Evolving Cardiovascular Disease Prevalence, Mortality, Risk Factors, and the Metabolic Syndrome in China

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ABSTRACT

The rapid growth transformation of China from a rural agrarian society to an industrial society with increased wealth has impacted the cardiovascular health of the entire population. The increasing prevalence of cardiovascular disease (CVD) and CVD risk factors mirror in some regards the disease prevalence in western industrialized countries and in other areas present unique public health issues. This article reviewed recent population surveys, reports, and clinical trials conducted in China. It was found that the prevalence of CVD and many of the risk factors such as hypertension, obesity, and diabetes contributing to disease mortality are increasing in China. However, compared with the United States, disease mortality is lower. Also, cerebrovascular disease is far more common than ischemic heart disease in China. The low prevalence of disease may suggest a reduced role of diagnostic imaging studies as compared with the US, while the increased percentage of strokes may point to the need for widely available emergent computed tomography (CT) imaging in hospitals in China. This article also discusses the occurrence of metabolic syndrome, obesity, glucose intolerance, diabetes, and their unique features in the Chinese population. Of interest, compared with the Caucasian cohort of the same body mass index (BMI), the Chinese had a higher percentage of body fat. Metabolic syndrome was found to be associated with increased cardiovascular mortality rate. With one fifth of the world's population, China can anticipate a dramatic rise, in absolute numbers, of CVD. It is imperative that national and regional programs are initiated to detect and treat the disease.

Introduction

This review examines the results of published Chinese and Chinese–International disease specific mortality reports, multi-year population surveys, and reports that address cardiovascular disease (CVD) prevalence and CVD risk factors in China from 1957 to the present. The prevalence and disease impact of the risk factor cluster termed the metabolic syndrome is a specific focus of this review. We also draw attention to specific studies that support the utilization of lower body mass index (BMI) and waist measurements for Chinese men and women in risk assessment and in the diagnosis of the metabolic syndrome than those published by major western medical organizations. There were 6 studies of significant duration, involving large populations in China that are the basis for this review. These studies are identified and described in the Table. 1

Cardiovascular Disease Prevalence and Mortality

In 2004, Liu et al compares heart disease and risk factor prevalence in China (from the Chinese Multi-provincial Cohort Study) and the United States (from the Framingham Heart Study).[7] The 10 year coronary heart disease (CHD) event rates in China were 1.5% for men and 0.6% for women. It is contrasted with the Framingham cohort who had event rates of 8% for men and 2.8% for women. This finding is, in part, the basis for the overestimation of CHD event risk for Chinese men and women using the Framingham Risk Score.

Critchley et al noticed a steep ascent in coronary artery disease (CAD) mortality in Beijing between the years 1984 and 1999. Age adjusted CAD mortality rates increased by approximately 50% in men and 27% in women[8] (Figures 1A and 1B). They noted rising overall mortality rates and that CAD age adjusted mortality for men was double that of women. They accumulated the data on risk factors and events from the World Health Organization (WHO's) Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (Sino-MONICA) project, the China Multicenter Collaborative Study, and routine hospital statistics. Their analysis of changing risk factor prevalence lead them to estimate that 77% or 1397 of the additional CVD deaths per year in Beijing were attributable to a greater than 1 mmol/L (>39 mg/dL) rise in total cholesterol levels. A total of 19% or 349 additional deaths were attributable to the 6% increase in the prevalence of diabetes mellitus (DM), 4% or 67 additional deaths were attributable to the 1.0 kg/m^2

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Table 1. Major Studies Addressing Prevalence of Cardiovascular Disease in China

Study Name	Study Date	Subjects	Location	Objectives
The Sino-Monica Project[1–3]	Jan. 1, 1987 to Dec. 31, 1993	749 251 men and women between ages 24 and 74	8 provinces in the northern areas and 5 provinces in the southern areas of China	To study trends of CVD in the Chinese population
The InterAsia Study[4]	2000–2001	15 540 men and women between ages 35 to 74	5 provinces in north and 5 provinces from south, each province is then divided into urban and rural	Cross-sectional survey with the risk factors to compare for US adults obtained from the National Health and Nutrition Survey
The PRC-USA Collaborative Study[5]	1981–2000	"Chunk samples" of 4 populations of working men and women	2 cities: Beijing and Guangzhou	Survey questions addressed the use of antihypertensive medications, oral contraceptives, smoking, angina, or claudication and alcohol consumption. Comparison to the US population was based on the US National Health and Nutritional Study II
The China Multicenter Collaborative Study of Cardiovascular Epidemiology Cohort[6]	Enrolled during 1991–1995 and followed up for 11 years	17 329 participants	15 populations in China	More recent version of PRC-USA cohort
The CMCS[7]	1992–2002	30 121 Chinese adults aged 35–64	11 provinces with 12 centers (80.3%) in urban areas and 4 centers in rural areas	After excluding with baseline history of myocardial infarction or angina, new CHD events were followed

Abbreviations: CHD, coronary heart disease; CMCS, Chinese Multi-provincial Chohort Study; CVD, cardiovascular disease; InterAsia, International Collabroative Study of Cardiovascular Disease in Asia Study; PRC-USA, P.R. of China - United States of America; Sino-Monica, Multinational Monitoring of Trends and Determinants in Cardiovascular Disease.

increase in BMI, and 128 recent deaths were attributed to an 8% increase in the prevalence of smoking. They noted a dramatic (100%) increase in the number of cigarettes smoked by men. Female smoking rates actually declined during the study period, from 16% to 9%, which by their calculations prevented 111 deaths in women (Figure 2).

A prior study by Yao et al, from the Beijing Institute of Heart Lung and Blood Vessel Diseases reported that mortality from CVD (CHD, hypertensive heart and vascular disease, and ischemic and hemorrhagic stroke) in China had almost tripled from 1957 (86 per 100 000 people) to 1990 (214 per 100 000 people), despite an overall decline in mortality during this time period.[9] In a separate study, Wang et al noted that cardiovascular disease prevalence had increased and that prevalence of hypertension had more than doubled.[10]

Unique Features of Cardiovascular Disease in China

Of profound importance are the findings from Sino-MONICA study which found that the northern population of China has a dramatically higher CVD mortality than the population living in the south of China.[1–3] The coronary event mortality rate for men in the 1992 survey was 43.5 per 100 000 people in Beijing (northern China) and 3.5 in Shanghai (southern China). A complementary finding (as confirmed by the International Collabroative Study of Cardiovascular Disease in Asia Study [InterAsia] survey[4]) was that dyslipidemia, hypertension, DM, and being overweight were more common among men and women living in northern China as was the clustering of risk factors.

Sino-MONICA and other studies in China noted that the mortality from CVD exceeds that of CHD,[1–3] which is the opposite of the respective mortality in the United States.[11]

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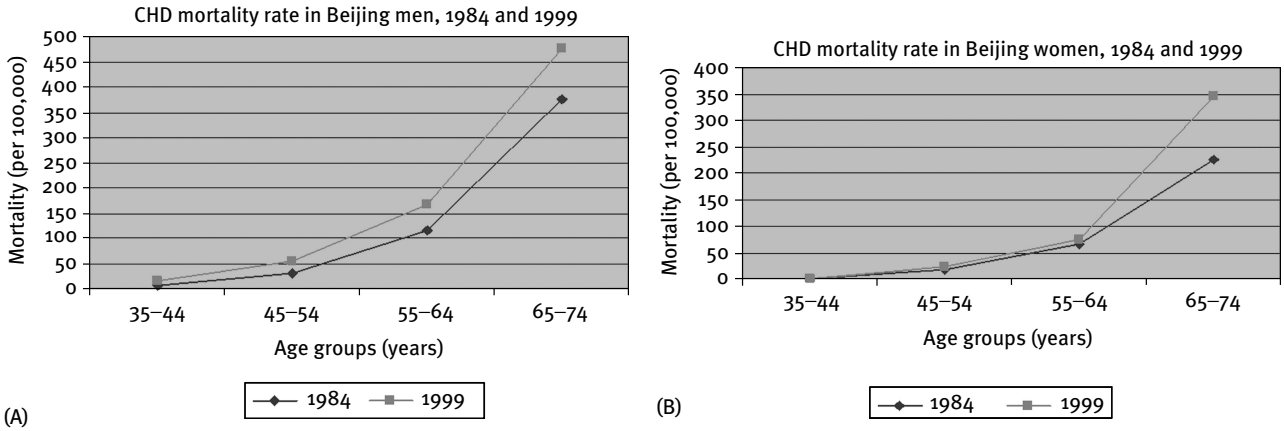

Figure 1. (A) CAD mortality rates in Beijing men, 1984 and 1999. (B) CHD mortality rate in Beijing women, 1984 and 1999. Note the drastic increase in CAD mortality rate between 1984 and 1999 in men (A) and women (B).[8] Abbreviations: CAD, coronary artery disease; CHD, coronary heart disease.

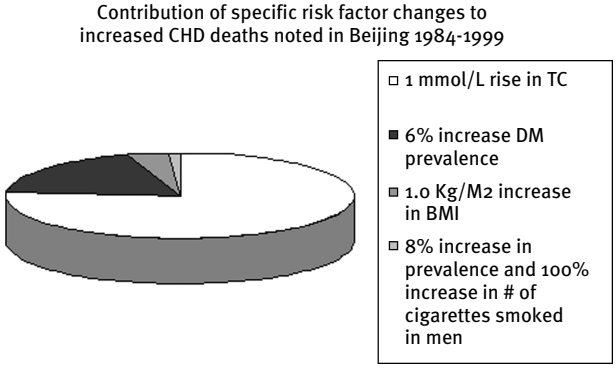

Figure 2. Contribution of specific risk factor changes to increased CHD deaths noted in Beijing 1984–1999. Figure 2 is modified from Critchley et al.[8] Abbreviations: BMI, body mass index; CHD, coronary heart disease; DM, diabetes mellitus.

The Sino-MONICA Beijing study noted an ischemic heart disease mortality from 1984 to 1986 of 29/100 000 for men and 14/100 000 for women and a cerebrovascular mortality of nearly 2-fold greater (Figures 3A and 3B), 59/100 000 for men and 52/100 000 for women.[3,11] Actual incidence rates of stroke were 249-273/100 000 for men and 161-205/100 000 for women. Ischemic stroke was more common than hemorrhagic stroke in China, but the relative frequency of hemorrhagic stroke in both men and women was greater than that reported in the United States.[11]

CVD Risk Factor Prevalence and the Metabolic Syndrome in China

InterAsia and the Sino-MONICA Beijing studies evaluated the prevalence and extent of CHD risk factors in China.[3,4] The InterAsia study noted that, in the 2000 data set, dyslipidemia was found in 54% of the subjects, hypertension in 26%, diabetes in 5 %, current smoking in 34%, and being overweight in 28% of subjects. Hypertension, dyslipidemia, and obesity had increased since the initial survey. This was compared with data in the United States (Figure 3). With regard to the "clustering" of risk factors, the studies determined that 35% of their population had 1 risk factor, 29% had 2 risk factors, and 17% had 3 or more risk factors. The clustering of risk factors was about equal for men and women and increased with age.[4] The findings were similar to values for US adults obtained from the National Health and Nutrition Survey shown in Figure 4.

Clustering of risk factors is of interest, not only in regard to global risk of CVD, but also in the context of the metabolic syndrome, a cluster of risk factors comprising elevated fasting glucose, dyslipidemia (reductions in high-density lipoprotein cholesterol [HDL-C], elevation in serum triglyceride levels and modest elevations in low-density lipoprotein cholesterol [LDL-C]), hypertension, obesity, and central obesity. The mortality associated with this syndrome exceed that of the individual risk factors and is currently understood to be mediated, in part, by insulin resistance.

Obesity and central obesity, primary components of the metabolic syndrome, are increasing in the Chinese population. Recent data suggests that it is best studied using different ranges of measurements than those that have been developed for white populations.[12,13]

The WHO BMI criteria for being overweight is 25–30 kg/m^2 and for obesity >30 kg/m^2. In 2002, the Working Group on Obesity in China published a meta-analysis of surveys performed in China (239 972 subjects) that included BMI, waist circumference, and risk factors for related diseases.[14] A BMI criteria of 24–28 kg/m^2 for being overweight and greater than 28 kg/m^2 for obesity had the best sensitivity (and specificity of 90%) for an association with concurrent hypertension, diabetes, and dysglycemia.

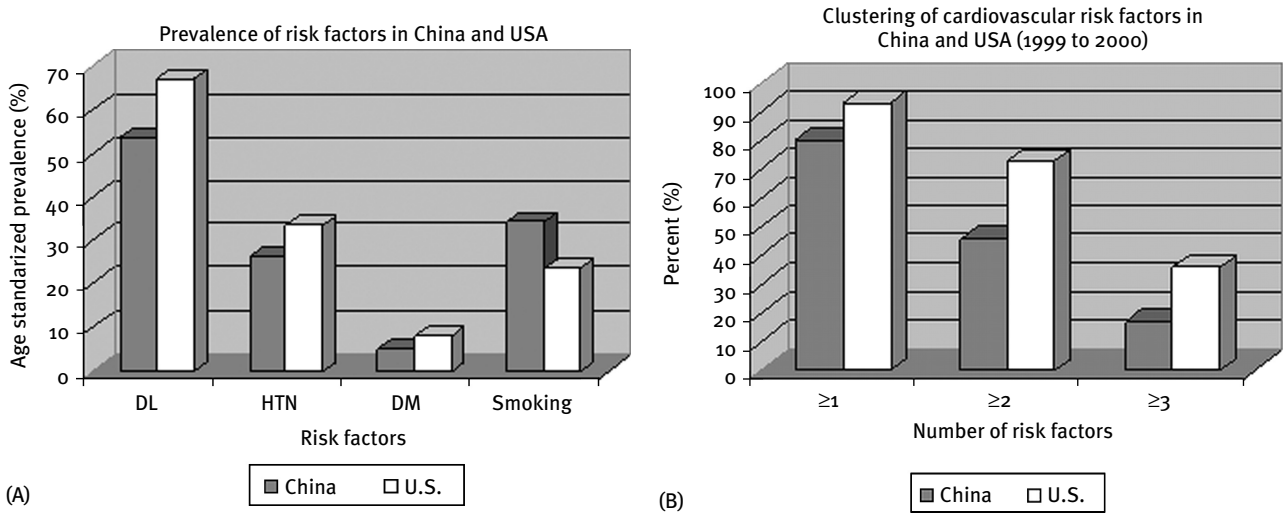

Figure 3. (A) Mortality due to coronary event (per 100 000) in Beijing (north) and Shanghai (south). (B) Mortality due to stroke (per 100 000) in Beijing (north) and Shanghai (south).[1] Figures 3A and 3B based on table 2 (age-standardized incidence and mortality rate of coronary event [1 of 100 000] and their trends during 1987 to 1993 by population 35 to 64 years of age.) Beijing represents the north of China and is abbreviated as BJ-N and Shanghai represents the south of China and is abbreviated as SH-S.

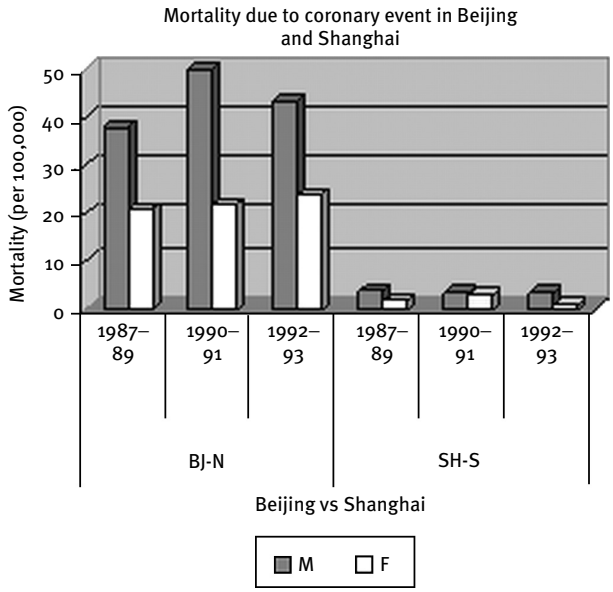

Figure 4. The comparison of age-standardized prevalence of risk factors in China and the United States. Figure 4 derived its data on age-standardized prevalence of risk factors in China from results of InterAsia.[4] The age-standardized prevalence of dislipidemia, hypertension, diabetes, and smoking in China were 53.6%, 26.1%, 5.2%, and 34.4%, respectively (each $P < 0.001$). This is compared with 67.1%, 33.6%, 8%, and 23.5%, respectively, in the United States.

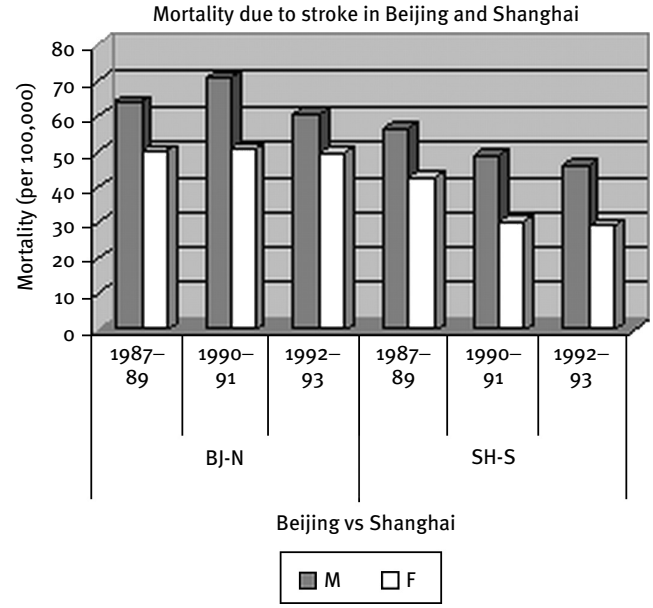

Figure 5. Clustering of cardiovascular risk factors in China and the United States (1999 to 2000). Figure 5 derived its data from the number of cardiovascular risk factors in China from results of the InterAsia study as seen in Table 3 (age standardized prevalence of ≥1, ≥2, and ≥3 major cardiovascular disease risk factors in rural and urban China and the United States).[4]

Additional support for lower BMI ranges for Chinese people comes from the studies of Chang et al[12] and He et al.[13] They surveyed Taiwan (n = 1079) and Hong Kong Chinese (n = 330), respectively, using dual energy x-ray absorptiometry (DEXA) to determine percentage of body fat at a specific BMI. Percent body fat prediction, using the formula developed in white populations, underestimated the percentage of body fat found with DEXA in both populations. A BMI of 25 kg/m^2 in whites corresponded to 23–23.6 kg/m^2 in Chinese people and 30 kg/m^2 corresponds to 25–25.3 kg/m^2, respectively.

Waist circumference, a measurement of central obesity was an independent predictor of CVD in Chinese in a study by Wildman et al.[15] The InterAsia study noted that waist circumference served as a predictor of CVD risk that is independent of BMI in a population of 15 540 Chinese adults aged 35 to 74 years old. Higher waist circumference tertiles were associated with higher blood pressure, total cholesterol, triglycerides, and glucose within each tertile of BMI and vice versa, especially in subjects with BMI $\geq$24 kg/m^2 and waist circumference increases from $\leq$71.1 cm to 71.9–80.3 cm to $\geq$80.3 cm.

Li et al from the China-Japan Friendship Hospital in Beijing studied 2856 adults in Da Qing City and followed them for 6 years.[16,17] They noted that the risks of hypertension and triglyceride levels were approximately doubled at a BMI of 23 to 24.9 kg/m^2. The risk of DM is increased 4-fold at a BMI greater than 27 kg/m^2 as compared with a BMI of less than 23 kg/m^2. Zhou et al using a 9-year follow-up of cohorts from the P.R. of China - United States of America (PRC-USA) Collaborative Study calculated that that reducing BMI and waist circumference to normal range (BMI $<$24 kg/m^2, waist circumference to $<$85 cm for men and $<$80 cm for women, respectively) could prevent 45% to 50% of metabolic syndrome.[5] Additionally, stratified analysis of participants from Beijing showed that BMI was independently associated with CAD, stroke, and peripheral artery disease.[18] Each 2 unit increase in BMI independent of other risk factors was associated with 23% increase in risk of CAD, a 9% increase in risk of stroke, and a 13% increase in risk of ischemic stroke.[19]

Diabetes and Glucose Intolerance

Glucose intolerance is an independent risk factor of hypertension in Chinese women.[20,21] When glucose intolerance was present without hypertension, it was a predisposing factor for the development of hypertension. The odds ratio of having hypertension in Chinese women with impaired glucose intolerance or DM were 2.93 and 5.94 ($P < 0.001$ for both), respectively as compared with women without glucose intolerance.[21] Clinical trials are pending in China to investigate whether addition of insulin sensitizers such as metformin (ClinicalTrials.gov identifier NCT00538486) and thiazolidinediones (ClinicalTrials.gov identifier NCT00155350) can improve blood pressure control in Chinese woman.

Determining the actual prevalence and the increase within the population of DM in China is confounded by the different definitions used in the various studies performed at different times. However some trends could be delineated when they were present within the same study. The InterAsia Collaborative Group Study (n = 15 540) reported that the rate of self-reported diagnosed DM was 1.3%, undiagnosed DM was 4.2%, and impaired fasting glucose was 7.3% between the years of 2000 and 2001.[22] This study also noted that the prevalence of DM in urban areas was higher than in rural China and the rates were higher in northern China (7.4%) than in southern China (5.4%).[22]

Although prevalence rates are important, actual case numbers may reflect more accurately the medical structural demands and population risk factor modification efforts that need to be addressed by a geo-political unit. New diabetes cases in China in the coming years can be conservatively estimated by applying the present incidence rate in selected populations to the anticipated population of China. Using this equation, there will be more than 700 000 new cases of diabetes per year when the population of China reaches 1.3 billion which is projected to occur early in the twenty-first century.

