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Testing if the BCG vaccine alters exacerbations in people with chronic obstructive pulmonary disease

Submission date 13/12/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 19/02/2025	**Overall study status** Ongoing	
Last Edited 09/11/2026	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
The vaccine for tuberculosis known as BCG has been in use to prevent this disease for over 100 years. More recently studies have shown that in both adults and children, giving this vaccine can result in other benefits, including helpful changes within the immune system that can protect against many other infections, and may prevent hospital admissions in older people as a result. Studies on these effects, sometimes referred to as “trained immunity” have been small, and we do not know if the effect is true until properly designed studies have been done. The main benefit of BCG seems to be in terms of rates of chest infections, which are more common in people who have a lung disease already, such as chronic obstructive pulmonary disease (COPD). Flare-ups of lung disease are usually called exacerbations and are mainly (but not always) due to infection. Preventing exacerbations in people with lung disease is particularly important because frequent infections can cause lung disease to progress, and every time an infection happens quality of life may get worse. Using the BCG vaccine as a means of prevention in such people could therefore be helpful for long-term health by breaking the vicious cycle of recurrent exacerbations and progressive lung pathology.

Who can participate?
Patients aged 18 years and over who have COPD and who have had at least two exacerbations in the last 12 months

What does the study involve?
Half of the patients will receive the vaccine and half will not. Patients will then be followed up for a year and their rate of exacerbations compared. The researchers will also study symptoms, quality of life and hospital admissions in the two groups. To understand how the vaccine works, they will send tests at enrollment and at 1 year to look at the function of the immune system. Patients will also send tests at the time of exacerbation from their own home - these will look for the presence of viruses and bacteria.

What are the possible benefits and risks of participating?
BCG vaccine has been used for over 70 years and side effects are well documented. As per the

BNF, known side effects of all vaccines commonly include abdominal pain; appetite decreased; arthralgia; diarrhoea; fatigue; fever; headache; lymphadenopathy; malaise; myalgia; nausea; skin reactions; and vomiting. Patients will be counselled as to these common side effects in order to better self-manage them. Rarely, a vaccine can cause hypersensitivity reactions. Rates of anaphylaxis in BCG vaccination in the UK are around 1 in 900,000. It will be difficult to assess the risk of an individual patient having a hypersensitivity reaction. However, patients will be counselled for this side effect, and vaccines will be administered in appropriate clinical environments to monitor for and provide first aid for anaphylaxis. Side effects specific to BCG vaccination include lymphadenitis suppurativa. Rarely BCG vaccination can cause osteitis or osteomyelitis; rates in one study of compulsory childhood vaccinations were 0.39 cases per million. This risk will be minimised by having appropriately trained staff giving the intradermal injections. Seizures and syncope are listed as side effects, but the frequency is not known. BCG vaccination contains a live attenuated strain derived from Mycobacterium bovis, and therefore should not be given to patients with concomitant immunodeficiency, which forms one of the exclusion criteria for the study. However, it is not impossible for a patient with undiagnosed immunodeficiency to receive the BCG vaccine in this study, which presents a very small but significant risk of contracting BCG-related non-tubercular mycobacterial disease. Risks will be minimised by excluding anyone immunosuppressed in the opinion of the investigator (including, but not restricted to: Human immunodeficiency viral (HIV) infection, common variable immunodeficiency, chemotherapy, disease-modifying agents for rheumatic diseases), anyone who has had >20 mg prednisolone for >14 days in the last 3 months, or anyone pregnant. Participants will be asked to send samples by post when they have an exacerbation and this may cause some inconvenience. Patients were specifically asked about this when the study was being designed and the majority indicated that it would be practical to post a sample quickly after producing it, as long as materials were provided. This has been addressed and all necessary materials will be provided to minimise any inconvenience. In general side effects beyond local skin reaction to BCG vaccine are rare.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
December 2024 to December 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
stabilise@trials.bham.ac.uk

Contact information

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Principal investigator

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Integrated Research Application System (IRAS)
1007306

Central Portfolio Management System (CPMS)
67005

Protocol serial number
RG_23-012

Study information

Scientific Title
STABILISE: a multicentre, randomised, parallel-group, superiority trial to investigate the use of BCG vaccine in altering immune response and exacerbation in chronic obstructive pulmonary disease (COPD)

Acronym
STABILISE

Study objectives
The primary aim is to determine whether BCG reduces rates of moderate-severe AECOPD at 12 months in patients who have a clinical diagnosis of chronic obstructive pulmonary disease

(COPD), and a history of exacerbation in the preceding year. The hypothesis is that the vaccine will reduce infectious exacerbations and that there may be a greater effect for viral-driven events.

