**INTERNATIONAL COLLABORATIVE STUDY OF CARDIOVASCULAR DISEASE IN ASIA: DESIGN, RATIONALE, AND PRELIMINARY RESULTS**

**Objectives:** The overall objective of the International Collaborative Study of Cardiovascular Disease in Asia (InterASIA) was to estimate the prevalence and distribution of cardiovascular disease risk factors, including hypertension, hypercholesterolemia, diabetes, obesity, cigarette smoking, and physical inactivity, in the general population of both China and Thailand.

**Methods and Results:** A multistage cluster sampling method was used to select a nationally representative sample of 15,838 adults, aged 35–74 years, in China, and 5,350 similarly aged adults in Thailand. Data on medical history, cigarette smoking, alcohol consumption, diet, physical activity, and awareness and control of risk factors for cardiovascular disease, were collected. Blood pressure, body weight and height, and hip and waist circumferences, were measured using standard methods. Fasting blood specimens were collected to measure levels of total cholesterol, high-density lipoprotein cholesterol, triglycerides, glucose, and creatinine. All data were carefully collected by specially trained, experienced observers using standardized methods and a stringent level of quality control. The prevalence of self-reported cardiovascular disease in Chinese adults aged 35–74 years was 3.3% in men and 3.6% in women (representing 8,147,000 male and 8,270,000 female cases nationally). The prevalence of self-reported cardiovascular disease in Thai adults was 1.5% in men and 1.7% in women (representing 184,000 male and 226,000 female cases).

**Conclusions:** The InterASIA study provides important information on the current prevalence and control of both cardiovascular disease and its risk factors in the region. These findings will be useful for developing national strategies to reduce the large, and increasing, burden of cardiovascular disease in China and Thailand.

**Key Words:** Blood Pressure, Cardiovascular Disease Risk Factors, China, Coronary Heart Disease, Cross-sectional Studies, Lipids, Stroke, Thailand

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**INTRODUCTION**

Cardiovascular disease (CVD) is the leading cause of mortality worldwide, and was estimated to account for approximately 14.3 million deaths in 1990.1,2 The majority of those deaths (about 9.1 million) occurred in economically developing countries, with many occurring in Asia.1,2 The burden of CVD in this region is projected to increase, both in absolute terms, and as a proportion of total disease burden, during the next 20 years.3 The emergence of CVD as a leading cause of death in this region is due primarily to the rapid economic growth and associated sociodemographic changes that have occurred over the past few decades. During this period, while the burden of infectious disease decreased, changes in lifestyle and diet, and an increase in life expectancy, resulted in a greatly increased burden of CVD and other chronic diseases.4-6 Established risk factors for CVD, such as high blood pressure (BP), high levels of cholesterol, cigarette smoking, obesity, and diabetes mellitus, are likely to be the principal determinants of the current, and projected, CVD burden in Asia. However, reliable data about the prevalence and distribution of these risk factors in Asian populations are sparse. Information about the prevalence and treatment of risk factors would greatly facilitate the development of effective strategies for the control of CVD in this region.

The International Collaborative Study of Cardiovascular Disease in Asia (InterASIA) was a cross-sectional study of CVD risk factors in a nationally representative sample of the general populations of China and Thailand. The overall objective of the study was to estimate the prevalence and distribution of CVD risk factors in the general populations, aged 35 years and older, of China and Thailand. The specific aims of the study were to obtain the following for each country: reliable age- and gender-specific estimates of the prevalence of hypertension, dyslipidemia, diabetes, obesity, active and passive cigarette smoking, physical inactivity, alcohol consumption, stroke, coronary heart disease (CHD), and peripheral vascular disease; the mean levels and distributions of BP, serum lipids, serum glucose, serum creatinine, body mass index (BMI), and waist/hip ratio; and the extent to which CVD risk factors are being treated and controlled.

**METHODS AND PRELIMINARY RESULTS**

The study recruitment and examination period of InterASIA began in July 2000, and ended in March 2001.

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During this period, while the burden of infectious disease decreased [in Asia], changes in lifestyle and diet, and an increase in life expectancy, resulted in a greatly increased burden of CVD and other chronic diseases.$^4$-$^6$

Sample Design
A multiple-stage stratified sampling method was used to select nationally representative samples of the general population, aged 35 years and older from both China and Thailand. The prevalence of CVD risk factors was considered likely to vary by age, gender, and geographic area,$^4$-$^8$ and the sampling method in the InterASIA study was stratified accordingly.

Sampling Method in China
A 4-stage stratified sampling method was employed (Figure 1). In stage one, 31 provinces (and municipalities) were stratified into north and south China, as divided by the Yangtze River. Four provinces from North China (Jilin, Shandong, Qinghai, and Shanxi) and 4 from South China (Sichuan, Hubai, Fujian, and Guangxi) were selected to be representative of the geographic and economic developing status in their regions, in addition to the municipalities of Beijing (North China) and Shanghai (South China). In the second stage of sampling, one rural county and one urban area from each selected province or municipality were randomly selected, providing a total of 10 urban areas and 10 rural counties. In the third stage of sampling, one township or one street district (about 1,000–2,000 households) was randomly selected from each of the counties and urban areas, respectively.

In the final stage, individuals aged 35–74 years were randomly selected from the selected township or street district. The final sampling was stratified by gender, with 50% men and 50% women, and age distribution based on the 1990 China census data. Only one participant was selected from each household.

Sampling Method in Thailand
A similar 4-stage stratified sampling method was employed in Thailand (Figure 2). In stage one, a representative province was selected from each of the 4 administrative regions of Thailand (North, South, Northeast, and Central), and from Bangkok. In stage 2, 5 representative urban political districts (one from Bangkok and one from each chosen province), and 4 representative rural political districts (one from each chosen province) were selected. In stage 3, enumeration districts (EDs, containing 350–450 households) were stratified as slum or non-slum in urban districts, and as developed, developing, or underdeveloped in rural districts. Up to 6 slum EDs, and 3 non-slum EDs, were selected from each urban political district (except in Central Thailand, where there were no slum EDs in the selected urban district), and up to 3 developing, and 3 developed, EDs were selected from each rural district. In addition, 2 undeveloped EDs were selected from North Thailand, the only region in which the selected rural district included undeveloped EDs. The number of EDs selected from each political district was dependent upon the size of each ED, and the potential to recruit the required number of study participants. In the final stage of sampling, individuals within each selected ED were grouped...
by age (35–44 years, 45–54 years, 55–64 years, and ≥65 years), and by gender, using lists compiled from the local government registers of households. Individuals were then sampled at random, from each age and by gender. Over-sampling of some age and gender groups was performed to ensure that adequate numbers of participants were recruited, and that reliable risk factor estimates could be obtained. Only one participant was selected from each household.

**Study Participants and Response Rate**

After a study participant was selected, study staff made a home visit, accompanied by a local health professional. The objectives and examination procedures of InterASIA were explained to potential participants, and instructions were given for overnight fasting. In China, 19,012 individuals were randomly selected from the 20 primary sampling units (street district or township), and were invited to participate in the study. Of them, 15,838 individuals (7,684 men and 8,154 women) completed the examination (Table 1). The overall response rate was 83.3% in China: 82.1% of men, and 84.5% of women; 82.2% in urban areas, and 84.4% in rural areas. In Thailand, 7,909 persons were randomly selected from the 18 EDs, and were invited for an interview. Of them, 5,350 individuals (2,109 men and 3,241 women) participated in the study (Table 1). The overall response rate was 67.6% in Thailand: 56.8% of men, and 77.3% of women; 60.7% in urban areas, and 81.0% in rural areas.

The following specific measures were taken to facilitate and encourage the participation of all those selected for the study: 1) travel assistance or home visits were provided for those unable to travel to the examination centers; 2) various appointment times were offered to suit study participants’ needs; 3) reports of blood test and examination results were provided to participants; and 4) the participation of local health professionals and government organizations was secured.

**Data Collection**

Data collection was conducted by trained observers in examination centers established in the participants’ residential areas. In some cases, interviews and examinations were conducted in study participants’ homes, if they were unable to attend an examination center.

**Questionnaire**

During the clinic or home visits, a standard questionnaire was administered (Table 2). Information on demographic characteristics, including age, gender, education, occupation, and household income, was collected. Medical history regarding coronary heart disease (CHD), stroke, transient ischemic attack (TIA), congestive heart failure (CHF), cor pulmonale, chronic rheumatic heart disease (RHD), hypertension, hypercholesterolemia, diabetes, and chronic kidney disease, was obtained. The questionnaire included sections from the London School of Hygiene Cardiovascular Questionnaire relating to angina, myocardial infarction, transient ischemic attack/stroke, and intermittent claudication. Self-reported history of physician-diagnosed CVD was confirmed by hospital chart review. Information on awareness of, and drug treatment and lifestyle modifications for,
hypertension, hypercholesterolemia, and diabetes, was also obtained. In addition, family history of premature heart attack, stroke, hypertension, hypercholesterolemia, and diabetes, was collected.

