CLINICAL PATHWAYS FOR ACUTE CORONARY SYNDROMES IN CHINA

Phase 3
Quality Care Initiation and Evaluation

Protocol

Chinese Society of Cardiology

THE GEORGE INSTITUTE
for International Health

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1. Overview

Clinical Pathway for Acute Coronary Syndromes in China (CPACS) are a series of trials initiated and conducted by Chinese Society of Cardiology and The George Institute for Global Health, supported by the Ministry of Health of China, aiming at shortening the gaps between clinical practice and evidence-based medicine and improve the prognosis of patients with acute coronary syndrome (ACS) through optimizing clinical processes in diagnosis, treatment and hospitalization of ACS patients. These trials were expected to provide evidence on the improvement of hospital services' quality by the interventions with the implementation of clinical pathways for ACS as the core, as well as cost-effectiveness analysis and analysis of the barriers in implementation.

CPACS-1 was a prospective registry and follow-up study, involving 51 tertiary or secondary hospitals in 18 provinces across the country. A total of 2973 ACS patients were included. The study found that there was a big gap between Chinese hospitals and guidelines in the treatment of ACS, for example, the final diagnosis and objective examination indicators were not consistent among 20% of patients. Less than half of the ACS patients were prescribed with the four drugs recommended in the guidelines (aspirin, beta receptor blocker, angiotensin-converting enzyme inhibitor and statin drugs) when they left the hospital (Heart 2008;94:554-560；Am Heart J 2009;157：509-516).

Between 2005 and 2010, we conducted a trial (CPACS-2) in 15,000 patients admitted to 75 hospitals (from 17 provinces) throughout China to determine whether the routine use of a quality improvement initiative, could increase evidence-based management of ACS. The trial showed that although the intervention could improve certain aspects of care (for example, the appropriate prescription of recommended therapies at discharge increased from 51.2% to 61.6% (OR 1.42; 95% CI: 1.00 to 2.02; p=0.061)), major system-level barriers including a lack of top down support, prevented universal improvement. Most patients with ACS in China present to non-tertiary hospitals in poorer areas, where the financial burden of ACS is catastrophic. However, relatively few of these hospitals were included in the CPACS-2. Furthermore the study was not powered to measure the impact of the intervention

on clinical outcomes such as in-hospital mortality. As a result, the social and economic benefits of the intervention remain unclear.

This study, Clinical Pathways for the management of Acute Coronary Syndromes – Phase 3 (CPACS-3), aims to determine the effectiveness and cost-effectiveness of a complex, quality improvement initiative in 96 non-tertiary, non-PCI hospitals throughout China in reducing the risk of major adverse cardiovascular events in patients admitted with ACS.

2. Background

2.1 Burden of acute coronary disease in China

The burden of chronic, non-communicable disease, of which cardiovascular disease comprises a significant component, has increased rapidly and substantially in China over recent years[1]. Coronary heart disease now ranks first in the causes of all death as well as premature death. It is estimated that at least hundreds of thousands of people die of acute coronary events each year, and more than 10% of disability-adjusted life-year losses were caused by acute coronary events.[2,3]

2.2 The CPACS-1 study

CPACS-1 was a prospective registry and follow-up study. From Oct 30, 2004 to May 31, 2005, CPACS-1 study recruited 2973 patients with the diagnosis of ACS from 51 tertiary and non-tertiary hospitals in 18 provinces throughout China, and followed them up at 6 months and 12 months after discharge. Two-thirds of participating hospitals were tertiary hospitals. Almost all tertiary hospitals were capable to perform percutaneous coronary intervention (PCI) and coronary artery bypass surgery. In terms of the demographic characteristics and medical history of recruited ACS patients, CPACS-1 were basically the same as those of other foreign registration studies [12-15], as 63% of registered patients were men, with an average age of 65 years, 36% of whom had a history of coronary heart disease (CHD). CPACS-1 showed that the proportion of patients discharged on guideline recommended medical therapy (aspirin, β-blocker, ACEI/ARB, statin) for secondary prevention was low (Heart 2008;94:554-560； Am Heart J 2009;157:509-516) The CPACS-1 study

collected reliable information on the status of ACS patients at various levels of hospitals, revealing that there were gaps in the diagnosis and treatment of ACS patients between evidence-based medical guidelines and clinical practice in Chinese hospitals, providing important evidence for further researches.

2.3 CPACS-2

In order to narrow the gap between clinical practice and guidelines, we had designed and conducted a CPACS-2 study under the strong supports of the Disease Control Bureau and Department of Medical Administration of the Ministry of Health. CPACS-2 Study was the first cluster randomized controlled trial around the world, evaluating the effectiveness of quality of care initiatives (QCI) among ACS. The study was conducted in 75 hospitals from 17 provinces / cities across the country (50 tertiary hospitals and 25 secondary hospitals). After the pilot trial completed in 5 pre-trial centers, 70 hospitals were randomly divided into the early intervention group (A group) or the late intervention group (B group) using a stratified randomization. The initiation time of the intervention in B group was 12 month later than A group (Figure 1). In the CPACS-2 study, hospitals implementing QCI established a medical quality management team to coordinate the hospital departments and medical staff. Every half a year, data from 50 hospitalized ACS patients were continuously collected and entered into the web-based IT system. The IT system could feed medical quality management indicators back to the hospital's team in real time (Figure 2). The intervention also contained the implementation of ACS clinical pathways that includes risk stratification and different clinical pathways for unstable angina, non-STEMI and STEMI. The effectiveness of QCI intervention was evaluated by comparing the post-12-month-intervention characteristics of A group and the baseline characteristics of B group.

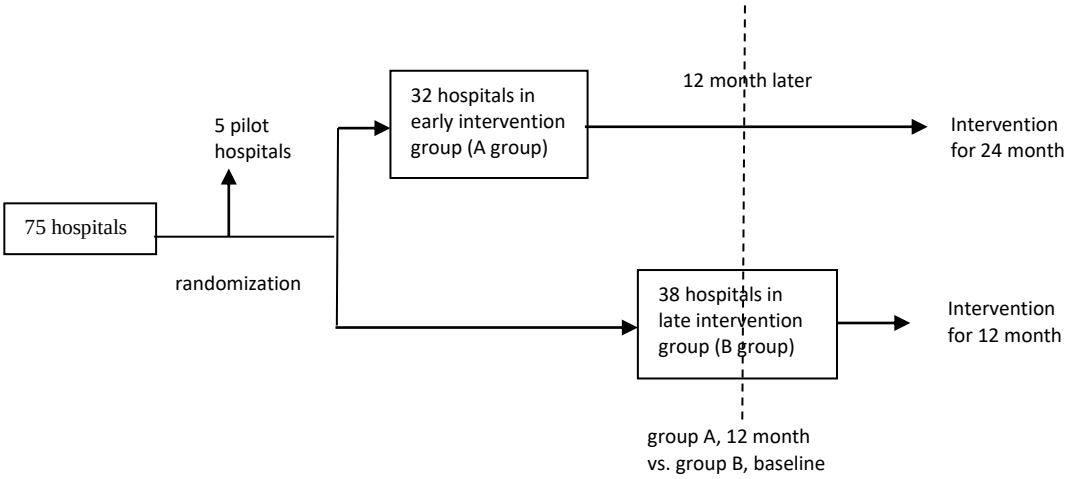


Figure 1. Design of CPACS-2, cluster randomized controlled trial.

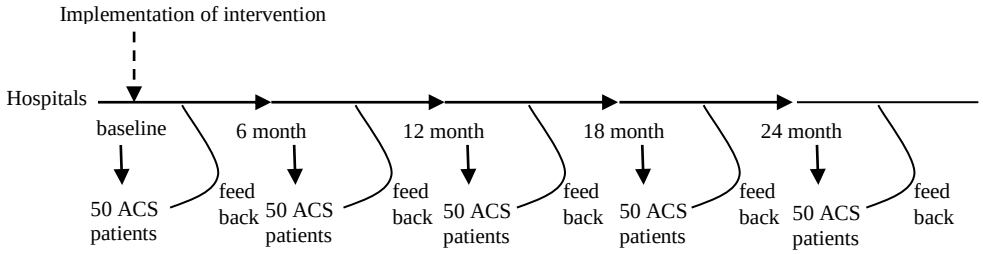


Figure 2. Intervention in CPACS-2.

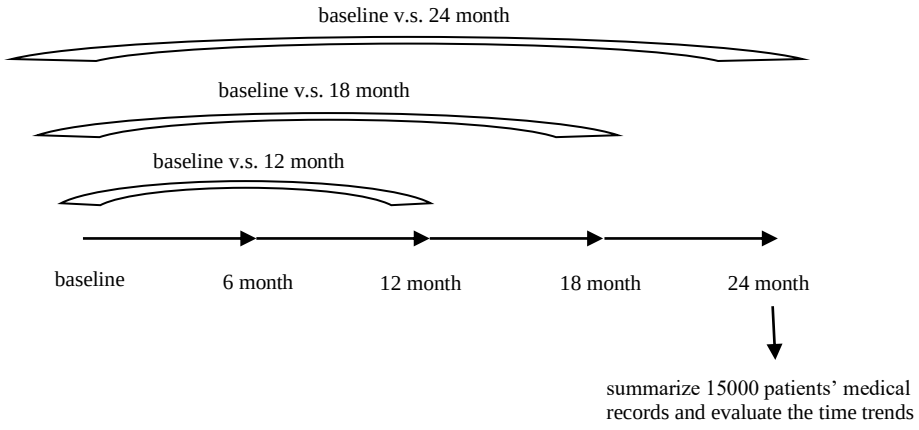


Figure 3. Design of CPACS-2, self-controlled trial.

The CPACS-2 study collected clinical data of 15140 ACS patients. The results showed that after comprehensive interventions, many medical quality indicators showed a trend of improvement. In randomized controlled design, comparisons of (group A, 12 months vs. baseline, group B) proportion of patients treated with guidelines

recommend four drugs (aspirin, beta-blockers, ACEI/ARB and statin) was 61.6% and 51.2% respectively (OR 1.42; 95% CI: 1.00-2.02; p=0.061); with the implementation of intervention, the hospital stay was significantly reduced (p=0.001) and the proportion of patients treated with the four drugs also significantly increased (p=0.004). Other indicators, such as the proportion of STEMI with reperfusion therapy, the door-to-needle time and door-to-balloon time also showed a trend of improvement, but not statistically significant. The incidence of major adverse events (including death, myocardial infarction, and stroke) in the hospital decreased, but which was only significant before controlling potential confounders (p=0.009).

To understand the implementation of the CPACS-2 study, obstacles to the application of clinical pathways, experience and lessons learned from this project and the impact of the medical environment on medical quality improvement measures, we conducted a process evaluation using semi-quantitative and qualitative methods. We conducted a questionnaire survey among 556 doctors, nurses and administrators from 75 hospitals participating in this study, as well as 40 in-depth interviews with doctors, nurses, administrators from 10 representative hospitals and experts from the working group to understand the problems in the implementation of QCI and the key points for future intervention. The results reflected the following issues: CPACS Phase 2 studies placed too much emphasis on scientific research rather than actions that improve quality of care; from the view of participating hospitals, there was a lack of good quality improvement (QI) teams and a lack of personnel dedicated to the work, the coordinators were overburdened, and the department leaders and the experts in this project had little time nor interest to truly participate in the implementation of this project. Besides, it was very difficult for large hospitals to change their service model, and secondary hospitals lacked the experience and infrastructure in doing academic research. The issue of medical insurance, the intense relations between doctors and patients, etc. affected the doctor's treatment decisions, and further hindered some effective treatments, such as the timely implementation of reperfusion therapy for acute myocardial infarction. Through process evaluation, we recognized that similar projects in the future should focus on one major issue (such as reperfusion treatment time), ask for more support

from the executive management, and conduct the project not only an academic research project but a quality improvement action.

3. CPACS phase 3 Study Plan

CPACS phase 3 study, as an ACS care quality improvement intervention, will be conducted in 15 provinces, including Hebei, Liaoning, Jilin, Jiangsu, Anhui, Gansu, Shandong, Shanxi, Henan, Hubei, Guangdong, Sichuan, Shaanxi, Inner Mongolia autonomous region, and Guizhou. These provinces cover all the different economic development status and geography in China and hence are having good representativeness. According to the experience and lessons learned from the CPACS-2 study, CPACS phase 3 study has adjusted its organizational structure. In order to strengthen administrative support, the CPACS phase 3 study will be led directly by the Department of Medical Administration, the Ministry of Health, and jointly implemented by the Chinese Society of Cardiology and The George Institute for Global Health. CPACS-3 study will mainly focus on county level hospitals that have limited medical resources, poorer ability of care and unable to transfer patients due to longer distance to tertiary centers. By implementing the ACS care quality improvement interventions in management of patients with ACS, the study will assists the participating hospitals to improve their technical and management capacity in ACS care. Through a rigorous controlled trial, we will evaluate the effect of the intervention, the costs and benefits, and we will conduct process evaluation.

3.1 Aim

To improve the diagnosis and treatment of patients with ACS, explore the mode of care suitable to local health resources, and maximize the application of evidence-based medicine in China's remote county-level hospitals.

3.2 Methods

3.2.1 Inclusion criteria for participating hospitals:

(1) The time taken to transfer an ACS patient to the nearest tertiary hospital with a cardiac catheter facility is more than 90 minutes;

(2) The hospital is highly unlikely to have the capacity to perform onsite

percutaneous coronary intervention (PCI) within the next 3 years;

(3) The director or deputy director responsible for medical care is a specialist in internal medicine and is able to set up a QCI team that is participated by directors of the internal medicine department, emergency department, and medical care management department;

(4) Already have established or are able to establish medical records for emergency patients and inpatients, as required by the project;

(5) Able to admit more than 40 ACS patients within 6 months;

3.2.2 Exclusion criteria for participating hospitals

Hospitals that participated in CPACS-2 will be excluded from CPACS-3.

3.2.3 Inclusion criteria for participating patients

Participants will be all patients who were admitted to participating hospitals (including outpatient departments and emergency department) with a final diagnosis of ACS (including those dead in hospital).

3.2.4 Exclusion criteria for participating patients

1) Age less than 18 years;
2) Dead on arrival or die within 10 minutes of arriving at hospital;
3) Patients who have been transferred to the Cardiology Department from another department within the same hospital;
4) Patients who have registered in CPACS-2 study.

3.2.5 Data collection

Data to be collected at discharge:

From the beginning of the study, all clinical data will be collected for all discharged or deceased patients who was diagnosed as acute coronary syndrome in the emergency department and inpatient department. Data to be collected include demography, clinical manifestations, the medical treatments at the emergency room, during hospital stay, and at discharge, as well as adverse events during hospitalization, and prognosis (basic questionnaire, appendix 1), costs during hospitalization (appendix 2) and the patients' quality of life (appendix 3). At the same time, the mobile phone numbers of patients or their families are registered for

conducting the patient satisfaction survey through the SMS platform (patient satisfaction survey questionnaire, appendix 4).

Data to be collected at follow-ups:

Patients who are alive at discharge and sign the informed consent will be followed up twice (at 6 months and 12 months). Data collection at follow-ups includes lifestyle, medical treatments, rehabilitation, adverse events (myocardial infarction, stroke, revascularization, hospitalization and death) (follow-up questionnaire, appendix 5). A quality of life survey will be conducted at the second follow-up visit (QoL35, appendix 3).

Data collectors:

The information at discharge and follow-ups (appendix 2, appendix 3 and appendix 5) and the informed consent to patients should be completed by the medical doctor in the department who is trained and assigned the responsibility specifically.

Data entry staff:

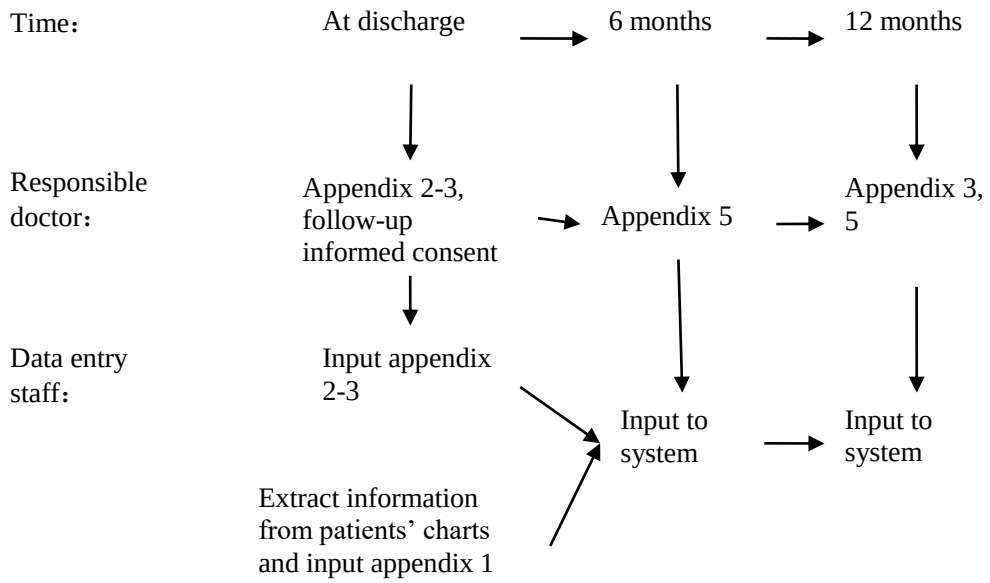
The entry of data (appendix 1, appendix 2, appendix 3, appendix 5) shall be completed by an independent staff at medical fair management office who are not responsible for medical diagnosis and treatment.

