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Treatment to prevent the narrowing of the oesophagus in a condition called oesophageal atresia (a disorder present at birth in which the oesophagus, the tube that carries food from the mouth to the stomach, does not develop properly)

Submission date
13/01/2023

Recruitment status
Not yet recruiting

Registration date
28/07/2025

Overall study status
Ongoing

Last Edited
28/07/2025

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Oesophageal atresia is a rare (about 1 in 2,500–3,000 births) condition where babies are born without an intact oesophagus (swallowing tube) and usually have a connection between their trachea (windpipe) and their stomach instead. It requires urgent lifesaving surgery in the first days of life. In the UK, every year around 150 babies are born with this condition
The surgery rebuilds the oesophagus, this is usually successful but sometimes there are problems. One of these problems is reflux where the acid content of the stomach comes back into the oesophagus and can cause regurgitation of feeds and/or damage to the oesophagus. Another problem that happens sometimes is that the join where the oesophagus has been rebuilt can narrow down (called a stricture) and cause difficulties with feeding and swallowing. It is thought that strictures can be caused or made worse by reflux.
Some surgeons who look after these babies use a medication to suppress the acid produced by the stomach even if there are no symptoms of reflux. A major reason for this is to reduce the risk of strictures forming. Despite this being an apparently popular option (about half of babies with oesophageal atresia are treated with this medication) the evidence for using this medication is weak. In fact, some studies of babies with oesophageal atresia have actually found that strictures are more common in babies treated with acid suppression than in those who were not. In addition, there is some suggestion that taking the medicine can increase the chance of certain types of infection.
We want to answer the question, “Should babies born with oesophageal atresia all be treated routinely with antacid medication to reduce strictures?”

Despite the common use of gastric acid suppression medication, we do not know for certain if there is any benefit to its use in babies following surgery. Indeed, some studies have indicated

that babies routinely given gastric acid suppression medication may be more likely to get a stricture, but the evidence is not conclusive. There are other reasons why giving gastric acid suppression medication as a preventative measure (rather than as a treatment for children who are diagnosed with gastro-oesophageal reflux disease) may not be a good idea, including that it may slightly increase the risk of gastro-intestinal infections. Also, there are concerns about giving medicines to babies when there is no proven benefit.

Who can participate?
Babies with oesophageal atresia.

What does the study involve?
In this randomised controlled trial, babies with oesophageal atresia are allocated at random to either being given acid suppressing medicine or not. They are then followed up for 2 years, to see if they develop a stricture and require any further treatments.

What are the possible benefits and risks of participating?
Benefits:
This study will not bring any immediate benefit to the participant.
Risks:
The treatments used in the study are used routinely for babies born with oesophageal atresia in UK hospitals and are known to be safe, so there are no extra risks involved from taking part in the study. The parent or carer will be asked to give trial medication/placebo once a day and record this on an app. We are asking the parents to record this once a day for the first week, but to reduce the burden, this is only once a week after the first month.
To further reduce the burden, we are only collecting data at routine visits that would occur as part of standard care following the surgery to repair the OA.
There are up to 7 questionnaires that the mother will be asked to complete. Links to these will be sent to them so they can complete at a convenient time or if they prefer they can complete on paper during their clinic visits.

Parents will be approached at a challenging and stressful time, soon after diagnosis of their child's OA. Due to this we have given 3 days to allow the parent(s) to be approached and then to think about taking part. If the child is diagnosed prior to birth, they will also be approached at this time to allow more time for their consideration. The person who approaches the parent about the trial will be someone from the direct clinical care team who are experts in OA and are sensitive to timings and so will know the appropriate way to approach them.

Any incidental findings that are identified during the course of the trial will be notified to the clinical team looking after the infant in question.

Where is the study run from?
National Perinatal Epidemiology Unit (NPEU), University of Oxford (UK)

When is the study starting and how long is it expected to run for?
May 2025 to October 2030

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

Who is the main contact?
Hayley Acton, toast@npeu.ox.ac.uk
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Study website
https://www.npeu.ox.ac.uk/TOAST

Contact information

Type(s)
Scientific

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Type(s)
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Additional identifiers

EudraCT/CTIS number

IRAS number
1005191

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
TOAST - A multicentre, randomised trial of gastric acid suppression medication for treating oesophageal atresia to prevent stricture

Acronym
TOAST

Study objectives
Primary objective:
To compare the severity of anastomotic stricture during the first year of life in infants randomised to receive routine gastric acid suppression medication versus those randomised to matched placebo.

Secondary objectives:
1. To compare the severity and incidence of anastomotic stricture during the first 2 years of life in infants randomised to receive routine gastric acid suppression medication versus those randomised to matched placebo
2. To investigate the influence of routine gastric acid suppression medication versus matched placebo on other important clinical outcomes in infants randomised to receive routine gastric acid suppression medication versus those randomised to matched placebo at 1 and 2 years of age
3. To investigate the cost and consequences of routine gastric acid suppression medication versus matched placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/05/2025, South Central - Berkshire Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048143; berkshire.rec@hra.nhs.uk), ref: 25/SC/0198

Study design
Interventional double blind randomized placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Infants born with oesophageal artesia (OA) with distal-oesophageal fistula (TOF) who have undergone primary repair

Interventions
Participants will be randomised using an online randomisation system to receive either esomeprazole (0.5mg/kg intravenously) once daily until infants are able to feed enterally followed by omeprazole (1mg/kg orally) once daily until 1 year of age, or a matched volume placebo given intravenously once daily until infants are able to feed enterally followed by matched volume placebo enteral administration, once daily until 1 year of age.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome measure
Severity of anastomotic stricture is defined as number of oesophageal dilatations from randomisation up to one year of age

Secondary outcome measures
1. Severity and incidence of anastomotic stricture during the first 2 years of life is measured by number of oesophageal dilatations up to 2 years of age.
2. Severity and incidence of anastomotic stricture during the first 2 years of life is measured by incidence of anastomotic stricture (one or more dilatations) up to 1 and 2 years of age.
3. Severity and incidence of anastomotic stricture during the first 2 years of life is measured by histological diagnosis of oesophagitis.
4. The influence of routine gastric suppression medication versus matched placebo is measured by all-cause mortality up to 1 year and 2 years of age.
5. The influence of routine gastric suppression medication versus matched placebo is measured by mortality directly related to OA up to 1 year and 2 years of age.
6. The influence of routine gastric suppression medication versus matched placebo is measured by any anastomotic complications (i.e., anastomotic leak, recurrent fistula) up to 1 year and 2 years of age.
7. The influence of routine gastric suppression medication versus matched placebo is measured by number of procedures performed under general anaesthetic (GA) related to OA up to 1 year and 2 years of age.
8. The influence of routine gastric suppression medication versus matched placebo is measured by number of serious adverse reactions up to 1 year of age.
9. The influence of routine gastric suppression medication versus matched placebo is measured by any non-GA diagnostic study related to OA, and findings, up to 1 year and 2 years of age
10. The influence of routine gastric suppression medication versus matched placebo is measured by duration of dose of any gastric acid suppression medication given in addition to study medication up to 1 year of age
11. The influence of routine gastric suppression medication versus matched placebo is measured by max level of intervention (based on the treatment flow diagram) reached for treatment of reflux symptoms in preceding 3 months (described using summary statistics) at 3, 6, 9 and 12

