Explaining the Increase in Coronary Heart Disease Mortality in Beijing Between 1984 and 1999

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Background—Coronary heart disease (CHD) mortality is rising in many developing countries. We examined how much of the increase in CHD mortality in Beijing, China, between 1984 and 1999 could be attributed to changes in major cardiovascular risk factors and assessed the impact of medical and surgical treatments.

Methods and Results—A validated, cell-based mortality model synthesized data on (1) patient numbers, (2) uptake of specific medical and surgical treatments, (3) treatment effectiveness, and (4) population trends in major cardiovascular risk factors (smoking, total cholesterol, blood pressure, obesity, and diabetes). Main data sources were the WHO MONICA and Sino-MONICA studies, the Chinese Multi-provincial Cohort Study, routine hospital statistics, and published meta-analyses. Age-adjusted CHD mortality rates increased by ∼50% in men and 27% in women (1608 more deaths in 1999 than expected by application of 1984 rates). Most of this increase (∼77%, or 1397 additional deaths) was attributable to substantial rises in total cholesterol levels (more than 1 mmol/L), plus increases in diabetes and obesity. Blood pressure decreased slightly, whereas smoking prevalence increased in men but decreased substantially in women. In 1999, medical and surgical treatments in patients together prevented or postponed ∼642 deaths, mainly from initial treatments for acute myocardial infarction (∼41%), hypertension (24%), angina (15%), secondary prevention (11%), and heart failure (10%). Multiway sensitivity analyses did not greatly influence the results.

Conclusions—Much of the dramatic CHD mortality increases in Beijing can be explained by rises in total cholesterol, reflecting an increasingly “Western” diet. Without cardiological treatments, increases would have been even greater. (Circulation. 2004;110:1236-1244.)

Key Words: coronary disease □ mortality □ risk factors □ prevention

Mortality rates from coronary heart disease (CHD) have been halved in many developed countries since the 1980s but are still rising in most developing countries, including China. CHD is projected to be the leading global cause of death and disability by 2020.

China, like many developing countries, has experienced rapid socioeconomic and health changes. Between 1985 and 1999, gross domestic product per capita rose by ∼8% per year, the second fastest increase globally. Life expectancy has increased owing to declines in infectious diseases and malnutrition; however, cardiovascular diseases and cancers are increasing. In 1998, cardiovascular diseases claimed ∼2.6 million lives, 40% of total deaths in China. Because of population aging, the burden of CHD will increase. Furthermore, rising trends in acute coronary events and mortality rates were reported in Beijing between 1984 and 1997, with a 1.7% average annual increase for those aged 35 to 74 years, even higher in older people.

These CHD trends are consistent with the risk factor paradigm. Evidence supports a causal association with the major cardiovascular risk factors: cholesterol, blood pressure, smoking, and physical inactivity. The relative importance of these different risk factors is unclear in China, with some studies suggesting that smoking is only a weak risk factor and given that cholesterol levels were relatively low until recently. Furthermore, many effective cardiovascular treatments have been introduced in Beijing since the 1980s, including thrombolysis, secondary prevention, and CABG surgery. It is uncertain what impact these therapies have had on trends in population mortality. Few attempts have been made to explore or explain increases in CHD mortality, reflecting the lack of adequate CHD data in most low- and middle-income countries. Beijing has successfully collaborated in the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease), SINO-MONICA, and Chinese Multi-provincial Cohort (CMCS) studies from 1984 onward, which makes it possible to exploit these extensive high-quality data sources.

A variety of CHD policy models have been developed to explain observed trends and predict future events. Model-
The IMPACT Model: Medical and Surgical Treatments

The model aimed to include all medical and surgical treatments in 1984 and 1999 (detailed in Table 3).26,27,37 The mortality reduction for each treatment, stratified by age and gender, was calculated as the relative mortality reduction reported in published meta-analyses multiplied by the age-specific case fatality observed in that group (Appendix). Case-fatality data came from the Beijing MONICA study27 and from large, unselected, population-based patient cohorts.46 Survival benefit over a 1-year time interval was used for all treatments.

