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Evaluating screening strategies for identifying undiagnosed COPD in China: a Breathe Well project

Submission date
11/09/2018

Recruitment status
No longer recruiting

Registration date
21/09/2018

Overall study status
Completed

Last Edited
06/11/2023

Condition category
Respiratory

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a group of lung diseases including chronic bronchitis, emphysema and asthma. People with COPD have damaged breathing airways which cause obstruction to breathing. Common symptoms are shortness of breath, cough and phlegm. The most common cause of COPD is smoking. COPD currently affects 5-10% of people worldwide and the number of people with the disease is increasing.
Experts estimate that more than half of people with COPD don't know they have the disease and miss out on early treatment that may slow or stop the disease getting worse. If patients with COPD can be identified and treated earlier, they may have longer, healthier lives. We want to find the best way of identifying people who have COPD.

Who can participate?
The study is taking place in China (Beijing, Chengdu, Shenyang and Guangzhou) and people can participate if they are 40 years of age or above and physically able to do simple blowing tests (spirometry).

What does the study involve?
All participants will do three blowing tests to measure lung function, and will also complete questionnaires about their lung health. The study assessment is likely to last approximately 1.5 hours.

What are the possible benefits and risks of participating?
At the end of the study assessment, researchers will explain participants' lung function results to them and answer any immediate questions they may have. The assessment measures pose no risk, and participants will only be recruited if they are physically able to do the blowing tests. Participants will be given an inhaler (salbutamol) before the final blowing test, which has a very small risk of drug allergy or side effects. Possible side effects are rare, and include feeling shaky, rapid heart rate or headache, which will disappear after several minutes.

Where is the study run from?
The study is being run by researchers at the Peking University First Hospital. The study aims to recruit about 2,000 participants from 8 community health centres in Beijing, Chengdu, Shenyang and Guangzhou.

When is the study starting and how long is it expected to run for?
February 2019 to November 2019 (updated 30/04/2019, previously: Participant recruitment is expected to start in October 2018 and the study is likely to finish in December 2019)

Who is funding the study?
The study is funded by the National Institute for Health Research (NIHR), using Official Development Assistance (ODA) funding.

Who is the main contact?
The main contact is Dr Zihan Pan (lead researcher)
panzihan@yeah.net

Contact information

Type(s)
Scientific

Contact name
Prof Chunhua Chi

Contact details
Peking University First Hospital
8# Xi Shiku Street
Xi Cheng District
Beijing
China
100034
+8613910987530
1504246723@qq.com

Type(s)
Public

Contact name
Dr Zihan Pan

Contact details
Peking University First Hospital
8# Xi Shiku Street
Xi Cheng District
Beijing
China
100034
+8618701291196
panzihan@yeah.net

Type(s)
Scientific

Contact name
Dr Rachel Jordan

ORCID ID
https://orcid.org/0000-0002-0747-6883

Contact details
Reader in Epidemiology & Primary Care
Institute of Applied Health Research
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT

Additional identifiers

Protocol serial number
Protocol v6 25/10/2018

Study information

Scientific Title
A study to evaluate the effectiveness and cost-effectiveness of different screening strategies for identifying undiagnosed COPD in China, amongst residents (≥40 years) in four cities.

Acronym
COPD screening in China (Breathe Well)

Study objectives
Objectives:
1. To identify the most cost effective screening strategy for identifying undiagnosed COPD in the general population in China.
2. To determine the test performance (sensitivity, specificity, positive predictive value, negative predictive value, area under the curve) of all screening tests and strategies in comparison with quality diagnostic spirometry.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 25/07/2018, Peking University First Hospital ethics committee, ref: 2018 R 141.
2. Approved 22/10/2018, University of Birmingham STEM international trials sub-committee, ref: ERN 18-1177.