Data collection process:

Data collectors complete the appendix 2 and 3 on the day or one day before the patient’s discharge, check the address and valid phone numbers, get informed consent for follow-up, make the appointment for follow-up time, as well as inform the data entry staff to enter the patient's medical records and questionnaires into the CPACS-3 IT system. All the patients' data should be entered within 2 weeks.

When patient is discharged from hospital, the IT system will send satisfaction questionnaire automatically via SMS platform to the patients or their family members, and invite this patient to reply message. The replied message will be automatically entered into the database system.

At 6 months and 12 months after discharge, the patient will be followed up by either face-to-face or telephone.



The data collection process.

Storage of original data:

Hospitals participating in the study were required to set up registers and medical records at emergency department. The nurses at emergency department are required to record each patient's visit time (accurate to minutes) and narratives, and keep the records at least for 7 years after the end of the project. All patients admitted to the emergency room shall uniformly use the emergency medical records (including patient narratives, medical advices and laboratory test results).

Hospital inpatient department is required to record all patients' (both ACS and non-ACS) information in either electronic or paper records. These records should be saved 7 years after the end of the study, in case of project supervision.

Protection of privacy of patients' information:

Patients' ID information will be kept in the local hospitals together with other medical information and will comply with the local medical record confidentiality regulations. The electronic records are stored in the CPACS IT system, which cannot be accessed by anyone except the authorized personnel. Moreover, all the authorized personnel have strict levels of authority and cannot browse or modify other data beyond their authority. All electronic data will be protected by password. During data analysis, all patients' information will be de-identified, and it is

impossible to identify who is included in the study in the reports and published articles from the study.

3.2.6 Quality of care assessment

The quality of care assessment indicators include key performance indicators (KPIs) recommended by the ACC/AHA acute myocardial infarction quality of care assessment guidelines and patient satisfaction.

The KPIs and its definitions used to evaluate the overall effect of QCI are shown in table 1. After receiving the patient's data, the CPACS-3 IT system will automatically produce the quality of care assessment report and update it in a real time. The web-based IT system can generate quality of care assessment report for any duration for each hospital. Hospital QCI team members can see the quality of care report of their own hospital in the system. Local health bureau and the provincial health department can view the reports of the hospitals within their respective authorities. The Ministry of Health and CPACS-3 study team can view all participating hospitals' quality of care reports.

Table 1. KPIs and definitions

	KPI	Definition
1	Door to ECG time	The mean time from door to first ECG; and the Proportion of patients who had the first ECG traced within 10 minutes after hospital arrival.
2	Early use of Aspirin	Proportion of patients who received aspirin within 24 hours of arrival at hospital
3	Early use of Clopidogrel	Proportion of patients who received Clopidogrel within 24 hours of arrival at hospital
4	Early use of Statins	Proportion of patients who received statins within 24 hours of arrival at hospital
5	Aspirin prescribed at discharge	Proportion of patients who are prescribed aspirin at hospital discharge
6	Clopidogrel prescribed at	Proportion of patients with STEMI and NSTEMI who are prescribed Clopidogrel at hospital discharge

	discharge	
7	Beta-blocker prescribed at discharge	Proportion of patients who are prescribed a beta-blocker at hospital discharge
8	Statins prescribed at discharge	Proportion of patients who are prescribed a statin at hospital discharge
9	ACEI or ARB for Patients with LVSD	Proportion of patients with left ventricular systolic dysfunction (LVSD) who are prescribed angiotensin-converting–enzyme inhibitors(ACEI) or angiotensin-receptor blockers(ARB) at hospital discharge (for purposes of this measure, LVSD is defined as chart documentation of an left ventricular ejection fraction less than 40% or a narrative description of left ventricular systolic function consistent with moderate or severe systolic dysfunction)
10	Reperfusion therapy for STEMI patients	Proportion of STEMI patients who arrive hospital within 12 hours of symptom onset receiving fibrinolysis
11	Door to needle time	Proportion of AMI patients with ST-segment elevation or LBBB on the ECG closest to hospital arrival time receiving fibrinolytic therapy within 30 min from arrival to the hospital.
12	Length of stay	Mean days of hospitalization
13	Diagnosis inconsistent with examination findings	Proportion of patients with a final diagnosis inconsistent with biomarker findings

Patient satisfaction survey will focus on the experiences that the patient just went through in seeking the medical care, in order to determine the patient satisfaction level. We will ask about the reasons for patients' dissatisfaction and the possible factors related to patient satisfaction including hygiene level of the ward, quietness

at night, communication satisfaction with nurses and doctors, timely responsive in case of problems, accessibility to the necessary information at discharge, overall satisfaction score and whether willing to recommend this hospital to others. The questionnaire will first be validated in a small group of people and to be used after proving its validity.

