

Quality Measurement and Improvement Study of Surgical Coronary Revascularization: Medication Adherence (MISSION-2)

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Abstract

Background: Secondary preventive therapies play a key role in the prevention of adverse outcomes after coronary artery bypass grafting (CABG). However, medication adherence after CABG is often poor, and conventional interventions for improving adherence have limited success. With increasing penetration of smartphones, health-related smartphone applications might provide an opportunity to improve adherence. Carefully designed trials are needed to provide reliable evidence for the use of these applications in patients after CABG.

Methods: The Measurement and Improvement Studies of Surgical Coronary Revascularization: Medication Adherence (MISSION-2) study is a multicenter randomized controlled trial, aiming to randomize 1000 CABG patients to the intervention or control groups in a 1:1 ratio. We developed the multifaceted, patient-centered, smartphone-based Heart Health Application to encourage medication adherence in the intervention group through a health self-management program initiated during hospital admission for CABG. The application integrated daily scheduled reminders to take the discharge medications, cardiac educational materials, a dynamic dashboard to review cardiovascular risk factors and secondary prevention targets, and weekly questionnaires with interactive feedback. The primary outcome was secondary preventive medication adherence measured by the Chinese version of the 8-item Morisky Medication Adherence Scale at 6 months after randomization. Secondary outcomes included all-cause death, cardiovascular rehospitalization, and a composite of death, myocardial infarction, stroke, and repeat revascularization.

Discussion: Findings will not only provide evidence regarding the feasibility and effectiveness of the described intervention for improving adherence to CABG secondary preventive therapies but also explore a model for outpatient health self-management that could be translated to various chronic diseases and widely disseminated across resource-limited settings.

Trial Registration: <https://clinicaltrials.gov> (NCT02432469).

Key words: Coronary Artery Bypass Grafting; Medication Adherence; Mobile Applications; Mobile Health; Secondary Prevention

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INTRODUCTION

Coronary heart disease (CHD) is the leading cause of death and disease burden worldwide.^[1] A proven method of coronary revascularization for >50 years, coronary

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artery bypass grafting (CABG), is the most durable and complete treatment of ischemic heart disease. However, in the months and years that follow CABG, patients remain at risk for subsequent ischemic events as a result of native CHD progression and the development of vein graft atherosclerosis. Secondary therapies play a key role in the maintenance of native and graft vessel patency and in the prevention of adverse cardiovascular outcomes.^[2-4]

Despite the importance of secondary prevention, many studies report poor medication adherence after CABG, with about 50% of patients failing to adhere to their prescribed drug regimens.^[5-12] Medication nonadherence is also a common health-care issue among other chronic disease patients,^[13] and it can lead to adverse health outcomes and excess health-care resource consumption. Nonadherent behaviors are estimated to account for 33–69% of medication-related hospitalizations and cost 100 billion dollars annually.^[14] Possible factors influencing adherence include the complexity of the treatment regimen, quality of information provided about the regimen, communication between provider and patient, patient ability to remember to take medications appropriately, concerns about adverse effects, and personal preferences and beliefs about the treatment.^[15]

Although a large number of factors are involved, common barriers to adherence are often under patient control, and attention to these patient-related factors is an important step in improving adherence.^[16] Forgetfulness is one of the most frequently cited patient-related reasons for nonadherence.^[16,17] A range of medication reminder interventions have been investigated with mostly mixed results.

Prior interventions for medication adherence

Traditional reminder packaging systems, such as weekly pill boxes, packaged calendars, and unit-of-use packaging,^[18] minimally involve the patients in the self-medication process and do not provide them access to their adherence data or other educational information.^[14] A review of reminder packaging for improving adherence to long-term medication noted evidence supporting the effectiveness of this type of intervention is of low quality, and it concluded that the packaging increased the proportion of people taking their medications, but the effect was not large.^[19,20] Additional questions remain regarding the types of packaging that are most helpful for different patient populations.^[19]

Methods of drug regimen simplification include formulations (e.g., slow release) that may be given fewer times daily or fixed-dose formulations such as a “polypill.”^[20] Studies have confirmed that the prescribed number of doses per day was inversely related to compliance, and simpler, less frequent dosing regimens resulted in better compliance across a variety of therapeutic classes.^[21] A review of these simplified drug regimens, however, noted that they did not consistently show benefit.^[22]

Systematic reviews and meta-analyses have indicated that telehealth interventions for secondary prevention,

limited to telephone calls, internet, and videoconferencing technologies, offer an effective alternative model of secondary prevention care.^[23] A study of nearly a million participants found that automated reminder telephone calls had no effect on nonadherence while live calls from pharmacists significantly decreased antihypertensive primary medication nonadherence, although many patients still abandoned their prescriptions.^[24] In a multicenter randomized controlled trial (RCT) of 16,280 participants, automated phone reminders using interactive voice response calls, either regular or enhanced, for participants due or overdue for a refill significantly increased the adherence by 1.6–3.7 percentage points for statins and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) compared with usual care.^[25]

Rationale for a smartphone-based intervention

Traditional reminder methods to enhance long-term medication adherence have been complex and labor intensive, and they were not widely available or consistently effective. Innovative strategies are needed that are practical for routine clinical use.^[14,26,27] A Cochrane review of RCTs of adherence interventions found that the studies mostly evaluated complex interventions that would be difficult to implement in “real-world” clinical practice settings.^[28] The limitations of these conventional interventions for medication adherence have prompted the development of innovative models of care. One example is smartphone technology-based applications, which can provide a platform for patient-centered programs that incorporate education, real-time feedback, motivation, reminders, and support.^[29] Such technology has the potential to revolutionize the landscape of secondary prevention.