The secondary aim is to compare the rate of hospitalisations for infective exacerbations, quality of life (QOL) and number of days of antibiotic and steroid therapy during follow-up between intervention and control groups. We will also determine acceptability.

Specific exploratory immunology objectives are to:
1. Characterise cellular and molecular immune responses induced by vaccination (BCG-specific and non-specific) and to pathogens identified during any exacerbations.
2. To relate responses induced by BCG to the level of protection BCG affords against exacerbations.
3. To relate exacerbating pathogen-specific response (if it occurs) to immune response induced by the BCG vaccine, and to identify biomarkers that predict BCG-associated protection from exacerbations.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 12/02/2025, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8284; hampstead.rec@hra.nhs.uk), ref: 25/LO/0027

Primary study design
Interventional

Study design
Randomized controlled open blinded endpoint parallel-group trial

Study type(s)
Treatment

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

Interventions
Bacillus Calmette–Guérin (BCG) vaccine. Participants need to get Interferon-Gamma Release Assay (IGRA) to test their TB status and only those who are negative will be eligible for the trial.

Eligible participants will be randomised at the level of the individual in a 1:1 ratio to either BCG vaccine or no vaccine via a central secure web-based Electronic Data Capture (EDC) system. After informed consent has been given and participant eligibility, excluding IGRA result, has been confirmed, the participant will be randomised into the trial using the online EDC system. All questions and data items on the online Randomisation Form must be answered appropriately prior to a potential participant being randomised into the trial and a Trial Number being issued.

Following randomisation, a confirmatory e-mail will be sent to the randomiser, local principal investigator, local research nurse, trial mailbox, and the administrating site pharmacist.

Participants allocated to the intervention arm will receive the vaccine injection within 6 weeks from the date of randomisation. They will receive BCG vaccine (after reconstitution, 1 dose [0.1 ml] for adults contains Mycobacterium bovis BCG [Bacillus Calmette-Guerin], Danish strain 1331, live attenuated, 2-8 x 105 cfu). The vaccine will be given as a one-off dose via the intradermal route of administration by a trained healthcare professional. Participants allocated to the control arm will not receive any extra treatment and will continue their standard care.

Participants will be followed up for 12 months from the date of the BCG vaccine if they are in the intervention arm or from the date of randomisation if they are in the control arm. Participants from both arms will need to complete an online form every time they experience an exacerbation and send some dried blood sample, nasopharyngeal swabs and sputum sample to the trial's laboratory in the University of Birmingham every time they experience an exacerbation. All participants will need to complete follow-up questionnaires at 3 and 12 months.

Intervention Type
Biological/Vaccine

Phase
Phase IV

Drug/device/biological/vaccine name(s)
BCG Vaccine AJV, powder and solvent for suspension for injection

Primary outcome(s)
Rate of moderate to severe acute exacerbations of chronic obstructive pulmonary disease (AECOPD) (number per person per year) over 12 months follow up from BCG administration date (or from the date of randomisation if no treatment was administered), measured using Participant Reported Outcomes (Questionnaires) at the time of exacerbation, 3- and 12-month follow up. In addition to lab results whenever they experience an exacerbation and a 12-month follow-up visit.

Key secondary outcome(s)
1. Hospitalisation rate for infective exacerbation at 12 months, measured using patient-completed exacerbation form and 3- and 12-month follow-up questionnaires
2. Quality of life (QOL) measured using the COPD Assessment Test (CAT) at 12 months
3. Total number of days of antibiotic therapy, whether for respiratory or other causes, at 12 months, measured using Participant Reported Outcomes (Questionnaires) at the time of exacerbation and 12-month follow-up
4. Total number of days of oral steroid therapy for exacerbations at 12 months, measured using Participant Reported Outcomes (Questionnaires) at the time of exacerbation and 12-month follow-up
5. Type of exacerbation (as they occur [rate over time]) defined by Anthonisen criteria defined by clinical adjudication committee (CAD) who will be meeting every 3 months to assess all the exacerbation-related forms, reports, and lab results
6. Host immune response measured using viral throat swab (PCR) and bacterial culture of sputum at the time of exacerbation

Completion date
31/12/2027

Eligibility

Key inclusion criteria
Any adult (age ≥18 years) patient with primary clinical diagnosis of COPD who has had ≥2 exacerbations in the last 12 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Positive IGRA at enrolment
2. Known pregnancy
3. Immunosuppressed in the opinion of the investigator (including, but not restricted to: Human immunodeficiency viral (HIV) infection, common variable immunodeficiency, chemotherapy, disease modifying agents for rheumatic diseases),
4. Anyone who has had >20mg prednisolone for >14 days in the last 3 months
5. previous experience of allergic reaction to vaccine
6. Unable to give informed consent

Date of first enrolment
21/10/2025

Date of final enrolment
30/11/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
-
-
-
England
-

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes