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Cellulitis optimal antibiotic treatment

Submission date 21/09/2022	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 01/06/2023	**Overall study status** Ongoing	
Last Edited 26/03/2026	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
Cellulitis is a deep infection of the skin and subcutaneous tissues and most often occurs in the legs. It is a painful condition that is associated with inflammation and swelling of the site, and often systemic symptoms such as fever, headache, muscle aches, malaise, and fatigue. Patients report feeling unwell and that it has a significant impact on their mobility and ability to carry out their usual activities. NICE guidelines recommend oral flucloxacillin 500–1000 mg four times daily for 5-7 days as first-line treatment for most patients with cellulitis in the community, but most prescriptions are dispensed for a 7-day course. We will be assessing the effectiveness and safety of a 5-day treatment versus the standard 7-day treatment. We also aim to evaluate the cost-consequences of a shorter course from an NHS and personal perspective.

Who can participate?
Adults presenting in primary care with unilateral cellulitis of the leg

What does the study involve?
Participants will be randomly allocated to one of two groups. In addition to usual care, participants will either be assigned to a 5-day oral flucloxacillin course or the standard 7-day flucloxacillin course. Participants prescribed a 5-day course of oral flucloxacillin, will be posted two additional days' worth of medication (8 capsules in total for two days), which will either be the antibiotic or placebo capsules. Participants will be asked to fill out daily questionnaires and express their experiences with their cellulitis and taking part in the trial.

What are the possible benefits and risks of participating?
Benefits include that participants may see an improvement in their cellulitis and avoid needing to use antibiotics or for longer than is necessary. participants will be helping to further our knowledge of how to treat patients with cellulitis and this will benefit others with the same condition in the future. However, possible risks include the listed side effects of oral flucloxacillin, risks to the participant's child if they were to become pregnant at any point during the trial, and the need to attend a clinic visit and fill out questionnaires that would not normally be asked of them if they were not part of the trial.

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

When is the study starting and how long is it expected to run?
June 2022 to July 2027

Who is funding the study?
Health Technology Assessment Programme (HTA) (UK)

Who is the main contact?
Miss Ella Bourke, coat@soton.ac.uk

Contact information

Type(s)
Scientific

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1006161

ClinicalTrials.gov (NCT)
NCT05584007

Protocol serial number
ERGO 67073

Central Portfolio Management System (CPMS)
54167

National Institute for Health and Care Research (NIHR)
NIHR134867

Study information

Scientific Title
A blinded, non-inferiority Phase III trial of 5 versus 7 days of oral flucloxacillin in primary care patients with lower limb cellulitis

Acronym
COAT

Study objectives
To determine whether a short course of oral flucloxacillin (5 days) is non-inferior to a standard course (7 days) in terms of pain over days 6-14 (indicative of persistence or recurrence associated with the symptoms of most importance to patients) in adults with cellulitis of the leg presenting in primary care.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 19/06/2023, North East - Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; -; tyneandwearsouth.rec@hra.nhs.uk), ref: 23/NE/0021

Study design
Randomized two-arm blinded multicentre Phase III non-inferiority study with a 6-month internal pilot

Primary study design
Interventional

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Cellulitis

Interventions
Intervention: Oral Flucloxacillin 500 mg capsules four times a day (QDS) for 5 days (unblinded NHS prescription) followed by blinded oral placebo capsules QDS for 2 days (5 days of antibiotic)
Control: Oral Flucloxacillin 500 mg capsules QDS for 5 days (unblinded NHS prescription) followed by oral flucloxacillin 500 mg capsules QDS (blinded) for 2 days (7 days of antibiotic)

Randomisation will be handled via an online system. Participants will be individually randomised between the arms, using a 1:1 allocation ratio, and using block randomisation, stratified by obesity (BMI≥30) and prior history of leg cellulitis.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Flucloxacillin

Primary outcome(s)
Self-reported pain measured using the Pain Numeric Rating Scale (0-10)) via an electronic patient-reported outcome (ePRO) system over days 6-14.

Key secondary outcome(s))
The effectiveness and safety of 5 days versus standard 7 days of oral flucloxacillin for lower leg cellulitis by assessing:
1. Total number of days of antibiotics taken between days 0 and 28 measured using the ePRO system at days 7, 12, 21 and 28
2. Use of additional antibiotics measured using the ePRO system at days 7, 12, 21 and 28
3. Patient-reported assessment of how unwell they are feeling measured using the ePRO system over days 6-14
4. Health-related quality of life measured using the participant-reported EQ5D5L and individual dimension (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) over days 6-14
5. Leg swelling measured using the ePRO system on days 7, 14, 21 and 28
6. Time until self-reported recovery measured using the ePRO system on days 7, 14, 21 and 28
Time until the self-assessed extent of cellulitis starts to reduce (with no subsequent increase) measured using the ePRO system on days 7, 14, 21 and 28

Evaluate the cost-consequences of a shorter course from an NHS and personal perspective by assessing:
1. Hospital admissions measured using occurrences reported in the participant's primary care record at 12 months
2. Episodes of recurrent cellulitis over 12 months measured using occurrences reported in the participant's primary care record at 12 months

3. Incidence of complications over 12 months which include lymphedema, leg ulceration, venous insufficiency, sepsis, and death measured using occurrences reported in the participant's primary care record at 12 months

Completion date
31/07/2027

Eligibility

Key inclusion criteria
1. Aged 18 years and over
2. Currently showing symptoms of cellulitis (such as pain, tenderness, redness, other change in skin colour, warmth to touch) in one leg for 10 days or less
3. Pain rated as 3/10 or higher on a numerical rating scale (0-10) at baseline assessment
4. Be willing to be randomised to either trial arm (5-day or 7-day treatment)
5. Able to complete trial procedures in the English language.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Penicillin allergy
2. Bilateral cellulitis
3. Antibiotics for cellulitis within the past month
4. Post-operative cellulitis (within 30 days of operative procedures on the same leg)
5. Cellulitis resulting from human/animal bite injury
6. Cellulitis associated with chronic (>6 weeks) leg ulceration
7. Require immediate hospital admission or out-patient intravenous antibiotic therapy

Date of first enrolment
18/08/2023

Date of final enrolment
30/04/2026

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
CRN Wessex
Berrywood Business Village
Hedge End
Southampton
England
SO30 2UN

Study participating centre
CRN East of England
20 Rouen Road
Norwich
England
NR1 1QQ

Study participating centre
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Sponsor information

Organisation
University of Southampton

ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication. Individual investigators may not publish data concerning their patients that are directly relevant to questions posed by the trial until the Trial Management Group (TMG) has published its report. The TMG will form the basis of the Writing Committee and advise on the nature of publications.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1	06/12/2022	11/07/2023	No	No
Protocol file	version 3	19/07/2024	09/09/2024	No	No
Protocol file	version 4	16/12/2024	08/04/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes