ISRCTN38860497 https://doi.org/10.1186/ISRCTN38860497

Staphylococcus aureus: early human responses to skin infection

Submission date
24/07/2026

Recruitment status
Not yet recruiting

Registration date
31/07/2026

Overall study status
Ongoing

Last Edited
11/09/2026

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background study and aims
This study aims to better understand how the human body responds to skin infections caused by a common bacteria called Staphylococcus aureus (or 'S. aureus'). This bacterium is the leading cause of skin infections and is getting harder to treat because of antibiotic resistance. Currently, there are no vaccines to prevent these infections. This research will help develop a safe, controlled way of studying S. aureus infections in people, which will allow faster progress in the development of new vaccines and future treatments.

Who can participate?
Healthy adult volunteers aged 18–55.

What does the study involve?
First, volunteers will go through a health check to make sure they are in good health and it is safe for them to participate. They will be allowed to change their mind and stop the study at any time. If they agree to continue, they will be asked to come to the hospital 15 times over six months. The research team will apply a small amount of bacteria to their skin in a controlled and safe way using a watch-like device. The research team will monitor volunteers closely, especially in the first few days after the bacteria is applied. If anyone develops signs of infection, they will be reviewed straight away and given antibiotics. This type of study is known as a human challenge study.

What are the possible benefits and risks of participating?
While there are no direct benefits to volunteering, the study will help to advance medical science. The findings may lead to new ways to prevent and treat infections caused by S.aureus bacteria. Participants who complete the entire study are offered up to £755 to compensate for their time, travel, and the inconvenience of the procedures and the donation of samples. This includes blood and poo samples, skin swabs, microbiopsies and punch biopsies conducted as part of the study.

There are risks to be aware of when taking part in the study. Skin challenge with S.aureus bacteria may lead to local infection with redness, pain and blistering. General symptoms such as headache, fevers and nausea may be experienced. There is a small risk of severe infections like

bloodstream and heart infections and of passing on the infection to others. Therefore, those living with vulnerable older adults of very young children cannot participate. Additionally, the procedures performed such as biopsies and blood tests may lead to pain, bleeding, scarring, infection and/or bruising.

Where is the study run from?
The STARS study is run by the University of Sheffield and takes place at Sheffield Teaching Hospitals NHS Foundation Trust, UK.

When is the study starting and how long is it expected to run for?
August 2026 to December 2028.

Who is funding the study?
UK Research and Innovation (UKRI)

Who is the main contact?
Eva Zincone, eva.zincone@nhs.net

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Scientific

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Integrated Research Application System (IRAS)
373888

UK Research and Innovation/Medical Research Council grant reference
MR/X032736/1

Study information

Scientific Title
Investigating the early responses to Staphylococcus aureus infection of the skin using a human infection model. The STARS study.

Acronym
STARS

Study objectives
The primary objective of the study is to determine the dose (number colony forming units, CFU) of live S. aureus strain SAUCHAL16 and duration of exposure needed to produce local infection in 60-75% of healthy adult volunteers when administered following microneedle epidermal abrasion. A co-primary objective is to assess the safety and tolerability of skin challenge with live S. aureus strain SAUCHAL16.

The secondary objectives of the study are:
1. (Clinical) To determine the S. aureus infection rate when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration.

2. (Clinical) To determine the S. aureus infection rate when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers by baseline S. aureus colonisation status.
3. (Clinical) To characterise the systemic response to S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration and by baseline S. aureus colonisation status.
4. (Clinical) To describe the severity of S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level /exposure duration and by baseline S. aureus colonisation status.
5. (Clinical) To profile the daily change in signs and symptoms related to S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration.
6. (Microbiological) To compare the microbiological features of S. aureus carriage following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level /exposure duration.
7. (Microbiological) To compare the microbiological features of S. aureus infection following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level /exposure duration.
8. (Immunological) To assess early differences in the local host immune response to microneedle epidermal abrasion and S.aureus challenge in healthy adult volunteers at each dose level /exposure duration.
9. (Immunological) To measure the systemic host immune response to S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration.

Exploratory objectives are to:
1. (Imaging) Describe features of the local skin architecture by non-invasive imaging before and after S. aureus challenge in healthy adult volunteers at each dose level/exposure duration.
2. (Microbiological) Describe the evolution of the skin surface microbial population following challenge.
3. (Experience) Investigate volunteer willingness to participate in S. aureus challenge studies and their experience of participation.

