS was 7.6% according to the guideline for children suggested by the International Diabetes Federation.^[9]

A review^[10] that summarized nineteen reports published during 2004-2014 describing the prevalence of metabolic syndrome in Chinese children and adolescents between of 16 and 20, indicated that the prevalence

[1] Xiao J, Huang JP, Xu GF, et al. Association of alcohol consumption and components of metabolic syndrome among people in rural China. *Nutr Metab (Lond)*, 2015 Feb 28; doi: 10.1186/s12986-015-0007-4. eCollection 2015.12:5.

[2] Xiang Y, Hu YY, Xiao P, et al. The prevalence of metabolic syndrome in Han and Uyghur adults in Keramay. *Journal of Xinjiang Medical University*. 2015, 37 (12) : 1561-1563.

[3] Song QB, Zhao Y, Liu YQ, et al. Sex difference in the prevalence of metabolic syndrome and cardiovascular-related risk factors in urban adults from 33 communities of China: The CHPSNE study *Diab Vasc Dis Res*, 2015,12 (3) :189-198.

[4] Tao R, Wu M, Tan Y, et al. Jiangsu province adult metabolic syndrome epidemic characteristics and comparison among different diagnostic standard. *Journal of Jilin University (Medicine edition)* . , 2015, 41 (1) :181-189.

[5] Deng M, Deng HC, Wang H, et al. Metabolic syndrome epidemic survey in adults over 35 years in Chongqing. *Zhonghua nei fen mi dai xie za zhi*. 2014, 30 (9) :760-764.

[6] Metabolic syndrome survey among health check adults in five cities from Gansu province. *Zhonghua liu xing bing xue za zhi*. 2014,35 (9) :1015-1019.

[7] Luo XQ, Huang H, Peng GC, et al. The prevalence of the metabolic syndrome and its risk factors among perimenopausal and postmenopausal women in Dongguan East region. *Maternal and Child Health Care of China*, 2015, 30 (13) :2030-2033.

[8] Qiu JF, Children and adolescents obesity and metabolic syndrome epidemiological study in Zhejiang longquan mountains region. *Chinese Journal of Primary Medicine and Pharmacy*, 2015,8:1139-1142.

[9] Li P, Jiang R, Li L, et al. Prevalence and risk factors of metabolic syndrome in school adolescents of northeast China. *J Pediatr Endocrinol Metab*, 2014, 27 (5-6) :525-532.

[10] Ye P, Yan Y, Ding W, et al. Prevalence of metabolic syndrome in Chinese children and adolescents: a Meta-analysis. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2015 Aug; 36 (8) :884-888.

rate of MS in Chinese children was 1.8%, 2.6% and 2.0%, according to International Diabetes Federation (IDF), National Cholesterol Education Program III (NCEP III) and based on the definition and prevention recommendations of metabolic syndrome in Chinese children and adolescents (MS-CHN2012).

The prevalence rates of metabolic syndrome in children and adolescents from different studies are shown in Table 2-8-2.

Table 2-8-2 Prevalence of MS in Children and Adolescents by Study (%)

Region	IDF	NCEP III	MS-CHN2012
Zhejiang ^[1]			2.0
Obesity			42.0
Northcast ^[2]	7.6		
Male	10.9		
Female	3.8		
Meta analysis ^[3]	1.8	2.6	2.0
Male	2.9	7.1	2.4
Female	1.8	5.2	1.5
Normal Weight	0.2	0.7	0.
Overweight	4.7	6.6	9.6
Obesity	17.3	26.7	19.6

2.8.2 Risk Factors of Metabolic Syndrome

A study performed from 2009–2010 among 15 477 urban adults aged 18 to 74 years of age in northeast China indicated that men with higher levels of physical activity displayed a lower prevalence of metabolic syndrome [adjusted odds ratios (aORs) = 0.88, 95% confidence interval (CI) : 0.79–0.99], while women with higher levels of physical activity displayed a higher prevalence of metabolic syndrome (aOR = 1.14, 95% CI: 1.00–1.29). Compared with the population consuming rice as a staple food, cooked wheat foods were associated with lower adjusted odds for metabolic syndrome in both men (aOR = 0.72, 95% CI: 0.58–0.90) and women (aOR = 0.72, 95% CI: 0.56–0.92).^[4]

A study during 2007–2008 in Nantong was conducted among 20 502 participants. The MS prevalence in women was significantly lower for drinkers (20.6%) than non-drinkers (23.6%). No significant association was observed between the MS prevalence in male drinkers and non-drinkers (16.4% versus 17.1%)^[5].

[1] Qiu JF, Children and adolescents obesity and metabolic syndrome epidemiological study in Zhejiang longquan mountains region. *Chinese Journal of Primary Medicine and Pharmacy*, 2015, 8:1139-1142.

[2] Li P, Jiang R, Li L, et al. Prevalence and risk factors of metabolic syndrome in school adolescents of northeast China. *J Pediatr Endocrinol Metab*, 2014, 27 (5-6) :525-532.

[3] Ye P, Yan Y, Ding W, et al. Prevalence of metabolic syndrome in Chinese children and adolescents: a Meta-analysis. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2015; 36 (8) :884-888.

[4] Song QB, Zhao Y, Liu YQ, et al. Sex difference in the prevalence of metabolic syndrome and cardiovascular-related risk factors in urban adults from 33 communities of China: The CHPSNE study *Diab Vasc Dis Res*, 2015, 12 (3) :189-198.

[5] Xiao J, Huang JP, Xu GF, et al. Association of alcohol consumption and components of metabolic syndrome among people in rural China. *Nutr Metab (Lond)*, 2015 Feb 28; doi: 10.1186/s12986-015-0007-4. eCollection 2015.12:5.

2.9 Air Pollution

In recent years, numerous studies have concluded that particulate matter (PM) especially PM_{2.5} (fine particulate matter) is a risk factor for CVD^[1]. PM_{2.5} is identified as a major pathogenic composition in PM, which is more closely related to CVD^[2,3]. Many of the most recent studies were conducted to investigate the association between short-term exposure to air pollution (a few hours to a few days) and CVD mortality, incidence, treatment, etc. In China, several studies have demonstrated an association between PM_{2.5}, sulfur dioxide (SO₂), oxynitride (NO_x) and CVD^[4].

2.9.1 Short-Term Effects of Air Pollution on CVD

(1) The relationship between PM_{2.5} concentration and CVD mortality

In select cities in China, several studies have found a relationship between increases of 10 $\mu\text{g}/\text{m}^3$ or 100 $\mu\text{g}/\text{m}^3$ in average daily concentrations of PM_{2.5} and CVD mortality. Study results published over the past ten years are summarized in Table 2-9-1.

Table 2-9-1 Relationship between PM_{2.5} Concentrations and CVD Mortality

Monitoring Time	Regions	Average Concentrations	Outcome Indicator/No.	CVD Risk Resulting from 10 $\mu\text{g}/\text{m}^3$ Increases of SO ₂ or NO ₂ Concentrations (95% CI)
2004-2005	Guanghzou ^[5]	56.4 $\mu\text{g}/\text{m}^3$	Total Mortality /79 530	Every 10 $\mu\text{g}/\text{m}^3$ increase, mortality of CVD increases 0.41% (0.01%, 0.82%) .
2004-2008	Chaoyang District in Beijing ^[6]	178.7 $\mu\text{g}/\text{m}^3$	—	Every 10 $\mu\text{g}/\text{m}^3$ increase, mortality of CVD increases 0.27% (0.08%, 0.46%) , mortality of coronary heart diseases increases 0.39% (0.14%, 0.65%) .
2004-2008	ShanXian ^[7]	Median 2004 184.9 $\mu\text{g}/\text{m}^3$ 2005 194.9 $\mu\text{g}/\text{m}^3$ 2006 206.8 $\mu\text{g}/\text{m}^3$ 2007 193.7 $\mu\text{g}/\text{m}^3$ 2008 179.1 $\mu\text{g}/\text{m}^3$	Mortality /22 051	Every 100 $\mu\text{g}/\text{m}^3$ increases, mortality of CVD, coronary heart diseases and stroke increases 6.18%, 8.23% and 5.13%, respectively.

[1] Brook RD, Rajagopalan S, Pope CA 3rd, et al. Particulate matter air matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation*,2010,121 (21) :2331-2378.

[2] Wan Z, Bian B, Particulate matter air pollution: independent risk factors for cardiovascular diseases. *Chinese Journal of Evidence-based Cardiovascular Medicine*, 2011, 3 (5) : 332-335.

[3] Qin G, Lv JY. Research progress of particulate matter air pollution and atherosclerosis. *Chinese Journal of Cardiology*, 2011, 39(3) : 282-284.

[4] Shang Yu, Sun Z ,Cao J, et al. Systematic review of Chinese studies of short-term exposure to air pollution and daily mortality. *Environ Int*, 2013, 54:100-111.

[5] Kan H, London SJ, Chen G, et al. Differentiating the effects of fine and coarse particles on daily mortality in Shanghai, China. *Environ Int*, 2007, 33:376-384.

[6] Huang W,Cao J, Tao Y, et al. Seasonal variation of chemical species associated with short-term mortality effects of PM (2.5) in Xi'an, a Central City in China. *Am J Epidemiol*,2012,175 (6) :556-66.

[7] Zhao K, Cao JY, Wen XM. Correlation Between PM_{2.5} Pollution in Air and Mortality of Residents in Urban Area, Xi'an.[Chinese] *Journal of Preventive Meicine Information* 2011, 27 (4) : 257-262.

Table 2-9-1 Relationship between PM_{2.5} Concentrations and CVD Mortality (Continued)

Monitoring Time	Regions	Average Concentrations	Outcome Indicator/No.	CVD Risk Resulting from 10 μ g/m ³ Increases of SO ₂ or NO ₂ Concentrations (95% CI)
2006-2008	Shenyang ^[1]	75 μ g/m ³	Total Mortality/60 938	Every 10 μ g/m ³ increases, mortality of CVD increases 0.53% (0.09%, 0.97%); mortality of CVD in population aged \geq 75 years old increases 0.64% (0.02%, 1.24%)
2007-2008	Guangzhou ^[2]	70.1 μ g/m ³	Total Mortality/58 400	Every 10 μ g/m ³ increases, mortality of CVD increases 1.22% (0.63%, 1.68%) .
2006-2011	Shanghai ^[3]	55 μ g/m ³	Mortality of Out-of-hospital Coronary Heart Diseases /18 202	Every 10 μ g/m ³ increases, mortality of out-of-hospital coronary heart diseases increases 0.68% (0.14%, 1.21%) .
2010-2012	Beijing ^[4]	96.2 μ g/m ³	Mortality of Ischemic Heart Diseases /53 247	Every 10 μ g/m ³ increases, mortality of ischemic heart diseases increases 0.25% (0.10%, 0.40%)

(2) Relationship between PM_{2.5} concentration and CVD morbidity

The majority of CVD patients survive the acute phase of their disease due to prompt treatment. Therefore mortality cannot completely reflect the short-term effects of air pollutants on this kind of disease. In 2015, researchers published a study that investigated the relationship between PM_{2.5} concentration and 369 469 ischemic heart disease (IHD) events from 2010 to 2012 in Beijing. The researchers found that^[4] the mean daily PM_{2.5} concentration was 96.2 μ g/m³ in Beijing and that a 10 μ g/m³ increase in PM_{2.5} concentration was associated with a 0.27% (95% CI: 0.21%, 0.33%) increase in IHD morbidity. A significant hysteresis effect associated with PM_{2.5} and IHD morbidity was also observed. It showed that IHD morbidity would continue to increase one, two and three days after initial exposure to PM_{2.5} air pollution. Additionally, this study found that people aged \geq 65 years were more susceptible to PM_{2.5}: a significantly stronger association between same-day PM_{2.5} exposure and IHD morbidity on the same day was observed for people aged \geq 65 years.

(3) The relationship between sulfur dioxide (SO₂), oxynitride (NO_x) and CVD

Studies on the relationship between sulfur dioxide (SO₂), nitrogen dioxide (NO₂) and CVD from the past decade are summarized in Table 2-9-2.

[1] Yang C, Peng X, Huang W, et al. A time-stratified case-crossover study of fine particulate matter air pollution and mortality in Guangzhou, China. *Int Arch Occup Environ Health*, 2012, 85 (5) :579-585.

[2] Dai J, Chen R, Meng X, et al. Ambient air pollution, temperature and out-of-hospital coronary deaths in Shanghai, China. *Environ Pollut*, 2015, 203:116-121.

[3] Xie W, Li G, Zhao D, et al. Relationship between fine particulate air pollution and ischaemic heart disease morbidity and mortality. *Heart*, 2015, 101:257-263.

[4] Xie WX, Li G, Zhao D, et al. Relationship between fine particulate air pollution and ischemic heart disease morbidity and mortality. *Heart*, 2015, 101 (4) : 257-263.

Table 2-9-2 Studies on the Relationship between Sulfur Dioxide (SO₂), Nitrogen Dioxide (NO₂) and CVD

Monitoring Time	Regions	Average Concentrations	Outcome Indicator/No.	CVD Risk Resulting from 10µg/m ³ Increases of SO ₂ or NO ₂ Concentrations (95% CI)
2006-2007	Guangzhou ^[1]	SO ₂ - NO ₂ -	Person-time of Emergency Patients with CVD/9 901	Person-time of emergency patients with CVD increases 1.17% (0.41%, 1.94%); Person-time of emergency patients with CVD increases 1.28% (0.5%, 2.06%). Circulatory system deaths increase 0.36% (-0.13%, 0.85%); Circulatory system deaths increase 0.30% (-0.34%, 0.94%)
2004-2008	Chaoyang District in Beijing ^[2]	SO ₂ 63.9µg/m ³ NO ₂ 146.1µg/m ³	Circulatory System Deaths/19 241	Mortality of CVD increases 0.822% (0.17%, 1.48%); Mortality of CVD increases 0.28% (-0.45%, 1.01%).
2006-2009	Wuhan ^[4]	SO ₂ 53.2µg/m ³ NO ₂ 53.1µg/m ³	CVD Mortality Events/8 955	CVD mortality risk (RR) is 1.01 (1.000, 1.020); CVD mortality risk (RR) of people aged >65 years is 1.016 (1.001, 1.031); CVD mortality risk (RR) is 1.019 (1.005, 1.033).
2006-2011	Shanghai ^[5]	SO ₂ 53µg/m ³ NO ₂ 62µg/m ³	Mortality of Out-of-hospital Coronary Heart Diseases/18 202	Mortality of out-of-hospital coronary heart diseases increases 0.88% (0.14%, 1.62%); Mortality of out-of-hospital coronary heart diseases increases 1.60% (0.72%, 2.48%).
2010-2012	Shanghai ^[6]	SO ₂ 30µg/m ³ NO ₂ 56µg/m ³	Person-time of Emergency Patients with Coronary Heart Diseases/47 523	Emergency patients with coronary heart diseases increased 0.90% (-0.14%, 1.93%); Emergency patients with coronary heart diseases increased 1.44% (0.63%, 2.26%).

2.9.2 Long-Term Effects of Air Pollution on CVD

Some studies have also addressed the long-term effects of air pollution on CVD^[7]. The long-term effects of air pollution on CVD should be evaluated using a cohort study, but domestic investigations are scant. In the China National Hypertension Survey and its follow-up study^[8], investigators used zip codes to link fixed air quality monitoring sites to measure suspended particle (TSP), sulfur dioxide (SO₂) and nitrogen oxide

- [1] Ma YH, Li SM, Zeng ZH, et al. Relationship between air pollution and cardiovascular emergency visits in Guangzhou: a time-series study.[Chinese] *Journal of Environment and Health*, 2013, 30 (11) : 977-980.
- [2] Zhang JY, Meng HY, Zhang GB, et al. Relationship between Air Pollution and Daily Respiratory System Disease Mortality in Chaoyang District, Beijing: a Time-series Analysis.[Chinese] *Journal of Environment and Health*, 2011, 28 (9) : 788-791.
- [3] Yang C, Peng X, Huang W, et al. A time-stratified case-crossover study of fine particulate matter air pollution and mortality in Guangzhou, China. *Int Arch Occup Environ Health*, 2012, 85 (5) : 579-585.
- [4] Yisi L, Xi C, Shuqiong H, et al. Association between Air Pollutants and Cardiovascular Disease Mortality in Wuhan, China. *Int. J. Environ. Res. Public Health*, 2015, 12: 3506-3516.
- [5] Xie J1, He M, Zhu W. Acute effects of outdoor air pollution on emergency department visits due to five clinical subtypes of coronary heart diseases in shanghai, china. *J Epidemiol*, 2014, 24 (6) : 452-459.
- [6] Dai J, Chen R, Meng X, et al. Ambient air pollution, temperature and out-of-hospital coronary deaths in Shanghai, China. *Environ Pollut*, 2015, 203:116-121.
- [7] Qin G, Lv JY. Research progress of particulate matter air pollution and atherosclerosis. *Chinese Journal of Cardiology*, 2011, 39(3) : 282-284.
- [8] Cao J, Yang C, Li J, et al. Association between long-term exposure to outdoor air pollution and mortality in China: a cohort study. *J Hazard Mater*, 2011, 186:1594-1600.

(NO_x) levels. They then analyzed the relationship between baseline air pollution exposure and CVD mortality by combining results from a long-term follow-up on 70 947 subjects (from 1991 to 2000). They found that baseline air pollution exposure was strongly associated with CVD mortality: each 10 μg/m³ elevation in TSP, SO₂, and NO_x levels was associated with a 0.9% (95%CI: 0.3%–1.5%), 3.2% (95%CI: 2.3%–4.0%), and 2.3% (95%CI: 0.6%–4.1%) increased risk of CVD mortality, respectively. The results of a cohort study^[1] in Shenyang city that followed up on 24 845 individuals from three regions (Shenyang, Anshan, and Jinzhou) for an average of 3 years found that for every 20 μg/m³ increase in baseline SO₂ concentrations, the prevalence rate of hypertension in men increased by 19% (OR=1.19; 95%CI: 1.05–1.34), but no statistical significance was found in women. A cohort study in Hong Kong^[2] analyzed the relationship between baseline air pollution exposure in 66 820 participants >64 years old (from 1998 to 2001) and CVD mortality after 10–13 years (2011) of follow up. The results indicated that for each 10 μg/m³ increased in PM_{2.5}, CVD mortality increased by 22% (HR 1.22, 95%CI 1.08–1.39), IHD mortality increased 42% (HR 1.42, 95%CI 1.16–1.73), and mortality from cerebrovascular disease increased 24% (HR 1.24, 95%CI 1.00–1.53).

2.9.3 A Randomized, Double blind, Crossover Trial on Indoor Particulate Matter Reduction and Cardiopulmonary Function

In 2014, some investigators conducted a randomized, double-blind crossover trial of indoor particulate matter reduction and cardiopulmonary function in Shanghai city^[3]. This study enrolled 35 healthy college students that were randomized into two groups and alternated using functional or non-functional air purifiers for 48 h in a two week interval. The study results indicated that when using air purification, indoor PM_{2.5} concentration was reduced from 96.2 mg/m³ to 41.3 mg/m³; systolic BP and diastolic BP decreased by 2.7% and 4.8%, respectively; the exhaled carbon monoxide decreased by 17%, and several circulating inflammatory markers and thrombosis biomarkers decreased. This study demonstrated that the cardiorespiratory function of healthy young people could benefit from indoor air purification.

Although many epidemiological studies have shown that particulate matter levels are related to CVD events, most studies have been observational studies and more experimental studies are needed to further investigate the relationship between air pollution and CVD.

[1] Dong GH, Qian ZM, Xaverius PK, et al. Association between long-term air pollution and increased blood pressure and hypertension in China[J]. *Hypertension*, 2013, 61 (3) :578-584.

[2] Wong CM, Lai HK, Tsang H, et al. Satellite-Based Estimates of Long-Term Exposure to Fine Particles and Association with Mortality in Elderly Hong Kong Residents. *Environ Health Perspect*, 2015, 123 (11) :1167-1172.

[3] Chen R, Zhao A, Chen H, et al. Cardiopulmonary benefits of reducing indoor particles of outdoor origin: a randomized, double-blind crossover trial of air purifiers. *J Am Coll Cardiol*, 2015, 65 (21) : 2279-2287.

Part 3

Cardiovascular Diseases

3.1 Cerebrovascular Disease

3.1.1 The Prevalence, Mortality and Trends of Cerebrovascular Disease in China

(1) National Health Service Survey^[1]

The Ministry of Health has been conducting a National Health Service Survey every five years since 1993, and four surveys have been fielded as of 2008. According to the results of the four surveys, the prevalence of stroke increases rapidly. Stroke prevalence rates are higher in urban populations than rural ones (Figure 3-1-1).

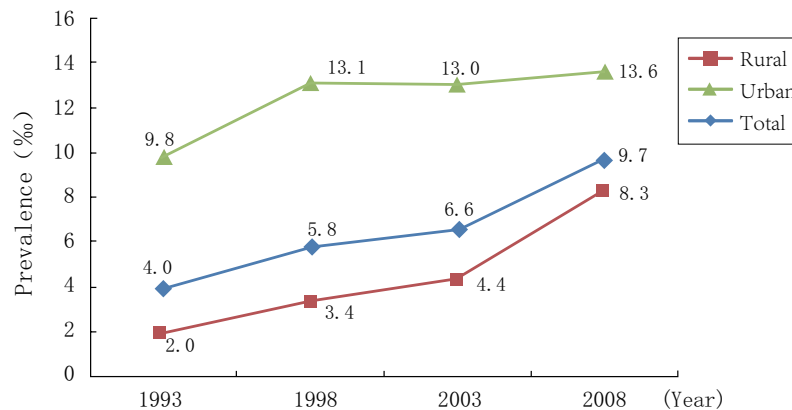


Figure 3-1-1 Stroke Prevalence in Urban and Rural Populations (China: 1993-2008)

(2) Cerebrovascular Disease Mortality in 2014^[2]

According to China Health Statistics Yearbook 2015, the mortality rate of cerebrovascular diseases for urban residents in 2014 was 125.78 per 100 000, and mortality rates from cerebral hemorrhage and cerebral infarction were 52.25 per 100 000 and 41.99 per 100 000, respectively. The mortality rate from cerebrovascular diseases was 151.91 per 100 000 in rural areas, and the mortality rates from cerebral hemorrhage and cerebral infarction were 74.51 per 100 000 and 45.30 per 100 000 respectively.

Based on the data from the Sixth National Population Census, 837 300 urban residents and 1 023 400

[1] Statistics Information Centre of Ministry of Health. China Health Service Survey. Peking Union Medical College Press.

[2] National Health and Family Planning Commission of the People's Republic of China. China Health and Family Planning Statistics Yearbook 2015. Peking Union Medical College Press, Beijing.

rural residents died from cerebrovascular diseases in 2014. In general the mortality rate was higher in rural areas than urban areas, and higher in men than in women (Figure 3-1-2).

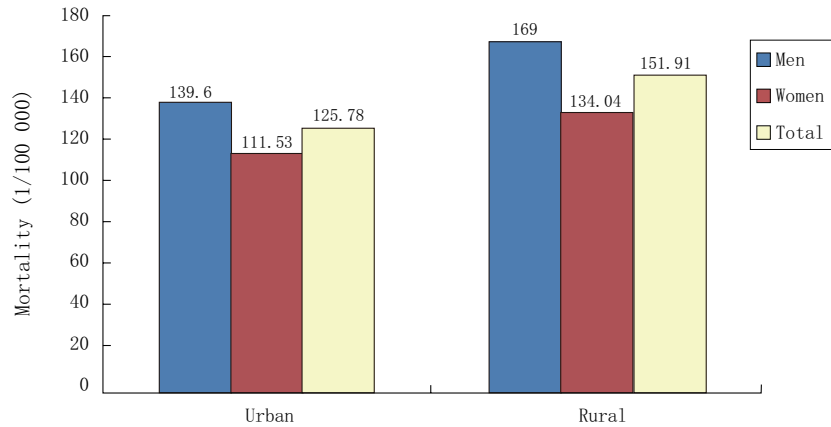


Figure 3-1-2 Stroke Mortality by Gender and Region (China: 2014)

(3) Cerebrovascular Disease Mortality by Gender and Age in 2014 (1/100 000)

The mortality rate from cerebrovascular diseases increased exponentially with age in both urban and rural areas. Mortality rates were higher for men than women across all age ranges, and higher in rural areas than in urban areas (Figure 3-1-3, Figure 3-1-4, Table 3-1-1, Table 3-1-2).

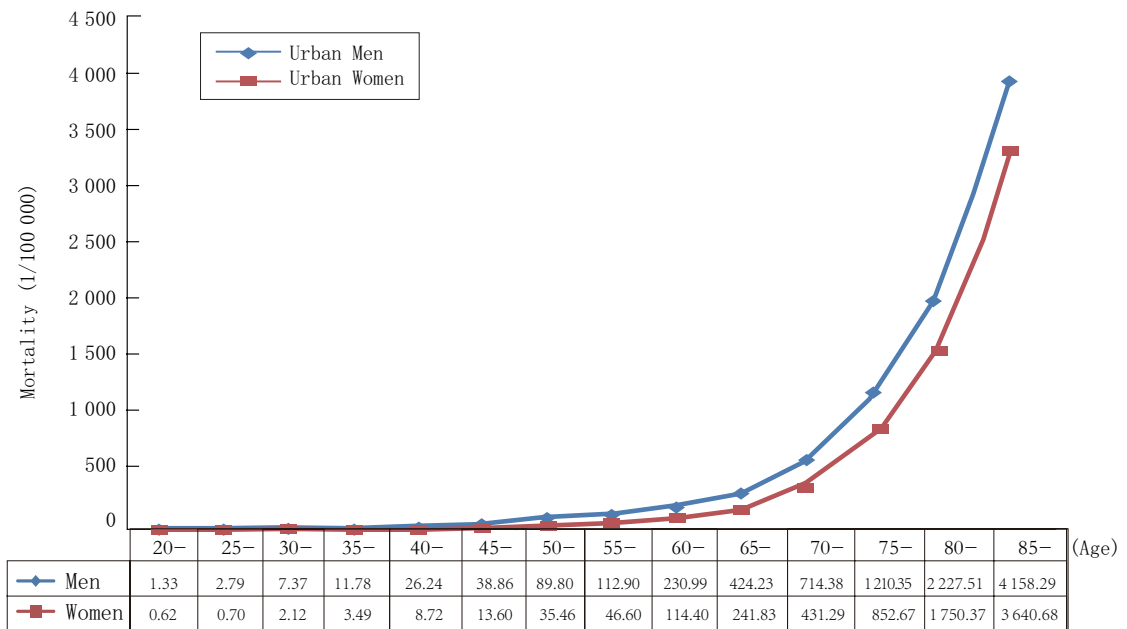


Figure 3-1-3 Stroke Mortality in the Urban Population by Gender and Age (China: 2014)

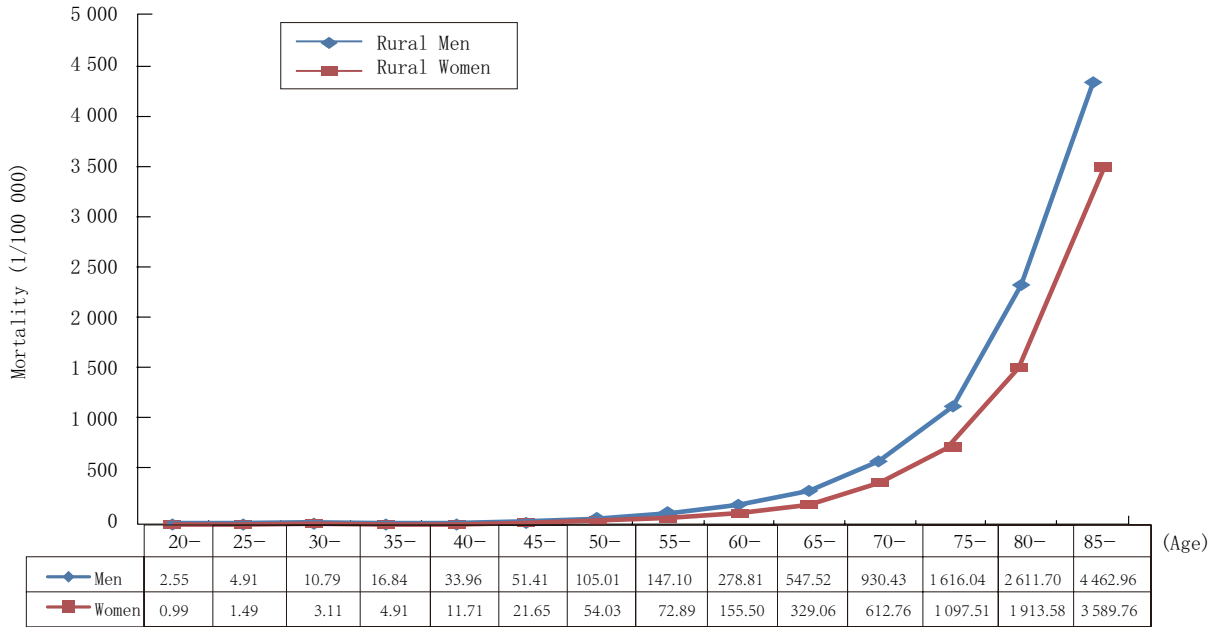


Figure 3-1-4 Stroke Mortality in the Rural Population by Gender and Age (China: 2014)

(4) Trends in Cerebrovascular Disease Mortality from 2003 to 2014

In general, cerebrovascular disease mortality rates were higher in rural areas than in urban areas from 2003 to 2014 (Figure 3-1-5).

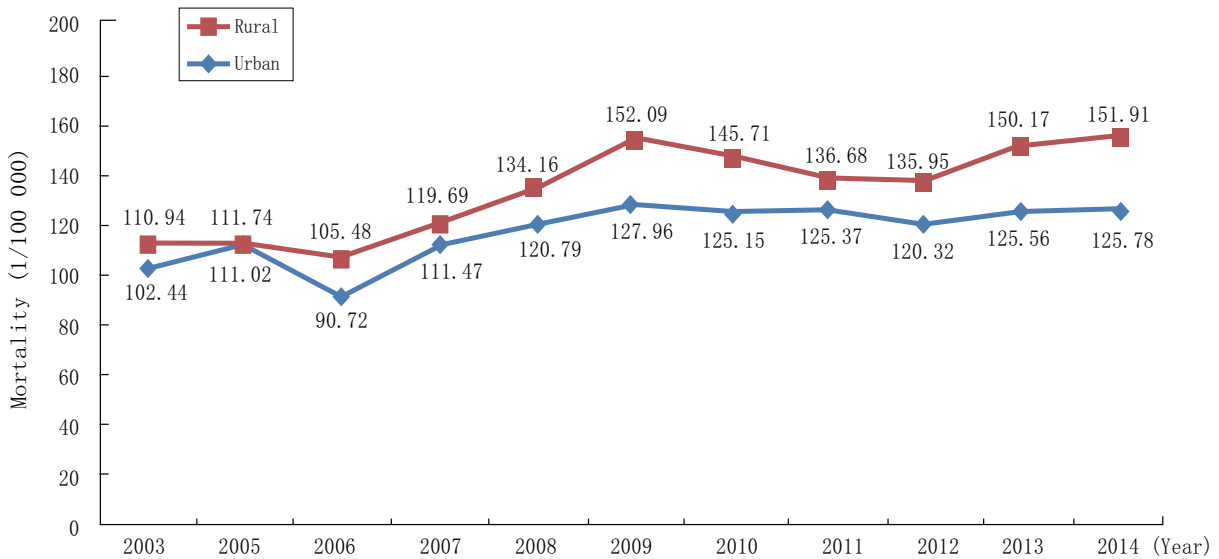


Figure 3-1-5 Trends in Stroke Mortality (China: 2003-2014)

(5) Trends in In-hospital Mortality among Patients with Stroke in China^[1]

A study recruiting the patients admitted to 109 grade III class A hospitals during 2007–2010 with a discharge diagnosis of stroke, assessed the trends in in-hospital mortality and influence factors. Overall stroke hospitalizations increased from 79 894 in 2007 to 85 474 in 2010, and in-hospital mortality of stroke decreased from 3.16% in 2007 to 2.30% in 2010. Compared with 2007, the mortality rate decreased for all types of strokes, including subarachnoid hemorrhage (OR 0.792, 95% CI=0.636 to 0.987), intracerebral hemorrhage (OR 0.647, 95% CI=0.591 to 0.708), and ischemic stroke (OR 0.588, 95% CI=0.532–0.649). Multivariable analyses indicated that age, male sex, no basic health insurance coverage, having multiple comorbidities and severity of disease were associated with higher odds of in-hospital mortality.

(6) Study on Survival Rate and Risk Factors of Mortality among First-ever Stroke Patients^[2]

In 2009, the Zhejiang Provincial Information System for Non-Communicable Diseases Surveillance and Management recruited and registered a total of 78 189 first-ever stroke patients. Patients with cerebral infarctions, intracerebral hemorrhages, subarachnoid hemorrhages and unspecified strokes respectively accounted for 61.65%, 30.42%, 2.32% and 5.62% of the sample. Survival status and cause of death were obtained from follow-up. Kaplan–Meier methods were employed for survival description. Mono-variant and multi-variant Cox's proportional hazard regression models were used to analyze the association of different risk factors on mortality. During the period of the study, 33 265 subjects died. A total of 27 147 deaths were stroke-related, accounting for 81.61% of all deaths. 6122 subjects died on the same day of stroke onset, with the one-day fatality rate at 7.83% and the overall 28-day fatality at 21.01%. The survival rates analyzed in the 1, 2, 3 and 4-year periods after the study were 72.04%, 68.92%, 66.27% and 64.29%, respectively. The 4-year survival rates of cerebral infarctions, intracerebral hemorrhages, subarachnoid hemorrhages and unspecified strokes were 80.06%, 50.15%, 71.80% and 21.41%, respectively. Age, gender, education level, diagnosis and quality of treatment in hospitals, hypertension, and the type of stroke incidences were considered the risk factors most associated with mortality.

3.1.2 Trends in Stroke Incidence and Mortality in Tianjin^[3]

In 1985, 15 438 urban/county residents were recruited to the Tianjin Brain Study, a study on population stroke surveillance. Stroke events and all deaths were registered annually. Since mature imaging technology was not available until 1992, investigators analyzed the incidence of first-ever stroke over three periods from 1992 to 2012, including 1992–1998, 1999–2005, and 2006–2012. The age-standardized incidence of first-ever stroke per 100 000 person-years rapidly increased from 124.5 in 1992–1998 to 190.0 in 1999–2005, and eventually approached 318.2 in 2006–2012. The incidence increased annually by 6.5%, and by

[1] He Q, Wu C, Luo H, et al. Trends in in-hospital mortality among patients with stroke in China. *Plos One*, 2014,9 (3) :e92763.

[2] Wu HB, Gong CC, Pan J, et al. Survival rate and risk factors of mortality among first-ever stroke patients. *Zhonghua Liu Xing Bing Xue Za Zhi*, 2014, 35 (7) :812–816.

[3] Wang J, An Z, Li B, et al. Increasing stroke incidence and prevalence of risk factors in a low-income Chinese population. *Neurology*. 2015, 84 (4) :374–381.

12% among men aged 45–64 years. From 1992 to 2012, the age at first-ever stroke in men decreased by 3.3 years, but no similar trend was observed in women. Concurrently, the prevalence of obesity and high levels of fasting glucose increased 8.8-fold and 11-fold from 1992 to 2012.

3.1.3 Low Rates of Knowledge and Treatment of Transient Ischemic Attack (TIA)

China Chronic Disease and Risk Factor Surveillance (CCDRFS) conducted a cross-sectional survey among 98 658 adults in 2010, and found that the age-standardized prevalence of TIA was 2.27%. The prevalence of TIA was higher in women and in patients who were older, less educated, current smokers, residents in rural or undeveloped areas, or with a history of stroke, hypertension, myocardial infarction, dyslipidemia, or diabetes. Approximately 3.08% of Chinese adults were informed and had knowledge of TIA. Among patients with TIA, only 5.02% received treatment and 4.07% received guideline-recommended therapy.^[1]

3.1.4 Treatment for and Prevention of Acute Phase of Stroke

(1) Double Antiplatelet Treatment Strategy

Non-disabling cerebrovascular events consist of TIA and minor stroke. Clopidogrel in High-risk patients with Acute Non-disabling Cerebrovascular Events (CHANCE) trial conducted by Tian Tan Hospital revealed that recurrent stroke was relevant to poor quality of life.^[2] The early benefit of clopidogrel-aspirin treatment in reducing the risk of subsequent stroke sustained during 1-year of follow-up.^[3] Compared with aspirin alone, cost-effective early treatment with a 90-day clopidogrel-aspirin therapy was higher for the treatment of nondisabling cerebrovascular events.^[4]

(2) Fixed-dose Combination Treatment Survey for Secondary Prevention of Stroke

China National Stroke Prevention Project screened 717 620 residents aged over 40 years from six provinces in China to investigate the prevalence of stroke from 2011 to 2012. The standardized prevalence rate of stroke was 1.9%. Up to 93.1% of patients with stroke were eligible for taking polypill containing at least two types of medications, with 75.3% eligible for a statin and antiplatelet agent and 70.6% for antihypertensive and antiplatelet medications. 54% of patients with stroke were eligible for antihypertensive, statin, and antiplatelet medications. The current treatment rate with all required combinations of separate pills

[1] Wang Y, Zhao X, Jiang Y, et al. Prevalence, knowledge, and treatment of transient ischemic attacks in China. *Neurology*. 2015;84(23):2354-2361.

[2] Wang YL, Pan YS, Zhao XQ, et al. Recurrent stroke was associated with poor quality of life in patients with transient ischemic attack or minor stroke: finding from the CHANCE trial. *CNS Neurosci Ther*. 2014;20(12):1029-1035.

[3] Wang Y, Pan Y, Zhao X, et al. Clopidogrel With Aspirin in Acute Minor Stroke or Transient Ischemic Attack (CHANCE) Trial: One-Year Outcomes. *Circulation*. 2015;132(1):40-46.

[4] Pan YS, Wang AX, Liu GP, et al. Cost - Effectiveness of Clopidogrel - Aspirin Versus Aspirin Alone for Acute Transient Ischemic Attack and Minor Stroke. *J Am Heart Assoc*. 2014;3(3):e000912.

was only 6.9%.^[1]

(3) Folic Acid

A population-based cohort study was conducted among 5 935 participants from 60 communities in Shenzhen, China. The results indicated that hyperhomocysteinemia in hypertensive patients was significantly associated with the risk of ischemic stroke, while folic acid supplementation for primary hypertension could efficiently down-regulate tHcy levels.^[2]

A randomized control trial was performed in Peking University First Hospital with the recruitment of 20 702 adults with hypertension from 32 communities in Jiangsu and Anhui provinces. The combined application of enalapril and folic acid, in contrast to enalapril alone, significantly reduced the risk of stroke.^[3]

3.1.5 Stroke Risk Factors

(1) Proteinuria

The Kailuan study followed up 92 013 participants for four years and indicated that proteinuria increased the risk of all subtypes of stroke.^[4]

(2) High-normal BP in addition to hypertension increased the incidence of asymptomatic intracranial arterial stenosis

Asymptomatic Polyvascular Abnormalities in Community Study was a sub-study of Kailuan study enrolling 4 422 participants. The results suggested that arterial pre-hypertension in addition to hypertension was associated with a higher incidence of asymptomatic intracranial arterial stenosis.^[5]

3.2 Coronary Heart Disease (CHD)

3.2.1 Mortality Rate and Trends of Coronary Heart Disease in Chinese Population^[6]

(1) Coronary Heart Disease Mortality in 2014

According to data from China Health and Family Planning Commission's Statistical Yearbook 2015, the

[1] Longde W, Ling Y, Yang H, et al. Fixed-dose combination treatment after stroke for secondary prevention in China: a national community-based study. *Stroke*. 2015; 46 (5) :1295-1300.

[2] Han L, Wu Q, Wang C, et al. Homocysteine, Ischemic Stroke, and Coronary Heart Disease in Hypertensive Patients: A Population-Based, Prospective Cohort Study. *Stroke*, 2015, 46 (7) : 1777-1786.

[3] Huo Y, Li J, Qin X, et al. Efficacy of folic acid therapy in primary prevention of stroke among adults with hypertension in China: the CSPPT randomized clinical trial. *JAMA*, 2015, 313 (13) : 1325-1235.

[4] Li Z, Wang A, Cai J, et al. Impact of proteinuria and glomerular filtration rate on risk of ischemic and intracerebral hemorrhagic stroke: a result from the Kailuan study. *Eur J Neurol*, 2015, 22 (2) : 355-360.

[5] Wang D, Zhou Y, Guo Y, et al. Arterial pre-hypertension and hypertension in intracranial versus extracranial cerebrovascular stenosis. *Eur J Neurol*, 2015, 22 (3) : 533-539.

[6] National Health and Family Planning Commission of the People's Republic of China .China Health and Family Planning Statistics Yearbook 2015. Beijing: Peking Union Medical College Press.

mortality rate from coronary heart diseases in 2014 was 107.5 per 100 000 in urban areas and 105.37 per 100 000 in rural areas, an increase over 2013 figures (urban: 100.86 per 100 000; rural: 98.68 per 100 000) . Overall, coronary heart disease mortality is higher in the urban populations than in the rural, and higher in men than women. (Figure 3-1-2, Table 3-2-1) .

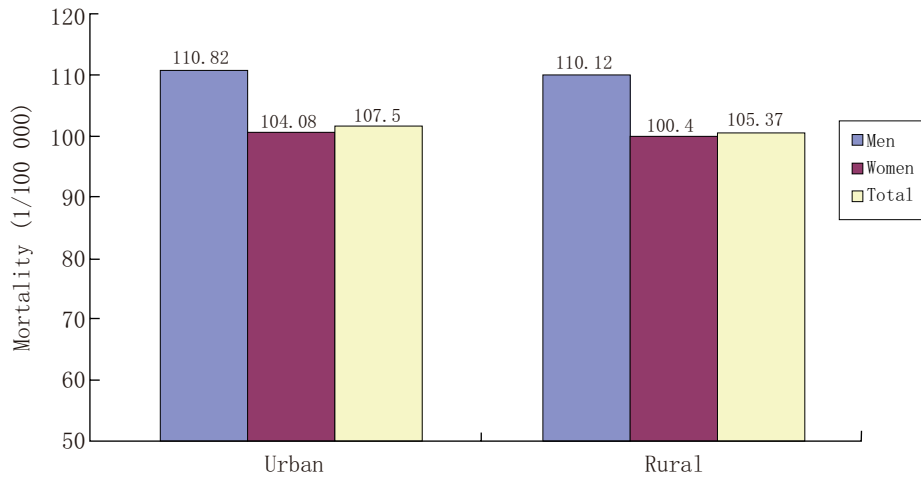


Figure 3-2-1 Coronary Heart Disease Mortality Rates in Urban and Rural Populations by Gender (China: 2014)

Table 3-2-1 Coronary Heart Disease Mortality Rates (1/100 000) in Urban and Rural Populations by Gender (China: 2014)

	Urban			Rural		
	Total	Men	Women	Total	Men	Female
AMI	55.32	60.23	50.26	68.6	74.19	62.76
Other CHD	52.18	50.59	53.82	36.77	35.93	37.64
Total CHD	107.5	110.82	104.08	105.37	110.12	100.4

AMI: acute myocardial infarction; CHD: coronary heart disease.

(2) Coronary Heart Disease Mortality Trends between 2002 and 2014

Mortality rates have increased from 2013 to 2014. Since 2012, the mortality rate of coronary heart disease in the rural population has increased rapidly, catching up to urban areas in 2014 (Figure 3-2-2) .

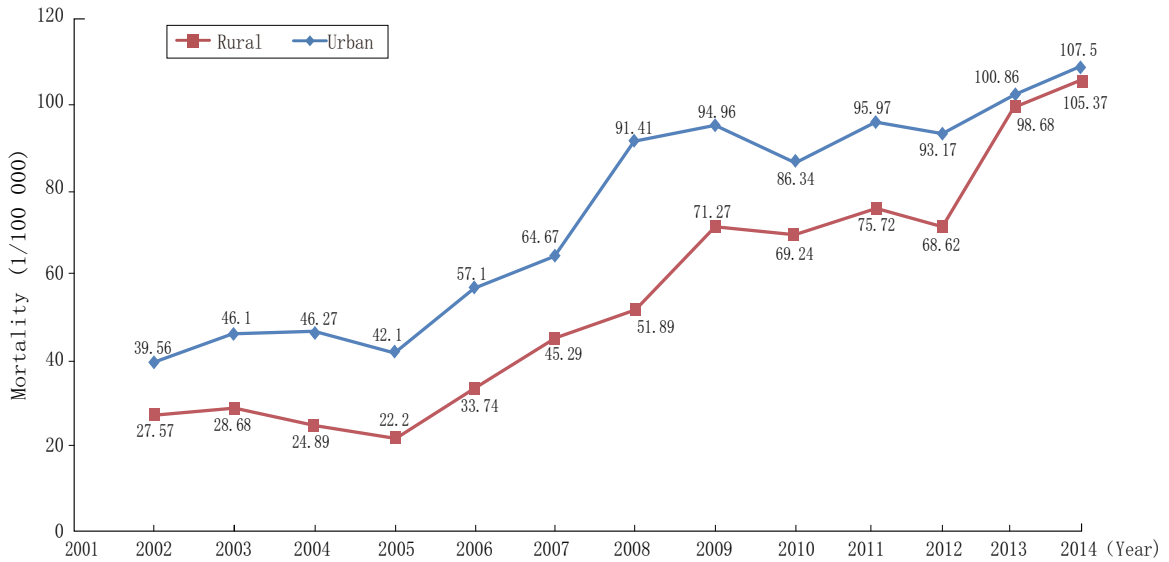


Figure 3–2–2 Coronary Heart Disease Mortality Trends in Urban and Rural Areas between 2002 and 2014

(3) Acute Myocardial Infarction Mortality Trends between 2002 and 2014

Acute myocardial infarction mortality rate increased from 2002 to 2014. Since 2005, the mortality rate of acute myocardial infarction has increased rapidly. AMI mortality in rural areas actually exceeded AMI mortality in urban areas in 2007, 2009 and 2011, increased dramatically in 2012, and significantly exceeded that of urban areas in both 2013 and 2014 (Figure 3–2–3).

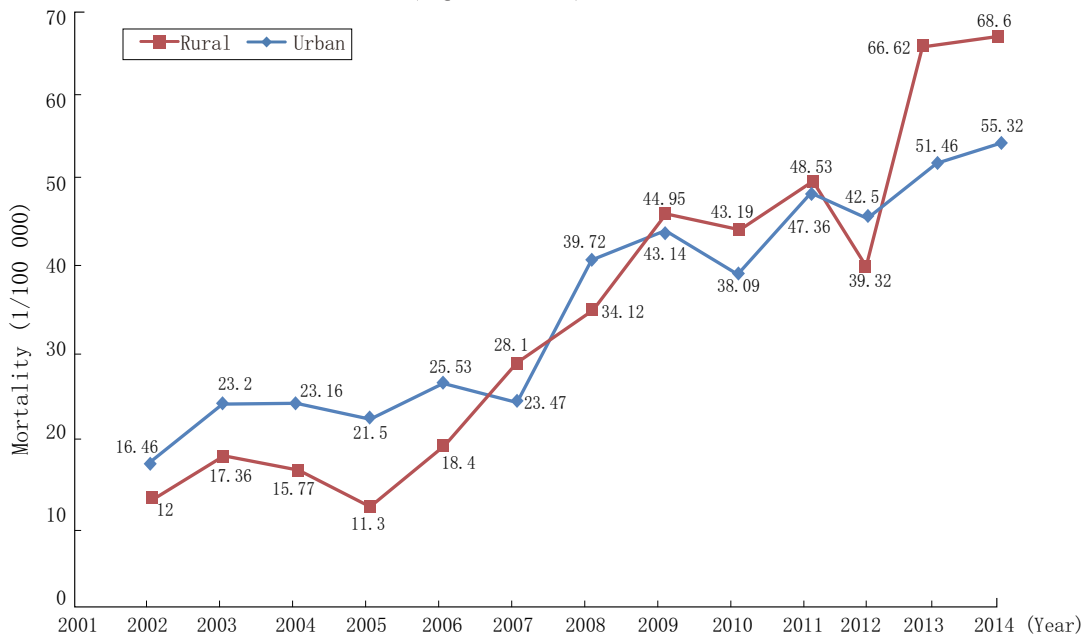


Figure 3–2–3 Acute Myocardial Infarction Mortality Trends in Urban and Rural Areas between 2002 and 2014

(4) Acute Myocardial Infarction Mortality Rate by Age and Gender between 2002 and 2014 (1/100 000)

AMI mortality increased with age regardless of gender or urban/rural distinction, and increased most significantly after age 40. The increase approaches an exponential relationship. (Figure 3-2-4, 3-2-5, 3-2-6, 3-2-7).

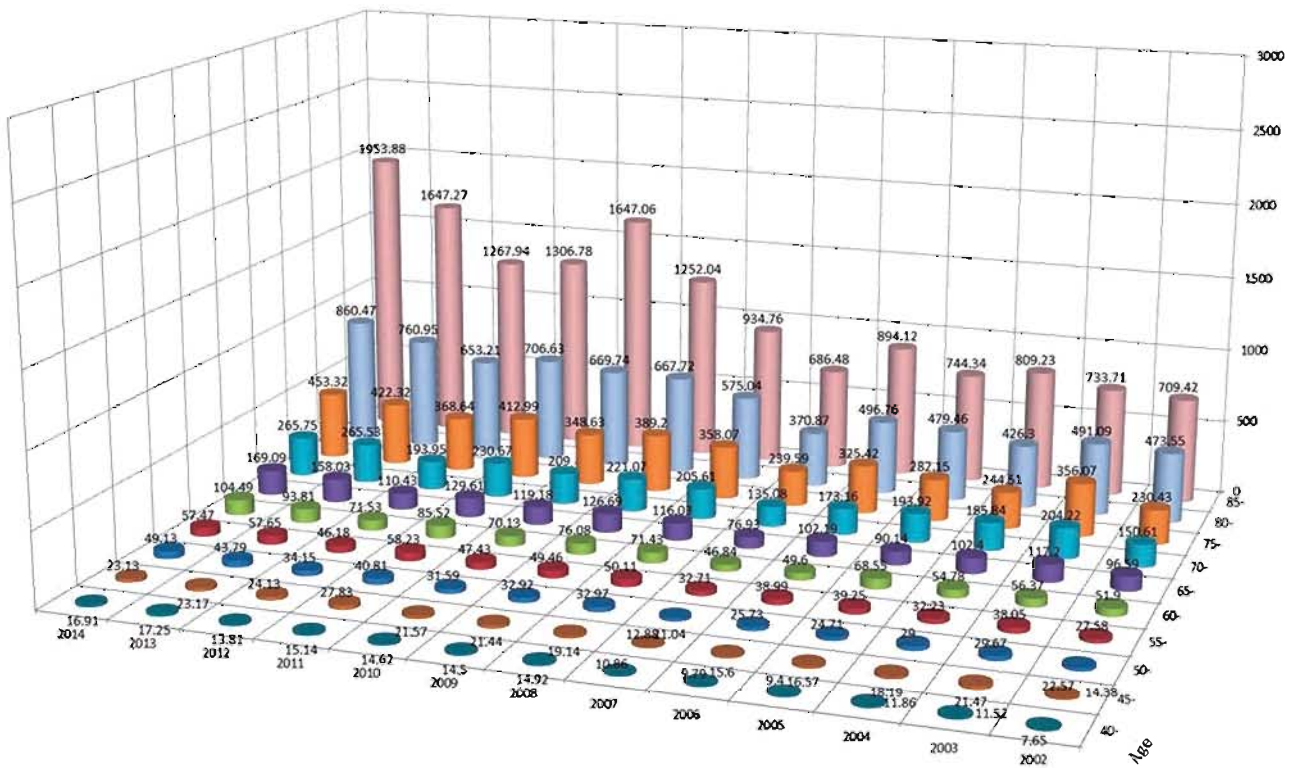


Figure 3-2-4 Trends in Acute Myocardial Infarction Mortality in Men from Urban Areas by Age (China: 2002–2014)

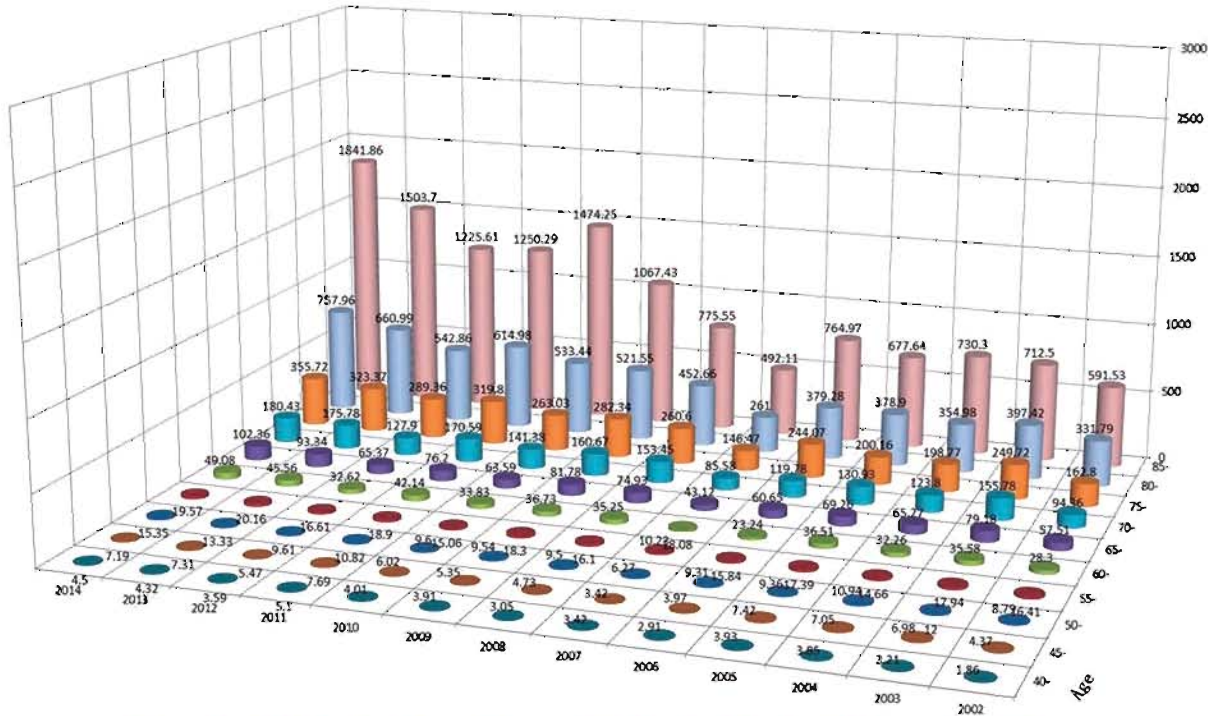


Figure 3-2-5 Trends in Acute Myocardial Infarction Mortality in Women from Urban Areas by Age (China: 2002-2014)

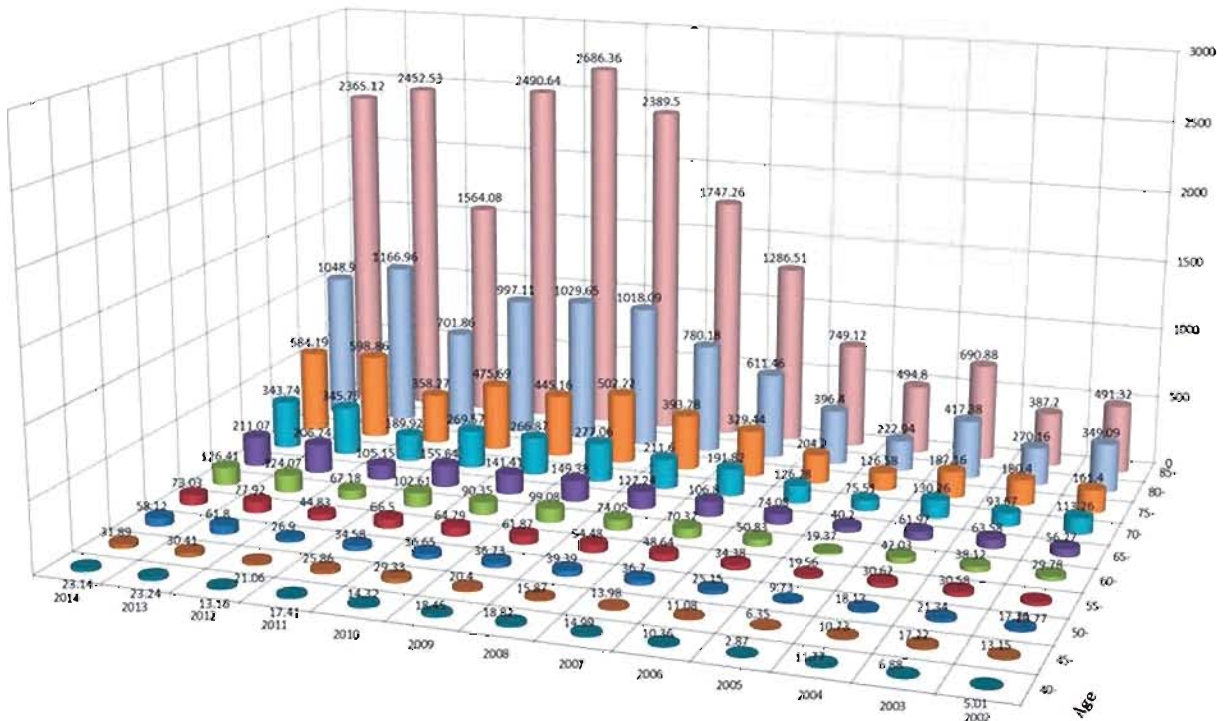


Figure 3-2-6 Trends in Acute Myocardial Infarction Mortality in Men from Rural Areas by Age (China: 2002-2014)

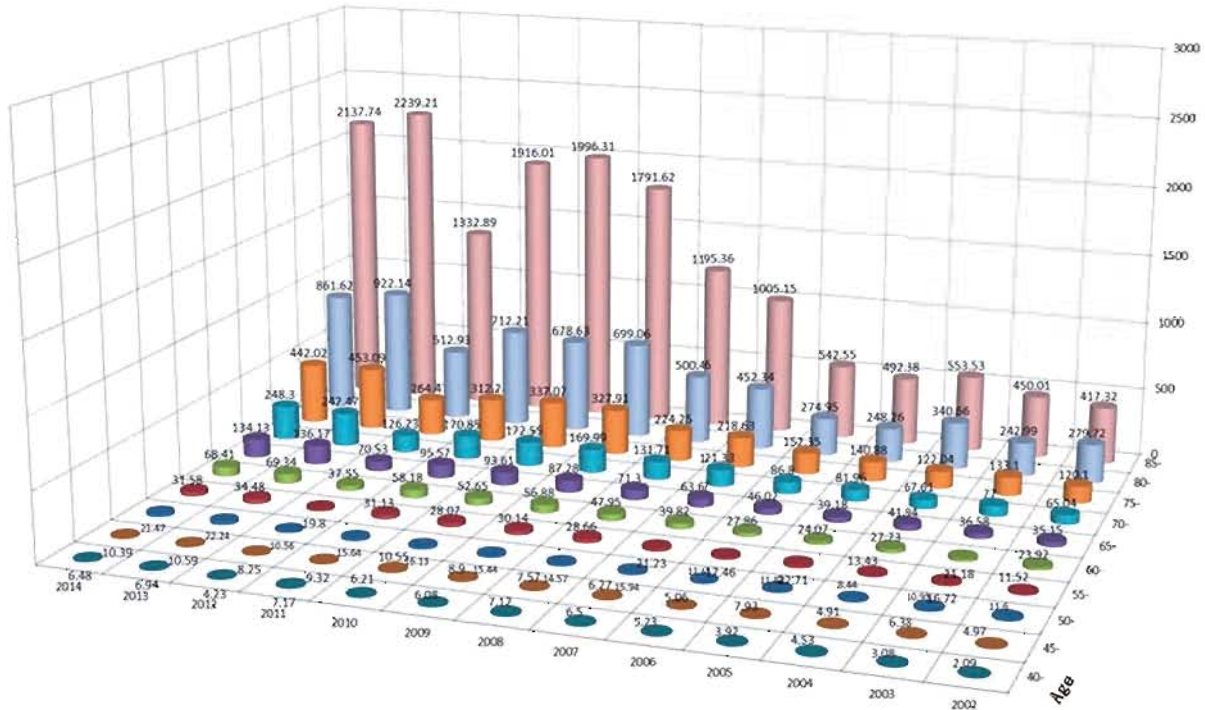


Figure 3-2-7 Trends in Acute Myocardial Infarction Mortality in Women from Rural Areas by Age (China: 2002-2014)

(5) Comparison of the Increase of Acute Myocardial Infarction by Different Gender and Age between 2012-2014 in Urban and Rural Areas (1/100 000)

From 2012 to 2014, AMI mortality increased significantly, especially in rural areas, significantly exceeding that in urban areas. The AMI growth rate increased with age when approaching 50 years old. The AMI growth rate in rural areas exceeded that of urban areas in all age groups. Regarding the group under 80, the increase of AMI in men in rural areas exceeded that in women. Regarding the group with the age above 80, the increase of AMI in women in rural areas exceeded that in men. Accordingly, AMI mortality increased among senior people over 80 and made a significant contribution to the substantial increase in total AMI mortality observed in the Chinese population during the 2012-2014 period. (Figure 3-2-8)

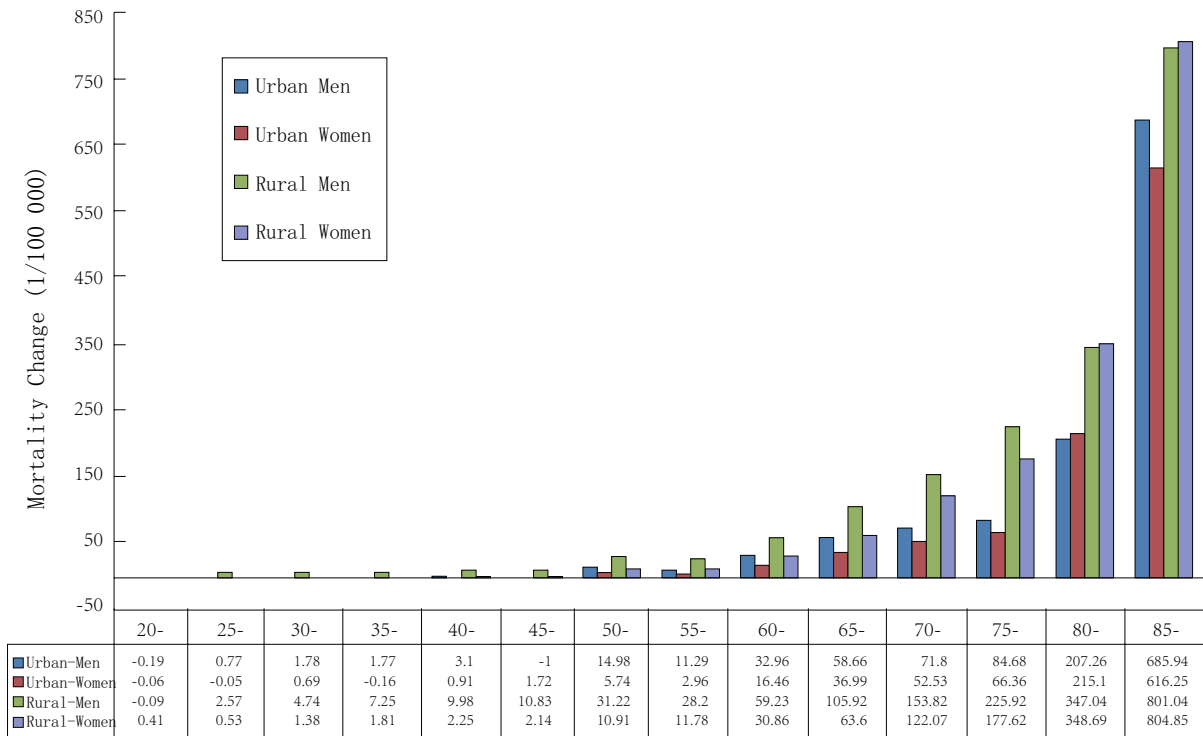


Figure 3–2–8 Acute Myocardial Infarction Increase Comparison by Gender and Age between 2012–2014 in Urban and Rural Areas

3.2.2 Prevalence of Coronary Heart Disease^[1]

The data from the 2008 4th Family Health Survey in China’s Health Services Survey demonstrated that the overall prevalence of ischemic heart disease was 7.7%: 15.9% in urban areas and 4.8% in rural areas. Compared with the data of the 3rd Family Health Survey in 2003 (4.6% for entire population, 12.4% for urban residents and 2.0% for rural residents), the prevalence of ischemic heart disease increased considerably.

In this survey, ischemic heart disease was defined as individuals diagnosed with ischemic heart disease within half a year of the survey, or diagnosed with ischemia heart disease before half a year of the survey and experienced recurrence within half a year of the survey, and received treatment. Prevalence was calculated for all ages.

Based on these data and according to the 2010 population of China being 1 339 724 852^[2], the total number of patients with IHD in mainland China is 10 315 881 in 2008. If evaluated based on the Fifth

[1] Ministry of Health Statistics Center. 2008 China Health Services Survey – 4th Family Health Survey. 2009.

[2] The main data bulletin of Sixth National Census in 2010 (the Second Order), National Bureau of Statistics of China, http://www.gov.cn/gzdt/2011-04/29/content_1854891.htm.2011.

National Census in 2000 (1 265 830 000)^[1], the number of patients with ischemic heart disease would be estimated to be 9 746 891.

3.2.3 Coronary Heart Disease Treatment

3.2.3.1 Current Status of Coronary Heart Disease Treatment in China

Based on data reported via the PCI network of National Health and Family Planning Commission Coronary Heart Disease Interventional Treatment Quality Control Center, the total number of PCI cases in China displayed a notably increasing trend. The increase showed a downward trend in recent years, 2014 exhibiting the lowest growth rate over the past five years (Figure 3–2–1).

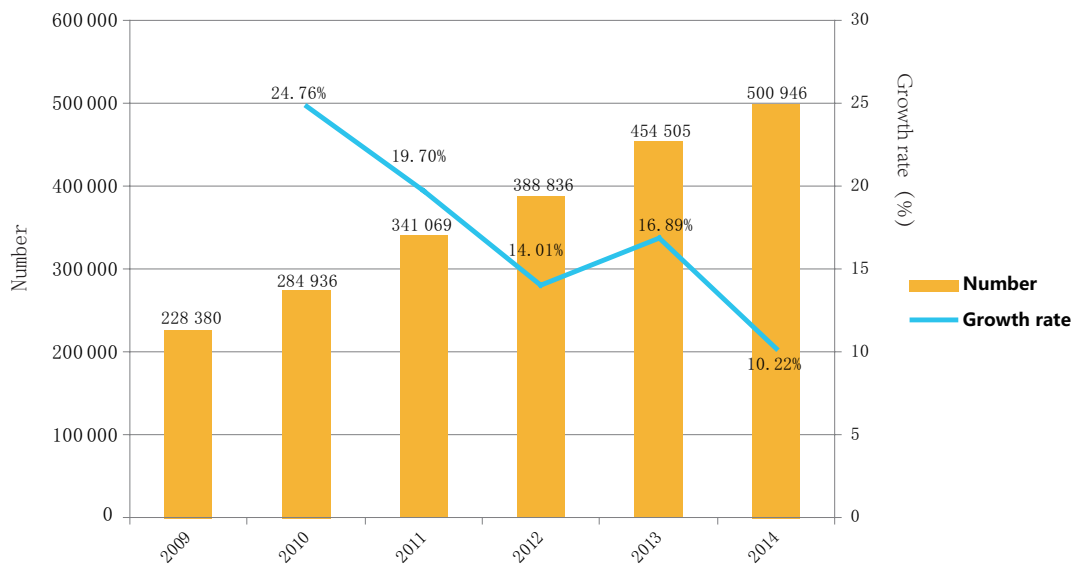


Figure 3–2–1 Coronary Heart Disease Intervention Treatment Number and Growth Rate

PCI network reporting data from National Health and Family Planning Commission indicated that:

(1) PCI Growth Rate

The number of patients with PCI increased steadily through 2014, but the PCI growth rate was significantly slower than before. The mortality rate of PCI has stabilized at a lower level and even continues to decrease, albeit it slightly. The proportion of patients with STEMI who received emergency PCI also increased. The national average number of people to receive PCI was 376/1 000 000, and increase of 21.47% compared with that in 2013. However, deficiency in PCI treatment for patients with acute coronary syndromes persists.

[1] The main data bulletin of Fifth National Census (the First Order), Nation Bureau of Statistics of China, http://www.gov.cn/tjsj/tjgb/rkpcgb/qgrkpcgb/200203/t20020331_30314.html.2001.

(2) Regional Difference

The number of provinces and cities with over 10 000 cases of PCI treatment per year increased to 20 in 2014. Beijing remained the PCI leader (with 48 314 cases). The overall level of a PCI operation varied greatly between China's eastern and western regions, but showed modest improvement since 2013.

(3) Stent Selection

The average number of cases of stent implantation also increased from 2009 to 2011. The nation-wide number of stent implantations per stented individual was 1.49 in 2014, similar to the year of 2013. The proportion of DES (drug-eluting stents) reached 99.67% in 2014.

(4) Artery Path

Excluding the requirement of a guide catheter with large diameter to provide better active support for complex lesions, most clinicians chose a radial artery path with less postoperative complications to perform PCI for coronary lesions.

(5) Quality Evaluation

PCI operation-related mortality remained below 3%.

(6) Indications

Among patients receiving PCI, 92% patients were diagnosed with acute coronary syndrome, and 59% of patients were diagnosed with unstable angina in 2014; both were similar to values in 2013.

(7) Myocardial Infarction Treatment

STEMI emergency treatment reflects the quality of first aid for cardiovascular disease, but also reflects issues in the social aid system. There were 117 039 admitted with a primary diagnosis of STEMI. However, only 39 191 patients received primary PCI within 12 hours. Two-thirds of patients with STEMI could not get primary PCI timely, and the proportion is slightly higher than it in 2013.

To date the lack of a PCI network system is noteworthy, as is the excessive concentration of PCI cases in certain areas. There is still substantial room for improvement in STEMI interventional treatment.

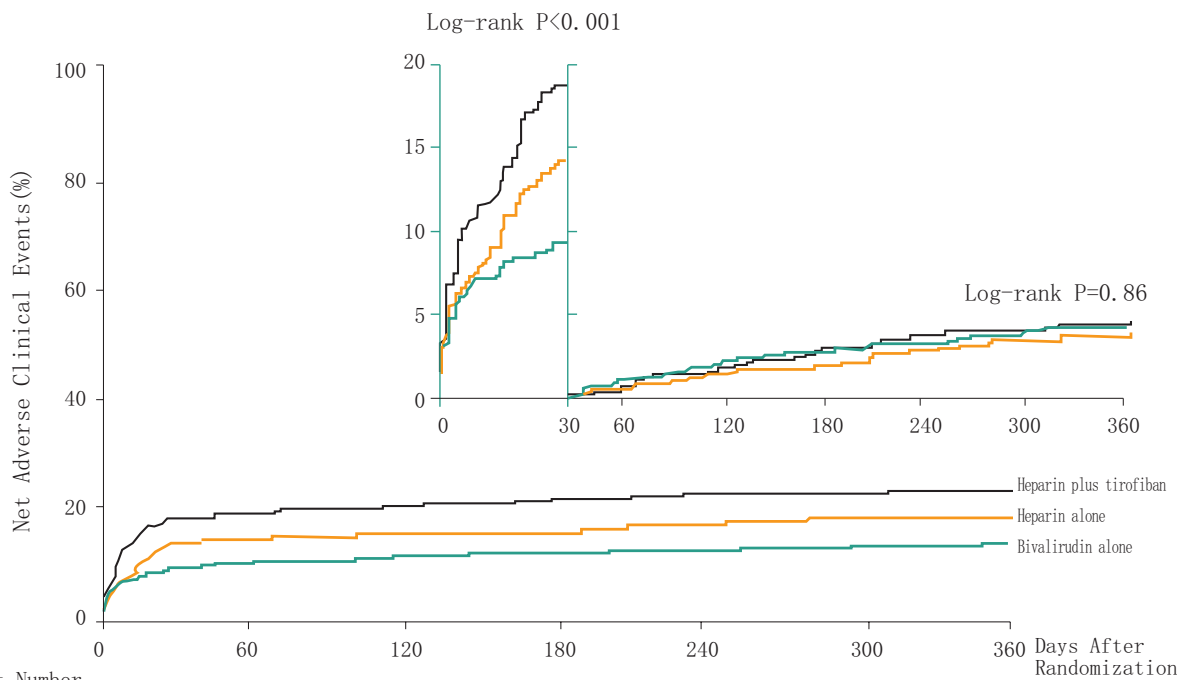
3.2.3.2 Study of Optimizing the Antithrombotic Therapy for Coronary Heart Disease-Bivalirudin in Acute Myocardial Infarction vs Heparin and GPI Plus Heparin Trial (BRIGHT)^[1]

BRIGHT was one of the subprojects of the Coronary Heart Disease Optimization Antithrombotic Therapy Study, funded by the 12th National Five-year Science and Technology Support Projects. A total of 2 194 patients with AMI were enrolled between August, 2012, and June, 2013, from 82 medical centers located in 23 provinces in China. The primary end point was the rate of net adverse clinical events at 30 days, a composite of major adverse cardiac or cerebral events (all-cause death, re-infarction, ischemia-driven target vessel revascularization, or stroke) or any bleeding. Patients were randomly assigned into three groups before PCI: bivalirudin alone, heparin alone, and heparin plus tirofiban. Study medications were administered

[1] Han Y, Guo J, Xu B, et al. Bivalirudin vs Heparin With or Without Tirofiban During Primary Percutaneous Coronary Intervention in Acute Myocardial Infarction The BRIGHT Randomized Clinical Trial. *JAMA*, 2015;313 (13) :1336-1346.

before coronary angiography in the catheterization laboratory. Bivalirudin was given as a bolus of 0.75mg/kg followed by infusion of 1.75mg/kg/h during the PCI procedure and for at least 30 minutes but no more than 4 hours afterwards.

Results showed that the bivalirudin group was superior to the other two groups in MACE (bivalirudin 8.8%, heparin alone 13.2%, heparin plus tirofiban 17.0%, $P < 0.001$), as illustrated in Figure 3-2-2. The rates of major adverse cardiac or cerebral events (MACCE) (5.0% vs 5.8% vs 4.9%, respectively, $P = 0.74$) were not significantly different between groups. Compared with heparin alone and heparin plus tirofiban, bivalirudin alone reduced bleeding events by 46% and 66%, respectively. There were also no statistically significant differences in acute stent thrombosis (<24h), sub-acute stent thrombosis (1-30d), or 1-year thrombosis.



Patient Number	0	60	120	180	240	300	360
Heparin plus tirofiban	735	656	650	646	641	636	634
Heparin alone	729	625	619	616	611	607	605
Bivalirudin alone	730	600	592	585	580	579	576

Figure 3-2-2 The Rates of Adverse Clinical Events after Randomization among Study Groups

The study reflected clinical practice characteristics for AMI treatment and emergency PCI in China: the application of radial access was close to 80%, and the application of thrombus aspiration was approximately 26%; the patients receiving emergency PCI approached 97%, and over 99% of patients received drug-eluting stents. Compared with heparin or heparin plus tirofiban, bivalirudin administered during the PCI procedure and after PCI for 3-4 hours reduced bleeding events, displaying no effect on ischemic events. This finding helped to resolve the issue of increased of stent thrombosis in previous studies, and offered “Chinese evidence” for patient-specific antithrombosis.

3.2.3.3 Registry of Acute Myocardial Infarction in China^[1,2,3]

The Cardiovascular Disease Key Treatment Technology Clinical Multi-center Research Platform, China Acute Myocardial Infarction (CAMI) study, recruited patients with AMI by web-based direct report from a total of 107 hospitals at three different levels across 31 provinces in China. The study was non-interventional, prospective and multi-centered, and sought to gather information on disease onset, diagnosis, treatment, and prognosis. The project was funded by the 12th National Five-year Science and Technology Support Projects. The CAMI registry was launched on January 1, 2013. As of September 2014, a total of over 20 000 patients who experienced AMI (STEMI/NSTEMI) within 7 days of acute ischemic symptoms have been followed up for 2 years. The results demonstrate that:

(1) The top three cardiovascular disease risk factors among AMI patients in China are smoking, overweight/obese and having hypertension, followed by diabetes and dyslipidemia. 90% patients had at least one of the following risk factors: hypertension, smoking, diabetes, overweight/obesity and high cholesterol. 35% patients had three or more risk factors. Compared to older patients, male gender, smoking, having hyperlipidemia, and a family history of coronary heart disease were more frequently observed among young patients. Compared with male patients, female patients were observed at a higher age, presented with higher prevalence of hypertension and diabetes, and were less physically active. However, compared with female patients, the number of male patients with smoking/smoking history and history of dyslipidemia was significantly higher. Patients at different ages also presented distinct profiles (Table 3-2-1).

Table 3-2-1 Risk Factors Analysis among Patients with AMI by Age (No, %)

	Total (n=15 998)	<55years (n=4 458)	>55 years (n=11 540)	P value
Age (year)	61.8±15.0	43.8±13.2	68.7±8.6	<0.0001
Male (%)	11 837 (74)	3 961 (88.9)	7 876 (68.2)	<0.0001
Body Mass Index	24.6±12.2	25.2±8.4	24.4±13.3	=0.0001
Hypertension	8 196 (51.2)	1 813 (40.7)	6 383 (55.3)	<0.0001
Dyslipidemia	1 236 (7.7)	448 (10.0)	788 (6.8)	<0.0001
Diabetes	3 116 (19.5)	679 (15.2)	2 437 (21.1)	<0.0001
Smoking	8 695 (54.4)	3 126 (70.1)	5 569 (48.3)	<0.0001

[1] Xu H, Li W, Yang J, et al. The China Acute Myocardial Infarction (CAMI) Registry: A National Long-term registry-Research-Education Integrated Platform for Exploring Acute Myocardial Infarction in China, *American Heart Journal*, 2015, doi: 10.1016/j.ahj.2015.04.014.

[2] Fu R, Yang YJ, Xu HY, et al. Clinical symptoms and triggering factor difference analysis by gender among Chinese patients with acute myocardial infarction. *Chinese Circulation Journal*, 2014.29 (12) : 964-967.

[3] Gao XJ, Yang JG, Yang YJ, et al. Cardiovascular Factors Analysis among Chinese patients with acute myocardial infarction. *Chinese Circulation Journal*, 2015 .30 (3) :206-210.

Table 3-2-1 Risk Factors Analysis among Patients with AMI by Age (No, %) (Continued)

	Total (n=15 998)	<55years (n=4 458)	>55 years (n=11 540)	P value
Family history of premature coronary artery disease	575 (3.6)	293 (6.6)	282 (2.4)	<0.0001
Lack of exercises	12 731 (79.6)	3 456 (77.5)	9 275 (80.4)	<0.0001
Fatty food	12 186 (76.2)	3 720 (83.4)	8 466 (73.4)	<0.0001

60% of patients in China presented with chest pain, sweating at AMI onset, and chest tightness with radiating pain. Persistent chest pain and sweating were the most common clinical symptoms. Men were more likely than women to have definite trigger factors. Physical stress and recent excessive/unhealthy lifestyles were also observed to be more common in men. Table 3-2-2.

Table 3-2-2 Acute Myocardial Infarction Trigger Factors Comparison

Trigger	Male n=2 297	Female n=582	P value
Physical stress	1 136 (49.5)	259 (44.5)	0.0325
Recent excessive/unhealthy lifestyle	353 (15.4)	51 (8.8)	<0.0001
Mental stress	222 (9.7)	82 (14.1)	0.0027
Weather and environment sudden change	109 (4.7)	48 (8.2)	0.0016
Disease/Operation/Trauma	65 (2.8)	46 (7.9)	<0.0001

Among STEMI patients receiving emergency reperfusion therapy, significant differences existed in time from admission to emergency reperfusion therapy. The median time was 165 minutes from admission to emergency PCI, and 130 minutes from admission to thrombolysis. The percent of patients receiving emergency reperfusion therapy also differed dramatically across hospital types: 36.1% for patients in provincial hospitals, and only 4.2% for patients in county hospitals. Late arrival at hospital was also common, which is concerning because effective reperfusion for AMI has to be performed in hospital as early as possible.

3.2.3.4 Clinical Characteristics and Prognosis Comparison of Chinese non ST-segment Elevation Acute Coronary Syndrome Patients in Different Time Periods^[1]

A total of 1 473 NSTEMI-ACS patients were recruited in this study. 749 cases were from the Organization to Assess Strategies for Ischemic Syndromes (OASIS REGISTRY) which was launched in 38 centers across China from April 1999 to December 2000, and the remaining 724 patients from The Timing of Intervention in Acute Coronary Syndromes (TIMACS) trial performed from April 2007 to June 2008 in 24 centers across the country. The follow-up period was 180 days. Compared with OASIS patients, TIMACS patients dis-

[1] Bai Y, Liang Y, Tan HQ, et al. Clinical characteristics and prognosis comparison of Chinese non ST-segment elevation acute coronary syndrome patients in two different time periods. *Zhong Hua Xin Xue Guan Bing Za Zhi*, 2014 .42 (8) : 655-660.

played lower rates of histories of coronary artery disease and myocardial infarction. After admission, compared with OASIS patients, TIMACS patients demonstrated a significantly higher proportion of PCI (74.9% vs. 49.3%, $P < 0.001$). Additionally for secondary prevention, TIMACS patients were more likely ($P < 0.05$) to be on standard medication treatments during hospitalization, at discharge and at 180 days follow up and had a higher compliance rate. The combined primary outcome event rate at 180 days was much lower in TIMACS than in OASIS patients (13.3% vs. 25.2%, $P < 0.001$, refractory angina accounting for 5.2% vs. 22.6%, $P < 0.001$). After adjustment for baseline levels and treatment during hospitalization by utilizing COX regression models, the results showed that the incidence rate for combination endpoint (HR = 0.39, 95%CI: 0.29–0.53, $P < 0.001$) and refractory ischemia/angina re-hospitalization (HR = 0.17, 95% CI: 0.11–0.25, $P < 0.001$) were both lower in TIMACS patients than in OASIS patients. The study indicated that PCI procedure and secondary prevention medication administration were more advanced in TIMACS patients than in OASIS patients, and that this was associated the lower incidence of primary outcomes at 180 days follow up. With progress on domestic and overseas treatment guidelines and clinical enhancements, China has made remarkable progress in effectively managing non-ST elevated ACS patients.

3.2.3.5 ABSORB China Trial^[1]

ABSORB China, a non-inferior trial, was designed to compare the angiographic efficacy, clinical safety and effectiveness of the metallic drug-eluting stent Xience CoCr-EES (cobalt-chromium everolimus-eluting stents) and the everolimus-eluting bioresorbable vascular scaffold (Absorb BVS). The primary endpoint was late loss (LL) of angiographic in-segment at 1 year.

A total of 480 patients from 24 medical centers in China were randomized into BVS or CoCr-EES in a 1:1 ratio. The primary endpoint of in-segment LL at 1 year was 0.19 ± 0.38 mm ($n=200$) for BVS versus 0.13 ± 0.38 mm ($n=195$) for CoCr-EES; achieving non-inferiority of BVS compared with CoCr-EES ($p_{\text{non-inferiority}} = 0.01$). BVS and CoCr-EES also showed similar 1-year rates of target lesion failure (TLF: cardiac death, target vessel myocardial infarction, or ischemia-driven target lesion revascularization; 3.4% vs. 4.2%, respectively; $p = 0.62$) and definite/probable scaffold/stent thrombosis (0.4% vs. 0.0%, respectively; $p = 1.00$). These data indicated that BVS was non-inferior to CoCr-EES for the primary endpoint of in-segment LL, clinical safety and efficacy at 1 year.

3.3 Arrhythmia

3.3.1 Pacemakers, Implantable Cardioverter-Defibrillators (ICD) and Cardiac Resynchronization Therapy (CRT)

The first application of an artificial cardiac pacemaker in China was in 1962 in Shanghai.^[2] Since then,

[1] Gao R, Yang Y, Han Y, et al. Bioresorbable Vascular Scaffolds Versus Metallic Stents in Patients with Coronary Artery Disease: ABSORB China trial. *J Am Coll Cardiol*, 2015, 66 (21) :2298-2309.

[2] Huo JJ, Fang ZP, Wang WN, et al. The experiment study and preliminary clinical use of two cardiac pacemaker. *Chinese J of Medicine*, 1964. 50:219-224.

pacemaker implant volume has increased annually, and the proportion of physiological pacemakers has also increased.^[1,2,3,4] According to statistics from the Ministry of Health’s online enrollment system (reported at the Introduction to Cardiovascular Disease in China Meeting in March 2015; military hospitals not included), about 52382 pacemakers were implanted in 2014:an increase of 3.2% when compared to 2013 (Figure 3–3–1) . Among the indications for cardiac pacing, 51.1% were associated with the treatment of sick sinus syndrome (SSS) , and 39.8% were related to atrioventricular block (Figure 3–3–2) . The proportion of dual-chamber pacemakers is nearly 67%, including 2 918 pacemakers that are remote monitoring pacemakers. From March 1st, 2009 to December 30th, 2010, 628 cases across 97 hospitals were selected for a national multicenter registry study of remote monitoring pacemakers. 22.9% of studied patients experienced at least one atrial fibrillation event at their six months follow-up. Atrial fibrillation occurred most frequently in the 2 months following pacemaker implantation. After medication, the atrial fibrillation event rate declined from 12% at the start to 2.5% at six months follow-up. The atrial fibrillation load also decreased significantly. It is evident that remote monitoring pacemakers are helpful to the early diagnosis of atrial fibrillation (especially to asymptomatic atrial fibrillation) and can bring long-term benefits to patients.^[5]

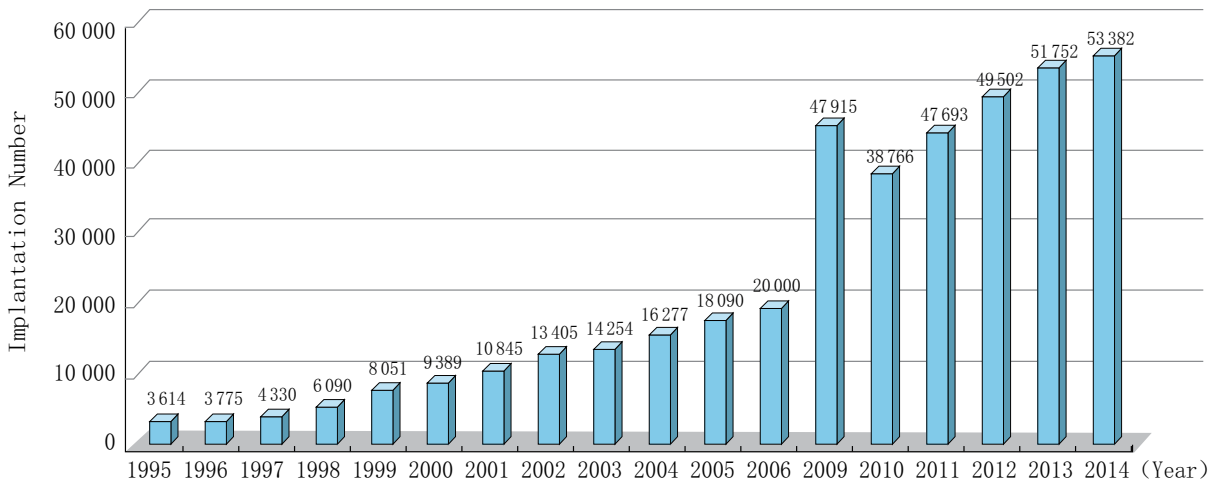


Figure 3–3–1 Pacemaker Implantation Volume (China: 1995–2014)

- [1] Wang FZ, Hua W, Zhang S, et al. National investigation of the clinical use of pacemaker in 1998-1999. *Chinese J of Cardiac Arrhythmias*, 2001. 5 (4) : 229-230.
- [2] Wang FZ, Hua W, Zhang S, et al. National investigation of the clinical use of pacemaker in 2000-2001. *Chinese J of Cardiac Arrhythmias*, 2003. 7 (3) : 189-191.
- [3] Wang FZ, Hua W, Zhang S, et al. National investigation of the clinical use of pacemaker from 2002 to 2005. *Chinese J of Cardiac Arrhythmias*, 2006. 10 (6) : 475-478.
- [4] Chen YH, Chen H, Wu Y, et al. Cardiac electrophysiology in China. *Heart Rhythm*, 2007. 4 (6) :862.
- [5] Chen KP, Dai Y, Hua W et al. Reduction of atrial fibrillation in remotely monitored pacemaker patients: results from a Chinese multicentre registry. *Chin Med J*,2013,126 (22) :4216-4221.

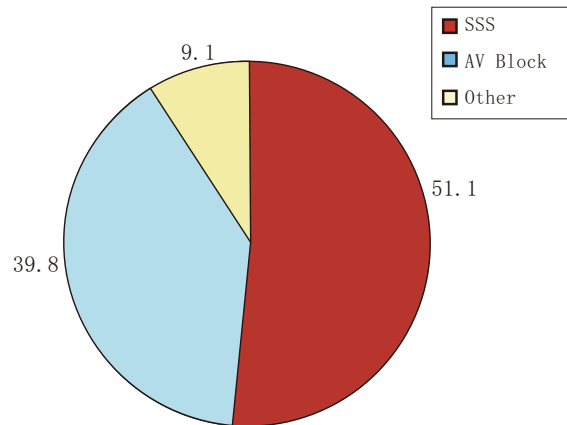


Figure 3–3–2 Indications for Pacemaker Implantation (China: 2014) (%)

In 1996, the first trans–jugular implantable cardioverter–defibrillator (ICD) placement was performed in China. A study of the indications for ICD implantation in 31 domestic hospitals showed that 85.2% of the patients met the 2002 criteria in the ACC/AHA/NASPE Class I ICD guidelines (secondary prevention), and only 10.6% matched with the Class IIa indication for primary prevention.^[1] But few patients who are eligible for ICD actually get them implanted. A recent study showed that among the 497 patients who met the Class I indication for ICD implantation, only 22.5% of those patients accepted ICD implantation. The remaining 77.5% of the patients refused ICD implantation for a number of reasons. An 11 ± 3 months follow–up survey showed that mortality rates were 1.8% in patients who received ICD and 9.4% in those who did not receive ICD. The incidence of sudden cardiac death was 6.7% for the latter group, much higher than that for individuals who received ICD.^[2] According statistics from the National Health and Family Planning Commission of the People’s Republic of China online enrollment system, the number of implanted ICD has increased steadily in recent years (Figure 3–3–3). However, ICD implantation annual growth rates have decreased: they were 23.5%, 15.2% and 2.9% in 2012, 2013 and 2014, respectively. This suggests that ICD implantation has reached the plateau phase in China. The percentage of single–chamber ICD implantations was 67.1%, and the percentage of dual–chamber ICD implantations was 32.9% in 2014. The proportion of ICD for secondary prevention was 52.1%, and for primary prevention was 47.9%. The proportion for primary prevention steadily increased compared to 2012 (42.7%) and 2013 (45%). This indicates that Chinese physicians have a better understanding of ICD implantations for primary prevention of sudden cardiac death.

[1] Hua W, Zhang S, Niu HX, et al. Primary and secondary prevention of sudden cardiac death with implantable cardioverter defibrillator: Analysis the indications of ICD in 31 hospital patients. *Chinese J of Cardiac Arrhythmias*, 2010. 14 (1): 9-11.

[2] Hua W, Niu H, Fan X, et al. Preventive effectiveness of implantable cardioverter defibrillator in reducing sudden cardiac death in the Chinese population: a multicenter trial of ICD therapy versus non-ICD therapy. *J Cardiovasc Electrophysiol*. 2012;23Suppl 1:S5-9.

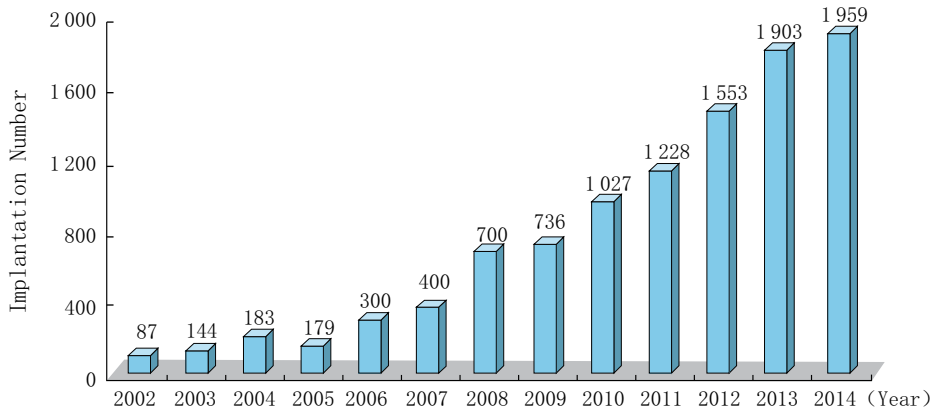


Figure 3-3-3 ICD Implantation Volumes by Year (China: 2002-2014)

Beginning in 1999, Chinese physicians started using biventricular pacing to treat heart failure. From 2002 to 2007, the number of CRT implantations increased by at least 30% each year. According to statistics from the National Health and Family Planning Commission of the People’s Republic of China online enrollment system (military hospitals not included), the CRT implantation rate increased 19.3% and 17.8% in 2011 and 2012, respectively. There was not much difference between 2012 and 2013, and rates increased by 8.2% in 2014 compared to 2013 (Figure 3–3–4). In 2014, among the people receiving CRT, CRT–D accounted for 55% of implantations and CRT–P for 45%. The most common indication of CRT (actually in over half of all cases) was no ischemic cardiomyopathy. The percent indicating with ischemic cardiomyopathy was 25.3% in 2013 and 26.5% in 2014. There are greater restrictions for receiving CRT treatment now than in the past, including left bundle branch block (76.3% of 1 814 cases), non–typical intraventricular block (456 cases), and right bundle branch block (109 cases). The remote monitoring CRT has been given perhaps greater importance. A study of 97 domestic hospitals was conducted by Fu Wai Hospital and analyzed 73 CRT cases of remote monitoring pacemaker. The six months follow–up showed that 92.7% of patients experienced abnormal alarm events, 85% of which were related to diseases (atrial arrhythmia events, ventricular arrhythmia events, low–frequency pacing, etc.) and 15% were system–related events (including conductor resistance disorder and sensory dysfunction). After implantation of CRT, it is easy to identify adverse events earlier, often well before 3 or 6 months follow–up. Furthermore adverse disease–related events decreased over time. This suggests that remote monitoring is reliable for CRT implanted patients who have heart failure and lends long–term benefits.^[1,2] However, the selection of CRT indications needs to become stricter: only heart failure patients with complete left bundle branch block should be selected, and this brings more benefits to the patients with high BMI.^[3]

[1] Chen KP, Dai Y, Hua W et al. Reduction of atrial fibrillation in remotely monitored pacemaker patients: results from a Chinese multicentre registry. *Chin Med J*, 2013, 126 (22) :4216-4221.

[2] Chen KP, Hua W, Dai Y, et al. Cardiac resynchronization therapy in remotely monitored pacemaker patients: results from a Chinese multicentre registry. *Chinese J of Cardiac Arrhythmias*, 2013, 17 (1): 46-49.

[3] Cai C, Hua W, Ding LG, et al. Association of body mass index with cardiac reverse remodeling and long-term outcome in advanced heart failure patients with cardiac resynchronization therapy. *Circ J*, 2014, 78 (12) :2899-2907.

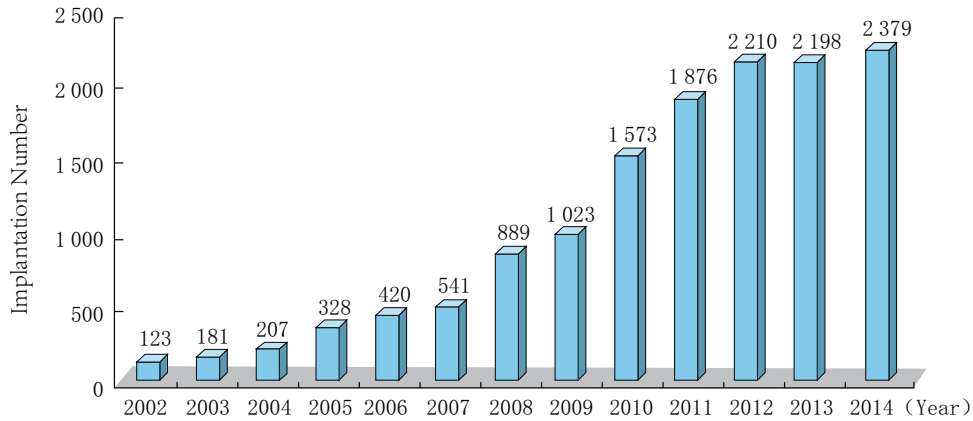


Figure 3-3-4 CRT Implantation Volumes by Year (China: 2002-2014)

3.3.2 Radiofrequency Catheter Ablation

China reported clinical practice of radiofrequency catheter ablation (RFCA) as early as 1991.^[1,2] Currently, the application of RFCA for pre-excitation syndromes and supraventricular tachycardia is well accepted in over 600 Chinese hospitals. Statistics from the National Health and Family Planning Commission of the People's Republic of China online enrollment system showed that the application of RFCA increased rapidly from 2010 to 2013 (Figure 3-3-5), with annual growth between 13.5% and 17.5%. The percentage of RFCA cases for atrial fibrillation also increased annually. The proportion of RFCA cases for atrial fibrillation out of all RFCA cases was 16.6% in 2012, 17.7% in 2013, and 19.7% in 2014.

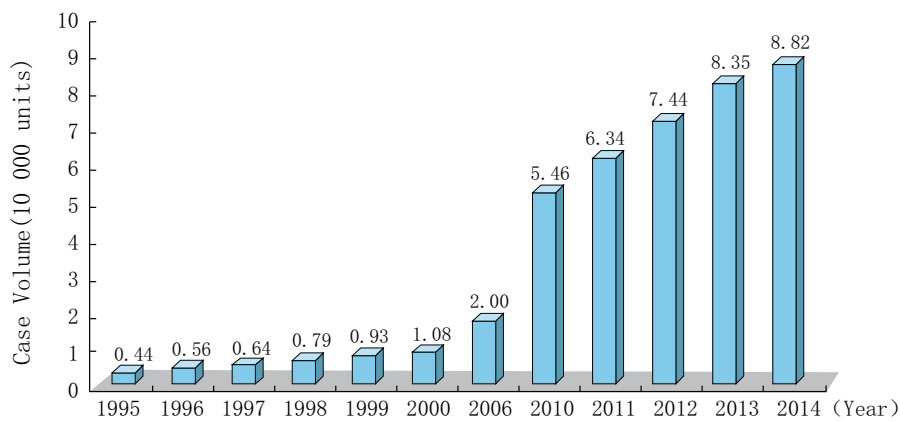


Figure 3-3-5 RFCA Case Volumes by Year (China: 1995-2014)

[1] Li GS, Gao HN, Xu JL, et al. "Treatment of pre-excitation syndrome through radiofrequency catheter ablation. Cardiac Pacing and Electrophysiology, 1991. 5 (2) : 57-59.

[2] Hu DY, Chen X, Ma CS, et al. National survey on radiofrequency catheter ablation in China. Chinese J of Cardiac Arrhythmias, 2002. 6 (2) : 124-127.

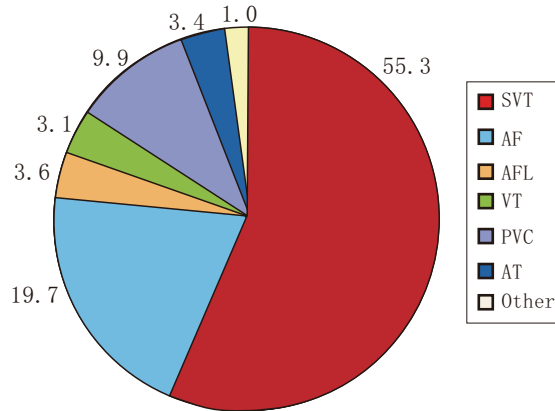


Figure 3-3-6 Diseases Treated by RFCA (China: 2014) (%)

3.3.3 Atrial Fibrillation

An early survey on atrial fibrillation (AF) showed that the prevalence of AF among patients at least 35 years old was 0.74% for men and 0.72% for women. Among all patients, 30.9% of AF cases were a first-time diagnosis, 33.0% were paroxysmal, 7.2% were sustained, and 28.9% were permanent.^[1] A recent publication, based on a survey conducted in 2004 in 10 different regions (4 cities and 6 rural areas), showed that the prevalence rate of AF in people 35–59 years was 0.42% and 1.83% in people over 60. After adjusting for age and gender, the prevalence rate was 0.77% (males 0.78%, females 0.76%). 19% of males and 30.9% of females with AF also had accompanying valvular heart diseases. After adjusting for age and gender, left ventricular hypertrophy, obesity, and alcoholism were identified as risk factors for AF.^[2] Recently, analysis from a study investigating 3 922 cases over 60 years old showed that the baseline prevalence rate of AF for males was 2.0% and for females was 1.6%. The average follow-up was 3 years, and the prevalence rate was 4.0/1 000 person-year. Only 1% of the AF patients received warfarin anticoagulant treatment. Patients with AF had significantly higher risks of all-cause (HR 1.87, 95 % CI, 1.09–3.20), cardiovascular mortality (HR 3.78, 95 % CI 2.17–6.58) and stroke mortality (HR 6.31, 95 % CI 2.81–14.19) when compared to patients with sinus rhythm disorder.^[3]

Led by Fu Wai Hospital, a prospective observational^[4] study recruited 2 016 patients (54.8% female) who were admitted to emergency departments due to atrial fibrillation or atrial flutter in twenty representative medical centers. The analysis of the baseline data showed that among the 2 016 patients, 30.7% of them

[1] Zhang S. Atrial fibrillation in mainland China: epidemiology and current management. *Heart*, 2009, 95 (13) : 1052-1055.

[2] Li Y, Wu Y, Chen K, et al. Prevalence of atrial fibrillation in China and its risk factors. *Biome Environ Sci*, 2013, 26 (9) : 709-716.

[3] Li LH, Sheng CS, Hu BC, et al. The prevalence, incidence, management and risks of atrial fibrillation in an elderly Chinese population: a prospective study. *BMC CardiovascDisord*, 2015, 15 (1) : 31.

[4] Zhang H, Yang Y, Zhu J, et al. Baseline characteristics and management of patients with atrial fibrillation/flutter in the emergency department: results of a prospective, multicenter registry in China. *Intern Med J*, 2014, 44 (8) : 742-748.

were diagnosed with paroxysmal AF, 22.4% with persistent AF, and 46.9% with permanent AF. Multiple factor analysis showed^[1] that the independent risk factors for stroke were female gender, age ≥ 75 , stroke or transient ischemic attack history, left ventricular systolic dysfunction, and previous major bleeding. The most common comorbidities were hypertension (55.5%), coronary artery disease (41.8%), and heart failure (HF, 37.4%). Overall, only 16.2% of all the patients received more than one anti-arrhythmic agent, whereas 68.4% patients received atrial rate control agents. Among the patients with valvular atrial fibrillation, 41.4% of patients received oral anticoagulant (OAC) treatment. Only 26.4% of these patients showed international normalized ratio values that were within the target range (2.0–3.0). This study also found^[2] that at 1-year follow-up, AF patients who had a lower body mass index (BMI) had higher all-cause mortality rates. However, the AF patients who were overweight and obese had relatively higher survival rates and lower clinical events risk compared to normal weight and underweight patients. Among the recruited senior patients (≥ 65 years old),^[3] those who were ≥ 75 were more likely to suffer from coronary artery disease, hypertension, previous stroke, cognitive disorder, and chronic obstructive pulmonary disease along with AF. They also showed higher CHADS2 scores but were less likely to accept anticoagulant treatment. The risk of death or adverse events increased by more than two-fold at 1-year follow-up. AF patients with COPD had significantly higher all-cause mortality and cardiovascular mortality at 1-year follow-up, and COPD was an independent risk factor for adverse clinical events.^[4]

A study on anticoagulation therapy for nonvalvular atrial fibrillation^[5] enrolled 988 patients at risk for thromboembolism and compared the safety and efficacy for the prevention of ischemic events among three therapy groups, including a standard-intensity warfarin group (international normalized ratio (INR) 2.1 to 2.5); a low-intensity warfarin group (INR 1.6 to 2.0); and an aspirin (200 mg per day) group. 15 months after randomization, the annual incidence of thromboembolism was 2.3%, 2.6%, and 6.4%, the annual incidence of excessive bleeding was 2.9%, 2.8%, and 1.0%, respectively. This survey found that there was no significance difference regarding the safety and efficacy between the two warfarin groups. In 2011, the Geriatrics Expert Group of the Chinese Medical Association published China's first Expert Opinion on the Treatment of Atrial Fibrillation for Elderly Patients,^[6] revealing the features of elderly patients concerning

[1] Yang YM, Shao XH, Zhu J, et al. Risk factors and incidence of stroke and MACE in Chinese atrial fibrillation patients presenting to emergency departments: A national wide database analysis. *Int J Cardiol.* 2014, 173 (2) : 242-247.

[2] Wang J, Yang YM, Zhu J, et al. Overweight is associated with improved survival and outcomes in patients with atrial fibrillation. *Clin Res Cardiol.* 2014,103 (7) :533-542.

[3] Wang J, Yang YM, Zhu J, et al. Overweight is associated with improved survival and outcomes in patients with atrial fibrillation. *Clin Res Cardiol.* 2014,103 (7) :533-542.

[4] Huang B, Yang Y, Zhu J, et al. Clinical characteristics and prognostic significance of chronic obstructive pulmonary disease in patients with atrial fibrillation: results from a multicenter atrial fibrillation registry study. *J Am Med Dir Assoc.* 2014, 15 (8) : 576-581.

[5] Chen KP, Huang CX, Huang DJ, et al. Anticoagulation therapy in Chinese patients with non-valvular atrial fibrillation: a prospective, multi-center, randomized, controlled study. *Chin Med J.* 2012. 125 (24) : 4355-4360.

[6] Expert Opinion on Treatment of Atrial Fibrillation for Elderly Patients, Writing Group. Expert Opinion on Treatment of Atrial Fibrillation for Elderly Patients. *Chinese J of Geriatrics.* 2011. 30 (11) : 894-908.

stroke risk evaluation, ventricular rhythm, antiarrhythmic medications, and antithrombotic therapies.

New oral anticoagulation medications have overcome the limitation of warfarin and made it unnecessary to constantly monitor levels during the course of treatment. So far, there are several kinds of new oral anticoagulation medications used in Chinese clinics, including direct thrombin inhibitors like dabigatran and direct factor Xa inhibitors like rivaroxaban. Large clinical trials have proven that new anticoagulation medications are able to effectively prevent the incidence of stroke and systemic embolism, and also safely reduce the risk of major bleeding and intracerebral hemorrhage among the nonvalvular atrial fibrillation patients.^[1,2] In China, there was a small study on the clinical efficacy and safety of dabigatran for treating nonvalvular atrial fibrillation. It showed dabigatran significantly reduced the incidence of left atrial thrombosis and stroke events compared to warfarin. But there was no difference in the rates of hemorrhage events between the dabigatran group and warfarin group.^[3] Multiple centers in China observed the effectiveness and safety of dabigatran in anticoagulation treatment for AF after ablation perioperative^[4] and ablation^[5] There was no difference in hemorrhage events between groups. Using dabigatran after ablation was not only safe and effective but also significantly reduced patient length of hospital stay.

Development of catheter ablation for atrial fibrillation: An analysis of registration data from 40 hospitals^[6] found that from 1998 to 2007, the number of patients treated with catheter-guided ablation for atrial fibrillation increased dramatically. The primary techniques employed for this therapy were circumferential pulmonary vein ablation and segmental pulmonary vein ablation. The total success rate was 77.1%, the recurrence rate was 22.9%, and the complication rate was 5.3%. Since 2008, China has been building a national online platform for atrial fibrillations statistics to facilitate data collection. Statistics have shown that RFCA therapies for atrial fibrillation have increased steadily. Currently, circumferential pulmonary vein isolation is still the most commonly used technique within RFCA for AF, accounting for 65.1% of all cases. The percentage of both pulmonary vein ablations with complex fractionated atrial electrograms and with stepwise ablation reached 11.3% and 13.6%, respectively.^[7] In recent years, the frozen cryoballoon ablation

[1] Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011; 365 (10): 883-891.

[2] Granger GB, Alexander JH, McMurry JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011; 365 (11) : 981-992.

[3] Yang GK, Xie B. Dabigatran clinical observation of patients with non-valvular atrial fibrillation anticoagulation. *Chinese J of Cardiac pacing and Electrophysiology*, 2014, 28 (06) : 550.

[4] Pan WQ, Hu WY, Lin ZJ, et al. Dabigatran in atrial fibrillation ablation perioperative application. *Chinese J of Cardiac Arrhythmias*. 2015, 19 (2) : 104-107.

[5] Wang X, Wang ZL, Yang GT, et al. Dabigatran for atrial fibrillation after radiofrequency catheter anticoagulant therapy effectiveness and safety of ablation. *J of Cardiac Arrhythmias*. 2015, 19 (2) : 99-103.

[6] Cao KJ, Chen X. Current situation and prospect of catheter-guided ablation for atrial fibrillation. *Chinese Journal of Cardiac Arrhythmias*, 2009. 13 (3) : 167-169.

[7] Huang CX, Zhang S, Ma CS, et al. National registry of catheter-guided ablation for atrial fibrillation-2008. *Chinese J of Cardiac Arrhythmias*, 2011. 15 (4) ; 247-251.

has started to be applied to pulmonary vein isolation in China. A primary clinical observation^[1] of patients with paroxysmal atrial fibrillation who received frozen balloon ablation, showed that 86.0% of patients continued to have sinus rhythm and fewer complications at their six-month follow-up. However, the long-term efficacy of frozen balloon ablation requires further observation. Since 2013, China has started the primary application of left atrial appendage closure.^[2] Left atrial appendage closure is mainly for the patients who are not able to receive anticoagulant treatment or have a high risk of atrial fibrillation thromboembolism. But it has not been applied widely as yet.

3.3.4 Sudden Cardiac Death (SCD)

A survey with one-year of follow-up^[3] among 678 718 people from July 2005 to June 2006 found that there were 2 983 deaths, with 9.5% (284 cases) attributed to sudden cardiac death (SCD). SCD occurred at a rate of 41.8/100 000 population and was more common in men than women (44.6/100 000 vs. 39.0/100 000). Most SCD cases occurred among people older than 65 years old. The estimated number of SCD cases across China was 544 000 per year.^[4]

Another survey on 497 patients with class I indication for ICD implantation recruited from 31 domestic hospitals between January 2005 and December 2006 was conducted. The study found that the incidence of SCD was 5%, 7%, and 8% in the 3-, 6-, and 12-month follow-up, respectively.^[5] A prospective observational study was conducted in Fu Wai Hospital^[6] from 2004 to 2009. A total of 1 018 consecutive patients who had LVEF \leq 35% and New York Heart Association (NYHA) Class II/III heart failure at least 40 days after myocardial infarction were enrolled. During a mean follow-up of 2.8 years, in the subjects who refused to have implantation, the SCD rate was 5% (the annual incidence of SCD was 1.8%), and the all-cause mortality rate was 7.4%. Independent predictors of SCD included age (HR 1.05, 95% CI 1.02–1.09), EF \leq 25% (HR 1.82, 95% CI 1.04–3.21), and non-revascularization (HR 3.97, 95% CI 2.15–7.31).

[1] Ling TY, Pan WQ, Jin Q, et al. Clinical application and safety of frozen balloon ablation for paroxysmal atrial fibrillation. *Chinese Journal of Cardiac Arrhythmias*, 2015, 19 (2) ; 115-117.

[2] Yao Y, Wu LM, Hou BB, et al. Three cases of the initial experience of percutaneous left atrial appendage closure in atrial fibrillation patients with high risks of stroke. *Chinese Journal of Cardiac Arrhythmias*, 2013, 17 (2) ; 154-155.

[3] Hua W, Zhang LF, Wu YF, et al. Incidence of sudden cardiac death in China: analysis of 4 regional populations. *J Am Coll Cardiol*, 2009, 54:1110-1118.

[4] Zhang S. Sudden cardiac death in China. *Pacing Clin Electrophysiol* 2009, 32:1159-1162.

[5] Hua W, Niu H, Fan X, et al. Preventive effectiveness of implantable cardioverter defibrillator in reducing sudden cardiac death in the Chinese population: a multicenter trial of ICD therapy versus non-ICD therapy. *J Cardiovasc Electrophysiol*. 2012;23 Suppl 1:S5-9.

[6] Fan X, Hua W, Xu Y, et al. Incidence and Predictors of Sudden Cardiac Death in Patients with Reduced Left Ventricular Ejection Fraction after Myocardial Infarction in an Era of Revascularization. *Heart*, 2014, 100 (16) : 1242-1249.

3.3.5 New Technology in the Arrhythmia Field

Implanted pacemakers are currently the first-line of treatment for bradyarrhythmia, but due to the lead displacements, lead fractures, venous thrombosis, and pacemaker pocket infection, leadless pacemakers have become a hot topic in recent years. On February 10th, 2015, Fu Wai Hospital performed the first leadless pacemaker implantation in China^[1] and opened a new era of leadless pacemaker therapy for treating bradyarrhythmia. Cardiac contractility modulation (CCM), also called absolute refractory period electrical stimulation or non-excitatory electrical stimulation, is mainly used in chronic heart failure patients with widened ECG QRS waves (<120ms). Fu Wai Hospital successfully implanted the first CCM in Mainland China on December 30th, 2014.^[2] ICD implantation is an effective treatment for primary and secondary prevention of SCD. Fu Wai Hospital implanted the first domestic station ICD (SICD) in Mainland China on the December 23rd, 2014.^[3] The SICD offers a new, safe, and effective treatment for those who are not eligible for conventional transvenous ICD implantation.

3.4 Heart Failure

3.4.1 Prevalence

A survey covering 15 518 people from 20 urban and rural areas in 10 provinces^[4] showed that the prevalence of chronic heart failure (CHF) among the Chinese population aged 35–74 years was 0.9% (0.7% for men, 1.0% for women, $P < 0.05$) in 2000. The prevalence of CHF was higher in the north than in the south (1.4% vs 0.5%, $P < 0.01$), and higher in urban than rural areas (1.1% vs 0.8%, $P = 0.054$). In addition, a survey of more than 8 459 adults over 35 years old in Xinjiang in 2010^[5] demonstrated that the overall prevalence of heart failure (HF) was 1.26%. There were significant differences among various ethnic groups: 0.89% in the Han, 1.11% in the Uygur, and 2.14% in the Kazakhs.

3.4.2 Demographic Characteristics of HF

Recently, the China HF Registration Collaborative Group released preliminary results of a prospective, multi-center, large-scale registry study on patients hospitalized with HF^[6]. It analyzed the etiology, clinical

[1] Chen KP, Dai Y, Zheng XL, et al. Non-wire Catheter Pacemaker Implantation One Case. *J of Cardiac Arrhythmias*, 2015,19 (2) : 145-146.

[2] Hua W, Fan XH, Wang J, et al. Implantable Cardiac Contractility Regulator Chronic Heart Failure One Case. *J of Cardiac Arrhythmias*, 2015 (1) :145-146.

[3] Hua W, Ding LG, Zheng LH, et al. Whole Subcutaneous Implantable Cardioverter Defibrillator Example. *J of Cardiac Arrhythmias*, 2014, 18 (6) :469-470.

[4] Gu DF, Huang GY, He J, et al. Investigation of prevalence and distributing feature of chronic heart failure in Chinese adult population. *Chinese Journal of Cardiology*, 2003,31 (1) :3-6.

[5] Yang YN, Mang YT, Liu F, et al. Incidence and distributing feature of chronic heart failure in adult population of Xinjiang. *Chinese Journal of Cardiology*, 2010,38 (5) :460-464.

[6] Zhang J, Zhang YH, et al. China Heart Failure Registry Study—A Multicenter, Prospective Investigation for Preliminary Analysis on Etiology, Clinical Features and Treatment in Heart Failure Patients. *Chinese Circulation Journal*, 2015,30 (5) :413-416.

features and treatment of HF. From January 2012 to December 2014, clinical data from 8 516 cases of HF patients in 88 hospitals (8 in the Northeast, 27 in the North, 18 in the East, 7 in the South, 5 in the Central, 15 in the Northwest, and 8 in the Southwest) were collected. The basic characteristics of patients and a comparison with previous domestic HF studies are shown in Table 3-4-1. The average age of patients with heart failure has been rising: the current average is 66 ± 15 years and 54.5% of cases are men and 84.7% of patients are NYHA Class III-IV heart failure. The main comorbidities have also changed significantly. The proportion of valvular heart disease (VHD) has gradually decreased and coronary artery disease (CHD) (49.4%), hypertension (54.6%), and chronic kidney disease (CKD) (29.7%) have become the main comorbidities in Chinese heart failure patients. 37.5% of the patients showed left ventricular ejection fraction (LVEF) $\leq 40\%$ by echocardiography, 20.5% showed 40%-50%, and 34.7% showed $\geq 50\%$. 34.7% of the patients were diagnosed as having diastolic HF.

Table 3-4-1 The Characteristics of HF Patients among Different Chinese Populations in Recent Years

Sites	Year	Sample Size	Population	Age	Male (%)	CHD	Hypertension	Diabetes	VHD	CKD
42 Hospitals ^[1]	1980	1 756	CHF	68 ± 17	56.0	36.8	8.0	—	34.4 ^a	—
	1990	2 181	CHF	64 ± 22	60.0	33.8	10.4	—	34.3 ^a	—
	2000	6 777	CHF	63 ± 16	55.0	45.6	12.9	—	18.6 ^a	—
Shanghai ^[2]	1980			52	55.1	31.1	8.5	—	46.8 ^a	—
	1990	2 178	CHF	59	58.2	40.6	10.3	—	24.2 ^a	—
	2000			69	58.3	55.7	13.9	—	8.9 ^a	—
PLA General Hospital ^[3]	1993 - 1997	1 623		56 ± 18	62.6	37.2	23.3	12.3	35.2 ^a	5.2 ^b
	1998 - 2002	2 444	CHF	58 ± 18	60.4	40.9	32.3	15.9	32.7 ^a	4.7 ^b
	2003 - 2007	3 252	CHF	63 ± 16	63.1	46.8	46.7	21.1	16.6 ^a	9.1 ^b
10 Hospitals ^[4]	2005 - 2009	2 154	CHF	64 ± 13	78.6	64.4	56.7	17.2	—	—
Hubei ^[5]	2000 - 2010	16 681	Chronic systolic HF	63 ± 11	59.3	—	47.6	16.2	—	—
China Heart Failure Registry Study ^[6]	2012 - 2014	8 516	In-hospital HF	66 ± 15	54.5	49.4	54.6	21.7	17.6	29.7 ^c

Notes: a: rheumatic valvular disease; b: creatinine clearance rate $< 50 \text{ ml/min}$; c: glomerular filtration rate $< 60 \text{ ml/min/1.73m}^2$; CHD: coronary heart disease; VHD: valvular heart disease; CKD: chronic kidney disease; CHF: chronic heart failure; HF: heart failure.

[1] Chinese Society of Cardiology of Chinese Medical Association. Retrospective investigation of hospitalized patients with heart failure in some parts of China in 1980, 1990 and 2000. *Chinese Journal of Cardiology*, 2002,30(8):450-454.

[2] Shanghai heart failure investigations Collaboration. The evolving trends in the epidemiologic factors and treatment of hospitalized patients with congestive heart failure in Shanghai during years of 1980,1990,2000. *Chinese Journal of Cardiology*, 2002,30(1):24-27.

[3] Pei ZY, Zhao YS, Li JY, et al. Fifteen-year evolving trends of etiology and prognosis in hospitalized patients with heart failure. *Chinese Journal of Cardiology*, 2011,39(5):434-439.

[4] Liu X, Yu H, Pei J, et al. Clinical characteristics and long-term prognosis in patients with chronic heart failure and reduced ejection fraction in China. *Heart Lung Circ*, 2014,23: 818-826.

[5] Yu SB, Zhao QY, Cui HY, et al. Investigation on the prevalence and related factors of medicinal therapy in patients with chronic systolic heart failure. *Chinese Journal of Epidemiology*, 2012,33(2):229-233.

[6] Zhang J, Zhang YH, et al. China Heart Failure Registry Study—A Multicenter, Prospective Investigation for Preliminary Analysis on Etiology, Clinical Features and Treatment in Heart Failure Patients. *Chinese Circulation Journal*, 2015,30(5):413-416.

3.4.3 Causes for the Onset of HF

Complicated infection was the most common predisposing factor for patients with HF hospitalized in Shanghai in 1980, 1990, and 2000, and accounted for 40.2%, 41.2% and 38.4% of HF patients, respectively^[1]. According to the China Heart Failure Registry Study (China-HF)^[2], infection (45.9%) remained the primary reason for the exacerbation of heart failure, followed by exertion or stress (26.0%), and then myocardial ischemia (23.1%) (Figure 3-4-1).

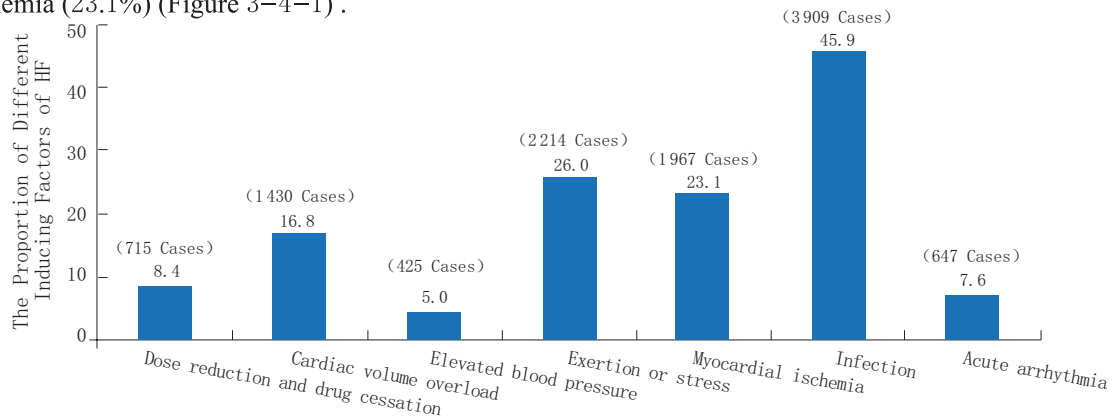


Figure 3-4-1 The Proportion of Different Inducing Factors of HF

3.4.4 Medicine Treatment for HF

The China Heart Failure Registry Study (China-HF)^[2] showed that the proportion of patients treated with intravenous diuretics during hospitalization has not changed significantly. The usage of digoxin showed a downward trend due to the effects of international clinical trials. The use of angiotensin II receptor antagonist (ARB), aldosterone receptor antagonist and beta-receptor blocker increased significantly (Table 3-4-2).

Table 3-4-2 Medicine Usage in the HF Patients

Site	Year	Sample Size	Medicine (%)							
			Nitrates	Diuretics	Digoxin	ARB	ACEI	AAs	BB	CCB
Tianjing ^[3]	1973-1982	542	30.3	58.7	61.3	—	—	5.9	9.0	14.8
	1983-1992	1 253	70.6	67.8	71.6	—	24.2	10.1	8.3	35.2
	1993-2002	3 394	91.4	75.4	67.9	4.0	70.9	23.1	25.3	21.6
42 Hospitals ^[1]	1980	1 756	44.7	63.7	51.7	0.4	14.0	10.0	8.5	6.1
	1990	2 181	36.0	70.2	45.5	1.4	26.4	8.4	9.5	16.4
	2000	6 777	53.0	48.6	40.3	4.5	40.4	20.0	19.0	10.5

[1] Chinese Society of Cardiology of Chinese Medical Association. Retrospective investigation of hospitalized patients with heart failure in some parts of China in 1980, 1990 and 2000. Chinese Journal of Cardiology, 2002,30 (8) :450-454.

[2] Zhang J, Zhang YH, et al. China Heart Failure Registry Study—A Multicenter, Prospective Investigation for Preliminary Analysis on Etiology, Clinical Features and Treatment in Heart Failure Patients. Chinese Circulation Journal, 2015,30 (5) :413-416.

[3] Ma JP, Wang L, Dang Q, et al. Retrospective analysis of drug treatment on inpatients with chronic heart failure. Chinese Journal of Epidemiology, 2007,28(1):78-82.

Table 3-4-2 Medicine Usage in the HF Patients

(Continued)

Site	Year	Sample Size	Medicine (%)							
			Nitrates	Diuretics	Digoxin	ARB	ACEI	AAs	BB	CCB
Shanghai ^[1]	1980	2 178	74.4	77.1	60.0	—	0.6	—	6.8	—
	1990	—	—	—	—	—	38.9	—	5.7	41.3
17 Districts	2000	—	—	—	—	11.5	70.8	—	25.0	14.2
Primary Hospitals ^[2]	2006	2 100	—	90.0	60.0	—	5.8	50.0	40.0	—
10 Hospitals ^[3]	2005–2009	2 154	—	74.4	—	66.0	66.0	74.6	68.3	—
Hubei ^[4]	2000–2010	16 681	—	69.1	46.2	18.7	51.6	—	46.6	—
China Heart Failure Registry Study ^[5]	2012–2014	8 516	41.6 ^a	67.2 ^b	26.1 ^b	24.6 ^b	30.1 ^b	55.4 ^b	50.6 ^b	10.6 ^b

Notes: a: Intravenous drugs during hospitalization; b: Oral medication after discharge. AAs: aldosterone receptor antagonists; BB: beta-receptor blocker; ACEI: angiotensin converting enzymes inhibitor; ARB: angiotensin II receptor antagonist; CCB: calcium channel blocker.

3.4.5 The Mortality Rates of Hospitalized Patients with HF

A retrospective analysis^[6] of hospitalized patients with CHF over the past 15 years in Beijing 301 Hospital showed that the 30-day mortality was 5.4%, and the mortality increased with age and additional comorbidities (Figure 3-4-2, 3-4-3). Another retrospective study analyzed 1 198 cases admitted to the emergency room in Xuanwu Hospital due to AHF between 2005 and 2011^[7], and demonstrated that 518 patients (43.2%) fell into the 70–79 age group, accounting for the highest proportion of AHF patients. 115 cases (9.6%) died in the emergency room, of which, 73 cases (63.5%) died within 24 hours and 93 patients (80.9%) within 48 hours. The China Heart Failure Registry Study (China-HF)^[5] showed that the median length of in-hospital stay was 11 days and the in-hospital mortality was 5.3%.

[1] Shanghai heart failure investigations Collaboration. The evolving trends in the epidemiologic factors and treatment of hospitalized patients with congestive heart failure in Shanghai during years of 1980,1990,2000. *Chinese Journal of Cardiology*, 2002,30(1):24-27.

[2] Cao YS, Hu DY, Wang HY, et al. A survey of medical therapies for chronic heart failure in primary hospitals in China. *Chinese Journal of Internal Medicine*, 2006,45(11):907-909.

[3] Liu X, Yu H, Pei J, et al. Clinical characteristics and long-term prognosis in patients with chronic heart failure and reduced ejection fraction in China. *Heart Lung Circ*, 2014,23: 818-826.

[4] Yu SB, Zhao QY, Cui HY. Et al. Investigation on the prevalence and related factors of medicinal therapy in patients with chronic systolic heart failure. *Chinese Journal of Epidemiology*, 2012,33(2):229-233.

[5] Zhang J, Zhang YH, et al. China Heart Failure Registry Study—A Multicenter, Prospective Investigation for Preliminary Analysis on Etiology, Clinical Features and Treatment in Heart Failure Patients. *Chinese Circulation Journal*, 2015,30(5):413-416.

[6] Yin QX, Zhao YS, Li JY, et al. The coexistence of multiple cardiovascular diseases is an independent predictor of the 30-day mortality of hospitalized patients with congestive heart failure: a study in Beijing. *Clin Cardiol*, 2011,34 (7) :442-446.

[7] Li XY, Qin J, Liang X, et al. A retrospective analysis of 1198 patients with acute heart failure treated in emergency department. *Chinese Journal of Geriatric Heart Brain and Vessel Diseases*. 2012,14 (10) :1045-1047.

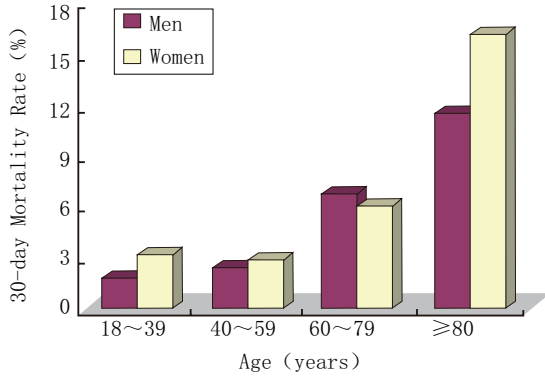


Figure 3-4-2 In-hospital Mortality by Age and Gender

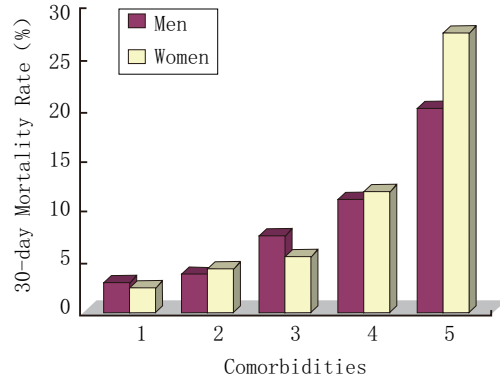


Figure 3-4-3 In-hospital Mortality by Gender and Number of Co-morbidities

3.4.6 Long-term Prognosis of Patients with HF

Henan Provincial People's Hospital did a long-term follow-up study in 685 HF patients with LVEF ≤ 45%^[1]. At the 31-month (8–61 months) mid-term follow-up, 191 cases (28%) died, including 127 cases (19%) due to pump failure and 42 cases (6%) of sudden death. Another prospective study^[2] including 2 154 patients with CHF from 10 hospitals showed that 850 patients died (39.5%) at the mid-term follow-up of 52 months, and the mortality rate was significantly higher in the dilated cardiomyopathy group than in the CAD group (46.8% vs. 35.4%, P < 0.001).

The HF Center of Beijing Fu Wai Hospital did a midterm follow-up on 1 440 HF patients hospitalized for 582 days during 2009–2013^[3]. During the period, 283 patients died (19.7%); among them, 169 cases died of worsened heart failure and 43 cases died of sudden death. Through the detection of protein markers, a novel protein marker, soluble growth stimulating gene expression protein 2 (sST2) was found as a predictor independent of renal function and it could provide additional prognostic information for the prediction model^[4]. The center also did a long-term follow-up (a mid-term follow-up is 31 months long) among 128 patients with recent onset of non-ischemic cardiomyopathy and HF^[5]. It demonstrated that 62 cases (48%) normalized their LVEF level via medication treatment alone, showing a significant increase in LVEF level

[1] Xu Y, Shi Y, Zhu Z, et al. Prognosis of patients with heart failure and reduced ejection fraction in China. *Exp Ther Med*, 2013, 6 (6): 1437-1442.

[2] Liu X, Yu H, Pei J, et al. Clinical characteristics and long-term prognosis in patients with chronic heart failure and reduced ejection fraction in China. *Heart Lung Circ*, 2014, 23: 818-826.

[3] Zhang Y, Zhang R, An T, et al. The utility of galectin-3 for predicting cause-specific death in hospitalized patients with heart failure. *J Card Fail*, 2015, 21 (1): 51-59.

[4] Zhang R, Zhang Y, An T, et al. Prognostic value of sST2 and galectin-3 for death relative to renal function in patients hospitalized for heart failure. *Biomark Med*, 2015, 9 (5): 433-441.

[5] Zou CH, Zhang J, Zhang YH, et al. Frequency and predictors of normalization of left ventricular ejection fraction in recent-onset nonischemic cardiomyopathy. *Am J Cardiol*, 2014, 113 (10): 1705-1710.

from $32 \pm 6\%$ to $58 \pm 5\%$. A multivariate regression analysis showed that normalization of LVEF was associated with a history of hypertension, higher systolic blood pressure, shorter QRS duration, smaller left ventricular end diastolic diameter, or higher left ventricular ejection fraction at baseline.

3.4.7 The Survey on Treatment of CHF in Chinese Primary Hospitals^[1]

A survey in 2006 summarized the drug usage among the patients with CHF in 2 066 primary hospitals (level 2 or below) in 17 regions (11 provinces, 3 municipalities and 3 autonomous districts). Several problems were discovered: the usage rate of digoxin at a dose of >0.25 mg/day was still as high as 10%; the usage rate of β -blocker was 40% with only 1% of patients at the target dose; the usage rate of angiotensin converting enzyme inhibitors (ACEI) was 80% with only 2% of patients at the target dose.

3.4.8 Studies of ACS and Acute HF

The BRIG study was a study completed in 2011 among domestic patients with ACS and acute HF^[2]. It examined the medical records of 3 168 patients who had a definitive diagnosis of ACS from 65 hospitals in 31 provinces of mainland China as well as Hong Kong district during March through June in 2006, including 1 329 cases of ST-elevation myocardial infarction (STEMI), 348 cases of non-ST-elevation myocardial infarction (NSTEMI), and 1 491 cases of unstable angina (UA). Among these ACS patients, 706 (22.3%) developed acute HF during hospitalization, 262 (8.3%) did not have an acute episode of HF, and 2 200 (69.4%) did not have HF.

The HF patients with acute episodes during hospitalization were younger than those without (67.8 ± 11.1 vs. 70.0 ± 9.3 , $p < 0.01$), with a higher proportion of men (70.3% vs. 60.3%, $p < 0.01$) and current smokers (26.6% vs. 20.2%, $p < 0.05$), a higher rate of STEMI (71.0% vs. 27.9%, $p < 0.01$), and a lower likelihood of having a history of ACS (24.6% vs. 33.6%, $p < 0.01$). Compared with the ACS patients without HF, those with HF had a lower compliance rate of β -blockers (66.5% vs. 71.1%, $p = 0.01$) and statins (67.4% vs. 72.2%, $p < 0.01$), as well as a lower rate of receiving PCI treatment (16.7% vs. 29.9%, $p < 0.01$).

Compared with those without HF, the ACS patients accompanying with HF had a higher rate of in-hospital mortality (8.4% vs. 0.8%, $p < 0.01$) and a higher occurrence of in-hospital composite endpoints (24.0% vs. 8.3%, $p < 0.01$). In addition, the in-hospital mortality and the occurrence of composite endpoints were higher in the patients with acute episodes than those without (10.8% vs. 1.9%, $p < 0.01$ and 30.3% vs. 6.9%, $p < 0.01$, respectively). Multivariate logistic regression analyses indicated that acute HF remained as a strong independent predictor of in-hospital mortality and the occurrence of composite endpoints in the

[1] Cao YS, Hu DY, Wang HY, et al. A survey of medical therapies for chronic heart failure in primary hospitals in China. *Chinese Journal of Internal Medicine*, 2006,45 (11) :907-909.

[2] Wang N, Zhao D, Liu J, et al. Impact of heart failure on in-hospital outcomes of acute coronary syndrome patients in China—Results from the Bridging the Gap on CHD Secondary Prevention in China (BRIG) project. *International Journal of Cardiology*, 2012,160:15-19.

patients (OR 7.50, 95% CI 4.32–13.02, and OR 2.74, 95% CI 2.15–3.48, respectively) .

3.4.9 2014 Chinese Guideline for the Diagnosis and Treatment of Patients with HF^[1]

“Chinese heart failure diagnosis and treatment guidelines 2014” was published in February 2014. This edition cited the latest results of both domestic and international studies, referred to the newest guidelines in Europe and America, and updated meticulously on the basis of the 2007 version. The main updates included: the addition of the flow chart for the treatment of acute and chronic HF clearly described the timing, options and conditions of medication use; in terms of improving the prognosis of the treatment, an early and combinational usage of ACEI, ARB and β -blockers without having to wait for the dry weight was proposed; the application timing of ARB was extended, from originally starting at NYHA III–IV to NYHA II; a flowchart for Chinese patients was made for the application of CRT/D and it proposed to relocate the patients if they are eligible after a standard treatment of 3–6 months; the management of patients after discharge was also emphasized, including pertaining to mental and physical rehabilitation; and the role of traditional Chinese medicine was updated for future treatment of HF.

3.5 Pulmonary Arterial Hypertension

3.5.1 Pulmonary Arterial Hypertension (PAH)

3.5.1.1 Prognosis for Connective Tissue Diseases Related PAH (CTD–PAH)

In May 2014, three hospitals in Beijing reported their findings on the prognosis of 129 patients with CTD–PAH.^[2] The breakdown of the different underlying connective tissue diseases (CTDs) is shown in Figure 3–5–1. The median follow–up time was 17.3 (1.4–55.1) months and 17 (14.9%) patients died. The 1– and 3–year survival rates in patients with different types of CTD–PAH are shown in Table 3–5–1. Factors affecting their survival rates are shown in Table 3–5–2.

[1] Chinese Society of Cardiology of Chinese Medical Association, Editorial Board of Chinese Journal Cardiology. 2014 Chinese guideline for diagnosis and treatment of patients with heart failure. Chinese Journal of Cardiology, 2014, 42 (2) :98–122.

[2] Hao YJ, Jing ZC, Zhang ZL. Connective tissue disease-associated pulmonary arterial hypertension in Chinese patients. Eur Respir J. 2014; 44 (4) :963–72.

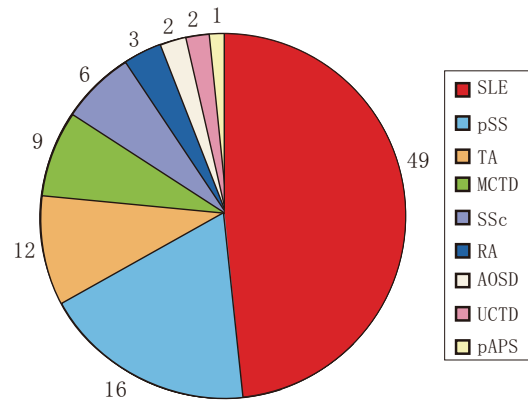


Figure 3-5-1 Proportions of Different Underlying Connective Tissue Diseases (CTDs) in 129 Patients with CTD-PAH(%)

AOSD: Adult-Onset Still's Disease; UCTD: Undifferentiated Connective Tissue Disease; pAPS: Primary Antiphospholipid Syndrome. SLE: Systemic Lupus Erythematosus; pSS: primary Sjogren's Syndrome; TA: Takayasu Arteritis; MCTD: Mixed Connective Tissue Disease; SSc: Systemic Sclerosis; RA: Rheumatoid Arthritis.

Table 3-5-1 One-and Three-year Survival Rates in Patients with CTD-PAH

Survival Rate	Total	SLE-PAH	pSS-PAH	TA-PAH	MCTD-PAH	SSc-PAH
1-year (%)	92	91	100	84	82	100
3-year (%)	80	88	86	72	64	60

Note: SLE-PAH: systemic lupus erythematosus-related pulmonary arterial hypertension; pSS-PAH: primary Sjogren's syndrome-related pulmonary arterial hypertension; TA-PAH: Takayasu Arteritis-related pulmonary arterial hypertension; MCTD-PAH: Mixed Connective Tissue Disease-related pulmonary arterial hypertension; SSc-PAH: systemic sclerosis-related pulmonary arterial hypertension.

Table 3-5-2 Factors Affecting the Prognosis of Patients with Connective Tissue Disease Related PAH

Parameters	HR (95% CI)	P value
Pulmonary Vascular Resistance	1.34 (1.04-1.73)	0.023
Alkaline Phosphatase	1.72 (1.01-2.93)	0.045

3.5.1.2 Long-term Survival Rate of Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Data from 504 patients with CTEPH admitted at Beijing Anzhen Hospital were collected from 1989 to 2008. Among this cohort, 360 patients underwent pulmonary thromboendarterectomy (surgery group) and 144 patients received medication (non-surgery group). The in-hospital mortality rates for the surgery and non-surgery groups were 4.44% and 3.50%, respectively. For patients with central CTEPH, those who underwent a surgical intervention demonstrated a higher long-term survival rate than patients treated with the medical regimen ($p=0.0004$). For peripheral CTEPH, there was no significant difference between the two

groups ($p=0.874$)^[1]. The long-term survival rates of patients with CTEPH are listed in Table 3-5-3. The long-term survival rates of CTEPH patients undergoing thromboendarterectomy from both domestic and international studies are shown in Table 3-5-4.

Table 3-5-3 Long-term Survival Rates of CTEPH

Groups	Central Type		Peripheral Type		P value*
	10-year survival rate (%)	15-year survival rate (%)	10-year survival rate (%)	15-year survival rate (%)	
Surgery	94.60 ± 2.38	90.96 ± 4.24	71.78 ± 4.66	29.57 ± 15.10	<0.0001
Non-surgery	81.4 ± 7.14	56.43 ± 14.70	69.84 ± 7.78	32.59 ± 13.70	0.5

Table 3-5-4 Long-term Survival Rates of CTEPH Patients Undergoing Thromboendarterectomy from both Domestic and International Studies

Country	Medical Center	Duration	Sample Size	In-hospital Mortality (%)	Long-term Survival Rate of Central CTEPH (%)
China	Beijing Anzhen Hospital	1989-2008	360	4	95 (10-year) 91 (15-year)
United States ^[2]	UCSD Medical Center	1997-2007	988	4	96 (1-year) 88 (5-year)
United Kingdom ^[3]	Papworth Hospital	2001-2006	236	16	98% to 99% (1-year) 93% to 94% (3-year)
Japan ^[4]	Chiba University	1990-2010	77	9	84 (5-year) 82 (10-year)

3.5.1.3 Long-term Survival Rates of Patients with PAH Following Lung Transplantation

244 lung transplants have been performed in 20 hospitals across China from January 1978 to December 2010, 100 cases of which were conducted in Wuxi People's Hospital, including 72 cases of single-lung and 28 cases of double-lung transplantation. Patients receiving the lung transplants were those with IPAH, CHD-PAH, and chronic lung disease related PAH. Survival rates are shown in Table 3-5-5^[5].

[1] Gan HL, Zhang JQ, Bo P, et al. The actuarial survival analysis of the surgical and non-surgical therapy regimen for chronic thromboembolic pulmonary hypertension. *J Thromb Thrombolysis*. 2010;29:25-31.

[2] Thistlethwaite PA, Kaneko K, Madani MM, et al. Technique and outcomes of pulmonary endarterectomy surgery. *Ann Thorac Cardiovasc Surg*. 2008;14(5): 274-282.

[3] Condliffe R, Kiely DG, Gibbs JS, et al. Improved outcomes in medically and surgically treated chronic thromboembolic pulmonary hypertension. *Am J Respir Crit Care Med*. 2008;15;177(10):1122-1127.

[4] Keiichi I, Masahisa M, Nobuhiro T, et al. Long-term outcome after pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension. *J Thorac Cardiovasc Surg*. 2012;144(2):321-326

[5] Mao W, Chen J, Zheng M, et al. Initial Experience of Lung Transplantation at a Single Center in China. *Transplantation Proceedings*. 2013,45:349-355.

Table 3–5–5 Survival Rates Following Lung Transplantation in China and Other Countries

Periods	Medical Center	Cases	1–Year Survival Rate (%)	3–Year Survival Rate (%)	5–Year Survival Rate (%)	10–Year Survival Rate (%)
1978.1–2010.12	20 Hospitals in China	244	50	30	20	—
2002.6–2010.12	Wuxi People's Hospital	100	73	54	41	—
1985.1–2012.6	ISHLT ^[1] (158 Centers)	47 000	80	65	53	32

Note: ISHLT: International Association of Heart and Lung Transplantation.

3.5.2 Pulmonary Embolism (PE)

3.5.2.1 Incidence and Mortality of Pulmonary Embolism among Hospitalized Patients

From 1997 to 2008, a registration study on patients with pulmonary embolism was conducted in 60 tertiary hospitals involved in the National Cooperative Project for the Prevention and Treatment of Venous Thromboembolism (NCPPT). A total of 18 206 patients were confirmed to have PE from the 16 972 182 hospital admissions. The annual incidence of PE was 0.1%^[2]. The incidence of PE in hospitalized patients by age and gender is shown in Table 3–5–6. The trends in incidence and case fatality rates for PE in hospitalized adults from 1997 to 2008 are shown in Figure 3–5–2. The discrepancies between the North and the South in incidence and case fatality rates for PE in China from 1997 to 2008 are shown in Figure 3–5–3.

Table 3–5–6 Incidence of PE in Hospitalized Patients by Age and Gender (%)

Age	Total	Men	Female
<30	0.07 (0.02–0.13)	0.12 (0.06–0.21)	0.05 (0.02–0.11)
31–40	0.06 (0.02–0.12)	0.14 (0.08–0.23)	0.03 (0.01–0.09)
41–50	0.13 (0.07–0.22)	0.16 (0.09–0.25)	0.10 (0.05–0.18)
51–60	0.12 (0.06–0.21)	0.14 (0.08–0.23)	0.10 (0.05–0.18)
61–70	0.14 (0.08–0.23)	0.19 (0.11–0.29)	0.12 (0.06–0.21)
71+	0.10 (0.05–0.18)	0.44 (0.32–0.59)	0.05 (0.02–0.11)
合计	0.11 (0.05–0.19)	0.18 (0.10–0.28)	0.07 (0.02–0.13)

[1] Jason D, Leah B, Anna Y, et al. The Registry of the International Society for Heart and Lung Transplantation: Twenty-seventh official adult lung and heart-lung transplant report—2010. *J Heart Lung Transplant*. 2010;29:1104-18.

[2] Yang Y, Liang L, Zhai Z, et al. Pulmonary Embolism Incidence and Fatality Trends in Chinese Hospitals from 1997 to 2008: A Multicenter Registration Study. *PLoS One*. 2011;6 (11) :e26861.

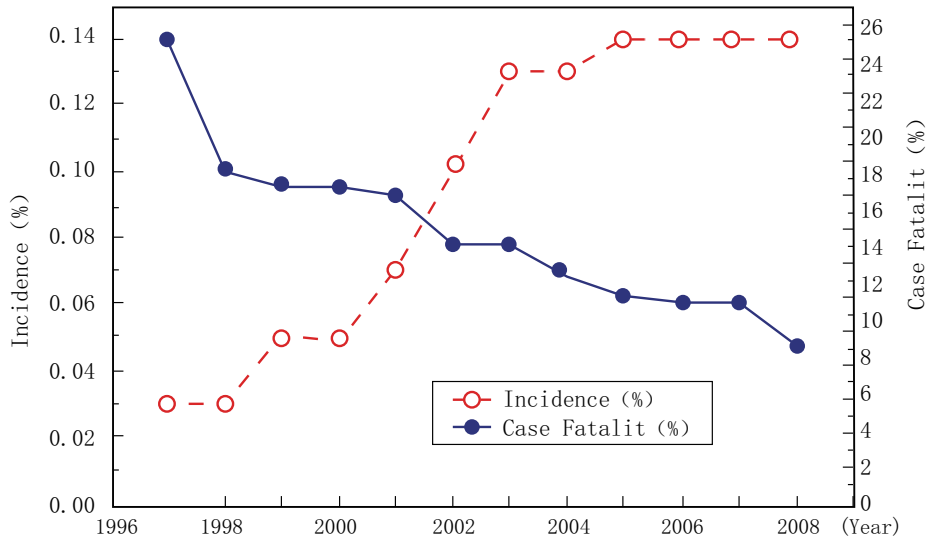


Figure 3-5-2 Incidence and Case Fatality Rates for PE in Hospitalized Adults from 1997 to 2008

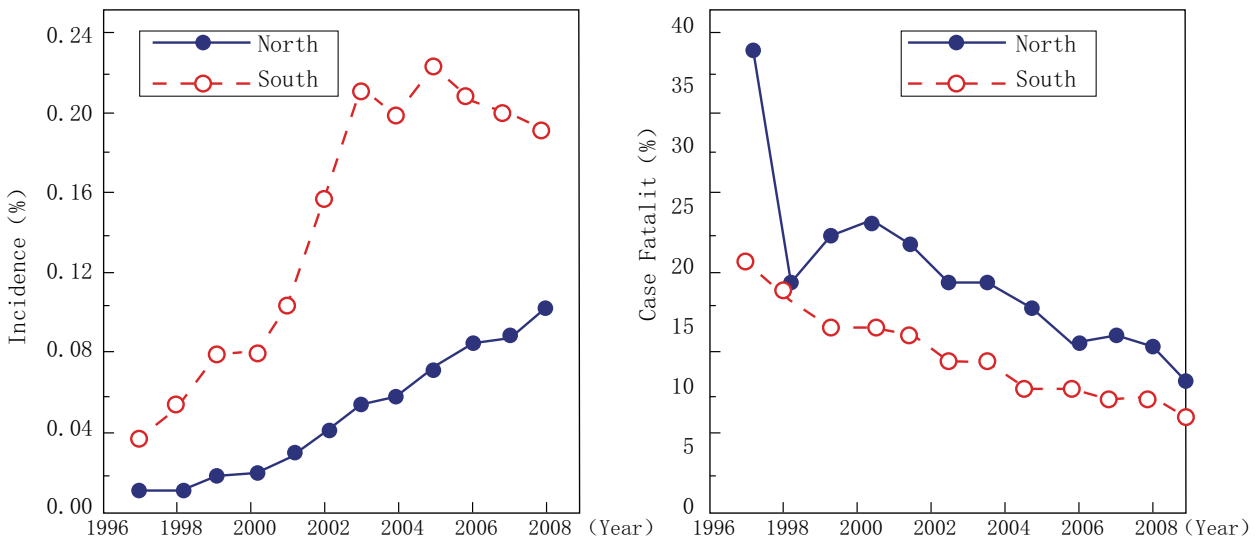


Figure 3-5-3 The Discrepancies between the North and the South in Incidence and Case Fatality Rates for PE in China from 1997 to 2008

3.5.2.2 Risk Factors for Venous Thromboembolism (VTE)

A retrospective study was conducted among 1 048 patients with VTE hospitalized in Hangzhou First People’s Hospital from 2004 to 2013, to investigate risk factors associated with VTE^[1]. The results showed that there were 229 cases with only pulmonary embolism (PE) , 552 cases with only deep venous thrombosis

[1] Wang H, Ye J, Wang LM, et al. Risk Characteristics of Venous Thromboembolism in Chinese Patients. Clinical and Applied Thrombosis Hemostasis, 2015, pii: 1076029615569272.

(DVT), and 194 cases with both PE and DVT. The incidence of VTE among hospitalized patients over ten years is shown in Figure 3-5-4, the distribution of patients with DVT by age and gender is shown in Figure 3-5-5, the risk factors for DVT stratified by gender are shown in Table 3-5-7, and a patient characteristics comparison in patients with DVT between China and western countries is shown in Table 3-5-8.

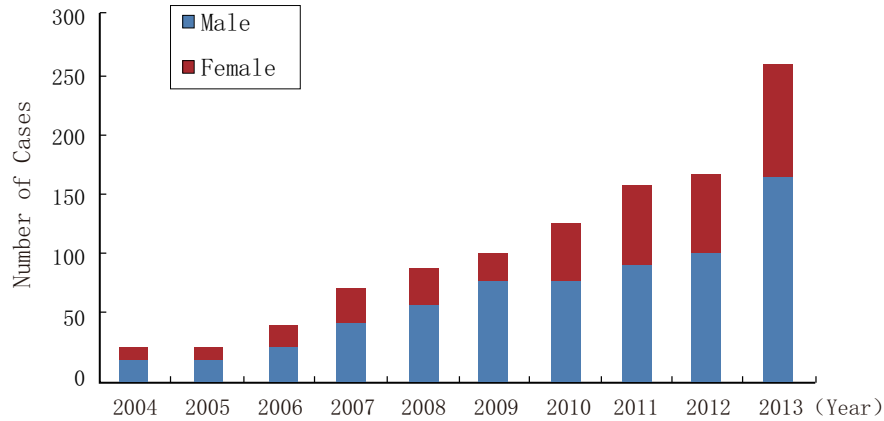


Figure 3-5-4 The Incidence of VTE among Hospitalized Patients over Ten Years

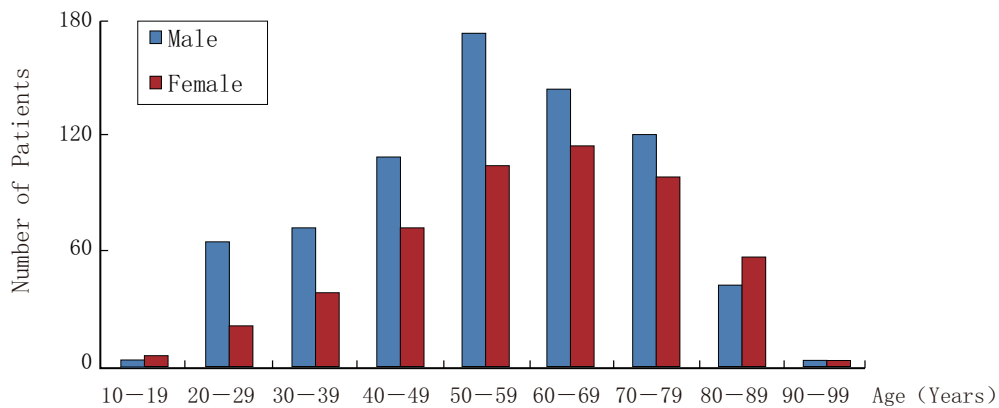


Figure 3-5-5 The Distribution of Patients with DVT by Age and Gender

Table 3-5-7 The Risk Factors for DVT Stratified by Gender

Characteristics	No. of Patients (%)	Male (%)	Female (%)	P Value
Age \geq 50 yrs	885 (73.0)	492 (71.2)	393 (75.3)	0.003
Gender	1 048	603 (57.5)	445 (42.5)	0.000
Prolonged Immobility	125 (11.9)	73 (12.1)	52 (11.7)	0.835
Cancer	109 (10.4)	61 (10.1)	48 (10.8)	0.725
Trauma/Surgery	68 (6.5)	43 (7.1)	25 (5.6)	0.326

Table 3–5–7 The Risk Factors for DVT Stratified by Gender

(Continued)

Characteristics	No. of Patients (%)	Male (%)	Female (%)	P Value
Infection	43 (4.1)	27 (4.5)	16 (3.6)	0.477
Diabetes Mellitus	32 (3.1)	20 (3.3)	12 (2.7)	0.564
Stroke	24 (2.3)	9 (1.5)	15 (3.4)	0.045
Autoimmune Diseases	20 (1.9)	8 (1.3)	12 (2.7)	0.109
Heart Failure	18 (1.7)	8 (1.3)	10 (2.2)	0.253
Myocardial Infarction	9 (0.9)	8 (1.0)	1 (0.2)	0.056
Pregnant/Post Partum	3 (0.3)	0 (0.0)	3 (0.3)	N/A

Table 3–5–8 Patient Characteristics Comparison between China and Western Countries

Risk Factors	Data from Hangzhou	Data from Western Countries
Have Primary Diseases	94%	22% ^[1]
Most Common Primary Diseases	Cancer, infection, Diabetes Mellitus	Heart failure, ABCOPD, septicemia ^[2]
Most Common Malignant Cancers	Lung, liver, uterus	Pancreas, stomach, bladder ^[3,4]
Elderly	Higher among elderly	Independent risk factor ^[5-7]
Gender Differences	Higher among male	Similar to data from Hangzhou, but different from that in Japan ^[8-12]

[1] Heit JA, O'Fallon WM, Petterson TM, et al. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism- A population-based study. *Arch Intern Med*, 2002,162 (11) :1245-1248.

[2] Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. *N Eng J Med*, 1999,341 (11) :793-800.

[3] Khorana AA, Francis CW, Culakova E, et al. Frequency, risk factors, and trends for venous thromboembolism among hospitalized cancer patients. *Cancer*, 2007, 110 (10) : 2339-2346.

[4] Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of venous thromboembolism and its effect on survival among patients with common cancers. *Arch Intern Med*, 2006, 166 (4) :458-464.

[5] Nakamura M, Sakuma M, Yamada N, et al. Risk factors of acute pulmonary thromboembolism in Japanese patients hospitalized for medical illness: results of a multicenter registry in the Japanese society of pulmonary embolism research *J Thromb Thrombolys*, 2006,21 (2) :131-135.

[6] Rothberg MB, Lindensauer PK, Lahti M, et al. Risk factor model to predict venous thromboembolism in hospitalized medical patients. *J Hosp Med*, 2011,6 (4) :202-209.

[7] Weill-Engerer S, Meaume S, Lablou A, et al. Risk factors for deep vein thrombosis in inpatients aged 65 and older: a case-control multicenter study *J Am Geriatr Soc*, 2004,52 (8) :1299-1304.

[8] Kishimoto M, Lim HY, Tokuda Y, et al. Prevalence of venous thromboembolism at a teaching hospital in Okinawa, Japan. *Thromb Haemostasis*, 2005,93 (5) :876-879.

[9] Bergqvist D. Are men more at risk of recurrent venous thromboembolism than women? *Nat Clin Pract Card*, 2007,4 (1) :12-13

[10] Tormene D, Ferri V, Carraro S, et al. Gender and the risk of venous thromboembolism. *Semin Thromb Hemost*, 2011,37 (3) :193-198.

[11] Heit JA. Venous thromboembolism: disease burden, outcomes and risk factors. *J Thromb Haemost*, 2005,3 (8) :1611-1617.

[12] McRae S, Tran H, Schulman S, et al. Effect of patient's sex on risk of recurrent venous thromboembolism: a meta-analysis. *Lancet*, 2006,368 (9533) :371-378.

3.5.3 Chronic Obstructive Pulmonary Disease

3.5.3.1 Prevalence of Chronic Obstructive Pulmonary Disease (COPD)

According to results from an epidemiological study in Beijing, Tianjin, Liaoning, Shanghai, Guangdong, Shanxi, and Chongqing in 2007, the prevalence of COPD in China was 8.2% among people over the age of 40, it is estimated that there were 43 million patients with COPD in China^[1]. COPD prevalence was significantly higher in rural (8.8%) areas compared with urban areas (7.8%) , and also higher in men (12.4%, 95% CI: 11.7–13.1) than women (5.1%, 95% CI: 4.7% –5.5%) . COPD prevalence in 7 provinces is displayed in Table 3–5–9.

Table 3–5–9 The Prevalence of COPD

Area	Urban		Rural		Total		P Value
	No.	Prevalence (%)	No.	Prevalence (%)	No.	Prevalence (%)	
Beijing	1 434	6.8 (5.5–8.1)	1 624	9.1 (7.7–10.5)	3 058	8.0 (7.1–9.0)	0.021
Tianjin	1 500	9.9 (8.4–11.4)	1 508	9.4 (7.9–10.9)	3 008	9.6 (8.6–10.7)	0.676
Liaoning	1 947	8.1 (6.9–9.3)	2 020	6.8 (5.7–7.9)	3 967	7.4 (6.6–8.3)	0.139
Shanghai	1 503	3.9 (2.9–4.9)	1 516	9.0 (7.6–10.5)	3 019	6.5 (5.6–7.4)	<0.001
Guangdong	1 818	7.4 (6.2–8.6)	1 468	12.0 (10.3–13.7)	3 286	9.4 (8.4–10.4)	<0.001
Shanxi	1 189	4.0 (2.8–5.1)	1 298	6.9 (5.5–8.2)	2 487	5.5 (4.6–6.4)	0.001
Chongqing	1 420	13.7 (11.9–15.5)	—	—	1 420	13.7 (11.9–15.5)	
Total	10 811	7.8 (7.2–8.3)	9 434	8.8 (8.2–8.4)	20 245	8.2 (7.9–8.6)	0.007

3.5.3.2 Mortality of Chronic Obstructive Pulmonary Disease

According to data released by the Ministry of Health in 2008^[2], COPD ranked as the fourth leading cause of death in urban areas and the third in rural areas. COPD mortality presented a downward trend from 1990 to 2008 (Figure 3–5–6) .

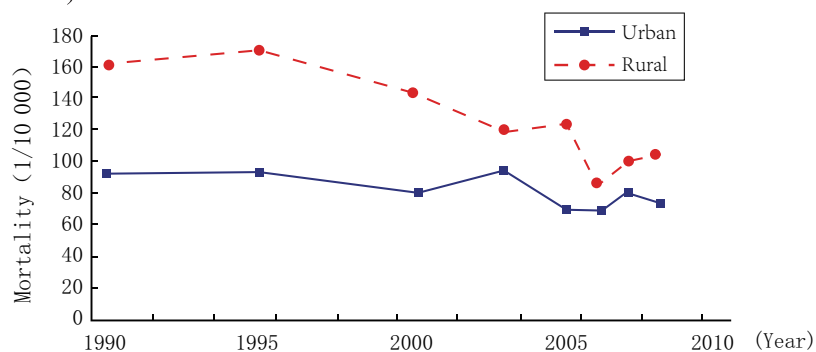


Figure 3–5–6 Trend of COPD Mortality in Urban and Rural Areas (China: 1990–2008)

[1] Zhong N, Wang C, Yao W, et al. Prevalence of chronic obstructive pulmonary disease in China: a large, population-based survey. *Am J Respir Crit Care Med.* 2007,176 (8) : 753-760.

[2] Fang X, Wang X, Bai C. COPD in China: the burden and importance of proper management. *Chest.* 2011, 139 (4) : 920-929.

3.6 Cardiovascular Surgery

3.6.1 Cardiovascular Surgery Volume in China

In 2014, 209 765 cardiovascular surgeries were performed in Mainland China, among which 159 108 cases were cardiopulmonary bypass surgeries. In Hong Kong (special administrative region, SAR), 1 704 cardiovascular surgeries were performed, among which 1 534 cases were cardiopulmonary bypass surgeries.

Table 3-6-1 Amount of Cardiac and Aortic Surgeries (Mainland China, Hong Kong: 2012-2014)

Region	Area	2012		2013		2014	
		Total	On-pump	Total	On-pump	Total	On-pump
North	Beijing	27 538	18 060	29 998	19 180	30 674	19 248
	Tianjin	5 688	4 137	5 662	4 287	5 973	4 153
	Hebei	3 784	2 217	3 959	2 523	4 770	2 928
	Shanxi	2 573	1 739	1 992	1 295	2 336	1 498
	Inner Mongolia	1 369	856	1 143	720	991	565
Northeast	Heilongjiang	4 940	3 402	5 040	3 407	5 489	3 320
	Jilin	3 386	2 172	3 316	2 304	2 610	1 751
	Liaoning	2 200	1 840	2 158	1 557	2 188	1 591
East	Shanghai	16 099	12 887	16 551	13 119	16 181	12 951
	Shandong	13 199	9 070	13 249	8 844	12 865	8 633
	Jiangsu	8 908	7 072	8 640	6 983	9 119	7 238
	Zhejiang	5 666	4 502	5 315	4 650	5 590	4 773
Central	Hubei	19 650	15 787	19 723	15 223	18 503	13 771
	Hunan	11 665	10 539	12 029	10 678	12 237	10 449
	Jiangxi	7 579	6 282	7 614	6 320	7 648	6 419
	Henan	4 823	4 330	4 698	4 111	4 719	3 912
	Anhui	4 200	3 808	4 103	3 743	4 263	3 782
South	Guangdong	15 036	13 018	15 677	13 365	15 662	13 678
	Guangxi	5 977	4 189	5 490	4 193	5 752	4 272
	Fujian	3 894	3 630	4 267	3 926	4 425	3 843
	Hainan	1 040	847	1 021	954	1 021	830
Northwest	Shanxi	6 997	5 778	6 944	5 786	7 701	5 772
	Gansu	5 030	3 477	4 412	3 528	3 442	2 439
	Qinghai	2 700	2 141	2 708	2 027	2 720	1 824
	Ningxia	910	568	1 158	528	1 161	546
	Xinjiang	364	309	384	369	476	417

**Table 3-6-1 Amount of Cardiac and Aortic Surgeries
(Mainland China, Hong Kong: 2012-2014)**

(Continued)

Region	Area	2012		2013		2014	
		Total	On-pump	Total	On-pump	Total	On-pump
Southwest	Chongqing	6 515	5 643	7 006	5 968	7 101	6 000
	Sichuan	5 634	5 085	5 591	5 016	5 599	4 683
	Yunnan	3 700	3 195	4 064	3 960	4 306	3 989
	Guizhou	2 049	1 949	2 376	2 197	2 436	2 221
	Tibet	82	68			103	78
Hong Kong		1 793	1 596	1 593	1 559	1 704	1 534
Total		204 988	160 193	207 881	162 320	209 765	159 108

Note: Data from the Extracorporeal Circulation Sub-committee of the Chinese Society of Biomedical Engineering

The annual volume of cardiovascular surgery in China has increased over the past decade, but with slowing growth since 2013 (Figure3-6-1, Figure3-6-2).

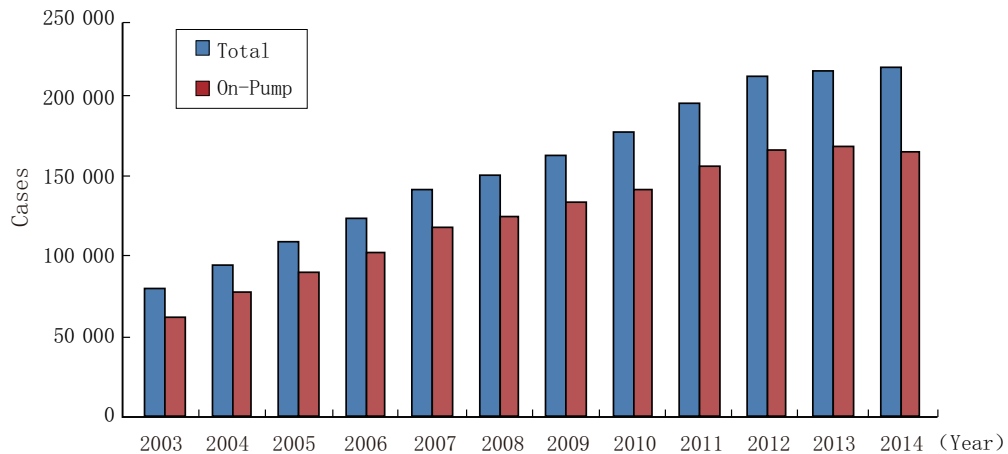


Figure 3-6-1 Volume of Cardiovascular Surgery (China: 2003-2014)

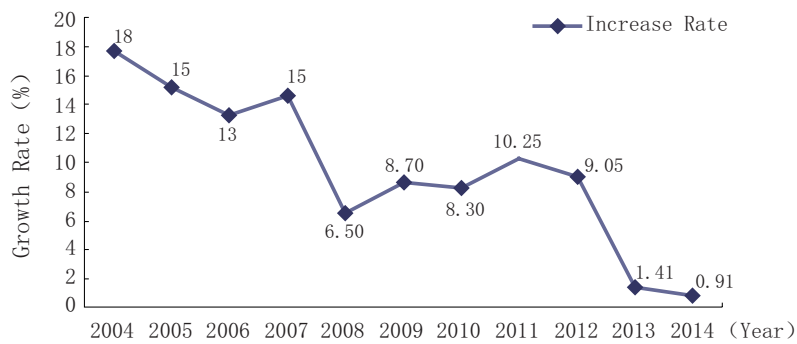


Figure 3-6-2 Growth Rate of Cardiovascular Surgery (China: 2004-2014)

Compared to the growth of treatments via Off-pump CABG and other interventions for aortic diseases, the increase in cardiopulmonary bypass (CPB) progressed at a significantly slower speed than that of other cardiovascular surgeries. The percentage of cardiopulmonary bypass surgeries among all cardiovascular surgeries for aortic disease has declined gradually since 2007 and reached 75.9% in 2014. The volume of CPB in 2014 was reduced by 3 200 compared with that in 2013 (Figure3-6-3).

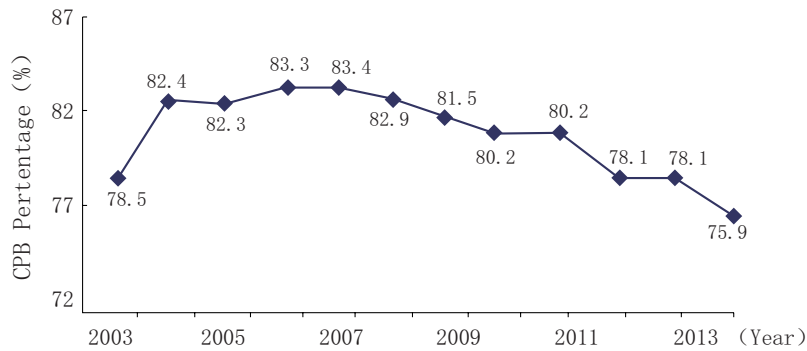


Figure 3-6-3 Percentage of Cardiopulmonary Bypass Surgery among All Cardiovascular Surgeries (2003-2014)

82 882 surgeries for congenital heart disease (CHD) were completed in 2014 in Mainland China and Hong Kong, and account for 39.5% of all aortic surgeries performed. Such surgeries were also listed as the most frequently performed surgery among all cardiac surgery categories (Figure 3-6-4). 60 485 valvular surgeries, 41 636 coronary artery bypass grafts, 11 013 aortic surgeries, 370 cases heart transplantations (including 12 heart-lung transplants), and 711 extracorporeal membrane oxygenation (ECMO) adjuvant treatments were performed.

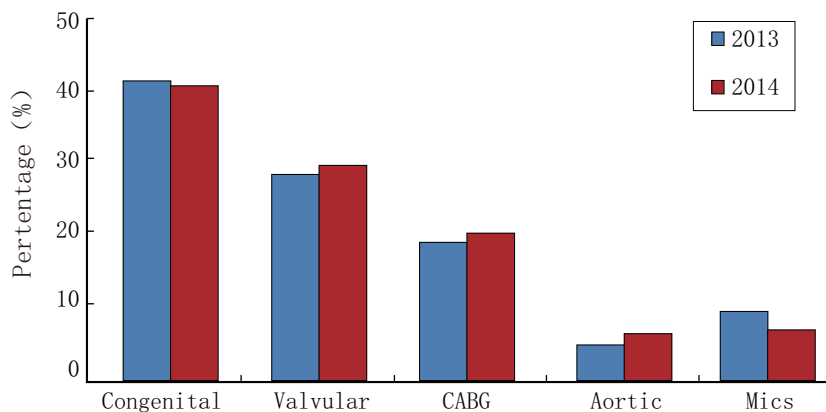


Figure 3-6-4 Proportions of Major Cardiac Surgeries in China, 2013-2014

Table 3-6-2 Cardiovascular Surgery Cases in Mainland China and Hong Kong, 2014

Region	Area	Surgery Category			Assisted Circulation			Transplant		
		CHD	Valvular	CABG	Valvular	IABP	ECMO	Heart	Lung	heart-lung
North China	Beijing	9 735	5 288	11 228	2 030	878	175	95		
	Tianjin	2 449	1 058	1 615	134	53	1			
	Hebei	1 641	548	2 172	101	196	23	5		
	Shanxi	949	753	719	85	13				
	Inner Mongolia	181	234	180	79	11				
Northeast	Heilongjiang	1 205	1 508	2 204	276	361	17	3		
	Jilin	845	584	511	105	108	6			
	Liaoning	644	688	544	185	36	15	1	5	
East	Shanghai	7 355	5 364	2 708	912	367	54	13	4	
	Shandong	4 510	3 204	3 579	504	19	6	14		
	Jiangsu	2 848	3 426	1 641	726	158	32	20	106	
	Zhejiang	1 692	2 604	674	252	66	43	7		
Central	Hubei	8 733	3 492	4 137	766	569	70			6
	Hunan	4 587	3 722	2 230	1 085	215	23	132	5	5
	Jiangxi	4 014	2 386	695	220	50	4	2	1	1
	Henan	1 753	1 890	605	153	92	1			
	Anhui	2 303	1 458	270	170	14	1			
South China	Guangdong	7 676	5 577	911	678	183	102	12	18	
	Guangxi	2 582	2 114	400	298	35	26	14		
	Fujian	1 836	1 851	232	161	50	45	20	3	
	Hainan	280	490	147	26	28				
Northwest	Shaanxi	3 388	1 770	1 283	664	83	2	7		
	Gansu	1 144	973	791	173	20	1			
	Qinghai	1 690	612	172	99	22	2	1		
	Ningxia	192	298	193	27	24				
	Xinjiang	321	84	19	9	5				
Southwest	Chongqing	2 475	3 371	504	342	61	5			
	Sichuan	2 249	2 306	323	279	46	10			
	Yunnan	2 279	1 426	323	224	44	2	3		
	Guizhou	1 182	907	123	77	13	1			
	Tibet	56	22							
Hong Kong		88	477	503	173	73	44	9	3	
Total		82 882	60 485	41 636	11 013	3 880	711	358	145	12

CHD, Congenital Heart Disease; ECMO, Extracorporeal Membrane Oxygenation

Note: Data from the Extracorporeal Circulation Sub-committee of the Chinese Society of Biomedical Engineering

3.6.2 Development of Cardiac Surgery^[1]

Since 2003, the Extracorporeal Circulation Sub-Committee of the Chinese Society of Biomedical Engineering has conducted an annual national survey of hospitals that perform cardiac surgeries, and collected data on surgery volume and related information, aimed at understanding the status and development of cardiac surgery in China.

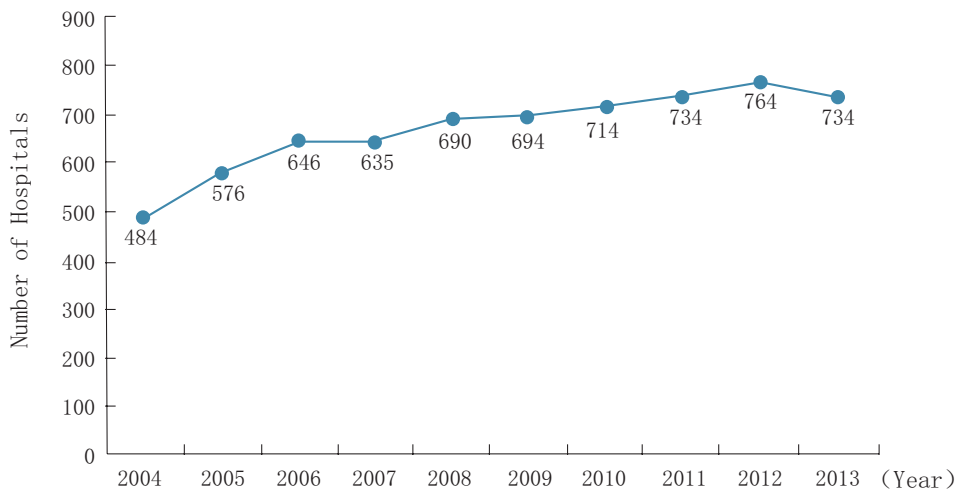


Figure 3-6-5 Number of Hospitals in China Participating in the Survey, 2004-2013

Since 2011, the number of hospitals participating in the survey has stabilized at around 740, significantly higher than the number in 2004 (around 500) (Figure 3-6-5). Hospitals were divided into subgroups based on their volumes of cardiac surgery (Figure 3-6-6): 8 hospitals were recorded to perform more than 3 000 aortic surgeries in 2013, including Fuwai Hospital, Beijing Anzhen Hospital, Wuhan Asian Heart Hospital, Guangdong General Hospital, Xijing Hospital, Shanghai Children’s Medical Center, The Second Xiangya Hospital of Central South University and Chongqing Xinqiao Hospital. The first four listed hospitals and the Shanghai Children’s Medical Center performed over 3 000 CPB annually. According to disease categories, Fuwai Hospital and Shanghai Children’s Medical Center performed more than 3 000 CHD surgeries each year.

[1] Wang W, Hei FL, et al. The development situation of cardiac surgery in China from 2004 to 2013. Chinese Journal of extracorporeal circulation. 2014,12 (4) :193-197.

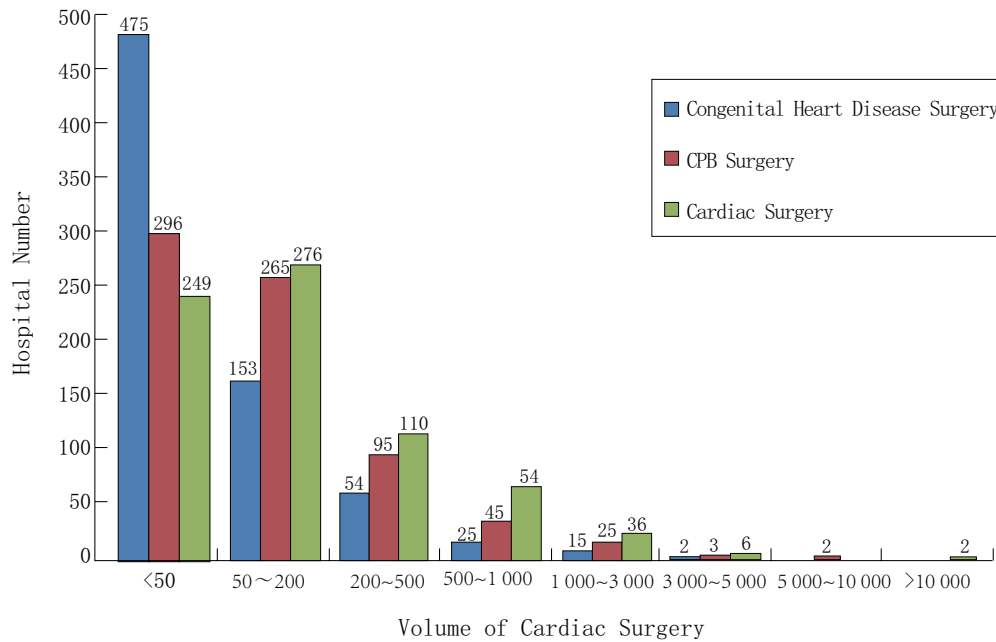


Figure 3-6-6 Distribution of Hospitals by Volume of Cardiac Surgery in 2013

There are 1.55 cardiac surgeries performed per 10 000 people in China based on the number of cardiac surgeries and the population of patients receiving surgery (Figure 3-6-7) . Beijing, Shanghai and Tianjin were the three cities/municipalities with the highest per capita rates of cardiac surgery. Beijing, Shanghai and Hong Kong were the top three in terms of CPB per 10 000 people (15.3, 7.09 and 2.25 respectively) .

The number of cardiac surgeries in Beijing and Shanghai is 10 times higher than that in other regions, exposing the unbalanced development of cardiac surgery across China. An unbalanced distribution of medical resource is considered one of the key reasons for poor access to medical services in some regions.

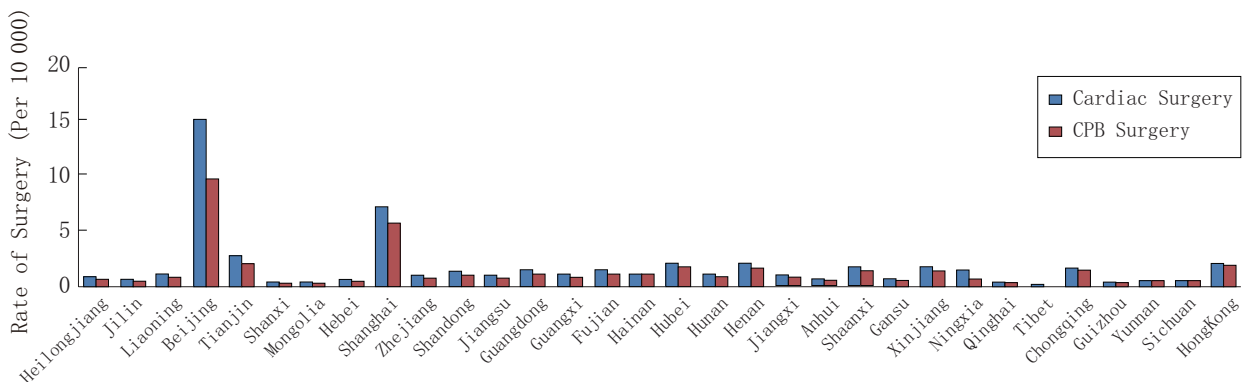


Figure 3-6-7 Rate of Cardiac Surgery and Cardiopulmonary Bypass Per 10 000 People in Each Province, Municipality and Autonomous Region in 2013

With the growth of cardiac surgery, the demand for oxygenators has also increased from 74 840 in 2004 to

162 245 in 2013. The demand for domestic bubble oxygenators declined dramatically over the same period (Figure 3-6-8).

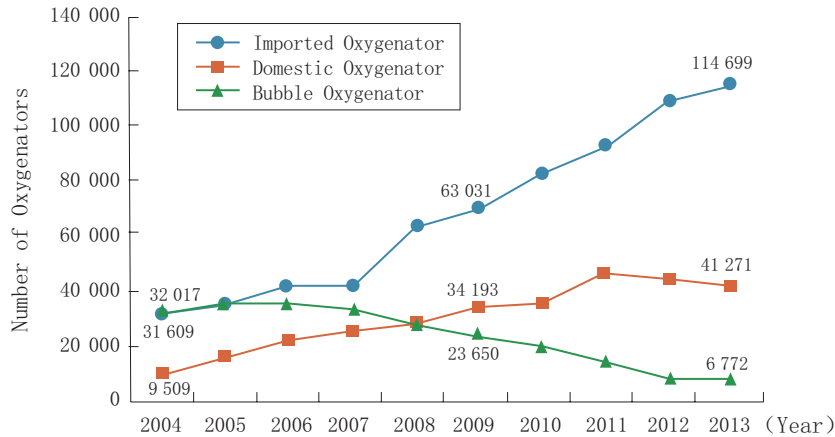


Figure 3-6-8 Demand for Oxygenators in China, 2004-2013

Although the number of CBP increased more than three-fold between 2004 and 2013, the growth in use of domestic oxygenators merely increased by 15.69%, far behind that of the imported oxygenators. The domestic medical devices industry in China has lagged behind that of developed countries in this field.

3.6.3 Congenital Heart Disease (CHD)

3.6.3.1 Epidemiology of CHD

Monitoring for birth defects has increased steadily in Mainland China. The incidence of CHD varies in different regions (Table 3-6-3).

Table 3-6-3 Incidence of CHD in Mainland China

Area	Number of Subjects	Survey Period	Incidence (‰)	Rank
Sichuan Province ^[1]	648 465	2001.1.1-2010	0.88	Fourth
Panzhihua, Sichuan Province ^[2]	30 111	2008.10.1-2011.9.30	1.49	
Hebei Province ^[3]	1 202 291	2001-2012	1.71	First
Cangzhou, Heibei Province ^[4]	256 420	2003-2012	5.55	

[1] Liu JT, Xu YZ, He LK, et al. Monitoring analysis of birth defects in Sichuan Province from 2001 to 2010 (Chinese). Practical Clinical Medicine. 2013,10 (6) : 63-65

[2] Xu YL, Tang J, Zhang FF, et al. Monitoring analysis of birth defects in Panzhihua from 2009 to 2011 (Chinese). Modern Preventive Medicine. 2013,40 (11) : 2052-2054.

[3] Li JH, Zhang YK, Zhao LN, et al. Monitoring analysis of birth defects in Hebei province from 2001 to 2012 (Chinese). Maternal & Child Health Care of China, 2013, 28 (29) : 4767-4771.

[4] Chen J, Zhao JH, Li HY, et al. Monitoring analysis of birth defects in Cangzhou from 2003 to 2012 (Chinese). Maternal & Child Health Care of China. 2014,29 (15) : 2377-2378.

Table 3-6-3 Incidence of CHD in Mainland China

(Continued)

Area	Number of Subjects	Survey Period	Incidence (%)	Rank
12 regions in Inner Mongolia ^[1]	62 544	2005.10.1-2008.9.30	1.71	Second
Beijing ^[2]	1 102 918	2007-2012	8.04	
Hunan Province ^[3]	714 071	2003-2012	4.36	First
Hunan Province ^[4]	293 053	2009-2011	5.57	First
Changsha, Hunan Province ^[5]	173 527	2001.1.1-2010.12.31	6.28	First
Xiangtan, Hunan Province ^[6]	94 799	2009-2012	2.03	First
Hengyang, Hunan Province ^[7]	197 635	2009.10-2013.9	0.83	Third
Ezhou, Hubei Province ^[8]	35 987	2008-2013	1.17	Third
Shiyan, Hubei Province ^[9]	204 908	2009.1.1-2013.12.31	1.88	Second
Shanxi Province ^[10]	363 363	2008-2012	0.96	
Changzhi, Shanxi Province ^[11]	37 231	2011	1.21	Fourth
Jilin Province ^[12]	913 998	2006.10.1-2011.9.30	1.23	First
Liaoyuan, Jilin Province ^[13]	51 513	2004-2010	1.36	Second

[1] Guo SY, Zhang XG. Monitoring analysis of birth defects in 12 regions in Inner Mongolia (Chinese). *Modern Preventive Medicine*. 2013,40 (21) : 3964-3973.

[2] Liu KB, Zhang W, Xu HY, et al. Analysis of the trend of perinatal congenital heart disease in Beijing area over 10 year period (Chinese). *Chinese Journal of Birth Health & Heredity*. 2013,21 (12) :127-128.

[3] Xie DH, Du QY, Wang H. Analysis of the trend of perinatal congenital heart disease in Hunan province from 2003 to 2012 (Chinese). *Chinese Journal of Birth Health & Heredity*. 2013,21 (11) : 72-74.

[4] Wang AH, Du QY. Monitoring analysis of birth defects in Hunan province from 2009 to 2011 (Chinese). *Practical Preventive Medicine*. 2013,20 (1) : 78-80.

[5] Zu YE, Zhu L, Zhou HN, et al. Monitoring analysis of birth defects in Changsha from 2001 to 2011 (Chinese). *Journal of Clinical Research*. 2013,30 (12) : 2447-2450.

[6] Zhang D, Han AH, Yang L, et al. Monitoring analysis of birth defects in Xiangtan from 2009 to 2012 (Chinese). 2013, 10 (volume one) : 5964-5965.

[7] Wang Z. Monitoring analysis of birth defects in Hengyang from 2010 to 2013 (Chinese). *Chinese Journal of Women and Children Health*. 2014, 5 (1) : 16-17.

[8] Li GY. Monitoring analysis of birth defects in Ezhou from 2008 to 2013 (Chinese). *Journal of Public Health and Preventive Medicine*. 2014, 25 (4) : 122-124.

[9] Zhao HB, Kuang E. Analysis of the reasons for the birth defects and the preventive strategy (Chinese). *Chinese Journal of Birth Health & Heredity*. 2015,23 (2) : 83-84.

[10] Zhang XJ, Zhao ZH, Huang J, et al. Monitoring analysis of congenital heart disease in Shanxi province from 2008 to 2012 (Chinese). *Chinese Journal of Reproductive Health*. 2013,24 (5) : 364-366

[11] Feng YH. Monitoring analysis of birth defects in Changzhi in 2011 (Chinese). *China Health Care & Nutrition*. 2013,02 (volume 2) : 924-925.

[12] Hao PK, Han JH, Zhang XQ, et al. Hospital-based monitoring analysis of birth defects in Jilin from 2007 to 2011 (Chinese). *Maternal & Child Health Care of China*. 2014, 29 (35) : 5888-5890.

[13] Yang W, Sun YC. Monitoring analysis of birth defects in Liaoyuan over 7 years (Chinese). *Chinese Journal of Birth Health & Heredity*. 2013, 21 (7) : 98-132.

Table 3-6-3 Incidence of CHD in Mainland China

(Continued)

Area	Number of subjects	Survey period	Incidence (‰)	Rank
Dunhua, Jilin Province ^[1]	15 987	2007-2012	2.81	First
Taonan, Jilin Province ^[2]	7 637	2008.10.1-2011.9.30	0.39	Second
Changchun, Jilin Province ^[3]	62 899	2010.10.1-2011.9.30	1.15	Second
Wuxi, Jiangsu Province ^[4]	296 244	2007-2011	0.93	Third
Yixing, Jiangsu Province ^[5]	60 021	2007-2012	0.38	Third
Shangyu, Zhejiang Province ^[6]	26 088	2007-2012	1.53	Second
Linhai, Zhejiang Province ^[7]	9 877	2013	2.23	First
Dongguan, Guangdong Province ^[8]	556 282	2008.1-2011.12	3.06	First
Shenzhen, Guangdong Province ^[9]	1 089 577	2008.1.1-2013.12.31	6.29	First
Haikou, Hainan Province ^[10]	118 199	2005.10.1-2013.9.30	1.85	First
Fujian, Fuzhou Province ^[11]	195 779	2007-2012	0.63	Fourth
Liu'an, Anhui Province ^[12]	11 274	2011	0.44	Fourth
Anqing, Anhui Province ^[13]	21 235	2009-2012	5.13	First

[1] Xu DM, Li L. Monitoring analysis of birth defects in Dunhua from 2007 to 2012 (Chinese). *China Journal of Modern Drug Application*. 2013,7 (17) : 259-260.

[2] Jiang HY. Monitoring analysis of birth defects in Taonan from 2009 to 2011 (Chinese). *China Journal of Modern Drug Application*. 2013; 7 (5) : 134.

[3] Wang S, Zhang YH. Monitoring analysis of birth defects in Changchun in 2011 (Chinese). *China Practical Medicine*. 2014; 9 (2): 261.

[4] Sui Q, Wei W. Monitoring analysis of birth defects in Wuxi from 2009 to 2011 (Chinese). *Maternal & Child Health Care of China*. 2013, 2 (28) : 4716-4718.

[5] Jin XL, Jiang LW, Wang XK. Monitoring analysis of birth defects in Yixing from 2007 to 2012 (Chinese). *Maternal & Child Health Care of China*. 2015,30 (2) : 180-181.

[6] Yu LP, Ruan XL. Monitoring analysis of birth defects in Shangyu from 2007 to 2012 (Chinese). *Zhejiang Journal of Preventative Medicine*. 2013,25 (8) : 79-81.

[7] Huang LF, Zhang XW, Jiang HM. Monitoring analysis of birth defects in Linhai area (Chinese). *Chinese Journal of Birth Health & Heredity*. 2014; 22 (12) : 88-89.

[8] Yi QY, Zhong BM, Liu JX. Monitoring analysis of birth defects in Yixing from 2008 to 2011 (Chinese). *Maternal & Child Health Care of China*. 2014,29 (5) : 770-773.

[9] Zhao J, Jin SY, Liu PH, et al. Monitoring analysis of birth defects in Shenzhen from 2008 to 2013 (Chinese). *Maternal & Child Health Care of China*. 2015,23 (3) : 71-72.

[10] Wang JS, Xie ZL, Liang ZQ, et al. Monitoring analysis of birth defects in Haikou from 2006 to 2013 (Chinese). *China Tropical Medicine*. 2014,14 (9) : 1122-1123.

[11] Liang XY, Chen LR, Yang Y. Monitoring analysis of birth defects in Haikou from 2007 to 2012 (Chinese). *Strait Journal of Preventive Medicine*. 2014,20 (6) : 81-83.

[12] Li YN, Tao FB. Monitoring analysis of birth defects in Liu'an Anhui Province from 2008 to 2011 (Chinese). *Maternal & Child Health Care of China*. 2013,28 (7) : 1201-1203.

[13] Li JP, Ju Y. Monitoring analysis of 447 birth defects in Anqing from 2009 to 2012 (Chinese). *China Tropical Medicine*. 2014,14 (9) : 1235-1237.

Table 3-6-3 Incidence of CHD in Mainland China

(Continued)

Area	Number of subjects	Survey period	Incidence (‰)	Rank
Anqing, Anhui Province ^[1]	18 864	2010.10.1–2013.9.30	5.14	First
Liuzhou, Guangxi Province ^[2]	239 343	2009–2013	3.70	First
Yulin, Guangxi Province ^[3]	146 366	2012	0.27	Fifth
Pulandian, Liaoning Province ^[4]	13 859	2010.10.1–2012.9.30	5.11	First
Weihai, Shandong Province ^[5]	9 057	2009.10.1–2010.9.30	2.43	First
Xintai, Shandong Province ^[6]	16 141	2012	1.67	First
Penglai, Shandong Province ^[7]	28 827	2004.1–2013.9	0.798	Third

Note: Monitoring subjects meet the requirement from "Protocol of birth defect monitoring in China" – perinatal infant from 28 gestational weeks to postpartum 7 days, including live births, stillbirth and newborn dead in 7 days and newborn of scheduled induced labor.

Among all monitoring analyses, the constituent ratios of diverse CHD types were reported by investigations from Beijing^[8], Liuzhou in Guangxi province^[2], and Dongguan in Guangdong province^[9] (Table 3-6-4, Table 3-6-5).

Table 3-6-4 Constituent Ratio and Incidence of Various Types of CHD in Beijing

Disease	Constituent Ratio (%)	Incidence (%)	Disease	Constituent Ratio (%)	Incidence (%)
Ventricular Septal Defect	14.5	1.17	Common Arterial Trunk	0.14	0.01
Atrial Septal Defect	11.4	0.92	Endocardial Cushion Defect	1.00	0.08
Patent Ductus Arteriosus	38.7	3.11	Single Ventricle or Atrial	0.97	0.08
Atrial Septal Defect and Patent Ductus Arteriosus	0.33	0.03	Mitral Atresia	0.01	

[1] Bai LP. Monitoring analysis of birth defects in Anqing from 2011 to 2013 (Chinese). *Jiangsu Journal of Preventative Medicine*. 2014,25 (5): 80-81.

[2] Nong Z, Qin HY, Guan HB, et al. Analysis of the incidence of congenital heart disease in Liuzhou area from 2009 to 2013. *Practical Preventative Medicine*. 2015,22 (1): 105-107.

[3] Zhang CL. Analysis of 146366 birth defects. *Maternal & Child Health Care of China*. 2015,30 (6): 924-926.

[4] Wang JP. Population-based analysis of birth defects in Pulandian from 2009 to 2013 (Chinese). *China Modern Medicine*. 2013,20 (34): 181-182.

[5] Cong QY. Monitoring analysis of birth defects in Weihai in 2010 (Chinese). *Maternal & Child Health Care of China*. 2013,28 (11): 1848-1849.

[6] Wei X. Monitoring analysis of birth defects in Xintai in 2012 (Chinese). *China Health Care Nutrition*. 2013,06 (volume one): 3301-3302.

[7] Li JP, Gao J. Monitoring analysis of 28827 birth defects in Penglai from 2009 to 2013 (Chinese). *Chinese Journal of women and children health*. 2014,5 (1): 45-46.

[8] Nong Z, Qin HY, Guan HB, et al. Analysis of the incidence of congenital heart disease in Liuzhou area from 2009 to 2013. *Practical Preventative Medicine*. 2015,22 (1): 105-107.

[9] Yi QY, Zhong BM, Liu JX. Monitoring analysis of birth defects in Yixing from 2008 to 2011 (Chinese). *Maternal & Child Health Care of China*. 2014,29 (5): 770-773.

Table 3-6-4 Constituent Ratio and Incidence of Various Types of CHD in Beijing (Continued)

Disease	Constituent Ratio (%)	Incidence (%)	Disease	Constituent Ratio (%)	Incidence (%)
Pulmonary stenosis	0.64	0.05	Ectocardia	0.14	
Tetralogy of Fallot	2.33	0.19	Interventricular septal bulged aneurysm	0.29	0.02
Complete transposition of great arteries	0.71	0.06	Cardiomyopathy	0.20	0.02
Coarctation of the aorta	0.17	0.01	Hypoplastic heart syndrome		

Ultrasound screening for CHD was performed on 15 627 newborns within the census registry in Yinzhou district, Ningbo from 2010 to 2012. The results revealed that the local incidence of CHD was 19.1%.^[1]

Table 3-6-5 Constituent Ratio of Various Types of CHD in Liuzhou, Dongguan and Ningbo

Disease	Liuzhou, Guangxi Province	Dongguan, Guangdong Province	Yinzhou District, Ningbo
Ventricular Septal Defect	10.84	7.17	11.74
Atrial Septal Defect	13.66	9.87	47.99
Patent Ductus Arteriosus	21.22	17.51	11.74
Patent Foramen Ovale	18.85	34.96	6.71
Atrial Septal Defect and Patent Ductus Arteriosus		2.70	
Ventricular Septal Defect and Atrial Septal Defect	2.48	1.59	
Pulmonary Stenosis		0.35	1.01
Tetralogy of Fallot		0.35	0.67
Ventricular Septal Defect and Patent Ductus Arteriosus		0.24	
Endocardial Cushion Defect		0.24	
Single Ventricle and Atrial		0.18	
Valvula Tricuspidalis		1.18	

3.6.3.2 Transcatheter Versus Surgical Closure of Perimembranous Ventricular Septal Defects^[2]

Perimembranous ventricular septal defect (pmVSDs) is one of the most common congenital heart diseases in children. From January 2009 to July 2010, three major medical centers (Xijing Hospital, Xi'an; Xi'an Children's Hospital, Xi'an; and Hanzhong Central Hospital, Hanzhong) in northwest China conducted prospective, randomized, controlled clinical trials to compare the safety and efficacy of the surgical versus transcatheter approaches to correct pmVSDs via utilizing domestic septal occluders.

[1] Jiang L. Monitoring analysis of birth defects in Ningbo Yinzhou from 2010 to 2013 (Chinese). Chinese Journal of Birth Health & Heredity, 2014,22 (9):132-133.

[2] Yang J, Yang L, Yu S, et al. Transcatheter versus surgical closure of perimembranous ventricular septal defects in children: a randomized controlled trial. J Am Coll Cardiol, 2014, 63:1159-1168.

229 patients with pmVSD were randomly assigned to surgical or transcatheter intervention, and were compared at two-year follow-up. The results suggested that no mortality or major complications (complete atrioventricular block, new-onset valvular regurgitation requiring surgical repair, etc.) was observed in patients from either group. However, statistically significant ($p < 0.001$) differences were found in minor adverse event rates (groin hematoma, blood loss requiring transfusion, device embolization with transcatheter removal, any cardiac arrhythmia that required medication, mild new or increased valvular regurgitation, etc.) between the two groups. During the median two-year follow-up, the left ventricular end-diastolic dimensions of both groups were restored to normal function, and there was no difference in closure rates, adverse events, or complications between groups.

Conclusions: both transcatheter device closure and surgical repair are effective interventions with excellent midterm results for treating pmVSD in children. Transcatheter device closure demonstrates relatively low incidence of myocardial injury, reduced blood transfused, fast recovery, short hospital stays, and low medical expenses.

3.6.4 Valvular Heart Disease

3.6.4.1 Anticoagulation Therapy Following Heart Valve Replacement^[1]

A meta-analysis was conducted by investigating the Chinese literature published from January 1990 to December 2010 regarding anticoagulation therapy following heart valve replacement. Studies involved in the final analysis were those using warfarin after valve replacement, and adopting prothrombin time ratio (PTR) or international normalized ratio (INR) as monitoring indicators. Subjects were divided into a regular intensity group (INR > 2.5, PTR > 1.5) and a low intensity group (INR ≤ 2.5, PTR ≤ 1.5) to observe the effects of different intensities of anticoagulation on patient outcomes.

Table 3-6-6 Comparison of Complications in Regular Intensity Group and Low Intensity Group

Group	Number of studies	Overall complications related to anticoagulation treatment (%)	Mortality due to complications related to anticoagulation treatment (%)	Bleeding (%)	Fatal Bleeding (%)	Percentage of major bleeding/all bleeding events (%)	Intracranial hemorrhage/mortality (%)	Embolization (%)	Fatal embolization (%)	Thrombus (%)
Intensity	27	10.66	1.16	9.14	9.15	25.79	1.24/0.65	1.26	26.09	0.26
Low intensity	30	7.86	0.49	6.39	5.50	14.66	0.49/0.22	1.39	9.64	0.08

Table 3-6-7 Comparison of Complications in Regular Intensity Group and Low Intensity Group by Study Year

Group	No. Of studies with Intensity anticoagulation	No. Of studies with low intensity anticoagulation (%)	Overall complications related to anticoagulation (%)	Mortality due to complications related to anticoagulation (%)	Bleeding (%)	Fatal Bleeding (%)	Percentage of major bleeding/all bleeding events (%)	Intracranial hemorrhage/mortality (%)	Embolization (%)	Fatal embolization (%)	Thrombus (%)
Before 2000	19	4	10.95	1.41	9.61	1.08	25.00	4.10/1.87	1.14	0.32	0.21
After 2000	8	26	8.77	0.67	7.31	0.45	18.72	0.27/0.15	1.29	0.21	0.17

Results showed that:

[1] Dong L, Shi YK, Fu B, et al. A systemic review of low intensity anticoagulation therapy for Chinese population with heart valve replacement (Chinese). National Medical Journal of China, 2014,94 (34) : 2673-2676.

(1) Among the literature published before 2000, 82.6% of studies adopted PTR as the monitoring indicator, and 80% used more intensive anticoagulation. In contrast, among the literature published after 2000, 88.2% of studies adopted INR as the monitoring indicator, and 76.5% used less intensive anticoagulation.

(2) The incidence of both overall complications and bleeding in the low intensity group was significantly lower than in the intensive group (both $P < 0.001$). No significant difference was found in embolization between the two groups ($P > 0.05$).

(3) The incidence of intracranial hemorrhage and mortality in both the low intensity group and studies conducted after 2000 declined when compared with their peer groups. Intracranial hemorrhage is the most severe complication following anticoagulation treatment with a mortality rate approaching 60%. A desire to avoid high hemorrhage rates is largely responsible for the significant decline in mortality and related complications associated with the widespread application of low intensity anticoagulation strategies over the last decade.

3.6.5 Cardiac Surgery for Coronary Artery Disease

3.6.5.1 The Impact of Body Mass Index on Outcomes in Patients Undergoing Coronary Artery Graft Bypass^[1]

4 916 Chinese who consecutively underwent isolated, primary CABG at the Cardiovascular Institute of Fu Wai Hospital from January 1, 1999 to December 31, 2005 were recruited into this study, and divided into subgroups based on BMI: underweight: $< 18.5 \text{ kg/m}^2$, normal weight: 18.5 to 23.9 kg/m^2 , overweight: 24 to 27.9 kg/m^2 , obese: 28 to 32 kg/m^2 , and severely obese: $> 32 \text{ kg/m}^2$. Short-term (in-hospital) and long-term (5-years) major post-operative complications and mortalities were compared among various BMI groups after initial revascularization.

The results showed that the variations of BMI groups were not significantly associated with 5-years mortality and MACCE, while advanced age, smoking, hypertension, myocardial infarction and heart failure were the risk factors most strongly associated with post-operative mortality; and old age, hypertension and heart failure were found to increase the rate of MACCE.

3.6.5.2 Influence of Diabetes Mellitus (DM) on Long-term Clinical Outcomes and Economic Burden after Coronary Artery Bypass Grafting (CABG)^[2]

Information on 9 240 consecutively enrolled patients who underwent isolated, primary, elective CABG between January 1999 and December 2008 was analyzed for long-term major adverse cardiovascular and cerebrovascular events and economic outcomes up to 2 years after the procedure. During the study, the

[1] Ao H, Wang X, Xu F, et al. The impact of body mass index on short- and long-term outcomes in patients undergoing coronary artery graft bypass. *PLoS One*, 2014, 9 (4) :e95223. doi: 10.1371/journal.pone.0095223. eCollection 2014.

[2] Zhang H, Yuan X, Qanabrugge RL, et al. Influence of diabetes mellitus on long-term clinical and economic outcomes after coronary artery bypass grafting. *Ann Thorac Surg*, 2014; 97 (6) : 2073–2079.

proportion of patients undergoing CABG who had DM increased from 20.1% to 31.8% in China. The DM patients were divided into DM subgroups, controlled either by diet, medication or insulin use. None of the DM subgroups was independently associated with in-hospital death, but DM was an independent predictor for long-term major adverse cardiovascular and cerebrovascular events (HR 1.29, 95% CI: 1.14 to 1.46). Medically controlled DM and insulin-dependent DM, but not diet-controlled DM, were independent predictors of long-term MACCE after CABG.

The cost of the index hospitalization was significantly higher for DM patients (76 782 RMB versus 65 521 RMB, respectively; $P < 0.001$) than non-DM patients. At two years post-CABG, the costs for DM patients (11 261 RMB) remained higher than for non-DM patients ($P < 0.001$).

3.6.6 Aortic Dissection

3.6.6.1 Clinical Feature of Acute Aortic Dissection (AAD) from Registry of Aortic Dissection in China

In 2011, Xijing Hospital established the first Registry of^[1] Aortic Dissection in China (Sino-RAD) that included 14 other major cardiovascular centers in China. Information from 1 003 patients with AAD in Sino-RAD enrolled from January 1st, 2012, to December 31th, 2013 was compared with that reported by the International Registry of Acute Aortic Dissection (IRAD). The results are show in Table 3-6-8 to Table 3-6-11.

Table 3-6-8 Demographic Data

Variable	Total			Type A			Type B		
	Sino-RAD (n=1003)	IRAD (n=464)	P Value	Sino-RAD (n=430)	IRAD (n=617)	P Value	Sino-RAD (n=573)	IRAD (n=498)	P Value
Age (y)									
Mean \pm SD	51.8 \pm 11.4	63.1 \pm 14.0	<0.01	50.5 \pm 11.2	61.1 \pm 14.1	<0.01	52.7 \pm 11.1	64.2 \pm 13.5	<0.01
>70 (n,%)	65 (6.5)			21 (4.9)	194 (31.4)	<0.01	44 (7.7)	197 (39.6)	<0.01
60-69 (n,%)	190 (18.9)			69 (16.0)			121 (21.1)		
50-59 (n,%)	306 (30.5)			129 (30.0)			177 (30.9)		
40-49 (n,%)	310 (30.9)			143 (33.3)			167 (29.1)		
<40 (n,%)	132 (13.2)			68 (15.8)			64 (11.2)		
Male sex	780 (77.8)	303 (65.3)	<0.01	328 (76.3)	413 (66.9)	<0.01	452 (78.9)	343 (68.9)	<0.01

Data presented as mean standard deviation or n (%). Sino-RAD, Registry of Aortic Dissection in China; IRAD, International Registry of Acute Aortic Dissection; SD, standard deviation.

[1] Wang W, Duan W, Xue Y, et al. Clinical feature of acute aortic dissection from the Registry of Aortic Dissection in China. *J Thorac & Cardiovasc Surg*, 2014,148 (6) : 2995-3000.

Table 3-6-9 Patient History

Variable	Total			Type A			Type B		
	Sino-RAD (n=1003)	IRAD (n=484)	P Value	Sino-RAD (n=430)	IRAD (n=617)	P Value	Sino-RAD (n=573)	IRAD (n=498)	P Value
Marfan Syndrome	25 (2.5)	22/449 (4.9)	0.02	22 (5.1)	38 (6.2)	0.48	3 (0.5)	13 (2.7)	<0.01
Hypertension	585/996 (58.7)	326/452 (72.1)	<0.01	221 (51.4)	408 (67.0)	<0.01	364/566 (64.3)	384 (77.9)	<0.01
Arteriosclerosis	150 (15.0)	140/452 (31.0)	<0.01	132 (30.7)	169 (27.7)	0.24	18 (3.1)	174 (35.8)	<0.01
Previous Aortic Dissection	25 (2.5)	29/453 (6.4)	<0.01	19 (4.4)	21 (3.4)	0.4	6 (1.0)	32 (6.6)	<0.01
Previous Aortic Aneurysm	35 (3.5)	73/453 (16.1)	<0.01	32 (7.4)	4.2 (6.8)	0.69	3 (0.5)	89 (18.2)	<0.01
Diabetes Mellitus	15 (1.5)	23/451 (5.1)	<0.01	8 (1.9)	24 (4.0)	0.06	7 (1.2)	31 (6.4)	<0.01
Previous Cardiac Surgery	20/986 (2.0)	83/463 (17.9)	<0.01	7/422 (1.7)			13/564 (2.3)	87 (18.4)	<0.01
Drinking	182/993 (18.3)		NA	99/426 (23.2)			83/567 (14.6)		
Smoking	350/993 (35.2)		NA	184/427 (43.1)			166/566 (29.3)		

Data presented as n (%) or n/N (%). Sino-RAD, Registry of Aortic Dissection in China; IRAD, International Registry of Acute Aortic Dissection; NA, not available.

Table 3-6-10 Presenting Symptoms

Variable	Total			Type A			Type B		
	Sino-RAD (n=1003)	IRAD (n=484)	P Value	Sino-RAD (n=430)	IRAD (n=617)	P Value	Sino-RAD (n=573)	IRAD (n=498)	P Value
Any Pain Reported	899 (89.6)	443 (95.5)	<0.01	397 (92.3)			502 (87.6)		
Abrupt Onset	687 (68.5)	379/447 (84.4)	<0.01	307 (71.4)	453 (91.0)	<0.01	380 (66.3)	418 (86.2)	<0.01
Chest Pain	173 (17.3)	331/451 (72.7)	<0.01	112 (26.0)	507 (84.6)	<0.01	61 (10.6)	349 (71.4)	<0.01
Back Pain	772 (77.0)	240/451 (53.2)	<0.01	309 (71.9)			463 (80.8)	329 (68.1)	<0.01
Abdominal Pain	120 (12.0)	133/449 (29.6)	<0.01	52 (12.1)			68 (11.9)		
Syncope	21 (2.1)	42/447 (9.4)	<0.01	17 (4.0)	106 (17.9)	<0.01	4 (0.7)	17 (3.5)	<0.01
Heart Failure	2 (0.2)	29/440 (6.6)	<0.01	1 (0.2)	47 (8.4)	<0.01	1 (0.2)		

Data presented as n (%) or n/N (%). Sino-RAD, Registry of Aortic Dissection in China; IRAD, International Registry of Acute Aortic Dissection.

Table 3-6-11 In-hospital Management and Outcomes

Variable	Total			Type A			Type B		
	Sino-RAD (n=1003)	IRAD (n=484)	P Value	Sino-RAD (n=430)	IRAD (n=617)	P Value	Sino-RAD (n=573)	IRAD (n=498)	P Value
Treatment									
Medical Treatment	275 (27.4)	221 (47.6)	<0.01	153 (35.6)	110 (17.8)	<0.01	122 (21.3)	354 (71.1)	<0.01
Surgery	251 (25.0)	243 (52.3)	<0.01	226 (52.6)	507 (82.2)	<0.01	25 (4.4)	78 (15.7)	<0.01
Endovascular Treatment	448 (44.7)			49 (11.4)			399 (69.6)	66 (13.3)	<0.01
Hybrid Treatment	29 (2.9)			2 (0.5)			27 (4.7)		

Table 3-6-11 In-hospital Management and Outcomes

(Continued)

Variable	Total			Type A			Type B		
	Sino-RAD (n=1003)	IRAD (n=484)	P Value	Sino-RAD (n=430)	IRAD (n=617)	P Value	Sino-RAD (n=573)	IRAD (n=498)	P Value
In-hospital Mortality									
Overall	104 (10.3)	127 (27.4)	<0.01	78 (18.1)	189 (30.6)	<0.01	26 (4.5)	61 (12.3)	<0.01
Medical Treatment	77/275 (28.0)	62/221 (28.1)	0.9893	65/153 (42.5)	64/110 (58.2)	<0.01	12/122 (9.8)	31/354 (8.8)	0.16
Surgery	14/251 (5.6)	65/243 (26.7)	<0.01*	12/226 (5.3)	125/507 (24.7)	<0.01	2/25 (8.0)	24/78 (30.8)	0.02
Endovascular	10/448 (2.2)			0/49 (0)			10/399 (2.5)	6/66 (9.1)	0.04
Hybrid Treatment	3/29 (10.3)			1/2 (50.0)			2/27 (7.4)		

Data presented as n (%) or n/N (%). Sino-RAD, Registry of Aortic Dissection in China; IRAD, International Registry of Acute Aortic Dissection. *: Sino-RAD (surgery plus endovascular plus hybrid) versus IRAD (surgery).

The results demonstrated that patients with AAD in Mainland China exhibit six major differences when compared with Western populations, including earlier onset, more male patients, a lower incidence of hypertension, a lower incidence of chest pain, a higher incidence of back pain, great differences in the choice of therapeutic strategies, and relatively lower in-hospital mortality.

3.6.6.2 Trends in Clinical Characteristics of Aortic Dissection Over 10 Years In Henan Province^[1]

The investigators collected data from 906 consecutively enrolled patients with AD over 10 years in the Henan Provincial People's Hospital, the First Affiliated Hospital of Zhengzhou University and the Henan Provincial Chest Hospital. Records and prognoses from the hospitals were collected over two 5-year periods (2003 to 2007 and 2008 to 2012). This served as a retrospective analysis to determine the clinical epidemiology features and changing trends in aortic dissection (AD) in Henan Province. The results are shown in Table 3-6-12 and Table 3-6-13.

[1] Song XR, Han XP, Chen ZY, et al. Change trend of clinical characteristics of aortic dissection over 10 years in Henan (Chinese). Chinese Journal of Thoracic and Cardiovascular Surgery. 2014,30 (3) :164-166.

Table 3-6-12 Baseline Characteristics

Group	No. of Patients	Male: Female	Age (years, mean±SD)	Hypertension, N (%)	Heavy Smoking History, N (%)
Group 1	287	3.51: 1	51.3±9.9	173 (60.1)	95 (33.1)
Group 2	619	3.47: 1	49.7±9.3	373 (60.8)	197 (31.2)
Total	906	3.49: 1	50.2±9.8	546 (60.3)	292 (32.2)

Note: Heavy smoking history indicates daily cigarette consumption >10 for more than 5 years.

Table 3-6-13 Subtypes and Treatment by Subgroups

Group	No. of Patients	Stanford Type		Cardiac Surgery	Intervention Therapy	Conservative Therapy
		A	B			
Group 1	287	133 (46.3)	154 (53.7)	96 (33.5)	58 (20.2)	183 (63.8)
Group 2	619	391 (63.2)	228 (36.8)	226 (36.5)	298 (48.1)	45 (7.3)
Total	906	524 (57.8)	382 (42.2)	322 (35.5)	356 (39.3)	228 (25.2)

The 10-year trend showed that:

(1) The increase in patients with type A dissection was more significant than that of patients with type B dissection. The prevalence of hypertension complicated with AD was 60.3%, which corresponds with results reported in the foreign literature.

(2) The age of patients with both types of AD is significantly lower than that reported in the foreign literature (Type A: 51.3±9.9; Type B: 49.7±9.3). Male patients were reported to be older than female patients.

(3) Patients with a history of heavy smoking accounted for 32.2% of all patients.

(4) 21.5% of patients with type A dissection underwent cardiac surgery before 2008, and this figure gradually increased by year. Since the introduction of endovascular repair for AD in 2005, the intervention method has become the major treatment for type B dissection. The total volume of intervention treatment has exceeded that of cardiac surgery.

3.7 Chronic Kidney Disease

3.7.1 Epidemiology of Chronic Kidney Disease (CKD)

A nationwide survey on CKD prevalence was performed from September 2009 to September 2010 by applying stratified multistage sampling with 47 204 adults across 13 provinces, municipalities, and autonomous regions. The results revealed that the overall prevalence of CKD, the adjusted prevalence of estimated GFR (eGFR) <60 ml/min/1.73m², and the urine albumin-creatinine ratio >30 mg/g were [10.8%, 1.7% and 9.4%], respectively. Based on the Sixth Nationwide Population Census in 2010, the number of patients with CKD was estimated to be approximately 120 million. The independent risk factors for CKD

included age, gender, hypertension, diabetes, history of cardiovascular disease, hyperuricemia, residence location and economic status.^[1]

A cross-sectional survey using four-stage cluster sampling was employed in the China Health and Retirement Longitudinal Study (CHARLS) during 2011–2012 on 17 708 adults ≥ 45 years of age from 450 villages/communities across 28 provinces. 8 659 participants with complete information were eventually recruited. eGFR was calculated using the creatinine–cystatin C equation. CKD was defined as a eGFR less than 60 mL/min per 1.73 m². The overall prevalence of CKD was 11.5% in people over 45. Rural populations displayed higher CKD rates than urban populations (13.0% vs 10.0%, $P < 0.05$). The prevalence of CKD also increased with age. 8.7% of the participants aware of having CKD and 4.9% received treatments. The awareness and treatment rates decreased with age.^[2]

The China National Stroke Registry study revealed that polyvascular diseases (defined as ischemic stroke with coronary heart disease and/or peripheral arterial disease) were observed in 1 387 out of 9 152 patients with ischemic stroke. Among the 1 351 cases displaying coronary heart disease, 56 cases displayed peripheral arterial disease, and 20 cases simultaneously displayed coronary heart disease, peripheral arterial disease and ischemic stroke. In contrast to ischemic stroke alone, the prevalence of CKD polyvascular disease was significantly higher (29.56% vs. 16.28% respectively, $P < 0.0001$). Patients in the polyvascular disease group presented significantly higher risk of lower eGFR (OR: 1.414, 95% CI: 1.202–1.665, $P < 0.0001$) compared with patients afflicted with ischemic stroke alone.^[3]

3.7.2 Renal Protection by Statins in Chronic Kidney Disease

Contrast medium can induce nephropathy in CKD patients. Statin drugs may prevent the progress of contrast-induced nephropathy. A prospective study on CKD patients undergoing elective percutaneous coronary intervention enrolled 1 078 subjects. An absolute increase of serum creatinine (≥ 0.5 mg/dL), or a $\geq 25\%$ relative increase from baseline within 48–72 hours after contrast medium exposure, was set as the diagnostic standard for contrast-induced nephropathy. The incidence of contrast-induced nephropathy was similar between patients pretreated with either rosuvastatin (10 mg) or atorvastatin (20 mg) (5.9% vs. 5.2%, $p = 0.684$). Multivariate logistic regression analysis revealed that rosuvastatin and atorvastatin displayed no significant difference in preventing contrast-induced nephropathy ($p = 0.623$). Moreover, no significant difference was found in terms of all-cause mortality (9.4% vs. 7.1%, respectively; $p = 0.290$) and major adverse cardiovascular events (29.32% vs. 23.14%, respectively; $p = 0.135$) during follow-up. These

[1] Zhang L, Wang F, Wang L, et al. Prevalence of chronic kidney disease in China: A cross-sectional survey. *Lancet*, 2012; 379 (9818) : 815-822.

[2] Wang S, Chen R, Liu Q, et al. Prevalence, awareness and treatment of chronic kidney disease among middle-aged and elderly: The China Health and Retirement Longitudinal Study. *Nephrology (Carlton)*, 2015, 20:474-84.

[3] Meng X, Chen Y, Jing J, et al. Association between polyvascular atherosclerosis and estimated glomerular filtration rate in patients with ischaemic stroke: data analysis of the patients in the Chinese National Stroke Registry. *Neurol Res*, 2015, 37 (5) :415-20.

findings indicated that rosuvastatin and atorvastatin have similar efficacies for preventing contrast-induced nephropathy in CKD patients undergoing PCI.^[1]

The TRACK-D study focused on the preventive efficacy of short-term treatment of rosuvastatin on contrast-induced nephropathy in patients receiving different volumes of contrast. 2 998 patients with type 2 diabetes and concomitant CKD at the point when receiving coronary or peripheral arterial angiography were randomized to groups of rosuvastatin therapy or standard care. Rosuvastatin treatment was found to significantly reduce contrast-induced nephropathy when compared with the control group (2.1% vs. 4.4%, $P=0.050$) in the overall cohort and in patients with moderate contrast volume (200–300 ml) (1.7% vs. 4.5%, $P=0.029$). However, no benefit was observed in patients with high contrast volume (≥ 300 ml) (3.4% vs. 3.9%, $P=0.834$).^[2]

3.8 Peripheral Arterial Disease

Peripheral arterial disease refers to arterial disease other than coronary artery disease and cerebrovascular disease. This report only covers lower extremity atherosclerotic disease (LEAD) and carotid atherosclerotic disease (CAD).

3.8.1 Lower Extremity Atherosclerotic Disease (LEAD)

3.8.1.1 Prevalence of LEAD

LEAD is a common disease in the middle-aged and elderly population. The diagnostic methods for investigating its prevalence include intermittent claudication questionnaires, ankle-brachial index (ABI), pulse wave velocity (PWV), and other noninvasive measures. Figure 3-8-1 shows the related epidemiological data on LEAD in China. The prevalence varies greatly across different populations, and increases with age. Most studies reported a higher prevalence of LEAD in women than men.

[1] Liu Y, Liu YH, Tan N, et al. Comparison of the efficacy of rosuvastatin versus atorvastatin in preventing contrast induced nephropathy in patient with chronic kidney disease undergoing percutaneous coronary intervention. *PLoS One*, 2014, 9 (10) :e111124.

[2] Zhang J, Li Y, Tao GZ, et al. Short-term rosuvastatin treatment for the prevention of contrast-induced acute kidney injury in patients receiving moderate or high volumes of contrast media: a sub-analysis of the TRACK-D study. *Chin Med J (Engl)*, 2015, 128 (6) :784–9.

Table 3-8-1 Epidemiological Data on the Prevalence of LEAD in China

Population (study year)	Number of People in Survey	Age (years)	Prevalence (%)		
			Male	Female	Average
Beijing Wanshoulu District Senior citizens (2003) ^[1,2]	2 124	60 – 95	12.7	18.1	16.4
Zhejiang Zhoushan fishermen (2005) ^[3]	2 668	35 –	3.0	1.2	2.1
Metabolic syndrome group (2006) ^[4]	2 115	32 – 91	21.7	23.4	22.5
MUCA Study Group (2007*) ^[5]	18 140	35 –	5.4	9.3	6.0
Diabetes group (2007) ^[6]	1 347	50 –	18.3	20.4	19.4
Hypertension group ^[7]	3 047	>50	—	—	27.5
Natural community group (2009) ^[8]	21 152	18 –	1.8	4.3	3.04
Wuhan Elderly Diabetes Group (2010) ^[9]	2 010	60 –	—	—	24.1

Note: The diagnostic criteria for LEAD studies listed in this table is ABI <0.90. MUCA: China cardiovascular disease epidemiology research multi-center collaborative study.

3.8.1.2 Risk Factors Associated with LEAD

Epidemiological studies show that the prevalence of LEAD increases with aging and atherosclerosis-related risk factors. Atherosclerosis is a main cause of LEAD, and the risk factors for atherosclerosis, including smoking, diabetes, dyslipidemia, hypertension, and homocysteinemia. 30% of patients with cerebrovascular disease and 25% of patients with ischemic heart disease also have complications with LEAD^[3,4]. Thus, LEAD heralds systemic atherosclerotic diseases. Early detection and treatment of LEAD significantly contributes to the diagnosis and treatment of systemic atherosclerosis.

Recent studies have revealed that Cystatin C level is an independent predictor for LEAD patients with diabetes. When Cystatin C is above 1.2 mg/L, the incidence of LEAD is significantly elevated (OR 21.79,

[1] Li XY, Wang J, He Y, et al. The association between lower extremity atherosclerotic disease and cardiac vascular disease: Survey of the elderly in Wanshoulu, Beijing.[Chinese] Chinese Medical Journal .2003,83 cross-sectional survey (21) : 1847- 1851.

[2] Wang J, Li XY, He Y, et al. The cross-sectional study of the lower extremity atherosclerotic disease among the elderly in Wanshoulu, Beijing. Chinese Journal of Epidemiology .2004,25 cross-sectional survey (3) : 221-224.

[3] Liu CG, Ruan LS. Survey of peripheral arterial disease in Zhoushan fishing area. Chinese Medical Journal of Gerontology 2005.24 (11) : 863-865.

[4] Wei YD, Hu DY, Zhang RF, et al. Study of the patients with metabolic syndrome and peripheral arterial disease.[Chinese] Chinese Medical Journal .2006, 86 (30) : 2114-2116.

[5] Li X, Wu FY. The distribution of the ankle-brachial index (ABI) among the elderly and the prevalence of atherosclerosis disease (PAD), Quanguo laonian zhouwei dongmaiyinghua jibing fangzhi zhuanli yantaohui lunwen huibian. 2007: 99.

[6] Guan H, Liu ZM, Li GW, et al. Peripheral arterial occlusive disease among patient aged 50 or older with diabetes and related factors.[Chinese] Chinese Medical Journal .2007, 87 (1) : 23-27.

[7] Li J. Serial of reports of the lower extremity arterial disease in China. All-cause of lower extremity arterial disease and the cardiovascular disease mortality among high-risk groups. Chinese Journal of Internal Medicine .2006, 26 (21) : 1685-1687.

[8] Wang Y, Li J, Xu YW, et al. The prevalence of peripheral arterial disease in the natural population and the associated risk factors in China.[Chinese] Chinese Journal of Cardiology. 2009, 37 (12) : 1127-1131.

[9] Wang L, Du F, Mao H, et al. Prevalence and related risk factors of peripheral arterial disease in elderly patients with type 2 diabetes in Wuhan, Central China. Chin Med J (Engl) .2011, 124 (24) : 4264-8.

95% CI: 10.05–47.28, $p < 0.001$ ^[1]. A recent community study including 4 748 subjects showed that, PAD was associated with all five MetS definitions in men, the odds ratios were 2.25 (1.27–3.99) (WHO), 2.09 (1.21–3.62) (CDS), 1.92 (1.2–3.09) (NCEP–ATPIII updated), 1.85 (1.14–3.00) (IDF) and 2.26 (1.40–3.66) (JIS) respectively. However, female MS patients were not at increased risk of peripheral artery disease^[2].

3.8.1.3 The Effects of LEAD on Mortality

The mortality rate of LEAD patients is significantly higher than that of non–LEAD subjects at the same age, and rates also increase as the ABI value decreases. Results from a 3–year follow–up study comparing the mortality rates of 3 210 patients with high risk of atherosclerotic diseases, categorized by their ABI, are shown in Figure 3–8–2^[3]. The all–cause mortality rate doubled in the group with ABI < 0.4 compared with that with ABI within 1.0 to 1.4 (95% CI: 1.936 to 4.979) and the mortality rate due to cardiovascular disease quadrupled (95% CI: 2.740 to 8.388). Few studies have examined the relationship between the increase of ABI and the incidence of coronary heart disease and PAD. A study including 2 080 outpatients with type 2 diabetes mellitus indicated that the prevalence of coronary heart disease and PAD was higher in patients with ABI > 1.3 compared to patients with normal ABI levels, but was lower than patients with ABI ≤ 0.9 . ABI > 1.3 is an independent risk factor for CVD and PAD. The threshold for ABI level as a predictor of PAD is 1.45^[4]. A five–year cross–sectional study in Hong Kong that enrolled 12 772 local residents investigated the risk for cardiovascular disease in type–2 diabetes mellitus patients with an ABI level within the threshold range (0.90–0.99)^[5]. The results showed that, after adjusting for traditional risk factors, an ABI level within the threshold range is an independent risk factor for diabetic microvascular and macrovascular lesions, with an associated increased risk for diabetic retinopathy of 1.19–fold (95%CI 1.03–1.37); for mass proteinuria of 1.31 fold (95%CI 1.10–1.56); for chronic kidney disease of 1.22–fold (95%CI 1.00–1.56) and for stroke of 1.31–fold (95%CI 1.05–1.64).

All–cause and CVD mortality in the four ABI categories after 3–year follow–up (Table 3–8–2).

[1] Liu F, Shen J, Zhao J, et al. Cystatin C: a strong marker for lower limb ischemia in Chinese type 2 diabetic patients? *PLoS One*.2013, 8 (7) :e66907.

[2] Wen J, Yang J, Shi Y, Liang Y, Wang F, Duan X, Lu X, Tao Q, Lu X, Tian Y & Wang N. Comparisons of different metabolic syndrome definitions and associations with coronary heart disease, stroke, and peripheral arterial disease in a rural chinese population. *PLoS One* 2015 10 e0126832.

[3] Li X, Luo Y, Xu Y, et al. Relationship of ankle-brachial index with all-cause mortality and cardiovascular mortality after a 3-year follow-up: the China ankle-brachial index cohort study. *J Hum Hypertens*.2010, 24 (2) :111-116.

[4] Li Q, Zeng H, Liu F, Shen J, Li L, Zhao J, Zhao J & Jia W. High Ankle-Brachial Index Indicates Cardiovascular and Peripheral Arterial Disease in Patients With Type 2 Diabetes. *Angiology*, 2015.

[5] Yan BP1, Zhang Y2, Kong AP3, et al; Hong Kong JADE Study Group. Borderline ankle-brachial index is associated with increased prevalence of micro- and macrovascular complications in type 2 diabetes: A cross-sectional analysis of 12,772 patients from the Joint Asia Diabetes Evaluation Program. *Diab Vasc Dis Res*, 2015 Sep; 12 (5) :334-341.

Table 3–8–2 Comparison of the Mortality Rates among Patients with High-risk of Atherosclerotic Diseases Categorized by ABI Levels after 3-year Follow-up (%)

Mortality Rate	ABI <0.4	0.41–0.9	0.91–0.99	1.0–1.4	Total	P-value
All-cause Mortality Rate	37.7	24.4	13.2	12.1	15.7	<0.001
CVD Mortality Rate	27.5	14.5	8.1	6.3	8.9	<0.001

3.8.2 Carotid Arterial Disease

3.8.2.1 Prevalence and Risk Factors for Carotid Arterial Disease

Carotid arterial disease is a common disease among the middle-aged and elderly population. Epidemiological diagnostic methods include atherosclerotic plaque detection and intima-media thickness (IMT) measurements via carotid ultrasound. Studies have shown that the prevalence of carotid arterial disease is associated with age, certain risk factors, and baseline diseases of the subject.

A collaborative cross-sectional study, involving investigators from China and the United States with 2 681 individuals enrolled from multiple regions reported that the ultrasound detection rate of carotid atherosclerotic plaques among patients from 43 to 81 years of age was 60.3% (males 66.7%, females 56.2%), with lesions predominantly located at the carotid sinus. Multivariable analysis showed that IMT among men and women increased with an increase in blood pressure, blood glucose, and LDL-C levels. Compared to patients with no risk factors, the rate for plaque detection was significantly higher in patients with hypertension, diabetes, smoking history, or high LDL-C^[1]. A recent study with a cohort of 1 195 patients investigated blood lipid levels and the carotid IMT in 1993–1994 and 2002. The data demonstrated that blood lipid levels (TC, LDL-C, non-HDL-C, TC/HDL-C, and LDL-C/HDL-C) were significantly correlated with carotid IMT; the correlation was much stronger between the baseline blood lipid levels and carotid IMT^[2]. A community-based study in Shanghai involving 3 381 individuals showed that the waistline-to-height ratio and the surface area of visceral fat are new risk factors for IMT independent of the body-mass index and traditional cardiovascular risk factors^[3]. Waistline, waist-to-hip ratio, and waistline-to-height ratio are all predictors of carotid atherosclerosis^[4].

A 2007–2010 survey of 13 896 people above 35 years old from the Uyghur, Kazakh, and Han Chinese ethnic groups reported that the overall detection rate of carotid atherosclerotic plaque was 10.2%, and 12.5%, 7.2%, and 10.4%, for each group, respectively. The relatively low detection rate in this study was probably

[1] Wang W, Wu YF, Zhao D, et al. Distribution characteristics and risk factors of carotid atherosclerosis in middle-aged and elderly Chinese. [Chinese] Chinese Journal of Cardiology, 2010, 38 (6) : 553-557.

[2] Huang Y, Yu X, Millican D, et al. The measurement of lipids currently and 9 years ago-which is more associated with carotid intima-media thickness Clin Cardiol, 2012, 35 (8) :512-517.

[3] Ren C, Zhang J, Xu Y, Xu B, Sun W, Sun J, Wang T, Xu M, Lu J, Wang W, Bi Y, Chen Y. Association between carotid intima-media thickness and index of central fat distribution in middle-aged and elderly Chinese. Cardiovasc Diabetol. 2014, 13 (1) :139.

[4] Zhang ZQ, He LP, Xie XY, Ling WH, Deng J, Su YX, Chen YM. Association of simple anthropometric indices and body fat with early atherosclerosis and lipid profiles in Chinese adults. PLoS One, 2014 Aug 4; 9 (8) :e104361.

due to the low average risk of cardiovascular disease in these populations.^[1]

3.8.2.2 The Risk of Carotid Arterial Disease and Ischemic Heart Disease

A 5-year follow-up study showed that the baseline IMT was an independent predictor of ischemic heart disease in patients without carotid atherosclerotic plaques (HR = 1.59, 95% CI: 1.04 – 2.45)^[2]. In patients with carotid plaques, the risk of ischemic heart disease increased with an increase in overall plaque surface area and number of plaques; hazard ratios for each were 1.29 (95% CI: 1.08 – 1.55) and 1.14 (95% CI: 1.02–1.27), respectively^[3].

[1] Yang YN, JiWN, Ma YT, et al. Survey of detection rate of carotid plaque among Xinjiang Uygur, Kazak and Han population[Chinese]Chinese Medical Journal 2011, 91 (4) :225-228.

[2] Xie W,Wu Y,Wang W,et al.A longitudinal study of carotid plaque and risk of ischemic cardiovascular disease in the Chinese population. J Am Soc Echocardiography 2011, 24 (7) :729-37.

[3] Xie W,Liang L,Zhao L,et al. Combination of carotid intima-media thickness and plaque for better predicting risk of ischaemic cardiovascular events. Heart, 2011, 97 (16) :1326-31.

Part 4

Community-based Prevention and Control of CVD

4.1 Overview

Community-based prevention of cardiovascular diseases in China has advanced for more than 40 years with increasing exploration and practice. By extending gradually from point to surface, developing a comprehensive intervention program focused on hypertension prevention and control, China's community-based prevention work is in the midst of continuous improvements with promising results. For example, the standardized mortality rate for stroke in residents has a significant downward trend since 2009.

The first CVD prevention and control center in China was established in 1969 at the Capital Iron and Steel Company by Fuwai Hospital and has been highly effective. This "Capital Iron Model" was recognized by the World Health Organization as the prevention and control model for developing countries. Since 1970s, various places have established similar community-focused centers and pilot programs based on administrative regions focused on comprehensive prevention and control of hypertension and cardiovascular diseases (CVD). Since 1997, 24 provinces, autonomous regions, and centrally administrative municipalities, including Beijing, Tianjin, Shanghai, and Zhejiang, have launched comprehensive prevention and control programs for chronic diseases. In 2009, the national government pushed forth new medical reform policies that brought community-based prevention and treatment of hypertension and diabetes into the agenda of national public health services and launched prevention-oriented work at the national level. This covered more than 86 000 000 hypertension patients in this community prevention and management network by the end of 2014. In 2010, the National Health Family Planning Commission initiated efforts to establish "China Chronic Disease Prevention and Treatment Demonstration Zones", creating 265 sites at national level by the end of 2014.

Over the course of more than 40 years, China's community-based prevention and treatment of cardiovascular diseases has undergone many changes. The efforts have gone from local pilot projects to regional comprehensive interventions to a fundamental component of the national public health service with equal treatment for all citizens. The projects have gone from only treating hypertensive individuals to large-scaled community management and comprehensive prevention and management of multiple chronic diseases. The projects' emphasis has shifted from the morbidity, prevalence, mortality, and risk factors of cardiovascular diseases (CVD) to improvement in the awareness, treatment and recovery rate, and prevention and control rate at the population level. The work has advanced from academic research conducted by experts and specialists to government-initiated and led preventative work through collaboration. Comprehensive prevention of cardiovascular diseases in China is gradually developing from spot targeting towards

standardization and large-scale information.

4.2 An Example of Community-based Prevention and Control of CVD—A Community-Based Information Management Model for Prevention and Control of Hypertension in Minhang District, Shanghai

Minhang District is located in the southwest of central area of Shanghai. At the end of 2014, its population was about 2 539 500 residents. Compared to all the other districts and counties in Shanghai, Minhang is not economically powerful and has a low level of allocated medical resources. But through creating an innovative medical reform model, Minhang has achieved an outstanding success and output in health service especially in CVD prevention and control such as hypertension with relatively limited investment in health resources. Under the district government's support, the Health Bureau of Minhang District began to establish a regional health information-based management platform based on the Electronic Health Record (EHR) from 2006, and continually established a "Trinitarian Management Model of CVD comprehensive prevention and control" in 2007. By circulating information, sharing resources and standardizing hypertension management processes, a scientific and efficient management system for hypertension patients has been achieved in the community.

(1) Establishing Trinitarian Management Model for CVD Comprehensive Prevention and Control for Co-management

Over the past few years, Minhang has emphasized community-based hypertension prevention and treatment, and has allocated a relatively high proportion of total public health funds to this cause. Such allocated funds were managed through a mechanism based on projects dedicated to this very specific purpose and serve as reliable guaranteed finances for the prevention and treatment of hypertension. For the management of hypertension, Minhang adopts a model called the "Trinitarian Management Model for CVD comprehensive prevention and control", indicating "no walls" between the district Center of Diseases Control, comprehensive hospitals, specialized hospitals, and community health service centers. It is a model of the cooperation of "borderless" multi-disciplines including the prevention, medical treatment and healthcare on the prevention and control of chronic diseases. Based on the regional health information platform, characterized by interoperability, interconnection, resource integration and information sharing, these institutions could achieve a continuous and dynamic prevention for hypertension throughout the whole process.

The District CDC is in charge of developing plans and strategies for hypertension prevention and control in the whole region, regulating blood pressure management processes, and conducting quality control, supervision, assessment and evaluation for hypertension prevention and control work in each community health service center. General hospitals and specialized hospitals in this district are primarily responsible for the diagnosis and treatment of hypertension and other related complications, as well as technical training and guidance to community health service centers that belong to the "medical consortium". Community health

service centers are considered to play the main role for hypertensive patient management. They conduct the entire process including screening, registration, follow-up, intervention and evaluation through the family doctor. The Trinitarian Management Model was adopted to optimize the utilization of resources, maximize the output and production, and substantially improve the capacity of community-based hypertension management.

(2) Achieving Community-Based Information Management for Hypertension Based on Technology

In 2006, Minhang took advantage of information technology and established the resident EHR, which could record all the health and medical care information of individuals, mimicking the real-time resident health management and disease rehabilitation services. In 2007, Minhang established a technology information based, intensive, scientific community hypertension management system, extending to the District Health Bureau, CDC, 5 hospitals, 13 community health service centers and all health service stations in the district with fiber optic network. The system has more than 180 kinds of function modules, covering all aspects of medical and health services and management (such as EHR, basic medical services, pharmaceutical logistics and management, performance evaluation, student health management, general practitioners workstation, Minhang Health Website, etc.) and their whole processes^[1]. With assistance of this information platform, the hypertension management in Mindang community achieved the information based management of hypertension patients in the community, through the resource sharing and multi-point real-time data collection and use of data. In 2008, Minhang continued to build the “Self-Help Health Management Cabin” in all community health service centers, which provided intelligent instruments such as self-service digital blood-pressure monitors, blood glucose meters and BMI instruments. The self-test results could be automatically stored and uploaded in the patient’s EHR. Residents could access to their own health profile information at any time via internet.

Through information technology, Minhang district community hypertension management system was able to help the “Chinese Hypertension Prevention Guideline (for Primary Care)” localize and grow. The information system can automatically evaluate cardiovascular risks of the covered hypertension patients, stratify them in to different groups (low risk, medium risk, high risk and very high risk) according to the guide’s requirements, and then provide hierarchical management and regular follow-up (once a month for the very high-risk and high-risk groups, once every two months for the medium risk group, and once every three months for the low risk group). During the follow-ups, CVD events and death would be recorded and verified by doctors. The system automatically sets dates and reminders for the next follow-up dates, shows the completion date of previous follow-up visit, and supports the real-time & dynamic query of patients requiring follow-ups to avoid duplicating or missing visits. As a result of one-on-one follow up and management, with the assistance of technological means to ensure the guide’s implementation, Minhang has greatly enhanced the rate of the standard management of patients, reduced the dropout rate of follow-up, and truly realized the real-time, dynamic and whole process management of hypertension in the community.

[1] Xu S. Exploration of health management model for residents under the support of information technology. *Chin J Health Manage*, 2012,6: 350-351.

EHR integrates the regular outpatient care and regular follow-up visits in community on the information platform with EHR as the core and has achieved a seamless transition and information sharing network between outpatient care and follow-up visits. Whether in the clinic, or at follow-up visits, as long as the hypertension patients access the system with their health cards, all the medical information (such as blood pressure, drugs and health prescriptions, etc.) can be uploaded directly to their own EHR via wired or wireless network. As a result, doctors in the outpatient clinics can simultaneously carry out about 50% of follow-up tasks. It completely solved the lack of communication and duplicated work problems between clinics and follow-up visits, greatly improving the efficiency of hypertension management^[1].

Because of these modules under the EHR, all the outpatient electronic medical records, prescriptions, laboratory tests, electrocardiogram, chest X-ray, as well as cardiovascular events during follow-up phase can be directly transmitted to the EHR. The automatic generation and upload of data help clinics avoid the input mistakes of paper information and data and enhance work efficiency. Such data are not only accurate, reliable, but are also dynamic and comprehensive with the entire process recorded. For example, each patient can get his or her own blood pressure curve which records all the dynamic changes and achieves the conformity assessment for hypertension control.

All the information including medical records, clinical and laboratory data, ECG and cardiac & vascular ultrasound image can be interconnected and shared between all levels of medical institutions in the district. When a hypertensive patient walks in any of the 13 community health centers in Minhang district, his medical treatment or follow-up information can be transmitted to his or her own EHR, which subsequently ensures the data sharing between various regional health service centers within this region. The information interconnection network also contributes to strengthening the linkage between medical institutions at different levels in the region. Imaging findings (such as chest X-rays) from community health service centers are synced to the Minhang District Central Hospital, and a diagnosis is made by the radiologist and returned on the same day, which helps community health service centers diagnose at the level of highly ranked hospitals^[2].

On the health information platform, the Minhang district has also developed a series of information modules for health service management, such as medical care quality control and personnel performance evaluation, which improved the quality of medical and health care, and simultaneously encouraged medical workers to become more proactive with incentives.

Currently, the Minhang district manages more than 200 000 hypertension patients in the district, which has increased by more than 100% since 2007. All the hypertension profiles are managed in the form of electronic information, with a standardized management rate of 98%. Compared to that of hypertension patients who were not included in the system, the blood pressure control rate of hypertension patients in the

[1] Chen LL, Yan YJ, Fang H, et al. Researches and effectiveness evaluation on the management model of hypertension and combination of clinic and prevention based on the electronic health record. *Chinese Primary Health Care*. <http://192.168.226.3/C/periodical-zgcjwzwbj.aspx>, 2015,29:63-64.

[2] Xu S, Jiang XH, Li GH, et al. Exploration of information Technology based exploration of regional health care reform. *CHINESE JOURNAL OF HOSPITAL ADMINISTRATION*, 2011,27:520-522.

system apparently increased, while stroke and myocardial infarction incidence rates decreased significantly^[1].

(3) Building Community-Based Hypertension Research Bases Jointly with Research Institutions, Achieving Remote Blood Pressure Monitoring

To better summarize and promote Minhang's experience with community-based management of hypertension, to further develop demonstration models in this regard, and to establish high-quality hypertension research bases focusing on the community's population, the "Shanghai Institute of Hypertension-Research Base on Community Hypertension Prevention and Control at Xinzhuang Community Health Service Center" was established in Minhang District in October 2011.

After the establishment of the base, Minhang hypertension database was first analyzed. Since then, multiple researches and investigations have been conducted.^[2,3,4,5,6] Besides introducing and promoting Minhang's experience with community-based hypertension information management to domestic and foreign academia, the research base has gradually been developing a system and management platform for automatic blood pressure measurement and direct transmission results since 2012 with the direct leadership and strong support from the Health Bureau of Minhang. With the adoption of the internationally certificated digital upper arm blood pressure monitors and the assistance of modern communications technology, fully automated and seamless processes of blood pressure measurement, hypertension data acquisition can occur. The data will then be imported into the management system and platform. This will ensure the accuracy, reliability and authenticity of data for blood pressure tests. Currently, at Xinzhuang community health service centers and all its subordinated service sites, automatic blood pressure measurement has been achieved and results are transferred directly to the doctor's workstation and the patient's EHR. Telemetry blood pressure monitors for home have also been configured to each community health service center in Minhang^[7].

The base conducted a series of trainings for hypertension-related knowledge and business skills for general practitioners in Minhang District. This specifically targeted new measurement technologies and organ damage screening and included 6 training sessions covering over 625 people. Currently, 24-hour dynamic

[1] Zhao YP, Fang H, He DD, et al. Application of Information-based Trinitarian Management Model of Chronic Diseases. *Chinese General Practice*, 2012,15:729-732.

[2] Wang Y, Wang YJ, Qian YS, et al. Longitudinal change in end digit preference in blood pressure recordings of patients with hypertension in primary care clinics: Minhang study. *Blood Press Monit*, 2015,20:74-78.

[3] Wang Y, Wang YJ, Gu H, et al. Use of home blood pressure monitoring among hypertensive adults in primary care: Minhang community survey. *Blood Press Monit*, 2014,19:140-144.

[4] Wang Y, Wang YJ, Qian YS, et al. Association of body mass index with cause specific deaths in Chinese elderly hypertensive patients: Minhang community study. *PLoS One*, 2013,8:e71223.

[5] Chen L, Qian YS, Zhu DL, et al. Analysis of antihypertensive drug use in Xinzhuang Community Health Service Center in Shanghai between 2007 and 2011. *Chinese General Practice*, 2014,17:101-104.

[6] Wang YJ, Qian YS, Wang Y. Comparison of blood pressures-lowering efficacy of 5 kinds of antihypertensive agents in the treatment of patients with hypertension in the community. *Shanghai Medical and Pharmaceutical Journal*, 2014,35:25-27.

[7] Zhu Dingliang. An information management model for community prevention and control of hypertension in Minhang District. Shen WF, Zhang RY. *New Theory and Technology of Cardiovascular Diseases (2015)*. Beijing: People's Military Medical Press, 2014:289-290.

blood pressure monitors have been used routinely in Xinzhuang communities. Seven days of the standardized home blood pressure measurement process have been widely carried out, and used for morning blood pressure research. The urinary albumin / creatinine ratio has been measured as a routine item and results can be transmitted directly to patients' health records. Community-based hypertension management in Xinzhuang has transformed from focusing solely on the completion of quantitative indicators to emphasizing the quality of blood pressure management gradually.

In the 3 years after its establishment, the base has carried out multiple studies on elderly patients with hypertension, high-normal blood pressure, refractory hypertension, hypertensive target organ damage, etc. These studies have successfully obtained the "three rate" of hypertension in community, the baseline prevalence of CVD risk factors and more. The base has acquired and established a biobank of the concerned population, developed a blood pressure monitoring management platform, and built a registration and verification system for CVD events, which has laid a foundation for its community population cohort study.



Part 5

Medical Treatment and Expenditure of Cardiovascular Diseases

Since 1980, the number of patients with CVD and diabetes discharged from hospitals in China has increased. The increasing trend accelerated quickly especially since 2000. Correspondingly, the total hospitalization expenditure on CVD has increased rapidly. Since 2004, the cost's average annual rate of increase has been growing faster than the annual rate of increase for China's GDP. The increase mainly springs from the increased number of hospitalization cases and the high proportion of inappropriate prescriptions.

5.1 Utilization Status of Inpatient Services by Patients with Cardio-cerebrovascular Diseases^[1,2,3]

5.1.1 Number and Trend for Patients Discharged with CVD

Among all hospital patient discharges in 2014, 12.75 % were related to CVD (17.94 million) . This includes 6.63% diagnosed with CVD (9.33 million) and 6.12% diagnosed with cerebrovascular disease (8.61 million) .

Among the cases of discharged patients with CVD, the leading causes were IHD (in total: 6.55 million, AMI: 0.54 million) and cerebral infarction (5.32 million) , which accounted for 36.53% and 29.66%, respectively. Other causes included hypertension (2.53 million, including 222 500 patients with hypertensive heart and renal disease) , intracranial hemorrhage (1.30 million) , and rheumatic heart disease (250 100) . Additionally, 3.2 million patients were discharged for diabetes.

From 1980 to 2014, the average annual growth rate of discharged patients with CVD in China was 10.10%. This was faster than the average annual growth rate of all-cause discharges (6.33% annually) . The annual average growth rates of different CVD in descending order were: cerebral infarction (12.30%) , IHD (11.74%) , intracranial hemorrhage (9.76%) , AMI (8.12%) , hypertension (8.06%) , hypertensive heart and renal disease (5.82%) . The number of discharged patients with rheumatic heart disease (1.43%) did not

[1] Ministry of Health of People's Republic of China. National health statistics annual report 1980-2001.

[2] Ministry of Health of People's Republic of China. China Health Statistics Yearbook 2002-2012.

[3] National Health and Family Planning Commission of the People's Republic of China. China Statistical Yearbook of Health and Family Planning 2013-2015.

change significantly. In addition, from 2008 to 2014, the annual average growth rate of patients with diabetes was 14.18%.

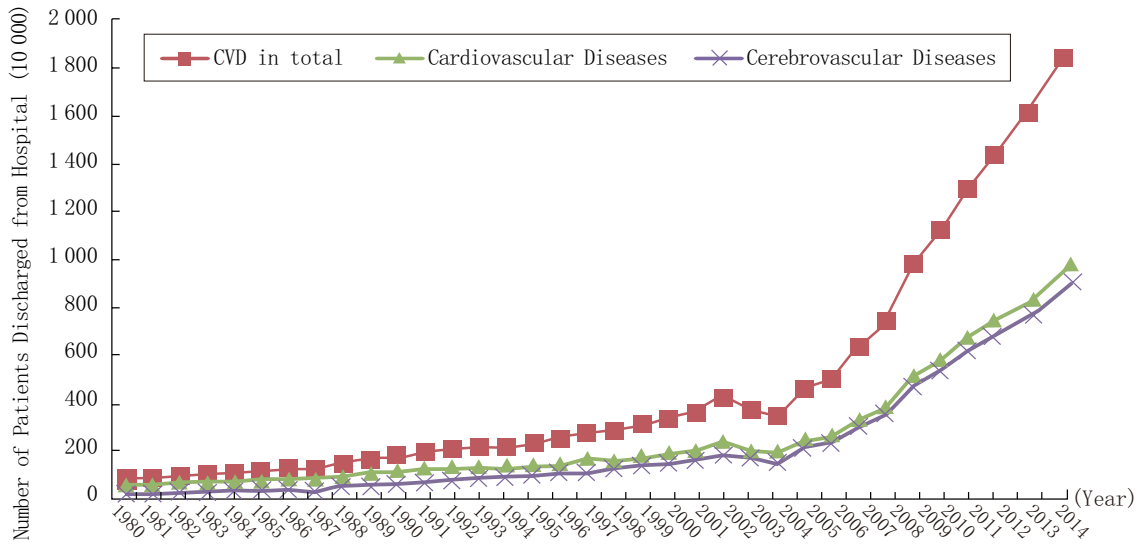


Figure 5-1-1 Trend in Number of Patients with CVD Discharged in China from 1980 to 2014

NOTE: CVD include IHD (angina, AMI, and other IHD) , chronic rheumatic heart disease, pulmonary heart disease, hypertension (including hypertensive heart and kidney disease) and cerebrovascular disease (intracranial hemorrhage and infarction) . Prior to 2002, IHD was listed as coronary heart disease in the Health Statistics Annual Report.

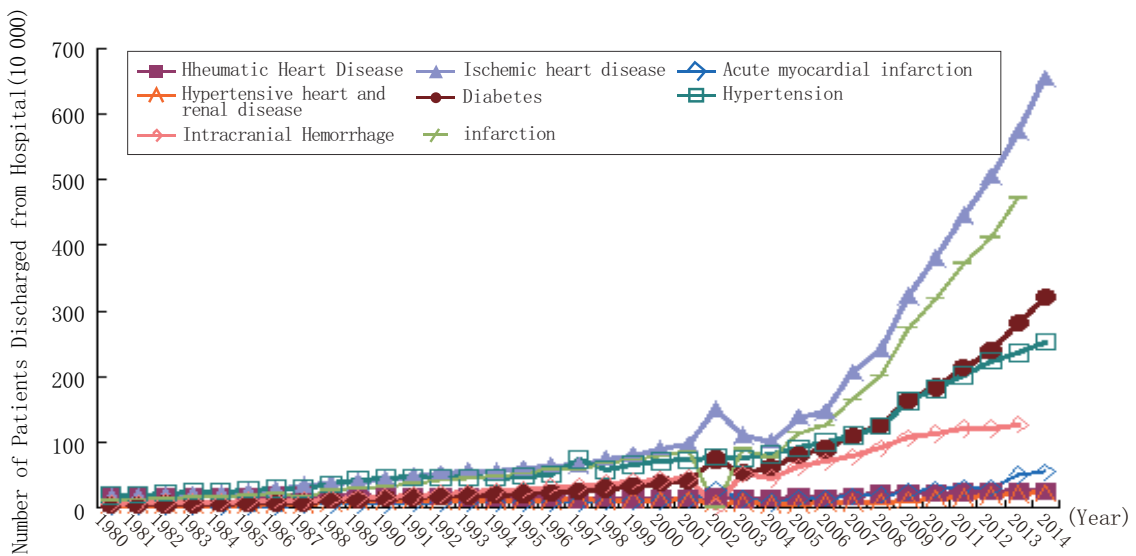


Figure 5-1-2 Trend in Number of Patients with CVD and Diabetes Discharged in China from 1980 to 2014

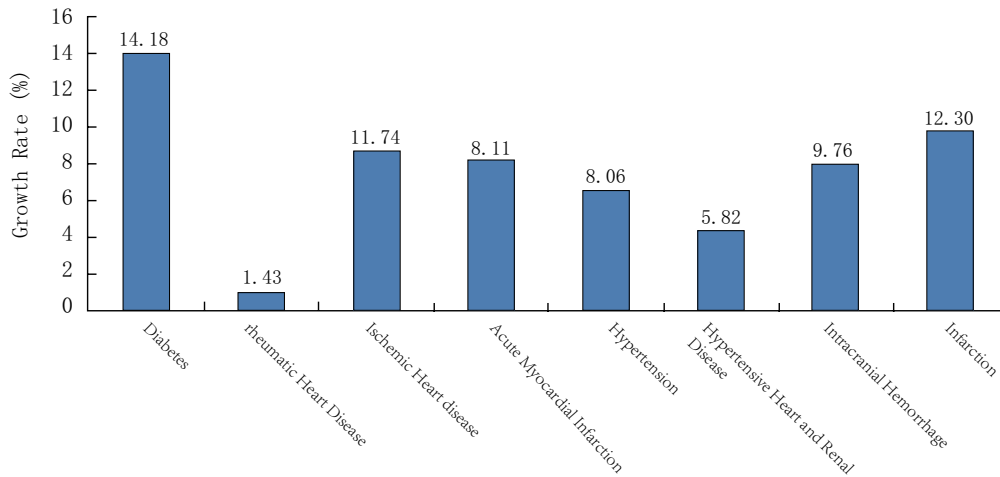


Figure 5–1–3 Average Annual Growth Rate of Number of Discharged Patients with CVD and Diabetes in China from 1980 to 2014

5.2 Hospitalization Cost of CVD

For hospitalizations associated with CVD in 2014, the total medical expenses for acute myocardial infarction, intracranial hemorrhage, and cerebral infarction were 13.375 billion, 20.707 billion, and 47.035 billion RMB respectively. After adjusting for annual price inflation, the expenses of these three diseases showed annual increases from 2004 by 32.02%, 18.90% and 24.96%, respectively.

The average individual expenses in 2014 for AMI, intracranial hemorrhage and cerebral infarction were 24 706, 15 929.7, and 8 841.4 RMB, respectively. After adjusting for annual price inflation, their average annual growth rates from 2004 were 8.72%, 6.63% and 2.81% respectively.

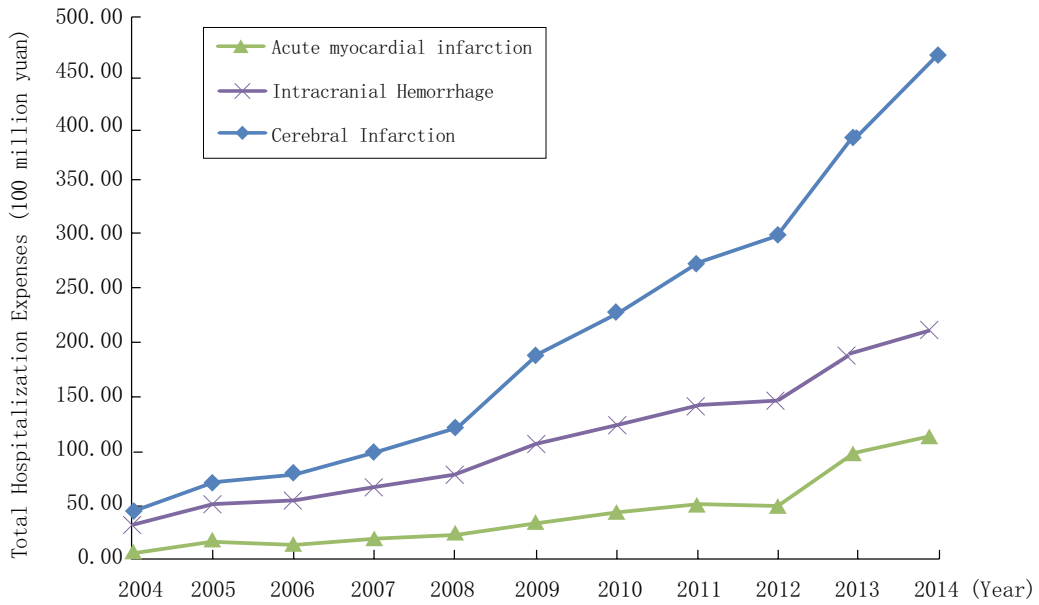


Figure 5-2-1 Trend of Hospitalization Expenses for CVD, 2004-2014

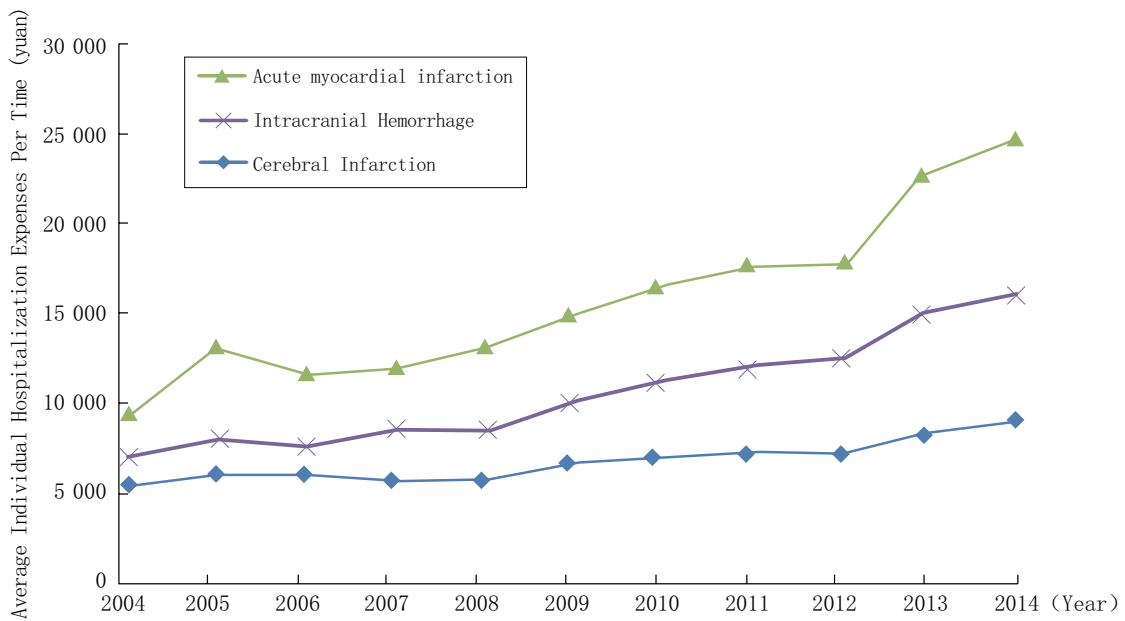


Figure 5-2-2 Trend of Average Hospitalization Expenses for Each Inpatient Period, 2004-2014

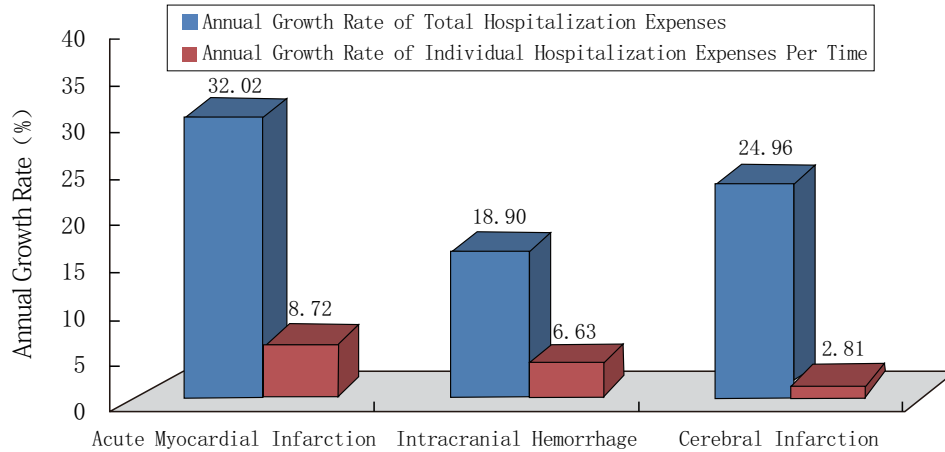


Figure 5–2–3 Annual Growth Rate of Hospitalization Expenses from 2004 to 2014

5.3 Pharmaceutical Market of CVD

In 2014, the total pharmacy expenses among hospitals in China with at least 100 beds totaled to RMB 614.76 billion. Out of this sum, 65.644 billion was used in CVD treatment. The five most frequently purchased medications were: cardiovascular circulation improving medications, other nutritional supplements and coronary circulation improving medications, lipid lowering drugs, calcium channel blockers (single medication), and an angiotensin receptor antagonist (single medication).

Table 5–3–1 The 15 Most Commonly Used Medications for Cardiovascular and Cerebrovascular Diseases in Chinese Hospitals, 2014 (RMB 100 000 000)

Category of Medicine	Sales Revenue
Overall	656.44
Cardiovascular Circulation Improving Medication*	173.45
Other nutritional Supplements and Coronary Circulation Improving Medications	145.79
Lipid Lowering Drugs	87.22
CCB (Calcium Channel Blockers) (Single Medication)	64.39
ARB (Angiotensin II Receptor Antagonist) (Single Medication)	45.30
β -Adrenergic Receptor Blocking Agents (Single Medication)	18.72
ARB (Angiotensin II Receptor Antagonist) (Combine Medication)	16.10
Nitrite and Nitrate	17.90
ACEI (Angiotensin Converting Enzyme Inhibitor) (Single Medication)	14.04
Medication for Varicose Veins, Systemic	13.79
Antianginal Medications (Excluding CCB and Nitrates)	9.58

Table 5-3-1 The 15 Most Commonly Used Medications for Cardiovascular and Cerebrovascular Diseases In Chinese Hospitals, 2014 (RMB 100 000 000) (Continued)

Category of Medicine	Sales Revenue
Diuretics	6.71
Antihypertensive Agents (Non Herb)	4.76
Cardiac Inotropes	4.33
Cardiac Stimulants Excluding Cardiac Glycosides	2.92
Others Medicine for Cardiovascular Diseases	31.46

*: cardiovascular circulation improving drugs include fleabane, Fick Chavez, Xingding, ginaton, Ginkgo Biloba Extract, Shuxuening, Sibelium Mailuoning, Dialis Lowe s.t.c.

Sources of data: The abovementioned data is extrapolated by IMS Health market research Consulting (Shanghai) Corporation Beijing Branch from the result of a survey of 2000 nationwide hospitals with at least 100 beds. It includes the western medicalized Chinese patent medicine, such as the compound Danahen dripping pills, Ginkgo agent, Erigeron breviscapus and etc.

5.4 Health Economics Assessment Research on CVD

In 2014, an international study was conducted jointly by Beijing Anzhen Hospital of Capital Medical University, Beijing Institute of Heart Lung and Blood Vessel Diseases, Fuwai Hospital, and Columbia University Medical Center. Using intergrated data resources to build the prediction model, this study aims to evaluate the cost-effectiveness of treatments recommended by Chinese guidelines to be used in acute phase of AMI (30 days after symptom onset)^[1]

In this study, treatments in acute phase for AMI include:

Strategy A1: Maximize the utilization of aspirin, β -blockers, statins and ACEI among hospitalized patients with AMI.

Strategy A2: Maximize the utilization of clopidogrel among hospitalized patients with AMI.

Strategy B: Maximize the utilization of heparin among hospitalized non-ST segment elevation myocardial infarction (NSTEMI) patients.

Strategy C1: Maximize the utilization of primary PCI among patients with ST segment elevation myocardial infarction (STEMI) in tertiary hospitals; simultaneously maximizing the utilization of thrombolytic drugs among STEMI patients in secondary hospitals.

Strategy C2: Improve the utilization of primary PCI among all STEMI patients.

Strategy C3: Maximize the utilization of primary PCI among high-risk NSTEMI patients in tertiary hospitals.

The maximized utilization calculation for each treatment is: 100%-current utilization rate-contraindications rate. For the criteria of cost-effectiveness, the researchers used the standard from Choosing Interventions That Are Cost Effective (WHOCCHOICE) standard, published by WHO (the World Health

[1] Miao W, Andrew EM, Jing L, et al. Cost-Effectiveness of Optimal Use of Acute Myocardial Infarction Treatments and Impact on Coronary Heart Disease Mortality in China. *Circ Cardiovasc Qual Outcomes*,2014,7:78-85.

Organization). The standard specifies: if the incremental cost effectiveness ratio (ICER) is less than the per capita gross domestic product (GDP), the intervention is considered very cost-effective; if the ICER value is larger than 1 time and less than 3 times the per capita GDP, the intervention is considered cost-effective; if the ICER is larger than 3 times the per capita GDP, the intervention is considered not cost-effective. Results of this study are shown as follows:

Strategy A1: Maximization of the utilization of aspirin, β -blockers, statins and ACEI among hospitalized patients with AMI could postpone or prevent 8 900 cases of coronary heart disease deaths annually in the next 10 years. It could also reduce the annual mortality rate of coronary heart disease by an average of 1.4%.

Strategy A2: Maximization of the utilization of clopidogrel among hospitalized patients with AMI could postpone or prevent 3 000 cases of coronary heart disease deaths annually.

Strategy B: Maximization of the utilization of heparin among hospitalized non-ST segment elevation myocardial infarction (NSTEMI) patients could postpone or prevent 1 800 cases of coronary heart disease deaths annually.

Strategy C1: Maximization of the utilization of primary PCI among patients with ST segment elevation myocardial infarction (STEMI) in tertiary hospitals, and maximization of the utilization of thrombolysis enhancing drugs among STEMI patients in secondary hospitals, could postpone or prevent 33 200 cases of coronary heart disease deaths annually. It could also reduce the total annual mortality rate of coronary heart disease by about 5.1%.

Strategy C2: Increasing utilization of primary PCI among all STEMI patients could postpone or prevent 49 100 cases of coronary heart disease deaths annually and reduce the total annual mortality rate of coronary heart disease by about 7.5%.

Strategy C3: Maximization of the utilization of primary PCI among high-risk NSTEMI patients admitted to tertiary hospitals could postpone or prevent 3,000 cases of coronary heart disease deaths annually.

Strategies A1 + A2 + B + C2 + C3: Overall, improved treatments of AMI acute phase, without considering the feasibility, could bring the coronary heart disease mortality rate down by at most 9.6%.

According to the standards established by WHOCHOICE, the implementation of Strategy A1 or Strategy B in China is very cost-effective, the implementation of Strategy C1 or Strategy C2 meets cost-effectiveness, while the implementation of Strategy A2 or Strategy C3 does not meet cost-effectiveness. Thus, most of the treatments for the acute phase of AMI recommended by the guidelines are cost-effective. A large proportion of patients with AMI, however, died outside of hospitals, due to their limited access to acute care; therefore, benefit of maximizing the use of guideline-recommended treatments for AMI is limited.

5.5 Content and Cited Data in This Part

Hospital expenditures for CVD in 2014: For representativeness and scientific value, the data here is based on hospitalization expenditures and trends of CVD related diseases (AMI, intracerebral hemorrhage and cerebral infarction), which are included in the 30 most common diseases reported on patient charts in a

nationwide hospital sample and reported in the Health Statistics Yearbook.

Number of discharges: The number of discharges for CVD in 2003 was excluded from this report because of the changes in definition and diagnosis standards based on guidelines in 1987 and 2002 from The Statistics Information Center of National Health and Family Planning Commission. Without exclusion, the data consistency would be affected.

Ischemic heart disease: Since different diagnosis standards are employed in different local hospitals, some systematic error exists in the estimation of the relevant discharge rate; however, the trend of hospitalization for ischemic heart disease is not influenced.

Eliminate price effects: In order to reflect the growth of medical costs accurately, we need to eliminate the impact of price factors on the costs, namely, changes in medicine price index. The medical care consumer price index (published in the Chinese Statistics Yearbook 2012) was used to adjust the medication expenses in this chapter to eliminate the effect of price inflation.