As of January 2014, 90% of American adults owned a mobile phone.^[30] By 2018, 50% of people worldwide will own a smartphone.^[31] Smartphone penetration is also increasing among groups with low socioeconomic status,^[32] poor access to medical care, and high prevalence of cardiovascular risk factors.^[33] Health-related smartphone applications may provide an opportunity for all patients, including those with traditional socioeconomic barriers to health care, to improve the outcomes of cardiovascular disease from primordial and primary prevention to secondary prevention strategies.^[34]

According to the Intercontinental Marketing Services Institute of Health Informatics, there were over 43,000 health-related smartphone applications available for download in August 2014 from the Apple iTunes App Store alone; together these applications have been downloaded more than 660 million times.^[35] Despite the vast number of applications, the capacity of these applications to improve long-term health behaviors remains under debate, and carefully designed RCTs are needed to provide reliable evidence for their efficacy and effectiveness.^[34,36-40] Among the few studies incorporating smartphone technology in the clinical setting, most were pilot or exploratory trials with small sample sizes or conflicting results.^[41-46] To our knowledge, there have been

no published studies testing smartphone applications as a medication reminder and lifestyle intervention for CABG secondary prevention.

The China National Center for Cardiovascular Diseases (NCCD) at Fuwai Hospital initiated a continuous quality improvement project nationwide >10 years ago. This project aims to improve the quality of medical care in cardiovascular disease across China. Guideline adherence is one of the goals of the project, and it is being pursued via the Measurement and Improvement Studies of Surgical Coronary Revascularization (MISSION) sister trials that commenced June 2015 with the target of improving CABG secondary prevention guideline adherence in clinical practice for physicians (MISSION-1)^[47] and patients (MISSION-2).

The primary objectives of the MISSION-2 trial are to evaluate the feasibility and effectiveness of a smartphone-based application on the medication adherence of patients after CABG and to explore a novel way of implementing secondary prevention for patients with chronic diseases. We hypothesize that our smartphone application will improve secondary preventive medication adherence, as measured by the Chinese version of the 8-item Morisky Medication Adherence Scale (C-MMAS-8) at 6 months after randomization, compared with standard care.^[48] We further hypothesize that the intervention will result in increased use of CABG secondary preventive medications (aspirin, β -blockers, statins, and ACEI/ARBs), improved cardiovascular risk factor control (as determined by the lipid profile, blood pressure, hemoglobin A1c [HbA1c], and smoking cessation), and decreased rates of death and major adverse cardiovascular and cerebrovascular events (MACCE) at the 6-month follow-up.

METHODS

Design overview

The study is designed as a multicenter, open-label, two-arm, parallel RCT with a targeted enrollment of 1000 CABG patients. Patients are randomly assigned to the smartphone application (Heart Health Application) intervention group or the usual care control group in a 1:1 ratio. The study design is displayed in Figure 1. The protocol was drafted in accordance with the Standard Protocol Items: Recommendations for Interventional Trials 2013 statement and the Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and onLine TeleHealth (CONSORT-EHEALTH) checklist.^[49-52]

Eligibility and recruitment

Patients aged ≥ 18 years are eligible to participate if they underwent isolated CABG and are prescribed secondary preventive oral medication (i.e., aspirin, β -blocker, statin, or ACEI/ARB) within 2 weeks of surgery. Participants must own or have sufficient access to a smartphone (e.g., shared access through a spouse or significant other; access must be available daily, and the phone owner must also agree to participation), and they must be able to operate the

smartphone application. Patients are excluded from the trial if they are unable to understand Chinese text or cannot attend the planned follow-up clinic visit at 6 months. We included patients who underwent isolated CABG but were not eligible for trial participation in a parallel nested registry designed to identify characteristics associated with the acceptability of the mobile health intervention strategy.

We invited five tertiary hospitals with annual CABG volume >100 cases to participate in this study. These hospitals are all major university-affiliated teaching institutions and members of the Chinese Cardiac Surgery Registry (CCSR), a nationwide adult cardiac surgery registry network launched in 2004 that currently includes nearly 100 coordinating centers across Mainland China.^[47,53] Participating institutions contribute to the CCSR database via a web-based data collection system that uses input items, common terminology, and variable definitions comparable to those of the Society of Thoracic Surgeons National Cardiac Database. The five hospitals included in this study are located in different regions across China, and they serve culturally and socioeconomically diverse populations. Patients undergoing CABG at these hospitals receive information on the study protocol and provide written informed consent for their participation.

Randomization

Randomization is performed using the password-protected computerized randomization program on the CCSR website (<http://ccsr.cvs-china.com>). The randomization process is stratified by study site and overseen by the National Coordinating Center (NCC). The computer-generated allocation is in a 1:1 fashion to the smartphone-based application intervention or usual care. Both researchers and patients are aware of randomization results.

Intervention

Application development

We developed a multifaceted, patient-centered, smartphone-based application, the Heart Health Application, which promotes medication adherence via a health self-management program initiated before hospital discharge. In developing the Heart Health Application, we first reviewed the adherence literature and adopted a user-centered design process – an evidence-based approach informed by the needs and understanding of a specific end-user group^[54] – to thoroughly investigate patient needs. We then translated these needs into a set of functional requirements and design guidelines, creating four modules focused on secondary prevention [medication reminders, cardiac health education, health questionnaire and feedback, and personal data center; Figure 2]. We conducted iterative cycles of prototyping and user testing to maximize the user experience and promote adoption by patients. To improve patient engagement (e.g., timely feedback to the medication reminders and frequent application use), we incorporated an incentive program into the application that provides credits toward rewards such as convenient clinical appointment

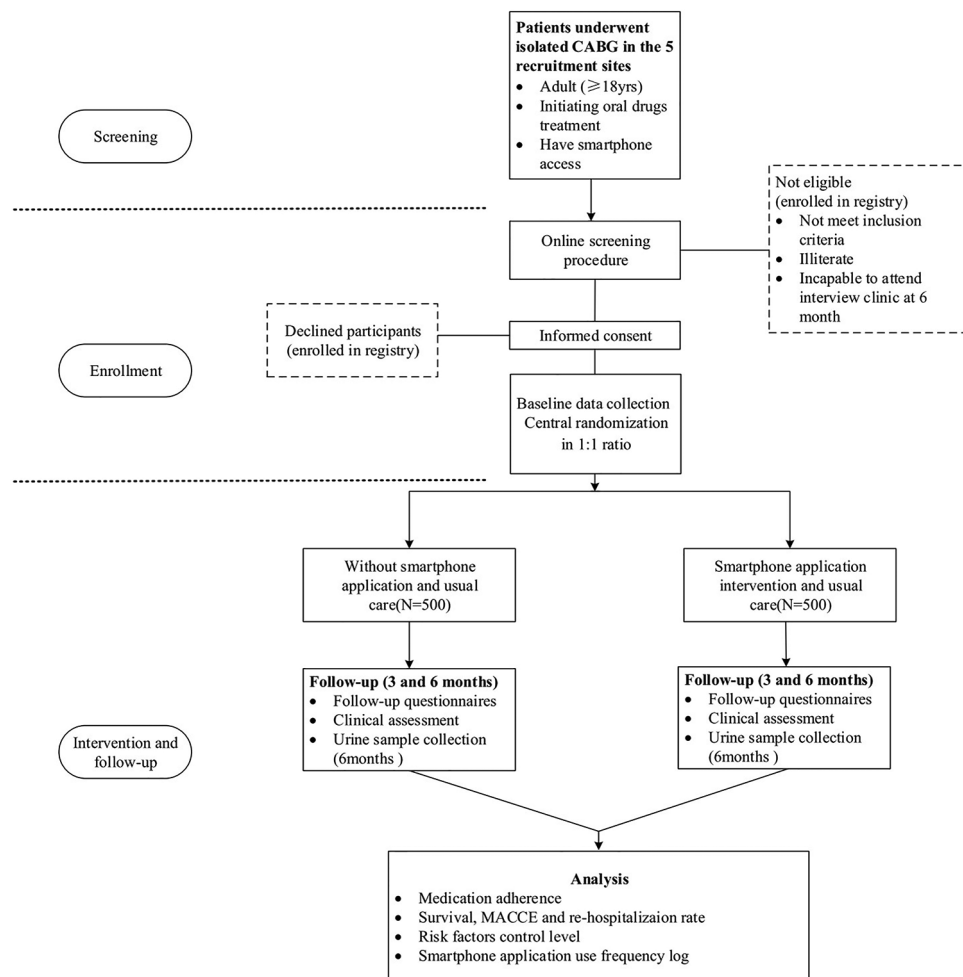


Figure 1: Overview of MISSION-2 study. CABG: Coronary artery bypass grafting; MACCE: Major adverse cardiovascular and cerebrovascular events. MISSION-2: Measurement and Improvement Studies of Surgical Coronary Revascularization: Medication Adherence.

scheduling. The different components of the Heart Health Application are discussed.

Medication reminders

Our research nurses input patient discharge medications and other relevant clinical information into the application before patient discharge from the hospital. This information is also synchronized with data on our web-based patient data collection platform. Participants are able to edit their medication regimen whenever a change is made. When it is time to take a medication, the application automatically alarms the patient. The patient taps the application bar for that reminder to confirm that the dose was taken as scheduled.

Cardiac health education

During initial development, we collected information from CABG patients on their concerns regarding cardiac rehabilitation and areas where they would like further instruction. We engaged a panel of cardiac surgeons and rehabilitation physicians to write patient-friendly answers to these questions. We combined these answers with content originating from scientific guidelines into a collection of educational readings on secondary preventive cardiac care that are easily accessible through the application.

Questionnaire and interactive feedback

Participants receive an 8-item questionnaire each week via the application messaging service [Table 1]. The questions relate to medication adherence and secondary prevention goals such as blood pressure and blood glucose control, physical activity, and healthy diet. After completing the questionnaire, participants receive preprogrammed interactive feedback, encouragement, and advice regarding their secondary prevention status and performance. This strategy for health self-management is based on social cognitive theory, and it has been successfully applied in mobile health technologies.^[55]

Personal data center

In this module, participants have access to a dashboard that dynamically tracks their individual cardiovascular risk factor control levels, recent blood biochemistry test results, and secondary prevention targets for behavior modifications such as smoking cessation and a low-salt diet. Patient health data are automatically populated based on records from the synchronized web-based data server platform.

Application training

Application training is provided to each participant in



Figure 2: Smartphone application interface depicting the four modules. (a) Four modules in Healthy Heart Application home interface; (b) Medication reminder; (c) Cardiac education readings; (d) Risk factor control targets in personal data center; (e) Blood pressure and biochemistry test results in personal data center; (f) Personal information in personal data center; (g) Weekly questionnaire; (h) Personalized feedback on questionnaire.

Table 1: Weekly health self-management questionnaire

| |
|--|
| Did you ever forget to take prescribed medicine this week? |
| Have you been keeping record of blood pressure this week and what is it? |
| Did you test your blood glucose this week and what is it? |
| Did you test your blood cholesterol this week and what is it? |
| Did you smoke or expose yourself to secondary smoke this week? |
| Did you exercise this week and what level is it? |
| Have you monitored your body weight and what was it? |
| Have you had a low salt and fat diet this week? |

the intervention group. Researchers help participants to download and install the application, and they demonstrate how to use the four modules. Application training is repeated at multiple points during the inpatient stay to ensure that participants are able to independently operate the application.

A telephone number is also provided within the application for patients to call with any application-related questions after hospital discharge.

Application transaction log file analysis

We record the application transaction log file on the application server station for each participant. We will use this file to assess how often the application was operated, which modules were used most frequently, whether the weekly questionnaire and the daily medication reminder feedback were completed in a timely manner, how usage patterns changed over the course of follow-up, and what participant characteristics were associated with consistent use.^[56]

Usual care

Patients randomized to the control arm receive standard post-CABG care without any additional intervention.

Regardless of the treatment arm, patients receive cardiology education, instruction on CABG secondary prevention, and promotion of self-care management from our research nurses and physicians during the inpatient stay after randomization; referral to cardiac rehabilitation; and pre-discharge planning.

Data collection

Because the recruiting sites are members of the CCSR network, the data collection and storage methods for our trial follow CCSR data regulations. All data related to hospital admissions, procedures, and follow-up are collected according to the definitions of the Society of Thoracic Surgeons National Adult Cardiac Database (<http://www.sts.org/>). The web-based CCSR data collection platform (<http://ccsr.cvs-china.com>) uses a high-level secure socket layer. The efforts made to ensure data accuracy and completeness have been described previously,^[53,57,58] and they are supervised by the NCC. The dataset for this study includes the following four modules: baseline in-hospital information, 3- and 6-month follow-up data, and interactive information from the application [Table 2].

