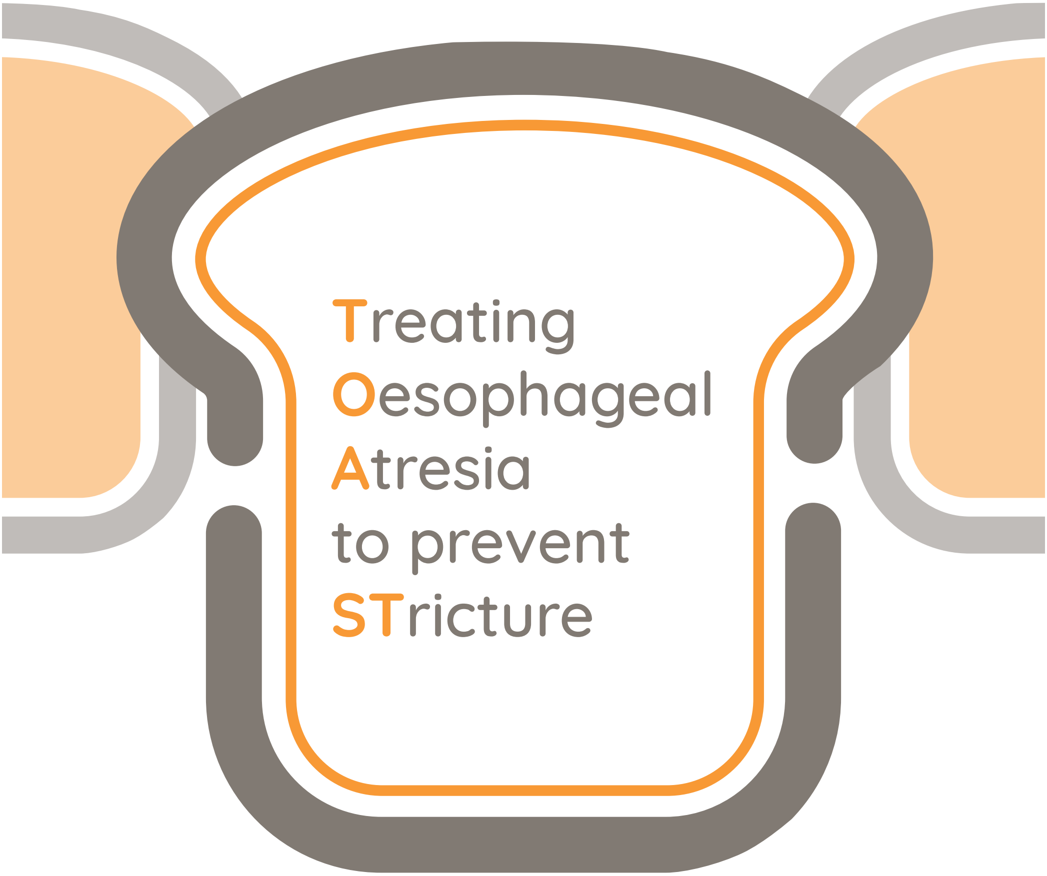
TOAST



Treating
Oesophageal
Atresia
to prevent
STricture

Parent Information Leaflet

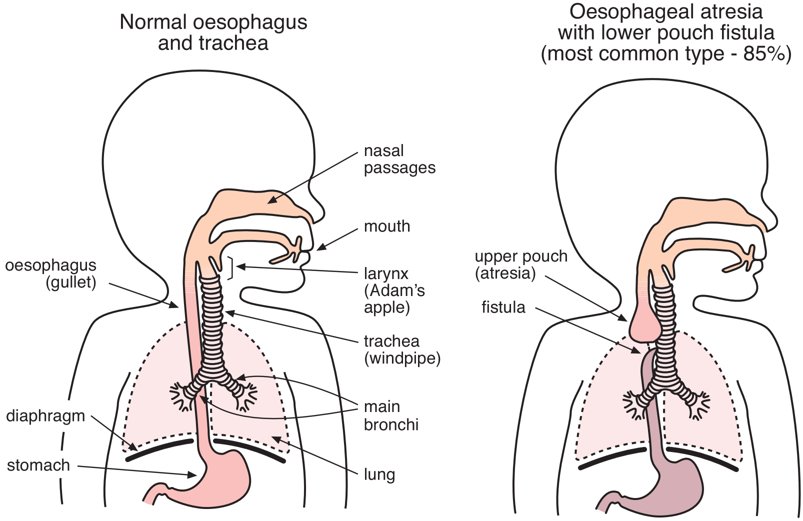
Important things to know about the TOAST Study