Primary study design
Observational

Study design
Cross-sectional screening test accuracy study

Study type(s)
Screening

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease

Interventions
Current interventions as of 30/04/2019:
The study will use a paired design, with all participants receiving the index tests and reference test during the same study assessment. The study will administer three index tests (peak flow, pre-bronchodilator microspirometry, screening questionnaires) and one reference test (post-bronchodilator quality diagnostic spirometry) to each participant.

INDEX TESTS
Lung function (peak flow):
A trained researcher will assess peak expiratory flow using a simple peak flow meter (USPE). Standardized researcher training will detail how to perform the technique and how to use the device. Each participant will perform three blows without administration of Salbutamol, after which the researcher will record the highest PEF. For the main analysis, peak expiratory flow rates (PEFR) of <350l/min for men and <250l/min for women will be used to indicate a positive test (Martinez et al, 2017).

Lung function (microspirometry):
Microspirometry will be performed with minimal coaching by a trained researcher using a simple handheld microspirometer (Vitalograph COPD6), to measure FEV1, FEV6 and FEV1/FEV6 ratio. Microspirometer devices will be checked for calibration errors at the start of the study by the researchers. Standardized researcher training will detail how to perform the technique and how to use the device. Each participant will perform three blows using the device, after which the researcher will record the highest FEV1 and FEV6 values and the FEV1/FEV6 ratio. For the main analysis, FEV1/FEV6 ratios of <0.75 (Frith et al, 2011) and <0.78 (Labor et al, 2016) will be used to indicate a positive test.

Screening questionnaires:
Three screening questionnaires will be used in the study, namely CAPTURE (Martinez et al 2017), CDQ (Price et al 2006) and a symptom-based questionnaire (Zhang et al 2016), as well as selected items from the COPD-SQ (Zhou et al 2013). The selection of questionnaires maximizes symptoms being assessed and minimizes duplication of items, whilst allowing comparison of the most relevant questionnaires. Recommended cut-points for each questionnaire will be used to identify those at risk of COPD, with potential additional analyses to explore optimal cut-points.

REFERENCE TEST
Post-bronchodilator quality diagnostic spirometry will be performed by a trained researcher using a portable spirometer (ndd Easy On-PC). The researcher will not be the same person who administered the peak flow and microspirometry tests, and they will not know the index test results. Lung function data such as FEV1, FVC and FEV1/FVC ratio will be recorded in the ndd software, and will also be imported to the study REDCap database. Accuracy of the device flowheads will be verified at the start of each assessment day the study by the researchers; calibration is not required. Standardized researcher training will detail how to perform the

technique and how to use the device. Participants will perform a maximum of six blows, or less if repeatability within 100mls or 5% is achieved.

A diagnosis of COPD (the reference standard) will be defined as airflow obstruction based on the lower limit of normal using the Global Lung Initiative (GLI) equations, according to post-bronchodilator quality diagnostic spirometry.

We will evaluate the performance of different single tests (e.g. questionnaires, peak flow or microspirometry), as well as different combinations of tests (e.g. a specific questionnaire followed by microspirometry) and conditional strategies where only those identified as positive through a screening questionnaire would perform peak flow and/or microspirometry.

The cost per true case detected will also be calculated for all strategies.

All analyses will be conducted once data collection has closed.

Statistical methods:
Test performance (sensitivity, specificity, positive predictive value, negative predictive value, area under the curve) of all screening tests and strategies will be compared against quality diagnostic spirometry. Cases will be defined using the lower limit of normal criteria for defining airflow obstruction, based on quality diagnostic spirometry data.

Resource use data will be collected alongside the study to estimate the cost of each screening strategy in terms of staff, equipment, medication and consumables. A fully incremental cost-effectiveness analysis will be undertaken from a health care perspective to calculate the cost per true case detected for all strategies. The strategies (including combinations) will be ordered by the number of true cases detected, from least to greatest, and the principles of dominance and extended dominance will be applied to eliminate redundant strategies from the analysis. Sensitivity analysis will be undertaken to explore the impact on results of any changes in assumptions (e.g. time taken for a strategy).

Previous interventions:
The study will use a paired design, with all participants receiving the index tests and reference test during the same study assessment. The study will administer three index tests (peak flow, pre-bronchodilator microspirometry, screening questionnaires) and one reference test (post-bronchodilator quality diagnostic spirometry) to each participant.

INDEX TESTS
Lung function (peak flow):
A trained researcher will assess peak expiratory flow using a simple peak flow meter (KOKA PEF-3). Standardized researcher training will detail how to perform the technique and how to use the device. Each participant will perform three blows without administration of Salbutamol, after which the researcher will record the highest PEF. For the main analysis, peak expiratory flow rates (PEFR) of <350l/min for men and <250l/min for women will be used to indicate a positive test (Martinez et al, 2017).

Lung function (microspirometry):
Microspirometry will be performed with minimal coaching by a trained researcher using a simple handheld microspirometer (COPD6), to measure FEV1, FEV6 and FEV1/FEV6 ratio.
Microspirometer devices will be checked for calibration errors at the start of the study by the researchers. Standardized researcher training will detail how to perform the technique and how to use the device. Each participant will perform three blows using the device, after which the

researcher will record the highest FEV1 and FEV6 values and the FEV1/FEV6 ratio. For the main analysis, FEV1/FEV6 ratios of <0.75 (Frith et al, 2011) and <0.78 (Labor et al, 2016) will be used to indicate a positive test.

Screening questionnaires:
Three screening questionnaires will be used in the study, namely CAPTURE (Martinez et al 2017), CDQ (Price et al 2006) and a symptom-based questionnaire (Zhang et al 2016), as well as selected items from the COPD-SQ (Zhou et al 2013). The selection of questionnaires maximizes symptoms being assessed and minimizes duplication of items, whilst allowing comparison of the most relevant questionnaires. Recommended cut-points for each questionnaire will be used to identify those at risk of COPD, with potential additional analyses to explore optimal cut-points.

REFERENCE TEST
Post-bronchodilator quality diagnostic spirometry will be performed by a trained researcher using a portable spirometer (ndd Easy On-PC). The researcher will not be the same person who administered the peak flow and microspirometry tests, and they will not know the previous test results. Lung function data such as FEV1, FVC and FEV1/FVC ratio will be recorded in the ndd software, and will also be imported to the study REDCap database. Accuracy of the device flowheads will be verified at the start of each assessment day the study by the researchers; calibration is not required. Standardized researcher training will detail how to perform the technique and how to use the device. Participants will perform a maximum of six blows, or less if repeatability within 100mls or 5% is achieved.

A diagnosis of COPD (the reference standard) will be defined as airflow obstruction based on the lower limit of normal using the Global Lung Initiative (GLI) equations, according to post-bronchodilator quality diagnostic spirometry.

We will evaluate the performance of different single tests (e.g. questionnaires, peak flow or microspirometry), as well as different combinations of tests (e.g. a specific questionnaire followed by microspirometry) and conditional strategies where only those identified as positive through a screening questionnaire would perform peak flow and/or microspirometry.

The cost per true case detected will also be calculated for all strategies.

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Statistical methods:
Test performance (sensitivity, specificity, positive predictive value, negative predictive value, area under the curve) of all screening tests and strategies will be compared against quality diagnostic spirometry. Cases will be defined using the lower limit of normal criteria for defining airflow obstruction, based on quality diagnostic spirometry data.

Resource use data will be collected alongside the study to estimate the cost of each screening strategy in terms of staff, equipment, medication and consumables. A fully incremental cost-effectiveness analysis will be undertaken from a health care perspective to calculate the cost per true case detected for all strategies. The strategies (including combinations) will be ordered by the number of true cases detected, from least to greatest, and the principles of dominance and extended dominance will be applied to eliminate redundant strategies from the analysis. Sensitivity analysis will be undertaken to explore the impact on results of any changes in assumptions (e.g. time taken for a strategy).

