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Evaluation of an innovative mobile health program for the self-management of chronic obstructive pulmonary disease (MH-COPD): protocol of a randomized controlled trial

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death globally. Resources to help patients self-manage COPD have long been available; however, patient adherence to these remains suboptimal. The objective of this study is to examine whether an innovative mobile health (mHealth)-enabled care program (MH-COPD) will improve the patient self-management and relevant health outcomes.

Methods and Analysis: A prospective open randomized controlled trial (RCT) has been designed. In the trial, patients with COPD will be recruited from The Prince Charles Hospital, Brisbane, Australia. They will then be randomized to participate in either the MH-COPD intervention group (n=50 patients), or usual care control group (UC-COPD) (n=50 patients) for 6 months. The MH-COPD program has been designed to integrate an mHealth system within a clinical COPD care service. In the program, participants will use a mobile health application at home to review educational videos, monitor COPD symptoms, use an electronic action plan, modify the risk factors of cigarette smoking and regular physical activity, and learn to use inhalers optimally. All participants will be assessed at baseline, 3 months and 6 months. The primary outcomes will be COPD symptoms and quality of life. The secondary outcomes will be patient adherence, physical activity, smoking cessation, use of COPD medicines, frequency of COPD exacerbations and hospital readmissions, and user experience of the mobile app.

Ethics and Dissemination

The clinical trial has been approved by The Prince Charles Hospital Human Research Ethics Committee (HREC/16/QPCH/252), and registered in the Australian New Zealand Clinical Trials Registry (Trial ID: ACTRN12618001091291). The recruitment and follow-up of the trial will be from Jul 2018 to Jun 2020. The study outcomes will be disseminated through a journal publication, approximately 6 months after finishing data collection.

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Trial registration: Registered with Australian New Zealand Clinical Trial Registry (Trial ID: ACTRN12618001091291).

Key words: Chronic pulmonary obstructive disease, randomized controlled trial, self-management, mobile health

Strengths and limitations of the study

- Integration of an innovative mHealth system with a clinical COPD care service can potentially improve the self-management of COPD by patients.
- The mHealth system being tested delivers core recommendations for the self-management of COPD as advocated by the evidence-based guidelines.
- Specific health outcomes of relevance to the self-management will be measured in this mHealth-study.
- The study is limited to a 6-month intervention period, and as a purely self-management program, the mobile phone application does not include remote, real-time monitoring of patient outcomes by clinicians.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive chronic lung disease, ranked as the fourth leading cause of death globally and affecting over 200 million people [1]. Patients with COPD have persistent respiratory symptoms and chronic airflow limitation, and are frequently impacted by episodic exacerbations of COPD. Consequently, they have high risks of hospital readmission, with reported 30-day readmission rates ranging from 10% to 20% [2,3].

The self-management of COPD, such as optimal use of medicines, lifestyle modification and avoidance of risk factors, is essential to improve health outcomes and prevent COPD progression [4,5]. Accordingly, evidence-based self-management principles are recommended in clinical guidelines for COPD. Unfortunately patient adherence with self-management is often suboptimal [6]. For example, studies have demonstrated that only 40% - 60% of patients with COPD adhere with their inhaled medicines to control COPD symptoms [7-9], and about 50% do not undertake physical activities regularly as recommended by the guidelines [10]. Similarly, over 24% of patients with COPD remain current cigarette smokers in Australia [11], although smoking has been well-known as the most important risk factor for COPD [12]. Moreover, many patients often take a wait-and-see approach with self-management, and, hence, fail to seek timely interventions for exacerbations [13]. Barriers to the patient adherence are complex and multifaceted, likely including limited health knowledge, difficulty to access resources, insufficient clinical support, and lack of motivation [13,14].

Recently, mobile health (mHealth) — defined as the use of mobile and wireless technologies for health care [15] - has become a new treatment approach which can empower self-management and enhance proactive clinical interventions [16]. For COPD, a number of mHealth applications are now available in the market [17]. Feasibility studies have demonstrated a high level of acceptance by patients [18] and many potential benefits such as knowledge gained, improved physical activities, reduced dyspnoea [19], and ability to remotely assess COPD exacerbations [20,21]. A recent systematic review, evaluating outcomes from six randomised controlled trials (RCTs), demonstrated the potential to use smartphone applications to reduce COPD exacerbation rates, but at the same time indicated the limitations of studies to date, including inadequate sample sizes (≤50) and heterogeneity in study design [22]. Therefore, additional high quality evidence remains essential to enable practical implementation of mHealth for the management of COPD in clinical settings.

In this study, we propose an innovative mHealth program for COPD (MH-COPD). The program has been specifically designed to integrate an mHealth system within an existing COPD care service to deliver all core components advocated by the evidence-based clinical guidelines in Australia. We hypothesize that the MH-COPD program would increase the self-management of COPD by patients that is consistent with guideline principles, and consequently improve health outcomes. We have therefore designed an RCT to evaluate the efficacy of the MH-COPD program.

Methods

Patient and Public Involvement

The research question on improving the self-management of COPD, and outcome measures were developed according to the clinical practice in Queensland, and suggestions from Lung Foundation Australia, a not-for-

profit organisation representing consumers with respiratory conditions. In design of the mobile health system, we employed an existing framework developed by The Australian e-Health Research Centre (Brisbane, Australia). This framework has been successfully used in a number of studies to assist patients in managing health conditions [23,24] and chronic diseases, including COPD [20,21], diabetes [25], and cardiovascular disease[26,27]. In this project, we also engaged with clinical nurses, general practitioners, thoracic physicians, and a group of patients with COPD in design of interventional components and user interface in the mobile app and clinician portal.

Patients with stable COPD will be recruited to examine the efficacy of the MH-COPD program. The study outcomes will be disseminated through a journal publication, approximately 6 months after finishing data collection. For the participants to be informed of the outcomes, we will send the final publication to them by email.

Trial Design and Clinical Setting

The clinical trial will be a prospective, open, parallel group, two-arm RCT. We will recruit 100 patients with COPD from The Prince Charles Hospital (TPCH), Brisbane, Australia. The study flow chart is shown in Figure 1. Written informed consent will be obtained. Using allocation concealment, participants will be randomised to receive either the MH-COPD program (n=50 patients) or usual care (UC-COPD) (n=50 patients) for a study duration of 6 months. All participants will be assessed at baseline, 3 months, and 6 months.

Patients with COPD attending the thoracic outpatient clinics at the hospital will be screened for eligibility. Each potential candidate will be provided with a participant information sheet about the research study and a consent form. If a candidate is willing to participate in the trial, written informed consent will be obtained. Each participant will be interviewed face-to-face by the clinical research staff (nurses or physicians) in the trial as a baseline assessment.

Eligibility Criteria

Adult patients with COPD will be invited to participate in this trial. The inclusion criteria will be: 1) diagnosis of COPD, defined according to the international GOLD guidelines [28], 2) chronic airflow limitation that is not fully reversible (post-bronchodilator FEV_1/FVC <70% and FEV_1 <80% predicted) and 3) current or former smokers, with a smoking history of >10 pack-years.

The exclusion criteria will be: a) women who are pregnant, b) with age less than 18 years, c) with an intellectual or mental impairment, d) other comorbid lung diseases that would potentially interfere with study outcomes (predominant asthma based on physician diagnosis, active lung cancer, interstitial lung disease, severe bronchiectasis); and e) limitations to the use of mobile technology (non-correctable vision, hearing, cognitive or dexterity impairment).

Randomisation

A series of random assignment forms with permuted blocks will be generated according to a published method [29]. The block size will be confidential. The randomisation will be stratified by participant's sex (male and

female) to ensure a balanced allocation. Assignment forms will be printed and sealed in opaque envelopes according to a predefined order. The envelopes will be stored in a secured cabinet. Following the order, the clinical research staff will open the next available envelope for each eligible participant, to reveal the assignment for the participant.

<Figure 1>

Baseline Assessment

Clinical characterisation will be undertaken at baseline:

1. **Demographics and respiratory history** will be obtained, including smoking history, respiratory symptoms, chronic bronchitis, respiratory medications, oxygen use, frequency of exacerbations of COPD requiring antibiotics and/or steroids in the past 12 months.
2. **COPD symptoms and quality of life**: The COPD Assessment Test (CAT), St George's Respiratory Questionnaire (SGRQ) and modified MRC (mMRC) dyspnoea scale will be administered.
3. **Lung function**: The most recent results for pre and post-bronchodilator spirometry, and gas transfer as physiological indicator of emphysema, will be recorded. These assessments will be performed, if they are unavailable within the previous 12 months.
4. **COPD knowledge** will be assessed with a questionnaire [30], based on the content of Lung Foundation Australia resources.
5. **Questionnaire on mobile technology**: Participants will be surveyed on their attitudes and beliefs about using mobile technologies (e.g. smart phones), and will be asked about their current use of mobile phone.

MH-COPD Intervention Group

The MH-COPD program will implement an mHealth system as an intervention, in addition to usual care. The mHealth system will comprise an Android smartphone application (app) and a secure online clinician portal. Participants will be informed that the MH-COPD program is not a replacement for their usual clinical care, but is an add-on, and they should contact their general practitioner, respiratory nurse or respiratory specialist as usual if they have any concerns about their COPD. The care model of the MH-COPD program is shown in Figure 2.

Resources Provided: In the intervention group, an Android smartphone with a prepaid SIM card will be provided to each participant, with the COPD app fully installed. If a participant wishes to use his/her personal smartphone, the research staff will ensure the participant's phone is compatible with the app and then will install the app. Participants using their own personal smartphone will be provided a mobile data voucher to cover the cost of Internet data transmission. A paper-based instruction manual of the MH-COPD program will be provided to help the participant to use the app and receive interventions.

Study Procedures and Interventions: Each participant will be provided with an education and training session, of up to one-hour duration, to provide instructions and demonstrate how to use the app. During the session, the research staff will introduce the MH-COPD program, and will then register the participant through the online clinician portal. After the registration, an SMS message, containing the log-in formation and a website for

downloading the app, will be automatically sent to the participant's mobile phone. The research staff will then guide the participant to receive the message, download the app, and log into the app. After the registration, the research staff will help the participant create self-management tools, according to the COPD app functions described below:

A. Health education: Ten video clips will be automatically provided to the participants via the app at scheduled times (Figure 3A), at a rate of two videos per week for the first 5 weeks. The video clips have been prepared and validated by Lung Foundation Australia [31]. Through the video clips, participants will gain essential knowledge on ten topics: 1) Managing your lung disease, 2) How do your lungs work? 3) Managing your breathlessness, 4) Managing treatment options, 5) Questions you can ask your health professional, 6) Who is your healthcare team? 7) Managing your fatigue and energy conservation, 8) Tips for looking after yourself and your condition, 9) Benefits of exercise programs and ongoing support, and 10) Supportive care and end-of-life issues. The duration of each video clip ranges from 6 to 12 minutes. The video clips are integrated in the app, and after each video, a questionnaire will be given to help participants self-assess the knowledge obtained. Links to the webpages of Lung Foundation Australia, Asthma Australia and the Australian Government Quitline for smoking cessation will be included in the app, to enable direct access from the smartphone to these sites.

B. Symptom monitoring: Participants will use the app each day to self-manage COPD symptoms, including breathlessness, cough, sputum colour, sputum volume, and wheezing (Figure 3B). The severity levels of the symptoms will be predefined, and scored on the app. The recorded symptoms of individual participants will be automatically compared with those in the previous day. If two or more symptoms of a participant are detected with increased scores, the participant will be notified via an automated smartphone notification to use an electronic COPD action plan in the app.

C. Electronic COPD action plan: Participants will work through an electronic COPD action plan in the app on a daily basis. The action plan will contain 3 sections based on symptom severity: danger signs (Figure 3C), signs of a flare-up, and staying well. It will contain recommendations for medicines prescribed for worsening symptoms and exacerbations. The medicines will include bronchodilators, antibiotics and oral steroids, and will be entered into the action plan in the app by the research staff during the education and training session. The sections and corresponding recommendations in the app will replicate a paper-based COPD action plan clinically validated and used in Queensland Health.

D. Physical activity: The app will use inbuilt motion sensors in the smartphone to automatically record walking steps. Participants will be asked to carry the smartphone with the app during normal activity in waking hours in order to capture walking activity. An initial personal goal for steps to walk will be prescribed [32] for each participant, and this goal will be automatically increased in the first 4 weeks. Motivational messages will also be automatically sent to the participant according to the number of steps and goal achievement each day.

E. Smoking cessation: For current smokers, the participants will use the app to record the number of cigarettes consumed each day, triggers and cues for smoking cigarettes, attempts to reduce cigarettes, and use of pharmacotherapy (such as nicotine replacement or varenicline). A goal of the maximum number of cigarettes consumed each day will be provided to each participant. The goal of cigarettes smoked will be

automatically reduced down to zero through the first six-week time period. Motivational messages will be automatically generated and sent according to the number of cigarettes recorded daily and the goal achievement through the 6-week period.

F. Inhaler technique: The participants will use the app to review videos to learn to how to use inhalers correctly. The videos have been prepared and validated by Lung Foundation Australia [33] and will be preloaded in the app, according to inhalers prescribed to individual participants. Videos of each participant actually using their inhalers will also be recorded by the research staff during the education and training session, and stored in the app for the participant to review.

Monitoring of Patient Adherence: All the data entries of the participants recorded via the app, such as symptoms, the action plan, and cigarettes, will be automatically uploaded to the online portal and analysed to assess the patient adherence. If a participant does not adhere to program for two days, alerts will be generated in the portal, and automated motivational messages will be sent to the participant via app notifications. The research staff will review the alerts in the portal and accordingly contact the participant to troubleshoot the nonadherence.

Diary Card for Exacerbations: Participants will keep a hard copy diary to record exacerbations and hospital admissions during the study. A COPD exacerbation will be defined as an increase in respiratory symptoms requiring treatment with systemic steroids and/or antibiotics [34]. Participants will record the start and end date of treatment for the exacerbation. The research staff based at The Prince Charles Hospital will phone each participant at 2 weeks, 2 months and 4 months, to ensure adherence to the exacerbation diary and reporting of exacerbations, as well as adherence to the app. The data in the diary will be collected and analysed to assess the frequency, duration and severity of exacerbations in the participants.

<Figure 2>

<Figure 3>

Usual Care Group

Usual care: Participants in the usual care (UC-COPD) group will receive standard care from respiratory clinics and primary care, throughout the trial period.

Resources provided: No COPD app will be provided to the usual care group. A standard care package will be provided to help participants with usual care, including general written advice about health education, the COPD action plan, symptom monitoring, physical activity, smoking cessation and inhaler technique. In the package, the information on the self-management of COPD from the Lung Foundation Australia and the corresponding web address will be provided.

Study procedures: After randomization and baseline assessment, the research staff will train the participant on study procedures and take them through the instruction manual. These training and procedures will be the same as those provided in usual care in Queensland Health.

Diary card for exacerbations: Participants will keep a written, hard copy diary to record exacerbations and hospital admissions during the study, similar to the methods described in the Intervention group.

Outcomes

The outcome measures of the study are shown in Table 1. The primary outcome measures will be COPD symptoms and quality of life, assessed by the CAT [35] , St George's Respiratory Questionnaire (SGRQ) [36] and mMRC [37] questionnaires at the baseline and 6-month time point. The secondary outcomes will include the inhaled medicine adherence (Test of the Adherence to Inhalers, TAI) [38], smoking cessation, and physical activity by Global Physical Activity Questionnaire (GPAQ) [39]. Smoking cessation will be defined as zero cigarettes smoked in the last 7 days of the 6 month follow-up period after commencement of the intervention, as assessed through the self-reported diary. To assess the risk of COPD exacerbation, we will analyse the rate of COPD exacerbations recorded in the diary and MH-COPD system. Additionally, we will assess the health care utilizations relevant to hospital readmissions and visits of the emergency department. These events will be obtained from the hospital information systems in the trial.

For the participants in the MH-COPD group, we will report the adherence quantified by the daily data entries recommended, and user experience assessed by a questionnaire previously applied in a previous mobile health based study [25].

Table 1. Study outcome measures and assessment tools and data resources.

Primary Outcome	**Baseline**	**Six months**	**Methods/Instruments**
COPD symptoms and quality of life	Y	Y	CAT, SGRQ and mMRC
Secondary Outcomes			
COPD knowledge	Y	Y	Lung Foundation Australia questionnaire on COPD knowledge
Inhaled medicine adherence	Y	Y	TAI questionnaire
Use of COPD action plan	N	Y	Self-reported in diary
Smoking cessation	Y	Y	Self-reported in diary
Physical activity	Y	Y	GPAQ (both groups), step count (intervention group)
Exacerbation rate	N	Y	Exacerbations recorded on hard copy exacerbation diary (both groups) and on the app (intervention group)
Health care utilisation	N	Y	Hospital readmissions and visits to the emergency department via hospital information systems
User experience of the mobile app	N	Y	Questionnaire (intervention group).

Sample Size

The sample size has been calculated based on the co-primary outcomes of the CAT score and SGRQ score. 100 patients, randomised 1:1 to intervention (MH-COPD) or usual care (UC-COPD), will have 80% power at

significance level (alpha) of 0.05 to detect a clinically important reduction of 3 in the CAT score [40] (primary outcome) in ~50% of intervention patients, compared to 20% in the control group, even with 40 patients in each final group (allowing for up to 20% withdrawal). In addition, this sample size will have 80% power at significance level (alpha) of 0.05 to detect a relative risk of 2 for a clinically important increase in SGRQ of 4 (co-primary outcome) in the intervention group, given a proportion of 30% of the control group achieving this with usual care, even with 40 patients in each final group (allowing for up to 20% withdrawal).