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Human challenge study

Study type(s)

Health condition(s) or problem(s) studied
Controlled human skin infection with Staphylococcus aureus bacteria in health adult volunteers.

Interventions
This study is an outpatient, single-centre, single-arm, ambulatory, controlled human infection model (CHIM). The study aims to establish a controlled human skin infection model for Staphylococcus aureus. This model aims to further our understanding of the early responses to skin infection and establish a reproducible platform to develop novel preventative vaccines, therapeutics and early diagnostics.

The primary aim is to establish the dose and duration of Staphylococcus aureus (strain SAUCHAL 16) exposure required to develop localised skin infection in 60-75% of healthy adult volunteers when challenged following microneedle epidermal abrasion. A Bayesian continual reassessment method (CRM) will be utilised to conduct dose escalation and determine the optimal challenge dose of SAUCHAL16. A total of 60 eligible, healthy adult volunteers aged 18-55 years will be enrolled after giving informed consent.

Volunteers will undergo screening to ensure eligibility for the study. This will include medical history, physical examination, and blood and urine tests to ensure fitness to participate as per the eligibility criteria. Electrocardiogram and echocardiogram will be performed to assess for valvular and structural heart disease. Screening will be undertaken no sooner than 120 days prior to challenge. Participants will be registered on The Over-Volunteering Prevention Database (TOPS).

During the pre-challenge phase, participants will self-collect Staphylococcus aureus carriage swabs at fortnightly intervals. These will be taken at home starting 28 days prior to the challenge. Decolonisation will be undertaken 7 days prior to the challenge, consisting of a standard 5-day course of a nasal antibiotic and topical body wash and shampoo. Compliance will be recorded on a daily eDiary, in addition to a paper record log and visual inspection of the packaging after completion by the study team. Baseline investigations will be performed including a punch biopsy, microbiopsies, optical coherence tomography for immunological profiling and analyses of the skin architecture. In addition, carriage swabs and stool samples, and microbiome swabs will be performed.

During the challenge phase, participants will attend daily as an outpatient. At the initial visit, skin preparation with 70% isopropyl alcohol will be performed prior to microneedle epidermal abrasion of the forearm challenge site. SAUCHAL16 will be applied in a bacterial watch application device for the pre-specified duration. A Bayesian continual reassessment method (CRM) will be undertaken to select the correct challenge agent dose and duration: dose range: 105-109 CFU (colony-forming units) and time range (exposure duration): 15-60 minutes. The site will then be wiped dry with a paper towel, a loose non-absorbent dressing will be applied to cover the challenge site, and participants will be reviewed 6 hours later to check the site integrity. Participants will then be reviewed daily as an outpatient for the following 7 days for

safety visits, physical examination and sampling, including safety and immunology blood tests, challenge site PCR swabs and carriage stool samples. If the clinical endpoint for infection is met, after sampling, topical antibiotics will be provided following NICE guidance for non-bullous impetigo or oral antibiotics if signs of systemic infection. At diagnosis, sampling will consist of bacterial culture swabs, a punch biopsy, microbiopsies, optical coherence tomography and blood cultures.

Participants will then be followed up at a further 4 visits over the following 6 months at day 14, 28, 90 and 180. At day 14, further optical coherence tomography will be performed. Then, at day 28, follow-up punch biopsies and microbiopsies will be conducted. A total of 3 participant experience and motivation questionnaires will be completed during the study, concluding at the final visit on day 180.

Intervention Type
Other

Primary outcome(s)
1. Primary. The dose (number colony forming units, CFU) of live S. aureus strain SAUCHAL16 and duration of exposure needed to produce local infection in 60-75% of healthy adult volunteers when administered following microneedle epidermal abrasion measured using the proportion of participants with evidence of local infection at the challenge site (defined as ≥3/5 SIRS signs/ symptoms with a skin infection rating score of ≥1, which must include exudate or pus, and a combined total score of ≥4) and confirmed by microbiological testing of surface swab, pus or microbiopsy (culture or molecular testing) at any time up to 7 days after challenge

2. Co-primary. The safety and tolerability of skin challenge with live S. aureus strain SAUCHAL16 measured using the proportion of participants experiencing: adverse events, adverse events of special interest, SAEs and concomitant medication usage based on clinical observation, examination findings and participant recording of solicited and unsolicited symptoms at any time during the 7 days before and up to 6 months after challenge

Key secondary outcome(s)
1. Clinical. The S. aureus infection rate when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration measured using the proportion of participants at each dose level/ exposure duration with any evidence of local infection at the challenge site (including any SIRS score >0, reported symptoms, or recorded visible skin alterations) at any time up to 14 days after challenge

2. Clinical. The S. aureus infection rate when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers by baseline S. aureus colonisation status measured using the proportion of participants with evidence of local infection at the challenge site and confirmed by microbiological testing of surface swab, pus or microbiopsy (culture or molecular testing) at any time up to 7 days after challenge

3. Clinical. The systemic response to S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level /exposure duration and by baseline S. aureus colonisation status measured using the proportion of participants with evidence of systemic signs/symptoms or perturbation of blood test results (full blood count, urea & electrolytes, liver function tests, c-reactive protein) at any time up to 14 days after challenge

4. Clinical. The severity of S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration and by baseline S. aureus colonisation status measured using the duration of abnormality, median and maximum measurements of symptoms or findings of local infection (SIRS score, other clinical signs/symptoms, or recorded visible skin alteration) and systemic response (any systemic signs/symptoms, or perturbation of blood test results) at any time up to 14 days after challenge

5. Clinical. The daily change in signs and symptoms related to S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration measured using per participant recordings of SIRS scores at daily measurements up to 14 days after challenge

6. Microbiological. The microbiological features of S. aureus carriage following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration measured using the proportion of participants with culture-confirmed growth or molecular detection and burden estimation (by qPCR) of S. aureus from surface swabs collected from site of challenge, or nose, groin and axilla swabs and stool cultures at the following timepoints: before decolonisation (Days -28, -14, -7), before challenge (Day 0), and after challenge (Days 7, 14, 28, 90, 180)

7. Microbiological. The microbiological features of S. aureus infection following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration measured using the proportion of participants with culture-confirmed growth or molecular detection (qPCR), and median bacterial density (quantified by qPCR) of the challenge strain (SAUCHAL16), in skin microbiopsy samples at the point of meeting infection diagnosis

8. Immunological. Early differences in the local host immune response to microneedle epidermal abrasion and S.aureus challenge in healthy adult volunteers at each dose level/exposure duration measured using levels of cytokines, chemokines, acute-phase reactants in punch biopsy samples at the following timepoints: before challenge and Day 28, and in samples collected at diagnosis of infection.

9. Immunological. The systemic host immune response to S. aureus infection when administered following microneedle epidermal abrasion and challenge in healthy adult volunteers at each dose level/exposure duration measured using assays assessing the total, functional, and antigen-specific IgA/IgG, cell-mediated response (including cell phenotyping, antigen-specific cell frequencies, B and T cell repertoire), cyto/chemokine and acute-phase reactants, transcriptome responses in peripheral blood samples at days 0, 1, diagnosis or Day7, and at Days 14, 28, 90, and 180

Completion date
01/12/2028

Eligibility

Key inclusion criteria
1. An informed consent form has been signed and dated by the participant and the Investigator
2. Adults aged between 18 and 55 years inclusive at time of consent
3. In good health as determined by:
3.1. Medical history

3.2. History-directed physical examination
3.3. Screening investigations performed (routine laboratory tests, ECG, echocardiography)
3.4. The clinical judgement of the study team
4. Willing to be available in Sheffield for all required appointments
5. Able and willing (in the study team's opinion) to comply with all study arrangements, including:
5.1. Availability for all required appointment windows
5.2. Able to use decolonisation treatment as directed
5.3. Willing to adhere to infection control precautions
6. Willing to allow study staff permission to contact their primary care provider to access medical history and to solicit opinion as to appropriateness for inclusion, where needed
7. Willing to allow study staff access to NHS health records as required for study purposes
8. Agree to have 24-hour contact with study staff during the 2-week period after challenge and be able to be contactable by mobile phone for the duration of study and until antimicrobial treatment completion
9. Have internet access to allow completion of the eDiary and real-time safety monitoring
10. Agree to avoid using medicated treatments (including shampoo and shower gel) until advised by a study doctor or until 14 days after challenge
11. Agree to provide their National Insurance/Passport number for the purposes of TOPS registration and for payment of reimbursement expenses