For baseline data, participating sites may directly import their in-hospital data from the Hospital Information System into the CCSR database if the data meet the safety and quality criteria established by the CCSR; otherwise, data must be manually entered into the CCSR system. Trained researchers who are blinded to the group allocation conduct face-to-face interviews with patients at the 3-month follow-up visit. Data collection includes C-MMAS-8, self-reported secondary preventive medication information (including names, dosage, and frequency of the drugs taken), and clinical

assessments of blood pressure, heart rate, body mass index, smoking status, and exercise level. Patients are also asked about the occurrence of any recent cardiovascular events or hospitalizations; a copy of the medical record for each event will be sent to the NCC for final adjudication by an expert clinical panel. A fasting blood sample is being collected for blood biochemistry tests. At the end of the interview, after the blinded follow-up assessment, participants are asked to identify their group assignment; participants in the intervention group then complete the application user feedback questionnaire. Participants who are unable to attend a face-to-face interview are asked to answer the questionnaires via telephone, with clinical information obtained through the medical practitioner. The data variables and interview procedures for the 6-month visit are consistent with those for the 3-month visit. In addition, a urine sample is collected for medication screening. For patients unable to attend the 6-month interview, a standardized cold-chain transportation service will collect the urine samples.

Researchers enter follow-up data directly into the CCSR web-based data collection platform while they are conducting the interviews to avoid the errors related to transcription from paper forms. To ensure completeness and accuracy of each module, the CCSR system incorporates logic checks with real-time feedback on input data that violate predetermined rules for format or range. The interactive information from the application is recorded in the server and will be exported for application usage analysis.

Biological samples

Blood samples collected during the index hospitalization are being stored for future genetic studies. We will use

Table 2: Variables collected in each module of the data platform

| Variables | Data source | | | |
|----------------------------------|----------------------|-------------------|-------------------|-------------------------|
| | Baseline information | 3-month follow-up | 6-month follow-up | Interactive information |
| Patient characteristics | • | • | • | • |
| Socioeconomic background | • | • | • | |
| Comorbidities | • | | | |
| Secondary preventive medications | • | • | • | • |
| Smoking status | • | • | • | • |
| Exercise level | • | • | • | • |
| Body mass index | • | • | • | • |
| Body weight | • | • | • | • |
| Height | • | • | • | • |
| Waist circumference | • | • | • | • |
| Resting heart rate | • | • | • | • |
| Blood pressure | • | • | • | • |
| Blood glucose | • | • | • | • |
| Fasting cholesterol | • | • | • | • |
| Physical activity capacity | • | • | • | • |
| Survival | • | • | • | |
| MACCE | | • | • | |
| Rehospitalization | | • | • | |
| C-MMAS-8 | | • | • | |
| Application user feedback | | • | • | • |

C-MMAS-8: Chinese version of the 8-item Morisky Medication Adherence Scale; MACCE: Major adverse cardiovascular and cerebrovascular events. Variables with "•" will be collected in the data sources respectively.

high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) to analyze the 6-month urine samples for the presence of the secondary preventive medications or their metabolites; results will be used for confirmation of self-reported medication adherence.^[59] Biological samples from each participating hospital will be transported to the NCC core laboratory for centralized management and analysis.

Outcome measures

The primary outcome is CABG secondary preventive medication adherence as measured by the C-MMAS-8 at 6 months after randomization. We obtained a license from the developer for the use of the linguistically certified C-MMAS-8.^[48] Low medication adherence will be defined as a C-MMAS-8 score of <6.

Secondary outcomes will be assessed at the 3-, 6-, and 12-month follow-up visits [Table 3]. MACCE is defined as the composite of death, myocardial infarction, stroke, and unplanned revascularization. Body mass index is calculated by dividing the weight in kilograms by the height in meters squared. Systolic and diastolic blood pressure will be assessed by an electronic sphygmomanometer. Glucose and cholesterol levels will be measured after 12 h of fasting and analyzed at the pathology department of the corresponding hospital in standard fashion. Smoking status will be assessed via self-report. HbA1c test results <6.5% will be defined as normal.

Adherence to specific secondary preventive medications (antiplatelet drugs, β -blockers, statins, and ACEI/ARBs) will be assessed via patient self-report at the 3- and 6-month visits. In addition, we will use HPLC-MS/MS to screen for these medications or their metabolites in the 6-month urine samples to confirm medication use.^[59] Adherence will be defined as the identification of the secondary preventive medication in the HPLC-MS/MS urinalysis.

Table 3: Primary and secondary outcomes

| |
|---|
| Primary outcome |
| Secondary preventive medication adherence at 6 months according to C-MMAS-8 |
| Secondary outcomes |
| Mortality |
| MACCE |
| Cardiovascular rehospitalization |
| Other prespecified outcome measures |
| Secondary preventive pharmacotherapy use according to urine analysis |
| Secondary preventive pharmacotherapy use according to patient self-report |
| Cardiovascular risk factors, including fasting glucose, fasting lipid levels, hemoglobin A1c, resting blood pressure, weight, body mass index, and self-reported smoking status |

C-MMAS-8: Chinese version of the 8-item Morisky Medication Adherence Scale; MACCE: Major adverse cardiovascular and cerebrovascular events (composite of all-cause death, myocardial infarction, stroke, and repeat revascularization).

Sample size

Approximately 45–55% of chronic disease patients poorly adhere to secondary preventive medications.^[8,11,12,60,61] We hypothesize that the smartphone application intervention will result in a 10–15% decrease in the percentage of patients with low adherence according to the C-MMAS-8. To detect a minimal clinically important difference in medication adherence between the groups with 80% power and a 5% level of significance, a sample size of 800 participants (400 per group) is required. To account for an estimated 20% loss to follow-up, 500 patients must be randomized to each study arm.

Statistical analysis

We will perform an intention-to-treat analysis. Categorical variables will be summarized as proportions, while continuous variables will be summarized as means and standard deviations or medians and interquartile ranges. We will compare baseline patient characteristics between the control and intervention groups to assess the adequacy of the randomization, using Chi-square tests for categorical variables and Student's *t*-tests or Mann-Whitney tests for continuous variables. We will also compare patient outcomes using these methods. We will calculate relative risks and 95% confidence intervals to further assess the relationship between the intervention and the primary and secondary outcomes.

We will conduct sensitivity analyses that consider participants who are missing follow-up data, withdrew from the study, or were lost to follow-up as nonadherent. If there are significant differences in baseline characteristics between the groups, we will consider adjusting for these variables in additional analyses. We will further assess the effect of the intervention on adherence in prespecified subgroup analyses based on age, sex, level of education, recruitment site, adherence at baseline, and level of application engagement. Statistical tests will be two-sided with $\alpha = 0.05$. All analyses will be performed using SAS version 9.3 (SAS Institute, USA).

Trial status

Patient enrollment began in June 2015. Recruitment, follow-up, and urine sample collection are ongoing. Using data from patients recruited early in the enrollment period, we identified a wide variety of medications being prescribed to patients after CABG, likely reflecting the multicenter nature of the study and diverse socioeconomic backgrounds of participants. A number of these medications have no established HPLC-MS/MS methods to identify the prototypes or metabolites in urine. We began establishing testing protocols for these medications in January 2018 and expect to finish by the end of June 2018.

Ethics and dissemination

The NCC is leading the study design, management, and data auditing and analysis for this study. The Ethics Committee of Fuwai Hospital approved the study design, and all participating sites accepted the central ethics approval or obtained local approval by internal ethics committees. All

patients must provide written informed consent for their participation in the trial. We plan to disseminate the findings of this study via the usual scientific forums, including peer-reviewed publications and presentations at international conferences.

DISCUSSION

MISSION-2 aims to evaluate the role of a smartphone application in improving secondary preventive medication adherence of outpatients after CABG. The benefits of comprehensive CABG secondary preventive medications, including aspirin, β -blockers, statins, and ACEI/ARBs, have been thoroughly established.^[11,62-66] With the development of mobile health technology, traditional health-care infrastructure to promote secondary prevention, such as face-to-face intervention at a clinic, may become less necessary.^[67] For patients in low- and middle-income countries, where >80% of cardiovascular deaths occur,^[68] smartphone technology might prove to be particularly helpful for increasing access to secondary prevention, bypassing traditional barriers to health information with efficiency and lower cost care. Smartphone technology could bridge the gap between scientific evidence and clinical practice. If effective, this mobile health intervention can potentially offer access to medical resources for large numbers of CABG patients.

The study strengths include the use of an application that integrates multiple technological elements to appeal to a range of patient preferences and learning styles and has the potential for sustainable provision within models of CABG outpatient care. In addition to the subjective medication adherence measurements from the C-MMAS-8 and patient self-reports of drug regimens, we also incorporate an objective measurement through the use of HPLC-MS/MS urinalysis. This technique has proved to be reliable, accurate, and precise in prior studies.^[59,69]

The reasons for medication nonadherence may be broadly categorized as unintentional or intentional. Reasons for unintentional nonadherence include forgetfulness or carelessness.^[70-72] Our application can intervene on such unintentional nonadherence by providing scheduled daily dose reminders. For intentional nonadherence, which involves a reasoned decision by the patient to not take a medication as instructed based on feelings or beliefs,^[27,28,30-32,71,72] our application provides educational information, which can better inform patients about the importance of treatment and potentially alter patient perceptions. Traditional reminder systems, such as weekly pill boxes, packaged calendars, and unit-of-use packaging, cannot achieve this goal.^[14,17,18]

There are also several potential limitations of the study. First, neither researchers nor patients will be blinded to the study allocation. However, those analyzing biologic samples and assessing outcomes will be unaware of patient allocation, which will ensure objective assessment of research outcomes. Second, several of the outcomes are collected by patient self-report. To confirm patient reports

of medication adherence, we have incorporated an objective assessment via HPLC-MS/MS urinalysis.

In conclusion, MISSION-2 will not only provide evidence regarding the feasibility and effectiveness of the described intervention for improving adherence to CABG secondary preventive therapies, but also explore a model for outpatient health self-management that could be translated to various chronic diseases and widely disseminated across resource-limited settings. The implementation of this trial will further inform the development of mobile smartphone technology to improve patient outcomes.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. WHO. Fact Sheet Number 310. The Top 10 Causes of Death. Available from: <http://www.who.int/mediacentre/factsheets/fs310/en/index.html>. [Last accessed on 22 Aug 20].
2. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, *et al.* 2011 ACCF/AHA guideline for coronary artery bypass graft surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2011;58:e123-210. doi: 10.1016/j.jacc.2011.08.009.
3. Kulik A, Ruel M, Jneid H, Ferguson TB, Hiratzka LF, Ikonomidis JS, *et al.* Secondary prevention after coronary artery bypass graft surgery: A scientific statement from the American Heart Association. *Circulation* 2015;131:927-64. doi: 10.1161/cir.000000000000182.
4. Alexander JH, Smith PK. Coronary-artery bypass grafting. *N Engl J Med* 2016;374:1954-64. doi: 10.1056/NEJMr1406944.
5. Liu JM, Ge L, Li J, Li X, Feng F, Zhang HB, *et al.* ACEI/ARB use among high risk patients with coronary heart disease in China: A cross-sectional study (In chinese). *Chin J Cardiol* 2013;41:18-22. doi: 10.3760/cma.j.issn.0253-3758.2013.01.005.
6. Li J, Chen YP, Li X, Armitage J, Feng F, Liu JM, *et al.* Use of secondary preventive medications in patients with atherosclerotic disease in urban China: A cross-sectional study of 16, 860 patients. *Chin Med J* 2012;125:4361-7. doi: 10.3760/cma.j.issn.0366-6999.2012.24.008.
7. Balasi LR, Paryad E, Booraki SH, Leili EK, Sadeghi Meibodi AM, Sheikhan NN. Medication adherence after CABG and its related to medication belief. *Biomed Pharmacol J* 2015;8:603-10. doi: 10.13005/bpj/804.
8. Barry AR, Koshman SL, Norris CM, Ross DB, Pearson GJ. Evaluation of preventive cardiovascular pharmacotherapy after coronary artery bypass graft surgery. *Pharmacotherapy* 2014;34:464-72. doi: 10.1002/phar.1380.
9. Thomas RJ, Goel K, Jumean M, Mullany C, Lahr B, Gibbons R, *et al.* Short- and long-term impact of an inpatient quality improvement initiative: Results of the CABG-GAP practice improvement project. *J Cardiopulm Rehabil Prev* 2013;33:212-9. doi: 10.1097/HCR.0b013e3182930cd0.
10. Khandaria U, Townsend KA, Erickson SR, Vlasnik J, Prager RL, Eagle KA, *et al.* Medication adherence following coronary artery

- bypass graft surgery: Assessment of beliefs and attitudes. *Ann Pharmacother* 2008;42:192-9. doi: 10.1345/aph.1K497.
11. Goyal A, Alexander JH, Hafley GE, Graham SH, Mehta RH, Mack MJ, *et al.* Outcomes associated with the use of secondary prevention medications after coronary artery bypass graft surgery. *Ann Thorac Surg* 2007;83:993-1001. doi: 10.1016/j.athoracsur.2006.10.046.
 12. Okraïnc K, Pilote L, Platt R, Eisenberg MJ. Use of cardiovascular medical therapy among patients undergoing coronary artery bypass graft surgery: Results from the ROSETTA-CABG registry. *Can J Cardiol* 2006;22:841-7. doi: 10.1016/S0828-282X(06)70302-6.
 13. Iihara N, Tsukamoto T, Morita S, Miyoshi C, Takabatake K, Kurosaki Y, *et al.* Beliefs of chronically ill Japanese patients that lead to intentional non-adherence to medication. *J Clin Pharm Ther* 2004;29:417-24. doi: 10.1111/j.1365-2710.2004.00580.x.
 14. Dayer L, Heldenbrand S, Anderson P, Gubbins PO, Martin BC. Smartphone medication adherence apps: Potential benefits to patients and providers. *J Am Pharm Assoc (2003)* 2013;53:172-81. doi: 10.1331/JAPhA.2013.12202.
 15. Patterson SM, Cadogan CA, Kerse N, Cardwell CR, Bradley MC, Ryan C, *et al.* Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev* 2014;10:CD008165. doi: 10.1002/14651858.CD008165.pub3.
 16. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005;353:487-97. doi: 10.1056/NEJMr050100.
 17. Rolnick SJ, Asche S, Pawloski PA, Bruzek RJ, Hedblom B. Barriers to and facilitators of medication adherence. *Am J Pharm Benefits* 2013;5:157. doi: 10.3121/cmr.2011.1020.ps2-32.
 18. Harbig P, Barat I, Damsgaard EM. Suitability of an electronic reminder device for measuring drug adherence in elderly patients with complex medication. *J Telemed Telecare* 2012;18:352-6. doi: 10.1258/jtt.2012.120120.
 19. Mahtani KR, Heneghan CJ, Glasziou PP, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. *Cochrane Database Syst Rev* 2011;9:CD005025. doi: 10.1002/14651858.CD005025.pub3.
 20. van Driel ML, Morledge MD, Ulep R, Shaffer JP, Davies P, Deichmann R, *et al.* Interventions to improve adherence to lipid-lowering medication. *Cochrane Database Syst Rev* 2016;12:CD004371. doi: 10.1002/14651858.CD004371.pub4.
 21. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther* 2001;23:1296-310. doi: 10.1016/S0149-2918(01)80109-0.
 22. Chapman S. Looking at medication adherence: An evidence review. *Br J Community Nurs* 2017;22:485-7. doi: 10.12968/bjcn.2017.22.10.485.
 23. Neubeck L, Redfern J, Fernandez R, Briffa T, Bauman A, Freedman SB, *et al.* Telehealth interventions for the secondary prevention of coronary heart disease: A systematic review. *Eur J Cardiovasc Prev Rehabil* 2009;16:281-9. doi: 10.1097/HJR.0b013e32832a4e7a.
 24. Fischer MA, Choudhry NK, Bykov K, Brill G, Bopp G, Wurst AM, *et al.* Pharmacy-based interventions to reduce primary medication nonadherence to cardiovascular medications. *Med Care* 2014;52:1050-4. doi: 10.1097/MLR.0000000000000247.
 25. Vollmer WM, Owen-Smith AA, Tom JO, Laws R, Ditmer DG, Smith DH, *et al.* Improving adherence to cardiovascular disease medications with information technology. *Am J Manag Care* 2014;20:SP502-10.
 26. Haynes RB, McDonald H, Garg AX, Montague P. Interventions for helping patients to follow prescriptions for medications. *Cochrane Database Syst Rev* 2002;2:CD000011. doi: 10.1002/14651858.CD000011.
 27. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008;5:CD000011. doi: 10.1002/14651858.CD000011.pub3.
 28. Nieuwlaar R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keenanasseril A, *et al.* Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2014;11:CD000011. doi: 10.1002/14651858.CD000011.pub4.
 29. Yudi MB, Clark DJ, Tsang D, Jelinek M, Kalten K, Joshi S, *et al.* SMARTphone-based, early cardiac REHABilitation in patients with acute coronary syndromes [SMART-REHAB trial]: A randomized controlled trial protocol. *BMC Cardiovasc Disord* 2016;16:170. doi: 10.1186/s12872-016-0356-6.
 30. Pew Research Center's Internet & American Life Project. Mobile Technology Fact Sheet. Available from: <http://www.pewinternet.org/fact-sheets/mobile-technology-fact-sheet>. [Last accessed on 2017 Aug 22].
 31. Fierce Wireless. Worldwide Smartphone Usage to Grow 25% in 2014. Available from: <http://www.fiercewireless.com/pressreleases/emarketerworldwidesmartphoneusagegrow252014>. [Last accessed on 2017 Aug 22].
 32. Krousel-Wood M, Reckelhoff J, Muntner P. Exploring demographic health differences – A foundation for addressing health disparities in cardiovascular disease. *Am J Med Sci* 2014;348:89-91. doi: 10.1097/maj.0000000000000316.
 33. Karlamangla AS, Merkin SS, Crimmins EM, Seeman TE. Socioeconomic and ethnic disparities in cardiovascular risk in the United States, 2001-2006. *Ann Epidemiol* 2010;20:617-28. doi: 10.1016/j.annepidem.2010.05.003.
 34. Neubeck L, Lowres N, Benjamin EJ, Freedman SB, Coorey G, Redfern J, *et al.* The mobile revolution – Using smartphone apps to prevent cardiovascular disease. *Nat Rev Cardiol* 2015;12:350-60. doi: 10.1038/nrcardio.2015.34.
 35. IMS Institute for Healthcare Informatics. Patient Apps for Improved Healthcare: From Novelty to Mainstream. Available from: http://www.imshealth.com/files/web/IMSH%20Institute/Reports/Patient%20Apps%20for%20Improved%20Healthcare/IIHI_Patient_Apps_Report.pdf. [Last accessed on 2017 Aug 22].
 36. Dubey D, Amritphale A, Sawhney A, Amritphale N, Dubey P, Pandey A, *et al.* Smart phone applications as a source of information on stroke. *J Stroke* 2014;16:86-90. doi: 10.5853/jos.2014.16.2.86. Epub 2014 May 30.
 37. de la Vega R, Miró J. MHealth: A strategic field without a solid scientific soul. A systematic review of pain-related apps. *PLoS One* 2014;9:e101312. doi: 10.1371/journal.pone.0101312.
 38. Buijink AW, Visser BJ, Marshall L. Medical apps for smartphones: Lack of evidence undermines quality and safety. *Evid Based Med* 2013;18:90-2. doi: 10.1136/eb-2012-100885.
 39. Breton ER, Fuemmeler BF, Abrams LC. Weight loss-there is an app for that! But does it adhere to evidence-informed practices? *Transl Behav Med* 2011;1:523-9. doi: 10.1007/s13142-011-0076-5.
 40. Abrams LC, Padmanabhan N, Thaweethai L, Phillips T. iPhone apps for smoking cessation: A content analysis. *Am J Prev Med* 2011;40:279-85. doi: 10.1016/j.amepre.2010.10.032.
 41. Varnfield M, Karunanithi M, Lee CK, Honeyman E, Arnold D, Ding H, *et al.* Smartphone-based home care model improved use of cardiac rehabilitation in postmyocardial infarction patients: Results from a randomised controlled trial. *Heart* 2014;100:1770-9. doi: 10.1136/heartjnl-2014-305783.
 42. Blasco A, Carmona M, Fernández-Lozano I, Salvador CH, Pascual M, Sagredo PG, *et al.* Evaluation of a telemedicine service for the secondary prevention of coronary artery disease. *J Cardiopulm Rehabil Prev* 2012;32:25-31. doi: 10.1097/HCR.0b013e3182343aa7.
 43. Worringham C, Rojek A, Stewart I. Development and feasibility of a smartphone, ECG and GPS based system for remotely monitoring exercise in cardiac rehabilitation. *PLoS One* 2011;6:e14669. doi: 10.1371/journal.pone.0014669.
 44. Korzeniowska-Kubacka I, Dobraszkiewicz-Wasilewska B, Bilińska M, Rydzewska E, Piotrowicz R. Two models of early cardiac rehabilitation in male patients after myocardial infarction with preserved left ventricular function: Comparison of standard out-patient versus hybrid training programmes. *Kardiol Pol* 2011;69:220-6.
 45. Tian M, Ajay VS, Dunzhu D, Hameed SS, Li X, Liu Z, *et al.* A cluster-randomized, controlled trial of a simplified multifaceted management program for individuals at high cardiovascular risk (SimCard trial) in rural Tibet, China, and Haryana, India. *Circulation* 2015;132:815-24. doi: 10.1161/CIRCULATIONAHA.115.015373.
 46. Gandapur Y, Kianoush S, Kelli HM, Misra S, Urrea B, Blaha MJ, *et al.* The role of mHealth for improving medication adherence in patients with cardiovascular disease: A systematic review. *Eur Heart J Qual Care Clin Outcomes* 2016;2:237-44. doi: 10.1093/ehjqcco/qcw018.