Information about current and former cigarette smoking, including age at which smoking was initiated, years of smoking, and the amount of cigarettes smoked per day, was obtained. Use of other forms of tobacco, and exposure to passive cigarette smoking in the work place or at home, was also assessed. Information about alcohol consumption, including the quantity and frequency of different types of alcoholic drinks, was ascertained. Data about the frequency and intensity of physical activity were collected, using questions that assessed both work-related and leisure-time physical activity. Finally, information on dietary habits, use of vitamin and mineral supplements, use of aspirin, and use of post-menopausal hormone replacement therapy, was collected. A brief 12-item semi-quantitative food frequency questionnaire was used to characterize several specific food intakes in the study participants.

**Blood Pressure and Anthropometric Measurements**

Trained and certified observers measured blood pressure (BP) during the clinic or home visits, according to a common protocol adapted from procedures recommended by the American Heart Association. The study participants were required to sit quietly for 5 minutes before their BP was measured. In addition, they were advised to avoid alcohol, cigarette smoking, coffee/tea, and exercise, for at least 30 minutes prior to their BP measurement. A standard mercury sphygmomanometer was used, and an appropriately sized cuff (pediatric, regular adult, large, or thigh) was chosen, as recommended in the American Heart Association's guidelines. The cuff was placed on the participant's right arm, and inflated in 10 mm Hg increments until the cuff pressure was 30 mm Hg above the level at which the radial pulse disappeared. Three BP measurements were obtained, with a 30-second interval between each cuff inflation. The first and fifth Korotkoff sounds were recorded, and used to identify systolic and diastolic BP.

During the clinic or home visits, body weight, height, and waist and hip girths were measured by trained observers using a standard protocol. Weight was recorded by trained staff, using a certified double balance beam scale placed on a firm level surface. Height was measured from a Frankfort plane positioned at a 90° angle against a wall-mounted metal tape. All body circumference measurements were taken with an anthropometric centimeter measuring tape. Waist girth was measured from the horizontal plane at one centimeter above the navel, which usually coincides with the narrowest circumference, but has the added advantage of being easily reproducible. The hip girth was measured at the level of the maximal protrusion of the gluteal muscles.

**Laboratory Measurements**

Overnight fasting blood samples were drawn by venipuncture to measure levels of serum lipids, glucose, and creatinine. Blood specimens were processed at the field center and shipped by air to central clinical laboratories in Beijing (China), or Bangkok (Thailand), where the specimens were stored at −70°C until laboratory assays could be performed. Levels of total cholesterol, HDL-cholesterol, and triglycerides were analyzed enzymatically, using commercially available reagents. LDL cholesterol levels were calculated using the Friedewald equation for the participants who had triglyceride levels <400 mg/dL: LDL cholesterol = total cholesterol − HDL cholesterol − triglyceride/5. For glucose measurement, whole blood was collected in vacuum tubes containing sodium fluoride. Plasma glucose was measured using a modified hexokinase enzymatic method. Serum creatinine was measured by the modified kinetic Jaffe reaction method.

**Study Outcomes**

Hypertension was defined as the mean systolic BP ≥ 140 mm Hg, and/or diastolic BP ≥ 90 mm Hg, and/or self-report of current use of antihypertensive medications. Overweight was defined as BMI ≥ 25 kg/m², and obesity as BMI ≥ 30 kg/m². Dyslipidemia was defined as total cholesterol ≥ 200 mg/dL, or LDL cholesterol ≥ 130 mg/dL, or HDL cholesterol < 40 mg/dL. Diabetes mellitus was defined as fasting plasma glucose ≥ 126 mg/dL, and im-
paired fasting glucose was defined as fasting plasma glucose between 110 mg/dL–125 mg/dL. A person was categorized as having CVD if they self-reported any of the following conditions diagnosed by a physician: CHD, stroke/TIA, CHF, cor pulmonale, PVD, or RHD.

Training and Quality Assurance

Training Program
All study investigators and staff members were required to successfully complete a rigorous central or local training program. All BP observers were required to participate in a special training session in the use of a standardized protocol for BP measurement. Certification of a BP observer included satisfactory performance on a written test of BP measurement knowledge, a standardized videotape examination, and concordant measurements of BP in the presence of an instructor. The certification of an anthropometric observer included participation in specific training sessions, and satisfactory performance of concordant measurements of body height, weight, waist and hip girth in the presence of an instructor.