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. History or evidence of organ dysfunction which could interfere with trial conduct or completion, including but not restricted to:
1.1. Cardiovascular disease, including diagnoses of valvular heart disease, hypertension, or previous episode(s) of infective endocarditis
1.2. Respiratory disease
1.3. Haematological disorders including anaemia felt to be clinically significant by the study team
1.4. Endocrine disease, including known or suspected diabetes mellitus
1.5. Renal or bladder disease
1.6. Autoimmune and metabolic disease
1.7. Psychiatric illness requiring in-patient stay or assessment
1.8. Known or suspected drug or alcohol dependence
1.9. Infectious disease, including personal or family history of severe infections including S.

aureus
1.10. acute or chronic dermatologic conditions, including eczema, psoriasis, folliculitis, vitiligo atopic dermatitis and/or keloid scar formation
2. Any genetic, inherited or acquired predisposition that may alter the immune response to S. aureus infection, including a personal or family (first-degree relative) history including severe or invasive staphylococcal infection, Hyper-IgE (Job's) syndrome (HIES), Chediak-Higashi syndrome, or Wiskott-Aldrich syndrome, IRAK-4 or MYD-88 deficiency, chronic granulomatous disease, HIV infection
3. Presence of implants (except for dental implants) or prosthetic material
4. Family history in 1st degree relative ≤50 years of age of aneurysmal disease, valvular heart disease, or sudden cardiac or unexplained death
5. Weight less than 50kg and/or a Body Mass Index (BMI) ≤18kg/m2 and ≥30kg/m2
6. Venous access deemed inadequate for the phlebotomy demands of the study
7. Scars or tattoos over or near the site of challenge
8. Detection of abnormal results from screening investigations including blood biochemistry, haematology, immunology and urinalysis i.e. grade 1 abnormality or above APPENDIX 6: Grading severity of laboratory results unless deemed not clinically significant and approved by the Principal Investigator.
19. 12-lead electrocardiogram recording with clinically relevant abnormalities, including a prolonged correct QT interval (QTc >450 milliseconds) as judged by a study physician/Principle Investigator
20. Echocardiography demonstrating evidence of structural cardiac abnormalities, in particular relating to valve dysfunction, including hypertrophic cardiomyopathy, rheumatic heart disease, mitral valve prolapse (with regurgitation) and/or mitral annulus calcification, aortic valve disease (regurgitation, stenosis and/or sclerosis), congenital cardiac disease, including aortic stenosis, bicuspid aortic valve, pulmonary stenosis, ventricular septal defect, and patent ductus arteriosus
21. Taking medication, including analgesia, anti-inflammatories or antibiotics that may affect the study integrity, symptom reporting or interpretation of the study results
22. Receipt of blood or blood products, or loss (including blood donations) of ≥550mL or more of blood during the 3 months prior to the planned date of challenge or planned during the 3 months following the final visit
23. Contraindication to use of:
23.1. Study decolonisation treatment, mupirocin (or naseptin) nasal ointment, chlorhexidine (or octenisan) washes
23.2. Study antimicrobial/antibiotic treatment, hydrogen peroxide or fusidic acid cream, flucloxacillin or clarithromycin (for those who report penicillin allergy)
24. Scheduled elective surgery or other programmed procedures requiring general anaesthesia during the study period.
25. People of childbearing potential (which excludes those who have undergone surgical sterilisation or are post-menopausal) who have a positive urinary pregnancy test at screening or prior to challenge, or who are unwilling to use an effective form of contraception for the duration of the study
26. Full-time, part-time, or voluntary occupations involving:
26.1. Clinical healthcare work (with direct patient contact),
26.2. Direct contact with young children (defined as those attending pre-school groups or nursery, or those aged <2 years), or other clinically vulnerable children or adolescents
27. Close household contact with:
27.1. Young children (defined as those attending pre-school groups or nursery, or those aged <2 years)
27.2. Any individual with severe immunocompromise
28. Adults over the age of 55 years
29. Any employee of the sponsor or research site personnel directly affiliated with this study or

their immediate family members
30. Any other reason that the Investigator considers makes the potential participant unsuitable for inclusion into the study
31. Participants with no knowledge of their family history

Date of first enrolment
26/10/2026

Date of final enrolment
01/08/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
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Study participating centre
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Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

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
Not expected to be made available