- You have been given this information sheet because your baby might be eligible to take part in the Treating Oesophageal Atresia to prevent STricture (TOAST) Study.
- Some babies with oesophageal atresia will develop a stricture (narrowing in the oesophagus, which can occur in 40-50% of babies with oesophageal atresia in the months following repair) despite taking gastric acid suppression medication. Others will not develop a stricture despite not taking gastric acid suppression medication.
- There is a lack of evidence about whether gastric acid suppression medication (e.g. omeprazole) increases or reduces the risk of stricture.
- There are differences in the treatment of babies with oesophageal atresia:
    - Some surgeons routinely prescribe gastric acid suppression medication (e.g. omeprazole) to all babies who have had oesophageal repair.
    - Some surgeons do not routinely prescribe gastric acid suppression medication after oesophageal atresia repair.
- In the TOAST Study, half the babies will be given gastric acid suppression medication (Esomeprazole 0.5mg/kg intravenously (if not feeding orally) once daily; Omeprazole 1mg/kg enterally or orally once daily) and half the babies will be given a ‘dummy’ medication called a placebo once daily for one year after their surgical repair.
- If your baby takes part in TOAST, when they are discharged home, we will ask you to give the medication to your baby once daily until they are one year old. The doctors and nurses will show you how to do this. The medication could be gastric acid suppression medication or placebo.
- If your baby has symptoms of reflux that need treatment, they can still have it, no matter what half of the trial your baby is in. Babies can still be prescribed gastric acid suppression medication if a doctor decides it is needed for treatment of reflux symptoms (see Reflux Management Plan flow chart on page 14).
- There are potential risks and benefits of taking this medication, these are detailed later in this leaflet.

- As part of this study, we will ask you to complete a questionnaire (online or on paper) at the start of the study and then when your baby is 3, 6, 9, 12, 18 months and 2 years old. The questionnaire aims to monitor your baby's progress, hospital visits and how you are feeling. We will also ask you to record whether you gave the study medication at regular intervals on a bespoke app or website.
- Your baby's progress will be monitored through routine hospital visits that all babies with oesophageal atresia need. We will also use information from your baby's medical records for this study.
- Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve for your baby and you. Please read the following information carefully and discuss it with relatives or friends if you wish.
- Taking part is voluntary. If you don't want your baby to take part, then you don't need to give a reason why. Deciding not to take part will not affect the standard of care for your baby.

Please ask a member of your baby's clinical team or the local research team research team (details at the end of this leaflet) if there is anything that is not clear, or if you would like more information.

Diagram of oesophageal atresia



From Jaffray, B. (2016) 'Introduction to OA/TOF', in Martin, V. and Crabbe, D. (Eds.) The TOF Book. 2nd Edition. Nottingham, UK: TOFS., p. 17. ISBN 978-0-9536265-1-9. Copyright 2016 by TOFS. Reprinted with permission.

We understand that this is a difficult time for you and your family. We would like to invite you to join a study that this hospital is taking part in for babies who have been born with oesophageal atresia. Before you decide, it is important that you understand why the research is being done and what it will mean for you and your baby. Please ask us if there is anything else that is not clear or you would like to know.

Why do we do research in healthcare?

Research is really important so that we can improve how we treat patients. If no research took place, then it would be difficult to improve outcomes for patients.

