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Evaluating screening strategies for identifying undiagnosed COPD in Brazil: 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
16/12/2022

Condition category
Respiratory

[X] Prospectively registered
[_] 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 São Bernardo do Campo in Brazil. People can participate if they are 40 years of age or above, diagnosed with systemic arterial hypertension (high blood pressure) 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?
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.
After the study assessment, all patients who show signs of airway obstruction will be invited to

attend a clinical assessment with a lung specialist. All patients with negative airway obstruction will be informed after the assessment, and it is possible that a sample of these patients may be followed up in the future, depending on resources.

Where is the study run from?
The study is being run by researchers at the ABC Medical School, São Paulo, Brazil. The study aims to recruit about 1080 participants from 9 basic health units in São Bernardo do Campo.

When is the study starting and how long is it expected to run for?
February 2019 to March 2020 (updated 28/01/2020, previously: November 2019) (updated 30/04 /2019, previously: October 2018 to 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?
Dr Sonia Maria Martins (lead investigator)
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Study website
https://www.birmingham.ac.uk/breathewell

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
3.0, 24/10/2018

Study information

Scientific Title
A study to evaluate the test accuracy of different screening strategies for identifying undiagnosed COPD in Brazil, amongst patients (≥40 years) with systemic arterial hypertension in primary care

Acronym
COPD screening in Brazil (Breathe Well)

Study objectives
Objectives:
1. To identify the most cost effective screening strategy for identifying undiagnosed COPD amongst patients with systemic arterial hypertension in Sao Bernardo de Campo, Brazil.
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 01/08/2018, Federal University of ABC Medical School ethics committee, ref: 2.793.862.
2. Approved 22/10/2018, University of Birmingham STEM international trials sub-committee, ref: ERN 18-1185.

Study design
Cross-sectional screening test accuracy study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
GP practice

Study type(s)
Screening

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Chronic obstructive Pulmonary Disease

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 (QVAR Mini Wright). 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 <350 l/min for men and <250 l/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 [added 30/04/2019] 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 (updated 30/04/2019, previously: 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 fewer if repeatability within 100 ml or 5% is achieved.

A diagnosis of COPD (the reference standard) will be defined as airflow obstruction detected in the study assessment and subsequent physician confirmation. Airflow obstruction will be defined by 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, using resource use data.

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).

Intervention Type
Other

Primary outcome measure
Current primary outcome measures as of 30/04/2019:
1. Pre-bronchodilator peak flow assessed using a Mini-Wright 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 Mini-Wright 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

Secondary outcome measures
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.

Overall study start date
01/06/2017

Completion date
30/09/2020

Eligibility

Key inclusion criteria
1. Aged ≥40 years
2. Residing in the catchment areas of the participating sites
3. Diagnosed with systemic arterial hypertension

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
A pragmatic approach will be taken and, based on what is feasible in the setting, approximately 1080 patients will be recruited i.e. 120 patients per BHU (~1080 in total). Using the Alonzo

method for paired test accuracy studies (Alonzo et al 2002), assuming independence of tests and a prevalence of 16%, we will have 85% power to detect a difference in sensitivity of 10% (95% vs 85% [Martinez et al 2017; Stanley et al 2014; Represas-Represas et al 2015; van den Bemt et al 2014]) with 1040 participants. If the sensitivity of tests is slightly lower in this population (91% vs 80%) we would have 80% power to detect this difference with the same sample size.

Total final enrolment
1201

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, coughing up blood in the last month, severe angina, high blood pressure (systolic BP ≥220 mmHg or diastolic ≥120 mmHg) or history in the last 3 months of tuberculosis, heart attack, detached retina, or surgery on chest/abdomen/brain /ears/eyes)
3. Previous adverse reaction to salbutamol

Date of first enrolment
21/02/2019

Date of final enrolment
11/10/2019

Locations

Countries of recruitment
Brazil

Study participating centre
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Sponsor information

Organisation
ABC Medical School

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Sponsor type
University/education

ROR
https://ror.org/028kg9j04

Funder(s)

Funder type
Not defined

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

Results and Publications

Publication and dissemination plan
Results of the study will be disseminated through academic peer-reviewed publications and at relevant national/international academic conferences.. All publications will be open-access, with links provided on the Breathe Well website (https://www.birmingham.ac.uk/breathewell). (The protocol is expected to be published around 31/12/2018, removed 30/04/2019). The results publication date is likely to be late-2020 (updated 30/04/2019, previously: mid-2020).

Intention to publish date
30/09/2021

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	13/12/2022	16/12/2022	Yes	No