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Role of the Intelligent Exercise Rehabilitation Management System on adherence of cardiac rehabilitation in patients with coronary heart disease: a randomized controlled crossover study protocol

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Title Page

Title of the article:

Role of the Intelligent Exercise Rehabilitation Management System on adherence of cardiac rehabilitation in patients with coronary heart disease: a randomized controlled crossover study protocol.

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Abstract

Introduction: The benefits of cardiac rehabilitation (CR) on the reduction of cardiac and all-cause mortality are well documented. However, adherence remains sub-optimal in China. It is clear that traditional CR does not meet the needs of many eligible patients and innovation is required to improve its application. Home-based CR (HBCR) is a cost-effective method that may be a valuable alternative for many individuals in China. In HBCR, it is essential to maintain an exercise intensity that is both effective and within safe limits. Mobile health interventions have the potential to overcome these obstacles and may be efficacious in improving adherence. The purpose of this study is to evaluate whether an Intelligent Exercise Rehabilitation Exercise System (IERMS)-based HBCR could improve adherence to CR and to assess the effects on exercise capacity, mental health, self-efficacy, quality of life and lifestyle-related risk factors.

Methods and analysis: We propose a single-blinded, two-arm, randomized control crossover study of 54 patients with coronary heart disease (CHD). Participants will be randomly assigned in a 1:1 ratio to one of two groups. Patients in Group 1 will receive the IERMS intervention together with usual care for the first six weeks and usual care for the last six weeks, while patients assigned to Group 2 will receive usual care for the first six weeks and will use IERMS in the last six weeks. The primary outcome is adherence to the program and secondary outcomes include

exercise capacity, psychological well-being, quality of life, self-efficacy and lifestyle-related risk factors. All secondary outcomes will be measured at baseline, six weeks and 12 weeks.

Ethics and dissemination: This study has been approved by the Human Research Ethics Committee of the School of Nursing, Jilin University (HREC 2019120901). The results will be published in peer-reviewed journals and at conferences.

Trial registration number: ChiCTR1900028182; Pre-results.

Key words: Cardiac rehabilitation, adherence, coronary heart disease

Strength and Limitations of this study

1. Our home-based cardiac rehabilitation program (HBCR) is technology-based and may improve adherence of CR in patients with coronary heart disease (CHD).
2. The measurements of plantar pressure and heart rate (HR) used in this study are accurate in evaluating exercise type and intensity. This is essential for reminding patients to exercise appropriately within safe limits during CR sessions at home.
3. The crossover study design allows us to observe the maintenance of effects after the three-week IERMS intervention.

4. The study is of relatively short duration and long-term effectiveness will not be observed after 12 months.

5. The study is limited to patients with smartphones and internet access.

1. Background

Coronary heart disease (CHD) is the leading cause of mortality in China and has increased by 20.6% from 1990 to 2017[1]. Studies over the past few decades have shown an increased prevalence and incidence of CHD and it was estimated that about 11 million patients suffered from it in 2017[2]. Patients with CHD have severe physical and often psychological problems and show reduced health-related quality of life (HRQoL) scores, which is associated with high mortality and additional cardiac events [3-4].

Cardiac rehabilitation (CR), an integral component of the continuum of care for patients with CHD[5], has been demonstrated to reduce mortality by up to 37% [6-7] to improve both physical functioning and quality of life[8-10], and is recommended by the American Heart Association (AHA)/ American College of Cardiology (ACC) and the European Society of Cardiology (ESC) guidelines for patients with CHD[11-12].

Despite proven benefits, the use of and adherence to CR remains sub-optimal, with participation rates of between 10.3% and 16.3% [13] and dropout rates of between 40% and 55% [14-15]. In China, access to CR

services remains very low, with the estimated availability of CR programs about two programs per 100 million inhabitants[16]. This may due to poor availability and problems with supplying CR in China, including a lack of facilities, funding, staff training, and reimbursements for participating patients [17-18]. Drop-out or non-adherence may lead to negative outcomes in CHD [19]. Therefore, innovation is needed to improve the implementation of CR in China.

Besides center-based CR, home-based CR (HBCR) is an alternative method recommended by AHA and ACC. HBCR may be more effective in the provision of CR to many patients in China[20] and has proved to be effective in improving adherence [21]. However, while effective performance of the prescribed exercises is essential, difficulties, such as managing the exercise type, intensity and duration appropriately at home, occur with HBCR [22]. With the development of science and technology, mobile health (m-health) interventions have emerged and have the potential to deliver HBCR safely and effectively [23-25]. The m-health interventions could help patients monitor exercise intensity, provide objective feedback data and encourage patients to track their own progress, which could help them self-manage their CR and may be useful in improving their adherence. In addition, patients with CHD have shown great interest in using m-health at home, providing clear signs of developing such interventions [26].

The Intelligent Exercise Rehabilitation Management system (IERMS) has been designed to meet these requirements. It introduces a closed-loop rehabilitation management system that supports the home-based management of prescribed CR and lifestyle-related risk factors for patients with CHD. The purpose of this study is to evaluate whether IERMS-based HBCR could improve adherence to CR and to assess its effects on exercise capacity, mental health, self-efficacy, quality of life and lifestyle-related risk factors. The results of the trial are expected to facilitate the development of effective m-health interventions for HBCR.

2. Methods

2.1 Study Design

A single-blinded, two-arm, randomized control crossover study will be conducted to evaluate the role of IERMS-based HBCR on adherence, exercise capacity, mental health, self-efficacy, quality of life and lifestyle-related risk factors. All participants will be recruited from the CR outpatient setting of a medical center in Changchun, China. A total of 54 participants will be randomly assigned to one of two groups. Patients in Group 1 will use IERMS in the first stage and receive usual care in the last stage, while patients in Group 2 will receive usual care in the first stage and IERMS-based HBCR in the last stage. Each stage of the study will last for six weeks. As one of our main objectives is to assess whether there is

an interaction at the end of the intervention and to observe the maintenance of the effects after the intervention, this study does not allow a wash-out period. The profile of the study design is displayed in Figure 1. The trial conforms to the SPIRIT reporting guidelines [27] and is registered at Clinical Trials.gov: ChiCTR1900028182.

2.2 Eligibility and Recruitment

Patients will be eligible to participate if they have: (1) a documented diagnosis of CHD and having had a hospitalization incident within six months prior to randomization; (2) been assessed as suitable by a cardiologist and a physical therapist to participate in their CR; (3) no contraindications to undergo a cardiopulmonary exercise test; (4) if they are willing and able to participate in the study and to provide written informed consent.

Exclusion criteria include: (1) severe heart failure (NYHA class IV); (2) unstable angina; (3) unstable clinical status; (4) coronary artery bypass grafting within the last three months; (5) patients are unable to use the IERMS-enabled devices after instruction; (6) lack of internet access at home; (7) requiring a walking aid for mobility; (8) participation in another clinical trial.

We will recruit participants at a medical center in Changchun, China. Patients admitted with CHD and eligible for CR will be screened and those

meeting the inclusion criteria will be invited to participate. We will inform them of the study details, and if they agree to participate in the study, they will be asked to sign the consent form.

2.3 Sample Size Calculation

This study selects the main outcome indicators of HBCR adherence as the calculation standard. A previous study has shown CR adherence rates of ~68% and ~94% for technology-based HBCR [28]. We will use two sample rate calculation formula: $N=[\frac{z_{\frac{\alpha}{2}}\sqrt{\pi_c\ (1-\pi_c)\ (Q_1^{-1}+Q_2^{-1})}}{\pi_1-\pi_2}+\frac{z_{\beta}\sqrt{\pi_1\ (1-\pi_1)\ /Q_1+\pi_2\ (1-\pi_2)\ /Q_2}}{\pi_1-\pi_2}]$ with 90% power (type I error = 5%) to calculate the sample size, and a total sample size of 54 across both arms will be used in this study.

2.4 Randomization, Blinding and Concealed Allocation

After signing an informed consent, patients will complete baseline measurement. They will then be randomized in a 1:1 ratio to either Group 1 or the Group 2 by a computer-generated randomization list, using block randomization and randomly selected block sizes of 4, 6, or 8. This assignment will be done by independent individuals who will not participate in the recruitment process. Given the characteristics of the intervention, the participants or researchers implementing the intervention cannot be blinded. However, researchers evaluating the results will be unaware of patient assignments. To ensure hidden assignments and

minimize selection bias, independent designated members of the School of Nursing, Jilin University will assign random numbers based on local researcher requirements.

2.5 Usual care

Regardless of the IERMS intervention, all patients will receive usual care. Patients will receive health education about CR provided by a cardiologist and a physical therapist will give them personalized exercise prescriptions according to the results of their cardiopulmonary exercise test (CPET). Patients will be free to participate in any type of exercise classes, Tai Chi programs, group dancing and available CR programs after discharge from rehabilitation facilities. All patients are required to record exercise logs, including exercise type, intensity and duration at home and will receive follow-up calls at six weeks and 12 weeks.

2.6 Key components of IERMS

The IERMS is a closed-loop rehabilitation management system which can facilitate management of exercise prescription and lifestyle-related risk factors and consists of three main components: Professional System, Patient Station and the Cloud (Figure 2). This system has been authorized as a China Invention Patent (Publication Patent Number (PPNO): 201810114305.3).

Patient Station

The Patient Station consists of one mobile application and two monitoring devices which including a pair of smart insoles and a heart rate (HR) monitor.

Smart insoles have been independently developed in this study and are able to measure gait parameters using inserted plantar pressure sensors and accelerometers during CR sessions. This has been shown to be accurate in identifying the type of exercise and in calculating energy expenditure [29-30]. The data collected by the smart insoles will be uploaded to the cloud which will analyze the metabolic equivalent (METs) and then present the results on the app. The HR monitor used in this study is tied around the chest and can monitor HR in real-time.

The mobile application and these monitoring devices are connected by Bluetooth. The mobile application is thus able to synchronize the data collected by the sensors and provide real-time motivational feedback automatically generated from actual exercise performances. Furthermore, the mobile application can present educational materials and exercise prescriptions prescribed by professionals and upload patients' data to the professional system.

The cloud

The cloud is the core part of the data processing, which stores and analyzes the data transmitted by the monitoring devices and then

distributes the results to the patient station and professional system. The cloud will use deep neural network models to train and evaluate the data and generate feedback on the patient's exercise and send them to the mobile application on the patient station. The cloud will also send a report of the exercise performance of patients in CR sessions to the professionals allowing them to update the exercise prescription for reference.

Professional System

The Professional System is a web-based tool for medical professionals, which can manage patients' CR exercise at home. Patient files are stored in the system, including the patient's medical history, past exercise prescriptions and lifestyle-related risk factors. The system can also synchronize the patient's exercise progress, weight, HR and BP, etc. The professionals can thus monitor the patient's health situations remotely through the system and perform continuity of care for patients.

2.7 Description of the IERMS intervention

Eligible and consenting participants will be enrolled prior to discharge from an outpatient ambulatory CR program and will learn and practice all features of the system in the hospital. Participants will be given a pair of smart insoles, an HR monitor and a mobile application will be installed on their smartphones.

Tele-monitoring CR sessions

In order to ensure the patients' safety, a series of confirmations will be performed before CR sessions including BP, HR and the presence or absence of cardiac symptoms, such as dyspnea and chest distress. Patients will receive immediate feedback on whether they are safe to exercise at that time, and if not, the exercise time will be changed.

During the exercise sessions, patients will be asked to wear a pair of smart insoles and an HR monitor, which can monitor the intensity and type of exercise to ensure both safety and effectiveness. Endurance and resistance training are both included in CR sessions. The goal of the endurance training is to reach the individual, pre-defined target zone[31], which will make sure the patient is safe while also allowing effective exercise. When the exercise intensity is not enough, the mobile application will automatically encourage the patients to speed up, and if the exercise intensity is excessive or the exercise type is not appropriate, the mobile application will remind the patients to slow down or change the type of training.

Encouraging self-management

The IERMS will provide an individualized exercise target according to the prescribed exercise program developed by the physical therapists, and which will be progressively updated weekly. The medical staff will be able to monitor the exercise frequency, intensity and type of participants

through the information collected by the monitoring devices and give feedback on the completion of the rehabilitation exercise and set goals, which can encourage patients to track their exercise progress. In addition, patients can communicate with the professionals through the mobile application and receive feedback within 24 hours.

The IERMS encourages patients to upload BP, HR, weight, smoking situation, and physical activity to the mobile application. This enables them to track their own progress to motivate them to quit smoking, lose weight, improve physical activity and reduce sedentary behaviors, which can, in turn, improve their self-monitoring, thereby increasing patients' adherence. Participants will also be encouraged to participate in other different types of physical activities, such as jogging, Tai Chi and group dancing.

2.8 Outcome Measures and data collection

Outcome measures will be analyzed by researchers blinded to the group allocation. All assessments will be performed at baseline, six weeks, and 12 weeks (Figure 3). The profile of the outcome measures for the study is outlined in Table 1.

Table 1 Completed SPIRIT diagram for the study

	STUDY PERIOD			
	Enrollmen	**Allocation**	**Post- Allocation**	**Close-out**

	t				
TIMEPOINT*	**-t1**	**0**	**t1**	**t2**	**t3**
ENROLLMENT:					
Eligibility screen	X				
Informed consent		X	X	X	
Randomization		X	X	X	
Allocation		X	X	X	
INTERVENTIONS:					
Group 1*		←	—	→	
Group 2**		←	—	→	
ASSESSMENTS:					
Adherence			X	X	
VO_2peak		X	X	X	
GAD-7		X	X	X	
PHQ-9		X	X	X	
SF-12		X	X	X	
GSES		X	X	X	
Life-related risk factors***		X	X	X	
Adverse event Reporting		←	—	→	
Satisfaction/usability			X	X	

Tests					

t1 = six weeks, t2 = 12 weeks

* IERMS in the first phase and usual care in the second phase.
** Usual care in the first phase and IERMS in the second phase.

***Part of routine care and therefore assessed before informed consent.

****Satisfaction/usability test will only be performed after IERMS intervention in each group.

GAD-7, Generalized Anxiety Disorder Scale-7; PHQ-9 Patients' Health Questionnaire Depression Scale-9; SF-12, the 12-item Short Form Health Survey; GSES, General Self -Efficacy Scale.

Primary outcome

The primary outcome will be adherence for CR. Adherence is defined as attendance for four weeks (eight or more sessions) for usual care or uploading of four weeks' data for IERMS-based HBCR, and attending six-week assessments (both groups), as described in a similar study by Dalal et al. (2007)[32]. The participation information in IERMS-based HBCR phase will be collected by the IERMS, while the adherence in the usual care phase will be analyzed from the training log.

Secondary outcomes

The secondary outcome measures for the trial are outlined in Figure 3. In general, all secondary outcomes will be measured at baseline, six weeks and 12 weeks. Secondary outcomes include VO_2peak, the Generalized Anxiety Disorder Scale-7 (GAD-7); Patients' Health Questionnaire Depression Scale-9 (PHQ-9); the 12-item Short Form

Health Survey (SF-12); General Self-Efficacy Scale (GSES) and lifestyle-related risk factors which include weight, smoking situation and physical activity. Satisfaction/usability tests will be measured at the end of the IERMS intervention in each group.

2.9 Adverse events monitoring

We will report all adverse events that occurred during the 12 weeks study period in the final paper. Adverse events during exercise training sessions are defined as deaths or other medical occurrences resulting in hospitalization during CR sessions or immediately after training sessions in an hour. Other adverse events are defined as medical occurrences resulting in hospitalization, disability or deaths without connection to training sessions. We will report all these adverse events to the Ethics Committee as required.

3.0 Data collection, management and analysis

All patients' data will be recorded by trained clinical researchers using a standardized case report form (CRF). We will record raw data appropriately and accurately and will keep copies of the laboratory reports. We will also store the CRFs in areas with restricted access.

3.2 Statistical analysis

Test for Significance

Categorical variables will be described as frequencies and percentages, and the difference between two groups will be compared using the $\chi 2$ test or Fisher's exact test. Continuous variables will be reported as mean and standard deviation, the t-test will be used if the data shows a normal distribution, and effects if the data does not show normal distribution. We will also compare the differences between patients who are adherent and those who are non-adherent to analyze the factors that influence adherence. Furthermore, the secondary comparison will be conducted according to the intent-to-treat comparison, which will include the full sample of randomized patients. All statistical analyses will be two-sided, and $P<0.05$ will be considered statistically significant. SPSS 20.0 will be used for data analysis.

Test for Carryover Effects

Carryover effects will also be analyzed in this specific context. We will analyze the changes in the two groups at 12 weeks, in other words, the changes in the first stage plus the changes in the second stage. Continuous variables will be analyzed using the t-test or rank test to compare the differences between the two groups. Categorical variables will be compared using the $\chi 2$ test. No significant difference indicates no carryover effect.

3. Ethics and dissemination

The Human Research Ethics Committee of the School of Nursing at Jilin University has approved for the study (HREC 2019120901). Research reports will be disseminated through scientific forums, including peer-reviewed publications and presentations at national and international conferences.

4. Discussion

The IERMS-based HBCR program developed in this study evaluates the role of HBCR by combining mobile health interventions (monitoring devices, internet and mobile applications) with evidence-based CR guidance strategies, including exercise intensity monitoring, feedback on CR progress and self-management life-style risk factors. The purpose of this study is to investigate whether HBCR using IERMS could improve adherence of CR in patients with CHD and the maintenance of the intervention.

CR is a Class I recommendation for managing CHD patients [33]. However, despite increasing evidence that has proven its cost-effectiveness and efficacy in reducing cardiovascular morbidity and mortality, CR services remain limited in China [8, 15]. HBCR is a method to increase the CR participation rate in CHD patients [21]. Setting the prescribed amount of exercise and monitoring its intensity are the key points of HBCR to ensure that the exercise is both appropriate and within safe limits [34]. The planter

pressure sensors have been proven to be accurate in measuring the patient's exercise type and intensity [29-30]. Combined with intelligent insoles and wearable HR monitors, our system can evaluate whether patients reach the required exercise intensity and are able to promptly alert patients should the intensity fall outside the preset range. Furthermore, before each CR session, the cardiologist will evaluate the suitability of the exercise program according to the patients' health data patients synchronized by IERMS to ensure patient safety. IERMS also encourages patients to upload BP, HR, weight and physical activity to track their own progress and give objective feedback, which could motivate self-monitoring, thereby improving patients' adherence.

Another key point which has impact on HBCR is the maintenance of the rehabilitation. The effectiveness of rehabilitation programs after stopping intervention has proven to be unsustainable in both CBCR and HBCR [35]. We will, therefore, also evaluate if there are any significant carryover effects in order to observe the maintenance of effects after the termination of the intervention.

An improvement in adherence may be associated with better physical and psychological states. We will also evaluate these in this study. CPET can be used to assess a patient's exercise performance and peak VO_2 which has been shown to be the strongest predictor of mortality [36] and which we have, therefore, chosen as a secondary outcome. In addition, mental status,

self-efficacy, quality of life and lifestyle risk factors are important for HBCR assessment, thus our study will also evaluate them.

In China and other lower middle-income countries (LMICs) where access to CR is often limited, mobile health interventions, such as IERMS used in our study, may effectively overcome barriers, such as inconvenience, geographical isolation and financial burden, and deliver the core components of HBCR to many patients with CHD.

Limitations

Our current study has several limitations. Firstly, as the study is of relatively short duration, no data will be available beyond 12 months and longer-term effectiveness will not be able to be evaluated. Secondly, the study is limited to patients with smartphones and internet access which may cause selective bias. Thirdly, we will not be able to allow participants to have a familiarization period of several weeks before using IERMS.

4. Conclusion

In conclusion, our study will evaluate the role of the IERMS intervention on the delivery of HBCR as advocated in various guidelines. If this technology-based HBCR intervention is shown to be effective, it may be an alternative method to implement evidenced-based CR for patients with CHD.

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Competing interests None declared.

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Data sharing statement For patient confidentiality concerns and the access possibilities of the data source, the clinical data collected will not be shared with the public. However, non-clinical data, such as educational

materials, will be shared with the public and other researchers.

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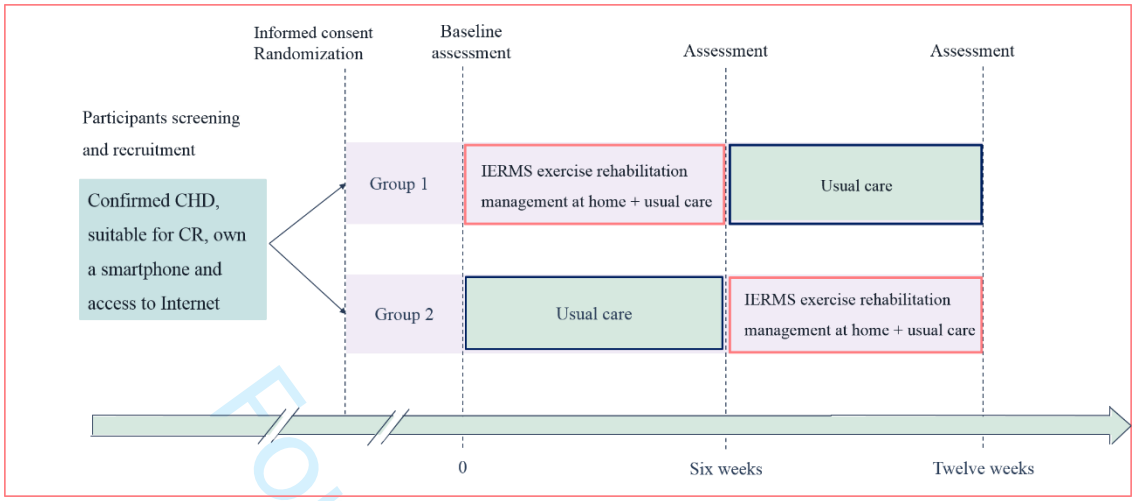
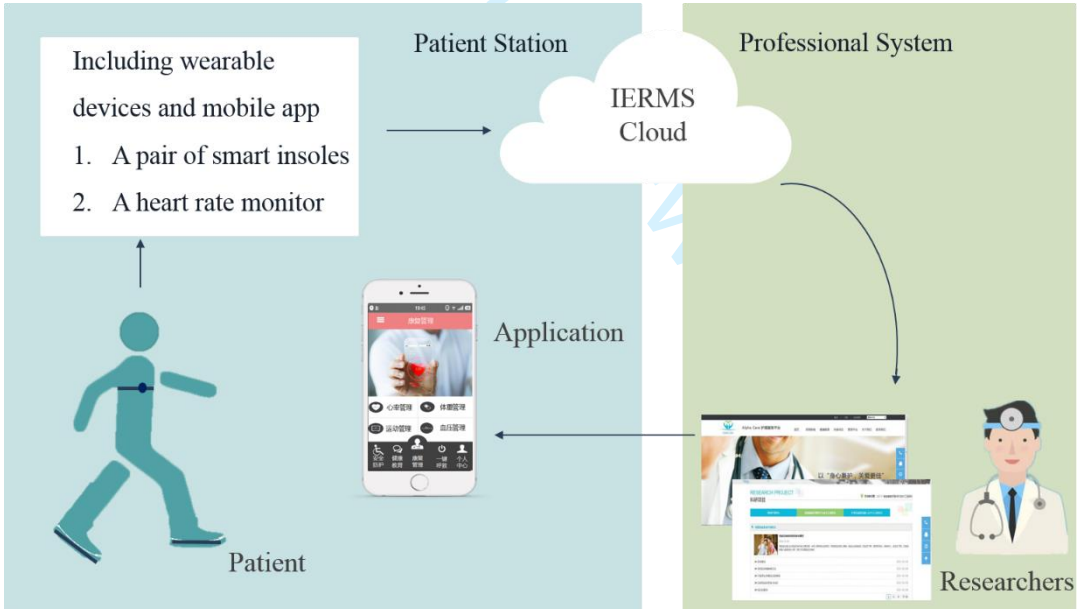
Figure 1 Profile of the randomized controlled crossover study design.



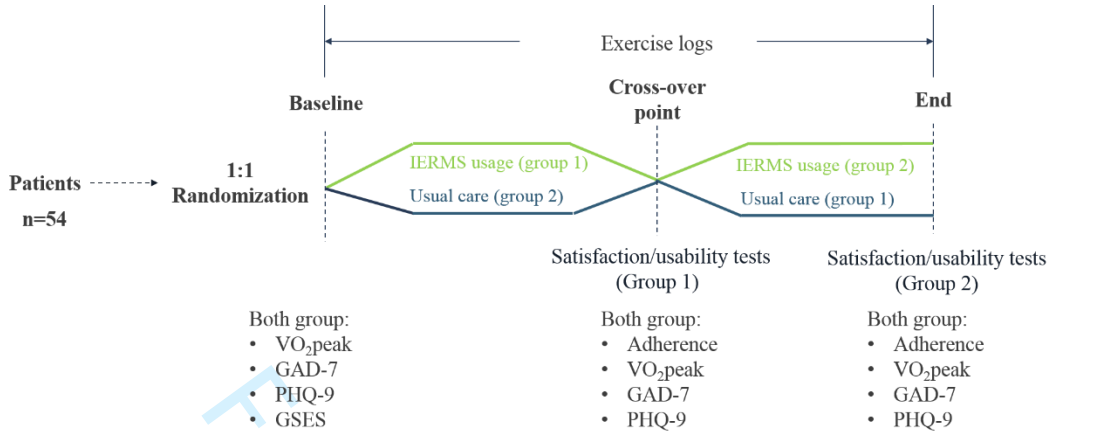
CHD, Coronary heart disease; IERMS, Intelligent Exercise Rehabilitation Management System.

Figure 2 Components of the IERMS.



IERMS, Intelligent Exercise Rehabilitation Management System.

Figure 3 Assessment time points for primary and secondary outcomes.



VO_2peak, peak oxygen uptake; GAD-7, the Generalized Anxiety Disorder Scale-7; PHQ-9, Patients' Health Questionnaire Depression Scale-9; SF-12, the 12-item Short Form Health Survey; GSES, General Self-Efficacy Scale.

吉林大学护理学院

涉及人的科研项目伦理审查表

审查编号：20191209 01

申报项目名称 （需与申请书完全一致）	智慧运动康复管理系统对冠心病患者居家心脏康复依从性的影响研究		
项目负责人及职称	李峰/教授	拟申报项目类别及资助金额 （或在研项目资金来源及金额）	无
研究目的	基于前期研发的智慧运动康复管理系统（IERMS），研究 IERMS 对冠心病（CHD）患者居家运动康复的参与率、依从性及完成率，从身体功能、运动能力及心理状态等多维度探讨 CHD 患者居家心脏康复运动依从性的影响因素；并通过设计交叉试验，探索干预效果的维持效应。		
立项依据（简述）	目前已有大量临床研究证据证实：心脏康复（CR）能够使 CHD 患者的预后得到充分的改善，使他们的生活质量有效提高，减少再次发病的可能，使患者患病后通过心脏康复重新恢复。虽然 CR 的益处已被证实，但并未能在实践中被大规模采用或在社区中成功实施，存在 CR 认知度和参与度低、依从性差等问题。随着移动医疗的快速发展以及智能电子设备的普及，基于移动医疗的 CR（eHealth CR）是指通过信息和通信技术（ICT）交付 CR，它已发展成为提高 CR 可用性和可访问性的替代方式。国外研究表明，基于移动技术的心脏康复提高了心肌梗死后患者心脏康复的参与度和依从性，而我国针对移动医疗在心脏康复中的研究较少。本项目基于前期研发的智慧运动康复管理系统（IERMS），可实时监测患者的运动康复过程。本项目通过设计随机对照试验，研究患者居家运动康复的参与率、依从性及完成率；从身体功能、运动能力及心理状态等多维度探讨 CHD 患者居家心脏康复运动依从性的影响因素；并通过设计交叉试验，探索干预效果的维持效应。		
受试者类别（医院患者/社区居民/健康志愿者等）	医院患者	受试者例数	54
受试者选择 （入选标准及排除标准）	纳入标准：①年龄 18-70 周岁；②诊断为冠状动脉粥样硬化性心脏病，（包括急性心肌梗死，不稳定心绞痛），并在入院期间接受 PCI 治疗；③经吉大一院心内科医生和理疗师评估为适合参加 CR；④愿意提供书面知情同意；⑤ 拥有智能手机；⑥精通中文。 排除标准：①运动康复的禁忌症（例如，未经治疗的室性心动过速，严重的心力衰竭，无法控制的高血压或低血压，明显的运动限制）；②指导后无法		

	使用 IERMS 的设备；③居住地没有互联网连接；④需要助行器才能行动；⑤参加其他临床试验。
是否有书面知情同意及履行保密原则	均提供知情同意书，尊重患者的履行保密原则
研究需要收集的具体材料【受试者信息，血液体液(ml、次数)、组织或病理标本等】	仅收集受试者一般资料、心肺功能测试以及问卷，无血液体液、组织或病理标本等。
所收集的受试者材料的检测实验室名称及地点（需具体说明）	所有资料、问卷的填写以及测试均在吉林大学第一医院心血管内科心脏康复中心进行，地点：吉林省长春市新民大街 71 号 7 号楼 4 层。
获取材料的方法、地点(手术切除标本、静脉穿刺、腹腔穿刺、住院病史摘录等)	心肺功能测试，问卷调查法，在吉大一院心血管内科心脏康复中心获得。
研究项目起止时间	2020.1~2021.12
审查结果	伦理委员会审批意见： 同意 伦理委员会主任委员签字（盖章）

项目负责人（签名）：

联系人及联系方式：17790089009 申请日期：2019.12.9

知情同意书·知情告知页

亲爱的患者：

医生已经确诊您为__冠状动脉粥样硬化性心脏病__。我们将邀请您参加一项研究，本研究为__2018年吉林大学白求恩计划__项目，课题编号：__2018A04__。本研究方案已经得到__吉林大学护理学院__伦理委员会审核，同意进行临床研究。

在您决定是否参加这项研究之前，请尽可能仔细阅读以下内容。它可以帮助您了解该项研究以及为何要进行这项研究，研究的程序和期限，参加研究后可能给您带来的益处、风险和不适。如果您愿意，您也可以和您的亲属、朋友一起讨论，或者请医生给予解释，帮助您做出决定。

一、 研究背景和研究目的

1.1 疾病负担和治疗现况

冠心病（Coronary heart disease，CHD）是由冠状动脉内的斑块积聚，导致动脉狭窄并减少富氧血液流入心脏引起的。WHO统计数据表明，全球有740万人死于冠心病，并预测到2020年冠心病将成为致残的主要原因。心脏康复（Cardiac rehabilitation, CR）是CHD处理中不可缺少的组成部分，被定义为涉及医学评价、药物处方、运动处方、营养处方、教育、咨询及行为干预的综合长期康复计划，且已经被美国心脏协会（AHA）和心脏病学会（ACC）、欧洲心脏病学会（ESC）列为CHD治疗的Ⅰ类推荐。目前已有大量临床研究证据证实：CR能够使CHD患者的预后得到充分的改善，使他们的生活质量有效提高，减少再次发病的可能，使患者患病后通过心脏康复重新恢复。虽然CR的益处已被证实，但并未能在实践中被大规模采用或在社区中成功实施，存在CR认知度和参与度低、依从性差等问题。因此，如何促进心脏康复的实施，改善心脏康复质量也成为医疗服务体系的巨大挑战。

1.2 本研究目的

本项目基于前期研发的智慧运动康复管理系统（IERMS），可实时监测患者的运动康复过程。通过设计随机对照试验，研究IERMS系统对患者居家运动康复的参与率、依从性及完成率的影响；从身体功能、运动能力及心理状态等多维度探讨CHD患者居家心脏康复运动依从性的影响因素；并通过设计交叉试验，探索干预效果的维持效应。

1.3 研究参加单位和预计纳入参试者例数

吉林大学护理学院、吉林大学第一医院，参试者54人。

二、哪些人不宜参加研究

①运动康复的禁忌症（例如，未经治疗的室性心动过速，严重的心力衰竭，无法控制的高血压或低血压，明显的运动限制）；②指导后无法使用IERMS的设备；③居住地没有互联网连接；④需要助行器才能行动；⑤参加其他临床试验。

三、如果参加研究将需要做什么？

1. 在您入选研究前，医生将询问、记录您的病史，并进行__问卷调查__。

   您是合格的纳入者，您可自愿参加研究，签署知情同意书。

   如您不愿参加研究，我们将按您的意愿施治。

2. 若您自愿参加研究，将按以下步骤进行：

   您在出院前，需要填写一部分问卷，出院以后，按照医生给您制定的运动处方，以及医生给与你的ECG监护仪、智能鞋垫，下载APP。回家进行居家心脏运动康复。出院后6周、12周需要回院进行复查。

3. 需要您配合的其他事项

您必须按医生和您约定的随访时间带着__病历、运动日志__来医院就诊（随访阶段，医生可能通过电话、登门的方式了解您的情况）。您的随访非常重要，因为医生将判断您接受的治疗是否真正起作用，并及时指导您。

您必须按医生指导用药，并请您及时、客观地填写您的服药记录。您在每次随访时都必须归还未用完的药物及其包装，并将正在服用的其它药物带来，包括您有其它合并疾病须继续服用的药物。

四、参加研究可能的受益

尽管已经有证据提示__移动健康技术对居家运动康复依从性__有满意的疗效，但这并不能保证对您肯定有效。本研究所采用的__智慧运动康复管理系统__也不是管理__心脏康复运动__的唯一的方法。如__智慧运动康复管理系统__对您的康复无效，您可以向医生询问有可能获得的替代管理方法。

五、参加研究可能的不良反应、风险和不适、不方便

如果在研究期间您出现任何不适，或病情发生新的变化，或任何意外情况，不管是否与研究有关，均应及时通知您的医生，他/她将对此作出判断并给与适当的医疗处理。

您在研究期间需要按时到医院随访，做一些检查，这些占用您的一些时间，也可能给您造成麻烦或带来不方便。

六、有关费用

本研究中智能鞋垫、ECG 监护仪的费用可免，回院复查时进行心肺运动试验（CPET）的费用需自己承担。

医生将尽全力预防和治疗由于本研究可能带来的伤害。如果在临床试验中出现不良事件，医学专家委员会将会鉴定其是否与本干预有关。申办者将按照我国规定对与试验相关的损害提供治疗的费用及相应的经济补偿。

对于您同时合并的其他疾病所需的治疗和检查，将不在免费的范围之内。

七、个人信息的保密

您的医疗记录（研究病历/CRF、化验单等）将完整地保存在您所就诊的医院。医生会将化验和其它检查结果记录在您的病历上。研究者、伦理委员会和药品监督管理部门将被允许查阅您的医疗记录。任何有关本项研究结果的公开报告将不会披露您的个人身份。我们将在法律允许的范围内，尽一切努力保护您个人医疗资料的隐私。

按照医学研究伦理，除了个人隐私信息外，试验数据将可供公众查询和共享，查询和共享将只限于基于网络的电子数据库，保证不会泄漏任何个人隐私信息。

八、怎样获得更多的信息？

您可以在任何时间提出有关本项研究的任何问题，并得到相应的解答。

如果在研究过程中有任何重要的新信息，可能影响您继续参加研究的意愿时，您的医生将会及时通知您。

九、可以自愿选择参加研究和中途退出研究

是否参加研究完全取决于您的意愿。您可以拒绝参加此项研究，或在研究过程中的

任何时间退出本研究，这都不会影响您和医生间的关系，都不会影响对您的医疗或有其他方面利益的损失。

出于对您的最大利益考虑，医生或研究者可能会在研究过程中随时中止您继续参加本项研究。

如果您因为任何原因从研究中退出，您可能被询问有关您使用试验药物的情况。如果医生认为需要，您也可能被要求进行实验室检查和体格检查。

十、现在该做什么？

是否参加本项研究由您自己（和您的家人）决定。

在您做出参加研究的决定前，请尽可能向你的医生询问有关问题。

感谢您阅读以上材料。如果您决定参加本项研究，请告诉您的医生，他/她会为您安排一切有关研究的事务。请您保留这份资料。

知情同意书.同意签字页

临床研究项目名称：基于 IERMS 的多维尺度心脏康复体系构建及实施科学研究

课题承担单位：吉林大学护理学院

课题协作单位：吉林大学第一医院

课题任务书编号：2018A04

同意声明

我已经阅读了上述有关本研究的介绍，而且有机会就此项研究与医生讨论并提出问题。我提出的所有问题都得到了满意的答复。

我知道参加本研究可能产生的风险和受益。我知晓参加研究是自愿的，我确认已有充足时间对此进行考虑，而且明白：

- 我可以随时向医生咨询更多的信息。
- 我可以随时退出本研究，而不会受到歧视或报复，医疗待遇与权益不会受到影响。

我同样清楚，如果我中途退出研究，特别是由于药物的原因使我退出研究时，我若将我的病情变化告诉医生，完成相应的体格检查和理化检查，这将对整个研究十分有利。

如果因病情变化我需要采取任何其他的药物治疗，我会在事先征求医生的意见，或在事后如实告诉医生。

我同意药品监督管理部门伦理委员会或申办者代表查阅我的研究资料。

我将获得一份经过签名并注明日期的知情同意书副本。

最后，我决定同意参加本项研究，并保证尽量遵从医嘱。

患者签名：_____ ＿＿＿＿年＿＿月＿＿日

联系电话：_____

我确认已向患者解释了本试验的详细情况，包括其权力以及可能的受益和风险，并给其一份签署过的知情同意书副本。

医生签名：_____ __ __ __ __ 年 __ __ 月 __ __ 日

医生的工作电话：_____

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	P1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	P7
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	P7
Protocol version	#3	Date and version identifier	n/a
Funding	#4	Sources and types of financial, material, and other support	P21
Roles and responsibilities:	#5a	Names, affiliations, and roles of protocol contributors	P21

contributorship			
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	P21
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	P21
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a, did not establish the committee
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	P4-6
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	P4-6
Objectives	#7	Specific objectives or hypotheses	P6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	P6-7
Methods: Participants, interventions, and outcomes			

Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	P6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	P7
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	P9-13
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	n/a, intervention did not involve harms or others
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	P9-13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	P9
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	P13-15
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions	P8

		supporting any sample size calculations	
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	P7-8
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	P8-9
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	P8-9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	P8-9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	P8-9
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a, not blind to participants or researchers
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate	P15-16

		measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	P9
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	P16
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	P16-17
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	P16-17
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	P17
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a, less safe risks in this study
Data monitoring:	#21b	Description of any interim analyses and stopping	n/a, not apply

interim analysis		guidelines, including who will have access to these interim results and make the final decision to terminate the trial	DMC in this trail
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	P16
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	P17-18
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	P8
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a, not needed in this study
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	P16
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	P21
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a, not needed in this study

Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a, not needed in this study
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	P17
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	P16-17
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	P16-17
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	n/a, not needed in this study
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a, not needed in this study

BMJ Open

Role of the Intelligent Exercise Rehabilitation Management System on adherence of cardiac rehabilitation in patients with coronary heart disease: a randomized controlled crossover study protocol

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Title Page

Title of the article:

Role of the Intelligent Exercise Rehabilitation Management System on adherence of cardiac rehabilitation in patients with coronary heart disease: a randomized controlled crossover study protocol.

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Abstract

Introduction: The benefits of cardiac rehabilitation (CR) on the reduction of cardiac and all-cause mortality are well documented. However, adherence remains sub-optimal in China. It is clear that traditional CR does not meet the needs of many eligible patients and innovation is required to improve its application. Home-based CR (HBCR) is a cost-effective method that may be a valuable alternative for many individuals in China. In HBCR, it is often difficult to maintain an exercise intensity that is both effective and within safe limits, factors that are essential for patient safety. Mobile health interventions have the potential to overcome these obstacles and may be efficacious in improving adherence. The purpose of this study is to evaluate whether an Intelligent Exercise Rehabilitation Exercise System (IERMS)-based HBCR could improve adherence to CR and to assess the effects on exercise capacity, mental health, self-efficacy, quality of life and lifestyle-related risk factors.

Methods and analysis: We propose a single-blinded, two-arm, randomized control crossover study of 70 patients with coronary heart disease (CHD). Participants will be randomly assigned in a 1:1 ratio to one of two groups. Patients in Group 1 will receive the IERMS intervention together with usual care for the first six weeks and usual care for the last six weeks, while patients assigned to Group 2 will receive usual care for the first six weeks and will use IERMS in the last six weeks. The primary outcome is adherence to the program and secondary outcomes include exercise capacity, psychological well-being, quality of life, self-efficacy and lifestyle-related risk factors. All secondary outcomes will be measured at baseline, six weeks and 12 weeks.

Ethics and dissemination: This study has been approved by the Human Research Ethics Committee of the School of Nursing, Jilin University (HREC 2019120901). The results will be published in peer-

reviewed journals and at conferences.

Trial registration number: ChiCTR1900028182; Pre-results.

Key words: Cardiac rehabilitation, adherence, coronary heart disease

Strength and Limitations of this study

1. Our home-based cardiac rehabilitation program (HBCR) is technology-based and may improve adherence of CR in patients with coronary heart disease (CHD).
2. The measurements of plantar pressure and heart rate (HR) used in this study are accurate in evaluating exercise type and intensity. This is essential for reminding patients to exercise appropriately within safe limits during CR sessions at home.
3. The crossover study design allows us to observe the maintenance of effects after the six-week IERMS intervention.
4. The study is of relatively short duration and long-term effectiveness will not be observed after 12 months.
5. The study is limited to patients with smartphones and internet access.

1. Background

Coronary heart disease (CHD) is the leading cause of mortality in China and has increased by 20.6% from 1990 to 2017[1]. Studies over the past few decades have shown an increased prevalence and

incidence of CHD and it was estimated that about 11 million patients suffered from it in 2017[2]. Patients with CHD have severe physical and often psychological problems and show reduced health-related quality of life (HRQoL) scores, which is associated with high mortality and additional cardiac events [3-4].

Cardiac rehabilitation (CR), an integral component of the continuum of care for patients with CHD[5], has been demonstrated to reduce mortality by up to 37% [6-7] to improve both physical functioning and quality of life[8-10], and is recommended by the American Heart Association (AHA)/ American College of Cardiology (ACC) and the European Society of Cardiology (ESC) guidelines for patients with CHD[11-12].

Despite proven benefits, the use of and adherence to CR remains sub-optimal, with participation rates of between 10.3% and 16.3% [13] and dropout rates of between 40% and 55% [14-15]. In China, access to CR services remains very low, with the estimated availability of CR programs about two programs per 100 million inhabitants[16]. This may be due to poor availability and problems with supplying CR in China, including a lack of facilities, funding, staff training, and reimbursements for participating patients [17-18]. Drop-out or non-adherence may lead to undesirable outcomes in CHD [19]. Therefore, innovation is needed to improve the implementation of CR in China.

Besides center-based CR, home-based CR (HBCR) is an alternative method recommended by AHA and ACC. HBCR may be more effective in the provision of CR to many patients in China[20] and has proved to be effective in improving adherence [21]. However, while effective performance of the prescribed exercises is essential, difficulties, such as managing the exercise type, intensity and duration appropriately at home, occur with HBCR [22]. With the development of new digital technologies, mobile

health (m-health) interventions have emerged and have shown the potential to deliver HBCR safely and effectively [23-25]. The m-health interventions could help patients monitor exercise intensity, provide objective feedback data and encourage patients to track their own progress, which could help them self-manage their CR and may be useful in improving their adherence. In addition, patients with CHD have shown great interest in using m-health at home, providing clear potential for developing such interventions [26].

In HBCR, m-health that could accurately monitor the intensity and type of exercise is required to ensure both safety and effectiveness. The Intelligent Exercise Rehabilitation Management system (IERMS) has been designed to meet these requirements. It introduces a closed-loop rehabilitation management system that supports the home-based management of prescribed CR and lifestyle-related risk factors for patients with CHD. The purpose of this study is to evaluate whether IERMS-based HBCR could improve adherence to CR and to assess its effects on exercise capacity, mental health, self-efficacy, quality of life, and lifestyle-related risk factors. The results of the trial are expected to facilitate the development of effective m-health interventions for HBCR.

2. Methods

2.1 Study Design

A single-blinded, two-arm, randomized control crossover study will be conducted to evaluate the role of IERMS-based HBCR on adherence, exercise capacity, mental health, self-efficacy, quality of life and lifestyle-related risk factors. All participants will be recruited from the CR outpatient setting of a medical center in Changchun, China. A total of 70 participants will be randomly assigned to one of two groups. Patients in Group 1 will use IERMS in the first stage and receive usual care in the last stage,

while patients in Group 2 will receive usual care in the first stage and IERMS-based HBCR in the last stage. Each stage of the study will last for six weeks. As one of our main objectives is to assess whether there is an interaction at the end of the intervention and to observe the maintenance of the effects after the intervention, this study does not allow a wash-out period. An illustration of the study design is displayed in Figure 1. The trial conforms to the SPIRIT reporting guidelines [27] and is registered at Clinical Trials.gov: ChiCTR1900028182.

2.2 Eligibility and Recruitment

Patients will be eligible to participate if they have: (1) a documented diagnosis of CHD and having had a hospitalization incident within six months prior to randomization; (2) been assessed as suitable by a cardiologist and a physical therapist to participate in their CR; (3) no contraindications to undergo a cardiopulmonary exercise test; (4) should own a smartphone and be willing and able to upload data and that they should have access to internet at home; (5) if they are willing and able to participate in the study and to provide written informed consent.

Exclusion criteria include: (1) severe heart failure (NYHA class IV); (2) unstable angina; (3) unstable clinical status; (4) coronary artery bypass grafting within the last three months; (5) patients are unable to use the IERMS-enabled devices after instruction; (6) requiring a walking aid for mobility; (7) participation in another clinical trial.

Our research group has formed a team with experienced clinical nurses and rehabilitation therapists in the cardiovascular department at a medical center in Changchun, China. Experienced clinical nurses and researchers in our team will be responsible for recruiting participants. Patients admitted with CHD and eligible for CR will be screened and those meeting the inclusion criteria will be invited to participate.

Rehabilitation therapists will inform them of the study details, and if they agree to participate in the study, they will be asked to sign the consent form. If complex clinical problems are encountered, our researchers, nursing experts, and rehabilitation therapists will work together to develop a solution.

2.3 Sample Size Calculation

This study selects the main outcome indicators of HBCR adherence as the calculation standard. A previous study has shown CR adherence rates of ~94% for technology-based HBCR and ~68% for traditional CR [28]. We will use two sample rate calculation formula: $N=[\frac{z_{\frac{\alpha}{2}}\sqrt{\pi_c\ (1-\pi_c)\ (Q_1^{-1}+Q_2^{-1})}}{\pi_1-\pi_2}+\frac{z_{\beta}\sqrt{\pi_1\ (1-\pi_1)\ /Q_1+\pi_2\ (1-\pi_2)\ /Q_2}}{\pi_1-\pi_2}]$ with 90% power (type I error = 5%) to calculate the sample size, and a total sample size of 54 across both arms will be used in this study. Allowing for an estimated 20% loss to follow-up, a total of 70 participants will be recruited.

2.4 Randomization, Blinding and Concealed Allocation

After signing an informed consent, patients will complete a baseline assessment. They will then be randomized in a 1:1 ratio to either Group 1 or the Group 2 by a computer-generated randomization list, using block randomization and randomly selected block sizes of 4, 6, or 8. This assignment will be done by independent individuals who will not participate in the recruitment process. Given the characteristics of the intervention, the participants or researchers implementing the intervention cannot be blinded. However, researchers evaluating the results will be unaware of patient assignments. To ensure hidden assignments and minimize selection bias, independent designated members of the School of Nursing, Jilin University will assign random numbers based on local researcher requirements.

2.5 Usual care

Regardless of the IERMS intervention, all patients will receive usual care. Patients will receive

health education about CR provided by a cardiologist and a physical therapist will give them personalized exercise prescriptions according to the results of their cardiopulmonary exercise test (CPET). Patients will be free to participate in any type of exercise classes, Tai Chi programs, group dancing and available CR programs after discharge from rehabilitation facilities. All patients will be required to upload exercise logs weekly at home, including exercise type, intensity and duration. Patients using IERMS will have exercise logs automatically recorded by the system and are required to upload them to the research team. Patients under usual care will record exercise logs in any form they like in the memorandum, and we will remind them to send them to us weekly through WeChat which is a popular social media site in China. In addition, all patients will receive follow-up calls at six weeks and 12 weeks.

2.6 Key components of IERMS

The IERMS is a closed-loop rehabilitation management system which can facilitate management of exercise prescription and lifestyle-related risk factors and consists of three main components: Professional System, Patient Station and the Cloud (Figure 2). This system has been authorized as a China Invention Patent (Publication Patent Number (PPNO): 201810114305.3).

Patient Station

The Patient Station consists of one mobile application and two monitoring devices which include a pair of smart insoles and a heart rate (HR) monitor.

Smart insoles have been independently developed in this study and are able to measure gait parameters using inserted plantar pressure sensors and accelerometers during CR sessions. This has been shown to be accurate in identifying the type of exercise and in calculating energy expenditure [29-30]. The data collected by the smart insoles will be uploaded to the cloud, and the cloud will analyze the metabolic

equivalent (METs) through an algorithm which has been developed specifically for this study, and then present the results on the mobile application. The HR monitor used in this study is attached around the chest and can monitor HR in real-time.

The mobile application and these monitoring devices are connected by Bluetooth. The mobile application is thus able to synchronize the data collected by the sensors and provide real-time motivational feedback automatically generated from actual exercise performances. Furthermore, the mobile application can present educational materials and exercise prescriptions prescribed by professionals and upload patients' data to the professional system.

The cloud

The cloud is the core part of the data processing, which stores and analyzes the data transmitted by the monitoring devices and then distributes the results to the patient station and professional system. The cloud will use deep neural network models to train and evaluate the data and generate feedback on the patient's exercise and send them to the mobile application on the patient station. The cloud will also send a report of the exercise performance of patients in CR sessions to the professionals allowing them to update the exercise prescription for reference.

Professional System

The Professional System is a web-based tool for medical professionals, which can manage patients' CR exercise at home. Patient files are stored in the system, including the patient's medical history, past exercise prescriptions and lifestyle-related risk factors. The system can also synchronize the patient's exercise progress, weight, HR and BP, etc. The professionals can thus monitor the patient's health situations remotely through the system and perform continuity of care for patients.

2.7 Description of the IERMS intervention

Eligible and consenting participants will be enrolled prior to discharge from an outpatient ambulatory CR program and will learn and practice all features of the system in the hospital. Participants will be given a pair of smart insoles and an HR monitor and a mobile application will be installed on their smartphones.

Tele-monitoring CR sessions

In order to ensure the patients' safety, a series of confirmations will be performed before CR sessions including BP, HR and the presence or absence of cardiac symptoms, such as dyspnea and chest distress. Patients will receive immediate feedback on whether they are safe to exercise at that time, and if not, the exercise time will be changed.

During the exercise sessions, patients will be asked to wear a pair of smart insoles and an HR monitor, which can monitor the intensity and type of exercise to ensure both safety and effectiveness. Endurance and resistance training are both included in CR sessions. The goal of the endurance training is to reach the individual, pre-defined target zone[31], which will make sure the patient is safe while also allowing effective exercise. When the exercise intensity is not enough, the mobile application will automatically encourage the patients to speed up, and if the exercise intensity is excessive or the exercise type is not appropriate, the mobile application will remind the patients to slow down or change the type of training.

Encouraging self-management

The IERMS will provide an individualized exercise target according to the prescribed exercise program developed by the physical therapists, and which will be progressively updated weekly. The

medical staff will be able to monitor the exercise frequency, intensity, and type of exercise through the information collected by the monitoring devices and give feedback on the completion of the rehabilitation exercise and set goals, which can encourage patients to track their exercise progress. In addition, patients can communicate with the professionals via short message service (SMS) built into the mobile application and receive feedback within 24 hours.

The IERMS encourages patients to upload BP, HR, weight, smoking situation, and physical activity to the mobile application. This enables them to track their own progress to motivate them to quit smoking, lose weight, improve physical activity and reduce sedentary behaviors, which can, in turn, improve their self-monitoring, thereby increasing patients' adherence. Participants will also be encouraged to participate in other different types of physical activities, such as jogging, Tai Chi and group dancing.

2.8 Outcome Measures and data collection

Outcome measures will be analyzed by researchers blinded to the group allocation. All assessments will be performed at baseline, six weeks, and 12 weeks (Figure 3).A summary of the outcome measures for the study is outlined in Table 1.

Table 1 Completed SPIRIT diagram for the study

	STUDY PERIOD				
	Enrollment	**Allocation**	**Post- Allocation**		**Close-out**
TIMEPOINT*	**-t1**	**0**	**t1**	**t2**	**t3**
ENROLLMENT:					
Eligibility screen	X				

Informed consent		X	X	X	
Randomization		X	X	X	
Allocation		X	X	X	
INTERVENTIONS:					
Group 1*		←	—	→	
Group 2**		←	—	→	
ASSESSMENTS:					
Adherence			X	X	
VO_2peak		X	X	X	
GAD-7		X	X	X	
PHQ-9		X	X	X	
SF-12		X	X	X	
GSES		X	X	X	
Life-related risk factors***		X	X	X	
Adverse event reporting		←	—	→	
Satisfaction/usability tests			X	X	

t1 = six weeks, t2 = 12 weeks

* IERMS in the first phase and usual care in the second phase.

** Usual care in the first phase and IERMS in the second phase.

***Part of routine care and therefore assessed before informed consent.

****Satisfaction/usability test will only be performed after IERMS intervention in each group.

GAD-7, Generalized Anxiety Disorder Scale-7; PHQ-9 Patients' Health Questionnaire Depression Scale-9; SF-12, the 12-item Short Form Health Survey; GSES, General Self -Efficacy Scale.

Primary outcome

The primary outcome will be adherence for CR. Adherence is defined as attendance for four weeks

(eight or more sessions) for usual care or uploading of four weeks' data for IERMS-based HBCR, and attending six-week assessments (both groups), as described in a similar study by Dalal et al. (2007)[32]. The participation information in IERMS-based HBCR phase will be collected by the IERMS, while the adherence in the usual care phase will be analyzed from the training log.

Secondary outcomes

The secondary outcome measures for the trial are outlined in Figure 3. In general, all secondary outcomes will be measured at baseline, six weeks and 12 weeks. Secondary outcomes include VO_2peak, the Generalized Anxiety Disorder Scale-7 (GAD-7); Patients' Health Questionnaire Depression Scale-9 (PHQ-9); the 12-item Short Form Health Survey (SF-12); General Self-Efficacy Scale (GSES) and lifestyle-related risk factors which include weight, smoking situation and physical activity. Satisfaction/usability will be measured at the end of the IERMS intervention in each group, using a 5-point Likert scale specifically designed for this study.

2.9 Adverse events monitoring

We will report all adverse events that occurred during the 12 weeks study period in the final paper. Adverse events during exercise training sessions are defined as deaths or other medical occurrences resulting in hospitalization during CR sessions or immediately after training sessions in an hour. Other adverse events are defined as medical occurrences resulting in hospitalization, disability or deaths without connection to training sessions. We will report all these adverse events to the Ethics Committee as required.

2.10 Data collection, management and analysis

All patients' data will be recorded by trained clinical researchers using a standardized case report

form (CRF). We will record raw data appropriately and accurately and will keep copies of the laboratory reports. We will also store the CRFs in areas with restricted access.

2.11 Statistical analysis

Test for Significance

Categorical variables will be described as frequencies and percentages, and the difference between two groups will be compared using the $\chi 2$ test or Fisher's exact test. Continuous variables will be reported as mean and standard deviation, the t-test will be used if the data shows a normal distribution, and effects if the data does not show normal distribution. We will also compare the differences between patients who are adherent and those who are non-adherent to analyze the factors that influence adherence. Furthermore, the secondary comparison will be conducted according to the intent-to-treat comparison, which will include the full sample of randomized patients. All statistical analyses will be two-sided, and $P<0.05$ will be considered statistically significant. SPSS 20.0 will be used for data analysis.

Test for Carryover Effects

Carryover effects will also be analyzed in this specific context. We will analyze the changes in the two groups at 12 weeks, in other words, the changes in the first stage plus the changes in the second stage. Continuous variables will be analyzed using the t-test or rank test to compare the differences between the two groups. Categorical variables will be compared using the $\chi 2$ test. No significant difference indicates no carryover effect.

2.12 Patient and Public Involvement

Patient and Public Involvement (PPI) has played an important part in this research. During the

IERMS development, CHD patients were invited to participate in surveys and discussions to help the research team better design the function and interface of the IERMS according to patients' priorities and preferences. In the pilot study, we also invited patients to give constructive feedback which allows us to better understand of their needs and barriers in HBCR and valuable suggestions in IERMS. In addition, patients were also invited to give reasonable recommendations for study design, questionnaire selection, and outcome measurements while considering the burden of intervention. The results of the study will be disseminated to participants who wish to be notified.

3. Ethics and dissemination

The Human Research Ethics Committee of the School of Nursing at Jilin University has approved for the study (HREC 2019120901). Research reports will be disseminated through scientific forums, including peer-reviewed publications and presentations at national and international conferences.

4. Discussion

The IERMS-based HBCR program developed in this study evaluates the role of HBCR by combining mobile health interventions (monitoring devices, internet and mobile applications) with evidence-based CR guidance strategies, including exercise intensity monitoring, feedback on CR progress and self-management life-style risk factors. The purpose of this study is to investigate whether HBCR using IERMS could improve adherence of CR in patients with CHD and the maintenance of the intervention.

CR is a Class I recommendation for managing CHD patients [33]. However, despite increasing evidence that has proven its cost-effectiveness and efficacy in reducing cardiovascular morbidity and mortality, CR services remain limited in China [8, 15]. HBCR is a method to increase the CR participation

rate in CHD patients [21]. Setting the prescribed amount of exercise and monitoring its intensity are the key points of HBCR to ensure that the exercise is both appropriate and within safe limits [34]. The planter pressure sensors have been proven to be accurate in measuring the patient's exercise type and intensity [29-30]. Combined with intelligent insoles and wearable HR monitors, our system can evaluate whether patients reach the required exercise intensity and are able to promptly alert patients should the intensity fall outside the preset range. Furthermore, before each CR session, the cardiologist will evaluate the suitability of the exercise program according to the patients' health data patients synchronized by IERMS to ensure patient safety. IERMS also encourages patients to upload BP, HR, weight and physical activity to track their own progress and give objective feedback, which could motivate self-monitoring, thereby improving patients' adherence.

Another key point which has impact on HBCR is the maintenance of the rehabilitation. The effectiveness of rehabilitation programs after stopping intervention has proven to be unsustainable in both CBCR and HBCR [35]. We will, therefore, also evaluate if there are any significant carryover effects in order to observe the maintenance of effects after the termination of the intervention.

An improvement in adherence may be associated with better physical and psychological states. We will also evaluate these in this study. CPET can be used to assess a patient's exercise performance and peak VO_2 which has been shown to be the strongest predictor of mortality [36] and which we have, therefore, chosen as a secondary outcome. In addition, mental status, self-efficacy, quality of life and lifestyle risk factors are important for HBCR assessment, thus our study will also evaluate them.

In China and other lower middle-income countries (LMICs) where access to CR is often limited, mobile health interventions, such as IERMS used in our study, may effectively overcome barriers, such

as inconvenience, geographical isolation and financial burden, and deliver the core components of HBCR to many patients with CHD.

Limitations

Our current study has several limitations. Firstly, as the study is of relatively short duration, no data will be available beyond 12 months and longer-term effectiveness will not be able to be evaluated. Secondly, the study is limited to patients with smartphones and internet access which may cause selective bias. Thirdly, we will not be able to allow participants to have a familiarization period of several weeks before using IERMS.

5. Conclusion

In conclusion, our study will evaluate the role of the IERMS intervention on the delivery of HBCR as advocated in various guidelines. If this technology-based HBCR intervention is shown to be effective, it may be an alternative method to implement evidenced-based CR for patients with CHD.

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Contributors LX and FL conceived the original concept of the study and wrote the first draft of the protocol manuscript. WX, JL, HS, MS, XZ, YP, YN, WZ, YL, LG, SZ, LZ contributed to the design of the study. LX, FL, JL, MS, XZ revised the manuscript. All authors read and approved the final manuscript.

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Qingdao Magene Intelligent Technology Co., Ltd, China. The funding source does not influence or comment on planned methods, protocol, data analysis or the draft report.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement For patient confidentiality concerns and the access possibilities of the data source, the clinical data collected will not be shared with the public. However, non-clinical data, such as educational materials, will be shared with the public and other researchers.

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Figure Legends

Figure 1 Illustration of the randomized controlled crossover study design.

CHD, Coronary heart disease; IERMS, Intelligent Exercise Rehabilitation Management System.

Figure 2 Components of the IERMS.

IERMS, Intelligent Exercise Rehabilitation Management System.

Figure 3 Assessment time points for primary and secondary outcomes.

VO_2peak, peak oxygen uptake; GAD-7, the Generalized Anxiety Disorder Scale-7; PHQ-9, Patients' Health Questionnaire Depression Scale-9; SF-12, the 12-item Short Form Health Survey; GSES, General Self-Efficacy Scale.

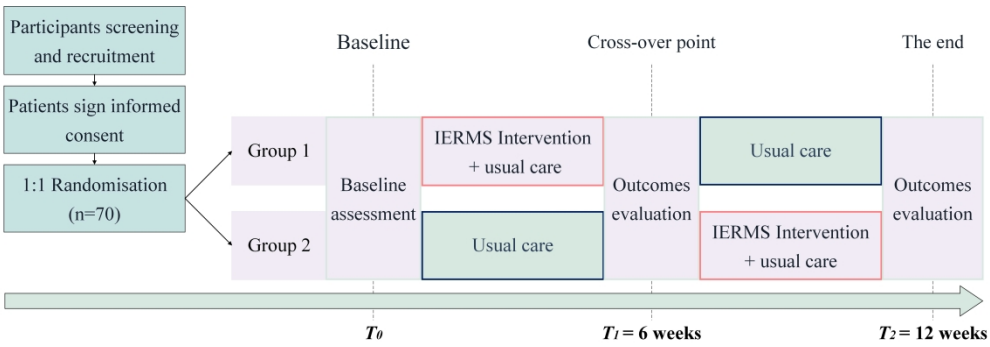

Figure 1 Illustration of the randomized controlled crossover study design.
CHD, Coronary heart disease; IERMS, Intelligent Exercise Rehabilitation Management System.

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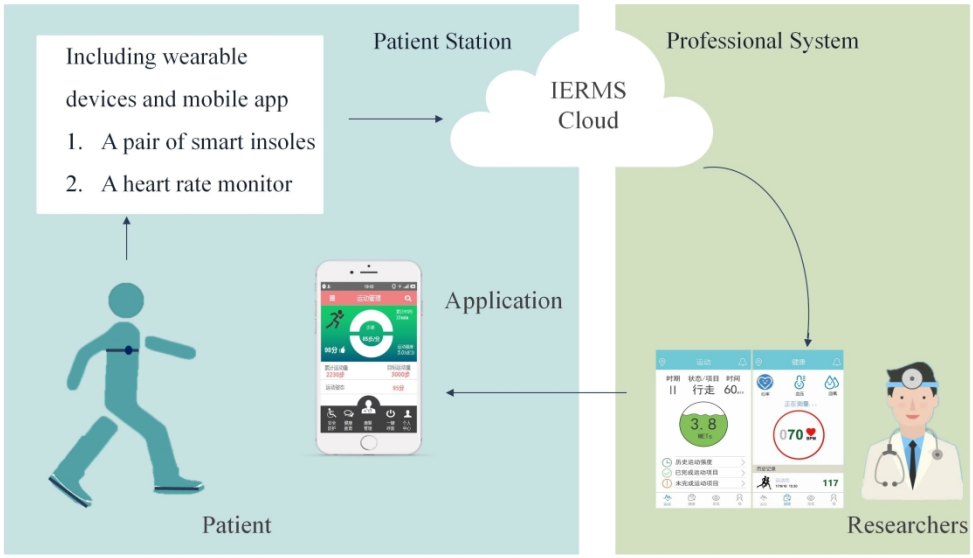

Figure 2 Components of the IERMS.
IERMS, Intelligent Exercise Rehabilitation Management System.

268x147mm (300 x 300 DPI)

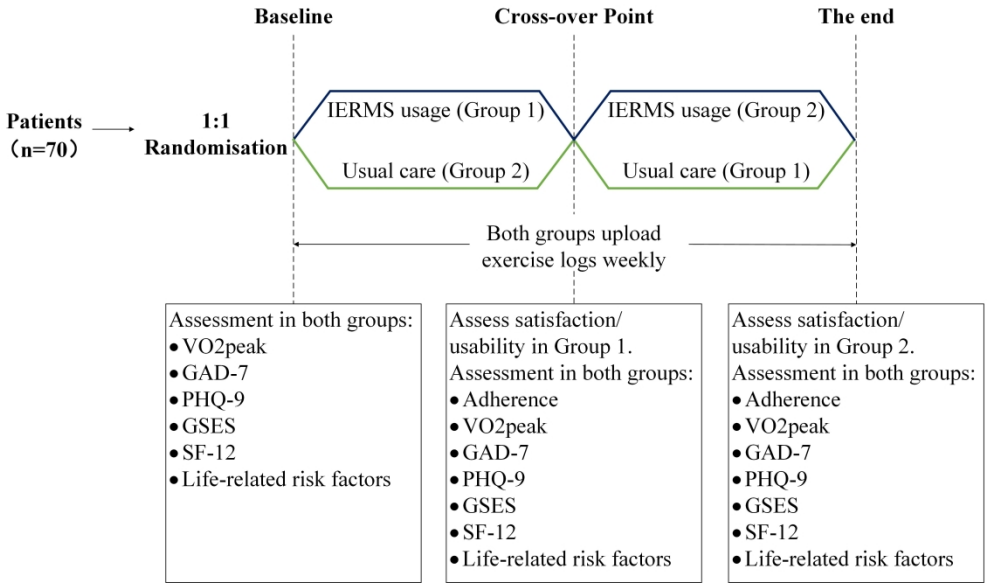

Figure 3 Assessment time points for primary and secondary outcomes.
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477x279mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	P1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	P6
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	P6
Protocol version	#3	Date and version identifier	n/a
Funding	#4	Sources and types of financial, material, and other support	P17-18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	P17
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	P18

Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	P18
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a, did not establish the committee
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	P3-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	P3-5
Objectives	#7	Specific objectives or hypotheses	P5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	P5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	P5-6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	P6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	P8-11
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or	n/a, intervention did not involve

		improving / worsening disease)	harms or others
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	P8-11
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	P8
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	P11-13
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	P7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	P6-7
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	P7
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	P7
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	P7
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	P7

Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a, not blind to participants or researchers
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	P11-13
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	P11-13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	P13-14
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	P14
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	P14
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	P14
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a, less safe risks in this study

Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a, not apply DMC in this trail
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	P15
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	P15
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	P8
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a, not needed in this study
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	P13-14
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	P18
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a, not needed in this study
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a, not needed in this study
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	P15

Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	P15
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	P14-15
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	n/a, not needed in this study
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a, not needed in this study