Why is my baby being asked to take part?

Your baby has been diagnosed with oesophageal atresia, where the oesophagus (swallowing tube) has not formed properly and so your baby's mouth is not connected to their stomach. The treatment for this condition involves surgery to reconstruct the oesophagus. The team looking after your baby will have talked to you about what this surgery involves.

We are asking you to help us with a research project to learn more about how treatment following this surgery can be made better. The study is called TOAST, which stands for Treating Oesophageal Atresia to prevent STricture.

Why are we doing this research?

One of the complications that can follow surgery to reconstruct the oesophagus is a narrowing called a stricture at the point where the repair is made. A stricture in the oesophagus would make it difficult for your baby to feed. Between 40% and 50% of babies get a stricture in the months after repair of oesophageal atresia[1]. A stricture is usually treated

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[1] *Jones, C. E., Smyth, R., Drewett, M., Burge, D. M., & Hall, N. J. (2020). Association Between Administration of Antacid Medication and Anastomotic Stricture Formation After Repair of Esophageal Atresia. Journal of Surgical Research, 254, 334–339. https://doi.org/10.1016/j.jss.2020.05.004*

by stretching the narrow section to make it wider in a procedure called a “dilatation”. This requires an admission to hospital and is done under general anaesthetic. Some babies require several dilatations during the first year of life.

Gastro-oesophageal reflux (where the stomach contents go back up into the oesophagus) is common after repair of oesophageal atresia and some surgeons think that reflux of acid into the oesophagus may make a stricture more likely or more severe. To try and prevent strictures from forming some surgeons use gastric acid suppression medication in all babies, even if they have no symptoms of reflux. A common medication of this kind is called Omeprazole. The aim of using this medicine is to reduce stomach acid secretion so that even if there is reflux it is not as acidic. Therefore a potential benefit could be that this medication could prevent stricture and unnecessary procedures for babies.

Despite the common use of gastric acid suppression medication by some clinicians to try to prevent strictures from forming, we do not know for certain if there is any benefit to its use in babies following surgery. Also, there are concerns about giving medicines to babies when there is no proven benefit. For these reasons, we are carrying out the TOAST study to find out if giving gastric acid suppression medication does help babies with oesophageal atresia. If it does, then all babies with oesophageal atresia can be given this treatment. If it does not, then we can stop asking parents to give medicine to their baby that has no benefit.

What will happen if my baby takes part?

The study we are asking you to give permission for your child to take part in is a randomised controlled trial (RCT). In the study, half of the babies will be given gastric acid suppression medication, starting from soon after their surgery to repair the oesophageal atresia. The other half will be given a ‘dummy’ medication called a placebo. Dividing babies into two groups in this way is called ‘randomisation’ and the most reliable way of finding out if the gastric acid suppression medication does or does not help babies. The chance of your baby receiving either gastric acid suppression medication or placebo is equal. Neither you nor the medical team will know whether your baby is receiving the gastric acid suppression medication or the placebo. The reason a placebo is important is to make sure that we are carrying out a fair test.

Your baby will be given the medication each day by the medical team in hospital. When your baby is discharged home, we will ask you to give the medication to your baby once daily for up to one year of age. The doctors and nurses will show you how to do this. The doctors and nurses will provide you with further medication supplies at your routine hospital visits and will be available to answer any questions you might have.

Your baby will be routinely followed up over the years and you won't be asked to come to extra visits for the study, as we will collect all our data at these routine visits. The study data will be copied from your NHS data.

You will be asked to complete questionnaires (either online or on paper) at the start of the study and then at 3, 6, 9, 12, 18 months and 2 years about you and your baby's progress. Some of these questionnaires are to be completed by the birth mother only. Permission for this will be asked on the consent form and if the birth mother is not available, these specific questionnaires will not be asked. This questionnaire contains questions of a sensitive nature and further action will not take place based on questionnaire responses. Mothers will be encouraged to get in touch with the site clinical staff if they have any concerns about the questionnaires or their responses.

We will also ask you to record whether you gave the study medication at regular intervals on an app or website and will send you reminders about this via text or email. If your baby does develop a stricture, then your doctor will talk to you about the treatment.

At 18 months into the study, the total numbers of babies taking part will be reviewed. If the number taking part is low, then consideration will be given whether to continue to recruit into the study.

At the end of the study, we hope to have included just over 200 babies in the study. This is a number which we believe is big enough to give valuable results and is far bigger than reported in any similar studies worldwide to date.

We have tried to make taking part in the study as easy as possible for you and your family. The follow-up has been designed around routine follow-up visits that would happen for all babies born with oesophageal atresia so it will not mean extra visits to the hospital and in some cases information might be gathered over the phone. Some visits might take a bit longer where some extra information is asked.

What are the possible benefits or risks of taking part?

The treatments used in the study are used routinely for babies in UK hospitals and are known to be safe, with low incidence of side effects, so there are no extra risks involved from taking part in the study.

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[2].

Babies can still be prescribed gastric acid suppression medication during and after the study if a doctor decides it is needed for treatment of reflux symptoms (see reflux management plan flow chart on page 14).

This study will not bring any immediate benefit to your child. We hope that we will get information about how best to treat children born with oesophageal atresia in the future. By participating, you will be helping us to learn whether treatment with gastric acid suppression medication helps babies with oesophageal atresia to inform the NHS whether or not to offer this routinely as a treatment for other children in the future. After we have finished the study, we will let you know the results.

Do we have to take part?

No, taking part is completely voluntary. If you decide not to take part, you do not have to give a reason and your child's routine care will not be affected in any way. If you agree to take part, we will ask you to sign a consent form which indicates your agreement to take part in the study and to let the researchers look at your child's health records. We will put a copy of this research consent form in your child's health records. We will give you a copy for your files.

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[2] *Terrin G, Passariello A, De Curtis M, Manguso F, Salvia G, Lega L, et al. Ranitidine is associated with infections, necrotizing enterocolitis, and fatal outcome in newborns. Pediatrics. 2012;129(1):e40-5.*

How long do I have to decide?

Because we would like to start treating your child soon after their operation to repair the oesophagus we will need to know if you are willing to take part up to 3 days after surgery. To help you decide please talk about the study to your doctor. Please ask them any questions you may have.

Will my details be kept confidential?

1. Your GP will be told that your baby is taking part in the study
2. We will ask permission to potentially contact you again in the future to find out how your baby is getting on as they grow up. If you agree, your personal details such as name, phone number and email address, will be stored by the TOAST Study team in Oxford and may be shared with the research teams in University of Southampton and Evelina, London.

What will happen to my data?

Data protection legislation requires that we, the University of Oxford (whose legal name is The Chancellor Masters and Scholars of the University of Oxford), state the legal basis for processing information about your child. In the case of research, this is a 'task in the public interest'. The University of Oxford is the sponsor for this study and is responsible for looking after your information and using it properly.

We will need to use information from your child's medical records for this research project. We will share your information related to this research project with the following organisations: University of Oxford (sponsor), Medicines and Healthcare products Regulatory Agency (MHRA), TOAST Study team and Host hospital trust.

This information will include:

- Your name, address, email address, and phone number
- Your baby's name, CHI number and DOB

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure by:

- Storing all electronic data in a secure place
- Access restricted to only those people who need it for the research, using individual logins and passwords
- Data will be backed up everyday
- Data will not be stored on individuals' computers

Your personal data will not be shared outside the UK.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep your study data for the minimum period of time required by the University of Oxford's Management of Data Policy - 25 years.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this. This would not affect the routine care your baby receives in any way.

If you choose to stop taking part in the study, we would like to continue collecting information about your baby's health from their medical records. If you do not want this to happen, tell us and we will stop.

You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

You can find out more about how we use your information by:

- Asking the local research team (see contact details at the back of this leaflet)
- Sending an email to ***toast@npeu.ox.ac.uk***
- Calling the TOAST Study team on 01865 289278

- Contacting the University's Data Protection Officer **data.protection@admin.ox.ac.uk**
- Looking at the University's privacy notice available at ***https://compliance.admin.ox.ac.uk/research-data***

If you would like to find out more about the use of confidential data in research, the HRA has developed a general information leaflet which is available at ***www.hra.nhs.uk/patientdataandresearch***

We may use third party service providers or subcontractors to help with some of the research activities we carry out (e.g. IT provision, survey provision, transcription services etc.). We may therefore share your personal data with these providers when it is necessary to do so to allow them to carry out the services we require them to provide. However, we require all our third-party providers to have appropriate security measures in place to protect your data and we only allow them to process your data for the specific purposes we have stated in our instructions.

The TOAST app requires your email address and your baby's DOB. Access to this personal identifiable data may be granted to the app provider (Blue Frontier) but only when troubleshooting any issues with the TOAST app. Your personal data will not be shared outside the UK. The app provider will not store any personal data relating to you or your baby. The app/website's main function is to gather medication information, but will also include an optional section for you to enter helpful notes about your baby, for example their weight or mood. Anything you enter in this optional section will not be used in the study. This optional data will be saved in a separate secure location by the TOAST Study team in Oxford and will be deleted at the end of the study. You will be able to download anything you entered prior to it being deleted and we will let you know when this will occur.

Who is organising and funding the study?

The study is funded by the National Institute for Health Research (NIHR) which is the research arm of the NHS. The study is sponsored by the University of Oxford and is being run by the National Perinatal Epidemiology Unit Clinical Trials Unit at the University of Oxford. The Chief Investigator is employed at University of Southampton and the other Senior Investigator is employed by Evelina London, Guys and St

Thomas Trust. The clinicians involved in the study are all experienced researchers, interested in improving the care given to babies born with oesophageal atresia. A number of parents of babies with oesophageal atresia have also helped design the study, as have TOFS, the UK support group for families affected by oesophageal atresia and tracheo-oesophageal fistula. Please see the back of this leaflet for TOFS contact details.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests and make sure it is done to the highest standards. This study has been reviewed and given favourable opinion by South Central Berkshire Research Ethics Committee (ref 25/SC/0198).

What will happen to the results of the research study?

At the end of the study, the results will be analysed and published in a medical journal. We will write our reports in a way that no one can work out who took part in the study. We will also share the results at medical and surgical conferences, on our website, with families of children with oesophageal atresia and with the TOFS support group. We will send you a copy of the results at the end of the study. Unidentifiable data from this study may also be shared with other groups who are carrying out similar work in the future.

What if there is a problem?

The investigators recognise the important contribution that volunteers make to medical research, and will make every effort to ensure your safety and wellbeing. The University of Oxford, as the research sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your taking part in this study. If something does go wrong, you are harmed during the research, and this is due to someone’s negligence, then you may have grounds for a legal action for compensation. While the Sponsor will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. The study doctor can advise you of further clinical action and refer you to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment provided.

In the first instance you can talk to the clinical team looking after your baby who will help you with your concern. You can also contact the local research team, either the research nurses or the Principal Investigator; their contact details are on the back page of this leaflet. If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact Professor Nigel Hall (details at the back of this leaflet) or you may contact the University of Oxford Research Governance, Ethics & Assurance Team (RGEA) on 01865 616480, or email ***RGEA.Complaints@admin.ox.ac.uk***

The Patient Advice and Support Service (PASS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PASS is unable to provide information about this research study. If you wish to contact the PASS team at your hospital, their contact details are on the back page of this leaflet, or please see the PASS website ***pass-scotland.org.uk/***.

How have patients and the public been involved in this study?

