A Chinese Immigrant Paradox? Low Coronary Heart Disease Incidence but Higher Short-Term Mortality in Western-Dwelling Chinese Immigrants: A Systematic Review and Meta-Analysis

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Background—Chinese form a large proportion of the immigrant population in Western countries. There is evidence that Chinese immigrants experience an increased risk of coronary heart disease (CHD) after immigration in part due to cultural habits and acculturation. This is the first systematic review and meta-analysis that aims to examine the risk of CHD in people of Chinese ethnicity living in Western countries, in comparison with whites and another major immigrant group, South Asians.

Methods and Results—Literature on the incidence, mortality, and prognosis of CHD among Chinese living in Western countries was searched systematically in any language using 6 electronic databases up to December 2014. Based on the meta-analysis, Chinese had lower incidence of CHD compared with whites (odds ratio 0.29; 95% CI: 0.24–0.34) and South Asians (odds ratio 0.37; 95% CI: 0.24–0.57) but higher short-term mortality after first hospitalization for acute myocardial infarction compared with whites (odds ratio 1.34; 95% CI, 1.04–1.73) and South Asians (odds ratio 1.82; 95% 1.33–2.50). There was no significant difference between Chinese immigrants and whites in long-term outcomes (mortality and recurrent events) after acute myocardial infarction.

Conclusions—These findings provide an important focus for resource planning to enhance early secondary prevention of CHD to improve short-term survival outcomes among Western-dwelling Chinese immigrants. (J Am Heart Assoc. 2015;4:e002568 doi: 10.1161/JAHA.115.002568)

Key Words: Chinese • coronary heart disease • mortality • outcome

Coronary heart disease (CHD) is a leading cause of mortality and morbidity worldwide. In particular, CHD is a major health problem in migrant populations in developed countries.1 Research has shown that immigrants tend to have a higher risk for CHD than the host population and the overall prevalence, mortality, prognosis and risk factors of CHD vary among subgroups of immigrants.2,3 Chinese are one of the fastest growing migrant populations in Western countries such as Australia, Canada, and the United States.4–6 The number of Chinese immigrants increased by 54% in Australia between 2006 and 2011 and by 43% in the United States between 2000 and 2010, respectively.7,8 Chinese immigrants have both higher prevalence and higher mortality rates from CHD compared with mainland Chinese.9 Chinese immigrants also appear to have a higher prevalence of cardiac risk factors such as hypertension and diabetes after migrating to Western countries when compared with Chinese living in China, and the risk increases with longer length of residence.9–11 Although there is limited literature comparing the absolute rates for mortality after acute myocardial infarction (AMI) between Chinese people living in China and Chinese immigrants in Western countries, a Canadian study described higher short-term mortality in Chinese immigrants (12.2%)12 compared to a study of Chinese in mainland China (7%).13 Moreover, there is some evidence that Chinese immigrants have a higher risk of mortality after AMI despite their much lower incidence rates of AMI compared to whites and South Asians.12

With an increasing number of Chinese immigrants in Western countries, their health has become a key issue to their host nations. While it is important to quantify the risks associated with CHD to inform population health strategies,
the risk for CHD among Chinese immigrants in comparison with other population subgroups has not been systematically reviewed. Furthermore, it remains unclear whether the discordance between the incidence and prognosis of CHD exists in Chinese immigrants, as the current evidence shows conflicting results.\textsuperscript{12,14}

This is the first study to systematically review and meta-analyze the incidence and prognosis of CHD among Chinese immigrants living in Western countries. To quantify differential risk and to contextualize findings, we compared Chinese immigrants with whites and South Asians in the same host country. Whites were selected because they are the most common racial group in Western countries. South Asian immigrants were selected because they are another fast-growing population in Western countries and they feature prominently in primary research studies included in this review, having higher cardiac mortality rates than other ethnic groups.\textsuperscript{15} Comparing incidence and prognosis of CHD with the host population and another major migrant group will help prioritize the related public health agenda and resource allocation at different stages of CHD prevention, allowing for the most effective and efficient programs and interventions to improve CHD outcomes at the population level.\textsuperscript{16}

Methods

This systematic review and meta-analysis is guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols and the Meta-Analyses of Observational studies in Epidemiology criteria.\textsuperscript{17,18}

**Definition and Eligibility Criteria**

Study subjects were Chinese and whites or South Asians (defined based on self-reported ancestry) living in Western countries including North America (United States, Canada), Europe, Australia, and New Zealand. Chinese and South Asian ethnicity were also identified by using surname analysis, which is proven to have high sensitivity and specificity.\textsuperscript{19,20} Chinese immigrants refers to Chinese born in, or having ancestry from, mainland China, Hong Kong, Taiwan, or Macao. South Asians refers to people from the Indian subcontinent (India, Pakistan, Bangladesh, and Sri Lanka) or those who self-identify as South Asians.\textsuperscript{16} Whites were defined as people of European ancestry\textsuperscript{2} and in some studies are described as Caucasians.\textsuperscript{12} For the purpose of this review, CHD is defined as myocardial infarction (MI), acute coronary syndrome, ischemic heart disease, or percutaneous coronary intervention or coronary artery bypass grafting surgery identified using International Classification of Diseases codes to define CHD. Case reports, editorials, expert opinions, and review articles were also excluded. In the case of multiple studies published based on the same data set, we selected the study with the most in-depth analysis.

**Inclusion and Exclusion Criteria**

We included studies where the incidence or prognosis of CHD was reported for Chinese immigrants and also for a comparison population (whites or South Asians). We only included studies based on registries or administrative data because these are not subject to selection or reporting bias.\textsuperscript{22} Exclusion criteria included studies on children, Chinese immigrants living in non-Western countries, studies that did not separate Chinese from other Asian groups and studies that reported Chinese only without comparison with whites and/or South Asians. We also excluded the studies that reported composite outcomes including heart failure or cerebrovascular disease, studies that only reported CHD mortality from the general population, and studies that did not use International Classification of Diseases codes to define CHD. Case reports, editorials, expert opinions, and review articles were also excluded. In the case of multiple studies based on the same data set, we selected the study with the most in-depth analysis.

**Search Strategies**

A comprehensive search of primary studies was independently conducted by 2 reviewers (K.J. and D.D.) based on search strategies developed by the research team. Databases included PubMed, PsychInfo, CINAHL, Scopus, Web of Science, and Cochrane library. In addition, we searched the reference lists of included studies or relevant reviews as well as the gray literature. We did not limit the search by study design, date, or language. The specific search terms and strategies are described in Appendices S1 and S2.

**Selection of Articles and Quality Appraisal**

All studies were imported to Endnote for screening. K.J. and D.D. independently screened papers based on the title, abstract, and full-text. The final results were reviewed by all authors. The Newcastle-Ottawa Scale was selected to guide a quality appraisal of these observational cohort studies.\textsuperscript{23} Any discrepancies or disagreements were resolved first by discussion between K.J. and D.D. and then by consultation with the team.

**Data Collection**

All data were extracted by K.J. and verified by D.D. When results were not available in published papers, corresponding authors of primary studies were contacted to clarify the reported data. Study characteristics were summarized including country, follow-up period, the comparison group, age range, sex, outcome measures, and the sample size. We
defined short-term prognosis outcomes as in-hospital mortality or mortality within 30 days and long-term outcomes as mortality or recurrent AMI beyond 30 days.

Data Synthesis and Statistical Analyses
An odds ratio (OR) with 95% CI was used to measure effect size to compare the incidence and short-term outcomes of CHD. Hazard ratios with 95% confidence were used to assess the long-term outcome after diagnosis of CHD. Statistical heterogeneity across the studies was tested using the $I^2$ statistic between studies. $I^2$ values can be categorized as 0% to 40% (might not be important); 30% to 60% (may represent moderate heterogeneity); 50% to 90% (may represent substantial heterogeneity); and 75% to 100% (considered heterogeneous). When statistical heterogeneity exceeded 70%, subgroup analysis was performed to explain the heterogeneity. If heterogeneity was deemed to be substantial, we also performed a narrative summary. Analyses were conducted using Comprehensive Meta-Analysis software, Version 2.0 (Biostat, Englewood, NJ; http://www.meta-analysis.com).

Results
Study Identification
The literature search identified 1424 potentially relevant records. After excluding 686 duplicates, the remaining 738 records were screened based on reading the title and abstract, which led to a further exclusion of 671 papers (Figure 1). The remaining 67 papers were subject to a more detailed review based on reading the full text, and of those, 31 papers remained. Ten additional papers were identified through manual review of references. Of these 41 papers, 33 papers were excluded after detailed evaluation of these articles, leaving a final 8 papers in our review (Table 1). All studies were cohort studies using registry data that were dated from 1987 to 2010. Country of study included Canada, the Netherlands, Scotland, and the United States with follow-up periods ranging from 3 to 12 years (Table 3). Two studies reported results separately for men and women. Three studies reported total participants and death events (total 1076 Chinese with 147 death events, 318 782 whites with 59 681 events, and 2907 South Asians with 195 events). One study reported OR for Chinese compared to whites.

A meta-analysis was performed to compare the risk of death after diagnosis of CHD between Chinese and whites as well as Chinese and South Asians. The random-effects summary of OR for Chinese compared to whites was 1.34 (95% CI, 1.04–1.73; Figure 4) with low heterogeneity ($I^2$=18%). The OR for Chinese compared to South Asians was 1.82 (95% CI, 1.33–2.50; Figure 5), also with low heterogeneity ($I^2$=23%).

Incidence of CHD in Chinese Compared With Whites or South Asians
Of the 8 studies, 3 reported the incidence of CHD in Chinese compared with whites and South Asians (Table 2). The number of Chinese participants in each study ranged from 6254 to 192 155, with duration of follow-up ranging from 7 to 10 years. All 3 studies reported results separately for men and women. For the meta-analysis, the results of Bansal et al were split into 2 based on the outcome of AMI incidence or mortality. Meta-analysis of all 3 populations in these studies (226 795 Chinese with 994 events; 11 136 183 whites with 350 625 events; 113 846 South Asians with 2536 events) showed that Chinese had a much lower incidence of CHD compared with whites (OR, 0.29; 95% CI, 0.21–0.40; $I^2$=90%) and South Asians (OR, 0.34; 95% CI, 0.16–0.73; $I^2$=97%). Subgroup analysis showed the OR of incidence for whites was 0.29 (95% CI, 0.24–0.34; $I^2$=74.5%) and South Asians 0.37 (95% CI 0.24–0.57; $I^2$=95%) (Figures 2 and 3). Although the heterogeneity between the analyzed studies was high, the direction and magnitude of the association based on the meta-analysis were consistent with the adjusted incidence rates reported in each primary study (Table 2).

CHD Outcomes for Chinese, Whites, and South Asians
Short-term mortality after first hospitalization for CHD
Four studies comparing Chinese with whites and South Asians reported short-term death after first hospitalization for AMI. These came from 4 countries including Canada, the Netherlands, Scotland, and the United States with follow-up periods ranging from 3 to 12 years (Table 3). Two studies reported results separately for men and women.

A total of 3 studies reported both long-term mortality and recurrent AMI after CHD in Chinese and whites with a follow-up time from 9 to 12 years with the exception of 1 study that reported second MI only (Tables 4 and 5). We were not able to compare Chinese with South Asians due to the lack of data. Meta-analysis showed risks of death and recurrent AMI in Chinese compared with whites were not statistically different (hazard ratio, 1.41; 95% CI 0.74–2.70; $I^2$=81%; hazard ratio, 1.05; 95% CI 0.74–1.48; $I^2$=54%, respectively) with moderate to substantial heterogeneity (Figures 6 and 7).
Discussion

This systematic review and meta-analysis evaluated the association between Chinese ethnicity and the incidence and prognosis of CHD in Western countries. While Chinese had much lower incidence of CHD, they had significantly higher short-term mortality after first diagnosis of CHD compared with whites and South Asians. This result is consistent with a previous international study, which found that AMI patients in China had a higher age-adjusted 28-day case fatality rate compared with those in Australia, Canada, and the United States. A similar finding was observed in an analysis of more than 15,000 AMI patients in Singapore; patients of Chinese ethnicity had the highest in-hospital mortality rates compared with South Asians and Malays. This presents a potential “paradox” where the risk of incident CHD and that of short-term mortality may be inconsistent.

Low incidence of CHD in Chinese immigrants may be explained by their favorable behavioral risk profiles, such as healthier diet, physical activity, and lower prevalence of obesity and smoking compared with whites and South Asians, as discovered by cross-sectional studies in Canada, the United Kingdom, and the United States. It is possible that poorer short-term survival in Chinese may not be explained alone by age or proximity to the hospitals and healthcare system. Although Chinese were older than South Africans have higher dietary intakes of vegetables and fruits, which may contribute to their lower risk of CHD.

Figure 1. Search, screening, and selection process of studies of incidence of CHD and outcome after CHD for Chinese living in Western countries. CHD indicates coronary heart disease; ICD, International Classification of Diseases.
Asians in this review, they had an age profile similar to whites. In addition, both Chinese and South Asians were more likely to live closer to hospitals compared with whites.12,29

Despite the limited data, due to the small number of available studies and particularly small samples of Chinese immigrants, several factors may explain the likely higher short-term mortality after CHD in Chinese. First, Chinese are less likely to have typical AMI symptoms (eg, midsternal pain and/or midsternal pressure),37 which could contribute to underdiagnosed heart disease leading to delay in definitive treatment and increased myocardial injury severity. Second, reporting of atypical symptoms is found to increase with age.37 Although both Chinese and South Asians are reported to have less typical AMI symptoms compared with whites,37 in this review, Chinese immigrants with AMI are much older than South Asians and this may exacerbate the diversity of presenting symptoms in this group.

Furthermore, Chinese patients have been found to have higher rates of cardiac catheterization within 1 day of AMI (22.8%, 15.3%, and 16.5% respectively) and percutaneous coronary intervention (27.6%, 18.1%, and 17.3%, respectively) compared with whites and South Asians.12 These results suggest Chinese patients may have more severe infarcts compared with other patients.38 This could be due to delayed medical attention and treatment, resulting in an unsuccessful response to thrombotic therapy or other treatments.12,38 The much lower incidence of CHD in Chinese compared with whites could also reflect poor data capture due to lower health literacy among Chinese immigrants; reduced awareness of heart disease may mean Chinese are less likely to recognize AMI symptoms compared to whites.37,39

Additionally, unsatisfactory control of risk factors subsequent to reduced medication adherence in Chinese immigrants may contribute to higher risk of mortality after CHD. One study from China found that history of hypertension was associated with 28-day mortality after AMI in men.40 Poor adherence to evidence-based antihypertensive medication among Chinese people was found to relate to their cultural preference for traditional medicine.41,42 Chinese immigrants were found to have the highest prevalence of alternative medicine use compared with other Asian ethnic groups.43 The common use of herbs such as garlic, ginseng, and ginkgo in Chinese culture37,44 can also lead to bleeding, a serious complication of percutaneous coronary diagnostic or interventional procedures.45 Furthermore, some studies suggest that Chinese patients may have different pharmacogenetic

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; CABG, coronary artery bypass grafting.

*No women death in the Chinese group.

Table 1. Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Period of Time</th>
<th>Study Population</th>
<th>Age Range (Years)</th>
<th>Sex</th>
<th>Identification of Ethnicities</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bansal et al (2013)14</td>
<td>Scotland</td>
<td>2001–2008</td>
<td>Chinese Whites South Asians</td>
<td>≥30</td>
<td>M/F</td>
<td>Self-reported</td>
<td>First occurrence of admission or death due to MI and time to event</td>
</tr>
</tbody>
</table>

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; CABG, coronary artery bypass grafting.

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responses to antiplatelet or anticoagulant therapy, which could potentially contribute to the higher risk of short-term mortality among Chinese participants. Research has shown that clopidogrel resistance, associated with significantly higher risk of major cardiovascular events such as bleeding, MI, and death, was 68% to 73% among Chinese immigrants compared with 5% to 44% among the mainstream Western population. Warfarin response variability also exists among Chinese patients, leading to a higher risk of bleeding events compared to whites.

Underutilization of healthcare services by Chinese immigrants has also been documented in the literature. Language barriers may cause delay in seeking early medical advice and treatment. One Canadian study showed Chinese immigrants are the least likely to speak fluent English compared with other ethnic groups, such as South Asians. Poor English is also associated with poor uptake of health check-ups, such as for lipid screening. Due to the collective nature of Chinese culture, older Chinese people are usually quieter and more stoic and less likely to voice symptoms or discuss treatment with doctors. Finally, physician bias could impact on diagnosis and management if the doctors are unaware of ethnic variations in AMI symptoms and CHD risk factors among Chinese patients.

Interestingly, in our study, outcome findings for South Asians were in contrast: having higher incidence but lower short-term mortality compared to Chinese and whites, which is consistent with previous research. The better survival rates found in the South Asian population may suggest doctors’ awareness of their increased coronary risk and better cardiac disease management for South Asians, including changes in health behaviors after AMI and better community support.

**Table 2. Studies on Incidence of CHD**

<table>
<thead>
<tr>
<th>Ethnic Group</th>
<th>Disease</th>
<th>Period of Time</th>
<th>Data Sources</th>
<th>Number of Cases/Total Participants</th>
</tr>
</thead>
</table>

**Strength and Limitations**

A major strength of this study is the robust and systematic nature of the evidence synthesis. Our meta-analysis of the prognosis after CHD may be particularly important in identifying Chinese immigrants as a unique “at risk” subgroup of patients. Another strength is the homogeneous nature of our study design: there is consistency among the included studies in administrative data sources covering broad populations, in settings (high-income countries dominated by European culture), in population selection, outcome measures, and in the similarity of universal health systems (with the exception of the United States), especially for the studies of prognosis. Our use of International Classification of Diseases codes to define CHD avoided the bias of using self-reported heart disease in survey studies.

The limitations of this review are related to the included primary studies. First, there are a small number of Chinese
participants compared with whites in most of the studies. However, this meta-analysis was based on the available data from national or state registry data sets, which are more generalizable. Second, the short-term mortality result between Chinese and whites is largely driven by Khan’s study12 which had a much larger sample of Chinese immigrants than other studies. While bias in the direction of overestimating the risk cannot be eliminated if all results are used, with the exception of Bansal14 (2013), the other ORs were in the direction of higher risk; however, only Khan’s study12 (2010) appears to have been adequately powered to detect the OR at a statistically significant level. Our results should stimulate further research with robust strategies. Third, the use of hospital data in the prognostic studies limits participants to those with a diagnosis of CHD, and may exclude those who may be misdiagnosed or die before coming to the hospital. Fourth, significant heterogeneity was noted in the analysis of incidence of CHD. However, the results of $I^2$ for heterogeneity need to be interpreted with caution when there are only limited studies included in the meta-analysis. In this analysis, only 3 studies were included and we had performed random-effects meta-analysis to incorporate heterogeneity among studies. Moreover, the demographics, follow-up duration, outcome measurement, and study quality were similar across the studies. Finally, the definition of ethnicity in this meta-analysis was not standardized and may involve misclassification. Bias could have been introduced by defining Western-born Chinese as whites when country of birth was used as a proxy for ethnicity. Surname analysis could also misclassify ethnic categories.12,16 In most cases, misclassification should involve defining Chinese immigrants as whites and therefore may underestimate the differences between them.

**Figure 2.** Incidence of coronary heart disease in Chinese compared with whites.

**Figure 3.** Incidence of coronary heart disease in Chinese compared with South Asians.
# Table 3. Studies on Short-Term Mortality After CHD in Chinese, White, and South Asians

<table>
<thead>
<tr>
<th>Study/Country</th>
<th>Disease Outcome</th>
<th>Follow-Up Period</th>
<th>Ethnic Group</th>
<th>Age (%)</th>
<th>Gender (%)</th>
<th>No. of Death/Total Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age</td>
<td>Chinese</td>
<td>Whites</td>
<td>South Asians</td>
</tr>
<tr>
<td>Khan et al (2010)</td>
<td>30-day mortality during the first hospitalization for AMI</td>
<td>1994–2003</td>
<td>Total</td>
<td>11 69</td>
<td>11 69</td>
<td>11 69</td>
</tr>
<tr>
<td>Van Oeffelen et al (2014)</td>
<td>28-day mortality after first AMI hospitalization</td>
<td>1998–2010</td>
<td>Total</td>
<td>Median age (IQR) 68 (57–75)</td>
<td>69 (58–78)</td>
<td>51 (46–57)</td>
</tr>
</tbody>
</table>

ACG indicates adjusted clinical group; ACS, acute coronary syndrome; AMI, acute myocardial infarction; CHD, coronary heart disease; IQR, interquartile range; SES, socioeconomic status.
Figure 4. Short-term mortality in Chinese compared with whites.

Figure 5. Short-term mortality in Chinese compared with South Asians.

Table 4. Studies on Long-Term Mortality After CHD

<table>
<thead>
<tr>
<th>Study</th>
<th>Country/Data Sources</th>
<th>Period of Time</th>
<th>Disease Outcome</th>
<th>Mortality After CHD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR (95%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chinese Versus Whites</td>
</tr>
<tr>
<td>Khan et al (2010)</td>
<td>Canada/Data from BC &amp; Alberta</td>
<td>1994–2003</td>
<td>Long-term mortality after first hospitalization for AMI, recurrent AMI</td>
<td>0.89 (0.77, 1.0)</td>
</tr>
<tr>
<td>Van Oeffelen et al (2014)</td>
<td>Netherlands/Nationalwide registers</td>
<td>1998–2010</td>
<td>5-year mortality and AMI readmission after first AMI</td>
<td>1.29 (0.77, 2.18)</td>
</tr>
</tbody>
</table>

AMI indicates acute myocardial infarction; CABG, coronary artery bypass grafting; CHD, coronary heart disease; HR, hazard ratios.

*Male only.

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Table 5. Studies on Recurrent AMI After CHD

<table>
<thead>
<tr>
<th>Study</th>
<th>Country/Data Sources</th>
<th>Period of Time</th>
<th>Disease Outcome</th>
<th>Recurrent AMI HR (95%)</th>
<th>No. of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dzayee et al (2014)²⁵</td>
<td>Sweden/National registers</td>
<td>1987–2007</td>
<td>MI occurring more than 28 days after first MI</td>
<td>1.03 (0.53, 1.9)</td>
<td>9 38 218</td>
</tr>
<tr>
<td>Khan et al (2010)¹²</td>
<td>Canada/Data from BC &amp; Alberta</td>
<td>1994–2003</td>
<td>Long-term mortality after first hospitalization for AMI, recurrent AMI</td>
<td>0.8 (0.65, 0.9)</td>
<td>— —</td>
</tr>
<tr>
<td>Van Oeffelen et al (2014)²⁹</td>
<td>Netherlands/Nationwide registers</td>
<td>1998–2010</td>
<td>5-year mortality and AMI readmission after first AMI</td>
<td>1.77 (0.66, 4.7)</td>
<td>&lt;10 6029</td>
</tr>
</tbody>
</table>

AMI indicates acute myocardial infarction; CHD, coronary heart disease; HR, hazard ratios.

Figure 6. Long-term mortality in Chinese compared with whites.

Figure 7. Recurrent acute myocardial infarction in Chinese compared with whites.
Conclusions

As compared with whites and South Asians, Western-dwelling Chinese immigrants showed a lower incidence of CHD, but a potentially poorer prognostic outcome after initial CHD diagnosis, hence a potential “Chinese immigrant paradox.” The poor short-term survival after CHD in Chinese immigrants may be explained by genetic differences, cultural habits, and acculturation. More rigorous research is required to monitor and compare short-term survival outcomes of population subgroups that may be at higher risk. Public health efforts should focus on early secondary prevention in this population to reduce mortality and reoccurrence from secondary events in the first 30 days. Ethnic variations in AMI presentation and disease management should be considered for healthcare providers caring for Chinese patients.

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Disclosures

None.

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