3.2.7 Intervention

Each hospital will implement a quality of care improvement (QCI) initiative comprising 6 components:

- ***Establishment of a quality improvement team:*** The Department of Medical Administration, the Ministry of Health of China will invite each hospital to establish an ACS quality improvement team with the Director of the hospital as the designated Team Leader. The team members will include directors of departments relevant to the treatment of ACS (i.e. Emergency and General Medical) and each team will take overall responsibility for the implementation of the quality improvement initiative at their hospital.
- ***Establishment of a web-based IT system for quality management (Hospital performance audit and feedback):*** Standard reports on the performance of each hospital in the quality of care provided to ACS patients will be generated at 6-monthly intervals by the web-based IT system and sent to the Hospital Director, local Health Bureaus and the Ministry of Health (Figure 4). The report will provide a summary report of the pre-specified key performance indicators (KPIs) (Table 1) at each hospital based on the results for all ACS patients admitted at the end of each 6 month cycle. The report will also provide a study benchmark, against which participating hospitals can assess their own performance. After receiving the feedback reports, the QCI group should meet to discuss about the solutions to the possible problems that are identified in the reports. The group should return the suggested solutions to the CPACS-3 study team and implement those solutions immediately.

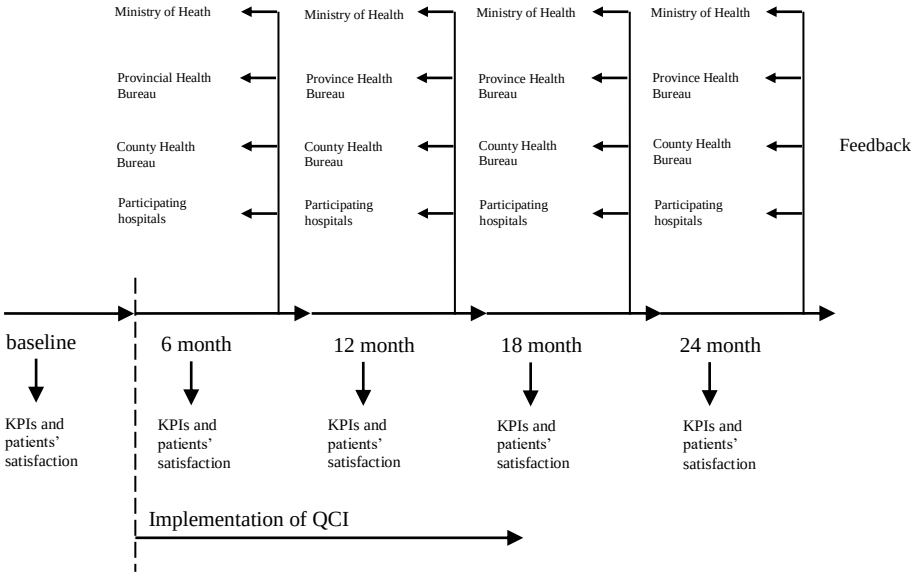


Figure 4. Web-based IT system of CPACS-3 study.

- ***Implementation of a clinical pathway:*** Clinical pathways for the management of STEMI and NSTEMI/unstable angina will be provided to each hospital and incorporated for use as part of the patient medical record. Hospitals will be encouraged to adapt the pathway to suit the local resources (including staff) and facilities. All participating hospitals should have a meeting every 6 months to summarize the KPIs of that time period, make corresponding adjustments to the clinical pathway and feedback them to the project team.
- ***Education and training for QCI teams:*** The participating hospital must receive the training provided by the project team when the QCI intervention starts, which includes introduction of intervention project, feedback pathway, introduction of online training, improvement and evaluation of medical quality, patient safety, and the conception of patient-centered services. Three key members of the hospital's QCI team are required to attend.
- ***Web-based education for relevant staff:*** Problem-based learning modules linked to professional Chinese Continuing Medical Education (CME)

programs, will be provided to clinical staff working at different levels (principally doctors and nurses) in each hospital. The education includes ACS diagnosis and treatment knowledge, and also patient safety and health care quality. Staff will be required to register to participate and complete the modules on-line. The website will record log-in details for all registered staff and a compulsory knowledge test on the website will be provided before the training started. The test also could be done at any time when after learning module started. CME points will be redeemed on passing the test (a score over 90 in 100 points totally).

- ***Online access to specialist advice using the "e-consultant" program:*** The e-consultant program allows hospital clinicians to access expert advice from clinical cardiologists via a web-based system. The program will have two kinds of expert advices, the first one is a web-answering system, in which doctors in the intervention group could ask questions that they face during the ACS patients' treatment and the expert will answer them in 24 hours; the second one is the case conference system, by which the hospital under intervention will received twice case discussion with cardiovascular experts on line.
- ***Patient education:*** Patient-oriented educational material will be provided to all ACS patients (and their families) during their admission to hospital. The material will focus on the importance of long-term medication use and lifestyle modification.

3.2.8 Study design

A stepped-wedge cluster randomized trial design will be used to evaluate the impact of the intervention. Using this design, the intervention will be implemented sequentially to the participating hospitals over 6-month time periods (Table 2). The period at which a hospital begins implementation of the intervention (or enters the "active phase" of the study) will be determined at random. The intervention will be applied at the level of the hospital (clusters). Participating hospitals will be randomized to one of four wedges, giving around 24 hospitals per wedge. Wedge

randomization will be computer-generated. The survivors will be followed up at 6 months and 12 months.

Table 2 Patient Selection and Intervention Plan

	0-6 month	7-12 month	13-18 month	19-24 month	25-30 month
A group (24 hospitals)	A0 (baseline)	A1 (intervention)	A2 (intervention)	A3 (intervention)	A4 (intervention)
B group (24 hospitals)	B0 (baseline)	B1 (baseline)	B2 (intervention)	B3 (intervention)	B4 (intervention)
C group (24 hospitals)	C0 (baseline)	C1 (baseline)	C2 (baseline)	C3 (intervention)	C4 (intervention)
D group (24 hospitals)	D0 (baseline)	D1 (baseline)	D2 (baseline)	D3 (baseline)	D4 (intervention)

3.2.9 Outcomes

The primary outcome will be the incidence rate of in-hospital major adverse cardiovascular events (MACE) comprising all-cause mortality, myocardial infarction or re-infarction and stroke. Secondary outcomes will be the key performance indicators (KPIs) and the patient satisfaction.

3.2.10 Sample Size

Sample size calculations are based on following assumptions:

- The baseline incidence rate of in-hospital major adverse cardiovascular events (MACE) is assumed as 8.4%. This parameter came previous findings from CPACS-1 (8.4%) and CPACS-2 studies (7.6%). Taking into account that participating hospitals in CPACS-3 come from remote areas with limited medical resources, a higher incidence of MACE in CPACS-1 is used to calculate the sample size;
- no delay in the effect of the intervention;
- an intra-class correlation coefficient of 0.10 (data from CPACS-2 study);
- 96 participating hospitals, 50 patients will be collected in each 6-month cycle in each hospital, and the intervention will be started in four steps;
- We select 4 hospitals from each province in Jiangsu Province, Guangdong Province, Gansu Province, Sichuan Province, Guizhou Province, and Inner Mongolia Autonomous Region and select 8 hospitals from each of the

remaining 9 provinces: Hebei Province, Liaoning Province, Jilin Province, Anhui Province, Shandong Province, Shanxi Province, Henan Province, Hubei Province, and Shaanxi Province.

This study will have 99%, 98% and 85% power to detect relative risk reduction of 25%, 20% and 15% respectively in the primary outcome (Table 3).

Table 3 Statistical power of CPACS-3

Relatively risk decline	Statistical power
25%	99%
20%	98%
15%	85%

3.3 Quality control

Each hospital will receive training of the research protocol before the start of the project and will receive the training on intervention protocol before the commencement of the intervention.

After the research protocol training but prior to the formal data entry a period of one month is blocked for practice. During this period, the data entry staff will be checked if he/she is qualified by examining whether the data inputted into the CPACS-3 IT system are matched with the medical charts separately sent to the coordinating center. After the qualification validated, the participating hospital could begin its formal recruitment.

Each participating hospital will receive the site monitoring visit at least twice, one within half a year after initiating the study and one within the last year before the end of the study. There is no difference in the time of the first monitoring visits. In the first six months of the project (February-June), the first monitoring visits of all 96 centers will be completed; the second monitoring visits will be done in 2-3 times. 20% to 40% of 96 centers will be checked at each time, and the second monitoring visits will be completed within one and a half years. Routine data queries will be conducted through the data management center.

The site monitoring visits should check the establishment and operation of the QCI team, documentation and filing, patient ID verification, original data sourcing, the implementation of clinical pathway, etc.

The site monitoring results will be reported back to the hospital QCI team as well as the project team, the corresponding local health bureaus and the Ministry of Health. The project team may raise critics and appraisals to the participating hospital on the basis of the monitoring results. The project team can withdraw hospitals that are seriously unqualified for data authenticity and data quality.

4. Statistical analysis plan

As the stepped-wedge cluster randomized trial design, we plan to analyse the study data at individual level. Considering that the response variables may be non-normal distribution or binomial distribution, and the sizes of the clusters may be unequal, we plan to use the generalized linear mixed models (GLMM) or generalized estimating equations (GEE) to do statistical analyses.

4.1 Effectiveness evaluation

For the primary end point (binary variable, in hospital major adverse cardiovascular events (MACE), including stroke, AMI, hospital readmission, vascular reconstruction and all-cause mortality), GLMM model will be used to evaluate the treatment effect (between intervention groups) and the time effect (between different patients in different time periods), with LOGIT/POSSION conversion of the end point. If there is neither the time effect nor the interaction term between time and intervention, the COX model or LOGISTIC regression model will be used to estimate the intervention effect after adjustment of covariates.

4.2 Basic situation evaluation

GLMM model will also be used to compare the socio-anthropometric variables between the intervention groups, and between time periods, as well as between patients with different discharge diagnosis (STEMI, NSTEMI, UAP). If there is neither the time effect nor the interaction with the intervention, *t* test will be used to compare the difference of continuous variables between the intervention groups.

4.3 QCI evaluation

For the secondary end points (quality evaluation index), GLMM model will be used to test treatment effect (comparison between intervention groups) and the time effect (comparison between time periods. The LOGIT transformation will be used for the binary variables.

5. Process evaluation

The overall goal of process evaluation is to evaluate the roles of each intervention component in CPACS-3 study, as well as the difficulties, obstacles, and possible ways for improvement in implementation of the quality improvement measures in present medical care environment.

Process evaluation will be conducted in combination of semi-quantitative and qualitative research. Semi-quantitative research will collect data on the acknowledgement, participation, comments and suggestions of CPACS-3 projects among different participating staff with different roles in participating hospitals through questionnaire survey. The qualitative study involves group discussions or in-depth interviews with local QCI team members, medical staff, patients, representatives from local health bureaus and medical administration department of the Ministry. The detailed study protocol for the process evaluation will be submitted for approval separately.

6. Economic evaluation

While proving that an intervention is effective, it is also important to assess the cost-effectiveness of the intervention, which plays a key role in policy-making. We invite health economists in CPACS-3 study to conduct an analysis of the cost-effectiveness evaluation of CPACS-3 intervention from both government and patient perspective. Detailed plans for economic evaluation will be reported separately later.

7. Time schedule

To ensure the successful completion of CPACS-3 study, the following tasks need to be completed within the planned time (Table 4):

Task 1: consent of the ethics committee, preparation of research materials, selection of hospitals, recruitment and training of personnel.

Task 2: collect baseline data.

Task 3: randomization, and start the interventions at the first 24 hospitals (group A).

Task 4: start the interventions in the second batch of 24 hospitals (group B).

Task 5: start the interventions in the third batch of 24 hospitals (group C).

Task 6: start the interventions in the fourth batch of 24 hospitals (group D).

Task 7: follow-up visits.

Task 8: data analysis and result report.

Table 4. CPACS-3 time schedule

2011				2012				2013				2014				2015			
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
preparation																			
		baseline																	
		baseline		Intervention on group A															
		baseline		baseline		Intervention on group B													
		baseline		baseline		baseline		Intervention on group C											
		baseline		baseline		baseline		baseline		Intervention on group D									
				Follow-up visits															
												data analysis and result report							

8. Ethics

Retrospective data collection every 6 months will be medical chart based and does not require the patient or family member to sign the informed consent; but the collected data is kept in a confidential database. However, written informed consent is required for discharged patients who have agreed to participate in the follow-up of the study. Patient instructions and informed consent are given in appendix 6.

9. Governance and Organization

CPACS3 will be led by a consortium comprising the Department of Medical Administration of the Ministry of Health, the Chinese Society of Cardiology and The George Institute for Global Health, China. A Steering Committee comprising

representatives of each organization will oversee the organization and conduct of the study.

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