

A staged dose-finding and challenge /rechallenge study of Staphylococcus aureus nasal colonisation in healthy adults

Submission date 20/03/2026	Recruitment status Recruiting	☐ Prospectively registered ☐ Protocol
Registration date 21/05/2026	Overall study status Ongoing	☐ Statistical analysis plan ☐ Results
Last Edited 21/05/2026	Condition category Infections and Infestations	☐ Individual participant data ☒ Record updated in last year

Plain English summary of protocol

Background and study aims

Staphylococcus aureus is a common bacterium that many people carry in their noses without feeling unwell. In some people it can lead to infections, but we do not fully understand why it lives harmlessly in some individuals and not others. This study aims to learn more about how the bacterium settles in the nose and whether being exposed once can protect someone from becoming colonised again in the future. To do this, the study team will place a small, carefully measured amount of the bacterium into the noses of healthy adult volunteers and monitor them closely.

Who can participate?

Healthy adults aged 18 to 55 years who meet the detailed health and lifestyle criteria set by the study team.

What does the study involve?

Participants will first attend a screening visit, where their general health will be checked. If eligible, they will then complete a standard 5 day course of decolonisation treatment that includes a nasal antibiotic ointment and an antiseptic hair and body wash. About two weeks later, they will return to receive the challenge, which means a small amount of Staphylococcus aureus will be dripped into their nose.

Participants will record any symptoms each day for 28 days, with some days involving in-person visits for safety checks, blood tests and nose or body swabs. They will take some nose samples at home using equipment provided. After this follow-up period, they will repeat the decolonisation treatment. Some participants may be invited to take part in a second challenge later in the study, depending on whether they became colonised the first time.

What are the possible benefits and risks of participating?

Participants will be contributing to important research that may help scientists develop new ways to prevent or treat Staphylococcus aureus infections in the future. However, taking part carries some risks. Mild infections such as small skin spots or pimples can occur, though more

serious infections are uncommon in healthy adults. There is a small chance volunteers could pass the bacteria to others, so they must avoid close contact with vulnerable people for a period of time. Blood tests may cause slight pain or bruising, and nasal swabs can be a little uncomfortable. The decolonisation products may cause mild irritation or, rarely, allergic reactions. Antibiotics will only be used if necessary.

Where is the study run from?

The study is run in Oxford, United Kingdom, at the Centre for Clinical Vaccinology and Tropical Medicine at Churchill Hospital.

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

April 2026 to December 2029.

Who is funding the study?

Ellison Institute of Technology (UK)

Who is the main contact?

Mr Conor Whelan at the Centre for Clinical Vaccinology and Tropical Medicine in Oxford.

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Contact information

Type(s)

Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
366748

Central Portfolio Management System (CPMS)
71824

Study information

Scientific Title

ReSET – Rechallenge Staphylococcus aureus Experimental nasal colonisation sTudy

Acronym

ReSET

Study objectives

Primary objectives:

Stage I: To determine the safety of *S. aureus* primary challenge in humans

Stage I co-primary: To determine the challenge doses required to achieve a 50-70% nasal colonisation rate with up to two strains of *S. aureus*

Stage II: To determine the safety of *S. aureus* primary challenge and rechallenge in humans

Stage II co-primary: To quantify the rate of *S. aureus* acquisition following primary challenge, homologous rechallenge $\pm$ heterologous rechallenge

Secondary objectives:

1. To explore immunological and microbiological markers including those induced by *S. aureus* exposure and how those may predict protection against re-infection
2. To describe pre-decolonisation *S. aureus* carriage within the study population
3. To determine time-course and bacterial density of colonisation with challenge strains
4. To determine rates and extent of colonisation spread to extra-nasal sites with challenge strains

Ethics approval required

Ethics approval required

Ethics approval(s)

Submitted 19/03/2026, South Central - Berkshire REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; no telephone number provided; berkshire.rec@hra.nhs.uk), ref: 26/SC/0123

Primary study design

Interventional

Allocation

Randomized controlled trial

Masking

Open (masking not used)

Control

Active

Assignment

Parallel

Purpose

Treatment

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Staphylococcus aureus nasal colonisation

Interventions

This study is a two-stage, unblinded, strain-randomised Controlled Human Infection Model (CHIM). It is multicentre, starting in one location with sequential opening of UK locations as required. It is designed to develop and evaluate a safe method of establishing temporary nasal colonisation with Staphylococcus aureus in healthy adults aged 18 to 55 years.

In stage I the aim is to find the best challenge dose of up to two strains of S. aureus in order to achieve colonisation in 50 to 70 percent of volunteers. Up to four strains of S. aureus will be trialled and the continuous reassessment method (CRM) will be used to identify the challenge dose. Up to 48 participants per strain will be enrolled.

Participants will be screened up to 6 months in advance of enrolment. Screening will involve written consent, a urine test for pregnancy where appropriate, blood tests to check general markers of health, a physical examination and measurement of vital signs. A medical and medication history will be taken. Next of kin information will be requested and they will be provided with a household contact information sheet. Details will also be taken to allow registration on TOPS (trial over-volunteering prevention service) and to allow reimbursement for time and inconvenience.

Once enrolled, participants will undergo a 5 day course of standardised decolonisation therapy (nasal antibiotic ointment and antiseptic hair and body wash) starting about 2 weeks before challenge. Participants will have a decolonisation e-diary to record adherence. They will be reviewed about 4 days before challenge for nose samples, body swabs and blood tests.

At challenge they will receive a carefully measured dose of liquid containing the candidate strain by dripping it into the nose. The dose will be determined by the continuous reassessment method, which takes into account the proportion of participants colonised up to that point to ensure the best chance of achieving a colonisation rate in the target range.

Participants will be followed up with a daily symptom e-diary for safety reasons. This lasts 28 days with a more intensive phase lasting 7 days. There will be a series of more time-intensive in-person reviews on days 1, 3, 7, 10 and 16 after challenge. These reviews are for safety monitoring as well as blood, nose and body swab sampling to check for immune responses and

presence of bacteria. On days without in-person review, participants will take nose samples at home and store them in the freezer using provided equipment. Additional home samples will be requested on day 22 and day 42.

There will be a further in-person visit on day 28 for blood, nose and body swab sampling. Participants will then be given a further 5 day course of decolonisation therapy. Two follow up visits by phone or email will occur on day 56 and day 182 for safety review.

Up to four strains will be trialled, but only up to two strains will progress to stage II once predefined criteria are met, including an estimated colonisation probability within the target range and no safety concerns. If no strain meets criteria, the study will stop. A formal DSMB safety review will be conducted before progression to stage II. Up to 48 participants will be challenged per strain, with a maximum of 192 for stage I.

The purpose of stage II is to assess whether colonisation after one challenge offers any protection against colonisation after a second challenge. A new set of participants will be recruited. Participants will be randomised 1:1 to receive either the first or second strain (at the doses selected in stage I) for their primary challenge. Only participants who become colonised at primary challenge will proceed to rechallenge.

Participants will undergo a very similar process to stage I, but the day 56 visit will be in-person and this is when they will receive their second decolonisation. Participants not successfully colonised after primary challenge will have their final contact with the study team at the day 182 phone or email visit.

Participants successfully colonised after primary challenge will undergo a second decolonisation starting at day 56. The schedule of visits will then repeat with a pre-challenge visit, rechallenge on day 70, and a more intensive follow up period lasting until 56 days after rechallenge, when they will receive their third decolonisation course. Their final contact will be a phone or email visit at day 182 after rechallenge.

Rechallenge will initially use the same strain as at primary challenge. The study team will review data as the study progresses, supported by formal interim analyses of rechallenge colonisation rates. Broadly, once 20 participants have demonstrated protection, the strain used for rechallenge will switch from the same strain used at primary challenge to the other strain in stage II, to assess whether protection applies across strains.

If only one strain progresses from stage I to stage II, there will be no randomisation and the same strain will be used for both primary challenge and rechallenge. Participants not colonised at primary challenge will not undergo rechallenge and will be followed up for approximately six months. Up to 192 participants will be enrolled in stage II.

Intervention Type

Other

Primary outcome(s)

1. Stage I: Occurrence of solicited and unsolicited adverse events, serious adverse events and adverse events of special interest measured using clinical assessment and safety reporting at D0–D6 (solicited), D0–D28 (unsolicited), study duration (SAEs & AESIs)
2. Stage I: Presence of *Staphylococcus aureus* in nasal wash measured using culture based microbiology at D3–D10

3. Stage II: Occurrence of solicited and unsolicited adverse events, serious adverse events and adverse events of special interest measured using clinical assessment and safety reporting at D0–D6 (solicited), D0R1–D6R1, D0–D28, D0R1–D28R1 (unsolicited), study duration (SAEs & AESIs)

4. Stage II: Presence of *Staphylococcus aureus* challenge strain in nasal wash measured using culture based microbiology at D3–D28, D3R1–D28R1

Key secondary outcome(s)

Completion date

31/12/2029

Eligibility

Key inclusion criteria

1. Adults between 18 to 55 years old (inclusive) at the time of enrolment (defined by the start of first decolonisation therapy)
2. Medically healthy, such that according to investigator judgement, hospitalisation within the study period is not anticipated, and the participant appears likely to be able to remain a study participant through to the end of protocol-specified follow-up. Planned elective procedures for pre-existing conditions may be allowable if *S. aureus* colonisation is not deemed to put the participant at increased risk of harm and if the elective procedure does not routinely involve, and is not likely to involve, decolonisation and/or antibiotic therapy
3. Fluent spoken English – to ensure a comprehensive understanding of the research project and their proposed involvement
4. Capacity to provide written informed consent in English for participation in the study
5. Able to attend the scheduled visits and to comply with all study procedures, including internet access for the recording of electronic diaries after issue of decolonisation therapy and *S. aureus* challenge
6. Able to follow and adhere to hygiene advice as well as the decolonisation protocol which includes daily shower and hair wash
7. Willing and able to avoid planned, non-essential non-study antibiotics for the duration of the study
8. Willing and able to avoid intranasal and inhaled products (including nasal steroids) unless prescribed by the study team for the duration of the study
9. Able to adhere to standard hygiene advice at home
10. Willing to allow confirmation of past medical history either through provision of, or access to, a medical record summary or other medical documentation or to allow investigators to obtain a copy of their medical history via their GP practice or via electronic patient records
11. Willing to allow their GP and/or consultant, if appropriate, to be notified of participation in the study
12. Willing to provide their national insurance number or passport number to be registered on The Trial Over-Volunteering Prevention System (TOPS)
13. For participants of childbearing potential only: Willing to use effective contraception for the duration of the study AND to have a pregnancy test on the day of screening, and challenge or as indicated by the study doctor

Healthy volunteers allowed

Yes

Age group

Adult

Lower age limit

18 Years

Upper age limit

55 Years

Sex

All

Total final enrolment

0

Key exclusion criteria**1. Research participants**

1.1. Participation in another research study in which procedures could compromise the integrity of this study (for example immune modulating or stimulating treatments) or the safety of the participant (for example significant volumes of blood taken), or planning to do so within the study period

2. Vaccination (self-reported with or without confirmation from GP questionnaire or medical records or summary if deemed necessary at clinician discretion)

2.1. Planned vaccination in the two months following final challenge

2.2. Live vaccination within the 4 weeks prior to first challenge

3. Allergy

3.1. Have an allergy or intolerance to beta-lactam antibiotics

3.2. Have an allergy or intolerance to more than one of doxycycline, co-trimoxazole, clindamycin and linezolid

3.3. Have an allergy or intolerance to any of the agents used for decolonisation

4. Specific health history (self-reported with or without confirmation from GP questionnaire or medical records or summary if deemed necessary at clinician discretion)

4.1. History of severe *S. aureus* infection, including PVL-associated disease

4.2. Atopic dermatitis

4.3. Psoriasis, eczema or other chronic skin condition requiring treatment in the last year

4.4. Compromised skin barrier function at the discretion of the investigator

4.5. Known structural heart issues at the discretion of the investigator, including but not limited to PFO, VSD and bicuspid AV

4.6. Implanted prosthetic material including but not limited to cochlear implants, orthopaedic implants, implantable cardiac devices, cardiac valves and neurological stimulators

4.7. Recurrent sinusitis

4.8. Previous sinus surgery

4.9. Planned surgical, dental, orthodontic, dental hygienist or pre-operative appointment over the study period

5. General health history (self-reported and or confirmed from GP questionnaire or medical records or summary if deemed necessary). Moderate to severe ill health including but not limited to:

5.1. Asplenia or dysfunction of the spleen

5.2. Chronic respiratory disease (for example asthma on medication, COPD, emphysema, bronchiectasis)

5.3. Chronic heart disease (for example angina, ischaemic heart disease, chronic heart failure).

- Controlled stable hypertension with or without angina may be included
- 5.4. Chronic kidney disease (for example nephrotic syndrome, kidney transplant, on dialysis)
 - 5.5. Chronic liver disease (for example cirrhosis, biliary atresia, hepatitis)
 - 5.6. Chronic neurological conditions
 - 5.7. Connective tissue disease
 - 5.8. Dementia
 - 5.9. Diabetes mellitus (including diet controlled)
 - 5.10. Immunosuppression or history of receiving immunosuppressive therapy at the discretion of the investigator
 - 5.11. Individuals with cochlear implants
 - 5.12. Individuals with major cerebrospinal fluid leaks (for example following trauma, major skull surgery or requiring CSF shunt)
 - 5.13. History of a bleeding disorder (for example factor deficiency, coagulopathy or platelet disorder) or prior history of significant bleeding or bruising following IM injections or venepuncture
 - 5.14. Any uncontrolled medical, surgical or mental health conditions at the discretion of the study doctor
 - 5.15. Significant mental health condition (for example previous admissions in a psychiatric unit, at the discretion of the clinician) that would impair the participant's ability to participate in the study
6. Taking medications
- 6.1. Any medication that may affect the immune system in the last 3 months (for example systemic steroids PO or IM or IV, Roaccutane, disease-modifying anti-rheumatoid drugs)
 - 6.2. Current or intended long-term or intermittent use of antibiotics over the course of the study
 - 6.3. Recent systemic antibiotic exposure in the last 1 month
 - 6.4. Use of any medication affecting blood clotting (any oral or injectable anticoagulants) except for aspirin for secondary cardiovascular prevention
 - 6.5. Use of any medication or other product (prescription or over-the-counter) for symptoms of rhinitis or nasal congestion within 4 weeks of enrolment
7. Volunteers who are pregnant, lactating or intending on becoming pregnant during the study
8. Volunteers who have close contact with individuals at higher risk of infection
- 8.1. Children under 5 years of age
 - 8.2. Chronic ill health or immunosuppression (adults or children)
 - 8.3. Older adults aged 65 years or above
 - 8.4. Household close contact with compromised skin barrier function, psoriasis, eczema or other chronic skin condition requiring treatment in the last year
9. Volunteers (including healthcare workers) who have close contact in high-risk occupational settings or with high-risk or vulnerable individuals during the study
10. Smoker
- 10.1. Current or ex-smoker (regular cigarettes, cigars, e-cigarette, vaping or smoking of recreational drugs) in the last 6 months
 - 10.2. Previous significant smoking history (more than 20 cigarettes per day for 20 years or the equivalent, meaning 20 pack years or above)
11. Suspected or known current hazardous or harmful alcohol or drug use, as per investigators' discretion
12. Intended overseas travel during the course of the study
13. Any other issue which, in the opinion of the study staff, may:
- 13.1. Put the participant or their contacts at risk because of participation in the study
 - 13.2. Adversely affect the interpretation of the study results
 - 13.3. Impair the participant's ability to participate in the study
14. Study staff or a partner or dependent child of study staff
15. Household close contact previously or currently involved in this study, provided they have

received challenge

16. Stage 2 exclusion only: enrolment in Stage 1

Date of first enrolment

01/01/2026

Date of final enrolment

31/12/2028

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Oxford Vaccine Group

Old Road

Headington

Oxford

England

OX3 7LE

Study participating centre

Liverpool Vaccine Group

Liverpool School of Tropical Medicine, Accelerator Building, 1 Daulby Street

Liverpool

England

L7 8XZ

Study participating centre

Sheffield Teaching Hospitals NHS Foundation Trust

Northern General Hospital

Herries Road

Sheffield

England

S5 7AU

Study participating centre

Oxford University Hospitals NHS Foundation Trust

John Radcliffe Hospital

Headley Way

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OX3 9DU

Sponsor information

Organisation

University of Oxford

ROR

<https://ror.org/052gg0110>

Funder(s)

Funder type

University/education

Funder Name

Elliston Institute of Technology

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

As part of this study, the University of Oxford will share relevant research data with the Ellison Institute of Technology, Oxford. The data they receive will not include participants names, contact details, NHS number or other direct identifiers. The data will be labelled only with a code.

IPD sharing plan summary

Other