Blinding

This is an open randomized controlled trial, due to the difficulty in effectively blinding participants and clinical researchers to the treatment groups. Data analysis of outcomes based on questionnaires and diary cards (common to both groups) will be analysed by a researcher not directly involved with recruitment and follow-up. In the analysis, only de-identified data will be provided.

Data Collection and Storage

The research staff will interview each participant at baseline to collect the data patient characteristics and conduct the assessments for those questionnaire-based outcomes. During the interview, the participant will receive paper-based assessment forms (questionnaires), and will be given sufficient time for completion of these. The completeness of each questionnaire will be checked at the end of the interview by the research staff for quality purposes.

All study files, including the questionnaire forms, master list of participants, and case report forms, will be stored securely, either in password-protected computer files (for electronic files) or in locked filing cabinets (for hard copies) in a secure area. Access to these files will only be granted to the study personnel trained in confidentiality and privacy procedures. All trial data provided for research analysis will be de-identified, including patient characteristics, primary and secondary outcomes, and data entries through the online portal systems used in the study.

All the trial files and data will be stored securely for a minimum of 5 years after completion of the study and, finally, be securely destroyed according to the Australian National Health and Medical Research Council code for responsible conduct of research guidelines [41].

Strategies for Participant Retention

Prior to the trial recruitment, the research team will discuss the importance of participant retention within the recruitment and care teams. During the trial, each participant will be provided with a telephone contact in the information package. Accordingly, the participants can contact the research staff for trial-related support. A structured procedure and log files will be in place to guide the research staff to document the participants' enquiries, and ensure timely responses and/or follow-ups. Additionally, we will reimburse the participants for trial-related expenses including Android smartphone handsets if needed, mobile Internet costs, and parking fees for interviews and assessments.

Statistical Methods

All participants randomized into this study will be included in the final comparative analysis on an intention-to-treat basis. A χ^2 test will be used to compare categorical variables between the MH-COPD and UC-COPD

group. ANOVA will be applied to compare continuous variables between the groups. We will also analyse fluctuations of monitored symptoms to predict COPD exacerbations for early intervention. In this predictive analysis, we will use a nonlinear regression method, such as the exponential regression model previously applied [20], to analyse the relationship between the changes in symptoms and occurrence of exacerbations. In these comparison and analysis methods, a p-value less than 0.05 (two-tailed) will be considered statistically significant. The analysis will be adjusted for confounding variables including age and sex. We will mainly use SPSS version 23 for the statistical analysis. Missing data at the case level will be imputed using a multiple imputation method implemented in SPSS.

Trial Management

A trial steering committee will convene monthly (with additional meetings if needed) and take overall responsibility for the conduct of the trial. The committee will comprise representatives of the chief investigators, research staff and project managers from the collaborating organizations. The responsibilities of the committee include managing the trial progress, reviewing adverse events, resolving technical issues, monitoring trial data, providing reports to the project sponsors and ethics committees, and deciding budget and administration issues. If necessary, the committee will advise and make changes to the clinical trial protocol. The committee will be independent from project sponsors and free from competing interests.

Trial Monitoring

A data monitoring committee (DMC), comprising four clinical researchers not directly involved in the study, will evaluate safety throughout the trial. The DMC will be independent from the trial sponsors and competing interests. The DMC will convene every 3 months (with additional meetings if needed) to review the risks and severity of adverse events or incidents reported. The DMC will assess the severity of adverse events and/or incidents, and provide recommendations if needed. If there are substantial differences in rates of serious adverse events (including mortality) or hospitalisation between the MH-COPD and UC-COPD groups, DMC may recommend a formal interim statistical analysis and, according, recommend whether the study should be terminated early.

Discussion

Currently many mobile apps for COPD are available in the market, but they often have limited features or focuses [17]. Importantly, the clinical evidence on the efficacy and effectiveness is generally absent [17,22,42]. Recently, several RCT studies evaluated potential benefits to use mHeath for COPD, but they are normally limited by small sample sizes ($n \leq 100$) and narrow scopes, such as intervention of worsening COPD symptoms [43-45], physical activities [19,46,47] or impacts of environment/climate change [48]. Moreover, many mHealth studies for COPD have been found with many issues, such as high drop-out rates (20% [45], 33% [47] and 36% [19]), large variations of patient adherence (20%[47] to 98%[44] adherence rates), and inconsistent user experience (mixed with technical challenges [19] and good satisfactions [47]). Therefore, further clinical validation remains essential to use the mHealth for improving COPD care.

The MH-COPD program has been deliberately designed to overcome those barriers stated before, and to focus on improving patient adherence to the self-management, consistent with the evidence-based clinical guidelines [4]. In the program, patients will use a mobile app to conveniently access educational videos to gain essential

knowledge and skills as recommended by the guidelines. The app will also assist the patients in monitoring COPD symptoms and risk factors (low physical activity and smoking of cigarettes). Patients will interact with the electronic COPD action plan to make decision for significant changes in the symptoms; and receive automated motivational messages for modification of the risk factors. The patients' data, including monitoring symptoms, risk factors and adherence, will be automatically uploaded to the portal. Using the portal, the care providers are able to remotely monitor the patient conditions and adherence, and accordingly provide timely interventions. Compared with the paper based approach in usual care, the use of mHealth would make it easier and simpler for the patients to access clinical resources and self-manage COPD. Additionally, it would allow the care providers to actively engage with the patients in COPD care. Therefore, we expect the MH-COPD program to improve the patient compliance and health outcomes.

Different from many existing studies, our MH-COPD program was designed to include all core components outlined by the evidence-based guidelines in Australia, and integrate within COPD clinics. Additionally, the program aims at improving patient self-management. Although the nurses and COPD physicians in the program will review the patients' data through the clinician portal, their interventions mainly focus on supporting and motivating patients to adhere to the program. Additionally, many automated messages and alerts will provided through the mHealth system to support the intervention. Therefore, the burden to the clinicians in the program would be minimum. In all, the MH-COPD study will provide a unique opportunity to help understand the potential to use mobile health innovations to improve patient self-management and health outcomes, and hence add evidence for the effectiveness of using mobile health to improve COPD care in the community.

Summary

The study will specifically integrate an innovative mHealth system with a clinical COPD service and evaluate this approach through a RCT. The evaluation will provide a unique opportunity to improve COPD care in the community through mobile health innovations.

Figure Legends:

Figure 1. Study flow chart of the randomized controlled trial designed to evaluate the MH-COPD program. UC=usual care, MH=mobile health.

Figure 2. The care model of the MH-COPD program includes the components of health education, electronic COPD action plan, symptom monitoring, physical activity, smoking cessation, and inhaler technique.

Figure 3. Selected screenshots showing the user interface of the mobile application. A: Scheduled educational videos preloaded in the app. B: User interface to record symptoms and risk factors. C: User interface showing an assessment of symptoms in the COPD action plan.

Author contributions

This study protocol was developed by I.Y. and H.D. The first draft of the manuscript was written by I.Y. and H.D. All authors contributed to design of the clinical study and critical revision of the manuscript.

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Conflicts of interest

There are no conflicts of interest in this project.

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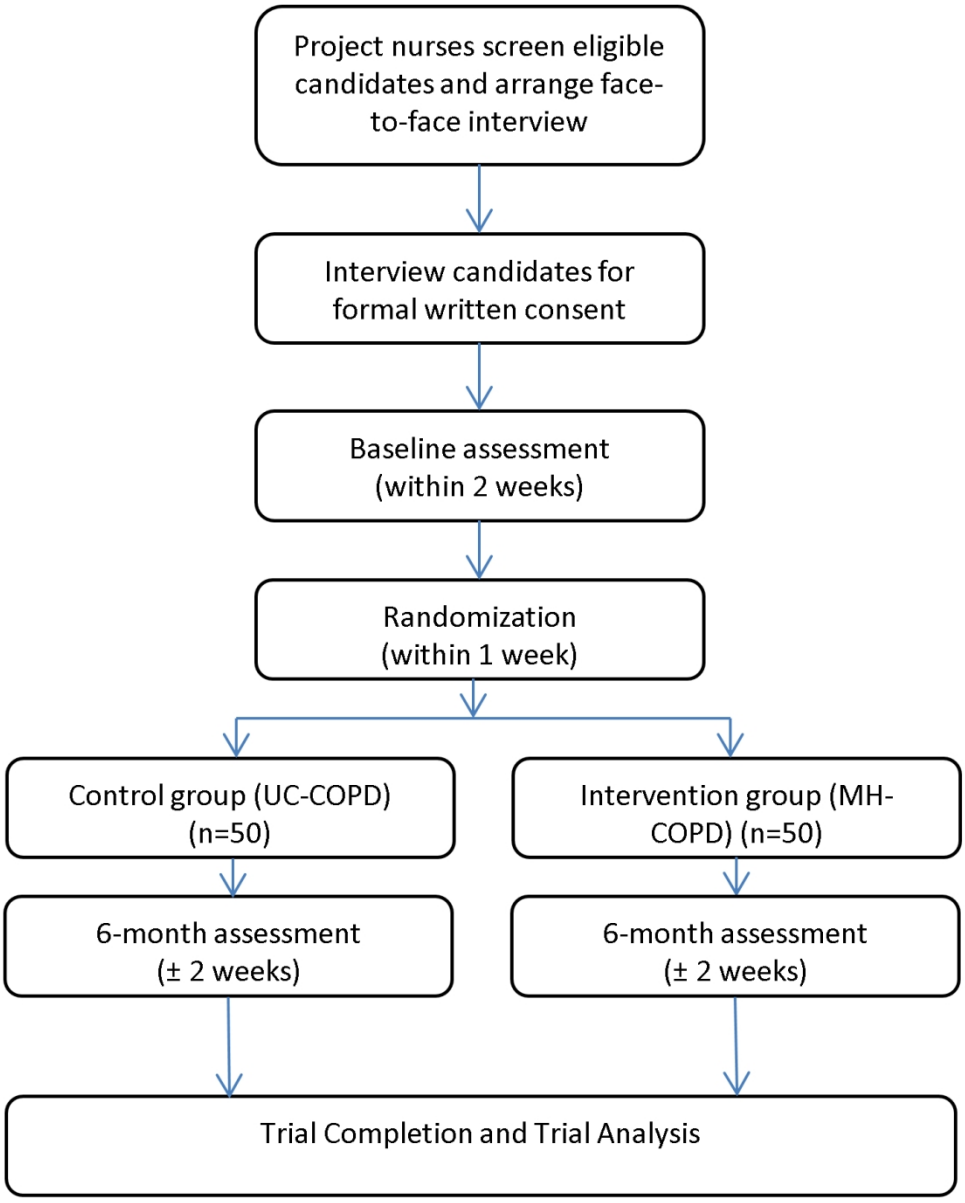

Figure 1. Study flow chart of the randomized controlled trial designed to evaluate the MH-COPD program. UC=usual care, MH=mobile health.

121x151mm (300 x 300 DPI)

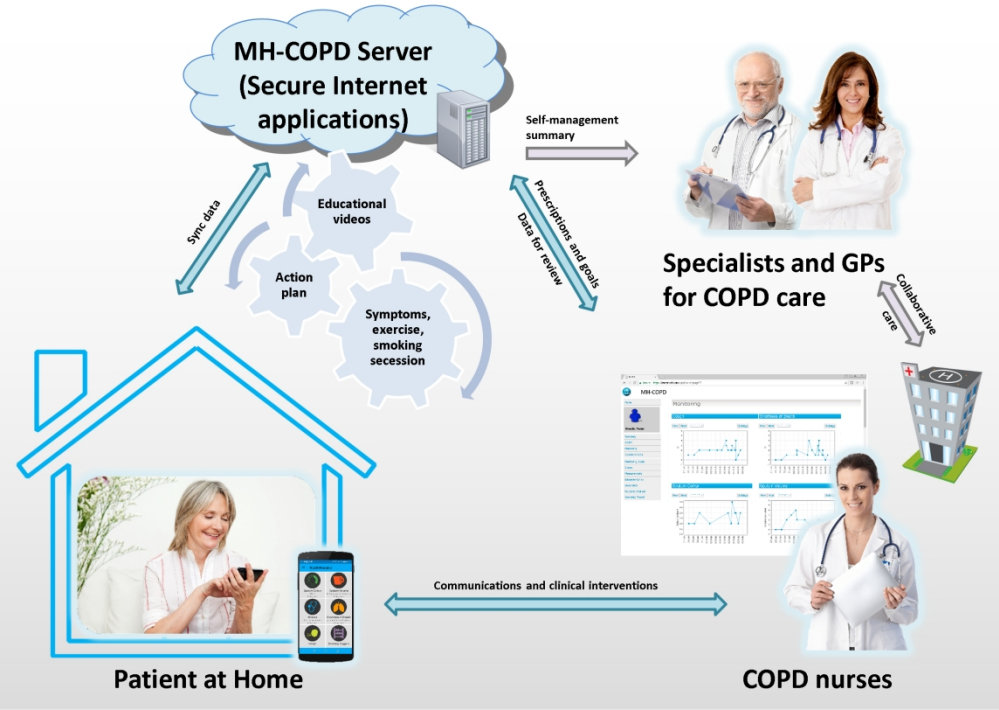

Figure 2. The care model of the MH-COPD program includes the components of health education, electronic COPD action plan, symptom monitoring, physical activity, smoking cessation, and inhaler technique.

215x154mm (300 x 300 DPI)

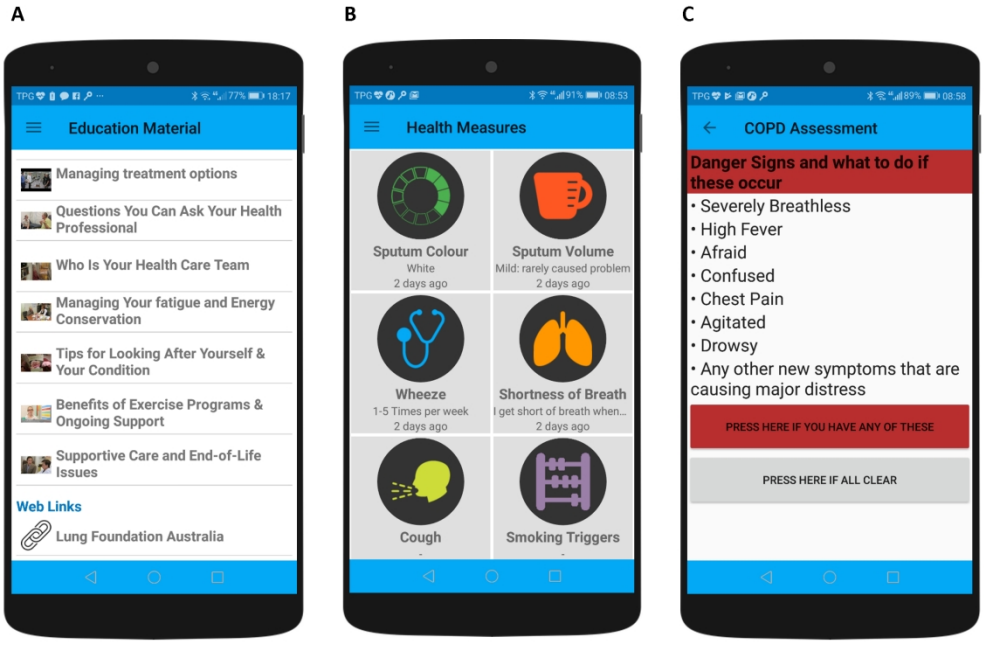

Figure 3. Selected screenshots showing the user interface of the mobile application. A: Scheduled educational videos preloaded in the app. B: User interface to record symptoms and risk factors. C: User interface showing an assessment of symptoms in the COPD action plan.

233x152mm (300 x 300 DPI)

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Evaluation of an innovative mobile health program for the self-management of chronic obstructive pulmonary disease (MH-COPD): protocol of a randomized controlled trial

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Evaluation of an innovative mobile health program for the self-management of chronic obstructive pulmonary disease (MH-COPD): protocol of a randomized controlled trial

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death globally. In outpatient care, the self-management of COPD is essential, but patient adherence to this remains suboptimal. The objective of this study is to examine whether an innovative mobile health (mHealth)-enabled care program (MH-COPD) will improve the patient self-management and relevant health outcomes.

Methods and Analysis: A prospective open randomized controlled trial (RCT) has been designed. In the trial, patients with COPD will be recruited from The Prince Charles Hospital, Brisbane, Australia. They will then be randomized to participate in either the MH-COPD intervention group (n=50 patients), or usual care control group (UC-COPD) (n=50 patients) for 6 months. The MH-COPD program has been designed to integrate an mHealth system within a clinical COPD care service. In the program, participants will use a mobile health application at home to review educational videos, monitor COPD symptoms, use an electronic action plan, modify the risk factors of cigarette smoking and regular physical activity, and learn to use inhalers optimally. All participants will be assessed at baseline, 3 months and 6 months. The primary outcomes will be COPD symptoms and quality of life. The secondary outcomes will be patient adherence, physical activity, smoking cessation, use of COPD medicines, frequency of COPD exacerbations and hospital readmissions, and user experience of the mobile app.