Treatment Adherence and Overlaps

Potential overlaps between different groups of patients were identified, and appropriate adjustments were made, as described previously.26,27,37 For example, approximately half the patients undergoing CABG surgery had a previous myocardial infarction. Deaths prevented by hypertension treatments were subtracted from those attributed to secular trends in population blood pressure. Adherence, the proportion of treated patients actually taking therapeutically effective levels of medication long term, was assumed to be 100% in hospital patients and 50% in community patients.49

Deaths Prevented or Postponed in 1984

A number of effective therapies were in limited use in 1984, including cardiopulmonary resuscitation in hospital, β-blockers for acute myocardial infarction, and therapy for moderate and severe hypertension (diastolic blood pressure >105 mm Hg). Precise patient data for some interventions were available from MONICA and others from unpublished reports.50

Sensitivity Analyses

Because of the uncertainties surrounding some of the values, multway sensitivity analyses using the analysis of extremes methodology were performed (examples in Appendix).

Model Validation: Comparison With Observed Decreases in Mortality

The model estimate for the changes in deaths attributed to all treatments plus all risk factor changes was summed and then compared with the observed increases in mortality for men and women in each specific age group.

Results

In Beijing between 1984 and 1999, CHD mortality rates increased by 50% in men and by 27% in women aged 35 to 74 years (Table 1; 1608 more CHD deaths than expected from baseline mortality rates in 1984). The increase in mortality rates showed a smooth negative age gradient in
men, decreasing from 111% among those aged 35 to 44 years to 16% in those aged 65 to 74 years, but no such gradient in women, with increases of 0%, 40%, 20%, and 20% in the respective age groups (Table 1).

### Risk Factor Changes Between 1984 and 1999

Changes in major cardiovascular risk factors together produced a best estimate of 1822 more deaths (minimum 969, maximum 2577; Figure 1; Table 2). The biggest contribution came from the very large increase in cholesterol (from a mean of 4.30 to 5.33 mmol/L), which led to an estimated 1397 additional deaths (minimum 798, maximum 2150). This was reduced to 1181 using the alternative method with age-attenuated coefficients. Smaller mortality contributions came from increases in smoking prevalence (from 49% to 57% in men) and in the number of cigarettes smoked (increased by 2 to 4 cigarettes per day among male smokers), which together generated 128 additional deaths in men (minimum 100, maximum 163). However, smoking prevalence decreased in women from 16% to 9%, which prevented ≈111 deaths (minimum 16, maximum 182; Figure 2). Diabetes prevalence increased from 3% to 9%, which led to 347 additional deaths (minimum 152, maximum 560), and body mass index increased from 23.9 to 24.9 kg/m², which resulted in ≈67 additional deaths (minimum 47, maximum 87; Table 2). Decreases in population blood pressure resulted in ≈160 (minimum 112, maximum 200) fewer deaths. This decreased to ≈5 after adjustment for hypertension treatment (Table 2).

### Medical and Surgical Treatments

Medical and surgical treatments in individuals together prevented or postponed ≈642 deaths in 1999 (minimum 456, maximum 1106), a large increase from the estimate of 72 for 1984 (Table 3). Substantial contributions came from treatments for acute myocardial infarction (41% of all deaths prevented by treatments) and hypertension (24%), with smaller contributions from treatments for angina and heart failure and from secondary prevention (15%, 10%, and 11%, respectively; Figure 3). Despite the very large numbers of eligible patients in the community, aspirin and secondary

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**TABLE 1. Population Sizes and Death Rates due to CHD in Beijing, 1984 and 1999**

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>Population, ×10³</th>
<th>Deaths, n</th>
<th>Death rates per 100 000</th>
<th>% Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, 35–44</td>
<td>1984 522</td>
<td>32</td>
<td>6.31</td>
<td>254</td>
</tr>
<tr>
<td>Men, 45–54</td>
<td>1984 581</td>
<td>182</td>
<td>36.8</td>
<td>176</td>
</tr>
<tr>
<td>Men, 55–64</td>
<td>1984 322</td>
<td>368</td>
<td>114</td>
<td>23</td>
</tr>
<tr>
<td>Men, 65–74</td>
<td>1984 179</td>
<td>673</td>
<td>376</td>
<td>12</td>
</tr>
<tr>
<td>Women, 35–44</td>
<td>1984 551</td>
<td>7</td>
<td>1.16</td>
<td>140</td>
</tr>
<tr>
<td>Women, 45–54</td>
<td>1984 537</td>
<td>88</td>
<td>16</td>
<td>40</td>
</tr>
<tr>
<td>Women, 55–64</td>
<td>1984 305</td>
<td>203</td>
<td>47</td>
<td>20</td>
</tr>
<tr>
<td>Women, 65–74</td>
<td>1984 191</td>
<td>431</td>
<td>226</td>
<td>20</td>
</tr>
</tbody>
</table>

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**Figure 1. CHD mortality trends in Beijing 1984 to 1999: additional deaths attributable to risk factor changes and deaths prevented or postponed by treatments. BMI indicates body mass index; AMI, acute myocardial infarction.**
prevention therapies prevented few deaths, which reflects the low prescribing levels. Revascularization interventions from coronary bypass surgery and angioplasty accounted for only 2% of the total mortality decrease (Table 3).

Model Validation
Table 4 shows the agreement between observed and expected deaths, stratified by age and gender. Model fit was highest among men and younger age groups and lowest among elderly women. Overall, the model was able to explain ~79% of the observed mortality trends, or 64% with age-attenuated cholesterol coefficients (Table 4).

Sensitivity Analyses
Irrespective of whether the best, maximum, or minimum estimates were used, most of the mortality increase was explained by large rises in total cholesterol levels (Figure 2; Table 2). Likewise, the biggest mortality reductions from treatments consistently came from therapies for acute myocardial infarction and hypertension (Figure 3; Table 3).

Discussion
CHD mortality in China has increased dramatically since the 1980s, particularly in urban populations.5,7 In Beijing, most of this rise can be attributed to substantial increases in total cholesterol levels, regardless of the method and coefficients used. Without improvements in treatments, the death rates would have been even higher.

Few studies have explained trends in CHD in the Far East.1,15,16 One Japanese study reported decreasing CHD mortality between 1980 and 1989, despite increases in total cholesterol levels.15 However, unlike in Beijing, blood pressure and smoking declined, and consumption of cardioprotective fish oils remained high. A recent comparison of CHD mortality rates in Beijing, Hong Kong, and Singapore found most risk factor levels were very similar, but Singapore had by far the highest CHD mortality and markedly higher cholesterol levels and dietary fat intake, particularly saturated fats.16

Cholesterol, Diabetes, Obesity, and Diet
Total cholesterol levels in Beijing have increased dramatically since the early 1980s, apparently accounting for most of
the increased CHD mortality. These trends are consistent with the observed changes from traditional to Western diet, such as a 5-fold increase in consumption of red meat, eggs, and oils between 1978 and 1992 and declines in fruit and vegetable intake. Unlike results from some studies, mortality increases occurred relatively quickly after the cholesterol increases. Studies from Eastern Europe also suggested a rapid response to changes in lifestyle and diet. Induction periods may be shorter when other causal factors are common. In Beijing, blood pressure and male smoking levels

<table>
<thead>
<tr>
<th>Treatments</th>
<th>No. of Patients Eligible</th>
<th>Treatment Uptake, %</th>
<th>Best Estimate</th>
<th>Minimum Estimate</th>
<th>Maximum Estimate</th>
<th>Proportion of Overall Deaths Prevented or Postponed, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myocardial infarction</td>
<td>6027</td>
<td></td>
<td>261</td>
<td>164</td>
<td>370</td>
<td>41</td>
</tr>
<tr>
<td>Hospital resuscitation</td>
<td>9</td>
<td>81</td>
<td>52</td>
<td>117</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombolysis and aspirin</td>
<td>22</td>
<td>38</td>
<td>18</td>
<td>41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin alone</td>
<td>66</td>
<td>86</td>
<td>55</td>
<td>123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombolysis alone</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>67</td>
<td>21</td>
<td>15</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>58</td>
<td>30</td>
<td>22</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary prevention after infarction</td>
<td>12,473</td>
<td></td>
<td>61</td>
<td>48</td>
<td>72</td>
<td>9</td>
</tr>
<tr>
<td>Aspirin</td>
<td>50</td>
<td>11</td>
<td>8</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>11</td>
<td>7</td>
<td>5</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin and β-blockers</td>
<td>21</td>
<td>10</td>
<td>8</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>24</td>
<td>13</td>
<td>10</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>23</td>
<td>9</td>
<td>7</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>12</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>32</td>
<td>6</td>
<td>5</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary prevention postrevascularization</td>
<td>1153</td>
<td></td>
<td>8</td>
<td>7</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3. Deaths Prevented or Postponed by Medical and Surgical Treatments in Beijing in 1999

![Figure 2. Proportional contributions of specific risk factor changes to trends in CHD deaths in Beijing 1984 to 1999 (sensitivity analysis).](http://circ.ahajournals.org/)
were already high before cholesterol levels increased. Autopsy studies in China had previously demonstrated significant levels of atheroma in young adults\textsuperscript{57}; the “coronary gun” was already loaded.

Increases were observed in obesity (body mass index) and diabetes, resulting in \approx 350 additional CHD deaths in 1999. This was consistent with dietary changes and possible decreases in physical activity.\textsuperscript{58} Furthermore, the 16 million diabetics in China are projected to more than double by 2025, to 38 million.\textsuperscript{59}

**Smoking**

It may seem surprising that smoking did not explain a higher proportion of the mortality increase, but our model focuses on change over a specific time period (1984 to 1999). In fact, increases in smoking by men were canceled out by decreases in women. Smoking has risen among Beijing men, reaching almost 70% in those aged 35 to 44 years. The proportion who consumed more than 20 cigarettes per day almost doubled, rising from 20% to 38%. The overall impact of smoking would be further compounded by the massive population exposure to passive smoking.

**Cardiological Treatments**

Modern cardiological treatments prevented or postponed \approx 642 additional deaths in 1999. Irrespective of whether best, minimum, or maximum estimates were used, the greatest contributions came from treatments for acute myocardial infarction and hypertension, with smaller contributions from treatments for angina and heart failure and from secondary prevention (Table 3). Prescribing levels in the community appeared to be very low for most interventions. Revascularization interventions played a minor role (Table 3), together accounting for only 2% of the total mortality fall, compared with 4% in Britain and 6% in the United States.\textsuperscript{28,60}

**Limitations of the Data and the IMPACT Model**

Modeling studies have a number of potential strengths, providing integration and simultaneous consideration of large amounts of data. However, all CHD models are dependent on the quality and extent of data available.\textsuperscript{47} China successfully supported the only MONICA center in a developing country. Additional high-quality epidemiological data for Beijing and beyond came from the subsequent Sino-MONICA project.\textsuperscript{61} Treatment data were also available from a variety of sources. However, assumptions had to be made about uptake and compliance across Beijing. Mant and Hicks corrections for polypharmacy were not considered necessary.\textsuperscript{35} Most risk factor coefficients came from very large international cohorts and meta-analyses and generally appeared comparable with the available Chinese data.\textsuperscript{41,43}

A robust sensitivity analysis was clearly essential.\textsuperscript{51} However, the relative contribution of each risk factor and treatment to the overall CHD mortality decline was little changed whether one considered the best, minimum, or maximum estimates (Figures 2 and 3). Overall, the model explained \approx 79% of the observed mortality trends (64% with age-attenuated cholesterol coefficients). This appears acceptable given imperfect death certification and risk factor measurement. Furthermore, most of the dramatic rise in mortality rates was attributable to increases in incidence, whereas case fatality actually improved slightly.\textsuperscript{1} Incidence, symptomatic

### Table 4. Model Validation: Estimated vs Observed Changes in CHD Deaths in Beijing Between 1984 and 1999

<table>
<thead>
<tr>
<th></th>
<th>Total Men and Women</th>
<th>Men, Age Groups, y</th>
<th>Women, Age Groups, y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>35–44</td>
<td>45–54</td>
<td>55–64</td>
</tr>
<tr>
<td>Observed change 1984–1999</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discrepancy</td>
<td>-355</td>
<td>-104</td>
<td>-34</td>
</tr>
<tr>
<td>Model fit, %</td>
<td>79</td>
<td>21</td>
<td>84</td>
</tr>
</tbody>
</table>
relief, life-years gained, and cost-effectiveness merit attention in future work.20,37 The generalization of efficacy estimates from randomized controlled trials to effectiveness in clinical practice appears reasonable.62 Finally, although the β-coefficients were all independent, having been adjusted for major confounders, some residual confounding may have remained.36

We cannot generalize these results to the rest of China. However, Beijing and the other large cities are leading dramatic socioeconomic trends with profound effects on health. Similar trends are likely in other middle-income countries.2 Primary prevention, particularly for diet and smoking, could potentially reverse these alarming trends.

Appendix

Examples of Mortality Reduction Estimation and Sensitivity Analyses

Example 1: Men Aged 55 to 64 Years Given Aspirin for Acute Myocardial Infarction
In the Antithrombotic Trialists’ Collaboration (ATT) meta-analysis, aspirin reduced relative mortality in men with acute myocardial infarction by 15% (see appendix 2 on World Wide Web site http://www.liv.ac.uk/PublicHealth/sc/bua/IMPACT_Model-Appendices.doc). In Beijing in 1999, 1149 men aged 55 to 64 years were eligible, and 65% were given aspirin.32 One-year case fatality in unselected men aged 55 to 64 years was therefore calculated as the number of deaths prevented or postponed. The minimum was 919 × 0.52 × 0.13 × 0.20 = 12 deaths prevented or postponed. The maximum was 1379 × 0.78 × 0.17 × 0.40 = 73 deaths prevented or postponed.

Example 3: Mortality Increase due to Rise in Total Cholesterol in Women Aged 55 to 64 Years
In Beijing, total cholesterol in women aged 55 to 64 years increased from 4.71 to 5.9 mmol/L between 1984 and 1999, an absolute increase of 1.19 mmol/L. Pooling of international cohort studies has demonstrated that the relationship between most continuously distributed risk factors and CHD is logarithmic (the relative change in CHD mortality is proportional to the absolute change in the risk factor) and produced a β-coefficient value of 0.65.37 (for every 1 mmol/L increase in total cholesterol, population CHD mortality would be expected to increase by ~65%).

The increase in deaths between 1984 and 1999 was then calculated as CHD deaths in that age and gender group in 1984 base year × risk factor change × β-coefficient. Thus, 203 × 1.191 × 0.65 = 157 additional deaths. This calculation was then repeated (1) for men and women in each age group and (2) for each risk factor, (3) using maximum and minimum values in each group, to generate a sensitivity analysis.

Example 4: Sensitivity Analysis: Mortality Increase due to Rise in Total Cholesterol in Women Aged 55 to 64 Years
Some uncertainty surrounds the estimates, particularly the precise levels of total cholesterol in 1984 and 1999, and the β-coefficients used. The 95% confidence levels for each risk factor in 1984 and 1999 were used as the maximum and minimum estimates; these were 4.71 (95% CI 3.77 to 5.65) in 1984 and 5.9 (95% CI 4.72 to 7.08) in 1999. The coefficients were assumed to vary by as much as 30%. The best estimate was 203 × 1.191 × 0.65 = 157 additional deaths. The minimum was 203 × 0.95 × 0.46 = 88 additional deaths. The maximum was 203 × 1.43 × 0.85 = 245 additional deaths.

Example 5: Population Attributable Risk Methodology for Diabetes in Men Aged 55 to 64 Years
The number of CHD deaths attributable to the increase in diabetes between 1984 and 1999 was calculated with the population attributable risk fraction. This required estimates of P, diabetes prevalence in both years, and RR, the relative risk of diabetes for CHD mortality, and the number of deaths from CHD in each year.

In Beijing, the diabetes prevalence in men aged 55 to 64 years was 4% in 1984 and 10% in 1999. Thus, 4% of CHD

<table>
<thead>
<tr>
<th>Diabetes Prevention</th>
<th>CHD Deaths</th>
<th>PAR Fraction</th>
<th>Mortality Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged 55 to 64 y</td>
<td>1984</td>
<td>1999 RR</td>
<td>1984</td>
</tr>
<tr>
<td></td>
<td>a</td>
<td>b</td>
<td>c</td>
</tr>
<tr>
<td>Best estimate</td>
<td>0.042</td>
<td>0.102</td>
<td>2</td>
</tr>
<tr>
<td>Minimum estimate</td>
<td>0.036</td>
<td>0.082</td>
<td>1.5</td>
</tr>
<tr>
<td>Maximum estimate</td>
<td>0.05</td>
<td>0.122</td>
<td>2.2</td>
</tr>
</tbody>
</table>

*""=[a×(c−1)]/[a×(c−1)+1]
†g=[b×(c−1)]/[b×(c−1)+1]
deaths were attributable to diabetes in 1984 and 10% in 1999 (Table 5). The difference between these 2 proportions was multiplied by the number of CHD deaths in 1999 to estimate the number of deaths theoretically attributable to the change in diabetes prevalence in the population between 1984 and 1999 (Table 5). This calculation was then repeated (1) for men and women in each age group, (2) for smoking prevalence (changes in proportions smoking 1 to 9, 10 to 19, and ≥20 cigarettes per day between 1984 and 1999), and (3) using maximum and minimum values in each group, to generate a sensitivity analysis.

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References


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