Monitoring Procedures
Quality monitoring of the data collection processes was conducted at local and central levels. The study coordinators at each field center monitored study personnel daily, and ensured that the data collection was being conducted according to the study protocol. The study equipment, including mercury sphygmomanometers and weight beam scales, was checked and calibrated regularly throughout the course of the project. Five percent of study participants were randomly selected for repeated measurements on all study variables. Central organized site visits were conducted to monitor all aspects of the data collection process.

Laboratory Quality Control
Study laboratories were standardized for lipid measurements, according to the criteria of the CDC and National Heart, Lung and Blood Institute Lipid Standardization Programs. Each laboratory technician working on the study completed a training program and used standardized protocols and procedures for the study analyses. Approximately 5% of randomly blinded blood samples were selected for repeated measurements, in order to estimate measurement variation and error.

Data Processing
Data entry and data processing were performed by the coordinating centers in Beijing and Bangkok. Questionnaire and examination data were recorded at the field centers on paper forms, and mailed to the coordinating centers periodically. The data entry personnel were trained in the use of the data entry system, and all data were double-entered.

Statistical Issues
Sample Size
The InterASIA study was designed to provide reliable estimates of prevalence of CVD, and levels of major CVD risk factors, for both men and women from 4 age groups (35–44 years, 45–54 years, 55–64 years, and 65–74 years) in rural and urban settings. In addition, the study provided reliable estimates of risk factors for southern and northern China. The study sample sizes were estimated to meet generally recommended requirements for precision in a complex survey. Assuming a design effect of 1.5 (the ratio of the variance of a statistic from a complex sample to the variance of the same statistic from a simple random sample of the same size) and a risk factor prevalence of 5%, it was estimated that a minimum of 240 study participants would be required for each final sample stratum. Individuals aged 65 years or older were over-sampled in some areas, in order to ensure a sufficient sample size in that group.

Data Analysis
The prevalence and levels of CVD risk factors were calculated, weighted by a sampling factor (weights that took into account several features of the survey design, including over-sampling for specific age or geographic subgroups, non-response, and other demographic or geographic differences between the sample and the total populations. Standard errors were calculated by a technique appropriate to the complex survey design. All data analyses were conducted using STATA 7.0 (Statistics/Data Analysis) software.

Ethics and Safety
The InterASIA study was approved by the Institutional Review Board at Tulane University Health Sciences Center, in addition to ethics committees and other relevant regulatory bodies in China and Thailand. Informed consent was obtained from each participant prior to data collection. During the study, participants with untreated conditions identified during the examination were referred to their usual primary healthcare provider for care, and, unless specifically requested otherwise, examination and laboratory findings were provided to study participants and their healthcare providers.

Prevalence of Cardiovascular Disease
The overall prevalence of self-reported history of physician-diagnosed cardiovascular disease (including CHD, stroke/TIA, CHF, cor pulmonale, peripheral vascular disease [PVD], and RHD) in Chinese adults, aged 35–74 years, was 3.3% in men, and 3.6% in women (representing 8,147,000 male and 8,270,000 female cases nationally). The prevalence of self-reported history of physician-diagnosed cardiovascular disease in Thai adults was 1.5% in men, and 1.7% in women (representing 184,000 male and 226,000 female cases nationally) (Figure 3).
Prevalence Rates in Chinese Adults

The prevalence of myocardial infarction in Chinese adults, aged 35–74 years, was 0.7% in men, and 0.5% in women (representing 1,790,000 male and 1,193,000 female cases nationally). The prevalence of stroke was 1.6% in men, and 1.3% in women (representing 3,774,000 male and 3,001,000 female cases nationally). The prevalence of congestive heart failure was 0.7% in men, and 1.0% in women (representing 1,684,000 male and 2,335,000 female cases nationally). The prevalence of peripheral vascular disease was 0.3% in both men and women (representing 675,000 male and 765,000 female cases nationally). The prevalence of rheumatic heart disease was 0.2% in men, and 0.8% in women (representing 487,000 male and 1,719,000 female cases nationally). The prevalence of cor pulmonale was 0.4% in both men and women (representing 938,000 male and 1,009,000 female cases). The prevalence of chronic renal disease was 0.6% in men, and 0.7% in women (representing 1,364,000 male and 1,655,000 female cases) (Figure 4).

Prevalence Rates in Thai Adults

The prevalence rate of myocardial infarction in Thai adults, aged 35 years and older, was 0.2% in men, and 0.4% in women (representing 22,000 male and 53,000 female cases, nationally). The prevalence of stroke was 0.5% in men, and 0.4% in women (representing 66,000 male and 55,000 female cases nationally). The prevalence of congestive heart failure was 0.3% in men, and 0.6% in women (representing 37,000 male and 81,000 female cases nationally). The prevalence of peripheral vascular disease was 0.3% in men and 0.2% in women (representing 37,000 male and 31,000 female cases nationally). The prevalence of rheumatic heart disease was 0.2% in men, and 0.1% in women (representing 23,000 male and 12,000 female cases nationally). The prevalence of cor pulmonale was 0.3%
Several studies suggest that the association between BP and risk of stroke may be even stronger in Asian, compared to Western, populations.23,24

Very few national surveys have been conducted in Asian populations to estimate simultaneously the prevalence of CVD and its major risk factors. The present study indicated that CVD was common in Chinese and Thai populations. The prevalence of CVD might be even higher than those reported, since these estimates were based on self-reported cases. Unlike those found among Western populations, the prevalence of cardiovascular disease was slightly higher in women than in men, for both Chinese and Thai populations. Among CVD risk factors, stroke prevalence was much higher than that of myocardial infarction. Based on data from the third National Health and Nutrition Examination Survey, the prevalence of CHD in the United States' general population was 6.7%, 13.1%, and 17.7% in men aged 45–54 years, 55–64 years, and 65–74 years, respectively; and 5.5%, 8.4%, and 11.1%, respectively, in women of the same age groups.29 The prevalence of stroke in the United States was 2.2%, 4.0%, and 5.9% in men, and 1.0%, 2.7%, and 5.8% in women, among the same age groups.

Three national hypertension surveys have been conducted in China during the past several decades.7,30,31 Although it is difficult to make direct comparisons, due to differences in sampling and measurement methods, the prevalence of hypertension in China has increased dramatically.30 The most recent 1991 national survey in China indicated that the prevalence of hypertension, defined as BP $\geq 140/90$ mm Hg, was 12.2% in men, and 10.3% in women.7 The 1991 Thailand National Survey used a somewhat more stringent definition of hypertension (BP $\geq 160/95$ mm Hg), and recorded a prevalence of hypertension of 6.3% in men, and 8.1% in women.4

Reliable information on population levels of serum cholesterol is sparse among Asian populations. In 1983–1984, the mean serum cholesterol levels in rural and urban populations in China ranged from 155 mg/dL to 187 mg/dL.8 The mean total cholesterol level was 187 mg/dL for men, and 198 mg/dL for women, in a representative 1991 population sample in Thailand.4 Mean serum total cholesterol levels in population-based surveys conducted in Taiwan, Hong Kong, and Singapore, ranged from 194 mg/dL to 207 mg/dL.32–34

Cigarette smoking is the single most important determinant of mortality risk, worldwide, and is anticipated to further increase in public health importance during the next 25 years.35 Results from the 1996 China National Prevalence Study indicated that the prevalence of current cigarette smokers was 63% among men, aged 15 years and older, and 4% among women of the same age.36 Both the prevalence of current cigarette smokers, and the average number of cigarettes smoked, have increased since the corresponding survey conducted in 1984.37 The prevalence of cigarette smoking is also high among men in other Asian populations.3,32–34

Diabetes is now a major public health challenge in many Asian populations, although the prevalence of diabetes remains somewhat lower than those observed in developed countries.38 In mainland China, among a sample of 110,660 men and women aged 25–74 years, living in an urban community in 1986, the prevalence of type 2 diabetes and impaired glucose tolerance were about 1% each for both genders.39 Eight years later, the 1994 China National Diabetes Survey (among 224,251 men and
women, aged 25–64 years) reported the prevalence of diabetes and impaired glucose tolerance to be 2.5% and 3.2%, respectively.\textsuperscript{40} Data from other Asian populations also indicate an increasing prevalence of diabetes.\textsuperscript{43,44}

The prevalence of obesity has been increasing in most developed countries for several decades, and there is now evidence that obesity is also increasing in developing countries.\textsuperscript{41} In 1991, the prevalence in China of individuals with a BMI$\geq25$ kg/m$^2$ was 9% among men, and 13% among women.\textsuperscript{42} In Thailand, the corresponding figures were 12.5% and 27.2%, respectively.\textsuperscript{4} In other Asian regions, such as Hong Kong, Taiwan, and Singapore, the prevalence of individuals with BMI$\geq25$ kg/m$^2$ was even higher.\textsuperscript{32–34}

The results of the InterASIA study provide the most reliable and up-to-date information on the current prevalence of CVD risk factors and their control in Chinese and Thai populations.

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**APPENDIX 1**

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