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Use of Intravenous Magnesium Sulfate among Patients with Acute Myocardial Infarction in China from 2001 to 2015: China PEACE-Retrospective AMI Study

Running head: Magnesium Sulfate for AMI in China

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ABSTRACT

Objective

To assess the trends and variation in use of IV magnesium sulfate among patient with acute myocardial infarction (AMI) in China.

Methods

In an observational study (China PEACE–Retrospective Study) of AMI care, we used a 2-stage, random sampling strategy to create a nationally representative sample of 28,208 patients with AMI at 162 Chinese hospitals in 2001, 2006, 2011, and 2015. The main outcome is use of IV magnesium sulfate over time.

Results

We identified 24,418 patients admitted for AMI, without hypokalemia, in the four study years. Over time, there was a significant initial decrease in IV magnesium sulfate use, from 32.1% in 2001 to 17.1% in 2015 ($p < .001$ for trend). The decline was greater in the Eastern (from 33.3% to 16.5%) and Western (from 34.8% to 17.2%) regions, as compared with the Central region (from 25.9% to 18.1%), with little difference between rural and urban areas. The proportion of hospitals using IV magnesium sulfate did not change over time (from 81.3% to 77.9%). The median odds ratios, representing hospital-level variation, were 6.03 in 2001, 3.86 in 2006, 4.26 in 2011, and 4.72 in 2015. IV magnesium sulfate use was associated with cardiac arrest at admission and receipt of reperfusion therapy, but no hospital-specific characteristics.

Conclusions

Despite recommendations against its use, IV magnesium sulfate is used in about 1 in 6 patients with AMI in China. Our findings highlight the need for more efficient mechanisms to stop using ineffective therapies to improve patients' outcomes and reduce medical waste.

Clinical Trial Registration

URL: https://www.clinicaltrials.gov. Unique identifier: NCT01624883

Keywords

acute myocardial infarction, Magnesium Sulfate, quality of health care

Strengths and limitations of this study

- This is the first large nationally representative registry demonstrating IV magnesium sulfate is still used in about 1 in 6 patients with AMI in China, despite recommendations against its use since 2000s.
- The study assessed the 15-year trend in the use of IV magnesium sulfate among patient with AMI in China.
- The study firstly reported both patients- and hospital-level resulted in the use of IV magnesium sulfate use, which could provide more targeted information for efficient mechanisms to stop using this ineffective therapy.
- The study adopted standardized procedures for abstraction of medical records that ensure the reliability of our results in describing the use pattern of magnesium sulfate in the real world.
- The very low prevalence of patients with some indications, such as magnesium sulfate deficiency would have little influence on the reliability of the results.

INTRODUCTION

The history of intravenous (IV) magnesium sulfate use for acute myocardial infarction (AMI) is convoluted. Once lauded in small, early trials as safe and highly effective,[1-3] it was later demonstrated to be ineffective, and even harmful, in two large clinical trials (MAGIC and ISIS-4) and in a subsequent meta-analysis.[4 5] Beginning in the early 2000s, AMI practice guidelines in the United States have specifically recommended against its routine use (Class III, level of evidence: C).[6 7] Similarly, China published guidelines in 2001 recommending against the use of IV magnesium sulfate in patients with AMI, except in the setting of hypomagnesemia or polymorphic ventricular tachycardia.[8]

Although several studies have evaluated the introduction and uptake of new therapies,[9-11] few have examine de-adoption of ineffective therapy in clinical practice.[12] The de-adoption of therapy is particularly important because the situation may involve greater resistance and barriers to discontinuing long-standing practices than simply introducing new and promising therapies into practice.[13] Characterizing the use of magnesium sulfate for AMI in clinical practice offers an opportunity to assess the speed with which providers stop using a therapy when new evidence has overturned prior dogma.

Accordingly, our objectives were to assess the trends and variation of regional and hospital-level use of IV magnesium sulfate among patient with AMI using data from the China PEACE Retrospective AMI Study between 2001 and 2015. These data, from a nationally representative network of hospitals throughout China, provided a unique opportunity to examine the trend for discontinuing routine IV magnesium sulfate over time and to describe the variations across hospitals in its discontinuation.

METHODS

Design Overview

The design and methods of the China PEACE-Retrospective AMI Study have been previously published.[14] In addition to a nationally representative sample of patients admitted for AMI in China during 2001, 2006, and 2011 created in the China PEACE-Retrospective AMI Study, we also included a more recent sample of patients admitted in 2015 using the same two-stage random sampling process. Briefly, in the first stage, we identified hospitals using a simple random sampling procedure within 5 economic-geographic regions: Eastern rural, Central rural, Western rural, Eastern urban, and Central/Western urban. We stratified on both location and urban-rural classifications because economic development and clinical capacities differed across these categories. We sampled representative hospitals from 2011 to reflect current practices and used the same hospitals for the 2006, 2001, and 2015 so as to describe temporal trends. In the second stage, we sampled AMI cases from hospital databases in 2001, 2006, 2011, and 2015 using random sampling procedures.

Trained personnel at the national coordinating centers abstracted data from the medical records using standardized data definitions. Data abstraction quality was rigorously monitored by randomly auditing 5% of the medical records, in a process that ensured that the overall variable accuracy exceeded 98%.[14] We also obtained information on the organizational learning culture of hospital in 2013 through questionnaires completed by the director and a physician of the Cardiology Department in each participating hospital (see Appendix B).[15]

The Ethics Committee at the National Center for Cardiovascular Diseases approved the study. All collaborating hospitals either accepted central ethics approval or obtained local ethics approval by their ethics committees. Given the retrospective nature of the data and the lack of personal identifiers, patient-level consent was not

required. The study was registered with ClinicalTrials.gov (NCT01624883).

Study Sample

Among the randomly sampled patients hospitalized for AMI in 2001, 2006, 2011, and 2015, only patients with a definite discharge diagnosis of AMI were included. We were unable to exclude patients with hypomagnesemia, because magnesium levels were not collected. However, we excluded patients with chart-documented hypokalemia during their hospitalization, which could also represent an indication for magnesium repletion. In hospital-level analysis, only hospitals with 10 or more cases in a study year were included.

Variables

Receipt of IV magnesium sulfate was ascertained from the medical record. Patient-level characteristics abstracted from the medical records included demographics (age, gender), medical history (hypertension, diabetes, dyslipidemia, current smoking, and history of myocardial infarction, coronary heart disease, ischemic stroke, coronary artery bypass grafting (CABG), or primary coronary intervention (PCI)), clinical presentation (chest discomfort, heart rate, systolic blood pressure on admission, and left bundle branch block on electrocardiogram), as well as in-hospital complications (cardiac arrest, cardiogenic shock, and acute stroke) and year of hospitalization (2001, 2006, 2011, 2015). The outcomes included: 1) in-hospital mortality or withdrawal from treatment due to a terminal status at discharge; and 2) in-hospital composite of major complications (including death, withdrawal from treatment, re-infarction, shock, ischemic stroke, or congestive heart failure (Appendix). Hospital characteristics included teaching status, PCI capability, economic geographic regions, and urban or rural location.

Organizational learning culture was measured with Learning Organization Survey

(LOS-27, an abbreviated version of the original Garvin et al. Learning Organization Survey).[16] The LOS-27 consists of 27 questions, grouped into 7 domains of organizational learning characteristics, including supportive learning environment, time for reflection, leadership that reinforces learning, experimentation, training, knowledge acquisition, and performance monitoring.

Statistical analysis

To examine the trends at both the population and hospital levels across different study periods, p-values for trends were reported using the Cochran–Armitage test. We described the hospital-level distribution of the IV magnesium sulfate use among the hospitals with at least 10 patients with AMI in the study years. To further understand the hospital-level variation in IV magnesium sulfate use, we quantified inter-hospital variation using the median odds ratio (MOR), by constructing generalized estimating equations in 2001, 2006, 2011, and 2015, respectively. MOR represents the average (median) OR for receiving IV magnesium sulfate for 2 AMI patients with similar clinical characteristics admitted to 2 randomly selected hospitals.

To understand the most current pattern in IV magnesium sulfate use, we constructed multivariable models using the data from 2015, which also adopted generalized estimating equations to account for the clustering of patients within hospitals. Factors were selected based on clinical judgment and literature review,[10,11] including patient and hospital characteristics. All covariates, except those with frequencies below 1%, were included in the multivariable model. We transformed continuous variables (e.g. age and heart rate) into categorical variables using clinically meaningful cut-off values, and then created dummy variables. From the multivariable model in 2015, we then computed risk-standardized rates for each hospital separately. The risk-standardized rate was calculated as the ratio of observed to predicted outcomes, multiplied by the overall unadjusted rate, a form of indirect standardization.

To compare the outcomes between patients with and without IV magnesium sulfate, we applied propensity score matching to adjust differences in observed characteristics between them. We obtained the log odds of the probability that patients received IV magnesium sulfate with modeling a function of all the variables in Table1. Then we performed a one-to-one no replacement match between the two groups based on the estimated propensity score. The no IV magnesium sulfate patients was matched if patient had the closest score with a randomly selected IV magnesium sulfate patient, and were considered eligible to match if the estimated logit within 0.6 standard deviation of the selected IV magnesium sulfate patient. This matching interval has been shown to eliminate approximately 90% of the bias in observed confounders (Appendix).[17]

For the questionnaire with LOS-27 (Appendix), we analyzed the responses at the hospital level by calculating the average of the 2 responses to each question. Responses were categorized as positive if they were ≥5 on a 7-point scale or ≥4 on a 5-point scale. We then calculated the positive response rate at each hospital as the proportion of questions that had a positive response by the hospital, and demonstrated the correlations between positive response rate and risk-standardize rate of IV magnesium sulfate use in 2015, as well as the reduction in IV magnesium sulfate use from 2011 to 2015.

All comparisons were two-sided, with statistical significance defined as p less than .05. Statistical analysis was done with SAS software, version 9.4, and R software, version 3.3.1.

Patient and Public Involvement statement

Patients or public were not involved in the development of the study protocol.

RESULTS

Study population

We identified 28,208 patients with AMI in 2001, 2006, 2011 and 2015 admitted to 162 hospitals. After excluding patients with hypokalemia (<3.5 mmol/L, n= 3,004), 24,418 patients remained, including 2,073 in 2001, 3,888 in 2006, 8,117 in 2011 and 10,340 in 2015 (**Figure 1**). In the study population, the average age was 65.1±12.7 years, 29.7% were female, almost three quarters had at least one cardiac risk factors (hypertension, diabetes, dyslipidemia or smoking), and about 10% had has a prior myocardial infarction or ischemic stroke (**Table 1**).

Temporal trends and regional variations in IV magnesium sulfate use

Over time, there was a significant initial decrease in the use of IV magnesium sulfate, from 32.1% (665) in 2001 to 18.4% (715) in 2006, 15.4% (1,251) in 2011 and 17.1% (1,763) in 2015 (p< .001 for trend) (**Figure 2**). There was significant variation in the temporal trends of use of IV magnesium sulfate across the five strata (p< .001 for interaction). In general, the decline was greater in the Eastern region [16.8% (from 33.3% in 2001 to 16.5% in 2015), p< .001] and Western region [16.6% (from 34.8% in 2001 to 17.2% in 2015), p< .001], compared with the Central regions [7.8% (from 25.9% in 2001 to 18.1% in 2015), p< .001]. There was a more modest difference between rural areas [16.3% (from 31.6% to 15.3%), p< .001] than in urban areas [13.9% (from 32.4% to 18.5%), p< .001]. No significant association was found between the positive response rate of LOS-27 in 2013 and the hospital-level reduction in IV magnesium sulfate use from 2011 to 2015 (R^2=0.011, p= .237) (Appendix C).

Hospital-level distributions in IV magnesium sulfate use

We examined hospital-level rates of IV magnesium sulfate use among hospitals with

10 or more cases per year, and observed a downward trend in the median, from 17.4% in 2001, 9.1% in 2006, 8.0% in 2011 to 10.7% in 2015 (**Figure 3**). However, the proportion of hospitals still using magnesium sulfate were 81.3% in 2001, 84.8% in 2006, 76.6% in 2011, and 77.9% in 2015, with no significant decline (p for trend = .26). Even in 2015, a quarter of hospitals had rates of IV magnesium sulfate use exceeding 25%. The MORs (95% CI) of each year characterized similar degrees of hospital-level variation (6.03 (3.93-8.52) in 2001, 3.86 (3.00-.4.77) in 2006, 4.26 (3.38-5.20) in 2011, and 4.72 (3.70-5.83) in 2015).

Patient and hospital characteristics associated with IV magnesium sulfate use

In univariate analysis, patients receiving IV magnesium sulfate were more likely to not have diabetes, dyslipidemia or a prior revascularization, were more likely to have had a prior ischemic stroke or cardiac arrest at presentation. They were more likely to receive reperfusion therapy, be at urban hospital, or be in Central or Western regions (**Table 1**). In the multivariable model, presence of cardiac arrest at admission (OR 3.41, 95% CI 2.2-5.26, P< .001) and receipt of reperfusion therapy (1.64 (1.38-1.94) for fibrinolytic therapy, 1.68 (1.44-1.97) for primary PCI, both P< .0001) were positively associated with IV magnesium sulfate use. No significant difference was identified across the teaching status, economic geographic region and rural/urban of hospitals **(Table 1)**. The risk-standardized rate of IV magnesium sulfate use in 2015 was not associated with the positive response rate of LOS-27 (R^2=0.027, p= .04) (Appendix C).

In-hospital outcomes of patients with and without IV magnesium sulfate use

In the patients treated with IV magnesium sulfate, the crude rates of in-hospital death (7.5% vs. 6.4%) (**Figure 4**), in-hospital death or treatment withdraw (10.8% vs. 9.5%), and in-hospital composite of major complications (22.0% vs. 17.6%) were higher than patients without IV magnesium sulfate therapy (P< .01 for all). After

adjusted for hospital characteristics, patient risk profiles and reperfusion therapies, using propensity score matching, the in-hospital death rates were not significantly different between the treated and non-treated patients (OR 1.13, 95% CI 0.96-1.33, P= .15). However, the patients treated with IV magnesium sulfate had still higher risk for in-hospital death or treatment withdraw (OR 1.19, 95% CI 1.04-1.37, P= .01), and in-hospital composite of major complications (OR 1.35, 95% CI 1.21-1.50, P< .001).

DISCUSSION

In this large nationally representative study, we found that despite an initial decline in the use of IV magnesium sulfate for patients with AMI in China after 2001, about 1 in 6 patients continued to be treated with it through 2015. Furthermore, there was substantial variation in the use of IV magnesium sulfate use across hospitals. No hospital characteristics were associated with IV magnesium sulfate use after adjusting for patient factors. including cardiac arrest and use of reperfusion therapy during hospitalization.

Our study is the first, to our knowledge, to characterize the rate of de-adoption of magnesium sulfate in patients with AMI in China. The only study on the use of magnesium sulfate to treat AMI, which was based on data from the National Registry of Myocardial Infarction (NRMI-2) in the United States, found that the use rate of magnesium sulfate in patients within first 24 hours after AMI was 5.1% in 2001 – 5 years after the US guideline recommended against the use of magnesium sulfate.[18] In contrast in 2015, three-fold more Chinese patients with AMI were receiving magnesium sulfate. This is congruent with a survey among cardiologists in 2012, where over one fifth reported that they were routinely using magnesium sulfate in patients with ACS.[19]

Several patient characteristics were identified to be associated with the use of IV

magnesium sulfate for AMI. It was plausible that the presence of cardiac arrest or reperfusion therapy may spur some physicians to use magnesium sulfate to prevent arrhythmias, according to prior studies in both China and other countries.[1 6 20-23] These explanations, even though not recommended by the guidelines, highlighted the gaps in physicians' practice and highlights the needs for targeted education in the future.

The hospital-level and regional variations in IV magnesium sulfate highlights the marked variability with which different hospitals adopted new evidence about the lack of benefit from IV magnesium sulfate use. On the one hand, magnesium sulfate use in 2015 was neither associated with hospital-specific characteristics, nor different across geographic or socio-economic regions. On the other hand, the regional variation in de-adoption of magnesium sulfate during the 15-year period seemed not directly related to the regional socio-economic development status that might be assumed to affect the resources available for acquiring and implementing guideline recommendation. Moreover, no evidence connects organizational learning culture with high performance, even much has been observed in studies of US hospitals.[24] Given our findings, more research is needed to better understand current practice patterns that cause some hospitals to still use ineffective therapies.

Our findings raise several questions about the dissemination and implementation of evidence and guidelines in China, particularly regarding education for physicians when long-standing therapies are demonstrated to be non-beneficial, and need to be de-adopted. We hypothesized that several factors may explain why the rate of magnesium sulfate use has remained relatively high in China. First, few actions have been taken to disseminate guidelines – after China published the guideline against IV magnesium sulfate for AMI in 2001,[8] the textbook used in all Chinese medical colleges had not stopped recommending IV magnesium sulfate use in patients with

AMI until 2009.[25] Second, China's hospital system is short for mechanisms to facilitate the implementation of guideline recommendations, and systematic approaches for monitoring the performance of hospitals and physicians in following the guidelines are lacking in China.[26]

The successful de-adoption of non-beneficial or potentially harmful therapies for corresponding disease, which could reduce costs and potentially prevent complications, requires more than increased efforts from the part of guideline developers.[12] After the dissemination of the guideline, more complicated issues need to be addressed, including how to develop tools reminding and alerting physicians when non-recommended therapies are ordered, how to establish a system to report feedback periodically on the appropriateness of treatment by practitioners and hospitals, how to design an accountability-oriented mechanism to prohibit ineffective regimen being prescribed, etc. These issues could only be properly addressed through collaborations with researchers, educators, policymakers and other stakeholders.[27 28]

This study has several limitations that warrant consideration. First, we could not exclude patients with some indications, such as magnesium sulfate deficiency and episodes of Torsade de pointes. However, we estimate that this number is relatively small given previous reports documenting a low prevalence of magnesium sulfate deficits in AMI patients.[29 30] Second, we did not have the ability to prospectively ask clinicians why they were prescribing IV magnesium sulfate, which limited our capability to gain better understanding of the use pattern and influencing factors. Third, our data were acquired retrospectively through medical record abstraction. Thus, the quality of our data depends on the accuracy and completeness of prior documentation and abstraction. Nevertheless, the standardized procedures for abstraction of medical records ensure the reliability of our results in describing the

use pattern of magnesium sulfate in the real world. Finally, we analyzed the data at the hospital level and were not able to determine whether the observed patterns were due to only a few physicians, or were common throughout a hospital's staff.

In conclusion, the de-adoption of magnesium sulfate for patients with AMI is suboptimal, moreover, the decrease of rate was slowing down recently, steady at an unacceptably high level. Our findings highlight the need for more efficient mechanisms to translate evidence-based therapies into clinical practice in China to improve patients' outcomes and reduce medical waste.

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CONTRIBUTORS

XL, JL and HMK conceived the China PEACE study and take responsibility for all aspects of it. XW, XD, JL, FAM, JAS, JL, HMK and XL designed the study. XW and XD wrote the first draft of the article, with further contributions from HY, EB, ND, JAS, FAM, JL, WG, HMK and XL. SH, YG and XB did statistical analysis. XL had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors interpreted data and approved the final version of the article.

DISCLOSURES

There are no relevant conflicts of interest.

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DATA SHARING STATEMENT

Extra data is available by emailing xi.li@fwoxford.org.

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Table 1. Baseline characteristics of using IV magnesium sulfate

Characteristics	Overall	Use N(%)	Non-Use(%)	P value
Patient characteristics				
Age				.234
<55	5262(21.5)	938(21.3)	4324(21.6)	
55-64	5821(23.8)	1072(24.4)	4749(23.7)	
65-74	6989(28.6)	1290(29.4)	5699(28.5)	
>=75	6346(26)	1094(24.9)	5252(26.2)	
Gender				.144
Female	7257(29.7)	1346(30.6)	5911(29.5)	
Male	17161(70.3)	3048(69.4)	14113(70.5)	
Hypertension	12551(51.4)	2247(51.1)	10304(51.5)	.7
Diabetes	4758(19.5)	768(17.5)	3990(19.9)	<.001
Dyslipidemia	1588(6.5)	235(5.3)	1353(6.8)	<.001
Currently smoking	8084(33.1)	1496(34)	6588(32.9)	.144
Prior ischemic stroke	2706(11.1)	546(12.4)	2160(10.8)	.002
Prior myocardial infarction	2504(10.3)	416(9.5)	2088(10.4)	.057
Prior CABG/PCI	713(2.9)	104(2.4)	609(3)	.016
Chest discomfort	22211(91)	4021(91.5)	18190(90.8)	.161
Left branch block at presentation	342(1.4)	65(1.5)	277(1.4)	.624
Cardiac arrest at presentation	271(1.1)	81(1.8)	190(0.9)	<.001
Cardiogenic shock at presentation	1436(5.9)	279(6.3)	1157(5.8)	.145
Acute stroke at presentation	530(2.2)	77(1.8)	453(2.3)	.036
Heart rate at presentation, bpm				.052
<50	1019(4.2)	177(4)	842(4.2)	
50-110	21760(89.1)	3886(88.4)	17874(89.3)	
>110	1639(6.7)	331(7.5)	1308(6.5)	
SBP at presentation, mmHg				.004
<120	8181(33.5)	1565(35.6)	6616(33)	
120-139	7534(30.9)	1299(29.6)	6235(31.1)	
140-159	5041(20.6)	913(20.8)	4128(20.6)	
>=160	3662(15)	617(14)	3045(15.2)	
Reperfusion therapies				<.001
No reperfusion	18720(76.7)	3130(71.2)	15590(77.9)	
Fibrinolytic therapy	3136(12.8)	746(17)	2390(11.9)	
Primary PCI	2562(10.5)	518(11.8)	2044(10.2)	
Hospital characteristics				
Teaching hospital	19081(78.1)	3462(78.8)	15619(78)	.252
Hospital level				.075

Secondary or lower	9045(37)	1576(35.9)	7469(37.3)	
Tertiary hospital	15373(63)	2818(64.1)	12555(62.7)	
Economic geographic region				.01
Eastern	13614(55.8)	2360(53.7)	11254(56.2)	
Central	5886(24.1)	1115(25.4)	4771(23.8)	
Western	4918(20.1)	919(20.9)	3999(20)	
Urban/Rural				.003
Rural	10064(41.2)	1724(39.2)	8340(41.7)	
Urban	14354(58.8)	2670(60.8)	11684(58.3)	

Figure 1. Flowchart of study cohort

Figure 2. Trends of intravenous magnesium sulfate therapy in 2001, 2006, 2011 and 2015 in five economic-geographic regions.

Figure 3. IV magnesium sulfate use in 2001, 2006, 2011 and 2015 among all hospitals.

Figure 4. In-hospital outcomes between patients with and without IV magnesium sulfate.

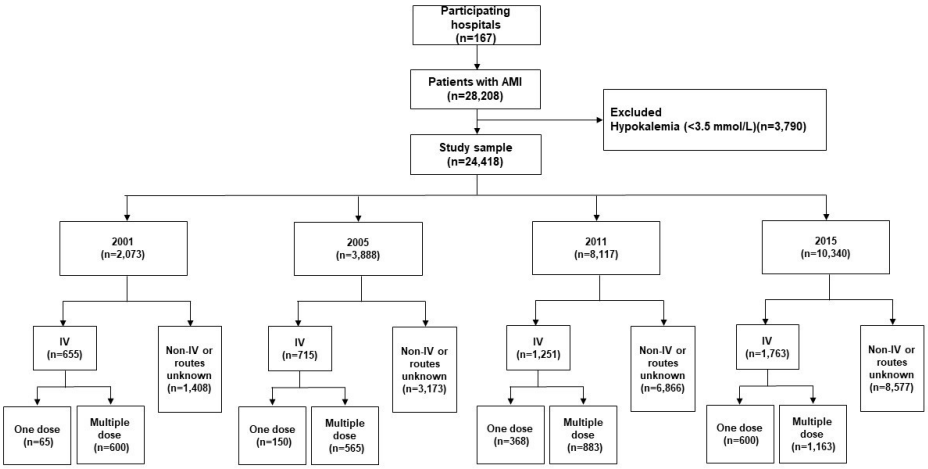


Figure 1

338x190mm (96 x 96 DPI)

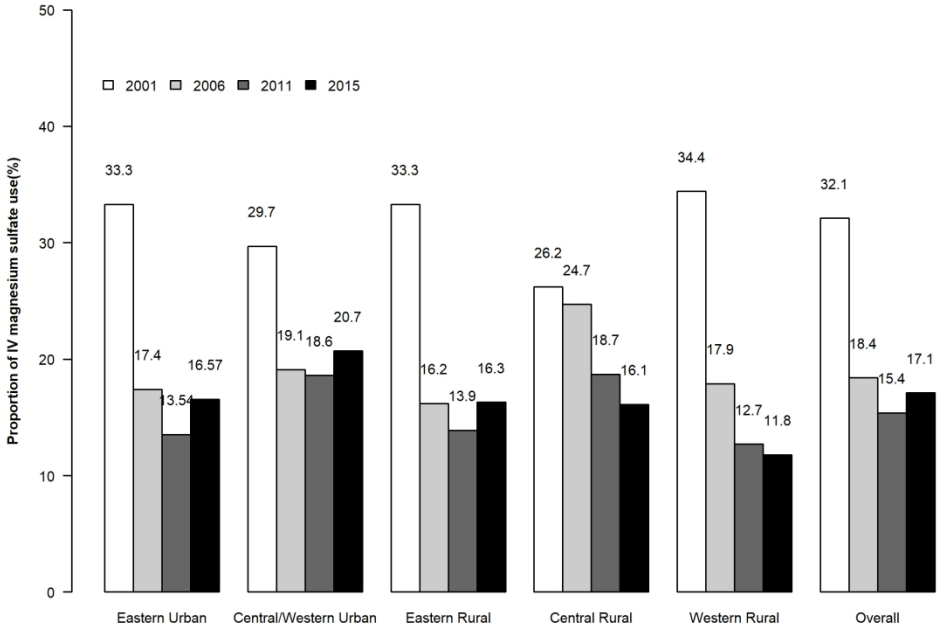


Figure 2

179x119mm (300 x 300 DPI)

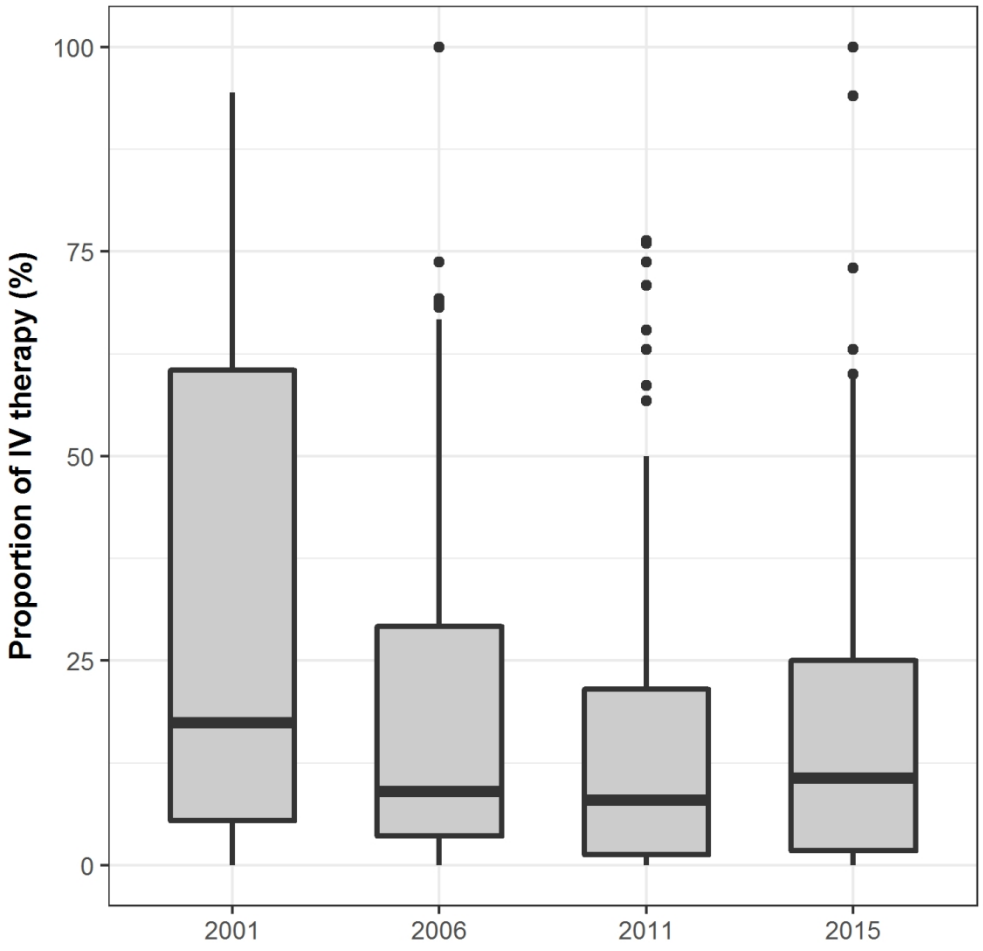


Figure 3

127x127mm (300 x 300 DPI)

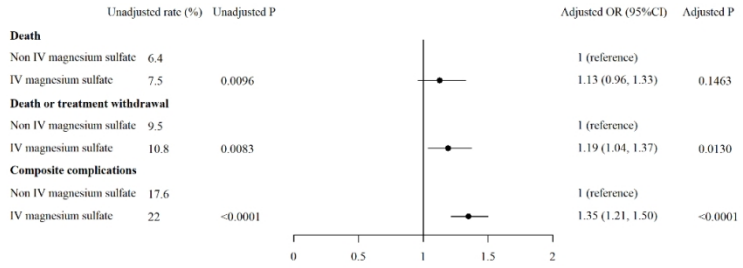


Figure 4

163x78mm (220 x 220 DPI)

APPENDIX

A. China PEACE-Retrospective AMI Study Site Investigators by Hospital

Aba Tibetan and Qiang Autonomous Prefecture People's Hospital, ShipingWeng, ShuyingXie; Affiliated Hospital of Guiyang Medical College, Lirong Wu, Jiulin Chen; Affiliated Hospital of Hainan Medical College, Tianfa Li, Jun Wang; Affiliated Zhongshan Hospital of Dalian University, Qin Yu, Xiaofei Li; Alxa League Central Hospital, Zhong Li, ShiguoHao, Yuzhen Zhang, Xuemei Wu; Baiquan County People's Hospital, Yachen Zhang, Zhifeng Liu; Biyang People's Hospital, Zhongxin Wang, HaoJia; Bortala Mongol Autonomous Prefecture People's Hospital, Bayin Bate, BadengQiqige; Changda Hospital Of Anshan, Xiang Jin, Ting Cai; Chengwu County People's Hospital, Fengqin Liu, Dayong Xu; Chenxi County People's Hospital, Xuejin He, Shui Yang; Chongren County People's Hospital, Chun Yuan, Jiping Wang; County People's Hospital of Jinning, LihuaGu, Lin Li, Shijiao Chen; Dalian Municipal Central Hospital, YongchaoZhi, Lili Sun; Dao County People's Hospital, Shengcheng Zhou, Lingjiao Jin; Daofu County People's Hospital, Yong Leng, Liangchuan Zhang, Tianyun Deng; Dingyuan County People's Hospital of Anhui Province, Yuanjin Wang, Wenhua Zhang, Xinmin Ma; Dongyang People's Hospital, Weimin Li, Liang Lu, Xuan Ge; Dulong and Nu Autonomous County People's Hospital of Gongshan, Xiaoping Wu, Yanming He; Dunhua City Hospital of Jilin Province, FanjuMeng, Jia Li; Fenghuang County People's Hospital, Dexi Liao, Guangyong Liu, Wen Qin; Fengshan County People’s Hospital, Wen Long, Xiangwen Chen; Fourth Hospital of Baotou City, Baohong Zhang, Yonghou Yin, Bin Tian; Fourth People's Hospital of Zigong City, Yong Yi, Chaoyong Wu; Fugu County People's Hospital of Shaanxi Province, Baoqi Liu, Zhihui Zhao, Haiming Li; Fujian Provincial Hospital, YansongGuo, Xinjing Chen; Fuling Center Hospital of Chongqing City, Liquan Xiang, Lin Ning; Gannan County People's Hospital, Mei Chen, Xin Jin, Guiling Li; General Hospital of the Yangtze River Shipping, Xiuqi Li, Xing’an Wu; Gongcheng Yao Autonomous County People's Hospital, Congjun Tan, Mingfang Feng, Meili Wang; Guangchang County People's Hospital, Liangfa Wen, Xiang Fu, QunxingXie; Guilin People's Hospital, Wei Zhang, Yanni Zhuang, Hua Lu;Guiping People's Hospital, Jiaqian Lu, Yu Huang; Haerbin 242 Hospital, Yin Zhou, Qiuling Hu; Haiyan People's Hospital, Chunhui Xiao, Xiaoli Hu; Heling Ge Er County People's Hospital, Yongshuan Wu, Qiuli Wang; Helong Municipal People's Hospital, Youlin Xu, Xuefei Yu;

Henan Provincial People's Hospital, Chuanyu Gao, Jianhong Zhang, You Zhang; Heze Municipal Hospital, WentangNiu, Xiaolei Ma, Yong Wang; HGKY Group Company General Hospital, Xiaowen Pan, Yanlong Liu; Hua Xin HospitalFirst Hospital of Tsinghua University, Lifu Miao, Yanping Yin, Zhiying Zhang; Huairen People's Hospital, Shutang Feng; Huayin People's Hospital, Aiping Wang, Jiangli Zhang, Feipeng Li; Huaying People's Hospital , Hong Wang; Hunchun Hospital, Lijun Yu, Xinxin Zhao; Huizhou Municipal Central Hospital, Yuansheng Shen, Zhiming Li, Lizhen He; Hunan Province Mawangdui Hospital, ZhiyiRong, Wei Luo; Ji'an Municipal Central People's hospital, Xueqiao Wang; Jianghua Yao Autonomous County People's Hospital, Rongjun Wan, Jianglin Tang, Guanghan Wu; Jiangsu Haimen People's Hospital, Jie Wu, Bin Xu; Jiangxi Provincial People's Hospital, Qing Huang, Xiaohe Wu; Jiangzi County People's Hospital, Sang Ge, Pian Pu, PingcuoDuoji; Jilin Province People's Hospital, Hui Dai, Yuming Du, Wei Guo; Jilin Integrated Traditional Chinese & Western Medicine Hospital, Jilin Province, Jianping Shi; Jinghai County Hospital, Peihua Zhao, Jingsheng Sun; Jingxi County People's Hospital, Hongxiang Li, Wen Liang; Jingxing County Hospital, Zhiwen Dong, Zhenhai Zhao; Jingzhou Central Hospital, Xin Li, Qin Xu; Jiuquan City People’s Hospital, Yaofeng Yuan, Zhirong Li; Jixi People's Hospital of The Jixi Municipal People's Hospital Medical Group, Jinbo Gao; Jize County Hospital, Qiu’eGuo; Kangbao County People's Hospital, Ruiqing Zhao, Guangjun Song; Keshiketengqi Hospital of Chifeng City, Lize Wang, Haiyun Song; Lanping Bai and Pumi Autonomous County People's Hospital, Jinwen He, Jinming He; Laoting County Hospital, Keyong Shang, Changjiang Liu, Kuituan Xi; Liaoyang Central Hospital, Rihui Liu, Peng Guo; Liaoyuan Central Hospital, ChaoyangGuo, Xiangjun Liu, Rujun Zhao, Zeyong Yu; Lindian County Hospital, Wenzhou Li, Xudong Jing, Huanling Wang; Linxiang People's Hospital, Xiyuan Zhao, Chao Zhang, Long Chen; Liujiang County People's Hospital, Meifa Wei, Yan Liu, Shengde Chen; Longyan First Hospital, Kaihong Chen, Yong Fang, Ying Liao; Luancheng County Hospital, Junli Wang, Tianyu Liu, Suzhe Cheng; Lucheng People's Hospital, Yunke Zhou, XiaoxiaNiu, Huifang Cao; Luchuan County People's Hospital, Zebin Feng, Min Feng; Luxi County People's Hospital, FeilongDuan, Haiming Yi; Luyi County People's Hospital, Yuanxun Xu, AnranGuo; Macheng People's Hospital, Xianshun Zhou, HongzhuanCai, Peng Zheng; Mengcheng First People's Hospital, GaofengGuo; MenglianLahudaiwa autonomous counties People's Hospital, Xiang Li; Min County

People's Hospital, MinwuBao, Yuhong Liu; Nanjing First Hospital, Shaoliang Chen, HaiboJia, Hongjuan Peng; Nan'an Hospital, Duanping Dai, Shaoxiong Hong; Nantong Third People's Hospital, Song Chen, Dongya Zhang, Ying Wang; Nanyang Central Hospital, Yudong Li, Jianbu Gao, Shouzhong Yang; Ningwu County People's Hospital, Junhu An; Peking University People's Hospital, Chenyang Shen, Yunfeng Liu; Peking University Shenzhen Hospital, Chun Wu, Huan Qu, Saiyong Chen; People's Hospital of Jingyu, Yuhui Lin, Dehai Jiao; People's Hospital of Yueqing City, Manhong Wang, Qiu Wang; Pianguan County People's Hospital, YingliangXue, Ruijun Zhang; Puding County People's Hospital, Cheng Yuan, Lei Wu; Qinghai Red Cross Hospital, Jianqing Zhang, Chunmei Wei, Yanmei Shen; Qinshui County People's Hospital, Hehua Zhang, Hongmei Pan, Yong Gao; Qinyang People's Hospital, Xiaowen Ma, Yanli Liang, Tianbiao Wang; Queshan County People's Hospital, Daguo Zhao; Quzhou People's Hospital, XiaomingTu, Zhenyan Gao; Rongjiang County People's Hospital, Fangning Wang, Qiang Yang; Rudong County People's Hospital, Xiaoping Kang, Jianbin Fang, Dongmei Liu; Ruyang County People's Hospital, Chengning Shen, Mengfei Li; Shangluo Central Hospital, Yingmin Guan, Wenfeng Wang, Ting Xiao; ShangqiuChangzheng People's Hospital, Qian Wang; Shaoyang County People's Hospital, Fengyun Jiang, Kaiyou Wu; Shengsi People's Hospital, Songguo Wang; Shenyang Weikang Hospital, Xujie Fu, Shu Zhang,Lifang Gao; ShougangShuicheng Iron & Steel (Group) Co·, Ltd. General Hospital, Min Zhang, Kai Fu, XiaojingDuan; Shuangshan Hospital Of Anshan, Rui Xiao, Ruixia Wu, Bin Li; Siziwang County People's Hospital, Hongtu Zhang, Yuerong Ma, Zhonghui Cao; SunanYugur Autonomous County People's Hospital, Zhansheng Ba, Wanhai Fu; Taizhou Hospital of Zhejiang Province, Jianjun Jiang, YafeiMi, Weiwei Zhou; The Affiliated Hospital of Beihua University, Feng Sun, Qi Zhang, Shiyu Zheng; The Fifth People's Hospital of Dalian, Jing Zhang, Yang Zhong; The First Affiliated Hospital of Hebei North University, Fangjiang Li, Xiaoyuan Wang; The First Affiliated Hospital of Henan University of Science & Technology, Pingshuan Dong, Laijing Du, Wei Liu; The First Affiliated Hospital Of Jia Mu Si University, Zhaofa He, Meihua Jin; The First Hospital of Fuzhou City, Ting Jiang, Zhuoyan Chen; The First Hospital of Xi'an, Manli Cheng, YuqiangJi; The First People's Hospital of Danzhou, Youhua Zhou, Jvyuan Li; The First People's Hospital of Guangzhou, Yizhi Pan, Jian Liu; The First People's Hospital of Guangyuan, Tianxun Wang, Ping Yang; The Fourth People's

Hospital of Shangqiu Shi, Guiyu Huang, JianjunPan,QingliangCai,Qianying Wang; The General Hospital of Yongzhou, Hunan Province, MingliLv; The people's hospital of Wuchuan, Yuanming Yi, Xuelian Deng; The People's Hospital of Yuanling, Wenhua Chen, RongCai; The People's Hospital of Zhijiang City, Bing Zhang; The Second Affiliated Hospital of Harbin Medical University, Bo Yu, Yousheng Xu, Zhengqiu Wang; The Second Affiliated Hospital of Kunming Medical University, Jun Shu, Ge Zhang, Kai Li; The Second Central Hospital of Baoding City, Guang Ma, PuxiaSuo; The Second People's Hospital of Liaoyuan City, Aimin Zhang, Yongfen Kang; Tianjin Medical University General Hospital, Zheng Wan,Yuemin Sun, Bo Bian; Tibet Autonomous Region People's Hospital, Xuejun Hu, DawaCiren; Tongchuan Mining Bureau Central Hospital, GuojiongJia, Jieli Pan; Tongliang County People's Hospital, Guofu Li, Hongliang Zhang, Longliang Zhan; Tongliao City Horqin District First People's Hospital, Junping Fang, Xinli Yu; Ulanqab Central Hospital, Dacheng Wang, Dajun Liu, Xinhong Cao; Wencheng County People's Hospital, Yi Tian, HaishengZhu,Wanchuan Liu; Wuhai People's Hospital, Zhaohai Zhou, Lei Shi; Wuhu Second People's Hospital, Wuwang Fang, Manxin Chen; Wulate County People's Hospital, ,FuqinHan,JianyeFu,Yunmei Wang; Wuqiang County People's Hospital, Binglu Liu, YanliangZhang,Xiupin Yuan; Wuyishan Municipal Hospital, Qingfei Lin, Yun Chen; Xiangtan County People's Hospital, Yuliang Zhu, ZhiqiangCai; Xing County People's Hospital, Xingping Li, LirongAo; Xingshan County People's Hospital, Shubing Wu, Hui Zhang; Xinmi First People's Hospital, Fusheng Zhao, Guangming Yang; Xinshao County People's Hospital, Renfei Liu, Wenwei Ai; Xiuwu County People's Hospital, JianbaoChang,Haijie Zhao; Xuanhan County People's Hospital, Qijun Ran, Xuan Ma; Xupu County People's Hospital, Shijun Jiang, Xiaochun Shu; Yanggao County People's Hospital, Zhiru Peng, Yan Han; Yanqing County Hospital, Jianbin Wang, Li Yang; Ying County People's Hospital, Yu Shen, Xingcun Shang; Yitong Manchu Autonomous County First People's Hospital, Haifeng Wang; Yongxing County People's Hospital, Hongyan Li, Zhisong Liao, Yang Cao; Yuanzhou District People's Hospital of Guyuan City, Xiaoping Gao, MeiyingCai, Lining You; Yuncheng Central Hospital, Xuexin Li, Shuqin Li, Yingjia Li; Yunlong County People's Hospital, Jianxun Yang, Song Ai, Jianfei Ma; Yuyao People's Hospital, Lailin Deng; ZhangjiachuanHui Autonomous County First People's Hospital, Keyu Wang, Shitang Gao, Jian Guan; Zhouning County Hospital, Banghua He,

Youyi Lu; Zhuoni County People's Hospital, Weirong Yang, Hong Li; Zhuozi County People's Hospital, Zhizhong Zhang, Xiaohong Chi; Zuoyun County People's Hospital, Ru Duan, Guangli Wang.

B. China PEACE hospital survey: design, conduction, and materials

Participants

In the collaborative network, we invited the principal investigator and the coordinator of each hospital to participate in the survey. The definitions of the roles were established during the planning phase of the China PEACE-Retrospective AMI Study: typically, the director of the Cardiology Department or Internal Medicine Department at each hospital served as the principal investigator, and the China PEACE study coordinator was most often a physician selected by the principal investigator.

Survey design

We organized the survey in 4 sections: personal information of the respondent (part A); general information about the hospital and the department in charge of AMI care (part B); information about hospital practices relating to the diagnosis and treatment of cardiovascular heart disease (part C); and organizational learning characteristics and quality improvement for AMI care (part D). Organizational learning culture was measured using questions from the Short-Form Learning Organization Survey (LOS-27) and the Survival after AMI (SAMI) study.

The survey was written in English and translated into Chinese. To ensure accuracy, a double translation was conducted in which the survey was translated into Chinese and then back into English independently by 2 bilingual Chinese medical researchers. Modifications were made to the Chinese translation accordingly. Participants were informed at the start of the survey that their responses would be used to study institutional characteristics and medical care patterns.

Survey conduction

The survey was piloted using a convenience sample of 6 hospitals with percutaneous coronary intervention capability. The principal investigators were invited to participate in the pilot, and one study coordinator also volunteered to participate. The responses of the 6 principal investigators (3 via in-person interviews and 3 via self-administered paper-based survey) and 1 study coordinator (via self-administered paper-based survey) were collected. The cognitive interviewing methodology, in which individual in-person interviews were conducted with each pilot participant, was used to assess understanding of the pilot survey. For paper-based pilot surveys, cognitive interviewing consisted of retrospective (post-survey) probes; for in-person interviews, concurrent (during survey) probes allowed

participants to provide survey feedback in real-time. Based on the experience from the pilot, minor revisions were made to clarify the meaning of certain questions, and the sequence of questions was modified to improve logic and flow. No questions were removed or added. All data from the pilot testing were included in the final data set.

The survey was available in 2 forms: web-based e-survey, in which each participant was able to log in with a unique password to a website where the survey was hosted, and PDF-based survey, in which subjects digitally marked their answers in PDF files and returned the files via email. We applied 2 methods to ensure the quality of the responses. We checked the response data for completeness, either by automatic verification (web-based) or by manual check by our staff (PDF-based), and on the basis of logic. For the web-based e-survey submissions, we used automatic logic check and verification while subjects were responding to the survey, and recorded total time spent on the survey. For the PDF-based survey submissions, we conducted a manual logic check, focusing on whether subjects correctly skipped inapplicable questions as indicated by the instructions in other parts of the survey. In cases of missing or illogical (e.g., questions incorrectly skipped or completed) data for PDF-based surveys, we contacted respondents by email and/or phone, informed them of which questions needed to be resolved, and asked them to resubmit the survey with the necessary changes.

Survey questionnaires

A. Personal information

A.1 Gender:
○ Male ○ Female

A.2 Education
○ Junior high school
○ Senior high school (technical school or technical secondary school)
○ College (junior college)
○ Postgraduate

A.3 Clinical job title:
○ Consultant ○ Attendant ○ Resident ○ Nurse ○ Other, please specify: ___

A.4 Senior administrative position in hospital:
○ No ○ Yes, please specify: ___

A.5 You have been working in the department for __ years.

B. General Information of the hospital and the department

Instructions: This section focuses on characteristics of your hospital and department. For all questions, please reflect upon them during the 1-year period from 1/1/2011 to 12/31/2011 (for some of them, please consider 1/1/2001 to 12/31/2001, and 1/1/2006 to 12/31/2006, as specified). Even some questions in this section might be somewhat hard to answer immediately, especially those about the characteristics of your hospital or department in 2001 and 2006. Please try best to find the answer - as accurate as possible - to every applicable question.

B.1 Affiliated hospital of medical college:
○ No ○ Yes, please specify the name of the college: _____ **[Skip to B3]**

B.2 Teaching hospital of medical college:
○ No ○ Yes, please specify the name of the college: _____

Total No. in your department

		In 2001	In 2006	In 2011
B.3	Beds			
B.4	Consultants			
B.5	Attendants			
B.6	Residents			
B.7	Nurses			

B.8 Is there any other department in your hospital providing inpatient treatment for AMI?
○ No ○ Yes, please specify the name of the department: _____

B.9 Coronary Care Unit (CCU) in hospital?
○ No ○ Yes, please specify the No. of beds: _____

B.10 Cath lab in hospital?
○ No **[Skip to B12]** ○ Yes, please specify when started: _____

B.11 How many qualified cardiac interventionalist there are in your hospital: _____ ○ unknown

B.12 Could CABG be performed in hospital?
○ No ○ Yes, please specify the No. of cases in 2011: _____

B.13 Independent emergency department?
○ No ○ Yes, please specify the No. of cardiologists in charge in emergency department normally: _____

B.14 Formal GCP training of clinical staff in your department?
○ No ○ Yes ○ Unknown

B.15 Have your apartment participated in international clinical trials?
○ No ○ Yes, please specify the names of the trials: _____ ○ Unknown

B.16 SFDA certified site for CVD drug trials?
○ No ○ Yes ○ Unknown

B.17 Existence of Ethics Committee in hospital?
○ No ○ Yes ○ Unknown

Total No. in your hospital

		In 2001	In 2006	In 2011
B.18	Patients with stroke			
B.19	Patients with ischemic stroke			
B.20	Patients with hemorrhagic stroke			

B.21 Independent neurology department?
○ No ○ Yes, please specify the No. of beds in the department: _____

B.22 Carotid endarterectomy performed in hospital?
○ No ○ Yes, please specify when started: _____ ○ Unknown

B.23 Carotid stenting performed in hospital?
○ No ○ Yes, please specify when started: _____ ○ Unknown

The average cost of the following items in your hospital

	Items	Cost, ¥
B.24	Biochemical test, including glucose, lipid, liver function, renal function, CRP or hsCRP	
B.25	Coagulation function test	
B.26	BNP or NT-proBNP	
B.27	Stress test	
B.28	UCG	
B.29	Cardiac CT	
B.30	Carotid US	

C. Diagnosis and treatment for CHD

Instructions: This section focuses on hospital processes and care of patients with AMI. For all questions, please reflect upon them during the 1-year period from 1/1/2011 to 12/31/2011.

C.1 Routine diagnostic test of CK for ACS patients after admission?

○ No ○ Yes, please specify the average time delay in reporting results: _____ ○ Unknown

C.2 Routine diagnostic test of CK-MB for ACS patients after admission?

○ No ○ Yes, please specify the average time delay in reporting results: _____ ○ Unknown

C.3 Routine diagnostic test of troponin for ACS patients after admission?

○ No ○ Yes, please specify the average time delay in reporting results: _____ ○ Unknown

C.4 Are patients who are stable after PCI admitted to an intensive care unit? SAMI-Q25

○ Always ○ Usually ○ Sometimes ○ Rarely ○ Unknown

C.5 Did your emergency department use a uniform protocol to care for patients who arrived to the emergency department with **STEMI**? SAMI-Q26

○ No ○ Yes ○ Unknown

C.6 Did your emergency department use a uniform protocol to care for patients who arrived to the emergency department with **Unstable Angina/NSTEMI**? SAMI-Q27

○ No ○ Yes ○ Unknown

C.7 Did your hospital use simulations (i.e., trial exercises, dry-runs) to practice any of the following AMI care processes? ***[Check all that apply]*** SAMI-Q28

□ Door-to-balloon or door-to-drug protocols

□ Chest pain in hospitalized patients

□ Inpatient codes (e.g., cardiac arrest, respiratory failure)

□ None above

□ Unknown

C.8 To which patient care unit were patients who were stable with Unstable Angina/NSTEMI most likely admitted? SAMI-Q29

○ CCU ○ ICU ○ Step-down unit ○ Designated chest pain/telemetry/cardiology floor ○ General medicine floor ○ We did not have a routine method of assigning beds for patients with Unstable Angina/NSTEMI ○ Unknown

C.9 Did all, or nearly all, patients with AMI have a cardiologist as their primary attending physician? SAMI-Q30

○ No ○ Yes **[Skip to C11]** ○ Unknown

C.10 Were cardiology consults required for all patients with AMI? SAMI-Q30a

○ No ○ Yes ○ Unknown

C.11 In the intensive care unit, who was primarily responsible for the care of patients with AMI? ***[Check all that apply]*** SAMI-Q31

□ Critical care physicians (i.e., intensivists)

□ Cardiologist/s based exclusively in the unit

□ Other cardiologists

□ Other, please specify: _____

□ Unknown

C.12 Electronic medical record?

○ No **[Skip to C14]** ○ Yes, please specify when started: _____ ○ Unknown

C.13 Did your hospital use an electronic medical record (EMR) in the following areas? ***[Check all that apply]*** SAMI-Q34

□ Emergency department

□ Inpatient floors

□ Critical care units

□ Affiliated ambulatory offices/clinics

□ None above

C.14 On the inpatient floors, did your hospital have the following electronic capabilities? ***[Check all that apply]*** SAMI-Q35

□ Computerized assisted physician order entry

□ Computer prompts to alert user to potential drug-drug interactions or allergies

□ Computer prompts to alert user to potential errors in dosing and information

□ Computer prompts to alert user to medication order expiration

□ Computer prompts to improve adherence to core measures for AMI care (e.g., beta-blocker use)

□ None above

C.15 In the emergency department, were prior ECG's electronically available at the time of care? SAMI-Q36

○ No ○ Yes ○ Unknown

C.16 Did physicians regularly use explicit protocols or clinical pathways for patients with AMI? SAMI-Q37

○ No ○ Yes ○ Unknown

C.17 Did clinicians on the inpatient care units regularly use order sets (either paper-based or electronic) for patients with STEMI? SAMI-Q38

○ No ○ Yes ○ Unknown

C.18 Did clinicians on the inpatient care units regularly use order sets (either paper-based or electronic) for with Unstable Angina/NSTEMI? SAMI-Q39

○ No ○ Yes ○ Unknown

C.19 Which of the following types of physicians were at the hospital 24-hours/day and 7-days/week? ***[Check all that apply]*** SAMI-Q42

□ Critical care physicians (i.e., intensivists)

□ Non-interventional cardiologists

□ Interventional cardiologists

□ Cardiology fellows (including non-interventional and interventional)

□ Hospitalists

□ None above

C.20 Are there any protocols used to guide nurses on when to call the attending cardiologist for patients with AMI? SAMI-Q43

○ No ○ Yes ○ Unknown

C.21 Patients with acute coronary syndrome who arrived by Emergency medical service (ambulance):

○ None **[Skip to C25]** ○ 1–25% ○ 26–50% ○ 51–75% ○ 76-100% ○ Unknown

C.22 Emergency medical service routinely gives pre-alert calls?

○ No ○ Yes ○ Unknown

C.23 Patients with acute coronary syndrome who undergo ECG en route to hospital:

○ None ○ 1–25% ○ 26–50% ○ 51–75% ○ 76-100% ○ Unknown

C.24 Emergency medical service routinely tell your hospital the results of ECG?

○ No ○ Yes ○ Unknown

C.25 Formal training of triage staff for assessing acute coronary syndrome?

○ No ○ Yes ○ Unknown

C.26 Dedicated space in triage area for immediate ECG?

○ No ○ Yes ○ Unknown

C.27 Written criteria for immediate ECG in emergency department?

○ No ○ Yes ○ Unknown

C.28 Expected interval between patients' arriving and ECG?

○ ≤5 min ○ 6–20 min ○ >20 min ○ No expected time ○ Unknown

C.29 Dedicated ECG technicians in emergency department?

○ No ○ Yes, only some shifts ○ Yes, always ○ Unknown

C.30 Thrombolysis for AMI patients in hospital?
○ No **[Skip to C38]** ○ Yes, please specify when started: _____

C.31 Does your hospital have a set protocol to identify eligible patients for thrombolysis?

○ No ○ Yes ○ Unknown

C.32 Does your hospital have a set protocol to assess contraindications of thrombolysis?

○ No ○ Yes ○ Unknown

C.33 Who makes the decision about thrombolysis in your hospital?

○ Emergency medicine physician alone

○ Emergency medicine physician with a cardiac consultation

○ Only Cardiologist

○ Unknown

C.34 In your hospital, where do patients with AMI receive thrombolysis?

○ In the emergency department

○ In the cardiology department (or general medicine department)

○ In the ICU or CCU

○ Unknown

C.35 Where are the thrombolytic medicines stored and prepared?

○ Stored and prepared in the department where thrombolysis is done

○ Prepared in the department where thrombolysis is done, but stored in another location

○ Stored and prepared in some location other than the department where thrombolysis is done

○ Unknown

C.36 Informed Consent before thrombolysis?

○ Not necessary

○ Only orally obtained informed consent is needed

○ One written informed consent form is needed

○ More than one written informed consent form is needed

○ Unknown

C.37 Prepayment before thrombolysis?

○ No

○ Yes, please specify the average amount approximately: ___ ("-1" if unknown)

○ Unknown

C.38 Primary PCI was performed in your hospital for STEMI patients?

○ No **[Skip to C60]** ○ Yes, please specify when started: ___

C.39 Activation of catheterization laboratory on weekdays?

○ Emergency medicine physician with cardiologist

○ Cardiologist alone

○ Emergency medicine physician alone

○ Unknown

C.40	Activation of catheterization laboratory at night and on weekends? ○ Emergency medicine physician with cardiologist ○ Cardiologist alone ○ Emergency medicine physician alone ○ Unknown
C.41	Process for activating catheterization team? ○ After communicating with the emergency department, interventional cardiologist activates catheterization laboratory by calling staff or a central page operator ○ Emergency department makes at least two calls: one to the interventional cardiologist and another to a central page operator, who pages catheterization laboratory staff ○ Emergency department makes a single call to a central page operator, who then pages interventional cardiologist and catheterization laboratory staff ○ No standard approach ○ Other ○ Unknown
C.42	Activation of on-call staff for catheterization laboratory? ○ Page operator is not used ○ Page operator is used; confirmation of page receipt is required ○ Page operator is used; no confirmation of page receipt is required ○ No standard approach ○ Unknown
C.43	First physician notified after STEMI diagnosis in emergency department? ○ Cardiologist ○ Interventional cardiologist ○ Patient's primary care physician ○ Other or variable ○ Unknown
C.44	Laboratory and radiographic results are needed to activate catheterization laboratory? ○ Yes ○ No ○ No standard approach ○ Unknown

C.45	Process after emergency medical service transmits ECG results? ○ Emergency department waits for patient to arrive at hospital to determine whether catheterization laboratory should be activated ○ Emergency department contacts cardiologist while the patient is en route to determine whether catheterization laboratory should be activated ○ Emergency department activates catheterization laboratory while the patient is still en route to the hospital ○ No standard approach or variable approach ○ Not applicable because ECG data not transmitted en route ○ Not applicable because ECG never performed en route ○ Unknown
C.46	Expected interval between page and arrival of staff in catheterization laboratory? ○ ≤20 min ○ 21–30 min ○ >30 min ○ No expected time ○ Unknown
C.47	Expected interval between page and arrival of interventional cardiologist? ○ ≤20 min ○ 21–30 min ○ >30 min ○ No expected time ○ Unknown
C.48	Someone is always available to transport patients from emergency department to catheterization laboratory? ○ No ○ Yes ○ Unknown
C.49	Initiation of patient transport from emergency department to catheterization laboratory? ○ After catheterization laboratory notifies emergency department it is ready ○ A set interval after the decision is made regarding PCI ○ No standard approach ○ Other approach ○ Unknown

C.50	Minimum number of nurses and technicians required in catheterization laboratory before patient is transported from emergency department? ○ Interventional cardiologist must be present ○ Interventional cardiologist may not be present but need presence of 1 staff person ○ Interventional cardiologist may not be present but need presence of 2-4 staff person ○ No set number ○ Unknown
C.51	Elective catheterization cases rescheduled for emergency PCI? ○ Yes ○ No ○ It depends ○ Unknown
C.52	If interventionalist is present, number of staff required to begin PCI? ○ 1 ○ 2 ○ 3 ○ 4 ○ Unknown
C.53	Catheterization laboratory is left so that next PCI can begin promptly? ○ Yes ○ No ○ No standard policy ○ Unknown
C.54	Cardiology fellows participate in performing PCI? ○ No ○ Yes ○ Unknown
C.55	Staff in critical care area are routinely cross-trained to cover catheterization laboratory? ○ No ○ Yes ○ Unknown
C.56	Location of catheterization laboratory? ○ Elevator required to travel from emergency department ○ Same floor as emergency department
C.57	An attending cardiologist is always at the hospital? ○ No ○ Yes ○ Unknown

C.58 Informed Consent before primary PCI?

○ Not necessary

○ Only orally obtained informed consent is needed

○ One written informed consent form is needed

○ More than one written informed consent form is needed

○ Unknown

C.59 Prepayment before primary PCI?

○ No

○ Yes, please specify the average amount approximately ___ ("-1" if unknown)

○ Unknown

C.60 Does your hospital measure the following time intervals? ***[Check all that apply]***

□ Door to ECG

□ Door to needle

□ Door to balloon

□ None above

□ Unknown

C.61 Do your hospital feedback the time intervals to someone? ***[Check all that apply]***

□ No

□ Yes, to physician staff involved in the care

□ Yes, to nursing staff involved in the care

□ Yes, to pharmacy staff involved in the care

□ Yes, to other staff involved in the care

□ Unknown

C.62 Do your hospital report the analyze results about the time intervals regularly? ***[Check all that apply]***

□ No

□ Yes, to departments involved in the care (the emergency department, the cardiology department)

□ Yes, to other department in your hospital

□ Yes, to other institutions outside your hospital

□ Unknown

D. Organizational learning characteristics

Instructions: This section focuses on the organizational learning and measurements to improve AMI care, including supportive environment and leadership, experimentation and training, knowledge acquisition, reflection and performance monitoring, etc. Please draw on your own experiences in your current role working with clinical staff and administration. For all questions, please reflect upon them during the 1-year period from 1/1/2011 to 12/31/2011.
Although some questions in this section look similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each question fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems most reasonable.
The definition of "workgroup" below is the department, unit, ward, or group caring AMI patients that you are working at.
This section adopts 7-point (from highly inaccurate to highly accurate). If you think the options are difficult to understand or distinguish, please grade the accuracy here using actual numbers, while 1 is the lowest (highly inaccurate), 7 is the highest (highly accurate), then choose the corresponding option.

D.1 In this workgroup, people value new ideas.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.2 Clinicians are encouraged to creatively solve problems related to AMI care processes. (60)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.3 Innovative ideas about AMI care are shared widely in the hospital. (61)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.4 Differences in opinions are welcomed in this workgroup.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.5 In this workgroup, people are open to alternative ways of getting work done.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.6 People in this workgroup are eager to share information about what doesn't work as well as to share information about what does work.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.7 This workgroup frequently compares its performance to: Best-in-class organizations.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.8 This workgroup frequently compares its performance to: Other similar workgroups.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.9 This workgroup consistently collects information on technological trends.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.10 If you make a mistake in this workgroup, it is often held against you. (Among clinicians taking care of patients with AMI, there is a tendency to blame individuals for errors in patient care). (66)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.11 Clinicians caring for patients with AMI are easily able to address problems and tough issues with their department heads/chiefs. (56)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.12 Department heads/chiefs are easily able to address problems and tough issues with senior level administration.(57)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.13 Nurses are comfortable checking with physicians if they have concerns about patient care.(65)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.14 Clinicians involved in the care of patients with AMI value each others' skills and talents (e.g., physicians value nurses' skills and talents and vice-versa).(58)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.15 Clinicians involved in the care of patients with AMI avoid sharing responsibility for medical errors. ○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always. (59)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.16 Were physicians explicitly encouraged to disclose medical errors to patients or their family members? (7)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.17 This workgroup engages in productive conflict and debate during discussions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.18 In this workgroup, we frequently identify and discuss underlying assumptions that might affect key decisions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.19 The hospital has the resources and information it needs to reduce 30-day mortality rates in patients with AMI. (51)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.20 Senior-level administration is supportive of efforts to improve AMI care. (52)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.21 There is simply no time for reflection in this workgroup.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.22 In this workgroup, people are too busy to invest time in improvement.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.23 My manager(s) establish(es) forums for and provide(s) time and resources for identifying problems and organizational challenges.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.24 My manager(s) establish(es) forums for and provide(s) time and resources for reflecting and improving on past performance.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.25 My manager(s) listen(s) attentively.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.26 My manager(s) invite(s) input from others in discussions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.27 This workgroup experiments frequently with new product/service offerings.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.28 This workgroup experiments frequently with new ways of working.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.29 This workgroup frequently employs pilot projects or simulations when trying our new ideas.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.30 This workgroup has a formal process for conducting and evaluating experiments or new ideas.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.31 Experienced employees in this workgroup receive training when new initiatives are launched.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.32 Experienced employees in this workgroup receive training when shifting to a new position.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.33 Newly hired employees in this workgroup receive adequate training.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.34 Did your hospital provide training to EMS providers about AMI care? (17)

○ Yes, about monthly

○ Yes, about quarterly

○ Yes, about annually

○ Yes, other: _____

○ No

○ Unknown

D.35 This workgroup has forums for meeting with and learning from: Experts from outside the organization.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.36 This workgroup has forums for meeting with and learning from: Experts from other departments/teams/divisions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.37 This workgroup has forums for meeting with and learning from: Customers/clients.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.38 This workgroup regularly conducts post-audits, after-action reviews, and debriefings.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.39 Did your hospital have regular 'morbidity and mortality' conferences (or another educational session) for discussing individual cases involving patients with AMI? (5)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.40 Did your hospital review the deaths of patients with AMI? (4a)

○ No, we did not review these cases **(go to D44)**

○ Yes, we reviewed only deaths with potential quality issues (i.e., unexpected deaths)

○ Yes, we reviewed *all* deaths

○ Other, please specify: _____

○ Unknown

D.41 Did your hospital have a **designated person or group** to review the deaths of patients with AMI (i.e., on an individual case level) that occurred during hospitalization? (4)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.42 How long after the occurrence of the death were the cases typically reviewed? (4b)

○ Within one week of the death

○ Within one month of the death

○ Within 3 months of the death

○ Other, please specify: _____

○ We did not have a set timeframe for reviewing these cases

○ Unknown

D.43 Who usually reviewed these cases? (4c)

a. Senior management of the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Cardiology chiefs

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Nursing directors

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Other physicians participating in the care of patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

e. Quality Improvement/Quality Management department staff

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.44 Did your hospital have a **designated person or group** to review any of the following **adverse events** in patients with AMI (i.e., on an individual case level)? (6)

a. Sentinel events (unexpected occurrence involving death or serious physical or psychological injury) that occurred during hospitalization

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Unexpected transfers from a floor (non-monitored unit) to an intensive are unit

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Catastrophic complications that occurred immediately after discharge from the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.45 How long after the occurrence of these adverse events were the cases typically reviewed? (6a)

○ Within one week of the adverse event

○ Within one month of the adverse event

○ Within 3 months of the adverse event

○ Other, please specify: _____

○ We did not have a set timeframe for reviewing these cases

○ Unknown

D.46 Who usually reviewed these cases? (6b)

a. Senior management of the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Cardiology chiefs

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Nursing directors

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Other physicians participating in the care of patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

e. Quality Improvement/Quality Management department staff

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

f. Other, please specify: ___

D.47 Did your hospital use root cause analysis or a similar method to understand the following problems in AMI care?

a. Poor adherence to the core medication (i.e., anti-platelet agents) measures

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Delay to fibrinolytic therapy or percutaneous coronary intervention (PCI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.48 Did your hospital review data on **30-day mortality rates** (deaths occurring within 30 days of admission, including both inpatient and post-discharge deaths) in patients admitted with AMI (Check all that apply) (10)

□ Yes, through the medical insurance data system

□ Yes, through a regional database system

□ Yes, we internally collect our own data on deaths

□ Yes, other, please specify: ___

□ No **[Skip to D52]**

□ Unknown

D.49 How quickly were **mortality rates** in patients with AMI available to your hospital (i.e., what was the most current data available to your hospital)? (10a)

○ Within 6 months of care delivery

○ 6 months to 1 year after care delivery

○ 1 - 2 years after care delivery

○ Less frequently than 2 years of care delivery

○ Unknown

D.50 Did your hospital regularly compare its performance to other hospitals on either **inpatient** in patients with AMI? (14)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.51 Did your hospital have **efforts** to improve any of the following inpatient acute myocardial infarction (AMI) quality measures? (1)

a. Adherence to the core medication (i.e., anti-platelet agents) measures

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Time to fibrinolytic therapy or percutaneous coronary intervention (PCI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.52 Beyond these quality measures, did your hospital initiate **efforts** to improve any of the following in patients admitted with AMI? (2)

a. Inpatient mortality in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. **Post-discharge** mortality (death occurring after discharge, but within 30 days of admission) in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Readmission within 30 days from prior admission in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.53 Did your hospital have a quality improvement **team(s)** devoted to improving: (3)

a. Inpatient mortality in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Post-discharge mortality (death occurring after discharge, but within 30 days of admission) in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.54 3a. Please indicate members of either the inpatient or post-discharge mortality **team(s)**.

a. Senior management of the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Hospital governing board

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Chief of cardiology

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Nursing directors

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

e. Other physicians participating in the care of patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

f. Quality Improvement/Quality Management department staff

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

g. Other please specify: _____

D.55 Nurses are engaged in efforts to improve AMI care. (53)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.56 Cardiologists are engaged in efforts to improve AMI care. (54)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.57 Emergency medicine physicians are engaged in efforts to improve AMI care. (55)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.58 Did your hospital have one or more physician champions focused on improving either **inpatient** or **30-day mortality** in patients with AMI? (12)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.59 Did your hospital have one or more nurse champions focused on improving either **inpatient** or **30-day mortality** in patients with AMI? (13)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.60 After we make changes to improve AMI care, we fail to evaluate their effectiveness. (67)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.61 Did cardiology and emergency department staff meet together to review care for patients with AMI? (15)

○ Yes, about monthly

○ Yes, about quarterly

○ Yes, about annually

○ Yes, other: _____

○ No **[Skip to D63]**

○ Unknown

D.62 What was typically discussed at these meetings? (15a).

a. Care of patients with ST-elevation myocardial infarction (STEMI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Care of patients with Unstable Angina/**non**-STEMI (NSTEMI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Care of patients with chest pain, in general

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.63 Did clinicians from your hospital meet with emergency medical system (EMS) providers to review the care of patients with AMI? (16)

○ Yes, about monthly

○ Yes, about quarterly

○ Yes, about annually

○ Yes, other: _____

○ No

○ Unknown

D.64 There is good coordination among the different departments involved with the care of patients with AMI. (62)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.65 Departments caring for patients with AMI (e.g., cardiology, emergency medicine) communicate easily with each other.(64)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.66 Clinicians caring for patients with AMI share new evidence-based approaches with the AMI team.(63)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.67 Which best describes the quality of your interaction with hospitals **that referred patients to you with AMI**?(18)

○ Very collaborative (we shared data along with strategies for improving AMI care) ○ Somewhat collaborative (we communicated regularly, but we did not share data and strategies)

○ Not collaborative (we had no or minimal contact with the referring hospital/s)

○ Not applicable **[Skip to D69]**

D.68 Did your hospital routinely give feedback to the referring hospital/s on any of the following? (18a.)

a. Time to transfer

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. AMI-related procedures performed

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Patient outcome

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Other please specify: _____

D.69 Which best describes the quality of your interaction with hospitals **that you referred patients to with AMI**? (19)

○ Very collaborative (we shared data along with strategies for improving AMI care) ○ Somewhat collaborative (we communicated regularly, but we did not share data and strategies)

○ Not collaborative (we had no or minimal contact with hospitals in our region)

○ Not applicable

D.70 Was your hospital part of a regional effort or consortium of hospitals to improve AMI care? (20)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

C. Definition of In-hospital Complications

1) Re-infarction

Indicate if there is physician documentation of recurrent myocardial infarction during hospitalization.

2) Cardiogenic shock

Indicate if there is physician documentation of cardiogenic shock during hospitalization.

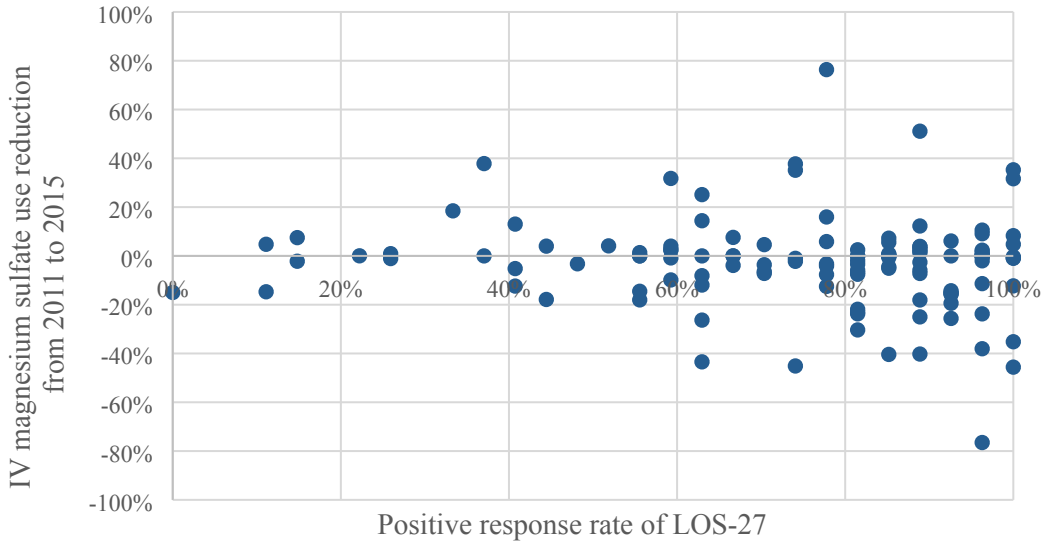
3) Ischemic stroke

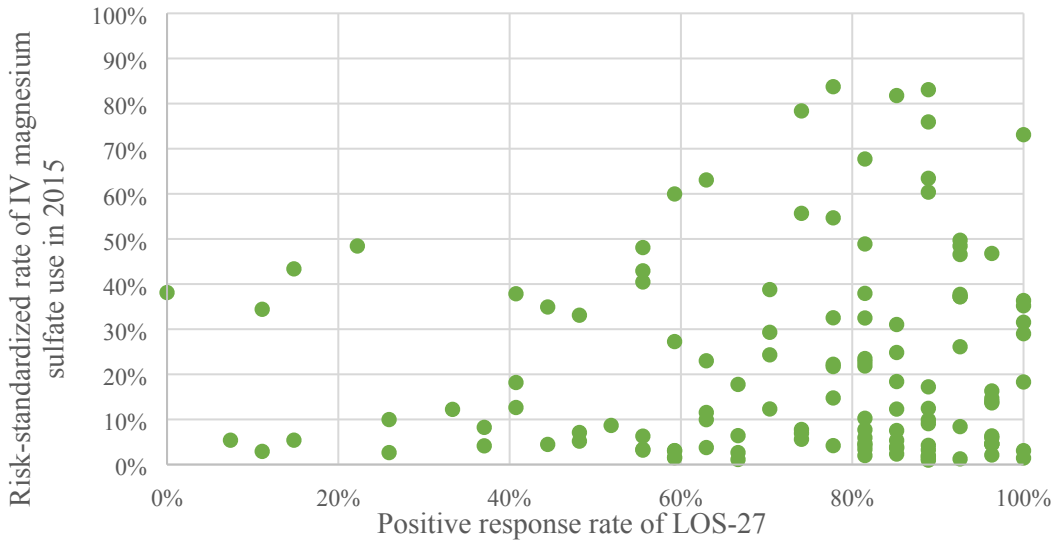
Indicate if there are physician documentations of new-onset ischemia stroke and stroke-related symptoms during hospitalization. The stroke-related symptoms include: trouble walking/loss of balance/incoordination, one-sided numbness or hemi-anesthesia, one-sided facial numbness or hemi-anesthesia, mouth askew and drooling, dysarthria or slurred speech, loss of vision or blurred version in one or both eyes, dizziness with vomiting, severe headache and vomiting, unconsciousness, and hyperspasmia.

4) Congestive heart failure

Indicate if there is physician documentation of heart failure during hospital stay. This include those without a history of heart failure but develop heart failure during hospitalization, and those with a history of heart failure as a chronic comorbidity and develop worsening heart failure during hospitalization.

D. Correlations between positive response rate of LOS-27 and IV magnesium sulfate use





E. Comparisons between patients with and without IV magnesium sulfate therapy after propensity score matching

Characteristics	Use N(%)	Non-Use(%)	P value
Patient characteristics			
Age			
55-64	1072(24.4)	1037(23.6)	.794
65-74	1290(29.4)	1283(29.2)	
<55	938(21.3)	959(21.8)	
>=75	1094(24.9)	1115(25.4)	
Gender			
Female	1346(30.6)	1299(29.6)	.274
Male	3048(69.4)	3095(70.4)	
Hypertension	2247(51.1)	2196(50)	.277
Diabetes	889(20.2)	878(20)	.77
Dyslipidemia	235(5.3)	244(5.6)	.672
Currently smoking	1496(34)	1470(33.5)	.558
Number of risk factors			
1	2055(46.8)	1997(45.4)	.445
2	1049(23.9)	1047(23.8)	
>=3	232(5.3)	229(5.2)	
None	1058(24.1)	1121(25.5)	
Prior ischemic stroke	546(12.4)	484(11)	.04
Prior myocardial infarction	416(9.5)	382(8.7)	.207
Prior CABG/PCI	104(2.4)	107(2.4)	.834
Chest discomfort	4021(91.5)	4046(92.1)	.331
Left branch block at presentation	65(1.5)	44(1)	.043
Cardiac arrest at presentation	81(1.8)	79(1.8)	.873
Cardiogenic shock at presentation	279(6.3)	236(5.4)	.051
Acute stroke at presentation	77(1.8)	66(1.5)	.354

Heart rate at presentation, bpm			.733
<50	177(4)	183(4.2)	
50-110	3886(88.4)	3898(88.7)	
>110	331(7.5)	313(7.1)	
SBP at presentation, mmHg			.621
<120	1565(35.6)	1607(36.6)	
120-139	1299(29.6)	1307(29.7)	
140-159	913(20.8)	899(20.5)	
>=160	617(14)	581(13.2)	
Reperfusion therapies			.941
No reperfusion	3130(71.2)	3131(71.3)	
Fibrinolytic therapy	746(17)	754(17.2)	
Primary PCI	518(11.8)	509(11.6)	
Hospital characteristics			
Teaching hospital	3462(78.8)	3530(80.3)	.072
Hospital level			.451
Secondary or lower	1576(35.9)	1610(36.6)	
Tertiary	2818(64.1)	2784(63.4)	
Economic geographic region			
Central	1115(25.4)	1186(27)	.191
Eastern	2360(53.7)	2288(52.1)	
Western	919(20.9)	920(20.9)	
Urban/Rural			
Rural	1724(39.2)	1721(39.2)	.948
Urban	2670(60.8)	2673(60.8)	

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6，7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	7
		(*b*) For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8，9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how matching of cases and controls was addressed	9
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	23
		(c) Consider use of a flow diagram	23
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	21，22
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	11，25

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	25 26
		(*b*) Report category boundaries when continuous variables were categorized	21， 22
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	12,13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14,15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Methods Paper

The China Patient-Centered Evaluative Assessment of Cardiac Events (China PEACE) Retrospective Study of Acute Myocardial Infarction: Study Design

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Background—Cardiovascular diseases are rising as a cause of death and disability in China. To improve outcomes for patients with these conditions, the Chinese government, academic researchers, clinicians, and >200 hospitals have created China Patient-Centered Evaluative Assessment of Cardiac Events (China PEACE), a national network for research and performance improvement. The first study from China PEACE, the Retrospective Study of Acute Myocardial Infarction (China PEACE-Retrospective AMI Study), is designed to promote improvements in acute myocardial infarction (AMI) quality of care by generating knowledge about the characteristics, treatments, and outcomes of patients hospitalized with AMI across a representative sample of Chinese hospitals during the past decade.

Methods and Results—The China PEACE-Retrospective AMI Study will examine >18 000 patient records from 162 hospitals identified using a 2-stage cluster sampling design within economic–geographic regions. Records were chosen from 2001, 2006, and 2011 to identify temporal trends. Data quality will be monitored by a central coordinating center and will, in particular, address case ascertainment, data abstraction, and data management. Analyses will examine patient characteristics, diagnostic testing patterns, in-hospital treatments, in-hospital outcomes, and variation in results by time and site of care. In addition to publications, data will be shared with participating hospitals and the Chinese government to develop strategies to promote quality improvement.

Conclusions—The China PEACE-Retrospective AMI Study is the first to leverage the China PEACE platform to better understand AMI across representative sites of care and during the past decade in China. The China PEACE collaboration among government, academicians, clinicians, and hospitals is poised to translate research about trends and patterns of AMI practices and outcomes into improved care for patients.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01624883.

(*Circ Cardiovasc Qual Outcomes*. 2013;6:732-740.)

Key Words: epidemiology ■ morbidity ■ mortality ■ myocardial infarction

Ischemic heart disease has significant public health importance in China.[1,2] Unlike in the United States,[3,4] age-standardized ischemic heart disease incidence is rising in China.[5–10] Reasons for this trend include the increasing prevalence of traditional risk factors for atherosclerosis,[6,7,10–12] including hypertension,[6,7] hyperlipidemia,[7,13] diabetes mellitus,[7,13] obesity,[13–16] and inadequate physical activity[6,7] in the presence of significant exposure to cigarette smoke[7,17,18] and air pollution.[19] Population aging is further contributing to rising ischemic heart disease incidence.[10]

To improve outcomes for ischemic heart disease and other cardiovascular diseases in China, the China National Center for Cardiovascular Disease (NCCD), the Yale-New Haven Hospital Center for Outcomes Research and Evaluation, the Chinese

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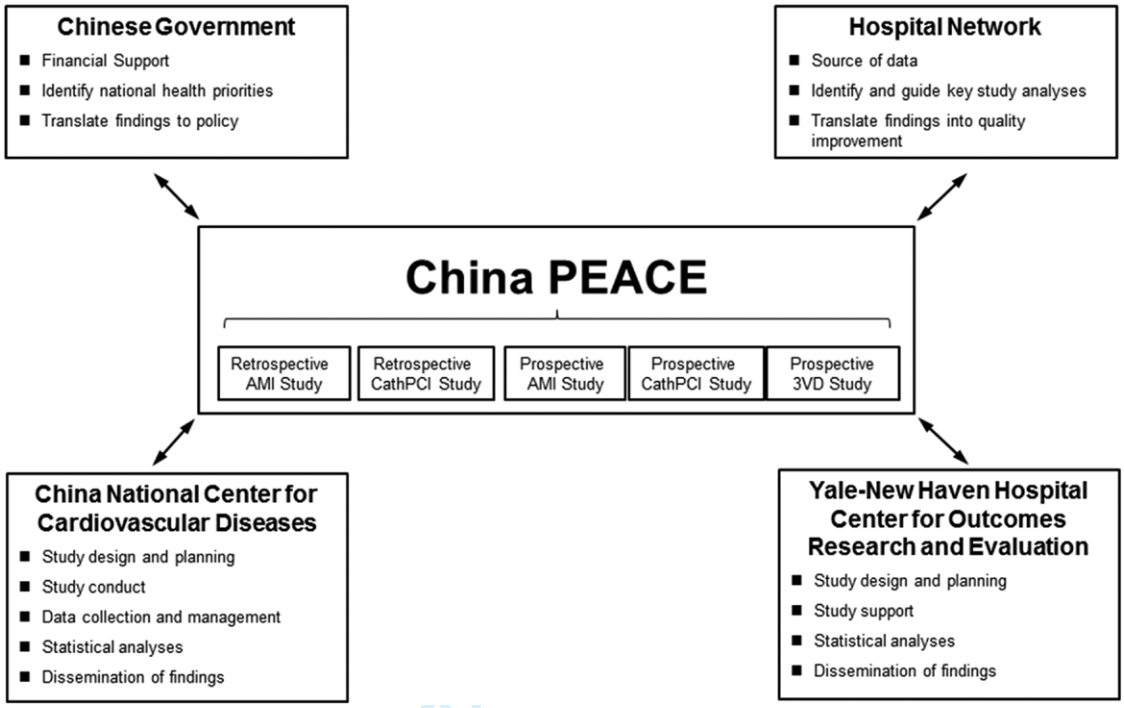

Figure 1. The China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE) initiative. Key partners include the Chinese government, collaborating hospitals, the China National Center for Cardiovascular Disease, and the Yale-New Haven Hospital Center for Outcomes Research and Evaluation. The China PEACE-Retrospective AMI Study is 1 of 5 initial studies from the China PEACE initiative. The topic areas for these 5 projects concern acute myocardial infarction, coronary catheterization/percutaneous coronary intervention, and multi-vessel coronary artery disease. Future studies will focus on cerebrovascular disease and other cardiovascular conditions. 3VD indicates revascularization in patients with triple-vessel disease; AMI, acute myocardial infarction; and PCI, percutaneous coronary intervention.

government, and >200 Chinese hospitals have collaborated to create a national network for research and performance improvement. This platform, entitled China PEACE (Patient-Centered Evaluative Assessment of Cardiac Events), will permit rapid bidirectional flow of information between partnering hospitals and the coordinating center at the NCCD (Figure 1). With funding from the Chinese government, China PEACE will elucidate the clinical epidemiology of cardiovascular disease treatment and its associated outcomes across patients, hospitals, regions, and time. China PEACE, envisioned as a combined research and quality improvement initiative, will disseminate findings of the greatest relevance to participating hospitals and the Chinese government in a manner suitable for the evaluation of care and the development of projects to improve clinical quality and patient outcomes. Through the use of strategies most often used by clinical trials, data quality will be ensured by rigorous monitoring by the central coordinating center at the stages of case ascertainment, data abstraction, and data management. The collaborative research and performance improvement network created by China PEACE will ultimately be leveraged to improve patient outcomes for a broad range of conditions and may be a model for research and quality improvement in other international settings.

The first study from the China PEACE collaboration is the Retrospective Study of Acute Myocardial Infarction (China PEACE-Retrospective AMI Study). Previous research on the characteristics, treatments, and outcomes for patients hospitalized with acute myocardial infarction (AMI) in China has contributed important knowledge but has been largely limited to studies from tertiary care centers in urban regions,[20–22] major metropolitan areas,[23–25] a small subset of provinces,[26,27] or to patients from clinical trial databases,[28] all of whom may not be representative of typical patients. Research involving a larger and more diverse distribution of study sites has contributed to our understanding of the use of evidence-based therapies after AMI,[29] including differences in treatment between secondary and tertiary hospitals[30] as well as in-hospital complications such as bleeding[31] and recurrent angina,[32] but it has not involved a large, nationally representative study population and has not examined temporal trends in AMI treatment and outcomes. These trends over time, in particular, may reflect major changes in the Chinese healthcare system that have occurred in the past decade such as the expansion of health insurance from 30% to 90% of the population between 2001 and 2011,[33] greatly increased resources for rural healthcare beginning in 2003,[34] and further health reforms starting in 2009.[35] Data relating these health reforms to changing healthcare practices are limited. To address these gaps in knowledge, the China PEACE-Retrospective AMI Study will identify trends using a nationally representative sample of >18 000 patient records from 162 randomly selected hospitals for 2001, 2006, and 2011. The hospitals represent diverse geographic regions and include institutions with a range of cardiovascular facilities. Thus, this is the first truly national assessment of practice patterns and outcomes for AMI performed in China.

The China PEACE-Retrospective AMI Study broadly aims to promote improvements in AMI quality of care by generating knowledge about the characteristics, treatments, and outcomes of patients hospitalized with AMI across a representative

sample of Chinese hospitals during the past decade. The study is largely descriptive, and rather than test a specific hypothesis, it seeks to characterize current AMI care and associated patient outcomes to provide a foundation for future quality improvement and research. We do anticipate that there will be marked variation in practice and outcomes, demographic and geographic disparities, and ample opportunities for improvements. The specific aims of the China PEACE-Retrospective AMI Study are to (1) describe the characteristics of patients hospitalized with AMI in China, including their clinical and demographic attributes such as occupation and insurance status; (2) characterize patterns of in-hospital treatment, including the use of traditional Chinese medicines; (3) describe mortality rates and other in-hospital outcomes, including the development of heart failure and complications of treatment; (4) determine trends over time in patient characteristics, treatments, and outcomes; (5) develop and test prognostic scores to stratify risk; (6) compare treatment across regions and hospitals and determine whether differences in treatment patterns by setting may be associated with differences in outcomes; (7) examine the alignment of diagnostic testing and treatment strategies with quality measures; (8) compare differences in patient characteristics, treatment approaches, and outcomes between China and other countries; (9) determine the quality of documentation within the medical record; and (10) collaborate with participating hospitals and the Chinese government to disseminate study findings to improve quality of care and outcomes.

This article describes study methodology, abstracted data elements, analytic plan, and preliminary findings of the China PEACE-Retrospective AMI Study. Findings will identify opportunities for quality improvement and guide the development of strategies and tools to improve outcomes for AMI in China.

Methods

Design Overview

The China PEACE-Retrospective AMI Study will examine >18 000 hospitalizations for AMI from a nationally representative network of Chinese hospitals during 2001, 2006, and 2011. The study includes hospitalizations with a principal discharge diagnosis of AMI (International Classification of Diseases, Ninth Revision, Clinical Modification codes 410.xx or International Classification of Diseases, Tenth Revision, Clinical Modification codes I21.xx), including ST-segment–elevation myocardial infarction and non–ST-segment–elevation myocardial infarction. We did not include hospitalizations with a principal discharge diagnosis of unstable angina.

To study 10-year trends in patient characteristics, treatment patterns, and outcomes nationally and within regions of different socioeconomic development, we drew a random, representative sample of patient discharges for each year. We intentionally drew a larger sample for 2011 to study differences in treatment patterns and outcomes across hospitals.

The central ethics committee at the China NCCD approved the PEACE-Retrospective AMI Study. All collaborating hospitals accepted the central ethics approval except for 5 hospitals, which obtained local approval by internal ethics committees. The study is listed at www.clinicaltrials.gov (NCT01624883).

The Chinese government, which provided financial support for the study, had no role in the design or conduct of the study; in the collection, management, analysis, and interpretation of the data; or in the preparation or approval of the article.

Sampling Design

We intended study hospitals to reflect diverse sites of care in China. As hospital volumes and clinical capacities differ between urban and rural areas, as well as among the 3 official economic–geographic regions of Mainland China, we separately identified hospitals in 5 strata: Eastern-rural, Central-rural, Western-rural, Eastern-urban, and Central/Western-urban regions. We considered an area urban if it is part of a downtown or suburban area within a direct-controlled municipality (Beijing, Tianjin, Shanghai, Chongqing) or 1 of 283 prefectural-level cities. We considered surrounding county-level regions, including counties and county-level cities, to be rural. Within this framework, Mainland China is composed of 287 urban regions and 2010 rural regions. We considered Central and Western-urban regions together given their similar per capita income and health services capacity.[36]

We identified cases for study inclusion using a stratified 2-stage cluster sampling design (Figure 2). In the first stage, we identified hospitals using a simple random sampling procedure within each of the 5 study strata. In the 3 rural strata, the sampling framework consisted of the central hospital in each of the predefined rural regions (2010 central hospitals in 2010 rural regions). Within each rural region, the central hospital is the largest general hospital with the greatest clinical capacity for treating acute illness, including AMI. In each of the 2 urban strata, the sampling framework consisted of the highest-level hospitals in each of the predefined urban regions (833 hospitals in 287 urban regions). Hospital level is officially defined by the Chinese government based on clinical resource capacity.[37] For example, secondary hospitals have ≥100 inpatient beds and the capacity to provide acute medical care and preventive care services to populations of ≥100 000, whereas tertiary hospitals are large referral centers in provincial capitals and major cities.[29] We excluded military hospitals, prison hospitals, specialized hospitals without a cardiovascular disease division, and traditional Chinese medicine hospitals. We decided to select representative hospitals from 2011 to reflect current practices and trace this hospital cohort backward to 2006 and 2001 to describe temporal trends. As the hospital number has grown by ≈18% during the past decade,[36,38] the study cohort should be most representative of national treatment patterns and outcomes in 2011.

In the second stage, we drew cases based on the local hospital database for patients with AMI at each sampled hospital using systematic random sampling procedures. In each of the 5 study strata, we determined the sample size required to achieve a 2% precision for describing the primary outcome, in-hospital mortality, which we had estimated to be ≈9% in urban hospitals and 7% in rural county-level hospitals.[5] To achieve a precision of 2% with an α of 0.05 in each of the 3 rural strata, assuming an intraclass correlation of 0.02 and design effect of 1.8, we would need to sample 1150 medical records among hospitals with an average cluster size of 40. Analogously, to achieve a precision of 2% with an α of 0.05 in each of the 2 urban strata, assuming an intraclass correlation of 0.02 and design effect of 2.2, we would need to sample 1750 medical records among hospitals with an average cluster size of 60. These cluster sizes in rural and urban settings seemed reasonable based on our previous survey of treatment for acute coronary syndromes at >1000 hospitals in 2010, which demonstrated that the median volume of hospitalization for AMI was ≈180 annual cases in urban hospitals and 95 annual cases in rural county-level hospitals. Assuming a participation rate of 85% among selected hospitals, we approached 35 hospitals for participation in each stratum for a total of 175 hospitals (70 urban and 105 rural). We doubled cluster sizes for 2011 to improve precision in the description of hospital-level treatment patterns and outcomes. Consequently, the total expected sample volume with the above assumptions was ≈6950 cases in 2001, 6950 cases in 2006, and 13 900 cases in 2011. A more detailed description of the sampling strategy used in the PEACE-Retrospective AMI Study is provided in the supplemental material.

Data Collection

We trained staff at participating hospitals to identify all hospitalizations for AMI from their respective local hospital databases for the years 2001, 2006, and 2011. After we sampled cases at each hospital, we assigned each case a unique study ID. We then required local investigators to gather the original record, scan it, and transmit the scanned copy to the coordinating center. To facilitate this process, the coordinating center provided each study site with a high-speed scanner. To verify compliance with the case finding strategy, research

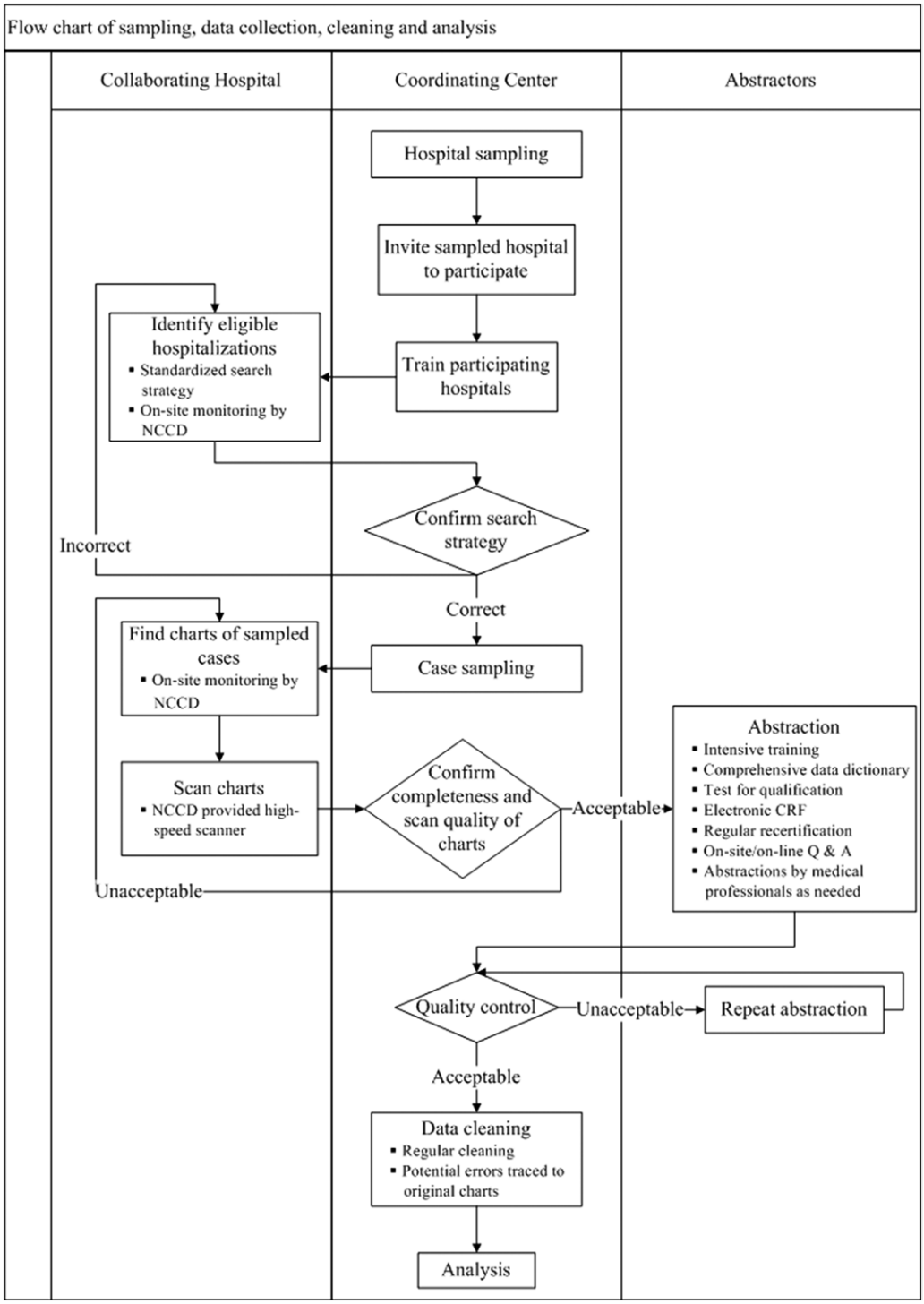

Figure 2. China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE) Retrospective Study of Acute Myocardial Infarction flow chart and associated quality assurance strategies. Flow chart should be read from top to bottom. CRF indicates case report form; NCCD, China National Center for Cardiovascular Diseases; and Q&A, questions and answers.

staff from the study coordinating center visited 46 study sites to repeat the case finding process, confirm that the list of hospitalizations with AMI was complete, and assist in acquiring the sampled cases (Figure 2). These 46 sites provided ≈50% of sampled cases for the China PEACE-Retrospective AMI Study.

After identifying all medical records for sampled cases, participating hospitals copied and transmitted the records to the NCCD after deidentification. Research staff ensured the completeness and quality with which each medical record was scanned; incomplete or poorly scanned records were rescanned and retransmitted (Figure 2). We instructed study sites to include all parts of the medical record, including the face sheet, admission note, daily progress notes, procedure notes, medication administration record, diagnostic procedure reports, laboratory test results, physician orders, nursing notes, and discharge summary. These subdivisions of the medical record are routinely present throughout China.

The China PEACE-Retrospective AMI Study has adhered to rigorous standards for abstraction. Before initiating chart review, each

abstractor received 2 weeks of training that included an introduction to the study and instruction about coronary heart disease and its subtypes, component parts of the inpatient medical record including specialized sections such as catheterization reports, and the China PEACE-Retrospective AMI Study data dictionary. We provided all material, including the data dictionary, in Chinese. After training, we certified trainees who were able to abstract 10 sample medical records with >98% accuracy (online-only Data Supplement).

The China PEACE-Retrospective AMI Study used several strategies to improve the accuracy of abstraction. Inexperienced abstractors began with exclusively typewritten rather than hand written medical records. In addition, we randomly audited ≈5% of the abstracted records. If the records were not abstracted with 98% accuracy, all medical records in the audited batch were considered unqualified and were rereviewed by a different abstractor. We used abstractors with formal medical training to identify data elements requiring more advanced medical knowledge for recognition, such as the presence of comorbidities, evidence of pulmonary edema on hospital presentation, and the development of postprocedural complications, such as bleeding or arrhythmia. A physician was always present in the room with abstractors or was available online to answer questions as they arose. As problems were identified, we updated the data dictionary and web-based data management program built for the China PEACE-Retrospective AMI Study into which data were directly entered. We have additionally customized this program to expedite the identification of medications that may have multiple trade names. Finally, we assigned medical records belonging to the same hospital and year to a broad group of reviewers to avoid potential residual disparities in quality among abstractors (online-only Data Supplement).

Data Management

We have treated all data as protected health information and have securely stored it in an encrypted and password-protected database at the coordinating center. We have securely stored paper charts in locked rooms.

We perform ongoing data cleaning systematically. Data managers regularly query data for invalid and illogical values, as well as for duplicate record entries. They identify potential invalid values by searching for outliers in continuous data distributions. Records with identical study identification numbers, hospital identification numbers, medical record identification numbers, and dates of discharge trigger a search for duplicate records. Once a potential error is found, data managers trace and review the relevant records to resolve the issue.

Data Elements

We examined both the English language and the Chinese literature for relevant studies to create a candidate list of potential data elements. Where possible, we included elements particular to the Chinese context such as the use of traditional Chinese medicines. We supplemented these elements with variables used in the Get with the Guidelines ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry of the National Cardiovascular Data Registry (NCDR) and the Variation in Recovery: Role of Gender on Outcomes of Young Acute Myocardial Infarction Patients (VIRGO) study. ACTION is an outcome-based registry and quality improvement program that focuses on patients hospitalized with ST-segment–elevation myocardial infarction and non–ST-segment–elevation myocardial infarction.[39] VIRGO is a large, observational study of the presentation, treatment, and outcomes of young women and men with AMI.[40] The use of standardized elements from ACTION and VIRGO permit cross-country comparisons (Table 1). We performed pilot testing of the case report form on >500 medical records from study sites across China to enhance clarity of wording and further guide variable selection. We present data relevant to performance measures during the first 24 hours of hospitalization and at hospital discharge in Table 2. Where possible, we collected data that would allow us to construct the core quality measures used and reported by the Centers for Medicare & Medicaid Services in the United States. Each participating hospital has also completed a survey, modeled on the annual survey of hospitals performed by the American Hospital Association, of its major structural and organizational characteristics.[41] Key variables assessed include bed size, annual volume of AMI, teaching status, and capacity to perform invasive revascularization procedures. The patient case report form and associated data dictionary are available in the online-only Data Supplement.

Statistical Analyses

We will report summary statistics for patient characteristics, use of diagnostic tests, treatments received, and in-hospital outcomes including complications of care across study sites. Weighting will reflect the reciprocal of sampling probability. For each aim, we will use standard parametric and nonparametric techniques for observational data, including *t* tests, χ^2 tests, Wilcoxon rank-sum tests, and generalized linear models. Because patient characteristics, treatments, and outcomes may be correlated within study sites, analyses will account for the effect of clustering. To examine and adjust for differences between comparison groups, we will use linear, logistic, Cox proportional hazard, and Poisson models with a generalized estimating

Table 1. China PEACE-Retrospective Study of Acute Myocardial Infarction Data Elements

Category	Example Elements
Patient demographics	Age, sex, ethnicity, postal code, occupation, and insurance status
Medical history	Diabetes mellitus, hypertension, hyperlipidemia, vascular disease, and prior revascularization
Initial cardiac status	Heart rate, blood pressure, Killip class, heart failure, and cardiac arrest
Laboratory values	Troponin, CK, CK-MB, BNP, sodium, BUN, creatinine, WBC count, and hemoglobin
Medications including dose	Antithrombotic therapy, β-blocker, ACE inhibitor/ARB, statin, and traditional Chinese medicines
Revascularization	Fibrinolysis, PCI (access, anatomy, stent number, stent type, contrast dose, closure device), and CABG surgery
Diagnostic procedures	Echocardiogram, CT angiogram, stress testing, and chest radiograph
Outcomes including in-hospital complications	Death, heart failure, shock, arrhythmia, stroke, bleeding, transfusion, and infection

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; CK, creatine kinase; CK-MB, creatine kinase-MB fraction; CT, computed tomography; PCI, percutaneous coronary intervention; PEACE, Patient-Centered Evaluative Assessment of Cardiac Events; and WBC, white blood cell.

Table 2. China PEACE-Retrospective Study of Acute Myocardial Infarction Performance Measures

First 24 h	Discharge
Aspirin	Aspirin
Heparin	Clopidogrel
Evaluation of left ventricular function	β-blocker
Time to primary PCI	ACE inhibitor or ARB for LV systolic dysfunction
Time to fibrinolysis	Statin
Overall reperfusion therapy	Smoking cessation counseling
	Cardiac rehabilitation referral

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; PEACE, Patient-Centered Evaluative Assessment of Cardiac Events; LV, left ventricle; and PCI, percutaneous coronary intervention.

equation approach and hierarchical models, where appropriate. We will develop models to stratify patients according to their risk of adverse outcomes. We will assess the relationship of candidate variables to in-hospital outcomes using appropriate statistical techniques for the dependent variable. We will further refine the list of candidate variables based on their clinical relevance.

Progress to Date

As of May 2013, 162 hospitals have agreed to participate in the China PEACE-Retrospective AMI Study (Figure 3). Of the 13 that did not participate, 7 did not have admissions for AMI, and 6 declined participation. Examination of patient databases from participating hospitals yielded 31 601 hospitalizations for AMI (3859 in 2001, 8863 in 2006, and 18 879 in 2011). Of these, we sampled 18 631 for the China PEACE-Retrospective AMI Study (2801 in 2001, 5199 in 2006, and 10 631 in 2011). Of these 18 631 sampled hospitalizations, we acquired medical records for 18 110 (97.2%) and began data abstraction in August 2012. Medical records from 95% (154) of study sites contained all expected sections and represent 89% of all hospitalizations in the China PEACE-Retrospective AMI Study. In the remaining 8 study sites, we did not have access to daily progress notes because of local administrative policies of hospital archives departments. However, these records were considered adequate for inclusion in the study. The use of electronic medical records increased with time: 0% of hospitals used electronic medical records in 2001, 7% of hospitals used electronic medical records in 2006, and 46% of hospitals used electronic medical records in 2011. We will code hospital-level variables for the presence of daily progress notes and electronic medical records to better understand whether these factors introduce bias into study results.

To verify the accuracy of principal discharge diagnoses, we randomly selected 300 medical records and examined concordance between principal discharge diagnosis and electrocardiographic findings consistent with the subtype of AMI (ST-segment–elevation myocardial infarction versus non–ST-segment–elevation myocardial infarction). We found concordance in 95% of cases.

Discussion

Akin to the Cooperative Cardiovascular Project in the United States,[42] China PEACE provides a platform through which government, healthcare providers, and research organizations can translate knowledge of the clinical epidemiology of cardiovascular disease into improved care for patients. In the United States, collaboration between the Healthcare Financing Administration, hospitals, and academic researchers demonstrated frequent underuse of evidence-based therapies for AMI.[43] Rapid feedback of these findings to hospitals resulted in significant improvement in performance on all studied quality indicators and reduced mortality.[44] China PEACE has similar potential to serve as a foundational project that evaluates and, if necessary, elevates cardiovascular care more generally within China. As with the United States in the early 1990s, China is turning increased attention to the treatment of patients hospitalized with acute cardiovascular conditions[45] to improve outcomes across diverse patient populations and sites of care. China PEACE will leverage the unique resources of the Chinese government, a diverse hospital network, and an international research team to translate study findings into action for the benefit of patients.

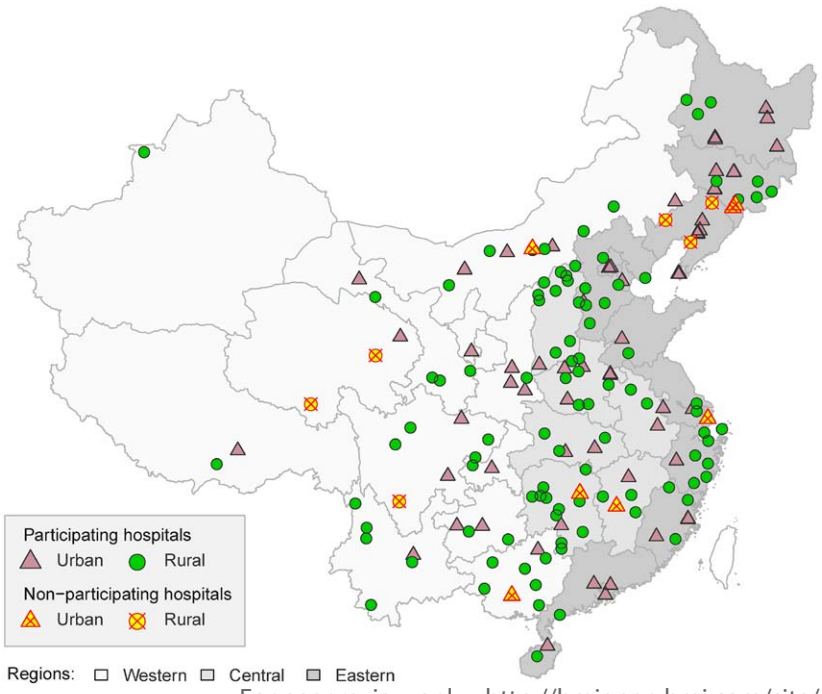

Figure 3. Geographic distribution of participating hospitals in the China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE) Retrospective Study of Acute Myocardial Infarction (AMI). Of 175 sampled hospitals, 13 were unable or unwilling to participate, and 162 provided cases for the China PEACE-Retrospective AMI Study.

The partnership among government, hospitals, and researchers is a critical source of strength for China PEACE. For example, clinical champions have informed the content of case report forms, thereby increasing the likelihood that study questions and findings are relevant at the front lines of care. Continuing conversations with hospitals will help align planned analyses to the areas of greatest concern and uncertainty for providers. The NCCD will tailor performance feedback reports to the information needs and clinical goals of each hospital. For example, the NCCD will be able to benchmark site-specific data on patient characteristics, receipt of evidence-based treatment, and outcomes to nearby hospitals, hospitals with similar case mix, top performing hospitals, the full spectrum of Chinese hospitals, or international institutions. In addition, the research teams will serve as hubs to ensure the rapid transfer of data, including information on best practices, between hospitals, and the Chinese government. The direct ties to government will increase the likelihood that study findings influence policy pertinent to AMI and cardiovascular care. Such an arrangement may also facilitate the creation of clinical tools to improve care, such as standing order templates, risk stratification algorithms, and dosing pocket cards.

China PEACE is further distinguished by its use of data quality control strategies, which are much more common in multinational clinical trials than in large retrospective studies. In particular, the China PEACE-Retrospective AMI Study has devoted significant attention to data quality at the stages of case ascertainment, data abstraction, and data management. For example, research staff rigorously monitored study sites to identify all hospitalizations for AMI from census databases. Staff also ensured that medical records for sampled cases were physically found, properly copied, and transmitted in full whenever possible. In addition, the China PEACE-Retrospective AMI Study provided central training for abstractors and required rigorous standards for both initial certification and recertification. Medical records from abstractors who did not achieve recertification requirements were reabstracted by a second reviewer. In developing these systems, China PEACE is also positioned for future studies.

The China PEACE-Retrospective AMI Study has several additional strengths. It contains the largest representative sample of hospitalizations for AMI in China and therefore includes patients from diverse geographic regions and institutions with widely varying resource capacities. Its inclusion of data from 2001, 2006, and 2011 will permit the assessment of trends in patient characteristics, care patterns, and outcomes. Information will be available on topics that have not been well studied (eg, the use of traditional Chinese medicines after AMI). Cross-country comparisons will be possible given the alignment of key data elements with the NCDR ACTION Registry and VIRGO. Finally, further targeted examination of additional data elements not included in the initial case report forms can be performed as novel questions arise, as the NCCD will maintain a physical copy of all charts after the initial abstraction.

The China PEACE-Retrospective AMI Study has some limitations. Study findings depend on the accuracy and completeness of the abstracted medical records. However, this limitation pertains to all retrospective chart reviews, including those performed by the Cooperative Cardiovascular Project and registries. Lack of completeness may signal problems with documentation that are important to note, as detailed and reliable record keeping is needed to measure key processes and outcomes in quality improvement. Therefore, the assessment of the quality of the medical record can be an important contribution of this effort. The China PEACE-Retrospective AMI Study is also restricted to measuring in-hospital outcomes, as we are unable to link patient-level data to a national registry of deaths. However, the length of stay in Chinese hospitals, extended compared with that of many Western countries,[5,36,46,47] should permit more robust estimates of short-term complications including death. Next, we are unable to report on hospital costs and cost-effectiveness related to care for AMI, as well as patient out-of-pocket costs, as this information is not available in the standard medical record, which only contains information on the total charge for hospitalization. Finally, study precision will be slightly lower than anticipated, as we collected data from ≈18 000 medical records rather than the anticipated 28 000. This discrepancy resulted from the substantially lower volume of hospitalizations for AMI than had been anticipated for the years 2001 and 2006, in particular. Our estimates, which were based on 2010 survey data, did not fully account for the marked increase in AMI hospitalizations that we identified between 2001 and 2011. However, the smaller sample size than expected should not substantively affect the precision with which major outcomes such as mortality are described, as expected strata-level precision for mortality decreased by no more than 2% in rural areas and no more than 1% in urban areas (online-only Data Supplement).

China PEACE will ensure transparency in research design, performance, and reporting. Although the Chinese government has funded China PEACE, it has no role in conduct of the study. We will perform all analyses in academic research units at the China NCCD and the Yale-New Haven Hospital Center for Outcomes Research and Evaluation. Government approval of articles will not be required before publication.

China PEACE is intended to spur similar collaborations among government, healthcare institutions, and academic researchers to better understand cardiovascular disease incidence, treatment, and outcomes. Partnerships among local hospitals at the front line of care, domestic research organizations with local expertise and previous track records of success, international experts in research design, and policymakers intent on improving population health can identify important targets for study, build novel research networks, and generate tools useful in improving health outcomes. These partnerships can support a research and health improvement infrastructure that is unconstrained by particular diseases or conditions and is capable of facilitating clinical trials and performance improvement activities. In the future we will seek to involve patients and caregivers in the research team. The China PEACE-Retrospective AMI Study is the first of many projects that can leverage the China PEACE platform to elucidate the patterns of care and outcomes of cardiovascular disease across patients, hospitals, and regions within China.

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Disclosures

None.

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July 01, 2019

Dr. Adrian Aldcroft,
Editor,
BMJ Open

Dear Dr. Aldcroft,

We are writing to submit our manuscript entitled "Use of Intravenous Magnesium Sulfate among Patients with Acute Myocardial Infarction in China from 2001 to 2015: China PEACE-Retrospective AMI Study" for your consideration for publication in *BMJ Open*. We believe this manuscript is a valuable contribution to the literature examining de-adoption of ineffective therapy in clinical practice in China and other countries.

This manuscript submitted provided a detailed analysis of the trends and variation in use of IV magnesium sulfate in a nationally representative sample of about 24,000 patients with AMI over the past fifteen tears. To our knowledge, limited data in China and other countries substantiate this subject. In our study, we found that the de-adoption of magnesium sulfate for AMI is suboptimal, with 17% of patients with AMI given IV magnesium sulfate in 2015. The decrease of rate was slowing down and stabilized around an unacceptably high level recently. Furthermore, IV magnesium sulfate use is neither associated with particular hospital characteristics, nor geographic/socio-economic regions. The findings highlighted the gaps in performance and called for further researches on the causes.

Our work provides a critical evaluation of the ineffective therapy in healthcare across the country, and implies that efforts aiming to more efficient mechanisms to translate evidence-

based therapies into clinical practice in China are needed. China's experiences could be highly relevant to many low- and middle-income countries facing similar challenges over the world. We believe this study will be of major interest to the readership of *BMJ Open*.

As the corresponding author, I take full responsibility for the content of this submission. I had full access to all the data and final responsibility for the decision to submit for publication. All authors contributed substantively to the manuscript and have approved the submission in its final form. The manuscript has not been submitted elsewhere, or published elsewhere in whole or in part in any language.

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We declare no relevant conflicts of interest.

We are grateful to you for considering our manuscript.

Yours sincerely

Dr. Xi Li

BMJ Open

Use of Intravenous Magnesium Sulfate among Patients with Acute Myocardial Infarction in China from 2001 to 2015: China PEACE-Retrospective AMI Study

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Keywords:	acute myocardial infarction, Magnesium Sulfate, quality of health care

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Use of Intravenous Magnesium Sulfate among Patients with Acute Myocardial Infarction in China from 2001 to 2015: China PEACE-Retrospective AMI Study

Running head: Magnesium Sulfate for AMI in China

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ABSTRACT

Objective

In 2001, Chinese guidelines for the care of acute myocardial infarction included a new recommendation against the routine use of magnesium. We studied temporal trends and institutional variation in the use of IV magnesium sulfate in nationally representative samples of individuals hospitalized with AMI in China between 2001-2015.

Methods

In an observational study (China PEACE–Retrospective Study) of AMI care, we used a 2-stage, random sampling strategy to create a nationally representative sample of 28,208 patients with AMI at 162 Chinese hospitals in 2001, 2006, 2011, and 2015. The main outcome is use of IV magnesium sulfate over time.

Results

We identified 24,418 patients admitted for AMI, without hypokalemia, in the four study years. Over time, there was a significant initial decrease in IV magnesium sulfate use, from 32.1% in 2001 to 17.1% in 2015 ($p < .001$ for trend). The decline was greater in the Eastern (from 33.3% to 16.5%) and Western (from 34.8% to 17.2%) regions, as compared with the Central region (from 25.9% to 18.1%), with little difference between rural and urban areas. The proportion of hospitals using IV magnesium sulfate did not change over time (from 81.3% to 77.9%). The median odds ratios, representing hospital-level variation, were 6.03 in 2001, 3.86 in 2006, 4.26 in 2011, and 4.72 in 2015. IV magnesium sulfate use was associated with cardiac arrest at admission and receipt of reperfusion therapy, but no hospital-specific characteristics.

Conclusions

Despite recommendations against its use, IV magnesium sulfate is used in about 1 in 6 patients with AMI in China. Our findings highlight the need for more efficient mechanisms to stop using ineffective therapies to improve patients' outcomes and

reduce medical waste.

Clinical Trial Registration

URL: https://www.clinicaltrials.gov. Unique identifier: NCT01624883

Keywords

acute myocardial infarction, Magnesium Sulfate, quality of health care

Strengths and limitations of this study

- This is the first large nationally representative registry demonstrating IV magnesium sulfate is still used in about 1 in 6 patients with AMI in China, despite recommendations against its use since 2000s.
- The study assessed the 15-year trend in the use of IV magnesium sulfate among patient with AMI in China.
- The study firstly reported both patients- and hospital-level resulted in the use of IV magnesium sulfate use, which could provide more targeted information for efficient mechanisms to stop using this ineffective therapy.
- The study adopted standardized procedures for abstraction of medical records that ensure the reliability of our results in describing the use pattern of magnesium sulfate in the real world.
- The very low prevalence of patients with some indications, such as magnesium sulfate deficiency would have little influence on the reliability of the results.

INTRODUCTION

The history of intravenous (IV) magnesium sulfate use for acute myocardial infarction (AMI) is convoluted. Once lauded in small, early trials as safe and highly effective,[1-3] it was later demonstrated to be ineffective, and even harmful, in two large clinical trials (MAGIC and ISIS-4) and in a subsequent meta-analysis.[4 5] Beginning in the early 2000s, AMI practice guidelines in the United States have specifically recommended against its routine use (Class III, level of evidence: C).[6 7] Similarly, China published guidelines in 2001 recommending against the use of IV magnesium sulfate in patients with AMI, except in the setting of hypomagnesemia or polymorphic ventricular tachycardia.[8]

Although several studies have evaluated the introduction and uptake of new therapies,[9-11] few have examined de-adoption of ineffective therapy in clinical practice.[12-14] The de-adoption of therapy is particularly important because the situation may involve greater resistance and barriers to discontinuing long-standing practices than simply introducing new and promising therapies into practice.[15] Characterizing the use of magnesium sulfate for AMI in clinical practice offers an opportunity to assess the speed with which providers stop using a therapy when new evidence has overturned prior dogma.

Accordingly, our objectives were to assess the trends and variation of regional and hospital-level use of IV magnesium sulfate among patient with AMI using data from the China PEACE Retrospective AMI Study between 2001 and 2015. These data, from a nationally representative network of hospitals throughout China, provided a unique opportunity to examine the trend for discontinuing routine IV magnesium sulfate over time and to describe the variations across hospitals in its discontinuation.

METHODS

Design Overview

The design and methods of the China PEACE-Retrospective AMI Study have been previously published.[16] In addition to a nationally representative sample of patients admitted for AMI in China during 2001, 2006, and 2011 created in the China PEACE-Retrospective AMI Study, we also included a more recent sample of patients admitted in 2015 using the same two-stage random sampling process. Briefly, in the first stage, we identified hospitals using a simple random sampling procedure within 5 economic-geographic regions: Eastern rural, Central rural, Western rural, Eastern urban, and Central/Western urban. We stratified on both location and urban-rural classifications because economic development and clinical capacities differed across these categories. We sampled representative hospitals from 2011 to reflect current practices and used the same hospitals for the 2006, 2001, and 2015 so as to describe temporal trends. In the second stage, we sampled AMI cases from hospital databases in 2001, 2006, 2011, and 2015 using random sampling procedures.

Trained personnel at the national coordinating centers abstracted data from the medical records using standardized data definitions. Data abstraction quality was rigorously monitored by randomly auditing 5% of the medical records, in a process that ensured that the overall variable accuracy exceeded 98%.[16] We also obtained information on the organizational learning culture of hospital in 2013 through questionnaires completed by the director and a physician of the Cardiology Department in each participating hospital (see Appendix).[17]

The Ethics Committee at the National Center for Cardiovascular Diseases approved the study. All collaborating hospitals either accepted central ethics approval or obtained local ethics approval by their ethics committees. Given the retrospective nature of the data and the lack of personal identifiers, patient-level consent was not

required. The study was registered with ClinicalTrials.gov (NCT01624883).

Study Sample

Among the randomly sampled patients hospitalized for AMI in 2001, 2006, 2011, and 2015, only patients with a definite discharge diagnosis of AMI were included. We were unable to exclude patients with hypomagnesemia, because magnesium levels were not collected. However, we excluded patients with chart-documented hypokalemia during their hospitalization, which could also represent an indication for magnesium repletion. In hospital-level analysis, only hospitals with 10 or more cases in a study year were included.

Variables

Receipt of IV magnesium sulfate was ascertained from the medical record. Patient-level characteristics abstracted from the medical records included demographics (age, gender), medical history (hypertension, diabetes, dyslipidemia, current smoking, and history of myocardial infarction, coronary heart disease, ischemic stroke, coronary artery bypass grafting (CABG), or primary coronary intervention (PCI)), clinical presentation (chest discomfort, heart rate, systolic blood pressure on admission, and left bundle branch block on electrocardiogram), as well as in-hospital complications (cardiac arrest, cardiogenic shock, and acute stroke) and year of hospitalization (2001, 2006, 2011, 2015). The outcomes included: 1) in-hospital mortality or withdrawal from treatment due to a terminal status at discharge; and 2) in-hospital composite of major complications (including death, withdrawal from treatment, re-infarction, shock, ischemic stroke, or congestive heart failure (Appendix). Hospital characteristics included teaching status, PCI capability, economic geographic regions, and urban or rural location.

Organizational learning culture was measured with Learning Organization Survey

(LOS-27, an abbreviated version of the original Garvin et al. Learning Organization Survey).[18] The LOS-27 consists of 27 questions, grouped into 7 domains of organizational learning characteristics, including supportive learning environment, time for reflection, leadership that reinforces learning, experimentation, training, knowledge acquisition, and performance monitoring.

Statistical analysis

To examine the trends at both the population and hospital levels across different study periods, p-values for trends were reported using the Cochran–Armitage test. We described the hospital-level distribution of the IV magnesium sulfate use among the hospitals with at least 10 patients with AMI in the study years. To further understand the hospital-level variation in IV magnesium sulfate use, we quantified inter-hospital variation using the median odds ratio (MOR), by constructing generalized estimating equations in 2001, 2006, 2011, and 2015, respectively. MOR represents the average (median) OR for receiving IV magnesium sulfate for 2 AMI patients with similar clinical characteristics admitted to 2 randomly selected hospitals.

To understand the most current pattern in IV magnesium sulfate use, we constructed multivariable models using the data from 2015, which also adopted generalized estimating equations to account for the clustering of patients within hospitals. Factors were selected based on clinical judgment and literature review,[10,11] including patient and hospital characteristics. All covariates showed in Table 1, except those with frequencies below 1%, were included in the multivariable model. We transformed continuous variables (e.g. age and heart rate) into categorical variables using clinically meaningful cut-off values, and then created dummy variables. From the multivariable model in 2015, we then computed risk-standardized rates for each hospital separately. The risk-standardized rate was calculated as the ratio of observed to predicted outcomes, multiplied by the overall unadjusted rate, a form of

indirect standardization. Regarding the different dosage of IV magnesium sulfate, we conducted a sensitivity analysis to compare patients receiving multiple doses to those receiving a single dose of or no IV magnesium sulfate.

To compare the outcomes between patients with and without IV magnesium sulfate, we applied propensity score matching to adjust differences in observed characteristics between them. We obtained the log odds of the probability that patients received IV magnesium sulfate with modeling a function of all the variables in Table1. Then we performed a one-to-one no replacement match between the two groups based on the estimated propensity score. The no IV magnesium sulfate patients was matched if patient had the closest score with a randomly selected IV magnesium sulfate patient, and were considered eligible to match if the estimated logit within 0.6 standard deviation of the selected IV magnesium sulfate patient. This matching interval has been shown to eliminate approximately 90% of the bias in observed confounders (Appendix).[19]

For the questionnaire with LOS-27 (Appendix), we analyzed the responses at the hospital level by calculating the average of the 2 responses to each question. Responses were categorized as positive if they were ≥5 on a 7-point scale or ≥4 on a 5-point scale. We then calculated the positive response rate at each hospital as the proportion of questions that had a positive response by the hospital, and demonstrated the correlations between positive response rate and risk-standardize rate of IV magnesium sulfate use in 2015, as well as the reduction in IV magnesium sulfate use from 2011 to 2015.

All comparisons were two-sided, with statistical significance defined as p less than .05. Statistical analysis was done with SAS software, version 9.4, and R software, version 3.3.1.

Patient and Public Involvement statement

Patients or public were not involved in the development of the study protocol.

RESULTS

Study population

We identified 28,208 patients with AMI in 2001, 2006, 2011 and 2015 admitted to 162 hospitals. After excluding patients with hypokalemia (<3.5 mmol/L, n= 3,790), 24,418 patients remained, including 2,073 in 2001, 3,888 in 2006, 8,117 in 2011 and 10,340 in 2015 (**Figure 1**). Almost half (41.2%) of the patients were hospitalized in rural areas. In the study population, the average age was 65.1±12.7 years, 29.7% were female, almost three quarters had at least one cardiac risk factors (hypertension, diabetes, dyslipidemia or smoking), and about 10% had has a prior myocardial infarction or ischemic stroke (**Table 1**).

Temporal trends and regional variations in IV magnesium sulfate use

Over time, there was a significant initial decrease in the use of IV magnesium sulfate, from 32.1% (665) in 2001 to 18.4% (715) in 2006, 15.4% (1,251) in 2011 and 17.1% (1,763) in 2015 (p< .001 for trend) (**Figure 2**). There was significant variation in the temporal trends of use of IV magnesium sulfate across the five strata (p< .001 for interaction). In general, the decline was greater in the Eastern region [16.8% (from 33.3% in 2001 to 16.5% in 2015), p< .001] and Western region [16.6% (from 34.8% in 2001 to 17.2% in 2015), p< .001], compared with the Central regions [7.8% (from 25.9% in 2001 to 18.1% in 2015), p< .001]. There was a more modest difference between rural areas [16.3% (from 31.6% to 15.3%), p< .001] than in urban areas [13.9% (from 32.4% to 18.5%), p< .001]. No significant association was found between the positive response rate of LOS-27 in 2013 and the hospital-level

reduction in IV magnesium sulfate use from 2011 to 2015 (R^2=0.011, p= .237) (Appendix).

Hospital-level distributions in IV magnesium sulfate use

We examined hospital-level rates of IV magnesium sulfate use among hospitals with 10 or more cases per year, and observed a downward trend in the median, from 17.4% in 2001, 9.1% in 2006, 8.0% in 2011 to 10.7% in 2015 (**Figure 3**). However, the proportion of hospitals still using magnesium sulfate were 81.3% in 2001, 84.8% in 2006, 76.6% in 2011, and 77.9% in 2015, with no significant decline (p for trend = .26). Even in 2015, a quarter of hospitals had rates of IV magnesium sulfate use exceeding 25%. The MORs (95% CI) of each year characterized similar degrees of hospital-level variation (6.03 (3.93-8.52) in 2001, 3.86 (3.00-.4.77) in 2006, 4.26 (3.38-5.20) in 2011, and 4.72 (3.70-5.83) in 2015).

Patient and hospital characteristics associated with IV magnesium sulfate use

In univariate analysis, patients receiving IV magnesium sulfate were more likely to not have diabetes, dyslipidemia or a prior revascularization, were more likely to have had a prior ischemic stroke or cardiac arrest at presentation. They were more likely to receive reperfusion therapy, be at urban hospital, or be in Central or Western regions (**Table 1**). In the multivariable model, presence of cardiac arrest at admission (OR 3.38, 95% CI 2.50-5.82, P< .001), receipt of aspirin within 24h (1.43(1.22-1.67), statin use (1.33(1.13-1.57), reperfusion therapy (1.67 (1.35-1.90) for fibrinolytic therapy, 1.69 (1.44-1.98) for primary PCI, both P< .0001), and onset of heart failure (OR 1.69, 95% CI 1.34-2.09, P< .001) were positively associated with IV magnesium sulfate use (Appendix). No significant difference was identified across the teaching status, economic geographic region and rural/urban of hospitals **(Table 1)**. The risk-standardized rate of IV magnesium sulfate use in 2015 was not associated with the positive response rate of LOS-27 (R^2=0.027, p= .04) (Appendix).

In-hospital outcomes of patients with and without IV magnesium sulfate use

In the patients treated with IV magnesium sulfate, the crude rates of in-hospital death (7.5% vs. 6.4%) (**Figure 4**), in-hospital death or treatment withdraw (10.8% vs. 9.5%), and in-hospital composite of major complications (22.0% vs. 17.6%) were higher than patients without IV magnesium sulfate therapy (P< .01 for all). After adjusted for hospital characteristics, patient risk profiles, medication and reperfusion therapies, using propensity score matching, the in-hospital death rates were not significantly different between the treated and non-treated patients (OR 1.13, 95% CI 0.96-1.33, P= .15). However, the patients treated with IV magnesium sulfate had still higher risk for in- hospital death (OR 1.18,95%CI 1.03-1.36, P=. 01), in-hospital death or treatment withdraw (OR 1.24, 95% CI 1.09-1.41, P= .001), and in- hospital composite of major complications (OR 1.32, 95% CI 1.19-1.47, P< .001).

Different Dose of IV magnesium sulfate

We hypothesized that that magnesium sulfate prescribed more than once was more likely to be a routine administration than the single dose that is commonly used for repletion or arrhythmias. Thus, we conducted a sensitivity analysis focusing on multiple doses. The sensitivity analysis showed that there was also a significant decrease in the multiple doses of IV magnesium sulfate, from 28.9% in 2001 to 14.5% in 2006, 10.9% in 2011 and 11.31% in 2015 (p< .001 for trend). Nearly identical predictors of IV magnesium sulfate use were found when we compared patients receiving multiple doses to those without IV magnesium sulfate (Appendix).

DISCUSSION

In this large nationally representative study, we found that despite an initial decline in the use of IV magnesium sulfate for patients with AMI in China after 2001, about 1 in 6 patients continued to be treated with it through 2015. Furthermore, there was substantial variation in the use of IV magnesium sulfate use across hospitals. No

hospital characteristics were associated with IV magnesium sulfate use after adjusting for patient factors, including cardiac arrest and use of reperfusion therapy during hospitalization.

Our study is the first, to our knowledge, to characterize the rate of de-adoption of magnesium sulfate in patients with AMI in China. The only real-word study on the use of magnesium sulfate to treat AMI, which was based on data from the National Registry of Myocardial Infarction (NRMI-2) in the United States, found that the use rate of magnesium sulfate in patients within first 24 hours after AMI was 5.1% in 2001 – 5 years after the US guideline recommended against the use of magnesium sulfate.[20] Questionnaire for chief cardiologist from 2500 hospital in China in 1998 revealed that 47% of physician would prescribe magnesium sulfate for patients with AMI.[21] In contrast in 2015, three-fold more Chinese patients with AMI were receiving magnesium sulfate. This is congruent with a survey among cardiologists in 2012, where over one fifth reported that they were routinely using magnesium sulfate in patients with ACS.[22]

Several patient characteristics were identified to be associated with the use of IV magnesium sulfate for AMI. It was plausible that the presence of cardiac arrest or reperfusion therapy may spur some physicians to use magnesium sulfate to prevent arrhythmias, according to prior studies in both China and other countries.[1 6 23-26] These explanations, even though not recommended by the guidelines, highlighted the gaps in physicians' practice and highlights the needs for targeted education in the future.

The hospital-level and regional variations in IV magnesium sulfate highlights the marked variability with which different hospitals adopted new evidence about the lack of benefit from IV magnesium sulfate use. On the one hand, magnesium sulfate use

in 2015 was neither associated with hospital-specific characteristics, nor different across geographic or socio-economic regions. The teaching status or tertiary level did not translate into the better performance in this measure, which underscores the widespread need for continued education and evaluation of clinical practice. On the other hand, the regional variation in de-adoption of magnesium sulfate during the 15-year period seemed not directly related to the regional socio-economic development status that might be assumed to affect the resources available for acquiring and implementing guideline recommendation. Moreover, no evidence connects organizational learning culture with high performance, even much has been observed in studies of US hospitals.[27] Given our findings, more research is needed to better understand current practice patterns that cause some hospitals to still use ineffective therapies.

Our findings raise several questions about the dissemination and implementation of evidence and guidelines in China, particularly regarding education for physicians when long-standing therapies are demonstrated to be non-beneficial, and need to be de-adopted. We hypothesized that several factors may explain why the rate of magnesium sulfate use has remained relatively high in China. First, few actions have been taken to disseminate guidelines – after China published the guideline against IV magnesium sulfate for AMI in 2001,[8] the textbook used in all Chinese medical colleges had not stopped recommending IV magnesium sulfate use in patients with AMI until 2009.[28] Second, China's hospital system is short for mechanisms to facilitate the implementation of guideline recommendations, and systematic approaches for monitoring the performance of hospitals and physicians in following the guidelines are lacking in China.[29]

The successful de-adoption of non-beneficial or potentially harmful therapies for corresponding disease, which could reduce costs and potentially prevent

complications, requires more than increased efforts from the part of guideline developers.[12] After the dissemination of the guideline, more complicated issues need to be addressed, including how to develop tools reminding and alerting physicians when non-recommended therapies are ordered, how to establish a system to report feedback periodically on the appropriateness of treatment by practitioners and hospitals, how to design an accountability-oriented mechanism to prohibit ineffective regimen being prescribed, etc.[30] These issues could only be properly addressed through collaborations with researchers, educators, policymakers and other stakeholders.[31 32]

This study has several limitations that warrant consideration. First, we could not exclude patients with some indications, such as hypomagnesaemia and episodes of Torsade de pointes. However, we estimate that the influence is relatively small given low prevalence of these conditions previously reported.[33 34] Second, we did not have the ability to prospectively ask clinicians why they were prescribing IV magnesium sulfate, which limited our capability to gain better understanding of the use pattern and influencing factors. Third, our data were acquired retrospectively through medical record abstraction. Thus, the quality of our data depends on the accuracy and completeness of prior documentation and abstraction. Nevertheless, the standardized procedures for abstraction of medical records ensure the reliability of our results in describing the use pattern of magnesium sulfate in the real world. Also, we analyzed the data at the hospital level and were not able to determine whether the observed patterns were due to only a few physicians, or were common throughout a hospital's staff. Finally, residual confounding of measured or unmeasured variables might affect the observed results about in-hospital outcomes of patients with and without IV magnesium sulfate use.

In conclusion, the de-adoption of magnesium sulfate for patients with AMI is

suboptimal, moreover, the decrease of rate was slowing down recently, steady at an unacceptably high level. Our findings highlight the need for more efficient mechanisms to translate evidence-based therapies into clinical practice in China to improve patients' outcomes and reduce medical waste.

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CONTRIBUTORS

XL, JL and HMK conceived the China PEACE study and take responsibility for all aspects of it. XW, XD, JL, FAM, JAS, JL, HMK and XL designed the study. XW and XD wrote the first draft of the article, with further contributions from HY, EB, ND, JAS, FAM, JL, WG, HMK and XL. SH, YG and XB did statistical analysis. XL had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors interpreted data and approved the final version of the article.

DISCLOSURES

There are no relevant conflicts of interest.

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DATA SHARING STATEMENT

Extra data is available by emailing xi.li@fwoxford.org.

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Table 1. Baseline characteristics of using IV magnesium sulfate

Characteristics	Overall	Use N(%)	Non-Use(%)	P value
Patient characteristics				
Age				0.234
<55	5262(21.5)	938(21.3)	4324(21.6)	
55-64	5821(23.8)	1072(24.4)	4749(23.7)	
65-74	6989(28.6)	1290(29.4)	5699(28.5)	
>=75	6346(26.0)	1094(24.9)	5252(26.2)	
Gender				0.144
Female	7257(29.7)	1346(30.6)	5911(29.5)	
Male	17161(70.3)	3048(69.4)	14113(70.5)	
Hypertension	12551(51.4)	2247(51.1)	10304(51.5)	0.7
Diabetes	4758(19.5)	768(17.5)	3990(19.9)	<.001
Dyslipidemia	1588(6.5)	235(5.3)	1353(6.8)	<.001
Currently smoking	8084(33.1)	1496(34.0)	6588(32.9)	0.144
Prior ischemic stroke	2706(11.1)	546(12.4)	2160(10.8)	0.002
Prior myocardial infarction	2504(10.3)	416(9.5)	2088(10.4)	0.057
Prior CABG/PCI	713(2.9)	104(2.4)	609(3.0)	0.016
Chest discomfort	22211(91)	4021(91.5)	18190(90.8)	0.161
Left branch block at presentation	342(1.4)	65(1.5)	277(1.4)	0.624
Cardiac arrest at presentation	271(1.1)	81(1.8)	190(0.9)	<.001
Cardiogenic shock at presentation	1436(5.9)	279(6.3)	1157(5.8)	0.145
Acute stroke at presentation	530(2.2)	77(1.8)	453(2.3)	0.036
Heart rate at presentation, bpm				0.052
<50	1019(4.2)	177(4)	842(4.2)	
50-110	21760(89.1)	3886(88.4)	17874(89.3)	
>110	1639(6.7)	331(7.5)	1308(6.5)	
SBP at presentation, mmHg				0.004
<120	8181(33.5)	1565(35.6)	6616(33.0)	
120-139	7534(30.9)	1299(29.6)	6235(31.1)	
140-159	5041(20.6)	913(20.8)	4128(20.6)	
>=160	3662(15.0)	617(14.0)	3045(15.2)	
New onset of heart failure	2506(10.3)	569(12.9)	1937(9.7)	<0.001
Medication within 24-hour				
Aspirin	13742(56.3)	2688(61.2)	11054(55.2)	<0.001
ACE inhibitors or angiotensin receptor blockers	13662(56)	2541(57.8)	11121(55.5)	0.006
β-blockers	10051(41.2)	1768(40.2)	8283(41.4)	0.169
Clopidogrel	10572(43.3)	1845(42)	8727(43.6)	0.054
Statins	13031(53.4)	2398(54.6)	10633(53.1)	0.076
Reperfusion therapies				<.001
No reperfusion	18720(76.7)	3130(71.2)	15590(77.9)	
Fibrinolytic therapy	3136(12.8)	746(17.0)	2390(11.9)	
Primary PCI	2562(10.5)	518(11.8)	2044(10.2)	
Hospital characteristics				
Teaching hospital	19081(78.1)	3462(78.8)	15619(78.0)	0.252
PCI-capable hospital	15876(65.0)	2768(63.0)	13108(65.5)	0.002
Hospital level				0.075

Secondary or lower	9045(37.0)	1576(35.9)	7469(37.3)	
Tertiary hospital	15373(63.0)	2818(64.1)	12555(62.7)	
Economic geographic region				0.01
Eastern	13614(55.8)	2360(53.7)	11254(56.2)	
Central	5886(24.1)	1115(25.4)	4771(23.8)	
Western	4918(20.1)	919(20.9)	3999(20.0)	
Urban/Rural				0.003
Rural	10064(41.2)	1724(39.2)	8340(41.7)	
Urban	14354(58.8)	2670(60.8)	11684(58.3)	

Figure 1. Flowchart of study cohort

Figure 2. Trends of intravenous magnesium sulfate therapy in 2001, 2006, 2011 and 2015 in five economic-geographic regions.

Figure 3. IV magnesium sulfate use in 2001, 2006, 2011 and 2015 among all hospitals.

Figure 4. In-hospital outcomes between patients with and without IV magnesium sulfate.

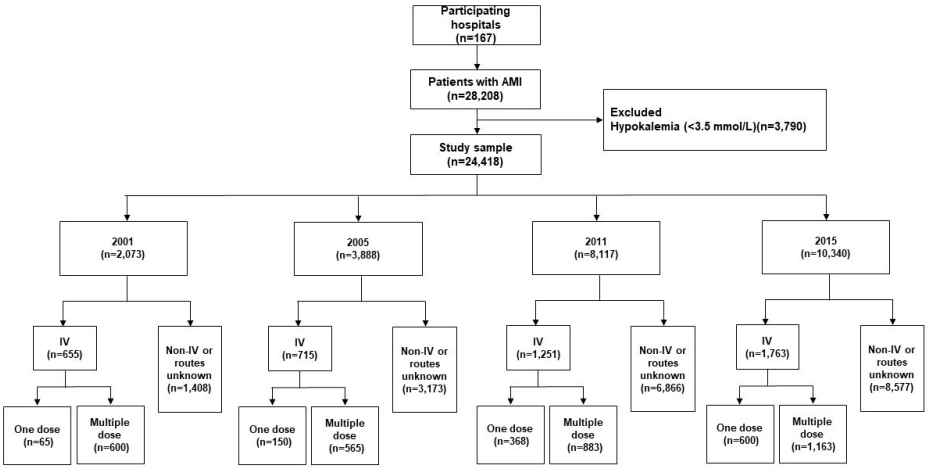


Figure 1

338x190mm (96 x 96 DPI)

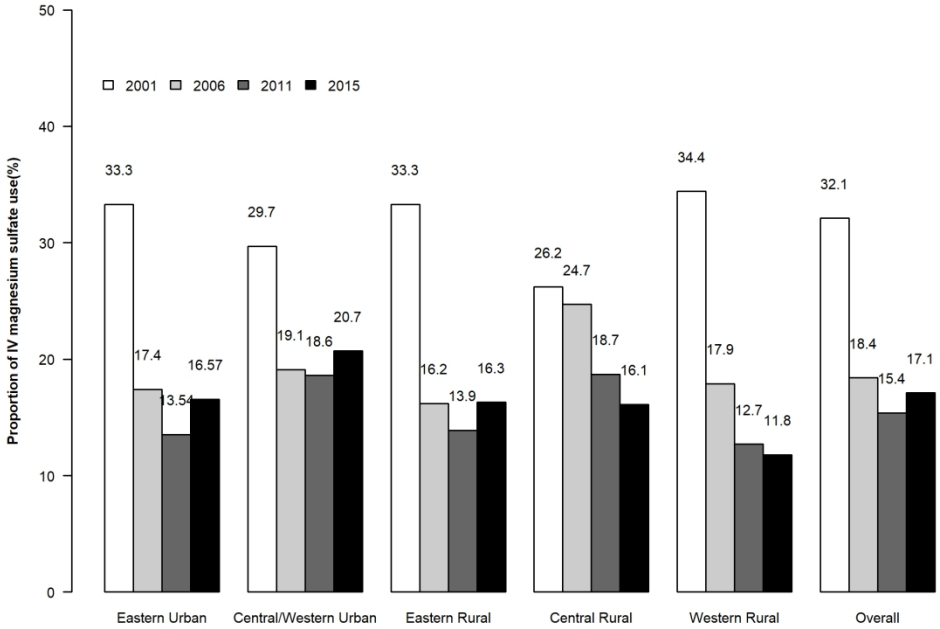


Figure 2

179x119mm (300 x 300 DPI)

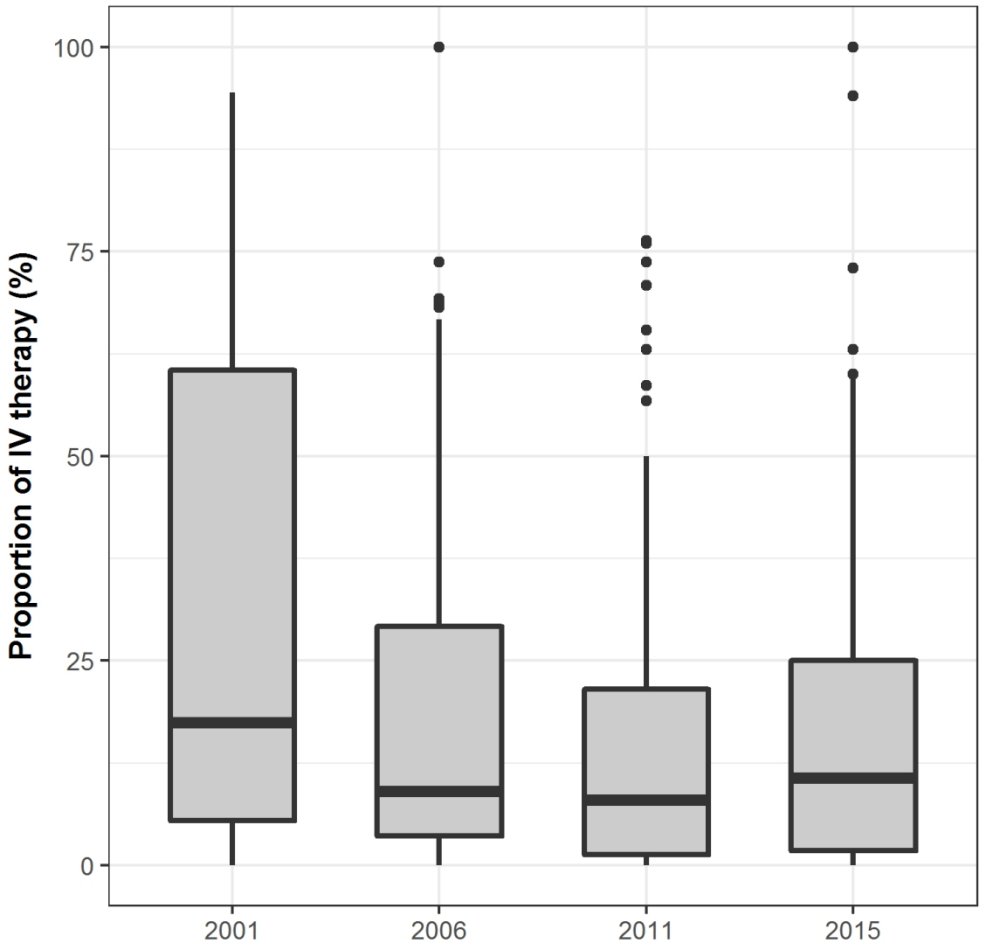


Figure 3

127x127mm (300 x 300 DPI)

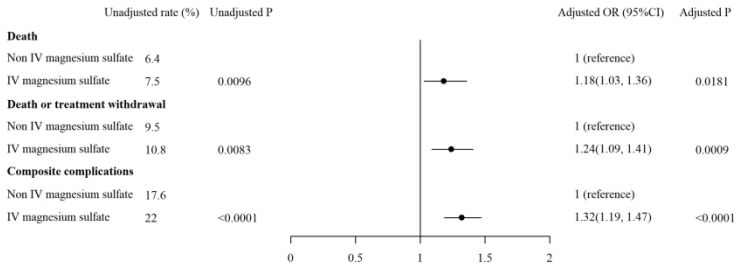


Figure 4

249x119mm (300 x 300 DPI)

APPENDIX

A. China PEACE-Retrospective AMI Study Site Investigators by Hospital

Aba Tibetan and Qiang Autonomous Prefecture People's Hospital, ShipingWeng, ShuyingXie; Affiliated Hospital of Guiyang Medical College, Lirong Wu, Jiulin Chen; Affiliated Hospital of Hainan Medical College, Tianfa Li, Jun Wang; Affiliated Zhongshan Hospital of Dalian University, Qin Yu, Xiaofei Li; Alxa League Central Hospital, Zhong Li, ShiguoHao, Yuzhen Zhang, Xuemei Wu; Baiquan County People's Hospital, Yachen Zhang, Zhifeng Liu; Biyang People's Hospital, Zhongxin Wang, HaoJia; Bortala Mongol Autonomous Prefecture People's Hospital, Bayin Bate, BadengQiqige; Changda Hospital Of Anshan, Xiang Jin, Ting Cai; Chengwu County People's Hospital, Fengqin Liu, Dayong Xu; Chenxi County People's Hospital, Xuejin He, Shui Yang; Chongren County People's Hospital, Chun Yuan, Jiping Wang; County People's Hospital of Jinning, LihuaGu, Lin Li, Shijiao Chen; Dalian Municipal Central Hospital, YongchaoZhi, Lili Sun; Dao County People's Hospital, Shengcheng Zhou, Lingjiao Jin; Daofu County People's Hospital, Yong Leng, Liangchuan Zhang, Tianyun Deng; Dingyuan County People's Hospital of Anhui Province, Yuanjin Wang, Wenhua Zhang, Xinmin Ma; Dongyang People's Hospital, Weimin Li, Liang Lu, Xuan Ge; Dulong and Nu Autonomous County People's Hospital of Gongshan, Xiaoping Wu, Yanming He; Dunhua City Hospital of Jilin Province, FanjuMeng, Jia Li; Fenghuang County People's Hospital, Dexi Liao, Guangyong Liu, Wen Qin; Fengshan County People’s Hospital, Wen Long, Xiangwen Chen; Fourth Hospital of Baotou City, Baohong Zhang, Yonghou Yin, Bin Tian; Fourth People's Hospital of Zigong City, Yong Yi, Chaoyong Wu; Fugu County People's Hospital of Shaanxi Province, Baoqi Liu, Zhihui Zhao, Haiming Li; Fujian Provincial Hospital, YansongGuo, Xinjing Chen; Fuling Center Hospital of Chongqing City, Liquan Xiang, Lin Ning; Gannan County People's Hospital, Mei Chen, Xin Jin, Guiling Li; General Hospital of the Yangtze River Shipping, Xiuqi Li, Xing’an Wu; Gongcheng Yao Autonomous County People's Hospital, Congjun Tan, Mingfang Feng, Meili Wang; Guangchang County People's Hospital, Liangfa Wen, Xiang Fu, QunxingXie; Guilin People's Hospital, Wei Zhang, Yanni Zhuang, Hua Lu;Guiping People's Hospital, Jiaqian Lu, Yu Huang; Haerbin 242 Hospital, Yin Zhou, Qiuling Hu; Haiyan People's Hospital, Chunhui Xiao, Xiaoli Hu; Heling Ge Er County People's Hospital, Yongshuan Wu, Qiuli Wang; Helong Municipal People's Hospital, Youlin Xu, Xuefei Yu;

Henan Provincial People's Hospital, Chuanyu Gao, Jianhong Zhang, You Zhang; Heze Municipal Hospital, WentangNiu, Xiaolei Ma, Yong Wang; HGKY Group Company General Hospital, Xiaowen Pan, Yanlong Liu; Hua Xin HospitalFirst Hospital of Tsinghua University, Lifu Miao, Yanping Yin, Zhiying Zhang; Huairen People's Hospital, Shutang Feng; Huayin People's Hospital, Aiping Wang, Jiangli Zhang, Feipeng Li; Huaying People's Hospital , Hong Wang; Hunchun Hospital, Lijun Yu, Xinxin Zhao; Huizhou Municipal Central Hospital, Yuansheng Shen, Zhiming Li, Lizhen He; Hunan Province Mawangdui Hospital, ZhiyiRong, Wei Luo; Ji'an Municipal Central People's hospital, Xueqiao Wang; Jianghua Yao Autonomous County People's Hospital, Rongjun Wan, Jianglin Tang, Guanghan Wu; Jiangsu Haimen People's Hospital, Jie Wu, Bin Xu; Jiangxi Provincial People's Hospital, Qing Huang, Xiaohe Wu; Jiangzi County People's Hospital, Sang Ge, Pian Pu, PingcuoDuoji; Jilin Province People's Hospital, Hui Dai, Yuming Du, Wei Guo; Jilin Integrated Traditional Chinese & Western Medicine Hospital, Jilin Province, Jianping Shi; Jinghai County Hospital, Peihua Zhao, Jingsheng Sun; Jingxi County People's Hospital, Hongxiang Li, Wen Liang; Jingxing County Hospital, Zhiwen Dong, Zhenhai Zhao; Jingzhou Central Hospital, Xin Li, Qin Xu; Jiuquan City People’s Hospital, Yaofeng Yuan, Zhirong Li; Jixi People's Hospital of The Jixi Municipal People's Hospital Medical Group, Jinbo Gao; Jize County Hospital, Qiu’eGuo; Kangbao County People's Hospital, Ruiqing Zhao, Guangjun Song; Keshiketengqi Hospital of Chifeng City, Lize Wang, Haiyun Song; Lanping Bai and Pumi Autonomous County People's Hospital, Jinwen He, Jinming He; Laoting County Hospital, Keyong Shang, Changjiang Liu, Kuituan Xi; Liaoyang Central Hospital, Rihui Liu, Peng Guo; Liaoyuan Central Hospital, ChaoyangGuo, Xiangjun Liu, Rujun Zhao, Zeyong Yu; Lindian County Hospital, Wenzhou Li, Xudong Jing, Huanling Wang; Linxiang People's Hospital, Xiyuan Zhao, Chao Zhang, Long Chen; Liujiang County People's Hospital, Meifa Wei, Yan Liu, Shengde Chen; Longyan First Hospital, Kaihong Chen, Yong Fang, Ying Liao; Luancheng County Hospital, Junli Wang, Tianyu Liu, Suzhe Cheng; Lucheng People's Hospital, Yunke Zhou, XiaoxiaNiu, Huifang Cao; Luchuan County People's Hospital, Zebin Feng, Min Feng; Luxi County People's Hospital, FeilongDuan, Haiming Yi; Luyi County People's Hospital, Yuanxun Xu, AnranGuo; Macheng People's Hospital, Xianshun Zhou, HongzhuanCai, Peng Zheng; Mengcheng First People's Hospital, GaofengGuo; MenglianLahudaiwa autonomous counties People's Hospital, Xiang Li; Min County

People's Hospital, MinwuBao, Yuhong Liu; Nanjing First Hospital, Shaoliang Chen, HaiboJia, Hongjuan Peng; Nan'an Hospital, Duanping Dai, Shaoxiong Hong; Nantong Third People's Hospital, Song Chen, Dongya Zhang, Ying Wang; Nanyang Central Hospital, Yudong Li, Jianbu Gao, Shouzhong Yang; Ningwu County People's Hospital, Junhu An; Peking University People's Hospital, Chenyang Shen, Yunfeng Liu; Peking University Shenzhen Hospital, Chun Wu, Huan Qu, Saiyong Chen; People's Hospital of Jingyu, Yuhui Lin, Dehai Jiao; People's Hospital of Yueqing City, Manhong Wang, Qiu Wang; Pianguan County People's Hospital, YingliangXue, Ruijun Zhang; Puding County People's Hospital, Cheng Yuan, Lei Wu; Qinghai Red Cross Hospital, Jianqing Zhang, Chunmei Wei, Yanmei Shen; Qinshui County People's Hospital, Hehua Zhang, Hongmei Pan, Yong Gao; Qinyang People's Hospital, Xiaowen Ma, Yanli Liang, Tianbiao Wang; Queshan County People's Hospital, Daguo Zhao; Quzhou People's Hospital, XiaomingTu, Zhenyan Gao; Rongjiang County People's Hospital, Fangning Wang, Qiang Yang; Rudong County People's Hospital, Xiaoping Kang, Jianbin Fang, Dongmei Liu; Ruyang County People's Hospital, Chengning Shen, Mengfei Li; Shangluo Central Hospital, Yingmin Guan, Wenfeng Wang, Ting Xiao; ShangqiuChangzheng People's Hospital, Qian Wang; Shaoyang County People's Hospital, Fengyun Jiang, Kaiyou Wu; Shengsi People's Hospital, Songguo Wang; Shenyang Weikang Hospital, Xujie Fu, Shu Zhang,Lifang Gao; ShougangShuicheng Iron & Steel (Group) Co·, Ltd. General Hospital, Min Zhang, Kai Fu, XiaojingDuan; Shuangshan Hospital Of Anshan, Rui Xiao, Ruixia Wu, Bin Li; Siziwang County People's Hospital, Hongtu Zhang, Yuerong Ma, Zhonghui Cao; SunanYugur Autonomous County People's Hospital, Zhansheng Ba, Wanhai Fu; Taizhou Hospital of Zhejiang Province, Jianjun Jiang, YafeiMi, Weiwei Zhou; The Affiliated Hospital of Beihua University, Feng Sun, Qi Zhang, Shiyu Zheng; The Fifth People's Hospital of Dalian, Jing Zhang, Yang Zhong; The First Affiliated Hospital of Hebei North University, Fangjiang Li, Xiaoyuan Wang; The First Affiliated Hospital of Henan University of Science & Technology, Pingshuan Dong, Laijing Du, Wei Liu; The First Affiliated Hospital Of Jia Mu Si University, Zhaofa He, Meihua Jin; The First Hospital of Fuzhou City, Ting Jiang, Zhuoyan Chen; The First Hospital of Xi'an, Manli Cheng, YuqiangJi; The First People's Hospital of Danzhou, Youhua Zhou, Jvyuan Li; The First People's Hospital of Guangzhou, Yizhi Pan, Jian Liu; The First People's Hospital of Guangyuan, Tianxun Wang, Ping Yang; The Fourth People's

Hospital of Shangqiu Shi, Guiyu Huang, JianjunPan,QingliangCai,Qianying Wang; The General Hospital of Yongzhou, Hunan Province, MingliLv; The people's hospital of Wuchuan, Yuanming Yi, Xuelian Deng; The People's Hospital of Yuanling, Wenhua Chen, RongCai; The People's Hospital of Zhijiang City, Bing Zhang; The Second Affiliated Hospital of Harbin Medical University, Bo Yu, Yousheng Xu, Zhengqiu Wang; The Second Affiliated Hospital of Kunming Medical University, Jun Shu, Ge Zhang, Kai Li; The Second Central Hospital of Baoding City, Guang Ma, PuxiaSuo; The Second People's Hospital of Liaoyuan City, Aimin Zhang, Yongfen Kang; Tianjin Medical University General Hospital, Zheng Wan,Yuemin Sun, Bo Bian; Tibet Autonomous Region People's Hospital, Xuejun Hu, DawaCiren; Tongchuan Mining Bureau Central Hospital, GuojiongJia, Jieli Pan; Tongliang County People's Hospital, Guofu Li, Hongliang Zhang, Longliang Zhan; Tongliao City Horqin District First People's Hospital, Junping Fang, Xinli Yu; Ulanqab Central Hospital, Dacheng Wang, Dajun Liu, Xinhong Cao; Wencheng County People's Hospital, Yi Tian, HaishengZhu,Wanchuan Liu; Wuhai People's Hospital, Zhaohai Zhou, Lei Shi; Wuhu Second People's Hospital, Wuwang Fang, Manxin Chen; Wulate County People's Hospital, ,FuqinHan,JianyeFu,Yunmei Wang; Wuqiang County People's Hospital, Binglu Liu, YanliangZhang,Xiupin Yuan; Wuyishan Municipal Hospital, Qingfei Lin, Yun Chen; Xiangtan County People's Hospital, Yuliang Zhu, ZhiqiangCai; Xing County People's Hospital, Xingping Li, LirongAo; Xingshan County People's Hospital, Shubing Wu, Hui Zhang; Xinmi First People's Hospital, Fusheng Zhao, Guangming Yang; Xinshao County People's Hospital, Renfei Liu, Wenwei Ai; Xiuwu County People's Hospital, JianbaoChang,Haijie Zhao; Xuanhan County People's Hospital, Qijun Ran, Xuan Ma; Xupu County People's Hospital, Shijun Jiang, Xiaochun Shu; Yanggao County People's Hospital, Zhiru Peng, Yan Han; Yanqing County Hospital, Jianbin Wang, Li Yang; Ying County People's Hospital, Yu Shen, Xingcun Shang; Yitong Manchu Autonomous County First People's Hospital, Haifeng Wang; Yongxing County People's Hospital, Hongyan Li, Zhisong Liao, Yang Cao; Yuanzhou District People's Hospital of Guyuan City, Xiaoping Gao, MeiyingCai, Lining You; Yuncheng Central Hospital, Xuexin Li, Shuqin Li, Yingjia Li; Yunlong County People's Hospital, Jianxun Yang, Song Ai, Jianfei Ma; Yuyao People's Hospital, Lailin Deng; ZhangjiachuanHui Autonomous County First People's Hospital, Keyu Wang, Shitang Gao, Jian Guan; Zhouning County Hospital, Banghua He, Youyi Lu; Zhuoni

County People's Hospital, Weirong Yang, Hong Li; Zhuozi County People's Hospital, Zhizhong Zhang, Xiaohong Chi; Zuoyun County People's Hospital, Ru Duan, Guangli Wang.

B. China PEACE hospital survey: design, conduction, and materials

Participants

In the collaborative network, we invited the principal investigator and the coordinator of each hospital to participate in the survey. The definitions of the roles were established during the planning phase of the China PEACE-Retrospective AMI Study: typically, the director of the Cardiology Department or Internal Medicine Department at each hospital served as the principal investigator, and the China PEACE study coordinator was most often a physician selected by the principal investigator.

Survey design

We organized the survey in 4 sections: personal information of the respondent (part A); general information about the hospital and the department in charge of AMI care (part B); information about hospital practices relating to the diagnosis and treatment of cardiovascular heart disease (part C); and organizational learning characteristics and quality improvement for AMI care (part D). Organizational learning culture was measured using questions from the Short-Form Learning Organization Survey (LOS-27) and the Survival after AMI (SAMI) study.

The survey was written in English and translated into Chinese. To ensure accuracy, a double translation was conducted in which the survey was translated into Chinese and then back into English independently by 2 bilingual Chinese medical researchers. Modifications were made to the Chinese translation accordingly. Participants were informed at the start of the survey that their responses would be used to study institutional characteristics and medical care patterns.

Survey conduction

The survey was piloted using a convenience sample of 6 hospitals with percutaneous coronary intervention capability. The principal investigators were invited to participate in the pilot, and one study coordinator also volunteered to participate. The responses of the 6 principal investigators (3 via in-person interviews and 3 via self-administered paper-based survey) and 1 study coordinator (via self-administered paper-based survey) were collected. The cognitive interviewing methodology, in which individual in-person interviews were conducted with each pilot participant, was used to assess understanding of the pilot survey. For paper-based pilot surveys, cognitive interviewing consisted of retrospective (post-survey) probes; for in-person interviews, concurrent (during survey) probes allowed

participants to provide survey feedback in real-time. Based on the experience from the pilot, minor revisions were made to clarify the meaning of certain questions, and the sequence of questions was modified to improve logic and flow. No questions were removed or added. All data from the pilot testing were included in the final data set.

The survey was available in 2 forms: web-based e-survey, in which each participant was able to log in with a unique password to a website where the survey was hosted, and PDF-based survey, in which subjects digitally marked their answers in PDF files and returned the files via email. We applied 2 methods to ensure the quality of the responses. We checked the response data for completeness, either by automatic verification (web-based) or by manual check by our staff (PDF-based), and on the basis of logic. For the web-based e-survey submissions, we used automatic logic check and verification while subjects were responding to the survey, and recorded total time spent on the survey. For the PDF-based survey submissions, we conducted a manual logic check, focusing on whether subjects correctly skipped inapplicable questions as indicated by the instructions in other parts of the survey. In cases of missing or illogical (e.g., questions incorrectly skipped or completed) data for PDF-based surveys, we contacted respondents by email and/or phone, informed them of which questions needed to be resolved, and asked them to resubmit the survey with the necessary changes.

Survey questionnaires

A.	**Personal information**
A.1	Gender: ○ Male ○ Female
A.2	Education ○ Junior high school ○ Senior high school (technical school or technical secondary school) ○ College (junior college) ○ Postgraduate
A.3	Clinical job title: ○ Consultant ○ Attendant ○ Resident ○ Nurse ○ Other, please specify: ___
A.4	Senior administrative position in hospital: ○ No ○ Yes, please specify: ___
A.5	You have been working in the department for __ years.

B.	**General Information of the hospital and the department**
	Instructions: This section focuses on characteristics of your hospital and department. For all questions, please reflect upon them during the 1-year period from 1/1/2011 to 12/31/2011 (for some of them, please consider 1/1/2001 to 12/31/2001, and 1/1/2006 to 12/31/2006, as specified). Even some questions in this section might be somewhat hard to answer immediately, especially those about the characteristics of your hospital or department in 2001 and 2006. Please try best to find the answer - as accurate as possible - to every applicable question.
B.1	Affiliated hospital of medical college: ○ No ○ Yes, please specify the name of the college: _____ **[Skip to B3]**
B.2	Teaching hospital of medical college: ○ No ○ Yes, please specify the name of the college: _____

Total No. in your department

		In 2001	**In 2006**	**In 2011**
B.3	Beds			
B.4	Consultants			
B.5	Attendants			
B.6	Residents			
B.7	Nurses			

B.8	Is there any other department in your hospital providing inpatient treatment for AMI? ○ No ○ Yes, please specify the name of the department: _____
B.9	Coronary Care Unit (CCU) in hospital? ○ No ○ Yes, please specify the No. of beds: _____
B.10	Cath lab in hospital? ○ No **[Skip to B12]** ○ Yes, please specify when started: _____
B.11	How many qualified cardiac interventionalist there are in your hospital: _____ ○ unknown
B.12	Could CABG be performed in hospital? ○ No ○ Yes, please specify the No. of cases in 2011: _____

B.13 Independent emergency department?
○ No ○ Yes, please specify the No. of cardiologists in charge in emergency department normally: _____

B.14 Formal GCP training of clinical staff in your department?
○ No ○ Yes ○ Unknown

B.15 Have your apartment participated in international clinical trials?
○ No ○ Yes, please specify the names of the trials: _____ ○ Unknown

B.16 SFDA certified site for CVD drug trials?
○ No ○ Yes ○ Unknown

B.17 Existence of Ethics Committee in hospital?
○ No ○ Yes ○ Unknown

Total No. in your hospital

		In 2001	In 2006	In 2011
B.18	Patients with stroke			
B.19	Patients with ischemic stroke			
B.20	Patients with hemorrhagic stroke			

B.21 Independent neurology department?
○ No ○ Yes, please specify the No. of beds in the department: _____

B.22 Carotid endarterectomy performed in hospital?
○ No ○ Yes, please specify when started: _____ ○ Unknown

B.23 Carotid stenting performed in hospital?
○ No ○ Yes, please specify when started: _____ ○ Unknown

The average cost of the following items in your hospital

	Items	Cost, ¥
B.24	Biochemical test, including glucose, lipid, liver function, renal function, CRP or hsCRP	
B.25	Coagulation function test	
B.26	BNP or NT-proBNP	
B.27	Stress test	
B.28	UCG	
B.29	Cardiac CT	
B.30	Carotid US	

C. Diagnosis and treatment for CHD

Instructions: This section focuses on hospital processes and care of patients with AMI. For all questions, please reflect upon them during the 1-year period from 1/1/2011 to 12/31/2011.

C.1 Routine diagnostic test of CK for ACS patients after admission?

○ No ○ Yes, please specify the average time delay in reporting results: _____ ○ Unknown

C.2 Routine diagnostic test of CK-MB for ACS patients after admission?

○ No ○ Yes, please specify the average time delay in reporting results: _____ ○ Unknown

C.3 Routine diagnostic test of troponin for ACS patients after admission?

○ No ○ Yes, please specify the average time delay in reporting results: _____ ○ Unknown

C.4 Are patients who are stable after PCI admitted to an intensive care unit? SAMI-Q25

○ Always ○ Usually ○ Sometimes ○ Rarely ○ Unknown

C.5 Did your emergency department use a uniform protocol to care for patients who arrived to the emergency department with **STEMI**? SAMI-Q26

○ No ○ Yes ○ Unknown

C.6 Did your emergency department use a uniform protocol to care for patients who arrived to the emergency department with **Unstable Angina/NSTEMI**? SAMI-Q27

○ No ○ Yes ○ Unknown

C.7 Did your hospital use simulations (i.e., trial exercises, dry-runs) to practice any of the following AMI care processes? ***[Check all that apply]*** SAMI-Q28

□ Door-to-balloon or door-to-drug protocols

□ Chest pain in hospitalized patients

□ Inpatient codes (e.g., cardiac arrest, respiratory failure)

□ None above

□ Unknown

C.8 To which patient care unit were patients who were stable with Unstable Angina/NSTEMI most likely admitted? SAMI-Q29

○ CCU ○ ICU ○ Step-down unit ○ Designated chest pain/telemetry/cardiology floor ○ General medicine floor ○ We did not have a routine method of assigning beds for patients with Unstable Angina/NSTEMI ○ Unknown

C.9 Did all, or nearly all, patients with AMI have a cardiologist as their primary attending physician? SAMI-Q30

○ No ○ Yes **[Skip to C11]** ○ Unknown

C.10 Were cardiology consults required for all patients with AMI? SAMI-Q30a

○ No ○ Yes ○ Unknown

C.11 In the intensive care unit, who was primarily responsible for the care of patients with AMI? ***[Check all that apply]*** SAMI-Q31

□ Critical care physicians (i.e., intensivists)

□ Cardiologist/s based exclusively in the unit

□ Other cardiologists

□ Other, please specify: _____

□ Unknown

C.12 Electronic medical record?

○ No **[Skip to C14]** ○ Yes, please specify when started: _____ ○ Unknown

C.13 Did your hospital use an electronic medical record (EMR) in the following areas? ***[Check all that apply]*** SAMI-Q34

□ Emergency department

□ Inpatient floors

□ Critical care units

□ Affiliated ambulatory offices/clinics

□ None above

C.14 On the inpatient floors, did your hospital have the following electronic capabilities? ***[Check all that apply]*** SAMI-Q35

□ Computerized assisted physician order entry

□ Computer prompts to alert user to potential drug-drug interactions or allergies

□ Computer prompts to alert user to potential errors in dosing and information

□ Computer prompts to alert user to medication order expiration

□ Computer prompts to improve adherence to core measures for AMI care (e.g., beta-blocker use)

□ None above

C.15 In the emergency department, were prior ECG's electronically available at the time of care? SAMI-Q36

○ No ○ Yes ○ Unknown

C.16 Did physicians regularly use explicit protocols or clinical pathways for patients with AMI? SAMI-Q37

○ No ○ Yes ○ Unknown

C.17 Did clinicians on the inpatient care units regularly use order sets (either paper-based or electronic) for patients with STEMI? SAMI-Q38

○ No ○ Yes ○ Unknown

C.18 Did clinicians on the inpatient care units regularly use order sets (either paper-based or electronic) for with Unstable Angina/NSTEMI? SAMI-Q39

○ No ○ Yes ○ Unknown

C.19 Which of the following types of physicians were at the hospital 24-hours/day and 7-days/week? ***[Check all that apply]*** SAMI-Q42

□ Critical care physicians (i.e., intensivists)

□ Non-interventional cardiologists

□ Interventional cardiologists

□ Cardiology fellows (including non-interventional and interventional)

□ Hospitalists

□ None above

C.20 Are there any protocols used to guide nurses on when to call the attending cardiologist for patients with AMI? SAMI-Q43

○ No ○ Yes ○ Unknown

C.21 Patients with acute coronary syndrome who arrived by Emergency medical service (ambulance):

○ None **[Skip to C25]** ○ 1–25% ○ 26–50% ○ 51–75% ○ 76-100% ○ Unknown

C.22 Emergency medical service routinely gives pre-alert calls?

○ No ○ Yes ○ Unknown

C.23 Patients with acute coronary syndrome who undergo ECG en route to hospital:

○ None ○ 1–25% ○ 26–50% ○ 51–75% ○ 76-100% ○ Unknown

C.24 Emergency medical service routinely tell your hospital the results of ECG?

○ No ○ Yes ○ Unknown

C.25 Formal training of triage staff for assessing acute coronary syndrome?

○ No ○ Yes ○ Unknown

C.26 Dedicated space in triage area for immediate ECG?

○ No ○ Yes ○ Unknown

C.27 Written criteria for immediate ECG in emergency department?

○ No ○ Yes ○ Unknown

C.28 Expected interval between patients' arriving and ECG?

○ ≤5 min ○ 6–20 min ○ >20 min ○ No expected time ○ Unknown

C.29 Dedicated ECG technicians in emergency department?

○ No ○ Yes, only some shifts ○ Yes, always ○ Unknown

C.30 Thrombolysis for AMI patients in hospital?

○ No **[Skip to C38]** ○ Yes, please specify when started: _____

C.31 Does your hospital have a set protocol to identify eligible patients for thrombolysis?

○ No ○ Yes ○ Unknown

C.32 Does your hospital have a set protocol to assess contraindications of thrombolysis?

○ No ○ Yes ○ Unknown

C.33 Who makes the decision about thrombolysis in your hospital?

○ Emergency medicine physician alone

○ Emergency medicine physician with a cardiac consultation

○ Only Cardiologist

○ Unknown

C.34 In your hospital, where do patients with AMI receive thrombolysis?

○ In the emergency department

○ In the cardiology department (or general medicine department)

○ In the ICU or CCU

○ Unknown

C.35 Where are the thrombolytic medicines stored and prepared?

○ Stored and prepared in the department where thrombolysis is done

○ Prepared in the department where thrombolysis is done, but stored in another location

○ Stored and prepared in some location other than the department where thrombolysis is done

○ Unknown

C.36 Informed Consent before thrombolysis?

○ Not necessary

○ Only orally obtained informed consent is needed

○ One written informed consent form is needed

○ More than one written informed consent form is needed

○ Unknown

C.37 Prepayment before thrombolysis?

○ No

○ Yes, please specify the average amount approximately: ___ ("-1" if unknown)

○ Unknown

C.38 Primary PCI was performed in your hospital for STEMI patients?

○ No **[Skip to C60]** ○ Yes, please specify when started: ___

C.39 Activation of catheterization laboratory on weekdays?

○ Emergency medicine physician with cardiologist

○ Cardiologist alone

○ Emergency medicine physician alone

○ Unknown

C.40	Activation of catheterization laboratory at night and on weekends? ○ Emergency medicine physician with cardiologist ○ Cardiologist alone ○ Emergency medicine physician alone ○ Unknown
C.41	Process for activating catheterization team? ○ After communicating with the emergency department, interventional cardiologist activates catheterization laboratory by calling staff or a central page operator ○ Emergency department makes at least two calls: one to the interventional cardiologist and another to a central page operator, who pages catheterization laboratory staff ○ Emergency department makes a single call to a central page operator, who then pages interventional cardiologist and catheterization laboratory staff ○ No standard approach ○ Other ○ Unknown
C.42	Activation of on-call staff for catheterization laboratory? ○ Page operator is not used ○ Page operator is used; confirmation of page receipt is required ○ Page operator is used; no confirmation of page receipt is required ○ No standard approach ○ Unknown
C.43	First physician notified after STEMI diagnosis in emergency department? ○ Cardiologist ○ Interventional cardiologist ○ Patient's primary care physician ○ Other or variable ○ Unknown
C.44	Laboratory and radiographic results are needed to activate catheterization laboratory? ○ Yes ○ No ○ No standard approach ○ Unknown

C.45	Process after emergency medical service transmits ECG results? ○ Emergency department waits for patient to arrive at hospital to determine whether catheterization laboratory should be activated ○ Emergency department contacts cardiologist while the patient is en route to determine whether catheterization laboratory should be activated ○ Emergency department activates catheterization laboratory while the patient is still en route to the hospital ○ No standard approach or variable approach ○ Not applicable because ECG data not transmitted en route ○ Not applicable because ECG never performed en route ○ Unknown
C.46	Expected interval between page and arrival of staff in catheterization laboratory? ○ ≤20 min ○ 21–30 min ○ >30 min ○ No expected time ○ Unknown
C.47	Expected interval between page and arrival of interventional cardiologist? ○ ≤20 min ○ 21–30 min ○ >30 min ○ No expected time ○ Unknown
C.48	Someone is always available to transport patients from emergency department to catheterization laboratory? ○ No ○ Yes ○ Unknown
C.49	Initiation of patient transport from emergency department to catheterization laboratory? ○ After catheterization laboratory notifies emergency department it is ready ○ A set interval after the decision is made regarding PCI ○ No standard approach ○ Other approach ○ Unknown

C.50 Minimum number of nurses and technicians required in catheterization laboratory before patient is transported from emergency department?

○ Interventional cardiologist must be present

○ Interventional cardiologist may not be present but need presence of 1 staff person

○ Interventional cardiologist may not be present but need presence of 2-4 staff person

○ No set number

○ Unknown

C.51 Elective catheterization cases rescheduled for emergency PCI?

○ Yes ○ No ○ It depends ○ Unknown

C.52 If interventionalist is present, number of staff required to begin PCI?

○ 1 ○ 2 ○ 3 ○ 4 ○ Unknown

C.53 Catheterization laboratory is left so that next PCI can begin promptly?

○ Yes ○ No ○ No standard policy ○ Unknown

C.54 Cardiology fellows participate in performing PCI?

○ No ○ Yes ○ Unknown

C.55 Staff in critical care area are routinely cross-trained to cover catheterization laboratory?

○ No ○ Yes ○ Unknown

C.56 Location of catheterization laboratory?

○ Elevator required to travel from emergency department

○ Same floor as emergency department

C.57 An attending cardiologist is always at the hospital?

○ No ○ Yes ○ Unknown

C.58 Informed Consent before primary PCI?

○ Not necessary

○ Only orally obtained informed consent is needed

○ One written informed consent form is needed

○ More than one written informed consent form is needed

○ Unknown

C.59 Prepayment before primary PCI?

○ No

○ Yes, please specify the average amount approximately ___ ("-1" if unknown)

○ Unknown

C.60 Does your hospital measure the following time intervals? ***[Check all that apply]***

□ Door to ECG

□ Door to needle

□ Door to balloon

□ None above

□ Unknown

C.61 Do your hospital feedback the time intervals to someone? ***[Check all that apply]***

□ No

□ Yes, to physician staff involved in the care

□ Yes, to nursing staff involved in the care

□ Yes, to pharmacy staff involved in the care

□ Yes, to other staff involved in the care

□ Unknown

C.62 Do your hospital report the analyze results about the time intervals regularly? ***[Check all that apply]***

□ No

□ Yes, to departments involved in the care (the emergency department, the cardiology department)

□ Yes, to other department in your hospital

□ Yes, to other institutions outside your hospital

□ Unknown

D. Organizational learning characteristics

Instructions: This section focuses on the organizational learning and measurements to improve AMI care, including supportive environment and leadership, experimentation and training, knowledge acquisition, reflection and performance monitoring, etc. Please draw on your own experiences in your current role working with clinical staff and administration. For all questions, please reflect upon them during the 1-year period from 1/1/2011 to 12/31/2011.
Although some questions in this section look similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each question fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems most reasonable.
The definition of "workgroup" below is the department, unit, ward, or group caring AMI patients that you are working at.
This section adopts 7-point (from highly inaccurate to highly accurate). If you think the options are difficult to understand or distinguish, please grade the accuracy here using actual numbers, while 1 is the lowest (highly inaccurate), 7 is the highest (highly accurate), then choose the corresponding option.

D.1 In this workgroup, people value new ideas.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.2 Clinicians are encouraged to creatively solve problems related to AMI care processes. (60)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.3 Innovative ideas about AMI care are shared widely in the hospital. (61)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.4 Differences in opinions are welcomed in this workgroup.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.5 In this workgroup, people are open to alternative ways of getting work done.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.6 People in this workgroup are eager to share information about what doesn't work as well as to share information about what does work.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.7 This workgroup frequently compares its performance to: Best-in-class organizations.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.8 This workgroup frequently compares its performance to: Other similar workgroups.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.9 This workgroup consistently collects information on technological trends.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.10 If you make a mistake in this workgroup, it is often held against you. (Among clinicians taking care of patients with AMI, there is a tendency to blame individuals for errors in patient care). (66)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.11 Clinicians caring for patients with AMI are easily able to address problems and tough issues with their department heads/chiefs. (56)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.12 Department heads/chiefs are easily able to address problems and tough issues with senior level administration.(57)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.13 Nurses are comfortable checking with physicians if they have concerns about patient care.(65)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.14 Clinicians involved in the care of patients with AMI value each others' skills and talents (e.g., physicians value nurses' skills and talents and vice-versa).(58)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.15 Clinicians involved in the care of patients with AMI avoid sharing responsibility for medical errors.

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always. (59)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.16 Were physicians explicitly encouraged to disclose medical errors to patients or their family members? (7)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.17 This workgroup engages in productive conflict and debate during discussions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.18 In this workgroup, we frequently identify and discuss underlying assumptions that might affect key decisions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.19 The hospital has the resources and information it needs to reduce 30-day mortality rates in patients with AMI. (51)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.20 Senior-level administration is supportive of efforts to improve AMI care. (52)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.21 There is simply no time for reflection in this workgroup.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.22 In this workgroup, people are too busy to invest time in improvement.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.23 My manager(s) establish(es) forums for and provide(s) time and resources for identifying problems and organizational challenges.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.24 My manager(s) establish(es) forums for and provide(s) time and resources for reflecting and improving on past performance.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.25 My manager(s) listen(s) attentively.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.26 My manager(s) invite(s) input from others in discussions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.27 This workgroup experiments frequently with new product/service offerings.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.28 This workgroup experiments frequently with new ways of working.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.29 This workgroup frequently employs pilot projects or simulations when trying our new ideas.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.30 This workgroup has a formal process for conducting and evaluating experiments or new ideas.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.31 Experienced employees in this workgroup receive training when new initiatives are launched.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.32 Experienced employees in this workgroup receive training when shifting to a new position.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.33 Newly hired employees in this workgroup receive adequate training.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.34 Did your hospital provide training to EMS providers about AMI care? (17)

○ Yes, about monthly

○ Yes, about quarterly

○ Yes, about annually

○ Yes, other: _____

○ No

○ Unknown

D.35 This workgroup has forums for meeting with and learning from: Experts from outside the organization.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.36 This workgroup has forums for meeting with and learning from: Experts from other departments/teams/divisions.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.37 This workgroup has forums for meeting with and learning from: Customers/clients.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.38 This workgroup regularly conducts post-audits, after-action reviews, and debriefings.

