Sino-MONICA Project
A Collaborative Study on Trends and Determinants in Cardiovascular Diseases in China, Part I: Morbidity and Mortality Monitoring

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Background—The Sino-MONICA project is a 7-year study monitoring trends and determinants of cardiovascular disease (CVD) in geographically defined populations in different parts of China.

Methods and Results—The study is a community-based prospective disease surveillance that uses the methodology and criteria of the World Health Organization’s Monitoring Trends and Determinants in Cardiovascular Disease (WHO MONICA) project, with slight modifications for local use. After a pilot study of 2 years (1985 through 1986), data collection started formally on January 1, 1987, and ended on December 31, 1993. The main results were as follows. By international standards, both the incidence and mortality rate of coronary heart disease in Chinese populations were low. The highest incidence was 108.7 of 100,000 (1987 to 1989), and the lowest was 3.3 for men 35 to 64 years of age, a 33-fold difference. Both the incidence and mortality rate of cerebrovascular disease were high. The highest incidence was 553.3 of 100,000 (1987 to 1989), and the lowest was 33.0 for men 35 to 64 years of age, a 17-fold difference. There were significant geographic variations in both CVD incidence and mortality rate, with higher rates in the north and lower rates in the south. During 1987 to 1993, increasing trends were found in CVD rates in some populations, whereas decreasing trends were found in others. The trends were not significant statistically in most cases.

Conclusions—Monitoring CVD with international standardized methods in China is feasible and urgently needed in view of the rapid socioeconomic development and transition of disease patterns taking place in China. The results are of significance in combating CVD both at home and abroad. (Circulation. 2001;103:462-468.)

Key Words: cardiovascular diseases ■ risk factors ■ mortality ■ trials

In 1981, a World Health Organization (WHO) working group developed a major international collaborative study, the Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) project, with the objective of measuring trends and determinants of cardiovascular disease (CVD) in many different populations over a period of 10 years. Specifically, the project focuses on trends in event rates for validated fatal and nonfatal coronary heart attacks and strokes and on trends in cardiovascular risk factors in men and women 25 to 64 years of age in the same defined communities. The Beijing Institute of Heart, Lung, and Blood Vessel Diseases (BIHLBD) has been involved in this study since the beginning and was then designated by WHO as a collaborating center for the WHO MONICA project. After a 2-year pilot study, the Beijing study started officially on January 1, 1984, and was called the Sino-MONICA-Beijing project. In 1983, the BIHLBD proposed and organized a national collaborative study on the same subject using the same methodology and criteria as that of the WHO MONICA project, with slight modifications for local use. After a pilot study from 1985 to 1986, this national study was formally launched on January 1, 1987, in 16 provinces, municipalities, and autonomous regions, covering a total population of ~5 million, and the study was then called the Sino-MONICA project. This article reports the 7-year outcome of the Sino-MONICA study from 1987 to 1993, with emphasis on organizational aspects of the study and results of event monitoring. CVD risk factor levels were also measured in the same populations at the beginning (1987 to 1988) and end (1992 to 1993) of the 7-year period through population surveys. The results will be reported later.

Methods
The Sino-MONICA collaborating centers (monitoring areas) were established and began data collection between 1985 and 1986 (pilot phase). CVD events in the community were registered, and core data from each center were reported to the Data Center at BIHLBD according to a common protocol.

Study Population
The Sino-MONICA populations were defined as all residents of 17 selected monitoring areas delineated by clear geographic and admin-
istrative boundaries in 16 provinces, totaling ~5 million people. The Figure is a map showing the populations under study. The names of the monitoring area are represented by the names of the province that are abbreviated by putting together the first letters of the Romanized Chinese characters (eg, BJ is for Beijing). Table 1 shows the average midyear population size in each monitoring area for men and women 35 to 64 years of age. Roughly two thirds of the study population is urban, and one third is rural. The size of the population of each of the 17 monitoring areas by 5-year age strata was obtained from the national population registers or censuses; the population size was updated annually and used as the denominator for calculation of event rates.

Because MONICA specifically concerns the exposure-disease association, it was decided that no intentional public health action on risk factors would be instituted in each population during the study period, so that biases in the ecological estimates of association would be minimized.3

**Case-Finding Procedures**

All acute coronary and stroke events occurring from 1985 through 1993 in men and women of the study areas who were 35 to 64 years of age were registered with WHO MONICA methodology and criteria,4 but only the data of 1987 to 1993 were used for analysis, because the data quality of 1985 to 1986 (pilot study period) was inadequate in terms of completeness and correctness of case registration and diagnosis. Case finding of CVD events was based mainly on 3 sources: reports from grassroots health station personnel, hospital records, and death certificates. A combination of “hot pursuit” (screening of hospital admission) and “cold pursuit” (identifying and extracting records after discharge) was used for hospitalized cases.5 For nonhospitalized cases, all possible efforts were made to collect from relevant informants the medical and social information used for diagnostic categorization. The case ascertainment and validation procedures have been described in detail previously.2 Briefly, a special system of CVD event monitoring and data collection (the so-called 3-level monitoring system) was developed. Each collaborating center of the study area served as a coordinating and data center for the study (first level). Regional hospitals formed the intermediate monitoring teams (second level). The basic unit of the system (third level) was at the residence health station (in urban areas) and village health station (in rural areas). When a CVD event occurred, members of the basic monitoring unit were informed first, and they reported the event to the intermediate monitoring team. A team physician was then sent to visit the patient at home or in the hospital. An interview was held with the patient or other suitable informants, and medical information was collected, with emphasis on symptoms and laboratory data (representative sets of ECGs and cardiac enzyme values). The diagnosis was validated according to MONICA diagnostic criteria, and a standard event form was completed by the physician; the form was sent to the coordinating center, where the case was reviewed again by a supervision group. After any possible errors in case registration were corrected, the final diagnostic classification of every event was ascertained. As a complementary way to find medically unattended fatal events, all death certificates of the deceased persons who resided in the study

**TABLE 1. Sino-MONICA Population: Average Midyear Population Size, 35 to 64 Years of Age**

<table>
<thead>
<tr>
<th>Province</th>
<th>Population Abbreviation</th>
<th>Years</th>
<th>Mean Population Size, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beijing</td>
<td>BJ</td>
<td>1987–1993</td>
<td>142,073</td>
</tr>
<tr>
<td>Hebei</td>
<td>HB</td>
<td>1987–1993</td>
<td>35,549</td>
</tr>
<tr>
<td>Nenenggu</td>
<td>NM</td>
<td>1987–1991</td>
<td>49,147</td>
</tr>
<tr>
<td>Liaoning</td>
<td>LN1</td>
<td>1987–1993</td>
<td>118,446</td>
</tr>
<tr>
<td>Liaoning</td>
<td>LN2</td>
<td>1987–1993</td>
<td>25,092</td>
</tr>
<tr>
<td>Heilongjiang</td>
<td>HLJ</td>
<td>1987–1993</td>
<td>91,649</td>
</tr>
<tr>
<td>Shanghai</td>
<td>SH</td>
<td>1987–1993</td>
<td>37,371</td>
</tr>
<tr>
<td>Jiangsu</td>
<td>JS</td>
<td>1987–1993</td>
<td>66,332</td>
</tr>
<tr>
<td>Anhui</td>
<td>AH</td>
<td>1987–1993</td>
<td>22,885</td>
</tr>
<tr>
<td>Fujian</td>
<td>FJ</td>
<td>1987–1989</td>
<td>17,215</td>
</tr>
<tr>
<td>Shandong</td>
<td>SD</td>
<td>1987–1989</td>
<td>32,119</td>
</tr>
<tr>
<td>Guangdong</td>
<td>GD</td>
<td>1987–1989</td>
<td>21,801</td>
</tr>
<tr>
<td>Sichuan</td>
<td>SC</td>
<td>1987–1993</td>
<td>45,895</td>
</tr>
<tr>
<td>Xinjiang</td>
<td>XJ</td>
<td>1987–1993</td>
<td>10,397</td>
</tr>
</tbody>
</table>

Map of populations under study in Sino-MONICA project. See Table 1 for definitions of populations.
areas were scrutinized to identify unrecognized fatal cases. For CVD or sudden deaths in patients between 25 and 64 years of age, further information was collected from the certifying agency or medical-legal authority. It was found that in ~15% to 20% of the fatal cases (mostly out-of-hospital unattended events or sudden deaths), diagnostic information was incomplete despite the efforts made for data collection, and pathological validations were not possible because of the very low autopsy rate (<1%) in China. However, MONICA diagnostic criteria were designed to cope with this problem by assigning these events to low-accuracy categories (coded as “possible” or “insufficient data”).

Quality Assurance of Data Collection
Quality control and standardization of event registration and validation, as well as of data collection and transfer, were maintained by several approaches. First, centrally organized seminars were conducted to train field workers in the use of the manual of operation, including ECG Minnesota coding, to ensure uniformity in data collection. Second, monthly working meetings for the monitoring teams at each area were held during the entire study period to supervise adherence to protocol and standardized coding. Third, principal investigators and other key personnel of the collaborating centers met once a year to discuss technical and administrative issues of the study, and intensive workshops were conducted for them during that meeting. Fourth, special site visits were made by BIHLBD staff to collaborating centers reporting technical difficulties or having problems with compliance. Fifth, to ensure uniformity in the coding of CVD events between the collaborating centers, centrally organized quality control tests were held at regular intervals (usually once every 2 years); for these tests, series of test case histories and ECGs (selected from WHO MONICA project test materials) were distributed to all participating centers. The results of the test were evaluated, graded, fed back to each center, and reported at the principal investigators’ meetings. Sixth, all the data (written in standard format) collected in each center were stored in a diskette and submitted to the data center in BIHLBD, where they were checked again for completeness, logical consistency, and possible duplicate registrations of the same event. After all the errors were corrected, the data were centrally analyzed at BIHLBD. Finally, a letter written in laymen’s terms describing the facts about major CVD events and the importance of the study was sent to every household in the monitoring area to encourage the prompt and correct reporting of events.

Diagnostic Categories
Coronary events were registered and assessed according to the protocol into 1 of the following diagnostic categories.4 Nonfatal events were classified as “definite” (NF1), “possible” (NF2), “ischemic cardiac arrest” (NF3), or “no myocardial infarction” (NF4). Fatal events were classified as “definite” (F1), “possible” (F2), “insufficient data” (F9), or “no myocardial infarction or coronary death” (F4). In this article, coronary event incidence refers to all coronary events, both first and recurrent, and is defined as NF1+NF2+F9+F4 per 100 000 people per year. Mortality rate is the number of fatal events (within 28 days) per year per 100 000 people.

Statistical Analysis
CVD incidence refers to all CVD, both first and recurrent events. It is the number of all events, both fatal and nonfatal, within a year per 100 000 people. Mortality rate is the number of fatal events (within 28 days) per year per 100 000 people.

Age-standardized incidence and mortality rates were calculated by the direct method with 5-year age-group rates in the range of 35 to 64 years. The weights 6, 6, 6, 5, 4, and 4 were derived from the age distribution of Segi’s World Population and used for the age groups 35 to 39, 40 to 44, 45 to 49, 50 to 54, 55 to 59, and 60 to 64 years, respectively.

Trends in CVD events were calculated from age-standardized annual event rates by the regression model $\log r_t = a + bt$, where $r_t$ denotes the event rate at time point $t$. The trend $b$ was estimated from the logarithms ($\log r_t$) of the annual age-standardized event rates with ordinary regression, and the CI of the trend was obtained in the usual manner from the SE of the regression coefficient, $b$. The instantaneous change rate per year at time point $t$ is a constant proportion, 100b percent of the event rate at time $t$, which is given in the tables. The estimated yearly change is $\exp(b)$, which is approximately $b$ for small changes.

Results
The average annual incidence and mortality rates for all coronary and stroke events are shown in Tables 2 and 3. The data for 3 years (1987 through 1989) were available in all 17 centers and are used for cross-sectional comparison. The data for 7 years (1987 through 1993) were available in only 12 of the 17 centers and are used for trend analyses.

The results have shown that according to international standards, both the incidence and mortality rate of coronary events in Chinese populations were low. The highest incidence among men and women was found in Shandong (108.7 per 100 000 for men and 34.0 per 100 000 for women) and the lowest in Anhui (3.3 per 100 000 for men and 0 for women). The incidence varied 33-fold among men. In addition, both the incidence and mortality rate of stroke events were high compared with world averages. The highest incidence among men and women was found in Heilongjiang (553.3 of 100 000 for men and 337.7 per 100 000 for women) and the lowest in Anhui among men (33.0 per 100 000) and in Fujian among women (29.7 per 100 000). The incidence varied 17-fold among men and 11-fold among women in the populations studied. In both men and women, CVD occurrence was higher in the northern than in the southern populations. Overall, significant geographic variations in CVD rates existed, with higher rates in the north and lower rates in the south. Finally, trend analyses have revealed that trends of incidence of coronary events were positive among men in 3 and among women in 4 of the 12 populations, whereas trends were negative among men in 9 and among women in 8 of the 12 populations in this study. All the trends, except 1 downward trend in Jiangsu, were not statistically significant at the 5% level, indicating that these trends were likely caused by random variations and other biases. Trends of stroke incidence were positive among men in 8 and among women in 8 of the 12 populations, whereas trends were negative among men in 3 and among women in 4 of the 12 populations. The increasing trend was statistically significant at the 5% level for men in Jilin, Heilongjiang, and Jiangsu and for women in Heilongjiang and Jiangsu, indicating that these populations were likely to be among those with real changes. None of the declining trends were statistically significant.
Discussion

An active and complete surveillance of CVD has been successfully performed for 7 years in a large population of >5 million in China by the methodology and criteria of the WHO MONICA project. The study, the first of its kind ever undertaken in China, produced a large quantity of internationally comparable data on CVD rates and their trends and determinants. Because the WHO MONICA project is a multinational study and China is the only Asian country involved, the Sino-MONICA study is especially significant and unique in reflecting the features of CVD patterns in this part of the world. The results of CVD monitoring by the Sino-MONICA study have also demonstrated that it is feasible to record CVD events with the use of the WHO MONICA protocol in a large Chinese community, which was thought to be impracticable for developing countries without adequate diagnostic facilities or population denominators. The success of the Sino-MONICA study has been well recognized.
However, organizing and coordinating such a large-scale, long-term study in a developing country such as China has proved to be a very challenging task. Indeed, we encountered a number of difficulties and logistical problems, particularly in CVD event validation and registration. First, there was a comparatively high rate of nonhospitalized CVD events, most of which were less severe or silent cases presenting minimum symptoms or signs. These events were not easily detectable by routine disease registry. Previous studies have shown that in China, ≈30% to 40% of stroke patients and 10% to 20% of heart attack patients were not admitted to hospital for various reasons. In addition, quite a number of patients with CVD events (especially in rural areas) were treated by local traditional doctors without proper diagnosis. In both cases, the patients might have been missed for registration as CVD events.

Second, the official death certificates were considered to be of low quality, which resulted in diagnostic inaccuracy in fatal CVD events. It has been reported that the current state of
medical knowledge, improper or varying coding practices, and insufficient clinical or laboratory data are the main causes of inaccuracies in death certification. In China, death certificates have been used traditionally both as legal documents and as public health records, but little attention has been paid to the quality of the death diagnosis. More seriously, because of the shortage of medical or medical-legal professionals, a certain proportion of death certificates (particularly those of sudden unattended deaths) are issued by administrative workers who have no knowledge of medicine, on the basis of reports by relatives of the deceased persons. Moreover, the very low autopsy rate, which is considered to be a cultural constraint in China, leads to inaccuracy and uncertainty in death diagnosis. Thus, the death certificates, which would have provided very important diagnostic information in most developed countries, are of limited value for case finding and validation in China.

Third, the medical information and personal identification systems in China are still underdeveloped, and a large-scale computerized data linkage system does not exist, even in big cities. Therefore, searching for CVD events by these sophisticated data retrieval and identification systems, as is done in most developed countries, was not possible in the Chinese setting.

Clearly, all these difficulties were related to an inappropriate medical care system, an underdeveloped medical information system, and the cultural background existing in many developing nations. Tunstall-Pedoe pointed out that the completeness of event identification and completeness and availability of the information obtainable for event recording and diagnosis depend on existing standards of medical care. To overcome the difficulties posed by the medical, cultural, and ethical constraints in China mentioned above, we developed a community-based, 3-level CVD monitoring system based on the existing primary healthcare organization. This monitoring system is an active surveillance that uses multiple and available sources, overlapping event finding methods, and detailed event validation. By using this system and several complementary quality control measures, we were able to get health workers at different levels of the healthcare system actively involved in the study, so that fairly high coverage and good quality of validation of CVD events were achieved. It has been reported that when community health personnel are asked to report cases, the identification rate increases by 10% to 30%. This is particularly true in regions with socialized medical care (as practiced in many developing countries) or when a high degree of interest and cooperation is maintained throughout the study. Therefore, the sustained high degree of cooperation and keen interest of the MONICA workers at all levels, together with a positively motivated and well-informed population, were very important in the coordination of such a long-term and large-scale study. In the Sino-MONICA study, we found that regular person-to-person contact through various activities such as monthly working meetings, principal investigators’ meetings, and site visits was very useful in promoting enthusiasm and cooperation. This kind of motivation would be rather difficult to achieve through modern technology such as teleconferences or computer networks. The essence of our monitoring system, therefore, was to mobilize all locally available resources by all possible means, so that the deficiencies in disease monitoring caused by medical and ethical constraints could be compensated for to the maximum extent.

The results of event monitoring in Sino-MONICA have shown that both the age-standardized incidence and mortality rate of stroke are high compared with world averages, but the same rates for coronary events are lower than world averages. This epidemiological pattern of CVD in China is very similar to that observed in Japan, Korea, and other oriental countries and regions. One significant feature of the occurrence of coronary and stroke events in China has been the very large difference between populations among both men and women, with higher rates in northern provinces and lower rates in southern provinces. This geographic difference in CVD mortality and incidence reported to exist between populations is considered to be real, which reflects the underlying differentials in risk factor profiles between north and south. A discussion of the causality of the north-south difference will be given later.

Trends of CVD rates are of significant interest in terms of epidemiology. Information on the trends of CVD in China has usually been based on routine mortality statistics, which are subject to a number of biases. No CVD incidence data were available in the past. The Sino-MONICA study provided, for the first time, very useful information on long-term mortality and incidence trends of CVD in China. Results have shown that increasing trends of CVD incidence and mortality were observed in a number of monitoring areas, whereas decreasing trends existed in others. Most of the trends did not reach statistical significance.

It has been thought that our data are not sufficient to warrant any firm conclusions about the trends of CVD events (especially coronary events) for the following reasons. First, the validity and comparability of data collected might not be good enough for trend analysis because of the methodological difficulties mentioned earlier. Second, the year-to-year fluctuations in event rates are obvious, especially in those areas with a small study population and low event rates (notably for coronary events), which leads to unstable estimates, as evidenced by the relatively broad CIs for the calculated yearly changes. The WHO MONICA project estimated that for centers wishing to monitor trends precisely, a target of 200 events per year was the minimum, but in the Sino-MONICA study, the number of coronary events per year in most monitoring areas was far below 200. Third, the time span of monitoring was only 7 years, which does not seem long enough to categorize the populations into those with increasing or decreasing trends. All these limitations underline the need for improvement of our monitoring system and the use of a larger population size and a longer period of registration time in the future. Therefor, the results of trend analysis in our study must be interpreted with caution.

The significance and implications of the Sino-MONICA study are 2-fold. First, China is a country of extraordinary contrasts with respect to geography and social and physical environment. On the other hand, it is a country of similarity in terms of culture and demography. One of the significant features of our study is that the populations are well defined.
and internally relatively homogeneous, both ethnically and socioeconomically. However, CVD rates in different populations vary by more than 12-fold. It has been recognized that the number of data points from internally homogeneous populations exhibiting contrasting trends in event rates is more important than the precision of the estimate of individual trends. Therefore, we believe that our data can provide a higher level of sensitivity for detecting some important associations between CVD and risk factors that are unlikely to be reproduced in other similar international studies based on heterogeneous populations. Second, China is now experiencing a rapid socioeconomic change in terms of economic reforms, particularly the increases in gross national product, average income, and personal expenditures. As a result, disease patterns have been undergoing a significant change, and China is now at a stage of epidemiological transition in which diseases of industrialization, such as CVD, are becoming more prevalent than diseases of underdevelopment, such as infectious diseases. However, in contrast to the wealth of socioeconomic statistics, there is a paucity of information on the impact of socioeconomic development on health. Accurate data on trends and determinants of CVD are therefore urgently needed in view of the epidemiological transition. In this regard, the Sino-MONICA study, which occurred at this critical time, provides an unprecedented opportunity to monitor the progress of CVD and suggest possible associated factors and causes so that the chance to prevent or halt the spread of CVD will not be missed.

In conclusion, despite its weaknesses and limitations, the Sino-MONICA study, in size, scope, and efficiency, establishes the feasibility of long-term monitoring of CVD events in Chinese communities. The study has also provided very useful data on CVD that are fairly generalizable to other parts of China. Because of its similarity to the WHO MONICA project, it can also be considered an important supplement to the WHO MONICA project, which has only 1 collaborating center in Asia. Organizing and coordinating a study like this in a developing country such as China is a major undertaking, and difficulties and logistical problems should not be underestimated. Furthermore, the imperfection of an observational study like ours does not justify firm conclusions on causality, even in China, and inferences and the use of our experience regarding the situation in other countries must be made with caution. Nevertheless, we are confident that our results have clear relevance to and could stimulate similar initiatives in other developing nations in which CVD is rapidly developing, as cautioned by WHO.

Acknowledgments

The Sino-MONICA study was funded predominantly by a China national research grant. Part of the work was supported by the World Health Organization.

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Circulation. 2001;103:462-468
doi: 10.1161/01.CIR.103.3.462

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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