Intervention Type

Other

Primary outcome(s)
Current primary outcome measures as of 30/04/2019:
1. Pre-bronchodilator peak flow assessed using a USPE peak flow meter on the day of recruitment
2. Pre-bronchodilator microspirometry of FEV1/FEV6 ratio measured using a Vitalograph COPD-6 microspirometer on the day of recruitment
3. Self-reported COPD symptoms assessed using CAPTURE, CDQ, a symptom-based questionnaire and selected items from the COPD-SQ on the day of recruitment
4. Post-bronchodilator spirometry using ndd Easy On-PC spirometer on the day of recruitment
5. Cost of screening measured at the end of the study

Previous primary outcome measures:
1. Pre-bronchodilator peak flow assessed using a KOKA PEF-3 peak flow meter on the day of recruitment
2. Pre-bronchodilator microspirometry of FEV1/FEV6 ratio measured using a Vitalograph COPD-6 microspirometer on the day of recruitment
3. Self-reported COPD symptoms assessed using CAPTURE and COPD Diagnostic Questionnaire (CDQ) questionnaires, plus a revised version of the International Primary Care Airways Guidelines (IPAG) questionnaire (Zhang et al 2016) on the day of recruitment
4. Post-bronchodilator spirometry using ndd Easy On-PC spirometer on the day of recruitment
5. Cost of screening measured at the the end of the study

Key secondary outcome(s)
1. Test performance of screening strategies, using a combination of spirometry data and clinical confirmation to define COPD
2. Test performance of screening strategies, using an FEV1/FVC ratio of <0.7 to define COPD
3. Optimal cut-points for the screening tests, assessed by repeating primary analyses while applying different thresholds to the questionnaires, peak flow and microspirometry tests to indicate possible COPD.

All analyses will be conducted once data collection has closed.

Completion date
31/03/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 28/01/2020:
1. Aged ≥40 years
2. Residing in the catchment areas of the participating community health centres or their satellite offices

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Previous inclusion criteria as of 30/04/2019:
1. Aged ≥40 years
2. Residing in the catchment areas of the participating community health centres

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Previous inclusion criteria:
1. Aged ≥40 years
2. Residing in the catchment areas of the participating community centres

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
2499

Key exclusion criteria
1. Unable to do spirometry (e.g. dementia, lack of teeth or otherwise cannot make a good seal)
2. Contraindicated for spirometry (chest infection in the last 3 weeks, coughing up blood in the last month, severe angina, uncontrolled high blood pressure, pneumothorax or history in the last 3 months of tuberculosis, heart attack, detached retina, or surgery on chest/abdomen/brain/ears/eyes
3. Currently pregnant/breastfeeding
4. Previous adverse reaction to salbutamol

Date of first enrolment
20/02/2019

Date of final enrolment
30/11/2019

Locations

Countries of recruitment
China

Study participating centre
Peking University First Hospital
8# Xi Shiku Street
Xi Cheng District
Beijing
China
100034

Sponsor information

Organisation
Peking University First Hospital

ROR
https://ror.org/02z1vqm45

Funder(s)

Funder type
Not defined

Funder Name
National Institute for Health Research, Official Development Assistance (ODA) funding

Results and Publications

Individual participant data (IPD) sharing plan
Quantitative anonymised individual participant data generated during and/or analysed during the current study will be available upon request from Dr Rachel Jordan (r.e.jordan@bham.ac.uk) from December 2020. It can be shared with academics. All types of analyses will be considered. Data acquisition forms will be available from the Investigator. Submitted forms will be reviewed by the Programme Directors, before contacting the applicant directly. Participant consent will be obtained to release anonymous data to other researchers and all identifiable data will be removed prior to sharing data with other researchers.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		23/09/2021	07/10/2021	Yes	No
Protocol article	protocol	27/11/2020	30/11/2020	Yes	No
Participant information sheet	Informed consent version 6.0	25/10/2018	06/11/2023	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes