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Omeprazole for babies born early or full-term, who are experiencing reflux

Submission date 09/06/2026	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 10/08/2026	**Overall study status** Ongoing	[ ] Statistical analysis plan [ ] Results
Last Edited 25/09/2026	**Condition category** Digestive System	[ ] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Gastro-oesophageal reflux (GOR) is when milk and acid come back up from the stomach after feeds. Mild symptoms of reflux, such as crying or being sick, are experienced by most babies, and often get better over a few months. In some babies, symptoms can be severe with pain, excessive crying and poor weight gain. Parents/caregivers find these symptoms distressing and ask for help from their doctor or health visitor, who may refer them onto specialist paediatricians. Simple things like keeping the baby upright during and after feeds or products that thicken milk can be useful. For severe symptoms, health professionals often use medicines such as omeprazole, that reduce stomach acid. Omeprazole is widely used, but it is not clear if it is effective, and some studies have suggested long-term effects like infections and broken bones.

Who can participate?
Term and preterm infants with gastro-oesophageal reflux.

What does the study involve?
We want to test omeprazole to find out if it is effective and safe in the long term. We will explain the study to parents/caregivers attending participating GP practices or hospitals with concerns about GOR in their baby. If they consent for their baby to participate, they will be prescribed omeprazole or a ‘placebo’ that looks and tastes like omeprazole but doesn’t contain any active medicine. The treatment will be selected at random by a computer, with babies having a 50/50 chance of receiving either treatment. Parents/caregivers and healthcare professionals will not know which treatment the baby will have. Treatment will be given for 4 weeks, followed by an online questionnaire about their baby’s symptoms. Follow up will continue for 6 months to look for longer-term effects of omeprazole and GOR on growth, infections, fractures and quality of life for parents/carers. Parents will be contacted regularly throughout this period to collect information on outcomes. We will also talk to parents and health professionals in-depth about their experiences of being in the study. The findings will help change practice and inform national guidelines.

What are the possible benefits and risks of participating?
Benefits:

Not provided at time of registration
Risks:
One of the concerns for infants taking drugs such as omeprazole that lower stomach acidity, is that longer term use can increase the risk of infections, and fractures. Omeprazole is widely used for treating infants with GOR, and as such the risk of the research is no greater than the risk with infants taking omeprazole as per standard care. However, this may cause concern for the parents/caregivers, and trial materials have been developed to ensure they are aware of that risk, and the limitation in our knowledge of the risks from current research evidence.
Parents/caregivers of infants with GOR often find the condition very distressing. To help provide support throughout the trial we have ensured that regular contact will be made in the form of a 2 week well-being phone call, and contact from the trial team during the longer follow up period to 6 months. Trial materials have made it clear that the care and well-being of the infant always comes first.
Parents/caregivers of babies in the trial and their clinicians will be blinded to the treatment allocation. If at any point during the trial, knowledge of the baby's treatment allocation becomes essential for clinical management in an emergency situation, emergency unblinding will be performed in the trial database by site staff who have been delegated the responsibility. The baby's clinical care team will then be able to decide whether to continue the trial treatment. If a SUSAR were to occur, emergency unblinding will take place as necessary to ensure the medical oversight of the CI and/or deputy medical monitor.
In order to minimise the burden of data collection by questionnaire we will be sending links to parents/caregivers by text or email so they can directly access the database on phone or computer. This will make outcome collection adaptable to the needs of different individuals. By providing a paper questionnaire where necessary we will avoid data poverty being an excluding factor to potential participants.

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

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

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

Who is the main contact?
OTTER@nottingham.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1013233

Central Portfolio Management System (CPMS)
62491

Sponsor's protocol code number
RHM CHI1309

Study information

Scientific Title
Omeprazole for Treatment of Term and preterm infants with gastro-oEsophageal Reflux (OTTER)

Acronym
OTTER

Study objectives
OTTER aims to find out if omeprazole, a medicine that reduces stomach acid, is effective for treating symptomatic gastro-oesophageal reflux in babies that are born early, and babies that are born at full term. Omeprazole will be compared with a placebo, that is an identical liquid to the omeprazole but contains none of the active medicine. OTTER is a basket trial as it will be looking at these 4 groups: 2 patient populations and 2 different treatments within those populations. OTTER will ask if omeprazole is more effective than the placebo in treating GOR.

OTTER will assess the safety of omeprazole treatment, including infections, fractures and growth, up to 6 months after trial entry. A qualitative process evaluation will be carried out by interviewing parents and healthcare professional to find out about experiences of the trial and acceptability of the treatment. Data relating to medications and resources used by participants

and their families will be analysed to find out if omeprazole is cost-effective in comparison to standard care in the two patient populations (preterm and term-born infants).