months of age.
12. The influence of routine gastric suppression medication versus matched placebo is measured by parent-reported symptoms of reflux using total score of I-GERQ-R at 3, 6, 9 and 12 months of age.
13. The influence of routine gastric suppression medication versus matched placebo is measured by any acute life-threatening event or cyanotic episode, either while in hospital, or leading to a 999 call and/or hospital attendance up to 1 year and 2 years of age.
14. The influence of routine gastric suppression medication versus matched placebo is measured by weight, length and height standard deviation scores at 1 year and 2 years of age.
15. The influence of routine gastric suppression medication versus matched placebo is measured by number of chest infections treated with antibiotics either in the community or hospital up to 1 year and 2 years of age.
16. The influence of routine gastric suppression medication versus matched placebo is measured by any other respiratory problem resulting in admission to hospital up to 1 year and 2 years of age.
17. The influence of routine gastric suppression medication versus matched placebo is measured by routine feeding via a tube after discharge home or 3 months chronological age, whichever is sooner, up to 1 year of age.
18. The influence of routine gastric suppression medication versus matched placebo is measured by number of re-admissions to hospital directly related to OA up to 1 year and 2 years of age.
19. The influence of routine gastric suppression medication versus matched placebo is measured by cumulative length of stay in intensive care post-surgery, directly related to OA up to 1 year and 2 years of age.
20. The influence of routine gastric suppression medication versus matched placebo is measured by number of re-admissions to intensive care directly related to OA up to 1 year and 2 years of age.
21. The influence of routine gastric suppression medication versus matched placebo is measured by cumulative length of stay in intensive care post-surgery, directly related to OA up to 1 year and 2 years of age.
22. The influence of routine gastric suppression medication versus matched placebo is measured by nature of feed tolerated using the International Dysphagia Diet Standardisation Initiative (IDDSI) score at 1 year and 2 years of age.
23. Health economic outcomes are measured by the Maternal Health Related Quality of Life using EuroQol EQ-5D-5L questionnaire at 6, 12, 18 and 24 months of age (infant).
24. Health economic outcomes are measured by the Maternal quality adjusted life years (QALYs) up to 2 years of age (infant).
25. Health economic outcomes are measured by parent reported infant Health Related Quality of Life using PedsQL Infant Scales at 6, 12, 18 and 24 months of age (infant).
26. Health economic outcomes are measured by healthcare and societal resource use and costs up to 1 and 2 years of age (infant).

Overall study start date
29/05/2025

Completion date
31/10/2031

Eligibility

Key inclusion criteria

1. Infants (of any sex and any gestational age) with OA with distal TOF who have undergone ligation of the fistula and oesophageal anastomosis at the same time during the first operative intervention.
2. Infants have written informed consent obtained from an individual with parental responsibility.
3. Infants are expected to survive beyond the first year of life.
4. Infants within the end of day 3 after surgery where day of surgery is day 0.
5. Infants up to 2 weeks postnatal age.
6. In the opinion of a clinical member of the local research team (appropriately trained and experienced doctor or nurse), parents(s)/carer(s) of the infant are able and willing to comply with all study requirements, (including having a good understanding of the English language), or can be supported to do so (including the use of translation services).

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
211

Key exclusion criteria
1. Infants with OA without distal TOF
2. Infants who have undergone an operative intervention (e.g. emergency tracheo-oesophageal fistula ligation without anastomosis, initial gastrostomy) prior to the one where they underwent oesophageal anastomosis
3. Infants with any additional significant disorder or disease that, in the opinion of a clinical member of the research team, makes entry into the study inappropriate
4. Infants taking any medication that, in the opinion of a clinical member of the research team, makes entry into the study inappropriate

Date of first enrolment
01/11/2025

Date of final enrolment
31/10/2030

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
University Hospital Southampton
Southampton University Hospital
Tremona Road
Southampton
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SO16 6YD

Study participating centre
Evelina London Children's Hospital
Westminster Bridge Road
London
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SE1 7EH

Study participating centre
Alder Hey Children's Hospital
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L14 5AB

Study participating centre
Royal Hospital for Sick Children (Glasgow)
1345 Govan Road
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G51 4TF

Study participating centre
Royal Manchester Children's Hospital
Oxford Road
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M13 9WL

Study participating centre

John Radcliffe Hospital
Headley Way
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OX3 9DU

Study participating centre
University Hospital of Wales
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CF14 4XW

Study participating centre
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50 Little France Crescent
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Study participating centre
St George's Hospital
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Study participating centre
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Study participating centre
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Steelhouse Lane, St Chads Tunnel,
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Study participating centre
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Study participating centre
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Study participating centre
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Sponsor information

Organisation
University of Oxford

Sponsor details

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Sponsor type
University/education

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ROR
https://ror.org/052gg0110

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

Publication and dissemination plan
Peer reviewed scientific journals
Conference presentation
Publication on website
Submission to regulatory authorities

Other
Data Sharing requests can be made at the end of the research inline with the NPEU Data sharing policy

Intention to publish date
31/10/2031

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date