To ensure that TOAST Study is carried out keeping the interests of OA-TOF parents and families at its centre, we have formed our research team to include a Patient and Public Involvement (PPI) co-applicant. This representative from the support charity TOFS, is also a parent of a patient (now an adult) born with OA. They have made significant contributions to TOAST Study by bringing a parental perspective of having a child with OA and providing insight into the acceptability of the care pathways proposed. They have also given advice on how and when is the best time to approach parents and importantly helped inform the selection of primary and secondary outcomes.

The NPEU research team are looking for ways to improve the research projects they run using Parent, Patient and Public Involvement and are looking for parents/carers to contact to help with this. This might include using your direct experience to help or advise how the research should be carried out or how to get any messages from the research out to future participants. If you agree to be contacted about this, it does not mean that you have to take part in the any of these activities. If you choose not to be contacted, it will not affect your baby’s participation in the TOAST Study.

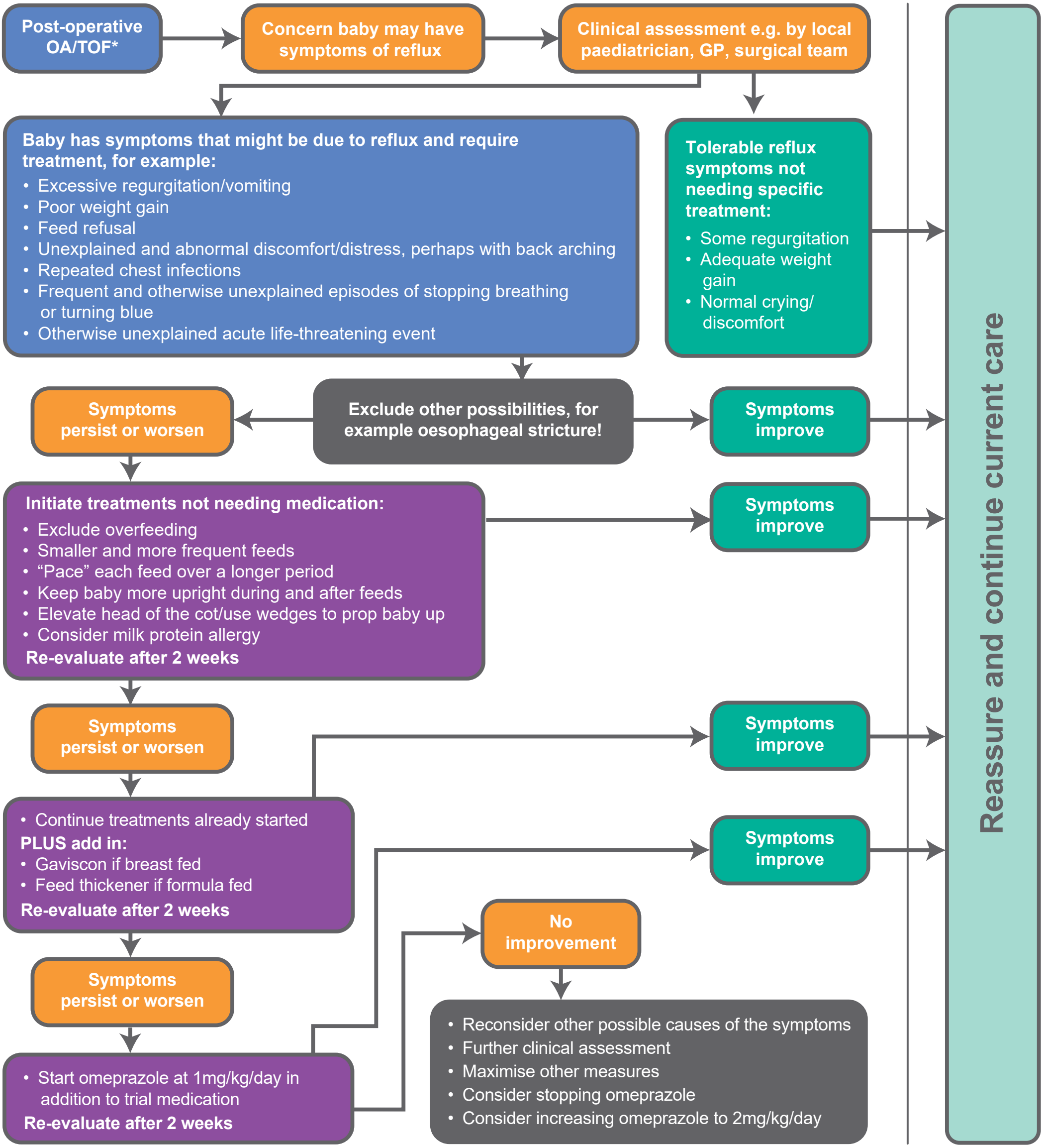
Contact Information:

Chief Investigator: Professor Nigel Hall, University of Southampton
n.j.hall@soton.ac.uk

Co-Lead: Mr Iain Yardley, Evelina London
i.yardley@nhs.net

Thank you for taking the time to read this information sheet

Symptomatic reflux treatment pathway - FAMILIES



Post-operative OA/TOF*

Concern baby may have symptoms of reflux

Clinical assessment e.g. by local paediatrician, GP, surgical team

Baby has symptoms that might be due to reflux and require treatment, for example:

- Excessive regurgitation/vomiting
- Poor weight gain
- Feed refusal
- Unexplained and abnormal discomfort/distress, perhaps with back arching
- Repeated chest infections
- Frequent and otherwise unexplained episodes of stopping breathing or turning blue
- Otherwise unexplained acute life-threatening event

Tolerable reflux symptoms not needing specific treatment:

- Some regurgitation
- Adequate weight gain
- Normal crying/ discomfort

Exclude other possibilities, for example oesophageal stricture!

Symptoms persist or worsen

Symptoms improve

Initiate treatments not needing medication:

- Exclude overfeeding
- Smaller and more frequent feeds
- "Pace" each feed over a longer period
- Keep baby more upright during and after feeds
- Elevate head of the cot/use wedges to prop baby up
- Consider milk protein allergy

Re-evaluate after 2 weeks

Symptoms improve

Symptoms persist or worsen

Symptoms improve

- Continue treatments already started

PLUS add in:

- Gaviscon if breast fed
- Feed thickener if formula fed

Re-evaluate after 2 weeks

Symptoms improve

Symptoms persist or worsen

- Start omeprazole at 1mg/kg/day in addition to trial medication

Re-evaluate after 2 weeks

No improvement

- Reconsider other possible causes of the symptoms
- Further clinical assessment
- Maximise other measures
- Consider stopping omeprazole
- Consider increasing omeprazole to 2mg/kg/day

Reassure and continue current care

IMPORTANT

- Your surgeon's decision always has priority, if treatment is felt to be urgent then it can be initiated sooner than described here but the steps should be followed in sequence and time given for them to have an effect before moving on.
- If you have already started some measures for reflux not needing a prescription before seeking medical attention, please inform your clinician.
- Every baby thought to need gastric acid suppression for reflux treatment can have this.

V3.0, 22-05-2025

*OA - Oesophageal Atresia TOF - Tracheo-oesophageal fistula

Who can I talk to if I have more questions?

Principal Investigator: {_LEAD_}

Local Research Nurse {_LRN_Nurse_}

Patient Advice and Support Service (PASS)
{_PASS_}

TOAST Study Team

NPEU Clinical Trials Unit,
National Perinatal Epidemiology Unit, University of Oxford,
Old Road Campus, OXFORD, OX3 7LF

☎ 01865 289278 ✉ toast@npeu.ox.ac.uk 🌐 www.npeu.ox.ac.uk/toast

Scan to visit
www.npeu.ox.ac.uk/toast

For more information about the TOFS support group please visit their website: ***www.tofs.org.uk/about-us.aspx***

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The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.