The Impact of Metabolic Syndrome, DM, and Cardiovascular Risk Factors in China on CVD Prevalence and Mortality

Studies confirmed the relationship of the increasing prevalence of risk factors in China and CVD prevalence.[3–5,7–10,18,19] However, data addressing the relationship of CVD risk factors and actual increases in mortality is less robust. One recent perspective cohort study by Thomas et al revealed that a significant relationship is present in the Chinese population. The investigators used the revised National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) Asian central obesity criteria to determine the impact of metabolic syndrome on mortality.[23] The study lasted 8.5 years for a total of 24/101 person/years. After adjustments were made for age, socioeconomic status, and lifestyle habits those with metabolic syndrome had a significantly higher risk of dying from all and vascular causes. With each additional risk factor, the hazard ratio increased proportionally. Those with metabolic syndrome had the highest risk and those with 0 to 2 components had the lowest—almost half the highest risk (Figure 6).

Conclusion

Studies in China over the past several decades have noted a low but rising prevalence and mortality from CHD. And the mortality from congenital ventricular aneurysm (CVA) is higher than CHD. Risk factors, especially smoking in men and the cluster of factors that define the metabolic syndrome, are increasing in China as is the CVD and

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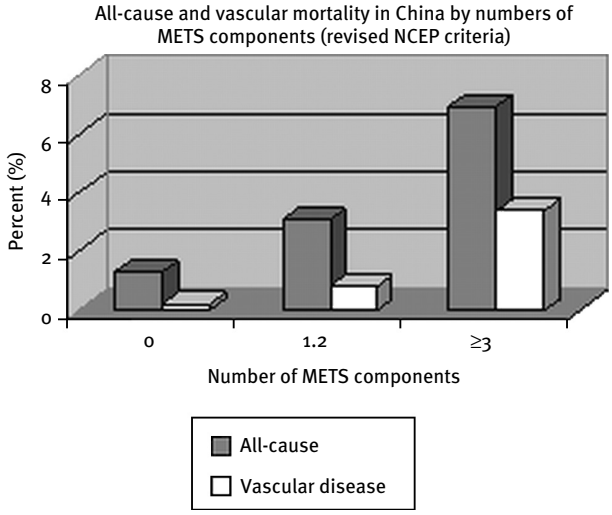

Figure 6. All-cause vascular mortality in China by number of METS components (revised NCEP criteria). Figure 6 derived its data from results of the study of Thomas et al as seen in table 2 (adjusted hazard ratio [and 95% confidence intervals] for all-cause and vascular disease mortality associated with the METS).[23] Abbreviations: METS, metabolic syndrome; NCEP, National Cholesterol Education Program.

mortality rates attributed to hypertension and to the metabolic syndrome. The very high rate of CVD mortality in the north of China as compared with the south of China is explained, in large part, by the increase in CVD risk factors found in the populations in the north (eg, Beijing) as compared with the south (eg, Shanghai).[3]

The combination of increasing risk factor prevalence and an aging population foretell the increase in CVD prevalence and mortality. The lower prevalence of CVD in China vs the United States and Europe will impact of the applicability of currently used western clinical noninvasive paradigms for detection of CVD, and the higher incidence of hemorrhagic stroke vs ischemic stroke will present, in the context of an early thrombolysis initiative, the need for widely available emergent CT brain imaging.

With finite resources, a challenge facing China in the next decade is where to invest healthcare research and clinical service funds. It is clear that hypertension will remain an important focus of preventive health care efforts in China. The growing appreciation of the number of people with elevated blood pressure and the impact of hypertension on heart disease, and of significant importance to the people of China, ischemic and hemorrhagic stroke make this an appropriate direction.

Of concern also is the increasing incidence of heart disease in women in Beijing, and most probably throughout China. Figures 1A and 1B make clear that although the incidence of heart disease is lower for women than men in Beijing, the rate of the increase of heart disease mortality in women is significantly greater than it is for men.

Over the next decade the impact of the metabolic syndrome will, as it is presently the case in the United States and Western Europe, dramatically increase cardiovascular morbidity and mortality in China. The opportunity, in China, to aggressively address these risk factors, and to avoid the negative impact already being felt in the United States is of special importance to healthcare programs, the government, and the people of China.

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