47. Rao C, Du J, Li X, Li J, Zhang H, Zhao Y, *et al.* Rationale and design of a randomized cluster trial to improve guideline-adherence of secondary preventive drugs prescription after coronary artery bypass grafting in China: Measurement and improvement studies of surgical coronary revascularization: Secondary prevention (MISSION-1) study. *Am Heart J* 2016;178:9-18. doi: 10.1016/j.ahj.2016.01.014.
48. Yan J, You LM, Yang Q, Liu B, Jin S, Zhou J, *et al.* Translation and validation of a Chinese version of the 8-item morisky medication adherence scale in myocardial infarction patients. *J Eval Clin Pract* 2014;20:311-7. doi: 10.1111/jep.12125.
49. Eysenbach G; Consort-Ehealth Group. CONSORT-EHEALTH: Improving and standardizing evaluation reports of web-based and mobile health interventions. *J Med Internet Res* 2011;13:e126. doi: 10.2196/jmir.1923.
50. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, *et al.* SPIRIT 2013 statement: Defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-7. doi: 10.7326/0003-4819-158-3-201302050-00583.
51. Chan AW, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, *et al.* SPIRIT 2013 explanation and elaboration: Guidance for protocols of clinical trials. *BMJ* 2013;346:e7586. doi: 10.1136/bmj.e7586.
52. Chan AW, Tetzlaff JM, Altman DG, Dickersin K, Moher D. SPIRIT 2013: New guidance for content of clinical trial protocols. *Lancet* 2013;381:91-2. doi: 10.1016/S0140-6736(12)62160-6.
53. Rao C, Zhang H, Gao H, Zhao Y, Yuan X, Hua K, *et al.* The Chinese cardiac surgery registry: Design and data audit. *Ann Thorac Surg* 2016;101:1514-20. doi: 10.1016/j.athoracsur.2015.09.038.
54. McCurdie T, Taneva S, Casselman M, Yeung M, McDaniel C, Ho W, *et al.* MHealth consumer apps: The case for user-centered design. *Biomed Instrum Technol* 2012; Suppl:49-56. doi: 10.2345/0899-8205-46.s2.49.
55. Winter SJ, Sheats JL, King AC. The use of behavior change techniques and theory in technologies for cardiovascular disease prevention and treatment in adults: A comprehensive review. *Prog Cardiovasc Dis* 2016;58:605-12. doi: 10.1016/j.pcad.2016.02.005.
56. Han JY. Transaction logfile analysis in health communication research: Challenges and opportunities. *Patient Educ Couns* 2011;82:307-12. doi: 10.1016/j.pec.2010.12.018.
57. Zhang H, Yuan X, Osnabrugge RL, Meng D, Gao H, Zhang S, *et al.* Influence of diabetes mellitus on long-term clinical and economic outcomes after coronary artery bypass grafting. *Ann Thorac Surg* 2014;97:2073-9. doi: 10.1016/j.athoracsur.2014.02.047.
58. Li Y, Zheng Z, Hu S; Chinese Coronary Artery Bypass Grafting Registry Study. The Chinese coronary artery bypass grafting registry study: Analysis of the national multicentre database of 9248 patients. *Heart* 2009;95:1140-4. doi: 10.1136/hrt.2008.146563.
59. Tomaszewski M, White C, Patel P, Masca N, Damani R, Hepworth J, *et al.* High rates of non-adherence to antihypertensive treatment revealed by high-performance liquid chromatography-tandem mass spectrometry (HP LC-MS/MS) urine analysis. *Heart* 2014;100:855-61. doi: 10.1136/heartjnl-2013-305063.
60. Baroletti S, Dell'Orfano H. Medication adherence in cardiovascular disease. *Circulation* 2010;121:1455-8. doi: 10.1161/CIRCULATIONAHA.109.904003.
61. Newby LK, LaPointe NM, Chen AY, Kramer JM, Hammill BG, DeLong ER, *et al.* Long-term adherence to evidence-based secondary prevention therapies in coronary artery disease. *Circulation* 2006;113:203-12. doi: 10.1161/CIRCULATIONAHA.105.505636.
62. Zhang H, Yuan X, Zhang H, Chen S, Zhao Y, Hua K, *et al.* Efficacy of long-term β -blocker therapy for secondary prevention of long-term outcomes after coronary artery bypass grafting surgery. *Circulation* 2015;131:2194-201. doi: 10.1161/circulationaha.114.014209.
63. Iqbal J, Zhang YJ, Holmes DR, Morice MC, Mack MJ, Kappetein AP, *et al.* Optimal medical therapy improves clinical outcomes in patients undergoing revascularization with percutaneous coronary intervention or coronary artery bypass grafting: Insights from the synergy between percutaneous coronary intervention with TAXUS and cardiac surgery (SYNTAX) trial at the 5-year follow-up. *Circulation* 2015;131:1269-77. doi: 10.1161/CIRCULATIONAHA.114.013042.
64. Mangano DT; Multicenter Study of Perioperative Ischemia Research Group. Aspirin and mortality from coronary bypass surgery. *N Engl J Med* 2002;347:1309-17. doi: 10.1056/NEJMoa020798.
65. Heart Outcomes Prevention Evaluation Study Investigators, Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, *et al.* Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;342:145-53. doi: 10.1056/NEJM200001203420301.
66. Campeau L, Knatterud GL, Domanski M, Hunninghake DB, White CW, Geller NL, *et al.* The effect of aggressive lowering of low-density lipoprotein cholesterol levels and low-dose anticoagulation on obstructive changes in saphenous-vein coronary-artery bypass grafts. *N Engl J Med* 1997;336:153-62. doi: 10.1056/NEJM199701163360301.
67. Bastawrous A, Armstrong MJ. Mobile health use in low- and high-income countries: An overview of the peer-reviewed literature. *J R Soc Med* 2013;106:130-42. doi: 10.1177/0141076812472620.
68. WHO. Noncommunicable Diseases and Mental Health. Global Status Report on Noncommunicable Diseases; 2010. Available from: [http://www.who.int/nmh/publications/ncd_report2010/en/\(2011\)](http://www.who.int/nmh/publications/ncd_report2010/en/(2011)). [Last accessed on 22 Aug 20].
69. Olah TV, McLoughlin DA, Gilbert JD. The simultaneous determination of mixtures of drug candidates by liquid chromatography/atmospheric pressure chemical ionization mass spectrometry as an *in vivo* drug screening procedure. *Rapid Commun Mass Spectrom* 1997;11:17-23. doi: 10.1002/(SICI)1097-0231(19970115)11:1<17::AID-RCM812>3.0.CO;2-N.
70. Daleboudt GM, Broadbent E, McQueen F, Kaptein AA. Intentional and unintentional treatment nonadherence in patients with systemic lupus erythematosus. *Arthritis Care Res (Hoboken)* 2011;63:342-50. doi: 10.1002/acr.20411.
71. Lehane E, McCarthy G. Intentional and unintentional medication non-adherence: A comprehensive framework for clinical research and practice? A discussion paper. *Int J Nurs Stud* 2007;44:1468-77. doi: 10.1016/j.ijnurstu.2006.07.010.
72. Wroe AL. Intentional and unintentional nonadherence: A study of decision making. *J Behav Med* 2002;25:355-72. doi: 10.1023/A:1015866415552.