Ethics and Dissemination

The clinical trial has been approved by The Prince Charles Hospital Human Research Ethics Committee (HREC/16/QPCH/252), and registered in the Australian New Zealand Clinical Trials Registry (Trial ID: ACTRN12618001091291). The recruitment and follow-up of the trial will be from Jan 2019 to Dec 2020. The study outcomes will be disseminated according to the CONSORT statement through a journal publication, approximately 6 months after finishing data collection.

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Trial registration: Registered with Australian New Zealand Clinical Trial Registry (Trial ID: ACTRN12618001091291).

Key words: Chronic pulmonary obstructive disease, randomized controlled trial, self-management, mobile health

Strengths and limitations of the study

- Integration of an innovative mHealth system with a clinical COPD care service can potentially improve the self-management of COPD by patients.
- The mHealth system being tested delivers core recommendations for the self-management of COPD as advocated by the evidence-based guidelines.
- Specific health outcomes of relevance to the self-management will be measured in this mHealth-study.
- The study is limited to a 6-month intervention period, and as a purely self-management program, the mobile phone application does not include remote, real-time monitoring of patient outcomes by clinicians.

Protocol version

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Authors: The research team of the MH-COPD study

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive chronic lung disease, ranked as the fourth leading cause of death globally and affecting over 200 million people [1]. Patients with COPD have persistent respiratory symptoms and chronic airflow limitation, and often experience episodic exacerbations of COPD. Consequently, they have high risks of hospital readmission, with reported 30-day readmission rates ranging from 10% to 20% [2,3].

The self-management of COPD through clinical and social support, such as optimal use of medicines, lifestyle modification and avoidance of risk factors, is essential to improve health outcomes and prevent COPD progression [4,5]. Accordingly, evidence-based self-management principles are recommended in clinical guidelines for COPD. Unfortunately patient adherence with self-management is often suboptimal [6]. For example, studies have demonstrated that only 40% - 60% of patients with COPD adhere with their inhaled medicines to control COPD symptoms [7-9], and about 50% do not undertake physical activities regularly as recommended by the guidelines [10]. Similarly, over 24% of patients with COPD remain current cigarette smokers in Australia [11], although smoking has been well-known as the most important risk factor for COPD [12]. Moreover, many patients often take a wait-and-see approach with self-management, and, hence, fail to seek timely interventions for exacerbations [13]. Barriers to the patient adherence are complex and multifaceted, likely including limited health knowledge, difficulty to access resources, insufficient clinical support, and lack of motivation [13,14].

Recently, mobile health (mHealth) — defined as the use of mobile and wireless technologies for health care [15] - has become a new treatment approach which can empower self-management and enhance proactive clinical interventions [16]. For COPD, a number of mHealth applications are now available in the market [17]. Feasibility studies have demonstrated a high level of acceptance by patients [18] and many potential benefits such as knowledge gained, improved physical activities, reduced dyspnoea [19], and ability to remotely assess COPD exacerbations [20,21]. A recent systematic review, evaluating outcomes from six randomised controlled trials (RCTs), demonstrated the potential to use smartphone applications to reduce COPD exacerbation rates, but at the same time indicated the limitations of studies to date, including inadequate sample sizes (≤100) and heterogeneity in study design [22]. Therefore, additional high quality evidence remains essential to enable practical implementation of mHealth for the management of COPD in clinical settings.

In this study, we propose an innovative mHealth program for COPD (MH-COPD). The program has been specifically designed to integrate an mHealth system within an existing COPD care service to deliver all core components advocated by the evidence-based clinical guidelines in Australia. The MH-COPD program will make it easy for patients to access validated educational materials, and self-manage clinical symptoms. The integration with the clinical service will also enable care providers to support and motivate patients to adhere to the self-management of COPD. We hypothesize that the MH-COPD program would enhance the self-management of COPD by patients that is consistent with guideline principles, and consequently improve health outcomes. We have therefore designed an RCT to evaluate the efficacy of the MH-COPD program.

Methods

Patient and Public Involvement

The research question on improving the self-management of COPD, and outcome measures were developed according to the clinical practice in Queensland, and suggestions from Lung Foundation Australia, a not-for-profit organisation representing consumers with respiratory conditions. In design of the mobile health system, we employed an existing framework developed by The Australian e-Health Research Centre (Brisbane, Australia). This framework has been successfully used in a number of studies to assist patients in managing health conditions [23,24] and chronic diseases, including COPD [20,21], diabetes [25], and cardiovascular disease [26,27]. In this project, we also engaged with clinical nurses, general practitioners, thoracic physicians, and a group of patients with COPD. With this engagement, we identified the care needs for the self-management of COPD. We accordingly designed the interventional components and care processes. Finally we worked with the clinician and patient groups to design the user interface for the mobile app and clinician portal.

Patients with stable COPD will be recruited to examine the efficacy of the MH-COPD program. The study outcomes will be disseminated through a journal publication, approximately 6 months after finishing data collection. For the participants to be informed of the outcomes, we will send the final publication to them by email.

Trial Design and Clinical Setting

The clinical trial will be a prospective, open, parallel group, two-arm RCT. We will recruit 100 patients with COPD from The Prince Charles Hospital (TPCH), Brisbane, Australia. The recruitment and follow-up of the trial will be from Jan 2019 to Dec 2020. The study flow chart is shown in Figure 1. Written informed consent will be obtained. Using allocation concealment, participants will be randomised to receive either the MH-COPD program (n=50 patients) or usual care (UC-COPD) (n=50 patients) for a study duration of 6 months. All participants will be assessed at baseline, 3 months, and 6 months.

Patients with COPD attending the thoracic outpatient clinics at the hospital will be screened for eligibility. Each potential candidate will be provided with a participant information sheet about the research study and a consent form. If a candidate is willing to participate in the trial, written informed consent will be obtained. Each participant will be interviewed face-to-face by the clinical research staff (nurses or physicians) in the trial as a baseline assessment.

Eligibility Criteria

Adult patients with COPD will be invited to participate in this trial. The inclusion criteria will be: 1) diagnosis of COPD, defined according to the international GOLD guidelines [28], 2) chronic airflow limitation that is not fully reversible (post-bronchodilator FEV_1/FVC <70% and FEV_1 <80% predicted) and 3) current or former smokers, with a smoking history of >10 pack-years.

The exclusion criteria will be: a) women who are pregnant, b) with age less than 18 years, c) with an intellectual or mental impairment, d) other comorbid lung diseases that would potentially interfere with study outcomes (predominant asthma based on physician diagnosis, active lung cancer, interstitial lung disease, severe bronchiectasis); and e) limitations to the use of mobile technology (non-correctable vision, hearing, cognitive or dexterity impairment).

Randomisation

A series of random assignment forms with permuted blocks will be generated according to a published method [29]. The block size will be confidential. The randomisation will be stratified by participant's sex (male and female) to ensure a balanced allocation. Assignment forms will be printed and sealed in opaque envelopes according to a predefined order. The envelopes will be stored in a secured cabinet. Following the order, the clinical research staff will open the next available envelope for each eligible participant, to reveal the assignment for the participant.

<Figure 1>

Baseline Assessment

Clinical characterisation will be undertaken at baseline:

1. **Demographics and respiratory history** will be obtained, including smoking history, respiratory symptoms, chronic bronchitis, respiratory medications, oxygen use, frequency of exacerbations of COPD requiring antibiotics and/or steroids in the past 12 months.
2. **COPD symptoms and quality of life**: The COPD Assessment Test (CAT), St George's Respiratory Questionnaire (SGRQ) and modified MRC (mMRC) dyspnoea scale will be administered.
3. **Lung function**: The most recent results for pre and post-bronchodilator spirometry, and gas transfer as physiological indicator of emphysema, will be recorded. These assessments will be performed, if they are unavailable within the previous 12 months.
4. **COPD knowledge** will be assessed with a questionnaire [30], based on the content of Lung Foundation Australia resources.
5. **Questionnaire on mobile technology**: Participants will be surveyed on their attitudes and beliefs about using mobile technologies (e.g. smart phones), and will be asked about their current use of mobile phone.

MH-COPD Intervention Group

The MH-COPD program will implement an mHealth system as an intervention, in addition to usual care. The mHealth system will comprise an Android smartphone application (app) and a secure online clinician portal. Participants will be informed that the MH-COPD program is not a replacement for their usual clinical care, but is an add-on, and they should contact their general practitioner, respiratory nurse or respiratory specialist as usual if they have any concerns about their COPD. The care model of the MH-COPD program is shown in Figure 2.

Resources Provided: In the intervention group, an Android smartphone with a prepaid SIM card will be provided to each participant, with the COPD app fully installed. If a participant wishes to use his/her personal smartphone, the research staff will ensure the participant's phone is compatible with the app and then will install the app. Participants using their own personal smartphone will be provided a mobile data voucher to cover the cost of Internet data transmission. A paper-based instruction manual of the MH-COPD program will be provided to help the participant to use the app and receive interventions.

Study Procedures and Interventions: Each participant will be provided with an education and training session, of up to one-hour duration, to provide instructions and demonstrate how to use the app. During the session, the research staff will introduce the MH-COPD program, and will then register the participant through the online

clinician portal. After the registration, an SMS message, containing the log-in formation and a website for downloading the app, will be automatically sent to the participant's mobile phone. The research staff will then guide the participant to receive the message, download the app, and log into the app. After the registration, the research staff will help the participant create self-management tools, according to the COPD app functions described below:

A. Health education: Ten video clips will be automatically provided to the participants via the app at scheduled times (Figure 3A), at a rate of two videos per week for the first 5 weeks. The video clips have been prepared and validated by Lung Foundation Australia [31]. Through the video clips, participants will gain essential knowledge on ten topics: 1) Managing your lung disease, 2) How do your lungs work? 3) Managing your breathlessness, 4) Managing treatment options, 5) Questions you can ask your health professional, 6) Who is your healthcare team? 7) Managing your fatigue and energy conservation, 8) Tips for looking after yourself and your condition, 9) Benefits of exercise programs and ongoing support, and 10) Supportive care and end-of-life issues. The duration of each video clip ranges from 6 to 12 minutes. The video clips are integrated in the app, and after each video, a questionnaire will be given to help participants self-assess the knowledge obtained. Links to the webpages of Lung Foundation Australia, Asthma Australia and the Australian Government Quitline for smoking cessation will be included in the app, to enable direct access from the smartphone to these sites.

B. Symptom monitoring: Participants will use the app each day to self-manage COPD symptoms, including breathlessness, cough, sputum colour, sputum volume, and wheezing (Figure 3B). The severity levels of the symptoms will be predefined, and scored on the app. The recorded symptoms of individual participants will be automatically compared with those in the previous day. If two or more symptoms of a participant are detected with increased scores, the participant will be notified via an automated smartphone notification to use an electronic COPD action plan in the app.

C. Electronic COPD action plan: Participants will work through an electronic COPD action plan in the app on a daily basis. The action plan will contain 3 sections based on symptom severity: danger signs (Figure 3C), signs of a flare-up, and staying well. It will contain recommendations for medicines prescribed for worsening symptoms and exacerbations. The medicines will include bronchodilators, antibiotics and oral steroids, and will be entered into the action plan in the app by the research staff during the education and training session. The sections and corresponding recommendations in the app will replicate a paper-based COPD action plan clinically validated and used in Queensland Health. This will make it easy for patients to access and use the action plan. Participants in the intervention program will still be required to engage with care providers to diagnose and treat clinical conditions, including acute exacerbations of COPD, as what they do in usual care.

D. Physical activity: The app will use inbuilt motion sensors in the smartphone to automatically record walking steps. Participants will be asked to carry the smartphone with the app during normal activity in waking hours in order to capture walking activity. An initial personal goal for steps to walk will be prescribed [32] for each participant, and this goal will be automatically increased in the first 4 weeks. Motivational messages will also be automatically sent to the participant according to the number of steps and goal achievement each day.

E. Smoking cessation: For current smokers, the participants will use the app to record the number of cigarettes consumed each day, triggers and cues for smoking cigarettes, attempts to reduce cigarettes, and use of

pharmacotherapy (such as nicotine replacement or varenicline). A goal of the maximum number of cigarettes consumed each day will be provided to each participant. The goal of cigarettes smoked will be automatically reduced down to zero through the first six-week time period. Clinicians in the program will discuss with individual participants to set the goal, and adjust the goal during follow-up. Motivational messages will be automatically generated and sent according to the number of cigarettes recorded daily and the goal achievement through the 6-week period.

F. Inhaler technique: The participants will use the app to review videos to learn to how to use inhalers correctly. The videos have been prepared and validated by Lung Foundation Australia [33] and will be preloaded in the app, according to inhalers prescribed to individual participants. Videos of each participant actually using their inhalers will also be recorded by the research staff during the education and training session, and stored in the app for the participant to review.

Monitoring of Patient Adherence: All the data entries of the participants recorded via the app, such as symptoms, the action plan, and cigarettes, will be automatically uploaded to the online portal and analysed to assess the patient adherence. If a participant does not adhere to program for two days, alerts will be generated in the portal, and automated motivational messages will be sent to the participant via app notifications. The research staff will review the alerts in the portal and accordingly contact the participant to troubleshoot the nonadherence.

Diary Card for Exacerbations: Participants will keep a hard copy diary to record exacerbations and hospital admissions during the study. A COPD exacerbation will be defined as an increase in respiratory symptoms requiring treatment with systemic steroids and/or antibiotics [34]. Participants will record the start and end date of treatment for the exacerbation. The research staff based at The Prince Charles Hospital will phone each participant at 2 weeks, 2 months and 4 months, to ensure adherence to the exacerbation diary and reporting of exacerbations, as well as adherence to the app. The data in the diary will be collected and analysed to assess the frequency, duration and severity of exacerbations in the participants.

<Figure 2>

<Figure 3>

Usual Care Group

Usual care: Participants in the usual care (UC-COPD) group will receive standard care from respiratory clinics and primary care, throughout the trial period.

Resources provided: No COPD app will be provided to the usual care group. A standard care package will be provided to help participants with usual care, including general written advice about health education, the COPD action plan, symptom monitoring, physical activity, smoking cessation and inhaler technique. In the package, the information on the self-management of COPD from the Lung Foundation Australia and the corresponding web address will be provided.

Study procedures: After randomization and baseline assessment, the research staff will train the participant on study procedures and take them through the instruction manual. These training and procedures will be the same as those provided in usual care in Queensland Health.

Diary card for exacerbations: Participants will keep a written, hard copy diary to record exacerbations and hospital admissions during the study, similar to the methods described in the Intervention group.

Outcomes

The outcome measures of the study are shown in Table 1. The primary outcome measures will be COPD symptoms and quality of life, assessed by the CAT [35] , St George's Respiratory Questionnaire (SGRQ) [36] and mMRC [37] questionnaires at the baseline and 6-month time point. The CAT and SGRQ questionnaires will be used because they are responsive to interventions [38]. We will also include mMRC because it is essential for assessing dyspnoea, and has been adopted in GOLD [28] and Australian COPD-X guidelines [4]. The secondary outcomes will include the inhaled medicine adherence (Test of the Adherence to Inhalers, TAI) [39], smoking cessation, and physical activity by Global Physical Activity Questionnaire (GPAQ) [40]. Smoking cessation will be defined as zero cigarettes smoked in the last 7 days of the 6 month follow-up period after commencement of the intervention, as assessed through the self-reported diary. To assess the risk of COPD exacerbation, we will analyse the rate of COPD exacerbations recorded in the diary and MH-COPD system. Additionally, we will assess the health care utilizations relevant to hospital readmissions and visits of the emergency department. These events will be obtained from the hospital information systems in the trial.

For the participants in the MH-COPD group, we will report the adherence quantified by the daily data entries recommended, and user experience assessed by a questionnaire previously applied in a previous mobile health based study [25].

Table 1. Study outcome measures and assessment tools and data resources.

Primary Outcome	**Baseline**	**Six months**	**Methods/Instruments**
COPD symptoms and quality of life	Y	Y	CAT, SGRQ and mMRC
Secondary Outcomes			
COPD knowledge	Y	Y	Lung Foundation Australia questionnaire on COPD knowledge
Inhaled medicine adherence	Y	Y	TAI questionnaire
Use of COPD action plan	N	Y	Self-reported in diary
Smoking cessation	Y	Y	Self-reported in diary
Physical activity	Y	Y	GPAQ (both groups), step count (intervention group)
Exacerbation rate	N	Y	Exacerbations recorded on hard copy exacerbation diary (both groups) and on the app (intervention group)
Health care utilisation	N	Y	Hospital readmissions and visits to the emergency department via hospital information systems
User experience of the mobile app	N	Y	Questionnaire (intervention group).

Sample Size

The sample size has been calculated based on the co-primary outcomes of the CAT score and SGRQ score. 100 patients, randomised 1:1 to intervention (MH-COPD) or usual care (UC-COPD), will have 80% power at significance level (alpha) of 0.05 to detect a clinically important reduction of 3 in the CAT score [38] (primary outcome) in ~50% of intervention patients, compared to 20% in the control group, even with 40 patients in each final group (allowing for up to 20% withdrawal). In addition, this sample size will have 80% power at significance level (alpha) of 0.05 to detect a relative risk of 2 for a clinically important increase in SGRQ of 4 (co-primary outcome) in the intervention group, given a proportion of 30% of the control group achieving this with usual care, even with 40 patients in each final group (allowing for up to 20% withdrawal).

Blinding

This is an open randomized controlled trial, due to the difficulty in effectively blinding participants and clinical researchers to the treatment groups. Data analysis of outcomes based on questionnaires and diary cards (common to both groups) will be analysed by a researcher not directly involved with recruitment and follow-up. In the analysis, only de-identified data will be provided.

Data Collection and Storage

The research staff will interview each participant at baseline to collect the data patient characteristics and conduct the assessments for those questionnaire-based outcomes. During the interview, the participant will receive paper-based assessment forms (questionnaires), and will be given sufficient time for completion of these. The completeness of each questionnaire will be checked at the end of the interview by the research staff for quality purposes.

All study files, including the questionnaire forms, master list of participants, and case report forms, will be stored securely, either in password-protected computer files (for electronic files) or in locked filing cabinets (for hard copies) in a secure area. Access to these files will only be granted to the study personnel trained in confidentiality and privacy procedures. All trial data provided for research analysis will be de-identified, including patient characteristics, primary and secondary outcomes, and data entries through the online portal systems used in the study.

All the trial files and data will be stored securely for a minimum of 5 years after completion of the study and, finally, be securely destroyed according to the Australian National Health and Medical Research Council code for responsible conduct of research guidelines [41].

Strategies for Participant Retention

Prior to the trial recruitment, the research team will discuss the importance of participant retention within the recruitment and care teams. During the trial, each participant will be provided with a telephone contact in the information package. Accordingly, the participants can contact the research staff for trial-related support. A structured procedure and log files will be in place to guide the research staff to document the participants' enquiries, and ensure timely responses and/or follow-ups. Additionally, we will reimburse the participants for trial-related expenses including Android smartphone handsets if needed, mobile Internet costs, and parking fees for interviews and assessments.

Statistical Methods

All participants randomized into this study will be included in the final comparative analysis on an intention-to-treat basis. A χ^2 test will be used to compare categorical variables between the MH-COPD and UC-COPD group. ANOVA will be applied to compare continuous variables between the groups. We will also analyse fluctuations of monitored symptoms to predict COPD exacerbations for early intervention. In this predictive analysis, we will use a nonlinear regression method, such as the exponential regression model previously applied [20], to analyse the relationship between the changes in symptoms and occurrence of exacerbations. In these comparison and analysis methods, a p-value less than 0.05 (two-tailed) will be considered statistically significant. The analysis will be adjusted for confounding variables including age and sex. We will mainly use SPSS version 23 for the statistical analysis. Missing data at the case level will be imputed using a multiple imputation method implemented in SPSS.

Trial Management

A trial steering committee will convene monthly (with additional meetings if needed) and take overall responsibility for the conduct of the trial. The committee will comprise representatives of the chief investigators, research staff and project managers from the collaborating organizations. The responsibilities of the committee include managing the trial progress, reviewing adverse events, resolving technical issues, monitoring trial data, providing reports to the project sponsors and ethics committees, and deciding budget and administration issues. If necessary, the committee will advise and make changes to the clinical trial protocol. The committee will be independent from project sponsors and free from competing interests.

Trial Monitoring

A data monitoring committee (DMC), comprising four clinical researchers not directly involved in the study, will evaluate safety throughout the trial. The DMC will be independent from the trial sponsors and competing interests. The DMC will convene every 3 months (with additional meetings if needed) to review the risks and severity of adverse events or incidents reported. The statistical analysis methods and outcomes will be reviewed by a statistician. The DMC will assess the severity of adverse events and/or incidents, and provide recommendations if needed. If there are substantial differences in rates of serious adverse events (including mortality) or hospitalisation between the MH-COPD and UC-COPD groups, the DMC will investigate the potential reasons for the differences. If significant adverse events are caused by the MH-COPD program, the DMC will recommend to terminate the trial early.

Limitations

A number of potential limitations should be considered. This study is limited to a 6-month intervention duration, which may be insufficient to reflect long-term effects of the intervention. The study is also not blinded to participants and clinicians, although analysis of 6 month outcomes will be blinded. This is a hospital-based study, which limits generalisability; however, future studies will address initiating of mHealth for patients with COPD in primary care.

Discussion

Currently many mobile apps for COPD are available in the market, but they often have limited features or focuses [17]. Importantly, the clinical evidence on the efficacy and effectiveness is generally absent [17,22,42]. Recently, several RCT studies evaluated potential benefits to use mHealth for COPD, but they are normally limited by small sample sizes (n≤100) and narrow scopes, such as intervention of worsening COPD symptoms [43-45], physical activities [19,46,47] or impacts of environment/climate change [48]. Moreover, many mHealth studies for COPD have been found with many issues, such as high drop-out rates (20% [45], 33% [47] and 36% [19]), large variations of patient adherence (20%[47] to 98%[44] adherence rates), and inconsistent user experience (mixed with technical challenges [19] and good satisfactions [47]). Therefore, further clinical validation remains essential to use the mHealth for improving COPD care.

The MH-COPD program has been deliberately designed to overcome those barriers stated before, and to focus on improving patient adherence to the self-management, consistent with the evidence-based clinical guidelines [4]. In the program, patients will use a mobile app to conveniently access educational videos to gain essential knowledge and skills as recommended by the guidelines. The app will also assist the patients in monitoring COPD symptoms and risk factors (low physical activity and smoking of cigarettes). Patients will interact with the electronic COPD action plan to make decision for significant changes in the symptoms; and receive automated motivational messages for modification of the risk factors. The patients' data, including monitoring symptoms, risk factors and adherence, will be automatically uploaded to the portal. Using the portal, the care providers are able to remotely monitor the patient conditions and adherence, and accordingly provide timely interventions. Compared with the paper based approach in usual care, the use of mHealth would make it easier and simpler for the patients to access clinical resources and self-manage COPD. Additionally, it would allow the care providers to actively engage with the patients in COPD care. Therefore, we expect the MH-COPD program to improve the patient compliance and health outcomes.

Different from many existing studies, our MH-COPD program was designed to include all core components outlined by the evidence-based guidelines in Australia, and integrate within COPD clinics. Additionally, the program aims at improving patient self-management. Although the nurses and COPD physicians in the program will review the patients' data through the clinician portal, their interventions mainly focus on supporting and motivating patients to adhere to the program. Additionally, many automated messages and alerts will provided through the mHealth system to support the intervention. Therefore, the burden to the clinicians in the program would be minimum. In all, the MH-COPD study will provide a unique opportunity to help understand the potential to use mobile health innovations to improve patient self-management and health outcomes, and hence add evidence for the effectiveness of using mobile health to improve COPD care in the community.

Summary

The study will specifically integrate an innovative mHealth system with a clinical COPD service and evaluate this approach through a RCT. The evaluation will provide a unique opportunity to improve COPD care in the community through mobile health innovations.

Figure Legends:

Figure 1. Study flow chart of the randomized controlled trial designed to evaluate the MH-COPD program. UC=usual care, MH=mobile health.

Figure 2. The care model of the MH-COPD program includes the components of health education, electronic COPD action plan, symptom monitoring, physical activity, smoking cessation, and inhaler technique.

Figure 3. Selected screenshots showing the user interface of the mobile application. A: Scheduled educational videos preloaded in the app. B: User interface to record symptoms and risk factors. C: User interface showing an assessment of symptoms in the COPD action plan.

Author contributions

The MH-COPD program was designed by I.Y, H.D, D.I, L.M, R.H, K.P and P.M. This study protocol was developed by I.Y and H.D. The first draft of the manuscript was written by I.Y and H.D. All authors (H.D, M.K, D.I, L.M, R.H, K.P, R.P, E.S, R.B, K.F, P.M and I.Y) contributed to the design of the clinical study and critical revision of the manuscript.

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Conflicts of interest

There are no conflicts of interest in this project.

Acknowledgement

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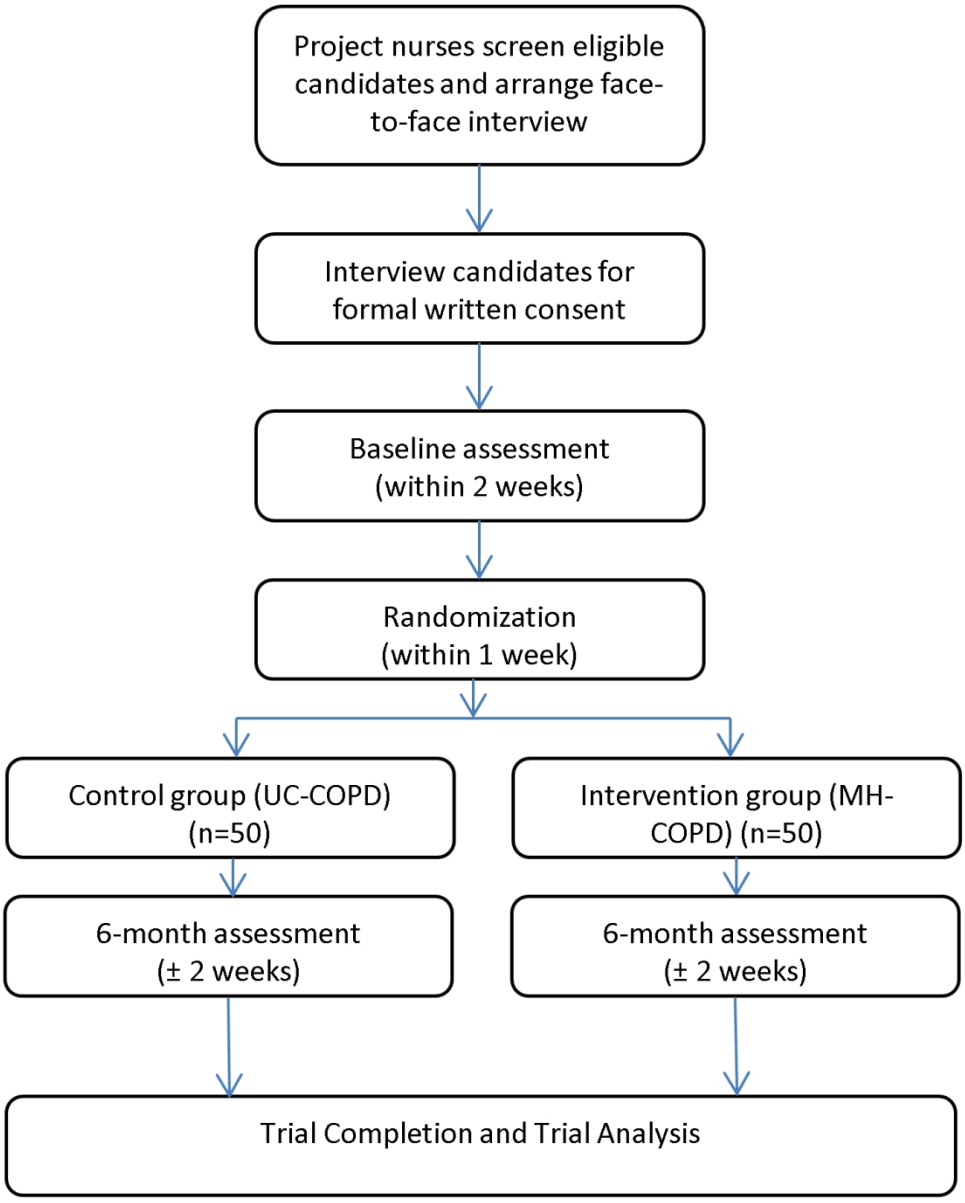

Figure 1. Study flow chart of the randomized controlled trial designed to evaluate the MH-COPD program. UC=usual care, MH=mobile health.

121x151mm (300 x 300 DPI)

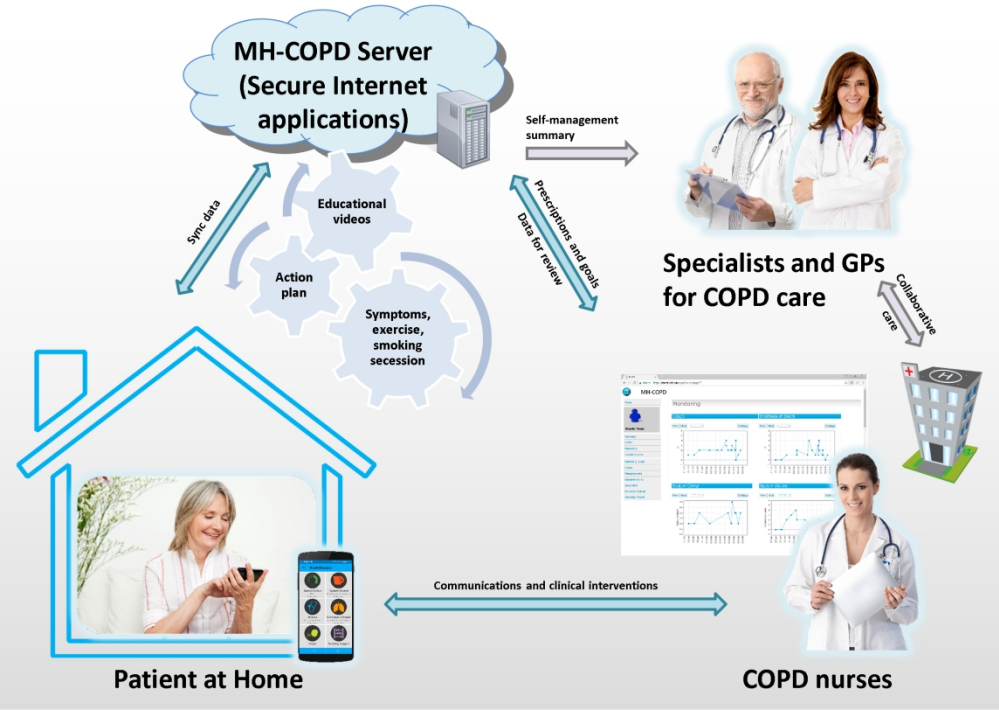

Figure 2. The care model of the MH-COPD program includes the components of health education, electronic COPD action plan, symptom monitoring, physical activity, smoking cessation, and inhaler technique.

215x154mm (300 x 300 DPI)

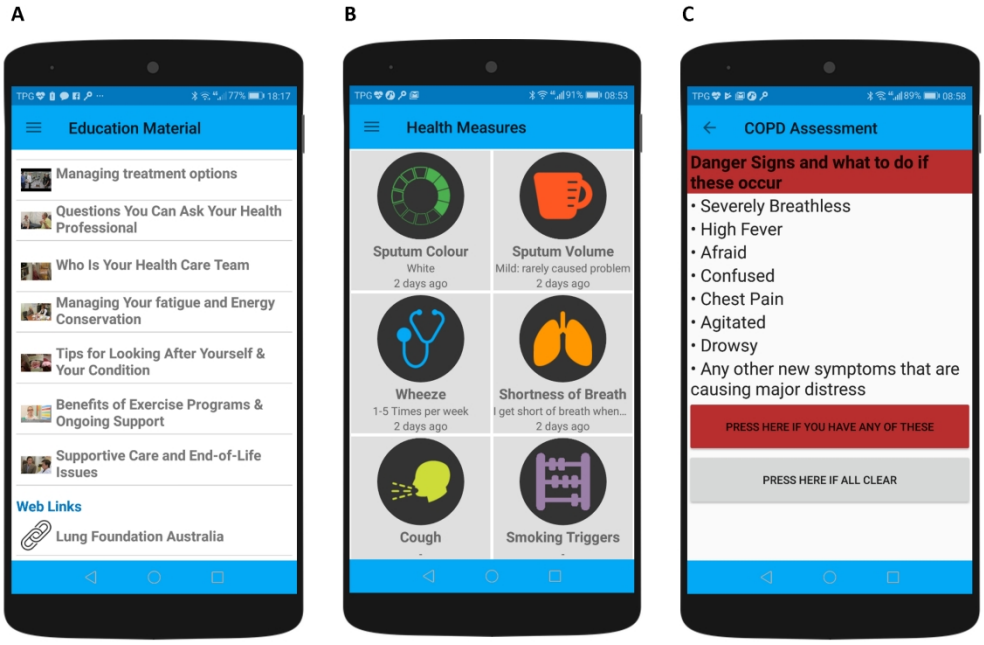

Figure 3. Selected screenshots showing the user interface of the mobile application. A: Scheduled educational videos preloaded in the app. B: User interface to record symptoms and risk factors. C: User interface showing an assessment of symptoms in the COPD action plan.

233x152mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
	2b	All items from the World Health Organization Trial Registration Data Set	1 (ANZCTR)
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,11
	5b	Name and contact information for the trial sponsor	12
	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	12
	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)	9-10

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	3
	6b	Explanation for choice of comparators	3
Objectives	7	Specific objectives or hypotheses	3
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, noninferiority, exploratory)	3-4

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	4
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)	4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-7
	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)	4-5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	n/a
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a
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	7,8
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)	4

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	8,9
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9
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	4,5
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	4,5
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection methods	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	9
	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	9

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	9
Statistical methods	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	9,10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	9,10
	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)	9,10
Methods: Monitoring			
Data monitoring	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	10
	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	10
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	10
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	1
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)	10

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3-4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
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	9
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	9
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
Dissemination policy	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	1
	31b	Authorship eligibility guidelines and any intended use of professional writers	n/a
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	4
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

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.