○ highly inaccurate ○ inaccurate ○ somewhat inaccurate ○ not sure ○ somewhat accurate ○ accurate ○ highly accurate

D.39 Did your hospital have regular 'morbidity and mortality' conferences (or another educational session) for discussing individual cases involving patients with AMI? (5)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.40 Did your hospital review the deaths of patients with AMI? (4a)

○ No, we did not review these cases **(go to D44)**

○ Yes, we reviewed only deaths with potential quality issues (i.e., unexpected deaths)

○ Yes, we reviewed *all* deaths

○ Other, please specify: _____

○ Unknown

D.41 Did your hospital have a **designated person or group** to review the deaths of patients with AMI (i.e., on an individual case level) that occurred during hospitalization? (4)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.42 How long after the occurrence of the death were the cases typically reviewed? (4b)

○ Within one week of the death

○ Within one month of the death

○ Within 3 months of the death

○ Other, please specify: _____

○ We did not have a set timeframe for reviewing these cases

○ Unknown

D.43 Who usually reviewed these cases? (4c)

a. Senior management of the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Cardiology chiefs

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Nursing directors

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Other physicians participating in the care of patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

e. Quality Improvement/Quality Management department staff

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.44 Did your hospital have a **designated person or group** to review any of the following **adverse events** in patients with AMI (i.e., on an individual case level)? (6)

a. Sentinel events (unexpected occurrence involving death or serious physical or psychological injury) that occurred during hospitalization

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Unexpected transfers from a floor (non-monitored unit) to an intensive are unit

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Catastrophic complications that occurred immediately after discharge from the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.45 How long after the occurrence of these adverse events were the cases typically reviewed? (6a)

○ Within one week of the adverse event

○ Within one month of the adverse event

○ Within 3 months of the adverse event

○ Other, please specify: _____

○ We did not have a set timeframe for reviewing these cases

○ Unknown

D.46 Who usually reviewed these cases? (6b)

a. Senior management of the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Cardiology chiefs

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Nursing directors

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Other physicians participating in the care of patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

e. Quality Improvement/Quality Management department staff

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

f. Other, please specify: ___

D.47 Did your hospital use root cause analysis or a similar method to understand the following problems in AMI care?

a. Poor adherence to the core medication (i.e., anti-platelet agents) measures

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Delay to fibrinolytic therapy or percutaneous coronary intervention (PCI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.48 Did your hospital review data on **30-day mortality rates** (deaths occurring within 30 days of admission, including both inpatient and post-discharge deaths) in patients admitted with AMI (Check all that apply) (10)

□ Yes, through the medical insurance data system

□ Yes, through a regional database system

□ Yes, we internally collect our own data on deaths

□ Yes, other, please specify: ___

□ No **[Skip to D52]**

□ Unknown

D.49 How quickly were **mortality rates** in patients with AMI available to your hospital (i.e., what was the most current data available to your hospital)? (10a)

○ Within 6 months of care delivery

○ 6 months to 1 year after care delivery

○ 1 - 2 years after care delivery

○ Less frequently than 2 years of care delivery

○ Unknown

D.50 Did your hospital regularly compare its performance to other hospitals on either **inpatient** in patients with AMI? (14)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.51 Did your hospital have **efforts** to improve any of the following inpatient acute myocardial infarction (AMI) quality measures? (1)

a. Adherence to the core medication (i.e., anti-platelet agents) measures

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Time to fibrinolytic therapy or percutaneous coronary intervention (PCI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.52 Beyond these quality measures, did your hospital initiate **efforts** to improve any of the following in patients admitted with AMI? (2)

a. Inpatient mortality in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. **Post-discharge** mortality (death occurring after discharge, but within 30 days of admission) in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Readmission within 30 days from prior admission in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.53 Did your hospital have a quality improvement **team(s)** devoted to improving: (3)

a. Inpatient mortality in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Post-discharge mortality (death occurring after discharge, but within 30 days of admission) in patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.54 3a. Please indicate members of either the inpatient or post-discharge mortality **team(s)**.

a. Senior management of the hospital

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Hospital governing board

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Chief of cardiology

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Nursing directors

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

e. Other physicians participating in the care of patients with AMI

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

f. Quality Improvement/Quality Management department staff

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

g. Other please specify: _____

D.55 Nurses are engaged in efforts to improve AMI care. (53)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.56 Cardiologists are engaged in efforts to improve AMI care. (54)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.57 Emergency medicine physicians are engaged in efforts to improve AMI care. (55)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.58 Did your hospital have one or more physician champions focused on improving either **inpatient** or **30-day mortality** in patients with AMI? (12)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.59 Did your hospital have one or more nurse champions focused on improving either **inpatient** or **30-day mortality** in patients with AMI? (13)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.60 After we make changes to improve AMI care, we fail to evaluate their effectiveness. (67)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.61 Did cardiology and emergency department staff meet together to review care for patients with AMI? (15)

○ Yes, about monthly

○ Yes, about quarterly

○ Yes, about annually

○ Yes, other: _____

○ No **[Skip to D63]**

○ Unknown

D.62 What was typically discussed at these meetings? (15a).

a. Care of patients with ST-elevation myocardial infarction (STEMI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. Care of patients with Unstable Angina/**non**-STEMI (NSTEMI)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Care of patients with chest pain, in general

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.63 Did clinicians from your hospital meet with emergency medical system (EMS) providers to review the care of patients with AMI? (16)

○ Yes, about monthly

○ Yes, about quarterly

○ Yes, about annually

○ Yes, other: _____

○ No

○ Unknown

D.64 There is good coordination among the different departments involved with the care of patients with AMI. (62)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.65 Departments caring for patients with AMI (e.g., cardiology, emergency medicine) communicate easily with each other.(64)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.66 Clinicians caring for patients with AMI share new evidence-based approaches with the AMI team.(63)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

D.67 Which best describes the quality of your interaction with hospitals **that referred patients to you with AMI**?(18)

○ Very collaborative (we shared data along with strategies for improving AMI care) ○ Somewhat collaborative (we communicated regularly, but we did not share data and strategies)

○ Not collaborative (we had no or minimal contact with the referring hospital/s)

○ Not applicable **[Skip to D69]**

D.68 Did your hospital routinely give feedback to the referring hospital/s on any of the following? (18a.)

a. Time to transfer

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

b. AMI-related procedures performed

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

c. Patient outcome

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

d. Other please specify: _____

D.69 Which best describes the quality of your interaction with hospitals **that you referred patients to with AMI**? (19)

○ Very collaborative (we shared data along with strategies for improving AMI care) ○ Somewhat collaborative (we communicated regularly, but we did not share data and strategies)

○ Not collaborative (we had no or minimal contact with hospitals in our region)

○ Not applicable

D.70 Was your hospital part of a regional effort or consortium of hospitals to improve AMI care? (20)

○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always

C. Definition of In-hospital Complications

1) Re-infarction

Indicate if there is physician documentation of recurrent myocardial infarction during hospitalization.

2) Cardiogenic shock

Indicate if there is physician documentation of cardiogenic shock during hospitalization.

3) Ischemic stroke

Indicate if there are physician documentations of new-onset ischemia stroke and stroke-related symptoms during hospitalization. The stroke-related symptoms include: trouble walking/loss of balance/incoordination, one-sided numbness or hemi-anesthesia, one-sided facial numbness or hemi-anesthesia, mouth askew and drooling, dysarthria or slurred speech, loss of vision or blurred version in one or both eyes, dizziness with vomiting, severe headache and vomiting, unconsciousness, and hyperspasmia.

4) Congestive heart failure

Indicate if there is physician documentation of heart failure during hospital stay. This include those without a history of heart failure but develop heart failure during hospitalization, and those with a history of heart failure as a chronic comorbidity and develop worsening heart failure during hospitalization.

D. Baseline characteristics of patients with hypokalaemia

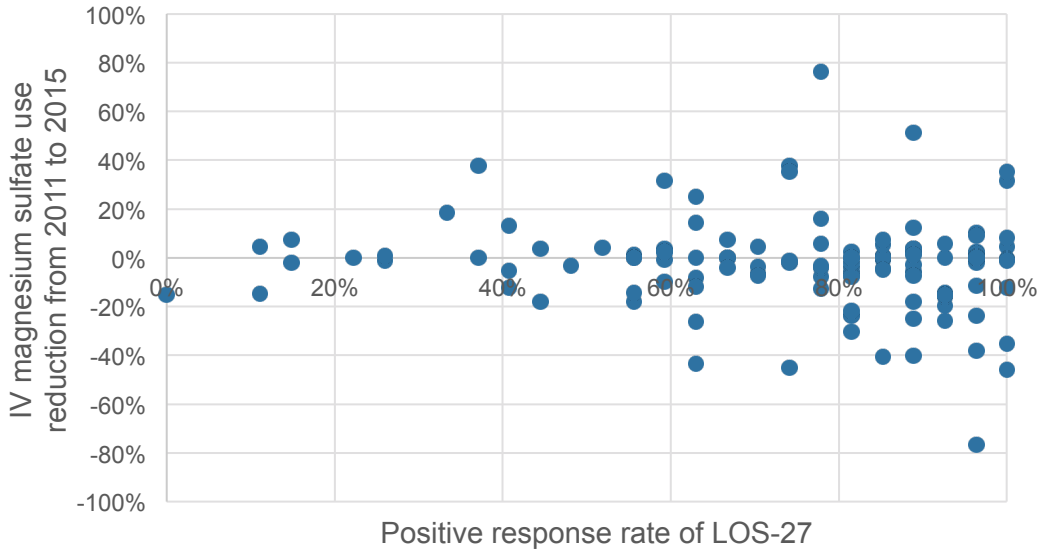
Characteristics	Overall	Use N(%)	Non-Use(%)	P value
Patient characteristics				
Age				0.005
<55	753(19.9)	170(20)	583(19.8)	
55-64	873(23)	225(26.5)	648(22)	
65-74	1135(29.9)	260(30.6)	875(29.8)	
>=75	1029(27.2)	195(22.9)	834(28.4)	
Gender				0.621
Female	1508(39.8)	332(39.1)	1176(40)	
Male	2282(60.2)	518(60.9)	1764(60)	
Hypertension	2318(61.2)	547(64.4)	1771(60.2)	0.060
Diabetes	655(17.3)	131(15.4)	524(17.8)	0.101
Dyslipidemia	212(5.6)	38(4.5)	174(5.9)	0.106
Currently smoking	1170(30.9)	286(33.6)	884(30.1)	0.057
Prior ischemic stroke	452(11.9)	102(12)	350(11.9)	0.940
Prior myocardial infarction	325(8.6)	91(10.7)	234(8)	0.012
Prior CABG/PCI	97(2.6)	23(2.7)	74(2.5)	0.759
Chest discomfort	3380(89.2)	764(89.9)	2616(89)	0.455
Left branch block at presentation	59(1.6)	16(1.9)	43(1.5)	0.384
Cardiac arrest at presentation	80(2.1)	28(3.3)	52(1.8)	0.006
Cardiogenic shock at presentation	306(8.1)	83(9.8)	223(7.6)	0.040
Acute stroke at presentation	102(2.7)	16(1.9)	86(2.9)	0.098
Heart rate at presentation, bpm				0.457
<50	163(4.3)	36(4.2)	127(4.3)	
50-110	3331(87.9)	739(86.9)	2592(88.2)	
>110	296(7.8)	75(8.8)	221(7.5)	
SBP at presentation, mmHg				0.046
<120	1263(33.3)	314(36.9)	949(32.3)	
120-139	1096(28.9)	223(26.2)	873(29.7)	

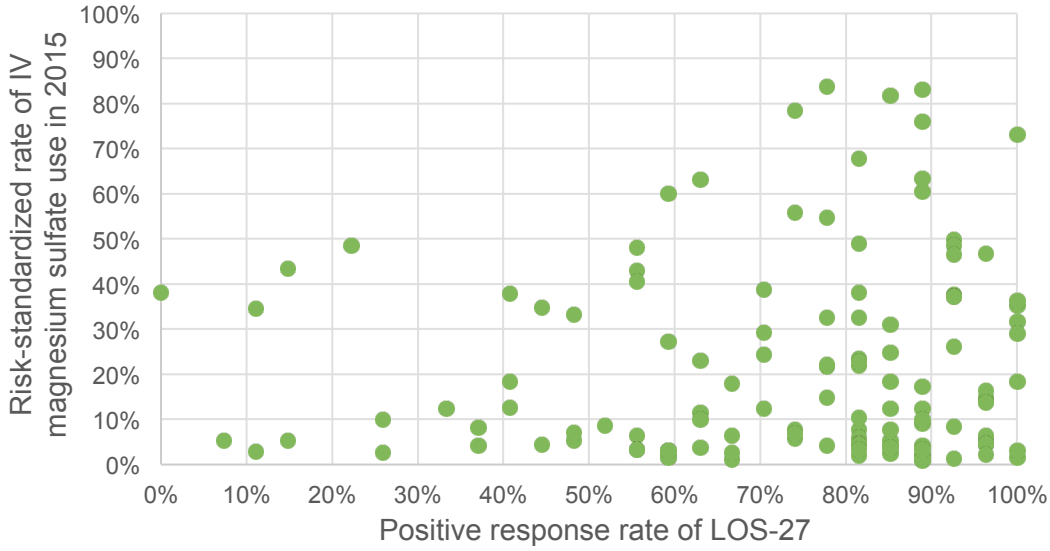
140-159	771(20.3)	162(19.1)	609(20.7)	
>=160	660(17.4)	151(17.8)	509(17.3)	
Reperfusion therapies				<0.001
No reperfusion	557(14.7)	156(18.4)	401(13.6)	
Fibrinolytic therapy	2809(74.1)	585(68.8)	2224(75.6)	
Primary PCI	424(11.2)	109(12.8)	315(10.7)	
Hospital characteristics				
Teaching hospital	3042(80.3)	707(83.2)	2335(79.4)	0.015
PCI capable hospital	2455(64.8)	581(68.4)	1874(63.7)	0.013
Hospital level				0.047
Secondary or lower	1507(39.8)	313(36.8)	1194(40.6)	
Tertiary hospital	2283(60.2)	537(63.2)	1746(59.4)	
Economic geographic region				0.682
Eastern	798(21.1)	184(21.6)	614(20.9)	
Central	2163(57.1)	474(55.8)	1689(57.4)	
Western	829(21.9)	192(22.6)	637(21.7)	
Urban/Rural				0.023
Rural	1739(45.9)	361(42.5)	1378(46.9)	
Urban	2051(54.1)	489(57.5)	1562(53.1)	

E. Predictors of the use of IV magnesium sulphate

	Unadjusted		Adjusted	
Variable	OR (95%CI)	P value	OR (95%CI)	P value
New onset of heart failure	1.86(1.51-2.28)	<0.0001	1.69(1.37-2.09)	<0.0001
Cardiac arrest at presentation	3.81(2.5-5.82)	<0.0001	3.38(2.19-5.21)	<0.0001
Aspirin within 24-hour	1.7(1.51-1.93)	<0.0001	1.43(1.22-1.67)	<0.0001
Statins within 24-hour	1.64(1.45-1.85)	<0.0001	1.33(1.13-1.57)	0.0005
Reperfusion therapies				
None	-		-	
Fibrinolytic therapy	1.57(1.33-1.85)	<0.0001	1.6(1.35-1.9)	<0.0001
Primary PCI	1.65(1.42-1.92)	<0.0001	1.69(1.44-1.98)	<0.0001

F. Correlations between positive response rate of LOS-27 and IV magnesium sulphate use





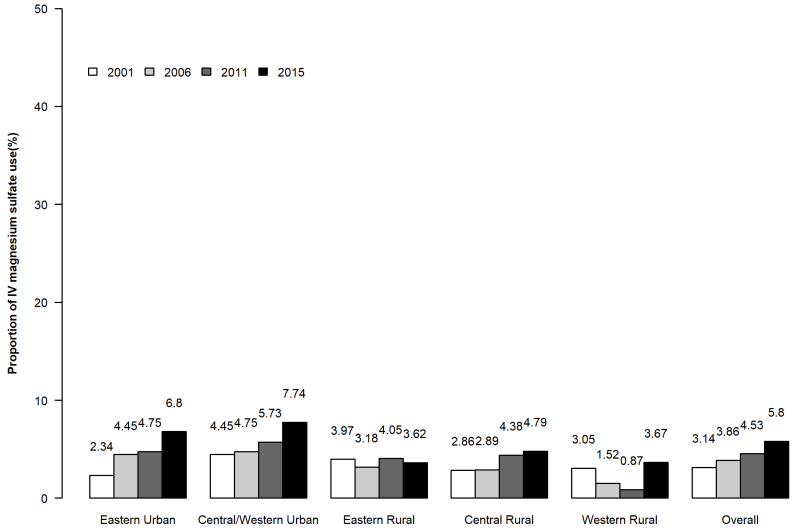
G. Comparisons between patients with and without IV magnesium sulfate therapy after propensity score matching

Characteristics	Use N(%)	Non-Use(%)	P value
Patient characteristics			
Age			
55-64	1072(24.4)	1037(23.6)	.794
65-74	1290(29.4)	1283(29.2)	
<55	938(21.3)	959(21.8)	
>=75	1094(24.9)	1115(25.4)	
Gender			
Female	1346(30.6)	1299(29.6)	.274
Male	3048(69.4)	3095(70.4)	
Hypertension	2247(51.1)	2196(50)	.277
Diabetes	889(20.2)	878(20)	.77
Dyslipidemia	235(5.3)	244(5.6)	.672
Currently smoking	1496(34)	1470(33.5)	.558
Number of risk factors			
1	2055(46.8)	1997(45.4)	.445
2	1049(23.9)	1047(23.8)	
>=3	232(5.3)	229(5.2)	
None	1058(24.1)	1121(25.5)	
Prior ischemic stroke	546(12.4)	484(11)	.040
Prior myocardial infarction	416(9.5)	382(8.7)	.207
Prior CABG/PCI	104(2.4)	107(2.4)	.834
Chest discomfort	4021(91.5)	4046(92.1)	.331
Left branch block at presentation	65(1.5)	44(1.0)	.043
Cardiac arrest at presentation	81(1.8)	79(1.8)	.873
Cardiogenic shock at presentation	279(6.3)	236(5.4)	.051
Acute stroke at presentation	77(1.8)	66(1.5)	.354
Heart rate at presentation, bpm			.733
<50	177(4.0)	183(4.2)	
50-110	3886(88.4)	3898(88.7)	
>110	331(7.5)	313(7.1)	
SBP at presentation, mmHg			.621
<120	1565(35.6)	1607(36.6)	
120-139	1299(29.6)	1307(29.7)	
140-159	913(20.8)	899(20.5)	
>=160	617(14)	581(13.2)	
Medication within 24 hours			
Aspirin	2688(61.2)	2686(61.1)	.965

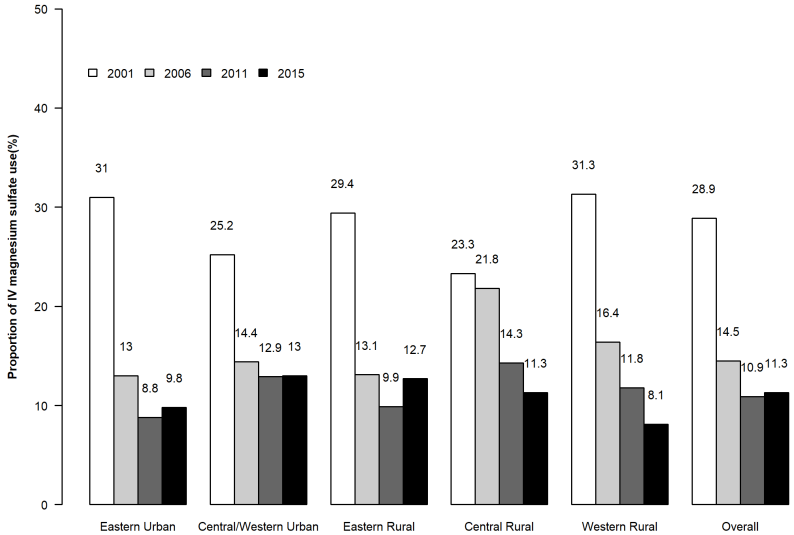
Statins	2398(54.6)	2442(55.6)	.345
ACE inhibitors or angiotensin receptor	2541(57.8)	2567(58.4)	.574
Beta-blockers	1768(40.2)	1748(39.8)	
Clopidogrel	1845(42)	1894(43.1)	.290
Reperfusion therapies			.941
No reperfusion	3130(71.2)	3131(71.3)	
Fibrinolytic therapy	746(17.0)	754(17.2)	
Primary PCI	518(11.8)	509(11.6)	
Hospital characteristics			
Teaching hospital	3462(78.8)	3530(80.3)	.072
PCI-capable hospital	2768(63.0)	2788(63.5)	.650
Hospital level			.451
Secondary or lower	1576(35.9)	1610(36.6)	
Tertiary	2818(64.1)	2784(63.4)	
Economic geographic region			
Central	1115(25.4)	1186(27.0)	.191
Eastern	2360(53.7)	2288(52.1)	
Western	919(20.9)	920(20.9)	
Urban/Rural			
Rural	1724(39.2)	1721(39.2)	.948
Urban	2670(60.8)	2673(60.8)	

H. Trends different dosage of intravenous magnesium sulfate therapy in 2001, 2006, 2011 and 2015 in five economic-geographic regions.

Single dosage of intravenous magnesium sulfate therapy

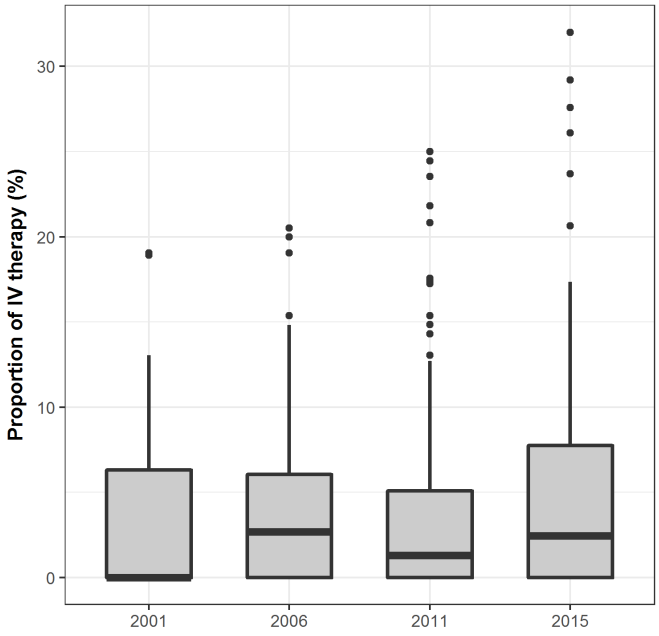


Multiple dosage of intravenous magnesium sulfate therapy

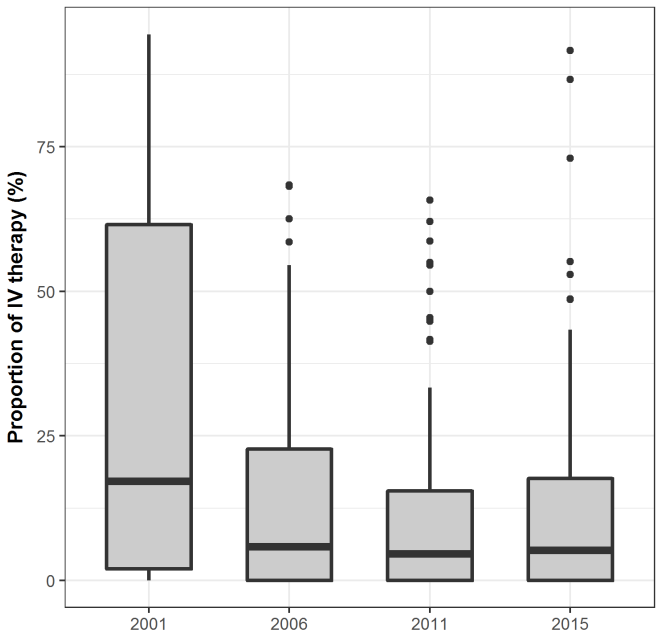


I. Different dosage of IV magnesium sulfate use in 2001, 2006, 2011 and 2015 among all hospitals.

Single dose of IV magnesium sulfate

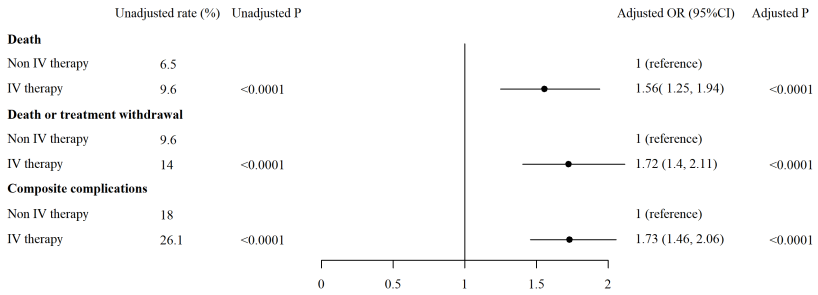


Multiple doses of IV magnesium sulfate

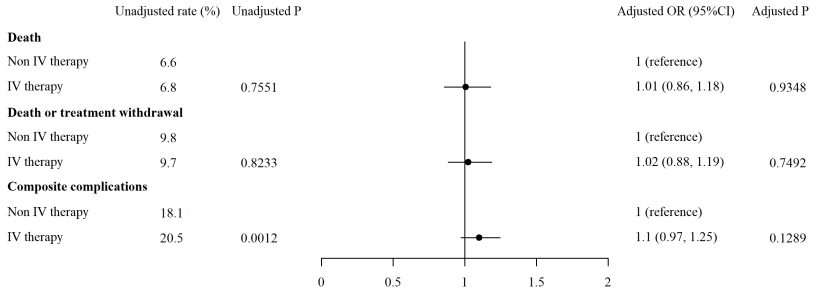


J. In-hospital outcomes between patients with different dosage of and without IV magnesium sulphate.

Single dose compared with no-use of IV magnesium sulphate



Multiple doses compared with no-use of IV magnesium sulphate



STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6，7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	7
		(*b*) For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8，9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how matching of cases and controls was addressed	9
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	23
		(c) Consider use of a flow diagram	23
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	21，22
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	11，25

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	25 26
		(*b*) Report category boundaries when continuous variables were categorized	21， 22
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	12,13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14,15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.