冠脉搭桥质量改善研究：患者二级预防用药依从性研究 (MISSION-2)

摘要

背景：冠脉搭桥术后的二级预防药物治疗，对减少术后心血管不良事件发生至关重要。然而，既往研究显示患者二级预防用药依从性差，并且传统提高依从性的干预手段效果有限。智能手机在全球范围内的普及，将有望改变传统的医疗模式，低成本、高效率地提供更多诊疗机会，改善搭桥术后二级预防水平和患者预后。但目前亟需相关的高质量临床研究提供可靠的临床应用证据。

方法：MISSION-2研究是一个前瞻性、多中心、开放标签、随机对照的临床试验，计划入选1000例搭桥术后患者，采用1:1随机分组。根据“用户中心”设计思路，我们研发了手机应用“心健康”APP，对干预组患者从术后住院期间开始提供用药提醒，心脏术后健康宣教，心脏康复指导，交互式个性化生活方式建议。该研究的一级终点为术后6个月的依据8-MMAS量表测量的用药依从性。二级终点包括全因死亡、心血管再住院以及死亡、心梗、中风、再次血运重建的复合终点。

讨论：该研究的结果，将为移动医疗技术在冠脉搭桥术后二级预防中应用的可行性和有效性提供可靠的临床证据。另外，试验的实施经验将为在医疗资源相对不足条件下，发展移动医疗技术改善慢病患者预后，探索患者院外自我管理新模式提供重要的借鉴。