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 08/06/2026, to be confirmed (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; no telephone number provided; -), ref: 26/WS/0074

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment, Safety

Study type(s)

Health condition(s) or problem(s) studied
Gastro-oesophageal reflux

Interventions
Eligible infants will be randomised in a 1:1 ratio to receive omeprazole or matched placebo after eligibility confirmation and parent/caregiver informed consent. Randomisation will be carried out by delegated site staff using REDCap, hosted by NCTU, and will be stratified within the preterm and term-born infant populations. A probabilistic minimisation algorithm will balance allocation by site, care setting, infant sex, feeding mode, and age or gestational age, as applicable. The trial is blinded, so parents/caregivers and recruiting site staff will not know the allocated treatment. Infants will receive either omeprazole oral suspension or matched placebo once daily for 28 days. Omeprazole dosing will be based on baseline or recent recorded weight, at 0.5 mL/kg once daily, equivalent to 1 mg/kg. The investigational medicinal product will be reconstituted by pharmacy and supplied ready to use, with inpatients receiving medication via the recruiting hospital pharmacy and outpatient/primary care participants receiving it by 24-hour home delivery from the central pharmacy.

Intervention Type
Drug

Phase

Phase IV

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

Primary outcome(s)
1. Severity of gastro-oesophageal reflux symptoms measured using Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R), 12-item caregiver-completed questionnaire at 4 weeks after randomisation (end of intervention period)

Key secondary outcome(s)
1. GOR symptom severity measured using Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R) at 2 weeks
2. Treatment escalation measured using parent or caregiver questionnaires and medical note review at 4 weeks and/or 6 months
3. Oesophagitis measured using medical note review at 4 weeks and/or 6 months
4. Haematemesis measured using parent or caregiver questionnaires and medical note review at 4 weeks and/or 6 months
5. Further GOR medication use measured using parent or caregiver questionnaires and medical note review at 4 weeks and/or 6 months
6. Hospital admissions measured using parent or caregiver questionnaires and medical note review at 4 weeks and/or 6 months
7. Length of hospital stay measured using medical note review at 4 weeks and/or 6 months
8. Crying or fussing measured using relevant IQI items at up to 6 months
9. Feeding difficulties measured using relevant IQI items at up to 6 months
10. Sleep quality measured using relevant IQI items at up to 6 months
11. Infant health-related quality of life measured using relevant IQI items at up to 6 months
12. Growth measured using change in weight standard deviation score at up to 6 months
13. Necrotising enterocolitis measured using medical note review at up to 6 months
14. Bacterial infections measured using parent or caregiver questionnaires and medical note review at up to 6 months
15. Gastrointestinal infections measured using parent or caregiver questionnaires and medical note review at up to 6 months
16. Respiratory infections measured using parent or caregiver questionnaires and medical note review at up to 6 months
17. Fractures measured using medical note review at up to 6 months
18. Healthcare use measured using parent or caregiver questionnaires and medical note review at up to 6 months
19. Parental health-related quality of life measured using EQ-5D-5L at up to 6 months
20. Parent experiences of the trial and treatment measured using semi-structured interviews during follow-up
21. Healthcare professional experiences of the trial and treatment measured using semi-structured interviews during follow-up

Completion date
31/08/2028

Eligibility

Key inclusion criteria

Population 1 (Preterm infants):
1. Infants born <37 weeks' gestation who are over 32 weeks corrected gestational age (8 weeks before their due date) and under 6 months past their due date at time of trial entry
2. Must be on full milk feeds at the time of eligibility assessment
3. Clinical diagnosis of symptomatic GOR made by a suitably qualified healthcare professional following clinical assessment
4. NICE guideline first-line interventions (including, but not limited to, feed thickeners and alginates) have either already been tried, or considered and are felt to be inappropriate by the treating clinician

Population 2 (Term-born Infants):
1. Infants born ≥37 weeks' gestation and who are under 6 months of age
2. Clinical diagnosis of symptomatic GOR made by a suitably qualified healthcare professional following clinical assessment
3. NICE guideline first-line interventions (including, but not limited to, feed thickeners and alginates) have either already been tried, or considered and are felt to be inappropriate by the treating clinician

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
0 Days

Upper age limit
6 Months

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Surgical conditions affecting feeding or the gastrointestinal tract, including but not limited to repaired oesophageal or intestinal atresia, congenital diaphragmatic hernia and gastroschisis /exomphalos
2. Progressive or severe neurological conditions affecting feeding
3. Infant has received any omeprazole or other proton-pump inhibitors in the preceding 2 weeks
4. Infant has known hypersensitivity to omeprazole or any of its excipients
5. Previous participation in the OTTER trial

Date of first enrolment
30/07/2026

Date of final enrolment
29/02/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Not provided at time of registration
-
-
England
-

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type

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

The datasets generated during and/or analysed during the current study may be available upon request from Nottingham Clinical Trials Unit (NCTU): OTTER@nottingham.ac.uk.

De-identified parent/caregiver and infant data may be shared with researchers external to the trial team, in accordance with NCTU's data sharing procedure. Requests will be reviewed and approved where appropriate, subject to ethical, legal, regulatory, confidentiality and information governance requirements.

Data will be available after trial completion, database lock and publication of the main trial results. Data sharing will be subject to an appropriate data sharing agreement or equivalent mechanism and will be limited to research or secondary analyses consistent with participant consent and trial governance requirements.

Any shared data will be de-identified, with participant confidentiality protected using unique trial identification numbers. Personal data will be held securely with restricted password-protected access.

IPD sharing plan summary

Available on request