SaFE | Swallowing, Feeding & Eating in children born with OA/TOF

A mixed methods exploration of early feeding and swallowing in children born with oesophageal atresia/tracheo-oesophageal fistula

Alexandra Stewart

Department of Language and Cognition, UCL

Thesis submitted in fulfilment of the requirements for the degree of PhD

December 2024

Declaration

I, Alexandra Stewart, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Background

Feeding and swallowing difficulties are widely recognised as long-term morbidities associated with OA/TOF, impacting on respiratory health, growth, and quality of life. However, evidence for their type, nature, prevalence, or severity is limited. This study aimed to investigate the nature of the swallow dysfunction in OA/TOF and explore the impact that the swallow dysfunction has on feeding and mealtimes within a family context.

Methods

This study used a convergent, parallel mixed methods design.

Work package 1: An embedded exploratory, sequential study of the impact of feeding difficulties from a parent perspective. Qualitative data were collected using an online forum and used to develop a questionnaire to determine contributing factors and prevalence of experiences.

Work package 2: A mixed methods systematic review synthesised existing data relating to swallow impairment, use of mealtime adaptations and eating and drinking-related quality of life.

Work package 3: A prospective, observational study of swallow physiology. Twelve infants born with OA/TOF underwent swallow assessment at 2-4 months and 8-10 months of age using videofluoroscopy and high-resolution impedance manometry. Feeding outcomes were assessed at 12 months.

Results

Parents described feeding difficulties throughout early childhood which led to anxiety and trauma in approximately 35%. Lower feeding-related quality of life was evident. Mealtime adaptations were reported by approximately 50%

of individuals with OA/TOF across the lifespan. Prospective study identified oesophageal stage swallow impairment in all children and oro-pharyngeal impairment in 25%. Synthesised data generated a bidirectional, dyadic model of eating and drinking demonstrating child and parent factors determine outcome.

Conclusions

This study provides novel data describing the nature of swallow impairment in OA/TOF. It also highlights the impact that this has on the child's broader eating and drinking experience and parent well-being. Evaluation and treatment of eating and drinking as a dyad is supported to optimise outcome.

Impact statement

Oesophageal atresia with or without tracheo-oesophageal fistula are rare but complex conditions which have lifelong gastrointestinal and respiratory impacts for the child. Burdens for the family include extra caring responsibilities and negative impacts on psychological well-being, personal finances, and personal relationships. The complex nature of the condition results in high demand use of healthcare resources. Thus, optimising outcome to minimise these burdens has individual and societal benefits. Work within this thesis contributes to optimising outcome in the following ways:

1. Providing a framework for treating eating and drinking difficulties

This thesis describes the multi-factorial nature of eating and drinking difficulties in this population. Where traditionally focus of intervention is on the child, this work highlights the role the parent role plays to determine overall outcome. It demonstrates that expressly including evaluation of parent anxiety, trauma and isolation within the assessment process could highlight barriers to treatment – providing advice or recommendations focused purely on the child's ability fails if a parent is too anxious to employ them. Generating family-centred, rather than child-centred, goals where ameliorating difficulties with broader eating and drinking, rather than isolated swallow impairment, is considered the goal of intervention, serves to address these barriers. That is treating the dyad, rather than the individual.

This work has been disseminated in the following ways:

- Peer-reviewed publication
- Engagement with patient support group
- Conference presentation
- Educational talks to Speech and Language Therapists

2. Developing use of high-resolution impedance manometry in children

Pharyngeal high-resolution impedance manometry (HRIM) is a relatively new assessment tool, but one which is increasingly being adopted in clinical practice and research. This study has demonstrated that it is feasible to carry out HRIM in children under one year of age and that it can be used to identify specific areas of impairment. Results have enlightened understanding of the nature of swallow impairment in OA/TOF by proposing different swallow phenotypes - those related to respiratory-swallow incoordination and those relating to compensatory behaviour of the upper oesophageal sphincter in relation to abnormal oesophageal clearance. Developed understanding of *why*, can support Speech and Language Therapists, or other clinicians, to reason a targeted, effective intervention or compensatory strategies. This study has also highlighted ways in which continued development of pharyngeal HRIM is required to unlock its potential when used with children. This includes exploring how analysis software could be adapted for use in young children, developing an agreed protocol and guideline for assessment and determining which metrics are most valuable to our understanding of how impairment relates to functional outcome.

This work has been disseminated in the following ways:

- Conference presentations
- Educational talks to multi-disciplinary team members

Co-author Royal College of Speech and Language Therapists position paper on use of HRIM

UCL Research paper declaration form

1. (a) Title: **Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula.**

(b) DOI: https://doi.org/10.1016/j.jpedsurg.2022.08.013

(c) Where was the work published?: **Journal of pediatric surgery 1;57(12):792-9.**

(d) Who published the work: **Elsevier**

(e) When was the work published?: **December 2022**

(f) Manuscript authors in order they appear on publication: **Stewart A, Smith CH, Govender R, Eaton S, De Coppi P, Wray J.**

(g) Was the work peer reviewed?: **Yes**

(h) Have you retained the copyright?: **Yes**

(i) Was an earlier form uploaded to a preprint server?: **No**

☑ I acknowledge permission of the publisher named under 1d to include in this thesis portions of the publication named as included in 1c

Statement of contribution: **AS, JW, CS, SE and PDC designed the study. AS collected the data. AS, JW, CS and RG analysed the data. AS drafted the manuscript. JW, CS, SE, RG and PDC reviewed and edited the manuscript.**

This work can be found in chapter 2.

2. (a) Title: **The characteristics of eating, drinking and oro-pharyngeal swallowing difficulties associated with repaired oesophageal atresia/tracheo-oesophageal fistula: a systematic review and meta-proportional analysis.**

(b) DOI: 10.1186/s13023-024-03259-x

(c) Where was the work published?: **Orphanet journal of rare diseases 4;19(1):253**

(d) Who published the work: **Springer**

(e) When was the work published?: **July 2024**

(f) Manuscript authors in order they appear on publication: **Stewart A, Govender R, Eaton S, Smith CH, De Coppi P, Wray J**

(g) Was the work peer reviewed?: **Yes**

(h) Have you retained the copyright?: **No**

(j) Was an earlier form uploaded to a preprint server?: **No**

☑ I acknowledge permission of the publisher named under 2d to include in this thesis portions of the publication named as included in 2c

Statement of contribution: **AS, JW, CS, RG, SE, PDC designed the study and were involved in study selection. AS extracted the data. JW, CS, RG and SE checked data extraction. AS and SE completed data analysis. AS drafted the manuscript. JW, CS, RG, SE and PDC reviewed and edited the manuscript.**

This work can be found in chapter 4.

Candidate: Date: 3rd December 2024

Supervisor/Senior Author signature (where appropriate):

Date: 3rd December 2024

Acknowledgements

First, I would like to thank my clinical and academic PhD supervisors, Prof Jo Wray, Dr Christina Smith, Prof Paolo De Coppi, Prof Simon Eaton and Dr Roganie Govender. Your guidance, support and commitment to me and this project have been outstanding. I would also like to thank Prof Nathalie Rommel and Dr Deborah Ridout for their time and expertise during the analysis phase. I would like to thank my funder, the National Institute for Health Research.

I would like to thank the Gastroenterology department at Great Ormond Street Hospital, particularly Dr Osvaldo Borrelli, Dr Kornilia Nikaki and Dr Anna Rybak for their time, flexibility, and enthusiasm throughout the project, as well as the nursing staff on Gastroenterology Investigations Suite, Kingfisher ward for freely sharing their friendly, helpful expertise. I would also like to thank the Speech and Language Therapy department, especially Vicky Thorpe, Emily Johnson, Lesley Cavalli, Martina Ryan and the inpatient team for their support and encouragement and for bearing with me over the last five years.

Thanks to go to the ORCHID team for their friendship and reassurance. Having peers with whom to celebrate, cogitate and deliberate has been invaluable. My particular thanks to Emma Shkurka for her friendship and support as we navigated the PhD journey from funding application to completion together.

My heartfelt thanks to all the participants in this study, those who shared their experiences so candidly and those who committed to being part of longitudinal study. To the steering group members, Julia Faulkner, Susan Morris, Neil Carding and Hayley Ramm, thank you for your time, insight, and knowledge. Your involvement positively impacted without doubt.

Finally, a huge thank you to my husband, Gareth and children, Wilf and Zadie. Their understanding and support have been unfailing, their humour and love sustaining.

Dedication

This thesis is dedicated to the memory of Kai Carding.

Table of contents

List of tables

List of figures

Abbreviations

ADVS	Airway dyspnoea voice swallowing scale
AirCl	Time to airway closure
BRS	Brief resilience scale
BRS	Bolus residue scale
CI	Chief investigator
CNS	Clinical nurse specialist
CT	Computerised tomography
DCI	Distal contractile integral
EA	Esophageal atresia
EGJ	Esophago-gastric junction
FEES	Fibreoptic endoscopic evaluation of swallowing
FSIS	Feeding swallowing impact survey
GAD	Generalised anxiety scale
GOR	Gastro-oesophageal reflux
GORD	Gastro-oesophageal reflux disease
GP	General practitioner
HCP	Healthcare professional
HRA	Health research authority
HRIM	High-resolution impedance manometry
IDDSI	International dysphagia diet standardisation initiative
IPA	Interpretive phenomenological analysis
IQR	Interquartile range
IRAS	Integrated research application service
IRP	Integrated relaxation pressure
IRP4s	4 second integrated relaxation pressure
LOS	Lower oesophageal sphincter
MaxAd	Maximum admittance
MCHFS	Montreal children’s hospital feeding scale

OA	Oesophageal atresia
PAS	Penetration aspiration scale
PhCI	Pharyngeal contractile integral
PFD	Paediatric feeding disorder
PIS	Participant information sheet
PHQ	Patient health questionnaire
PPIE	Patient and public involvement and engagement
PROM	Patient reported outcome measure
PTSD	post-traumatic stress disorder
PSS	Perceived stress scale
QOL	Quality of life
ResVol	Residue volume
RT	Relaxation time
SLT	Speech and language therapist
SpS	Sucks per swallow
TEF	Tracheo-esophageal fistula
TOF	Tracheo-oesophageal fistula
TPT	Total pharyngeal transit time
UOS	Upper oesophageal sphincter
VFSS	Videofluoroscopy swallow study

Chapter 1. Introduction

This chapter will outline the current literature relating to 1) swallow function and assessment, 2) feeding difficulties and 3) oesophageal atresia/tracheo-oesophageal fistula, which are cornerstones of this PhD. The aims and objectives of the thesis are presented with an overview of, and justification for, the research design.

1.1 An overview of anatomy and physiology of swallowing

Swallowing comprises three interconnected phases: oral, pharyngeal, and oesophageal, which will be outlined in the subsequent sections.

1.1.1 The oral phase

The oral phase describes the process of getting food or drink into the oral cavity, forming a cohesive bolus within the oral cavity and transporting it efficiently into the pharynx (Dodrill et al. 2015). This is a voluntary process and requires coordinated movement of the lips, jaw, tongue, cheeks, and palate to maintain bolus control. Additionally, the oral phase is influenced by sensory stimuli, such as taste, texture and temperature and external factors, such as hunger and alertness (Willging et al. 2019). Neural control of these muscles is cortical and brainstem mediated (Miller 2008). Information from mechanoreceptors, pain receptors, chemoreceptors, thermoreceptors, and taste receptors located throughout the oral cavity is coordinated by the cerebral cortex and information sent to the brainstem regarding the characteristics of the bolus. Motor and sensory innervation of the oral phase arises from cranial nerves V, VII, X and XII within central pattern generators (Willging et al. 2019). In neonates, the oral phase consists predominantly of reflexive sucking, mediated entirely by the central pattern generator in the brainstem. During a period of rapid development in the first year of life, volitional sucking develops and then mastication. A key component of sucking in infancy is coordination with the respiratory system. Once the bolus exits the oral cavity, the pharyngeal phase is initiated.

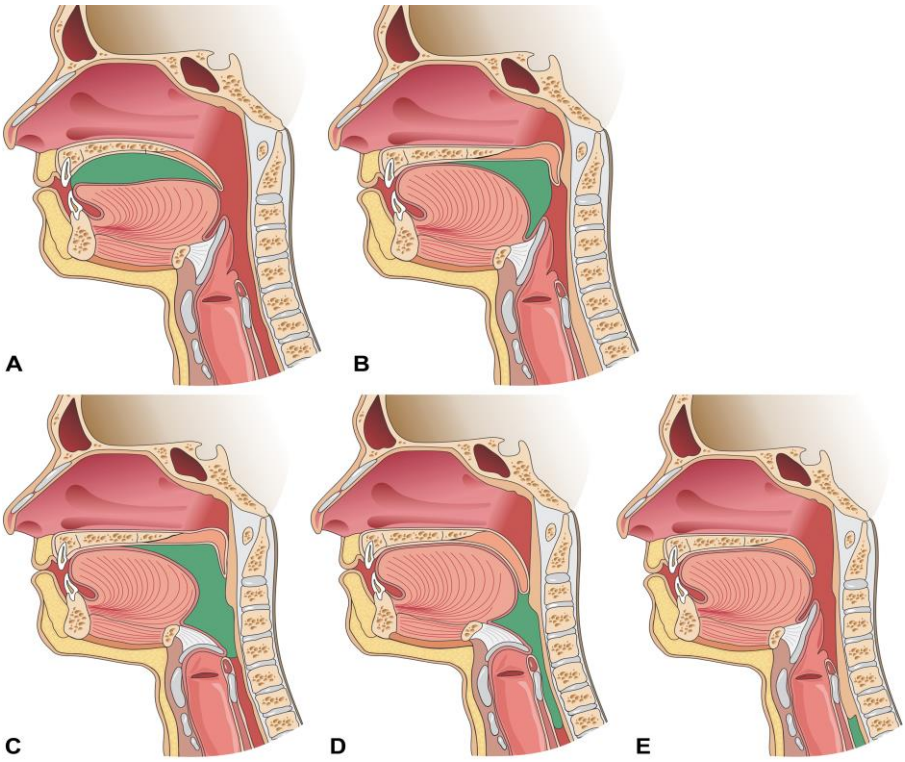


Figure 1-1. Schematic representation of the phases of swallowing

A = the oral phase, B = oral to pharyngeal transit and swallow initiation, C = the pharyngeal phase, D = entry through the upper oesophageal sphincter, E = the oesophageal phase.

Image reproduced with permission (Carbo et al. 2021)

1.1.2 The pharyngeal phase

The pharyngeal phase is a complex, involuntary phase of swallowing during which the bolus is propelled through the pharynx and the relaxed upper oesophageal sphincter into the proximal oesophagus (Figure 1-1. Schematic representation of the phases of swallowing). Simultaneously, epiglottic inversion, glottic closure and hyolaryngeal elevation close the airway, protecting it from bolus intrusion (laryngeal penetration and aspiration) (Willging et al. 2019). In addition to propulsive forces, negative pressure generated from a sealed pharyngeal cavity helps create a suction effect aiding bolus transfer into the proximal oesophagus (Ferris et al. 2021).

Motor innervation of the pharyngeal phase arises from five cranial nerves (trigeminal, facial, glossopharyngeal, vagus and hypoglossal) and cervical nerve roots of C1 and C2 (Willging et al. 2019). Sensory innervation occurs via the trigeminal, facial, glossopharyngeal and vagus nerves (superior and recurrent laryngeal nerve). A central pattern generator integrates sensory and motor information to produce a motor pattern modulated to the specific requirements of bolus size and consistency, ensuring effective clearance. Central pattern generators also ensure timely inhibition of respiration during pharyngeal transit of the bolus (Willging et al. 2019).

1.1.3 The upper oesophageal sphincter

The upper oesophageal sphincter (UOS) is a high-pressure zone separating the pharynx from the oesophagus. Comprising predominantly of the cricopharyngeal muscle, together with the inferior pharyngeal constrictor and cervical oesophageal muscle, cartilage and connective tissue, its primary purpose is to allow food and prevent air from entering the oesophagus, while also preventing retrograde movement of a bolus from the oesophagus back into the pharynx (Singh et al. 2005). The UOS is tonically activated at rest, with resting pressures in healthy adults observed between 35-200 mmHg (Singh et al. 2005). Lower resting pressures, ranging from 2-26 mmHg are reported in infants (Omari et al. 1999). Relaxation of the UOS occurs at the onset of swallowing resulting in a pressure drop. Bolus transit requires not only this relaxation but also opening of the UOS. Contraction of the mylohyoid, thyrohyoid and geniohyoid pulls the cricoid cartilage superiorly and anteriorly, which causes superior movement of the UOS. The UOS then opens and rises to meet the bolus (Cook et al. 1989). The extent and duration of UOS opening are dependent on intrabolus pressure exerted by the tongue base and pharyngeal constrictor muscles, hence are modulated by bolus size and consistency (Singh et al. 2005).

1.1.4 Oesophageal phase

The oesophageal phase begins once the bolus passes through the UOS. This is also an involuntary phase of swallowing. This phase of swallowing involves the efficient transit of the food, liquid or saliva bolus down the length

of the oesophagus by way of peristaltic contraction, through the lower oesophageal sphincter (LOS) and into the stomach (Willging et al. 2019). The upper part of the oesophagus consists of striated muscle and is under central control (originating in the brainstem). The distal oesophagus consists of smooth muscle and is under central and intrinsic control (from the smooth muscle itself). The segment between the proximal and distal oesophagus is known as the transition zone and contains both striated and smooth muscle fibres (Bajwa et al. 2023).

As a bolus enters the oesophagus, primary peristaltic waves are triggered, i.e. bolus-induced contractions. Secondary peristaltic waves can also be triggered. These are triggered by the presence of bolus residue or refluxate for the purposes of oesophageal clearance and occur in the absence of swallow initiation (Bajwa et al. 2023).

1.1.5 Lower oesophageal sphincter

As the bolus reaches the end of the oesophagus, it passes through the lower oesophageal sphincter (LOS). The LOS acts as a high-pressure zone, along with the crural diaphragm, separating the oesophagus from the stomach, preventing damage to oesophageal mucosa from refluxed acidic gastric contents (Figure 1-2) (Bajwa et al. 2023). The LOS consists of intrinsic and extrinsic elements. The intrinsic component consists of oesophageal smooth muscle fibres which are under neurohormonal control. The crural diaphragm and phrenoesophageal ligament constitute the extrinsic components (Rosen et al. 2023).

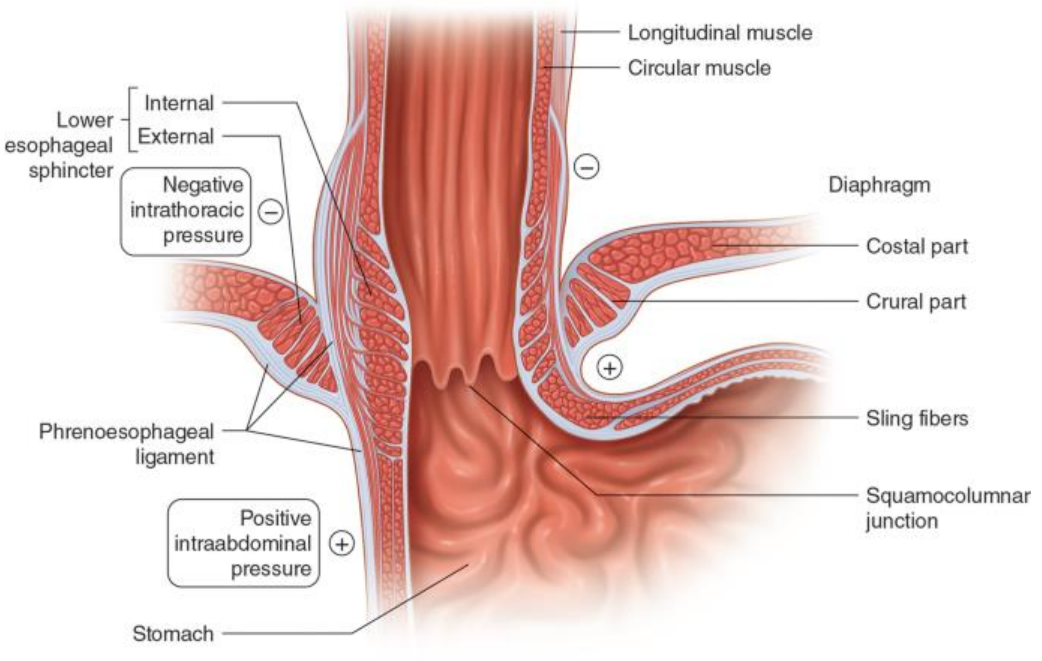


Figure 1-2. Anatomy of the gastro-oesophageal junction, including the lower oesophageal sphincter.

Image reproduced with permission from Kim (2023)

Resting pressure is lowered, and the sphincter relaxed by direct inhibition of the smooth muscle. This opens the sphincter and permits passage of a bolus. Unlike the UOS, opening relies on relaxation alone, there is no dilatory component (Rosen et al. 2023). Typical resting pressure is approximately 30 mmHg, dropping to approximately 3 mmHg during relaxation in both adults and children. Relaxation of the LOS occurs with onset of pharyngeal swallowing, ahead of the bolus, facilitating oesophageal peristalsis (Rosen et al. 2023). Transient LOS relaxation is relaxation that occurs outside of swallowing, believed to be triggered by gastric distension. This allows for release of excess gas. Excessive frequency of transient LOS relaxation is also observed in gastro-oesophageal reflux disease (Kim et al. 2013).

1.2 Assessment of swallow function in infants and children

Evaluation of swallow function can be divided into four main categories: observational, endoscopic, radiologic and catheter based. These will be summarised in the following section but further detail regarding the tools used within this thesis is provided in section 5.1.1.

1.2.1 Observational assessment of swallowing

Observational assessment, also known as bedside or clinical evaluation, involves direct observation of oral structures and function, oral sensorimotor skills, parent-child feed/mealtime interaction and feed/mealtime function and behaviours (Willging et al. 2019). Assessment is non-invasive and includes detection of signs and symptoms of swallow dysfunction, from which pharyngeal swallow function can be inferred (Garand et al. 2020). Such signs include coughing, wet/noisy breathing, throat clearing, colour change, eye tearing and an inability to complete a feed (Arvedson et al. 2020). The aims of the assessment are to describe the nature of the presenting eating/drinking difficulty, generate hypotheses regarding the underlying cause(s), provide initial advice to improve safety or efficiency of swallowing, and determine the need for further assessment or onward referral. It is not a screening test and therefore cannot be "passed" or "failed" (Garand et al. 2020). Observational assessment can be conducted in any environment including the child's home, enabling naturalistic assessment, and is readily repeatable. Observational assessment includes information gathering from medical notes and the caregiver, examination of oro-motor function (cranial nerve examination), communication skills (including parent-child interaction), and direct observation of eating/drinking (Garand et al. 2020). Standardised assessment tools for some elements of the observational assessment of swallowing in children exist, for example the dysphagia disorders survey (Sheppard et al. 2014) and the schedule of oro-motor assessment (Reilly et al. 1995) but more commonly workplace specific or "homemade" checklists are adopted (Garand et al. 2020). The validity and reliability of determining swallow function from observational assessment has been widely

questioned, with the limited use of standardised assessment adding to variability in practice (Garand et al. 2020). Current assessment provides invaluable information that will help to guide intervention but have limited ability to describe swallow physiology and identify the cause of presenting symptoms (Dodrill et al. 2015, Willging et al. 2019). To determine this direct observation of swallowing it is necessary to use instrumental measures.

1.2.2 Endoscopic evaluation of swallowing

Endoscopic evaluation of swallowing involves insertion of an endoscope through the child's nose to facilitate direct observation of the velum, pharynx, larynx, oesophagus, and stomach. Pharyngeal and oesophageal phases of swallowing are both assessed endoscopically but assessment is undertaken separately, as the goals and purpose differ.

Assessment of the pharynx is called fibreoptic evaluation of swallowing (FEES) and is conducted using local anaesthetic delivered to the nasal cavity immediately prior to scope insertion. The child is positioned in as natural a position as possible and provided with a variety of food and/or drink, often with added food colouring to optimise identification, while the pharynx and larynx are visualised (Miller et al. 2023). When FEES is conducted with young children, familiar foods and utensils are typically used. Protocolled assessment provides improved study validity and reliability but is more challenging to achieve with infants and young children, and no paediatric specific protocols exist (Miller et al. 2020, Zang et al. 2022, Pizzorni et al. 2024). In addition to enabling assessment of the safety and efficiency of food/drink swallowing, FEES uniquely facilitates assessment of saliva swallowing. The assessment allows for identification of abnormal anatomy (particularly the tongue base, pharyngeal wall, epiglottis and glottis) and physiology (timing of swallow initiation, airway closure before the swallow and pharyngeal constriction). Direct visualisation of the food and/or drink enables detection of the presence and volume of pre- or post-swallow airway penetration or aspiration and post-swallow residue thus aiding understanding

of the signs/symptoms of swallow dysfunction evident during observational assessment (Willging et al. 2019, Miller et al. 2023). However, bolus visualisation is lost during the swallow as pharyngeal contractility obscures the end of the endoscope, a process known as “white out” (Miller et al. 2023). A further limitation of FEES in children is a lack of validated analysis tools, resulting in the reliance on descriptive analysis methods (Zang et al. 2022, Pizzorni et al. 2024).

Upper gastrointestinal (oesophageal) endoscopy involves insertion of an endoscope, under general anaesthetic for children, which facilitates direct visualisation of the oesophagus, stomach and duodenum and enables biopsy (Zerbib et al. 2015). Unlike use of endoscopy for assessment of pharyngeal swallowing, endoscopy below the upper oesophageal sphincter is not a physiological assessment and does not involve swallowing of food or drink, rather it identifies anatomical or mucosal abnormalities which may have functional impacts (Lanzoni et al. 2022). Thus, endoscopy can identify a number of causes of dysphagia, including signs of gastro-oesophageal reflux (mucosal changes), oesophagitis (histological changes) and stricture (anatomical changes) but provides limited functional information about bolus flow other than evidence of acute bolus obstruction (Zerbib et al. 2015, Lanzoni et al. 2022).

1.2.3 Radiological evaluation of swallowing

Radiological assessment of oral and pharyngeal phases of swallowing is undertaken in a procedure known as a videofluoroscopy swallow study or modified barium swallow (Arvedson et al. 2017, Ingleby et al. 2021). For the remainder of this thesis the term videofluoroscopy swallow study (VFSS) will be adopted. A VFSS is a dynamic, radiological assessment during which the oral cavity, pharynx, upper trachea, and upper oesophagus are imaged using fluoroscopy while radiopaque contrast material is swallowed (Arvedson et al. 2017, Willging et al. 2019). Standardised presentation of a variety of food and fluid consistencies facilitates evaluation of swallow physiology. Movement and coordination of the lips, jaw, tongue, velum, pharyngeal wall,

epiglottis, larynx, upper oesophageal sphincter are evaluated alongside bolus transit (Martin-Harris et al. 2008). Outcome of VFSS involves a description of physiology and the impact of abnormal physiology on the safety and efficiency of bolus transit from the mouth to the proximal oesophagus (Re et al. 2019). The VFSS is described in greater detail in section 5.1.1.

Radiological swallow assessment of the oesophagus involves fluoroscopic imaging of the oesophagus, stomach and duodenum while the child swallows a radio-opaque liquid (for example, barium sulphate), typically in a supine position (Zerbib et al. 2015). It allows for assessment of oesophageal anatomy and bolus movement, identifying anastomotic or congenital strictures, oesophageal compression due to vascular rings, oesophageal webs, signs of achalasia and tumours (Lanzoni et al. 2022). Although frequently conducted in children presenting with dysphagia and vomiting, diagnostic yield is low in those without a history of bolus obstruction and is not diagnostic for gastro-oesophageal reflux (Goldman-Yassen et al. 2019, Lanzoni et al. 2022). Radiological imaging can identify bolus stasis but is limited in diagnostic utility for oesophageal motility disorders (Lanzoni et al. 2022).

1.2.4 Catheter-based evaluation of swallowing

High resolution impedance manometry (HRIM) is a catheter-based assessment of swallow muscle pressure (manometry) and bolus flow (impedance), used in the evaluation of dysphagia, chest pain and intractable regurgitation (Rosen et al. 2018, Omari et al. 2020). The assessment involves insertion of a catheter containing pressure and impedance sensors through the nose, pharynx, oesophagus and into the stomach, typically without sedation (Rosen et al. 2018). Assessment involves swallowing of food and fluid of prescribed bolus size and consistency which allows for assessment of numerous swallow parameters associated with contractility, distension and bolus flow. It is the accepted gold standard test for evaluation of oesophageal motor and motility disorders and lower oesophageal

sphincter function. Its role in the assessment of pharyngeal function is increasingly reported, particularly as a unique measure of upper oesophageal sphincter function (Ferris et al. 2016, Omari et al. 2020, Omari et al. 2023). Assessment is feasible in children and infants over 1500g (Rayyan et al. 2022). A detailed description of HRIM is provided in section 5.1.1.

The aim of all types of instrumental (endoscopic, radiologic, or catheter-based) assessment is to determine the presence, nature and severity of disordered swallowing, to inform treatment decisions.

1.3 Defining disordered swallowing patterns

The described measures of swallow function all provide information about different aspects of swallow physiology, providing unique information in the diagnosis of swallow impairment. These are then used to classify disordered swallowing by oro-pharyngeal or oesophageal phases.

1.3.1 Classification of oral and pharyngeal swallow dysfunction

No agreed taxonomy for oro-pharyngeal swallow dysfunction exists currently in the literature. Rather, dysphagia is typically defined by the impact that physiological impairment has on the safety and efficiency of swallowing. It is defined by the outcomes of impairment, rather than the impairment itself. Of primary concern are issues relating to swallow safety. That is, food, liquid or saliva entering the laryngeal inlet or trachea due to incomplete or mistimed closure of the airway before or during swallowing. The presence of material in the larynx above the level of the vocal cords is defined as laryngeal penetration. The presence of material below the level of the vocal cords, as aspiration (Rosenbek et al. 1996). Aspiration of food and fluid has been associated with an increased risk of respiratory infection in children, although the relationship is complex, and development of respiratory disease is not dependent on aspiration of food and drink alone (Weir et al. 2007, Pavithran et al. 2019, Tanaka et al. 2019). Incomplete airway closure may be rooted in abnormal neurological control of swallowing, failure of respiratory-swallow

coordination or an anatomical/structural abnormality, such as a laryngeal cleft (Willging et al. 2019).

Efficiency of swallowing describes the process of preparing and transporting food or fluid in an efficient manner, ensuring complete bolus clearance and adequate nutrition and hydration to maintain health. Oral impairments caused by abnormal muscle tone or persistence of primitive reflexes can limit movement and coordination of the lip, tongue, cheek, jaw, and palate which impair bolus formation, cohesion, and transfer. These impairments can lead to bolus residue in the oral cavity, loss of food or drink from the front of the mouth, uncontrolled spillage of a bolus into the pharynx resulting in prolonged mealtimes and inadequate nutritional intake (Arvedson 2008, Willging et al. 2019). Impairment at the pharyngeal level can result in inefficient or ineffective bolus clearance, due to incomplete propulsion of the bolus. This is known as post-swallow residue. Presence of pharyngeal residue can lead to laryngeal penetration or aspiration *after* the swallow (Arvedson 2008).

Diagnosis and severity of oro-pharyngeal dysphagia is typically derived from the degree to which safety or efficiency of swallowing is impacted, that is the degree to which aspiration or residue are present. However, no validated measures of impairment exist in paediatrics to further classify by severity or type.

1.3.1.1 Oesophageal motor disorder classification

Oesophageal phase swallow dysfunction is broadly classified as disorders of motility or obstruction. Classification of oesophageal motility disorders can be undertaken using the Chicago Classification 4.0 algorithm (Table 1-1) (Yadlapati et al. 2021). Disorders of oesophageal body motility (peristalsis) are assessed using the distal contractile integral (DCI) on oesophageal manometry. In adults cut off values for DCI are defined as <100 mmHg.s.cm = failed peristalsis, 100-≥450 mmHg.s.cm = weak peristalsis, >450-8000 mmHg.s.cm = normal peristalsis (Yadlapati et al. 2021). Disorders of oesophago-gastric junction, or outflow obstruction, are assessed using the

mean integrated relaxation pressure of the lower oesophageal sphincter in the 4 seconds (IRP4s) prior to upper oesophageal sphincter relaxation. Normal values for adults in upright position are <15mmHg (Yadlapati et al. 2021).

Applying these metrics directly to children is challenging (Singendonk et al. 2020). Evidence suggested that oesophageal length influences DCI and IRP4s, with higher values seen in younger children (Singendonk et al. 2014). This is related to organ size, rather than neurologically derived developmental changes (Goldani et al. 2010). Subsequent research indicated that DCI was less influenced by oesophageal length, due to the complex interaction between length, duration and pressure vigour in relation to catheter lumen size and oesophageal width, thus supporting use of Chicago classification cut-off values for distal contraction (Singendonk et al. 2020).

However, it is acknowledged that using the adult cut-off value of 15mmHg for IRP4s is problematic and no validated normative data are available. Rayyan and colleagues (2022) reported IRP4s values ranging from 2.5-22.1mmHg in 13 healthy term and preterm infants included in their characterisation of oesophageal motility in a neonatal intensive care unit. However, there is no widely accepted threshold for what constitutes impairment in children. Rather, it is recommended that thresholds are derived locally, dependent on the protocol and equipment used (Rosen et al. 2018, Singendonk et al. 2020). These are then applied to diagnose disorders of the lower oesophageal sphincter causing obstructed bolus flow.

Table 1-1 Chicago classification of oesophageal motor disorders

Classification	Disorder	Definition
Disorders of EGJ outflow	Type 1 Achalasia	Abnormal median IRP4s and 100% failed peristalsis
	Type 2 Achalasia	Abnormal median IRP4s, 100% failed peristalsis & ≥20% swallows with pan-oesophageal pressurisation.
	Type 3 Achalasia	Abnormal IRP4s & ≥20% swallows with premature/spastic contraction and no evidence of peristalsis.
	EGJ outflow obstruction	Abnormal IRP4s (supine and upright), ≥20% elevated intrabolus pressure (supine), and not meeting criteria for achalasia.
Disorders of peristalsis	Absent contractility	Normal median IRP4s (supine and upright) & 100% failed peristalsis.
	Distal oesophageal spasm	Normal median IRP4s & ≥20% swallows with premature/spastic contraction
	Hypercontractile oesophagus	Normal median IRP4s & ≥20% hypercontractile swallows
	Ineffective oesophageal motility	Normal median IRP4s, with >70% ineffective swallows or ≥50% failed peristalsis.

1.3.2 Eating and drinking development

Swallowing and broader eating and drinking skills are developmental. Rapid skill development occurs predominantly during the first 2-3 years of life. In the absence of impairment, development follows a predictable path which reflects the maturation of the central nervous system (Willging et al. 2019). The relationship of food texture to oro-motor skill development is outlined in Table 1-2. The process of moving from a liquid only diet to a wide range of family food is known as the weaning phase. Gross and fine motor skills develop alongside oro-motor skills, facilitating progression from being totally dependent on the feeder to establishing independent sitting and self-feeding, including utensil use (Willging et al. 2019). Acknowledging that eating and drinking is a developmental skill is fundamental to the work in this thesis.

Table 1-2. Relationship between food textures and oro-motor skill acquisition

Age range	Food type	IDDSI level	Oro-motor skill
Birth- 4 months	Liquid	0	Suckling and sucking
4-6 months	Smooth consistency food	3-4	Anterior-posterior tongue movements Phasic biting
7-9 months	Thicker smooth foods Fork mashed solids Dissolvable foods Emergent cup drinking	4 5 Transition foods	Emergent tongue lateralisation Vertical chewing
9-12 months	Fork mashed solids Easy to chew foods Emergent cup drinking	5 6-7 (easy chew)	Increasing tongue lateralisation Vertical chewing with emergent lateral tongue movements
12-18 months	Chopped, soft foods Easy to chew foods	3-6 7 (easy chew)	Consistent tongue lateralisation Emergent rotary chewing
19-24 months	Chewable foods Cup drinking established	3-7	Increased chewing efficiency
24 months	Wide range of family foods	3-7	Continued refinement of chewing skills

Adapted from Willging et al (2019). Pediatric dysphagia: etiologies, diagnosis, and management. Chapter 6: Oral Motor Development, p 76. IDDSI = International Dysphagia Diet Standardisation Initiative

Provided in Table 1-2 are International Dysphagia Diet Standardisation Initiative (IDDSI) levels for the different stages of weaning described (Cichero et al. 2017). The IDDSI framework (Figure 1-3) provides a shared language to define different food and drink textures, alongside evidence-based methods for assessing each level (Cichero et al. 2017). They are used to describe food and fluid consistencies throughout this thesis.

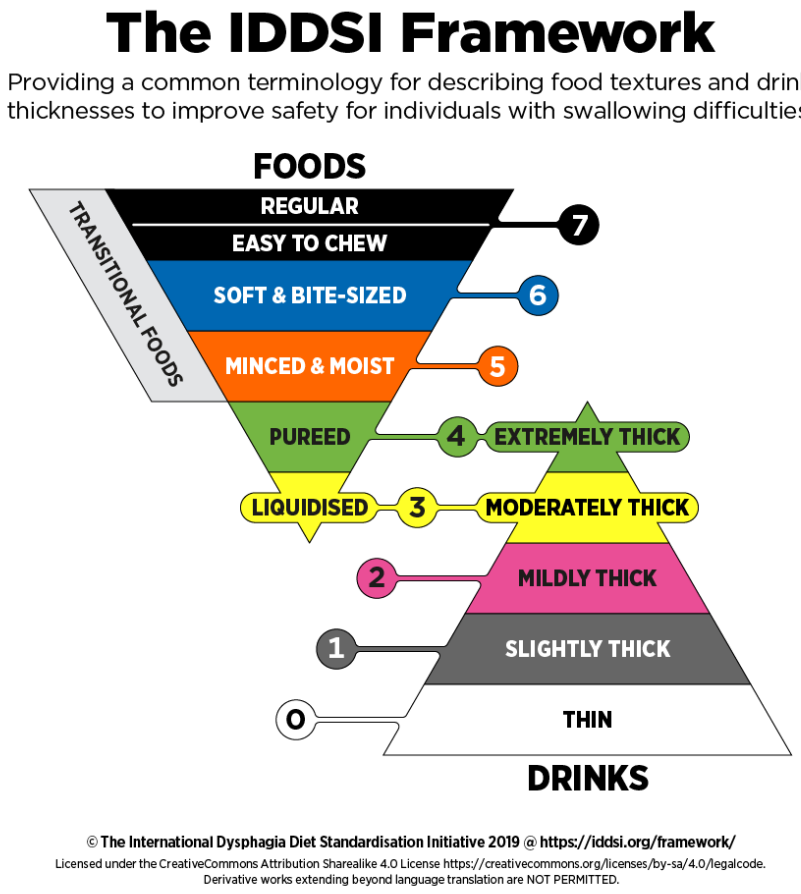


Figure 1-3. IDDSI framework

1.4 Defining feeding difficulty and disorder

The introduction so far has focused on the physiological process of swallowing, outlining the skills required to consume sufficient food and/or fluid to sustain life. A related but distinct concept from a swallowing difficulty

is that of a *feeding* difficulty. The term "feeding difficulty" is a broad term that describes a range of behaviours that make mealtimes or feeds challenging for the child and their family, including food refusal, food selectivity, prolonged mealtimes, stressful mealtimes and impaired child-parent interaction, in circumstances where food availability is not of concern (Estrem et al. 2017). It is accepted that such difficulties often arise because of an antecedent factor. Essential to understanding how feeding difficulties develop or are sustained is an acknowledgement that eating and drinking in childhood is dyadic, occurring between parent/caregiver and child (Arvedson et al. 2020). Thus, the antecedent may be related to the child or the parent (Estrem et al. 2017). Problematic feeding is one of the most commonly reported concerns of parents, with a prevalence of around 25% commonly reported in otherwise healthy, typically developing children (Manikam et al. 2000). Prevalence of feeding difficulties increases substantially in children with underlying medical conditions (Arvedson et al. 2020).

Several models have been developed to explain the development and maintenance of feeding difficulties. One prominent model is the Feeding Dynamics Model, based on work pioneered by Satter (Satter 1990). This model asserts that feeding difficulties arise when there is discordance between a child's hunger and satiety cues, and the parent provided mealtime structure. The Feeding Dynamics Model acknowledges the interaction between caregiver and child factors, in that the child's lack of ability to regulate can impact caregiver functioning – such as problem-solving ability, stressors – and consequently can lead to poor outcomes. Over time this can result in greater difficulty with child regulation and caregiver functioning, exacerbating the feeding difficulty. The model also acknowledges that eating and drinking occurs within a broader environment - the wider family, sociocultural and socioeconomic contexts. These factors can create risk or resilience for the development of a feeding difficulty.

Berlin et al. (2009) built upon the Feeding Dynamics model, developing the biopsychosocial model of feeding (Figure 1-4) . The biopsychosocial model builds upon the Feeding Dynamics Model by placing emphasis on the role of

biomedical factors on the child's ability to meet hydration and nutritional needs (i.e. to regulate their intake). The caregiver's ability to differentiate and respond to their child's cues and needs is fundamental to the degree to which biomedical risk factors impact on feeding. Where hunger/satiety, driven by biomedical factors such as dysphagia or gastro-oesophageal reflux, and suboptimal mealtime structures co-exist, feeding difficulties develop.

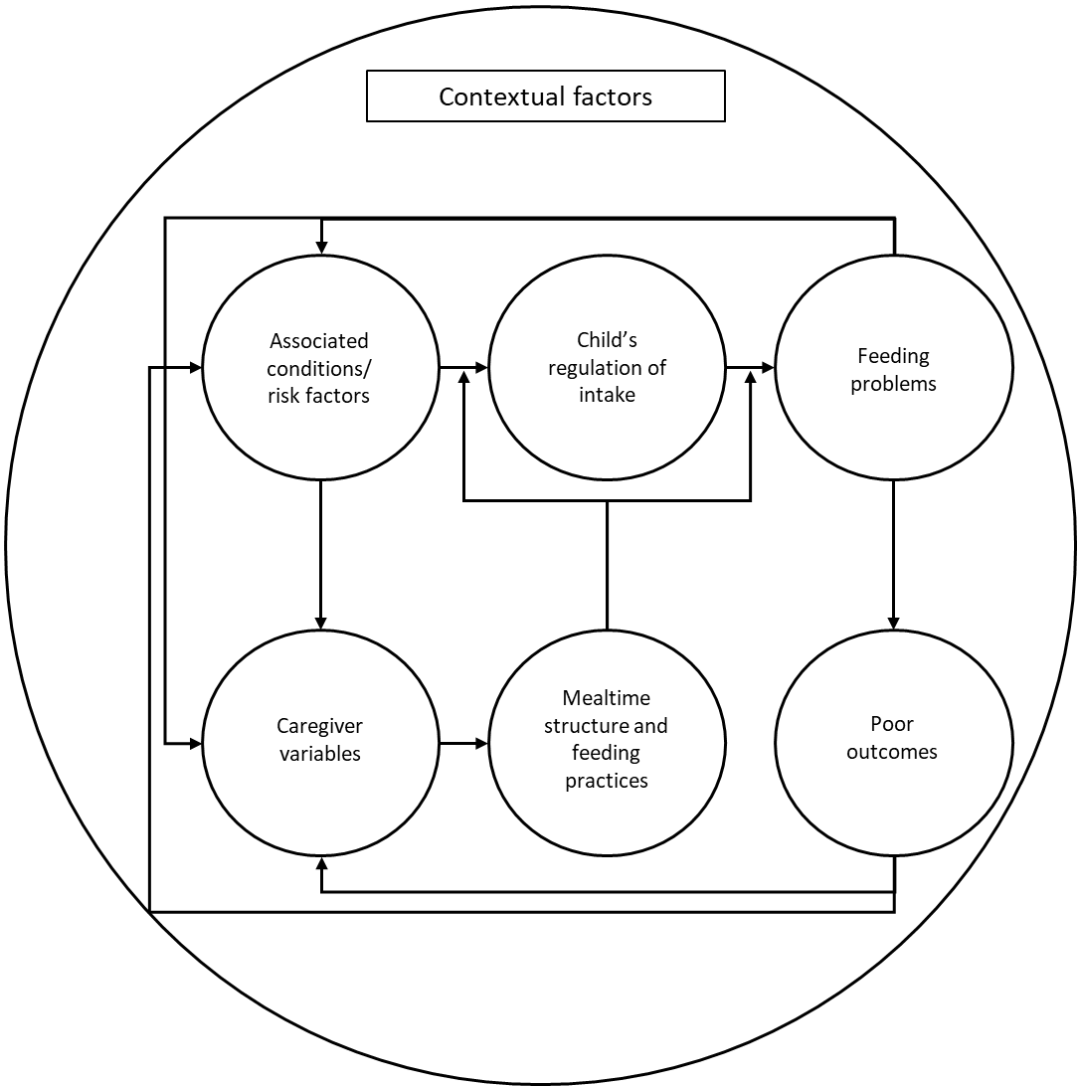


Figure 1-4. Biopsychosocial model of feeding and feeding difficulties

Yet, despite having these models, achieving a clear definition of what constitutes a "feeding difficulty" is challenging, in part due to difficulty differentiating between behaviours that are part of typical child development or parent-child interaction and those that are pathological. The field is also

inter-disciplinary, with problematic feeding addressed by those in medicine, psychology, speech and language therapy, dietetics, and occupational therapy, among others. As such, an array of terms to describe such difficulties exists, including feeding difficulty, feeding problem, feeding disorder, feeding issue and dysphagia (Estrem et al. 2017). These related concepts, arising from different but related disciplines, create a complex landscape from which to define feeding difficulty, understand why feeding difficulties occur and why they are maintained.

Recent work has conceptualised and defined feeding difficulty using the International Classification of Functioning, Disability and Health framework and acknowledging its inter-disciplinary nature. Goday et al. (2019) define a "pediatric feeding disorder" (PFD) as "*impaired oral intake that is not age-appropriate, and is associated with medical, nutritional, feeding skills, and/or psychosocial dysfunction* (p.125)". Within this paradigm, the medical domain refers to an impairment of structure or function within the gastrointestinal, cardiorespiratory, or neurological system that impairs any aspect of eating and drinking. The nutrition domain describes a restriction in the quality, quantity and/or variety of food/drinks consumed which places the individual at risk of malnutrition, overnutrition, micronutrient deficiency or toxicity and dehydration. The feeding skill domain describes developmental, sensory, or motor impairment of feeding skills. Any impairment to the safety or efficiency of feeding, or reliance on food textures or utensils that are not deemed "age appropriate", indicates a skill-based dysfunction. The psychosocial domain refers to any developmental, behavioural, mental health, social or environmental factors relating to the child and/or caregiver that contribute to the feeding disorder. This includes a mismatch between parent expectations and child feeding skill, parent or child anxiety at mealtimes, negative mealtime adaptations or behaviours, disruption to parent-child interaction and inadvertent reinforcement of problematic mealtime behaviours. The psychosocial domain acknowledges the bidirectional relationship that occurs at feeding/mealtimes between the caregiver and child. This framework aims to provide a shared language from which feeding difficulties can be both

defined and diagnosed. This framework, unlike the earlier models of feeding disorder, does not explicitly acknowledge interaction between domains.

1.5 Oesophageal atresia and tracheo-oesophageal fistula

Oesophageal atresia (OA) and tracheo-oesophageal fistula (TOF) are congenital abnormalities occurring in approximately 1 in 3500 live births, equating to 150 cases every year in the UK (Pedersen et al. 2013). Oesophageal atresia is the most common congenital abnormality of the oesophagus (van Lennep et al. 2019). Arising from incomplete separation of the embryonic foregut, the upper and lower parts of the oesophagus form unjoined pouches, rather than a continuous tube (Ioannides et al. 2009). Consequently, swallowed material cannot enter the stomach. A TOF is an abnormal connection (fistula) between the trachea and oesophagus, which allows swallowed material or stomach contents to enter the lungs or air to enter the stomach. In most cases, OA and TOF are diagnosed post-natally, when the baby presents with difficulty managing secretions or feeding. Diagnosis is suspected on passing a naso-gastric tube, which visibly coils in the upper oesophageal pouch on x-ray. Diagnosis of a TOF is confirmed endoscopically (van Lennep et al. 2019).

Typically, OA and TOF co-occur. As presented in Figure 1-5, there are five subtypes of OA/TOF, defined by two commonly used classification systems – Gross and Vogt (van Lennep et al. 2019). For the remainder of this thesis, the Gross classification system will be adopted. In three subtypes, OA occurs in combination with TOF, this includes the most common presentation (approximately 82-85%)– Gross type C – in which the lower oesophageal pouch creates a fistula with the trachea. In 1-4% of cases, the upper pouch creates a fistula (type B). In 3-4% of cases both upper and lower pouches form fistulae (type D). Type A is the second most common subtype, with a prevalence of approximately 7-8%. In this circumstance OA occurs in the absence of a fistula and may therefore be described as isolated OA. In type E, a TOF occurs in the absence of OA (van Lennep et al 2019). As OA and

TOF co-occur in most children, the abbreviation OA/TOF will be used in this thesis for ease of reading.

Without surgical repair these abnormalities are fatal. However, surgical advances have now resulted in survival rates of over 90%. Mortality risk is associated with cardiac abnormalities, prematurity, and very low birth weight, rather than the OA surgery itself (Sadreameli et al. 2016, van Lennep et al. 2019). Prior to repair of OA, the length of the gap between the upper and lower pouches is assessed. Where there is sufficient oesophageal tissue, repair involves thoracoscopic (minimally invasive) or open thoracotomy primary anastomosis of the upper and lower pouches. This approach can typically be employed for those with type C OA/TOF and is undertaken within the first day or two of life (van Lennep et al. 2019).

If the gap between the upper and lower pouches is too long, immediate primary anastomotic repair is not possible. So-called “long-gap” OA results in a longer, more complex surgical course. Almost all type A and B OA will be defined as long-gap. A recent consensus paper defines this as a gap that exceeds 2cm, although there are different definitions within the literature (Van der Zee et al. 2017).

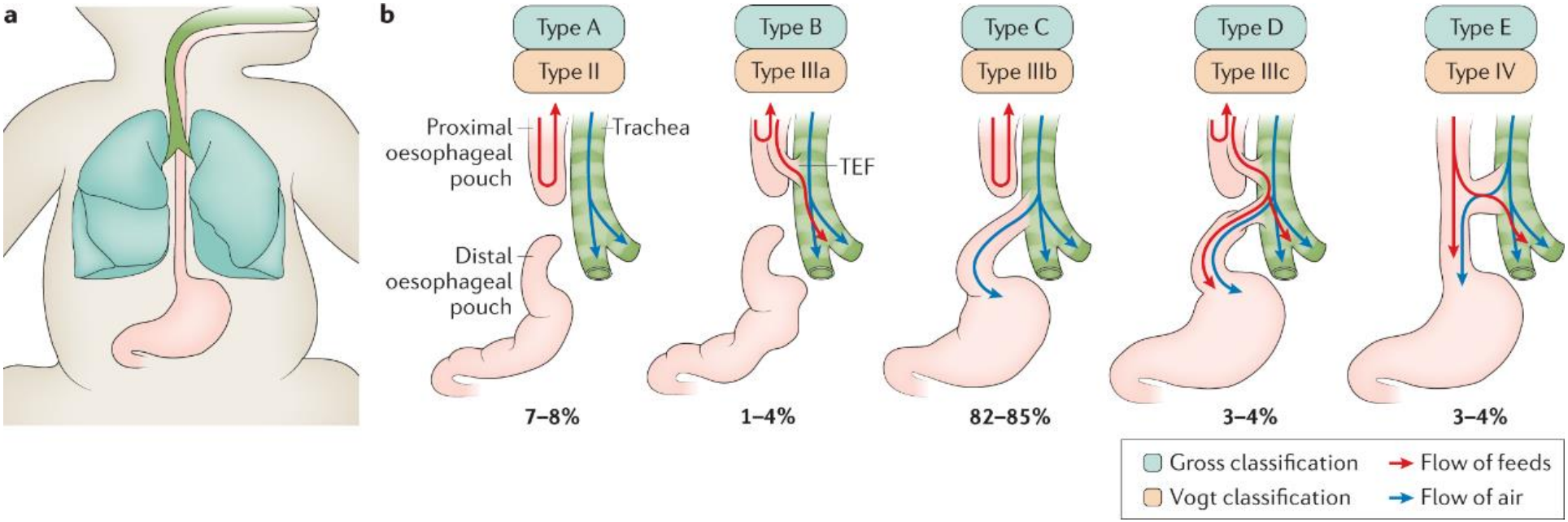


Figure 1-5 Types of oesophageal atresia and tracheo-oesophageal fistula.

A = typical anatomy of the trachea and oesophagus. B = types of oesophageal atresia and tracheo-oesophageal fistula. Image reproduced with permission from van Lennep et al. (2019)

Various surgical options exist to repair a long-gap and are typically dependent of the skills and knowledge of each surgeon or surgical centre (Shieh et al. 2017). One option is delayed primary anastomotic repair. In this case a TOF, if present, would be ligated, a gastrostomy inserted to allow nutrition/hydration needs to be met and a Replogle tube inserted into the upper pouch. A Replogle is a double lumen tube inserted through the nostril into the upper pouch. It is continuously suctioned to manage saliva and secretions, thus protecting the lungs from aspiration (van Lennep et al. 2019). The Replogle remains in situ until sufficient growth of the oesophagus allows for anastomotic repair.

Alternatively, or in cases of insufficient oesophageal tissue, an oesophageal replacement procedure is used. This involves use of the stomach, colon or jejunum to create a conduit from the pharynx to stomach, allowing for the transport of saliva, food and drink (Shieh et al. 2017). Use of non-native oesophageal tissue to form the conduit can lead to numerous complications, including severe gastro-oesophageal reflux disease, delayed gastric emptying, dilation of the conduit and poor long-term function (Shieh et al. 2017).

Oesophageal repair may also be delayed due to prematurity or complex cardiac comorbidities which prevent immediate anastomosis (van Lennep et al. 2019). In these cases, as with long-gap OA, the TOF is ligated with gastrostomy and Replogle tube inserted until such time that repair is possible. Hence, repair can be described as immediate or delayed, primary anastomotic or oesophageal replacement. It is generally accepted that immediate and primary repair involves a less complex course than delayed or replacement surgery.

Delayed surgical repair inevitably results in delayed introduction to oral feeding, which has been reported to lead to food avoidance or aversive eating/drinking behaviours (van Lennep et al. 2019). To reduce this impact, pre-repair oral experience using a technique known as “sham-feeding” has been described for children with a Replogle tube or oesophagostomy (Soyer

et al. 2022, Tollne et al. 2024). This involves offering a child food or drink by mouth, and either suctioning what is swallowed using the Replogle tube or collecting swallowed material in a stoma bag or on a cloth where an oesophagostomy has been formed. The child can receive feeds via gastrostomy simultaneously, mimicking satiation and allowing the child to develop sensori-motor eating/drinking skills.

Approximately 50% of babies with OA/TOF have at least one other congenital abnormality, 35% of which are cardiac-related (Pedersen et al. 2013, Sadreameli et al. 2016, van Lennep et al. 2019). There is emerging evidence that gene mutations play a role in OA/TOF, although in the majority of cases the mutation is spontaneous (Ioannides et al. 2009). There are a number of disorders arising from single gene mutations and chromosomal disorders that feature OA/TOF, the most common of which is VACTERL association (Ioannides et al. 2009). VACTERL association involves vertebral, anorectal, cardiac, trachea-oesophageal, renal and limb malformations.

Premature birth is also associated with OA/TOF. In a national cohort study of OA/TOF over 40% were born prematurely, 3.5% between 24- and 29-weeks' gestation and 38.5% between 30-36 weeks (Sfeir et al 2013). Those born prematurely have been shown to have delayed introduction to oral feeding, with greater likelihood of gastrostomy insertion and need for anti-reflux surgery but with similar levels of post-operative complication (Le-Nguyen et al, 2024).

1.5.1 Post-operative morbidity

Although survival rates are now excellent, increased reporting of longer-term outcomes has highlighted a complex intertwining of gastrointestinal issues, respiratory complications and feeding difficulties that place a considerable burden on patients, parents and health services (Svoboda et al. 2018). Morbidity can be relatively short-term, related to post-operative complications, or longer-term caused by underlying anatomical or physiological impairment. Longer term morbidity typically relates to

gastrointestinal (including eating, drinking, and swallowing) or respiratory issues. The following sections summarise these post-repair difficulties.

1.5.2 Post-operative complications

There are three primary post-operative complications reported: anastomotic leak, stricture, and recurrent fistula.

1.5.2.1 Anastomotic leak

Anastomotic leak refers to breakdown of the repair resulting in leak of oesophageal contents. It can occur at any time during the healing process but most commonly in the first week after surgery. Minor leak is reported in approximately 20% of cases and can be treated conservatively with a Replogle tube and post-pyloric or parenteral feeding until healed (van Lennep et al. 2019, Comella et al. 2021). Re-repair is required for major leak, occurring in 3-5% of patients (Teague et al. 2016). Episodes of leak can disrupt or delay introduction to oral feeding.

1.5.2.2 Oesophageal anastomotic stricture

Narrowing at the site of the anastomotic repair occurs as part of the natural wound healing process. Stricture is defined as narrowing that is associated with significant functional impairment and symptoms, including swallowing difficulties, drooling, regurgitation, vomiting, coughing, aspiration, and food impaction (Krishnan et al. 2016). Strictures are diagnosed by radiological imaging and/or endoscopy and can occur at any age, although occur most frequently in the first two years of life (Tambucci et al. 2017). However, no consensus exists as to the exact fluoroscopic or endoscopic definition of a stricture, thus they are diagnosed by visual appearance of narrowing and symptoms (Tambucci et al. 2017). Reported incidence varies, but a recent systematic review stated a median incidence of 29%, generated from 32 papers. However, the range was extremely wide – 2-100% (Comella et al. 2021). Numerous risk factors for developing strictures have been reported: lower gestational age, VACTERL association, long-gap OA, gastro-oesophageal reflux, high anastomotic tension, and leak (Tambucci et al.

2017). First line treatment is by endoscopic bougie or balloon dilatation. Current guidelines support dilatation in response to symptoms rather than at pre-determined time intervals (Krishnan et al. 2016). Persistent strictures, defined as three or more clinically relevant strictures, are reported in approximately 30% of cases (Lévesque et al. 2013). Treatment options include intralesional steroid injection and systemic steroid treatment.

Anastomotic strictures disrupt swallowing by preventing passage of food and, as the stricture worsens, fluid and saliva down the oesophagus. Treatment typically provides immediate relief of symptoms (Tambucci et al. 2017). A recent systematic review found that the presence of strictures did not increase the likelihood of long-term dysphagia (Soyer et al. 2022).

1.5.2.3 Recurrent tracheo-oesophageal fistula

Recurrent TOF describes the re-emergence of a connection between the trachea and oesophagus at the site of the initial TOF repair (Hua et al. 2020). It occurs most frequently between 2-18 months post initial repair and is suspected in the presence of coughing after swallowing with or without recurrent respiratory infection (Almog et al. 2022) . Diagnosis is typically made following visualisation on radiological assessment and confirmed with endoscopic images (van Lennep et al. 2019). Median incidence was reported as 7% (range 2-10%) in a recent systematic review (Comella et al. 2021). Treatment options include surgical re-repair, injection of glue or closure with trichloroacetic acid. Risk factors include higher anastomotic tension and leak and fistula ligation, rather than repair (as conducted in a two-stage repair when immediate, primary oesophageal atresia repair is not possible) (van Lennep et al. 2019).

There has been little specific research into the impact of recurrent TOF on feeding. However, impact on feeding development would be anticipated as the child is unable to feed orally until the fistula is re-repaired. In cases of complex or persistent fistula this may result in long periods without eating/drinking, often at important stages of development.

1.5.3 Oesophageal dysmotility

Inadequate peristalsis, or dysmotility, can lead to stasis or bolus retention within the oesophagus, increasing risk for aspiration of food, discomfort at mealtimes and contribute to bolus obstruction which may require surgical removal (Faure et al. 2017). Dysmotility is thought to be the primary contributing factor in the need for mealtime adaptations that are frequently reported in those with OA/TOF: a need to drink water when swallowing, eating slowly and modifying food textures (Lemoine et al. 2013, Birketvedt et al. 2020, Mikkelsen et al. 2022). Dysmotility can also result in damage to the oesophageal mucosa, causing oesophagitis or peptic stricture, as a result of prolonged exposure to gastric contents due to failure of normal clearance of gastro-oesophageal reflux (Faure et al. 2017). Dysmotility in OA/TOF is thought to arise from abnormal intrinsic and vagal oesophageal innervation, although it is hypothesised that surgical repair may further damage the vagus nerve and exacerbate dysmotility (Faure et al. 2017).

Using HRIM, three main dysmotility patterns in OA/TOF are described: distal contractions, aperistalsis and pressurization (Lemoine et al. 2013, Courbette et al. 2020, Comella et al. 2021). Those with aperistalsis exhibit a complete lack of oesophageal body contraction during swallowing. Those with pressurisation patterns demonstrate whole body oesophageal contraction in the absence of peristalsis following relaxation of the upper oesophageal sphincter. Distal contraction describes a pattern of limited oesophageal body contraction occurring in the middle or distal third of the oesophagus only (Lemoine et al. 2013). A recent systematic review reported a median prevalence for dysmotility of 76%, with a range of 7-100%, generated from meta-analysis of 25 studies. Dysmotility was the most prevalent oesophageal morbidity in this population (Comella et al. 2021). There is insufficient data at present to analyse motility type and prevalence by OA subtype (Comella et al. 2021).

Despite identification of different motility patterns, to date symptoms or dysphagia severity have rarely been shown to correlate with motility patterns. Only one study has positively correlated symptoms with severity of

dysmotility, identifying that longer bolus transit times were associated with dysphagia symptoms (Di Pace et al. 2011). However, an aperistaltic pattern has consistently been shown to be highly correlated with presence and severity of gastro-oesophageal reflux disease (Faure et al. 2017, Comella et al. 2021). Oesophageal motility has been assessed using manometry in neonates and throughout childhood, however there is a lack of repeated assessment or longitudinal study to document changes to motility that might occur with maturation (Lemoine et al. 2013, Courbette et al. 2020, Rayyan et al. 2022).

1.5.4 Gastro-oesophageal reflux disease

Gastro-oesophageal reflux is defined as “passage of gastric contents into the oesophagus with or without regurgitation and/or vomiting” (Rosen et al. 2018). It is a physiological process present in all children but becomes gastro-oesophageal reflux *disease* when episodes of reflux are accompanied by symptoms which affect daily functioning and/or lead to complications within the oesophagus or other systems, such as the respiratory system (Sintusek et al. 2023). Comella et al (2021), reported a median prevalence of gastro-oesophageal reflux disease (GORD) of 43% (range 9-100%) in individuals with repaired OA/TOF, established from a meta-analysis of 49 studies. This compares to prevalence in the general population of approximately 8% (Sintusek et al. 2023). The wide range is related to variation in diagnostic method, particularly differences between diagnosis from symptom report and use of more objective measures from endoscopy or pH impedance, as symptoms have been found to be poorly correlated, even with severe GORD as measured by objective means (Frohlich et al. 2008, Castilloux et al. 2010, Tong et al. 2016). When objectively measured, prevalence ranges between 30-70% (van Lennep et al. 2019). Gastro-oesophageal reflux prevalence also varies by OA type, being present in almost all those with long-gap atresia (Lindahl et al. 1995).

Numerous mechanisms are reported to cause GORD in OA/TOF. Van Wijk et al (2013) identified abnormal relaxation of the lower oesophageal sphincter as the most frequent cause of GORD. In a study of 50 patients,

Koziarkiewixz et al (2015) also identified impaired motility, displacement of the gastro-oesophageal junction and delayed gastric emptying as causal mechanisms. Increased intra-thoracic traction caused by tracheomalacia has also been identified as a potential cause of GORD in those with OA/TOF pressure (Tomaselli et al. 2003).

Presence of GORD has been shown to be associated with negative outcomes in OA/TOF: anastomotic stricture, faltering growth, oesophagitis, Barrett's oesophagus/metaplasia, cyanotic episodes and respiratory complications (Krug et al. 1999, Legrand et al. 2012, Krishnan et al. 2016). Reflux is also proposed to have a causal relation with feeding difficulties, although evidence from empirical studies is lacking (Mahoney et al. 2017). As a result, expert consensus recommendations are for all children with OA/TOF under one year of age to be treated for GORD with proton pump inhibitors, followed by objective evaluation and monitoring (Krishnan et al. 2016). However, recent evidence fails to demonstrate efficacy for proton pump inhibitors in the management of any symptoms, other than reducing oesophagitis, and highlights increased presence of eosinophilic oesophagitis (Dimitrov et al. 2024, Tang et al. 2024). Treatment with fundoplication is also controversial as poor motility coupled with a "tightened" lower oesophageal sphincter can result in an increase in dysphagia, gagging and feeding difficulties in those with OA/TOF. Van Lennep et al. (2019) reported that 82% of children with OA/TOF who underwent fundoplication experienced post-operative dysphagia, compared to 46% pre-operatively and 41% experienced new onset, sustained symptoms. At present, optimal management of GORD and its role in the development of feeding difficulties in OA/TOF is unclear.

1.5.5 Oro-pharyngeal dysphagia

Oro-pharyngeal dysphagia is increasingly acknowledged to be present in children with OA/TOF. To date, study has largely been retrospective report of the presence of aspiration or laryngeal penetration on VFSS, with prevalence ranging from 8-50% (Fraga et al. 2015, Yalcin et al. 2015, Coppens et al. 2016, Yasuda et al. 2022, Maybee et al. 2023). Maybee et al.

(2023) found symptoms of oro-pharyngeal dysphagia were present at a mean of 2.3 years, compared to those of oesophageal dysphagia which were reported at a mean age of 4.5 years. Determining true prevalence from these figures is challenging as VFSS is typically conducted as a provoked assessment, only in the presence of symptoms, rather than as a population surveillance assessment. Thus, the reported prevalence is likely an over-estimate. The largest study to date reported VFSS results conducted in 165 children, out of a total cohort of 330 (Yasuda et al. 2022). Assuming oro-pharyngeal swallow function was normal in all those who did not undergo VFSS, aspiration/penetration prevalence was 33%. In addition to aspiration/penetration a number of other features of abnormal pharyngeal swallow function are reported: swallow initiation delay, reduced base of tongue to pharyngeal wall contact, reduced velo-pharyngeal contact, reduced hyoid movement, reduced airway closure and reduced upper oesophageal sphincter opening (Hormann et al. 2002, Yalcin et al. 2015, Coppens et al. 2016, Soyer et al. 2022, Maybee et al. 2023). More extensive evaluation of the prevalence and nature of oro-pharyngeal dysphagia is presented in Chapter 4.

Numerous pathophysiological mechanisms for oro-pharyngeal dysphagia have been proposed, including anatomical abnormalities, iatrogenic causes and altered physiology. Laryngeal cleft is a congenital abnormality in which the posterior larynx fails to fuse in utero. This creates a connection between the hypopharynx and larynx, allowing swallowed material to enter the posterior larynx or upper trachea (Fraga et al. 2015, Baxter et al. 2018). Four types of cleft are described, type 1 extends to the level of the vocal cords, type 2 extends below the vocal cords but not below the cricoid cartilage, type 3 extends through the cricoid into the posterior cervical tracheal membrane and type 4 extends into the thoracic trachea (Benjamin et al. 1989). Laryngeal cleft is estimated to co-occur with OA/TOF in 3-19% of cases and has been identified as a cause of pharyngeal dysphagia and aspiration in this population (Baxter et al. 2018, Londahl et al. 2018, Lejeune et al. 2021).

Additionally, vocal cord palsy, incomplete abduction or adduction of the vocal cords, has been reported in 5-7% of OA/TOF children (Hseu et al. 2015, Kovesi et al. 2018, Lal et al. 2018). It is likely iatrogenic, caused by damage to the vagus nerve during surgical repair (Kovesi et al. 2018). Increased aspiration risk occurs due to incomplete adduction of the vocal cords during swallowing. Yasuda et al. (2022) identified vocal cord palsy to predict the need for enteral tube feeding, with aspiration proposed as the reason for tube feeding.

Maybee and colleagues (2023) detected increased risk of oro-pharyngeal dysphagia in those with tracheomalacia, with greatest risk in those with severe tracheomalacia. DeBoer et al. (2016) reported a statistically significant higher rate of aspiration on VFSS in those with severe tracheomalacia than those with mild/moderate disease. These findings were both identified in relatively small retrospective cohort studies, therefore causative relationships cannot be assumed. However, the findings suggest there is a relationship between tracheomalacia and oro-pharyngeal dysphagia.

Abnormal upper oesophageal sphincter function has been hypothesised as a mechanism for aspiration (Yalcin et al. 2015). Montgomery et al. (1998) identified shorter time between pharyngeal contractility and upper oesophageal sphincter relaxation in a small cohort of adults with repaired OA/TOF using low resolution manometry and videofluoroscopy, compared to healthy controls. There were no differences in basal relaxation pressures or duration of relaxation, but the authors proposed that incoordination of swallowing occurs, which increases the risk of aspiration. However, no participants presented with aspiration or laryngeal penetration in this study. Romeo et al. (1987) conducted low resolution manometry in 20 newborns with unrepaired OA/TOF. They found incomplete upper oesophageal sphincter relaxation in 2/20. This study did not attempt to identify the functional impact of the incomplete relaxation; therefore, the implications are unknown. Despite these findings, there has been little further study of upper

oesophageal sphincter function and its role in oro-pharyngeal dysphagia over the last 30 years.

With regard to the impact of oro-pharyngeal dysphagia, Maybee et al (2023) reported an increased risk of abnormal chest CT, including presence of bronchiectasis (risk ratio = 3.0), in children with abnormal VFSS but did not identify an increased risk for pneumonia. However, determining the causative role of aspiration from oro-pharyngeal dysphagia on respiratory function in this population is hampered by use of retrospective cohort studies that fail to accurately delineate different types of dysphagia i.e. oro-pharyngeal from oesophageal (Kovesi 2017). Thus, identifying the source(s) of aspiration requires assessment of oro-pharyngeal and oesophageal dysphagia.

Reports of treatment for oro-pharyngeal dysphagia in the literature predominantly describe compensatory modalities, such as thickened fluids (Yasuda et al. 2022, Maybee et al. 2023), change of utensils or positioning (Maybee et al. 2023) or non-oral (tube) feeding (Maybee et al. 2023). No efficacy studies specific to this population for any of the reported management strategies have been found. Serel Arslan and colleagues (2017) describe a swallow rehabilitation programme involving 20 therapy sessions over 4 weeks. A group of 24 children with repaired OA/TOF and aspiration on at least one consistency identified on VFSS were randomly assigned to treatment (rehabilitation, mean age 12.09 months ± 7.52) or control (nonnutritive stimulation, mean age 15.33 months ± 11.15). Rehabilitation involved neuromuscular electrical stimulation to activate anterior neck muscles, thermal tactile application to trigger swallowing reflex and hyolaryngeal mobilization to support hyolaryngeal elevation. The authors reported statistically significant improvements in liquid and food aspiration, swallow trigger and residue scores post-treatment in the rehabilitation group but not the control group. However, there was no report of blinded outcome assessment indicating high risk of bias. Additionally, although pre-treatment VFSS was undertaken and aspiration risk identified, there was no description of the mechanism of aspiration. Consequently,

there was no justification for treatment selection - there was a lack of evidence of impairment at which treatment was directed - that is, there was no justification for why these treatments *should* work in this population. These limitations highlight the need to understand the mechanisms for aspiration, the pathophysiology of the swallow dysfunction, rather than describing the presence or absence of outcomes of dysphagia.

1.1.1. Mealtime difficulties

In addition to swallowing difficulties, mealtime difficulties are widely reported in OA/TOF (Traini et al. 2020), with challenging mealtime behaviours, prolonged mealtimes, and food refusal reported in up to 79% of children with OA/TOF (Menzies et al. 2017, Ax et al. 2021, Pham et al. 2022). Conversely, a recent study found that although children presented with frequent “choking” episodes, 90% demonstrated high levels of curiosity about food and 94% were happy to eat (Bevilacqua et al. 2020). Parental anxiety at mealtimes has also been reported. Wallace and colleagues (2021) reported a significant correlation between a need for Speech and Language Therapy intervention (used as a proxy for feeding difficulties) and higher levels of parental anxiety. Increased frequency of parent-reported choking episodes was associated with higher levels of parental mealtime anxiety (Bevilacqua et al. 2020). Parent mealtime anxiety has also been shown to negatively impact on parent-child interaction in infants with repaired OA/TOF (Faugli et al. 2008). The nature and prevalence of all mealtime difficulty characteristics will be presented in greater detail in Chapter 4.

A small number of studies have examined risk factors for the presence of a feeding disorder. Pham et al. (2022) only identified presence of low weight and the need for cortico-inhaled steroids as significantly different when comparing those with and without feeding difficulties. Other factors including OA subtype, presence of cardiac co-morbidity, length of stay, repair type and presence of post-operative complications were not statistically different. However, measures of gastrointestinal factors, such as presence of oro-pharyngeal dysphagia, GORD or dysmotility, were not included as variables. In a small retrospective study, Menzies et al. (2017) found no association

between any demographic (including OA type, prematurity, delayed repair) or gastrointestinal/respiratory complications (including GORD, dysphagia, strictures or chest infections). Thus, questions remain as to why some children present with feeding difficulties while others do not. Understanding factors that contribute to the development and maintenance of mealtime difficulties is key to developing appropriate interventions and improving outcomes.

1.5.6 Growth

Suboptimal weight and height have been reported in numerous studies of adults and children born with OA/TOF (Presse et al. 2016, Traini et al. 2020, Harrington et al. 2021, Harrington et al. 2022, Sparre et al. 2022). Establishing true prevalence is difficult due to a lack of agreed definition for suboptimal growth/height, use of different measures (including weight/height for age, height potential, z-scores, percentiles) and a lack of differentiation between OA/TOF subtypes, but suboptimal growth/height is estimated to occur in 9-15% of children with OA/TOF (Traini et al. 2020).

There is a growing body of evidence to suggest that faltering growth impacts children under one year of age, and that after this age the majority achieve adequate catch up growth (Vergouwe et al. 2017, Ko et al. 2020, Harrington et al. 2022). This is likely related to the higher prevalence of complications in the first year of life, including anastomotic strictures and leak which disrupt the child's ability to feed effectively and efficiently. Other identified risk factors for poor growth include lower birth weight, VACTERL association, long gap OA and GORD (Traini et al. 2020). Interestingly, dysphagia has not been shown to consistently correlate with poor weight. Legrand et al. (2012) found no significant association between dysphagia and low weight in a cohort of children with a mean age of 13 years. However, Menzies et al. (2017) report poorer growth in those with identified aspiration risk in a cohort of children with a mean age of 3 years. Presse et al. (2016) reported underweight adults in their study were more likely to have severe difficulties swallowing dry foods than those with normal range body mass index. Inconsistencies are likely related to selection bias, small study sizes and

different methods for calculating both dysphagia and suboptimal weight gain. Evidence to date supports careful monitoring of growth and nutrition, particularly in the first year of life.

1.5.7 Respiratory complications

Recurrent respiratory tract infections, pneumonia, wheeze and asthma are all widely reported in children and adults born with OA/TOF (Schier et al. 2001, Connor et al. 2015, Porcaro et al. 2017, Nurminen et al. , Rayyan et al. 2019, Lejeune et al.). Approximately 30% of children will have at least one episode of pneumonia in the first 3 years of life (Porcaro et al. 2017, Nurminen et al.), with up to 64% presenting with non-pneumonia respiratory infections in the first year of life (Lejeune et al. 2021). Although the frequency of respiratory infections decreases with age, around 25% of those over 10 years of age continue to experience recurrent respiratory infections (Connor et al. 2015). There is evidence that these frequent infections can lead to long-term lung damage with bronchiectasis in childhood reported in up to 14% of those with OA/TOF (DeBoer et al. 2016, Porcaro et al. 2017). Mechanisms for respiratory sequalae are summarised in the following sections.

1.5.7.1 Tracheomalacia

Tracheomalacia has been highlighted as the most significant predisposing factor to all other respiratory complications in the OA/TOF population (Koumbourlis et al. 2020). Tracheomalacia describes the anterior-posterior collapse of the tracheal wall. Involvement can extend to the bronchi (bronchomalacia). As seen in Figure 1-6, it causes the usual horseshoe appearance of the trachea to flatten, obstructing airflow and hindering secretion clearance (Koumbourlis et al. 2020). It has been proposed that almost all those with OA/TOF have a degree of tracheomalacia (DeBoer et al. 2016, Bergeron et al. 2017) caused by intrinsically altered or weak tracheal cartilage, potentially exacerbated by mechanical ventilation or prolonged intubation (Koumbourlis et al. 2020). Fischer et al. (2020) identified higher incidence in those with TOF than those with isolated OA.

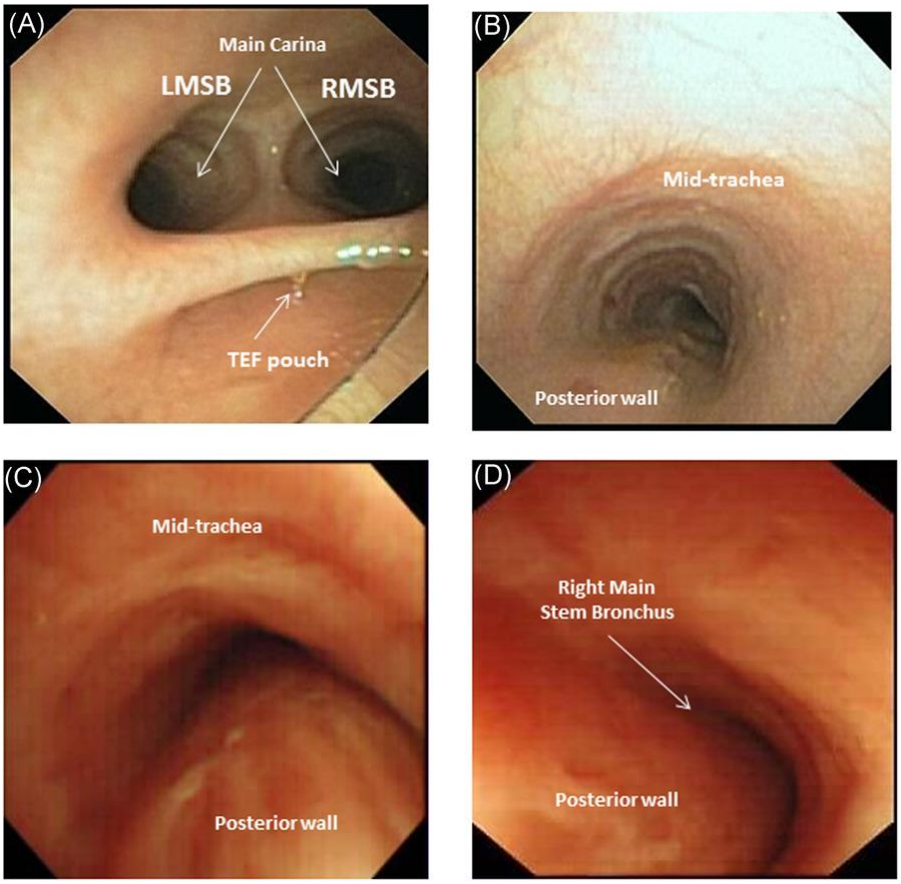


Figure 1-6. Appearance of tracheomalacia

Tracheoesophageal fistula and tracheobronchomalacia: A, TOF post repair. Note the ridge on the posterior tracheal wall above the carina as well a visible pouch (the pouch is often closed); B, At rest, the mid-trachea maintains its characteristic “horseshoe” shape; C, Severe obstruction of the trachea lumen and change in its shape due to the intrusion of the posterior membranous wall into the lumen during cough; D, Almost complete occlusion of the right main stem bronchus during cough. TEF, tracheoesophageal fistula.

Image reproduced with permission from Koumbourlis et al. (2020).

In addition to increasing risk of recurrent lower respiratory tract infections due to colonisation of retained secretions, tracheomalacia can lead to cyanotic episodes, particularly during episodes of increased intra-thoracic pressure, such as crying or feeding. Cyanotic episodes also occur during eating/drinking due to a bolus induced dilation of the oesophagus compressing the trachea (Wallis et al. 2019). Children present with a

distinctive sounding “brassy” cough (Fraga et al. 2016). Flexible tracheobronchoscopy is the gold standard method of diagnosis, during which the characteristic collapse of the tracheal lumen can be observed (Fraga et al. 2016, Wallis et al. 2019). Visual interpretation of percentage of lumen collapse is used to determine severity of malacia (Wallis et al. 2019). There is evidence to indicate that tracheomalacia improves with age, and treatment may be symptomatic until such time that tracheal cartilage “stiffens”. However, in cases of severe tracheal collapse causing cyanotic episodes, surgical treatment is aortopexy or tracheopexy is required (Wallis et al. 2019, Koumbourlis et al. 2020).

The presence of an association between tracheomalacia and oro-pharyngeal dysphagia has already been briefly described in section 1.5.5 and the presence of cyanotic episodes due to tracheal compression within the oesophagus described above. Thus, it is evident that tracheomalacia is of relevance to the exploration of feeding and swallowing difficulties. However, examination of the mechanism of the association, prevalence, and the impact on the development of feeding disorder remain unresearched.

1.5.7.2 Aspiration

Aspiration, defined as inhalation of oral or gastric contents into the lower respiratory tract, has been associated with chronic respiratory morbidity, including bronchiectasis, in those with OA/TOF (Kovesi 2017). Aspiration can lead to respiratory compromise, including aspiration pneumonitis (acute inflammation caused by inhalation of acidic or caustic material such as gastric contents) and aspiration pneumonia (infection caused by inhalation of bacteria typically residing in the oro-pharynx). Recurrent or repeated infection can lead to chronic lung damage, including bronchiectasis. Both oro-pharyngeal dysphagia and gastrointestinal conditions are risk factors for aspiration pneumonia and are of relevance to those with OA/TOF (Kovesi 2017).

Diagnosis of aspiration-related respiratory sequalae is challenging, with no gold standard assessment available. Typically, diagnosis is made by the

presence of risk factors, such as oro-pharyngeal dysphagia, GORD or oesophageal dysmotility in conjunction with evidence of respiratory sequalae on chest CT or broncho-alveolar lavage (Torres-Silva 2018). However, determining the contribution of specific risk factors when multiple factors co-occur, as is the case in OA/TOF, is not possible. Optimum management requires evaluation of all potential causes, as recognised in recent consensus recommendations (Koumbourlis et al. 2020).

In summary, those with OA/TOF are at risk of gastrointestinal and respiratory complications from many underlying conditions and abnormalities. These factors co-exist and interact with each other. Feeding and swallowing difficulties can both cause and exacerbate gastrointestinal and respiratory complications.

1.6 A summary of current knowledge of paediatric feeding disorder in OA/TOF

In Table 1-3 the PFD framework (Goday et al. 2019, Sharp et al. 2022) has been used to summarise the current knowledge of how feeding and swallowing difficulties are impacted in OA/TOF. The evidence supports the concept that it is a multi-dimensional phenomenon, with all PFD domains impacted. Gaps in current understanding regarding the nature, prevalence, and severity of feeding and swallowing in this population have been highlighted in this introductory chapter. At the end of the thesis, this framework will be revisited to consider how findings have enhanced understanding of the complex phenomenon that is feeding and swallowing.

Table 1-3 Existing knowledge of paediatric feeding disorder in oesophageal atresia/tracheo-oesophageal fistula

Medical domain	Nutritional	Feeding skill	Psychosocial
Delayed introduction to oral feeding	Reliance on non-oral feeding	Prolonged mealtimes	Food refusal
Intubation	Suboptimal growth	Diet not age typical	Altered caregiver-child interaction
Oro-pharyngeal dysphagia	Nutritional deficiency	Modified food textures	Caregiver stress and anxiety
Oesophageal dysmotility		Modified drink textures	
GORD		Needing to drink water when eating	
Anastomotic stricture, leak, recurrent TOF			
Tracheomalacia			
Congenital heart disease			

GORD = Gastro-oesophageal reflux disease, TOF = Tracheo-oesophageal fistula.

At present assessment of, and intervention for, feeding and swallowing difficulties in this population are based on knowledge “borrowed” from other conditions and are, as such, non-specific to OA/TOF. As has been highlighted throughout this introductory chapter, feeding difficulties in OA/TOF can potentially arise from numerous factors. Yet our understanding of their interaction and relative contribution to outcome is unknown. Generating a deeper understanding of the phenomenon will provide a firm grounding upon which to base care pathway decisions, such as which assessments are required and when, and to guide choice of intervention – be that use of an existing, or development of a new, treatment. While many of our interventions lack a strong evidence base, as traditional intervention studies are very difficult to achieve in rare populations, we can generate an understanding of the problem so that assessment or intervention decisions are based upon sound theory of why they *should* work.

1.7 Aims and objectives

Given the multi-dimensional nature of feeding and swallowing difficulties, a mixed methods exploration of feeding in children born with OA/TOF has been conducted to build on the evidence base for their nature, severity, and prevalence.

Aim

To characterise feeding and swallowing skills and difficulties in children with repaired OA/TOF.

Objectives

- To describe pharyngeal and oesophageal stage swallow physiology in children under 1 year of age with repaired OA/TOF.
- To describe the parental experiences of establishing feeding and mealtimes in children with OA/TOF.
- To determine how feeding difficulties associated with OA/TOF impact on parental quality of life and well-being.
- To determine the prevalence and characteristics of feeding and swallowing difficulties in OA/TOF
- To develop an interactional model of feeding difficulties in children with OA/TOF.

1.8 Thesis outline

The thesis contains data from three work packages, presented in four thesis chapters. Specific aims, objects and methods are described for each project within each chapter. Results are synthesised in a subsequent chapter.

Work package one, part one (Chapter 2) explored feeding and swallowing difficulties in OA/TOF from the parent perspective. Using a phenomenological approach, data relating to parents lived experience of

establishing eating and drinking with their child were collected using an online discussion forum. Data qualitatively described the nature of the eating, drinking, and feeding, and the impact that difficulties had on parental well-being and family functioning. Data were analysed using reflective thematic analysis and used to develop an initial model to explain the development and maintenance of feeding difficulties in OA/TOF.

Work package one, part two (Chapter 3) evaluated the phenomena described by parents in the qualitative study using a questionnaire design. Quantitative data regarding the nature of the feeding difficulties were collected using validated measures of feeding difficulty, alongside parent report of medical and demographic data. Validated measures were also used to assess aspects of parent mental health. Multiple regression analyses were used to explore potential causal relationships and associations between parent and child factors, to develop and strengthen the model developed from the qualitative data.

Work package two (Chapter 4) consisted of a mixed-methods systematic review of the characteristics of feeding and oro-pharyngeal swallowing difficulties. This included meta-proportional analyses to estimate prevalence of different characteristics of feeding and swallowing difficulties. These data were collated to enable use of existing data to inform development of the model.

Work package three (Chapter 5) was a study of swallow physiology. A small, prospective cohort design was used to collect data from 12 infants at three time points within the first year of life. Detailed assessment of oro-pharyngeal and oesophageal swallow function was undertaken using videofluoroscopy and high-resolution impedance manometry at between 2-4 months and 8-10 months of age, providing pre- and post-weaning data. Functional feeding outcome was evaluated by parent interview at 12 months of age. Using novel methods, this study provided rich data to further understanding of swallow physiology, mechanisms underlying pharyngeal impairment and the impact of dysphagia on functional outcome. These data

were used to evaluate the role of swallow function on feeding outcome within the proposed model.

Synthesis and clinical implications (Chapter 6). The PFD domains and the original model generated from the qualitative data are revisited to generate a hypothesis as to how different components of eating, drinking, and swallowing interact and ultimately impact on outcome. Development of the model provides a theoretical foundation to underpin decisions regarding appropriate timing and methods of assessment and intervention to optimise and improve outcomes for children and their families. These are summarised as clinical implications of the findings.

1.9 Methodology

This PhD employed a mixed methods approach. Mixed methods methodology is defined as research that employs both qualitative and quantitative data in response to research questions and hypotheses. A fundamental component of this methodology is the integration of the results from both quantitative and qualitative sources (Creswell et al. 2017). Mixed methods research is often used to explore broad, complex, and multi-faceted issues, such as feeding and swallowing difficulties. The integration of methods leads to better understanding of the phenomenon and can help develop and test theories to explain the causal mechanisms underlying said phenomenon (Mukumbang 2021). It is differentiated from multi-methods research, in which more than one quantitative or qualitative method is used within a study but methods are not mixed or integrated (Hesse-Biber et al. 2015).

Mixed methods research can be conducted for many different purposes, including the need to obtain more complete or corroborated results, to explain a result, to explore a phenomenon to inform instrument selection, to describe or compare cases, to include the participant or stakeholders' voice in research or when developing or evaluating an intervention (Creswell et al. 2017). In these scenarios the mixing of methods creates an output arguably

greater than the sum of its parts. It allows for some of the shortfalls of one method to be met by the advantages of another. For example, providing an understanding of context or individuality that might be absent from quantitative study, alongside generalisability that may be challenged in a pure qualitative study (Fetters et al. 2015).

As described by Creswell et al. (2017), research study design is determined by a research paradigm (a worldview determined by the researcher's beliefs – epistemology and ontology), which influences the theoretical rationale for the study, which then determines the methodology (such as qualitative or quantitative), from which the methods of data collection are determined (such as an experiment, questionnaire or interview). The following sections describe and justify the methodology, research paradigm and theoretical rationale adopted within this PhD.

1.9.1 Research paradigm

Research should be founded upon a philosophical framework, a set of values which consist of one's ontological commitments, epistemological beliefs and methodological preferences (Allemang et al. 2022). Quantitative research is typically founded upon a postpositivist belief system, whereby researchers acquire knowledge based upon a belief that a hypothesis can be generated from a theory that through research is rejected, or not. The belief is that there is a single truth. Qualitative research perceives that knowledge is generated from the individual, thus there are multiple truths. Research aims to *generate* theory, and answer the question, from enquiry at an individual level, rather than test a specific hypothesis. This is determined as a constructivist paradigm. As a result of these opposing belief systems, mixed methods research requires use of an alternative paradigm. The most commonly adopted, and the one adopted for this PhD, is pragmatism (Creswell et al. 2017). Pragmatism is founded upon a philosophy of understanding "what works" and understanding real-world practice. Where complex problems exist, the best methods are used in order to answer the research question, allowing for the integration of multiple data sources rather than being limited to methods aligned with a paradigm as with postpositivism

or constructivism (Allemang et al. 2022). The pragmatist researcher believes that both a single truth and multiple truths exist – there may be a theory to explain a phenomenon but it is important to assess how individual experiences change the nature of that phenomenon (Hesse-Biber et al. 2015, Creswell et al. 2017).

The aim of my research was to enhance understanding of feeding difficulties in OA/TOF. As discussed in section 1.4, feeding difficulties in childhood are multi-faceted, and can involve, for example, changes to swallow physiology, neurodevelopmental issues or neurodiversity, parent interaction and environmental factors. It is my belief that some of these factors are better suited to a hypothesis driven research question or, in a postpositivist framework, identification of a single truth. Within my research generating knowledge of swallow physiology fits this framework. However, other factors are more impacted by how the individual experiences the world. In my opinion, an individual's beliefs, attitudes, experiences, and environment will influence how swallowing difficulties impact on *feeding* or the whole mealtime experience. Therefore, a postpositivist stance, whereby a single truth is sought, is not the most effective way of generating new knowledge of this aspect of the phenomenon. Here, qualitative research can help to understand individual differences. This ontological perspective, which recognises singular and multiple realities, is supported by pragmatism. Epistemologically, use of a pragmatist framework, taking a "what works" approach, supported use of different methods to answer questions about different aspects of the feeding difficulty phenomenon. Methodologically, integration of the mixed methods built a more complete picture and understanding.

1.9.2 Theoretical perspective

A challenge within mixed methods research is the seemingly contradictory standpoints of postpositivist and constructivist use of theory. Within postpositivism, theory is used deductively, identified at the beginning of the study, to make and then test predictions. Within constructivism, theory is used inductively, often generated through the research to provide an

explanation of what was found (Creswell et al. 2017). Within mixed methods research, Creswell et al. (2017) assert that a social science theoretical approach can be applied. This involves identification of a theory which is used as an *a priori* framework to guide question development. The theory then provides a framework for the integration of quantitative and qualitative findings, which may involve development of the theory or model.

Within this study, the biopsychosocial model of feeding and feeding difficulties described by Berlin et al. (2009) was the guiding principle used to support the assertion that feeding is multi-faceted and interactional. Research questions were generated to investigate different factors within the model and research was designed using methods best suited to each of these questions.

The recent work developing the term “paediatric feeding disorder (PFD)” provides an opportunity to use a shared language and diagnostic criteria that are increasingly being adopted within clinical and research arenas (Goday et al. 2019). Therefore, I feel it is also important to frame my study’s findings within the PFD context. The biopsychosocial model is provided as the overall theoretical perspective, with the PFD framework used to provide a method for integrating study findings in a clinically relevant manner.

1.9.3 Research design

By their very nature, mixed methods research studies can be designed in a wide variety of ways. The design is dependent on the study goals, conceptual framework, research questions, methods and validity considerations (Maxwell et al. 2015). Creswell et al. (2017) describe three core mixed methods designs – explanatory sequential, exploratory sequential and convergent – one or more of which can be applied in a wide range of ways. Designs differ by the role and relative priority of the quantitative and qualitative elements. The choice of design is ultimately determined by the purpose of the study.

Briefly, convergent studies simultaneously obtain quantitative and qualitative data, which are then combined or contrasted to best understand a research problem. Historically, this has been associated with data triangulation (Moseholm et al. 2017). Within this design quantitative and qualitative data are collected independently of each other but concurrently. One does not rely on data from the other. Another key facet is that each dataset is of equal importance. Once the data are collected and analysed, results are merged with the researcher determining the extent to which the results diverge or converge and relate to each other. Results are then combined to generate an answer to the research question. Data may be merged by way of a joint table or graphic.

Explanatory sequential studies describe a design in which quantitative data are collected first, then specific components explained in follow up qualitative inquiry. This may be adopted to explain unexpected findings or outlier results (Morgan 2013). It is typical for the quantitative element to be seen as the primary component and qualitative as supplementary. Integration occurs in the design of the qualitative study and after completion of the qualitative study, during which the two sets of connected data are used to explain and detail the findings (Creswell et al. 2017).

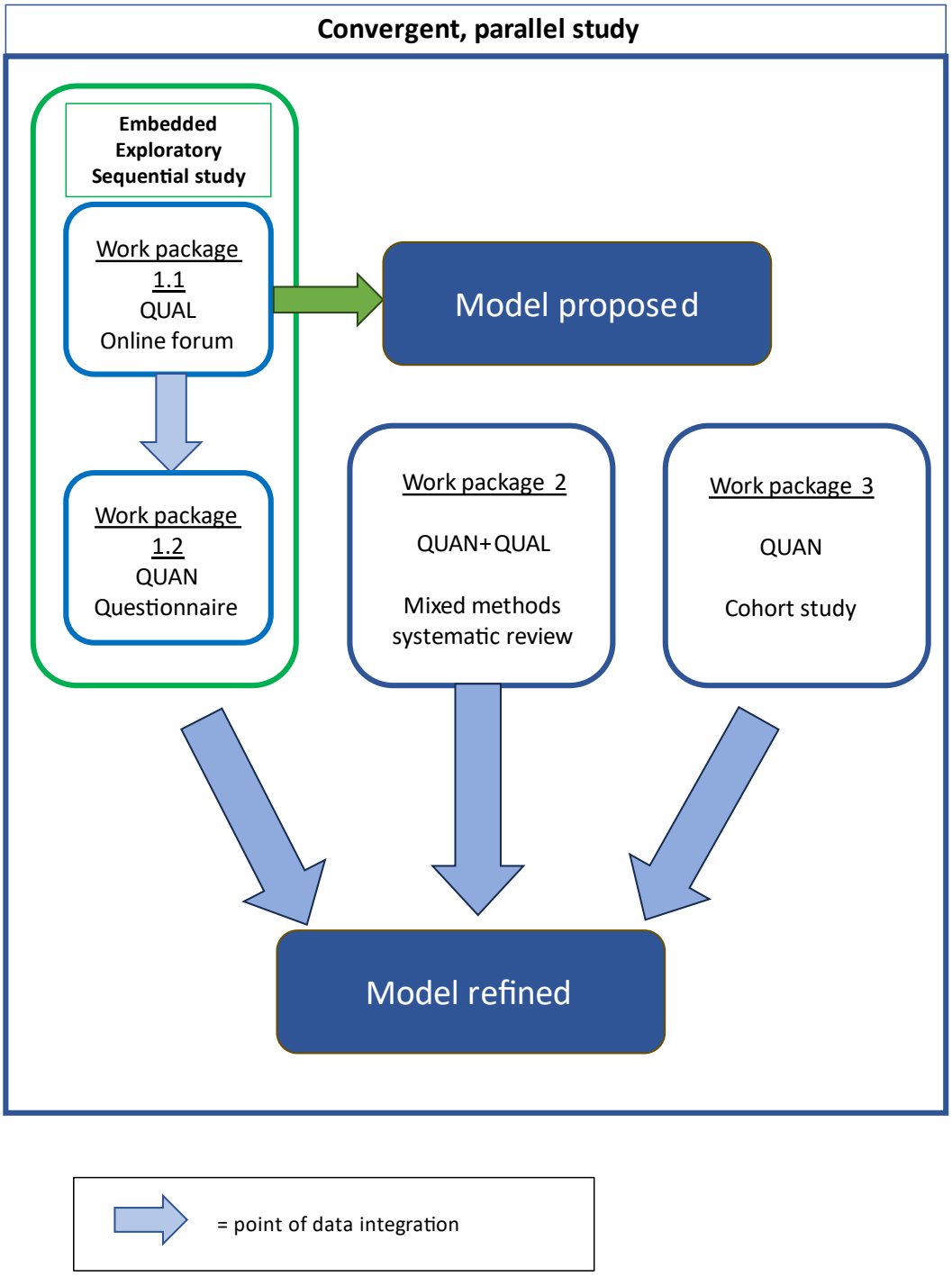
The final mixed methods typology is the exploratory sequential design. In this design, initial data collection and analysis is of a qualitative nature. Qualitative data inform development of a tool or intervention that is used to collect quantitative data. This enables the quantitative component of the research to be informed by participants or the community to whom the research is of relevance, rather than being pre-determined by the researcher themselves or pulled “off the shelf” (Creswell et al. 2017). This may be required when measures or instruments do not exist for the research in question, variables are unknown, there is no guiding framework or theory, or an existing tool requires adaption to meet the needs of the participants. It is also used to generalise results from qualitative research, test an emergent theory or measure the prevalence of findings (Morgan 2013). Integration

determines the ways and extent to which qualitative findings are generalisable or their results extended (Creswell et al. 2017).

As described by Creswell et al. (2017), these research typologies are not suitable for every study design. Core designs may be mixed or complemented by other methods in more complex studies. This was the case in my PhD. The overall design was influenced by two fundamental principles of the pragmatism paradigm. The first was that the research question should drive the choice of research design and second that problems are best defined by the individuals experiencing them, which leads to the development of actionable research questions (Allemang et al. 2022). It is also my assertion that to generate greater understanding, the concept of feeding difficulty in this population should be described by those experiencing it. In this context, this was the parents, as the focus of this study was early childhood. The overall study followed a convergent design but within this was an embedded exploratory sequential study (QUAN = quantitative study, QUAL = qualitative study.

Figure 1-7). The qualitative element of this exploratory study informed development of a model of feeding difficulties in TOF/OA. This model was tested and developed with data from the other studies within the PhD. The qualitative data were used to design a quantitative, questionnaire study forming a sequential, exploratory study. However, this questionnaire was not the most appropriate way of assessing all components of the "feeding" phenomenon. Evaluation of swallow physiology required use of direct swallow assessment within a prospective cohort study. As the qualitative data did not expressly inform the design of the cohort study, it cannot be determined a sequential study design. Rather the cohort study was determined as the most appropriate way to obtain data regarding a different component of the overall "feeding" phenomenon, i.e. swallow function. Likewise, a systematic review was determined the most appropriate way to determine prevalence data for characteristics of feeding and swallowing. Data from all four studies were then integrated and used to test the relationships within the model and refine its design and increase the generalisability of findings. This process is represented graphically in QUAN = quantitative study, QUAL = qualitative study.

Figure 1-7.



QUAN = quantitative study, QUAL = qualitative study.

Figure 1-7. Research study design

One of the major challenges associated with use of mixed methods research is the requirement for knowledge and skills with a range of methods and techniques. These challenges were addressed within my PhD by having a multi-disciplinary supervisory team, familiar and expert in different aspects of my research methods. Prof Jo Wray, my primary supervisor, Dr Roganie Govender and Dr Christina Smith are all experienced mixed methods researchers.

1.9.4 Research methods

The methods of data collection and analysis for each element of the study are described within the relevant thesis chapter.

1.9.5 Patient and public involvement and engagement

Patient and public involvement and engagement (PPIE) have been central to the development of this project. Following initial idea conception I engaged with 'TOFS', a national support group for individuals with OA/TOF and their families. My proposal was put to the charity council who recognised the lack of research in this area and were supportive of further investigation, writing a formal letter of support and providing £250 for PPIE activity. They facilitated recruitment of 10 families of pre-school children with TOF/OA with whom telephone interviews were conducted to develop the research questions and methods.

Key concerns raised by families related to lack of knowledge and understanding of the specific feeding and swallowing difficulties that children with OA/TOF experience. Parents felt that the information given was generic and did not take account of individual differences or the spectrum of abilities. Parents expressed frustration that local professionals had limited experience of OA/TOF, and that accessing specialist support was difficult. One mother had reviewed the literature and expressed surprise that there was no evidence-base for the current advice given. This project reflects this feedback, examining the underlying nature of the physiological and psycho-social aspects of feeding/swallowing difficulties. The PPIE group also guided overall study design by highlighting the frequency and enthusiasm with which

Facebook is used by support group members – thus informing use of the online forum method. The longitudinal nature and acceptability of the swallow assessment protocol was also informed by the PPIE members, ensuring favourable recruitment and retention within the cohort study.

At the start of the PhD fellowship a steering group was established, consisting of a dietitian, a speech and language therapist and four parents of children with OA/TOF. This group was consulted throughout the fellowship period on many aspects of study design. The steering group advised on appropriate methods of recruitment and advertising, ensuring recruitment was sensitive to the needs of families at a potentially traumatic time. The group were involved in writing all participant introductory and information leaflets, facilitating readability and inclusion of factors families felt important to decision-making, such as the length of time they might expect their child to experience discomfort during swallow assessment. One parent member of the steering group designed the layout of the leaflets to be more easily read and visually appealing. The steering group co-developed the questions for the online forum and questionnaire studies, providing advice on topic and wording. The steering group were also involved in cross-checking theme development from qualitative data, adding to the generalisability of findings. Specific contributions of the steering group to study design and analysis are outlined in each project chapter.

1.10 Chapter summary

In summary, this chapter outlines the concept of childhood feeding difficulties as a multi-faceted phenomenon impacted by biological, psychological, and social factors. It acknowledges feeding is a dyadic process, involving a feeder (typically a parent or caregiver) and the child. The chapter also introduces oesophageal atresia/trachea-oesophageal fistula as a rare, complex congenital abnormality that results in considerable gastro-intestinal and respiratory morbidity. It is acknowledged that feeding difficulties occur as part of the post-repair course. However, knowledge to date is limited by a lack of understanding of the underlying nature of these difficulties, their

prevalence and severity. Data to date have often been siloed, investigating one aspect of swallow function, or feeding difficulty, limiting awareness of how different components interact. This study aimed to develop understanding of this concept through generation of an OA/TOF specific model of feeding difficulty and mapping components onto the paediatric feeding disorder framework using a convergent mixed methods study design.

Chapter 2. Work package 1.1: Online forum

2.1 Introduction

[1]As outlined in Chapter 1, there is limited literature describing the exact type, nature and extent of the feeding difficulties experienced by children with OA/TOF. Symptoms are reported: coughing or choking when eating, difficulty with specific textures of food, needing water to move food through the oesophagus and prolonged mealtimes, but details of the underlying causes, severity and prevalence are lacking (Baird et al. 2015, Bevilacqua et al. 2020, Ax et al. 2021). Also outlined was the importance of acknowledging eating and drinking in children as a dyadic interaction, occurring between parent/caregiver and child. Understanding of OA/TOF-related feeding difficulties on the parent/caregiver aspect of the dyad is even less well understood.

2.1.1 Aims and objectives

The starting point for this thesis is a characterisation of eating and drinking in OA/TOF from a parent perspective. It was assumed that those with lived experience of feeding in OA/TOF would be best placed to describe the phenomenon. As eating and drinking difficulties exist from birth, the parent perspective can provide insight into the nature of childhood feeding and afford the opportunity to explore the impact of any difficulties on the feeding dyad. The objectives of the research were:

1. To describe parents' experiences of their child's eating and drinking through childhood.

2. To explore how the process of feeding their child impacts on a parents' well-being.

[1] This chapter is based on previously published work: Stewart A, Smith CH, Govender R, Eaton S, De Coppi P, Wray J. Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula. Journal of pediatric surgery. 2022 Dec 1;57(12):792-9.

3. To describe parental experiences of accessing support for managing eating and drinking difficulties.

2.2 Method

2.2.1 Theoretical framework

A phenomenological approach underpinned use of an online forum to explore parents' experiences of eating and drinking in children born with OA/TOF. Phenomenology aims to describe the essence of a phenomenon by exploring an individual's experience of said phenomenon (Neubauer et al. 2019). Exploring *what* and *how* the phenomenon is experienced by an individual generates understanding through new appreciations or reorientations (Neubauer et al. 2019). Although these experiences are examined at an individual level, acknowledging the individual's "lifeworld", this approach asserts that commonalities in individual experience exist that can be drawn together to generate a universal essence of the phenomenon (Smith 2015). Phenomenology can be divided into "descriptive" and "interpretive" approaches (Sundler et al. 2019). Descriptive phenomenology, initially conceived by Husserl, requires the researcher to suspend their own beliefs, knowledge, and life experience to describe the lived experience of others (Neubauer et al. 2019). Interpretative or hermeneutic phenomenology, developed by Heidegger, asserts that it is not possible for the researcher to suspend their own beliefs or experiences, but that interpreting the lived experience of others requires acknowledgement of one's own "lifeworld", a reflection of our own experience and how that may influence the interpretation we make of others experiences i.e. the research data (Neubauer et al. 2019). Interpretive phenomenology determines that deeper understanding can be generated by interpreting meaning beyond the immediately observable description (Smith 2015). Subsequently, researchers have argued that phenomenological research need not be rooted entirely in a descriptive or interpretative dimension (Sundler et al. 2019). The approach taken in this study was descriptive but, as described by Sundler et al. (2019), was based on the principles of openness,

acknowledging my pre-understanding of the phenomenon and adoption of a reflexive attitude to analysis.

2.2.2 Data collection

Data were collected using an online forum method. Online forums, such as Facebook groups, are often used by support groups to connect individuals, providing effective peer support, and are particularly useful for those with rare diseases (Titgemeyer et al. 2022). Such forums, conducted in collaboration with patient support groups, have been shown to be effective methods of rapid data collection in health research, facilitating participation from geographically wide areas (Wray et al. 2018). They allow participants to answer questions at a time and in a place convenient to them, particularly useful for participants with caring responsibilities and limited time. This type of communication has been defined as “asynchronous” i.e. do not require immediate feedback. This had led them to being determined as easier and safer than offline methods of communication, such as interviews (Stehr 2023).

Facebook discussion is a familiar medium through which parents share knowledge and experience (Bartholomew et al. 2012). Patient and public involvement conducted with 10 parents of children with OA/TOF at the point of project development identified active use of Facebook as a means of peer support for this population. Thus, an online forum was determined to be a particularly useful method of data collection for the target population.

TOFS is the largest UK support group for individuals born with OA/TOF and their families. At the time of writing, it has approximately 1520 parent members of children aged 6 months-11 years and 3200 members of the Facebook group. In collaboration with TOFS, a research-specific, private Facebook group was launched. A standard operating procedure was agreed between the research team and TOFS (Appendix 1). An experienced member of the TOFS Facebook group, who was herself a parent of a child born with OA/TOF but was independent of the research team, was paid to moderate the forum.

2.2.3 Ethical approval

This study was granted NHS/HRA ethical approval (NRES 20/LO/0098; IRAS 262966) as part of a single ethics application for all work packages in this PhD.

2.2.4 Participants

Convenience sampling was used to recruit parents of children aged 0-18 years with OA/TOF living in the UK. The TOFS support group advertised participation to their members by email and on their Facebook group. An electronic link to a full participant information sheet (PIS) was provided and potential participants were directed to this prior to joining the Facebook group. The PIS is provided in Appendix 2. Interested parents were asked to apply to join the research Facebook group, with access granted by the moderator after participants consented to participation by agreeing the group "rules":

1. I understand that I will provide basic personal information to allow the research team to know who took part in the forum but that they will not be able to identify me by name.
2. I understand that all my responses will be analysed anonymously. The results of the study will be reported for the forum discussion as a whole and I will not be identified in any report or publication.
3. I understand that the results of the study will be published and shared with professionals at conferences and in journals and a summary of the results will be available on the TOFS website and shared in the CHEW newsletter.
4. I understand that information I give in relation to this project in any online posts may be anonymised and directly quoted in publications and presentations.

2.2.5 Data collection

Twelve questions, provided in Table 2-1, were co-developed with the PPI group consisting of four parents of children with OA/TOF, one dietitian and one speech and language therapist and reviewed by the medical advisory

group at TOFS, ensuring pertinent issues were explored in a sensitive manner. After joining the Facebook group, participants provided demographic data via a link to a separate Survey Monkey questionnaire. These data were used to describe group characteristics but were not linked to individual responses. Each question was posted individually by the moderator. Participants provided a response to the question by posting a comment. Participants were able to read others' responses to the question and could "like" or respond to each comment. Participants could choose whether to answer any question. A new question was posted once there were no further comments to the existing question. The moderator answered participant questions and prompted for clarification or explanation if required, for example if answers were limited to practical details the moderator might ask the respondent to elaborate. Participants were also able to respond privately to the moderator. To facilitate access and participation, parents not using Facebook, or not wishing to share information on the forum, could participate via email.

Table 2-1. Online forum questions

What were your early experiences of feeding your child? How did you feel in those early days?
For those of you with children who are old enough, what were your experiences of starting weaning/pureed foods? How did offering your child food make you feel?
For those of you with children who are old enough, what were your experiences of moving on to chewable foods? How did moving on to chewable foods make you feel?
Thinking about your child's feeding, what has gone the best and what has been the most challenging aspect for you as a parent?
For those of you with older children, what were your experiences of supporting your child's eating/drinking when they started nursery/early years childcare and/or school?
How have you adapted mealtimes to support your child? How do you promote a positive relationship with food?
What are your experiences of other family members' or friends' involvement with your child's eating/drinking?
What are your experiences of eating out with your child? Do you feel confident eating out with your child (pre-COVID!)?
What has been your experience of supporting your child to feed themselves? How have you helped your child gain independence with eating/drinking?
What was your experience of seeking support or advice for feeding or swallowing related concerns, pre-COVID? Who provided you with the most useful information?
What has been your experience of explaining your child's swallowing to them and others?
If you could give another parent of a child with OA/TOF one piece of advice about feeding, what would it be?

2.2.6 Data analysis

All responses were anonymised by the moderator and sent by email the lead researcher in MS Word format. Data were analysed using reflexive thematic analysis (Braun et al. 2022). Phenomenological research requires a method for interpreting the data obtained. Typically this involves thematising to develop underlying meaning or interpretations (Sundler et al. 2019). There are numerous analysis methods available for achieving this, including grounded theory, interpretive phenomenology and discourse analysis (Braun et al. 2019, Braun et al. 2020). Reflexive thematic analysis was chosen as it provides a flexible method which can be used at a sematic or inductive level and is often aligned with phenomenological research (Braun et al. 2020). It involves the development of themes, generated by the researcher in response to the interpretation of data coding (Braun et al. 2022). However, unlike other interpretive methods, such as interpretive phenomenology analysis (IPA) or grounded theory, it is suited to analysis across the whole data set, rather than at an individual level (Braun et al. 2020). Use of an online forum data collection method resulted in anonymous data collection from a larger number of participants than is often achieved in qualitative research. Not all participants answered all questions. Data were provided to without identifiers and responses were not linked to demographic details. Thus, analysis at an individual level was not conducted. Using reflexive thematic analysis allowed for inductive analysis and theme generation in the absence of individual level data.

Data analysis was undertaken using the method described by Braun et al. (2022).

1. Initial analysis involved familiarisation with the data, reading through the transcripts and identifying initial ideas. Data familiarisation was undertaken by AS and members of the supervisory team (JW, CS and RG) to enable discussion and reflection. Data were then coded line-by-line by AS.

2. Coding was conducted at a semantic level to identify explicitly stated feeding behaviours and difficulties described by parents and experiences of

parents. Latent codes were also developed from data relating to parent experiences of feeding their children.

3. Codes were then organised into initial themes, summarising the parents' experiences, and discussed with the whole research team. Tables of codes with supporting quotes were reviewed by the PPI group providing reflections on the data from different personal perspectives.

4. Following discussion and reflection, themes were refined, further developed, and given names.

5. Themes were then described and illustrated in the writing up process.

2.2.7 Researcher reflection

An essential part of reflexive thematic analysis and phenomenological research is an awareness of the position of the researcher, acknowledging that interpretive research will be undoubtably influenced by the researcher's own life experience and that true "bracketing" of one's own experience in the interpretation of research data is impossible (Braun et al. 2019). This is typically achieved through self-reflection, locating oneself in relation to research participants considering how this might influence what you take from the data or what you may take for granted (Braun et al. 2022). Analysis of one's own position allows for optimal subjectivity in the interpretation of other's experiences (Braun et al. 2022). Thus, my position as both a speech and language therapist and mother are acknowledged, and their influence considered.

My interest and drive to engage with parents as a primary source of information for understanding the nature of feeding difficulties is influenced by the value I place on the parent being the expert in their child's difficulties. I have worked with children with feeding and swallowing difficulties since 2002, in hospital in-patient and out-patient settings, as well as in community settings, including people's homes. I have observed the long-term struggle that can result from having a child with a swallowing difficulty. Yet despite this

experience, I acknowledge that I will only ever have a limited understanding of the daily reality and true nature of the child's difficulties when in a position of professional "expert" from whom the families are expecting advice and support. Thus, undertaking this qualitative research is driven by a desire to gain a deeper understanding, giving a voice to those who I believe to be the true experts by virtue of their everyday experiences to enrich my own and others' understanding of the difficulties.

While there is distance between my own experience of a child with feeding difficulties given my professional standing, I share experiences of motherhood with the participants. Analysis was undertaken through the lens of an acknowledgement of and empathy with the stressors of motherhood. The importance of understanding and highlighting the impact of these stressors is in part driven by a belief that the child's outcome is inextricably linked to the behaviours of the parents, and the primary caregiver in particular. Empathy with research participants was heightened by similarities between me and many of the research participants, being a mother of young children. I have seen the benefit of being part of an online parenting community on Facebook, albeit not related to any specific difficulty or condition, which influenced my confidence that parents would be likely to feel comfortable and be familiar with sharing personal information within this forum.

2.3 Results

2.3.1 Participants

One hundred and twenty-seven individuals joined the research-specific Facebook group, 83 (65%) of whom provided demographic data, presented in Table 2-2. Forty-four of the Facebook group elected not to provide demographic details. Comparison of those providing and not providing demographic information was not possible. There were 85 unique responders to the Facebook forum.

Table 2-2. Demographic data provided by 83 respondents to the demographic survey.

		Number (% of 83 responders)
Relationship to child	Mother	74 (89)
	Father	4 (5)
	Individual with OA/TOF*	1 (1)
	Missing	4 (5)
Ethnicity	White	75 (90)
	Asian or Asian British	2 (2)
	Mixed Ethnicity	2 (2)
	Missing	4 (5)
Geographical location	England	53 (64)
	Scotland	10 (12)
	Wales	2 (2)
	Northern Ireland	0 (0)
	Outside of the UK	18 (22)
Respondent age	18-24	1 (1)
	25-34	31 (37)
	35-44	44 (52)
	45-54	7 (8)
	55-64	1 (1)
Age of child	Under 12 months	13 (16)
	12-23 months	16 (19)
	2-4 years	28 (34)
	5-11 years	16 (19)
	12 and over years	6 (7)
	Did not respond	4 (5)
Type of OA/TOF	OA and TOF repaired at birth	70 (84)
	OA and TOF delayed repair	7 (8)
	TOF only (repaired)	4 (5)
	OA only (repaired)	2 (2)
	OA unrepaired	1 (1)

*It was not possible to determine if this individual contributed to the forum.

As participants were predominantly parents, the term “parent” will be used to describe participants for the remainder of this chapter.

2.3.2 Themes

The results of the analysis are summarised in Figure 2-1.

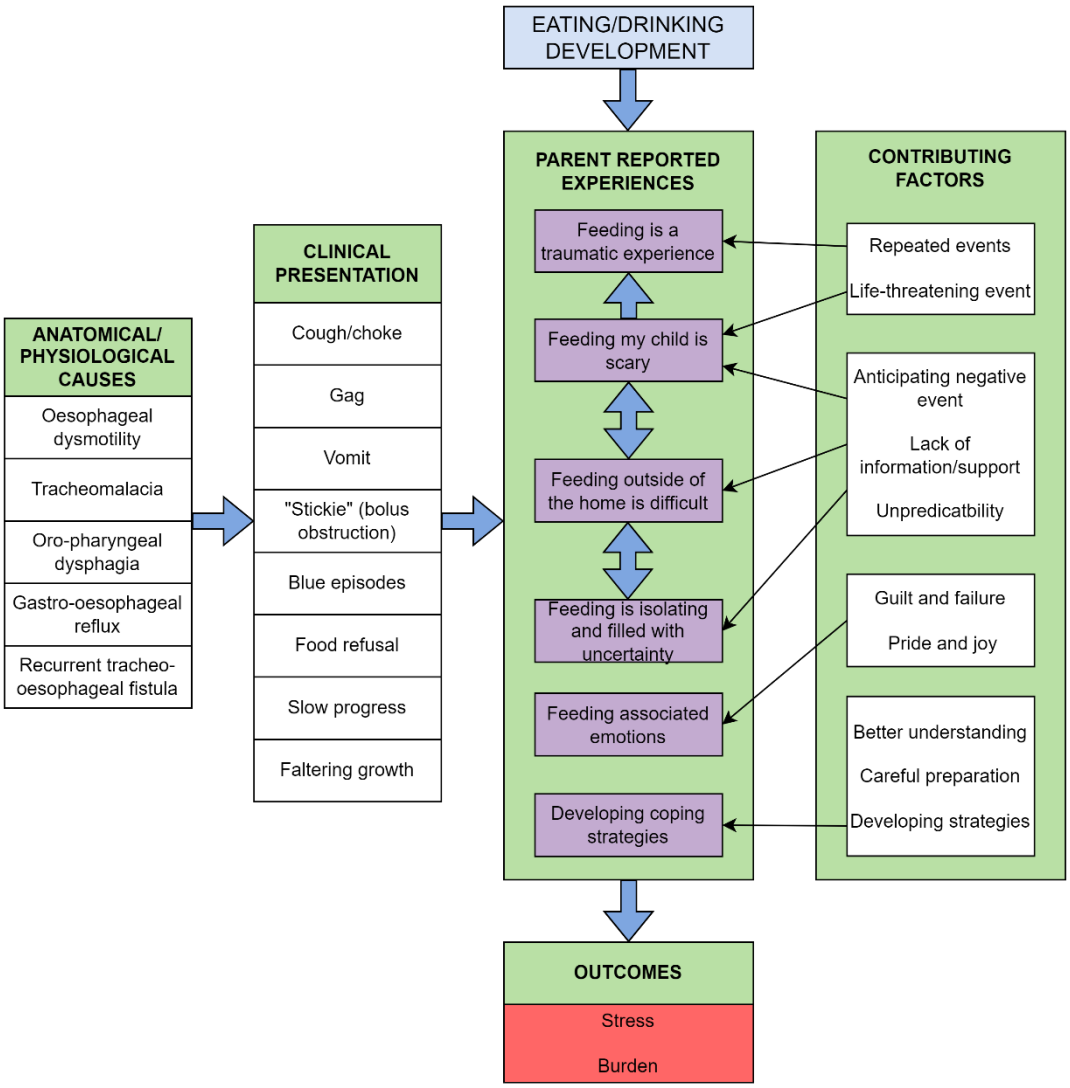


Figure 2-1. Visual summary of the online forum results

Parents described five anatomical and physiological abnormalities (far left boxes in Figure 2-1), that led to a wide variety of clinical presentations associated with feeding. Anatomical and physiological abnormalities related to gastroenterological, respiratory, and pharyngeal processes. Clinical presentations described physical responses at the time of eating/drinking - coughing, gagging, vomiting, bolus obstruction, blue episodes, as well as behavioural responses – food refusal - and longer-term outcomes of difficult feeding - slow progression with feeding milestones and faltering growth.

Six key themes, relating to parents' experiences of eating and drinking were generated and are outlined in the purple boxes. The data created an overall

impression of feeding being burdensome and stressful for parents. Parent experiences covered all stages of feeding development, signifying that feeding difficulties are not related to a single time point but, due to the developmental nature of eating and drinking in early childhood, can be pervasive over years, as represented by the light blue text box in the diagram. Ten additional factors, that were deemed to influence or contribute to the parent experience of eating and drinking, were identified in the data, and are summarised in the boxes on the far right of the diagram. The six themes will be described in detail in the following sections, with illustrative quotes.

2.3.3 Feeding my child is scary

Many parents expressed fear when feeding their child. Feeding was described as *"terrifying", "petrifying", "worrying"* and *"nerve-wracking".* For some this fear was associated with initial feeding attempts, which then lessened as feeding progressed successfully.

"*I was petrified the first few times I fed him"*

Others described a fear that was constant, seemingly not diminishing even with positive experiences.

"I'm always scared. Always, even when he goes through a long time of doing well."

Some parents identified a trigger for their fear of feeding, such as an episode perceived as a choking, which then persisted,

"After the first choke on milk at 3 months old, it was always on my mind."

"From that moment on every feeding was a nightmare for me that I tried to cover up as hard as I could."

Parents described being repeatedly exposed to this fear-inducing situation as it occurred at every mealtime, an unavoidable event happening multiple times a day.

"…every feed I worry and prepare for the worst. I am on edge, I hold my breath…I don't take my eyes off him for a second"

"Worst thing is deffo [definitely] *the constant fear of something getting stuck"*

"he started to have blue episodes during feeds which was terrifying. He would look like he was choking and then all of sudden be completely fine again. There was worry and anxiety at every feed."

Parents described multiple events where their child would experience food sticking, gagging, vomiting, or going blue. They expressed fear at never knowing what that meal would bring, identifying the unpredictable nature of each feed as anxiety-inducing.

"It was hard and often very nerve racking, never knowing what the outcome would be especially with new foods and textures."

"Now he has solids it really is a roller coaster. Some days he manages food well, other days he gets stickies from food that he has managed easily before."

Feeding was seen as an event that could end in needing to go to hospital to remove food that had become stuck or in the child having acute, blue episodes.

A few parents reported preparing for the worst when their child first started weaning onto pureed foods.

"It was nerve wracking. I used to have my phone in one hand ready to dial 999 [emergency services] *and a spoon in the other!".*

“First experience was horrifying! Even the tiniest lump would cause a stickie. Every feeding time I was petrified we might have to go to a&e [emergency department].”

Parents highlighted the ever-changing feeding landscape as difficult. Transitioning to new feeding milestones, including introducing smooth pureed foods, moving to lumpy and then chewable foods or a child eating away from the family, was identified as particularly challenging, causing increased fear.

"I’m always scared. Always, even when he goes through a long time of doing well. It only takes once to choke to death. I’m especially scared when he is away from me.”

Eating and drinking skill development occurs throughout early childhood and results in a change to feeds or mealtimes. Parents described fear in anticipation of a new milestone, as well as during the actual event.

“As with anything new it was quite daunting and hard to know what the next right step was and what we were looking for in terms of concerns”.

[speaking about moving between textures] “We started weaning 2 months ago…but I feel like I’m not moving on from smooth/runny purees because I’m too scared to try anything else.”

Several parents described being “brave” when feeding their child, particularly around offering different types of food.

“We then braved some finger foods which was very scary.”

Parents also demonstrated good awareness of their anxiety and the potential impact this may have on their child’s attitude towards eating, with some describing how they hid their fear from their child,

“However nervous I was I always tried hard not to show it so that the experience was positive for my daughter.”

"Gradually (with a nudge from my husband usually) I would become braver and give him lumpier textures and melty snacks etc but took it really slowly."

2.3.4 Feeding is a traumatic experience

Some parents felt that feeding was not just anxiety-inducing at the time, but that their experiences led to longer lasting trauma. Some recalled a single traumatic feeding event that then led to the development of trauma responses,

"*I think my first experience scarred me a little. Those earlier memories still haunt me and set me up to feel anxious about feeding*…"

"*the scariest blue-spell happened some 10 days upon being home…it was and still is the most horrifying moment of my entire life…this is one thing that stayed with me always and I still can feel the horror of it…from that moment on every feeding was a nightmare for me that I tried to cover up as hard as I could…but the PTSR* [post-traumatic stress response] *with me stays*…"

Others described repeated events during feeding that resulted in longer term trauma responses,

"We had many many blue episodes including the need for resuscitation as a result of drinking milk/early weaning foods. This has without a doubt left me with a degree of PTSD from everything we've seen him go through."

Descriptions of traumatic events included first feeding attempts and during weaning onto solids foods. Blue episodes, or those perceived as life-threatening, were vividly described as having a long-lasting impact for parents, although were not the only cause of trauma responses.

2.3.5 Feeding is isolating and filled with uncertainty

Many parents reported feeling uncertainty around their child's feeding. Parents felt unsure about what is "normal" and what is not. There was uncertainty about what foods to give, when to try new foods and the speed at

which to progress. Parents described this uncertainty as being stressful and unsettling.

"You're constantly asking yourself if your moving too fast or too slow or worrying about what could happen. It's stressful"

The uncertainty around feeding was compounded by feeling that there was no support and that parents were left making decisions on their own. Many parents felt that they were told to "have a go" when weaning their child. They felt dissatisfied that they were left to try different foods and find their way through the process.

"I felt completely on my own and isolated. Very little support or advice…very much on my own fighting to do the best I could every day"

"All of these questions….nobody seems to help or advise."

"…challenging is knowing what foods are safe to try and how to know when he is ready for something new. There is no support or advice (apart from tofs or Facebook)"

Some parents described needing to "fight" to get professional help. There were reports of not being believed that something was wrong with their child's feeding and delays in accessing the appropriate investigations or professionals.

"We could not access a dietitian. Every time the health visitor tried to refer she was told to advise as to wean as normal. I pushed and got referred through paediatrics…After finally getting a referral to salt [speech and language therapist] and a swallow study they have found that he has dysmotility".

"We….stressed that something wasn't right…it turns out at 4 weeks post op a recurrent fistula was present."

Parents also described lacking confidence in some professionals' understanding of their child's difficulties. Accessing specialists with knowledge of OA/TOF-specific feeding was particularly difficult.

"Most listen and pretend they understand but it's quite clear they have no idea what I'm talking about or little understanding to be able to provide a useful answer".

"Because doctors and even specialist could provide just basic information, that was not even close to our reality in most cases and I really felt lost without having a proper specialist guidance."

Parents not only felt isolated due to a lack of professional support, but also that their usual support - family and friends - did not understand their child's difficulties. This led to some feeling that they were the only one able to feed their child. For some this extended to not feeling confident that their partner could be involved in feeding their child.

"…seeing my husband act inappropriately or with panic and even my mother who was our rock when me and my siblings were growing up…she was too lost during such episodes with feeding issues so I relied exclusively on myself."

"It is extremely hard burden to wear, to think you are the only person to feed your child and you can never show fear or distress."

"No one would feed him except for myself and his dad….it was very tough mentally and emotionally."

"My mum won't feed my son anything unless I'm around as she's too worried about what to do if he gags or chokes."

Some parents expressed difficulty about family and friends not understanding the complexity of the situation, again adding to feelings of isolation.

"I don't think anyone really understands the condition and appreciates its challenges unless they have spent a period of time with us and experienced a choking episode."

Parents also described not feeling able to leave their child due to the feeding difficulties. This was related to feeling that others did not understanding the risks associated with offering the child the "wrong" foods or feeling that it was unfair to give someone else the responsibility of feeding their child given the risks.

"…my dad tried to push my little one too far by offering far too much on a spoon and doesn't break food up as small as I do so I worry about leaving my son alone with him in case he gives him something he can't manage."

"I didn't really let anyone else look after her or feed her as I didn't feel it was safe and not fair to put that responsibility on them."

Some parents described that because there was no visible impairment, it made it more difficult for others to understand what the problems were and the complexity of the feeding difficulties.

"Many people, including other family members, don't get the fact that this isn't something that was fixed at birth and I've even had people trying to feed him foods which I have told them time and time again are dangerous to him!"

"It's not been so easy explaining to others as I don't think they realise the gravity of having a child unable to swallow solids."

Some parents described only having a limited number of trusted people with whom they felt able to leave their child, resulting in limited access to practical help and childcare.

"Only a few have been involved with our little boy, my mum, sons and 2 trusted friends are completely trusted with him eating/drinking. Not only for

our peace of mind but there's many that are not confident in managing meals."

2.3.6 Feeding difficulties make eating outside of the home difficult

Numerous parents reported eating outside of the home was difficult. This was often due to concern about managing if food got stuck. Parents described it being easier to manage at home than out, hence avoided eating out. Other parents reported taking "easy" foods, such as pureed foods, with them when eating out or carefully checking the menu for suitable foods to avoid the risk of food getting stuck. The reluctance to eat out extended to attending family gatherings or meals with friends, as well as eating in a restaurant.

"I don't feel very comfortable eating out with my 4-year-old son as he sometimes gets food stuck and it is easier to manage the situation at home"

"We don't really eat out with her, if we do we always take along puree for her and she will sometime have chips from the menu…It's easier to eat at home where she is less distracted."

Numerous parents reported negative reactions from others, typically strangers, when food gets stuck when eating out. These reactions included panic, staring or negative remarks.

"I had several people tell me that I shouldn't bring my child out if she has croup/isn't well…if she struggled with some food and coughed….I would…throw long medical words at them to shut them up but it was still unpleasant and stressful".

Parents described needing to learn to be resilient to the negativity when eating out. For some this enabled them to continue eating out, for others it caused them to avoid these situations.

Eating outside of the home was also difficult when others were taking responsibility for feeding the child. Parents described situations where others

"pushed" feeding, by giving more challenging foods that the parent would not usually offer. For some this was positive, enabling them to gain confidence in their child's skills. For others this caused distress, distrust and conflict with family members or caregivers. There was discussion within the forum about how these situations were difficult to manage.

"They [nursery] were a little gung ho at times, I remember having to remind them no toast. But in hindsight, I think we were being more cautious than we needed to be, and actually nursery did get her eating!"

"My mum will casually say "oh he ate a cracker and cheese today, no problems". I would never have given him that! But now he has a new snack…sometimes it's helpful as I am very nervous."

Many parents described carefully preparing for eating outside of the home. There were numerous examples of parents training others and providing meticulous written guidance, particularly for childcare settings. Others described how family members had voluntarily done CPR/choking management training in preparation for feeding their child.

"I had to provide a lot of information and speak to her keyworker at length about what to look out for and what to do or not do."

2.3.7 Feeding associated emotions

Some parents identified that although feeding their child was a scary process, it was also exciting. A number expressed the immense pride that they felt when their child managed a new food or did better than they had expected.

"Apprehensive and frightened but if she managed it and/or enjoyed it then I felt huge pride."

Parents described the guilt and sadness when they felt feeding had gone wrong juxtaposed with the joy of seeing their child feed well.

“If she struggled or had a bad experience with a certain food. I would feel huge guilt. If she did well then the pride was overwhelming.”

Despite the challenges, there was also an awareness that their experience of supporting their child to establish oral feeding had been an enriching experience.

"I actually really feel that going through all this with my child has created even stronger bond and trust between us.”

Alongside feelings of failure and guilt when feeding was less successful, there was appreciation when feeding went well or better than expected that other parents would take for granted.

“I never get tired of watching him eat. Little big steps….I’m surprised by what he can manage… I’m also surprised when he can’t manage something that seems ok.”

“When you have a good day or try something new without a glitch it’s an amazing, happy and proud feeling!”

2.3.8 Developing coping strategies

Many parents described developing ways to cope and that, with time, the anxiety eases. Improvements related to being less worried about doing something wrong, gradually gaining confidence through taking small steps, having positive experiences, and having increased knowledge about what to do when feeding becomes difficult.

Parents identified a number of mechanisms that supported coping. Peer support and that of the TOFS support group were often cited as being very positive.

“We found the TOF group on Facebook invaluable for information.”

Knowledgeable professionals were also noted to be helpful in reducing anxiety around feeding.

"Surgical team and professionals very supportive and encouraging"

"We have had input from our local SALT team which has been really helpful".

Informal support networks, including family and friends also helped develop resilience to the feeding challenges.

"I have a group of friends with babies around the same age and they are just wonderful while out and about."

Some mothers reported that the child's father supported progression with feeding, particularly with initial attempts at weaning.

"At the start I kept shouting for my husband to come and help. I knew I could manage it but was scared in case the situation got worse."

"We had no idea what signs to look out for [when starting weaning] so I personally stood back and let my husband lead as I couldn't cope."

Many parents described the strategies that they had developed to support their child's feeding, such as eating slowly, taking small bites, chewing well, drinking after a mouthful of food, and making foods more liquid. Learning and adapting to their child's feeding difficulties over time enabled parents to cope with the feeding-related anxiety.

2.3.9 Proposed model of feeding in OA/TOF

Figure 2-2 presents a proposed model of the eating and drinking dyad in children born with OA/TOF. The lived experiences described in the data have been encapsulated in the concept of feeding-related quality of life (QOL), that is, the enjoyment of mealtimes, participating in social activities involving eating/drinking and feeling confident in their own and others' ability to feed their child. The derived themes highlight factors, relating to both the

child and the parent, which impact on feeding-related QOL. The recognition of feeding as a dyadic process, and thus the inter-relation of these factors, is supported.

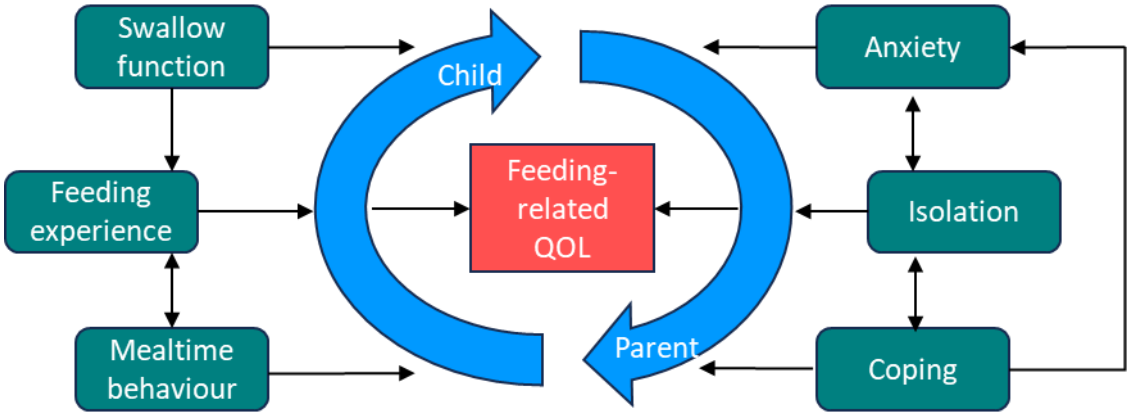


Figure 2-2. Proposed model of dyadic feeding in OA/TOF.

Table 2-3 illustrates how data derived directly from parent experiences informed the development of the model domains. "Swallow function" encapsulates any anatomical or physiological impairment that may impact on swallow function. "Feeding experience" captures events that occur during a mealtime, that cause an altered, and potentially negative, feeding experience. These often occur because of swallow function abnormalities. "Mealtime behaviour" describes the child's manner at mealtimes. These behaviours may be interpreted as challenging or enabling. "Anxiety" encapsulates any parent emotion associated with worry, nervousness, fear, stress, or anxiety at, or in response to, feeding or mealtimes with their child. "Isolation" incorporates parent perceptions of having inadequate support, either from social contacts or professional contacts, including healthcare, childcare and education settings. "Coping" describes the development or presence of behaviours parents identify as mitigating or managing negative mealtime/feeding experiences.

Table 2-3. Outline of feeding model domains informed by parent derived data.

Swallow function	Feeding experience	Mealtime behaviour	Anxiety	Isolation	Coping
Oro-pharyngeal dysphagia	Presence of cough/gag	Food refusal	Feelings of anxiety or fear	Feeling unsupported by family	Developing strategies
Dysmotility	Presence of blue episodes	Willingness to try new foods	Trauma responses	Feeling unsupported by professionals	Building confidence
Recurrent TOF	Presence of bolus obstruction				Seeing positives
GOR	Presence of vomiting				Parent teamwork
Stricture	Requirement for non-oral feeding				

TOF = tracheo-oesophageal fistula. GOR = gastro-oesophageal reflux

2.4 Discussion

This research provides insight into the reality of eating and drinking in children born with OA/TOF from the parent perspective. The research highlights the numerous ways in which feeding difficulties present and the considerable anxiety and uncertainty parents experience when feeding their child. It emphasises the importance of recognising feeding as a developmental process with new challenges faced at each developmental milestone. The data indicate that feeding difficulties can result in social isolation for parents. The need to consider these parent factors, alongside child factors, in the assessment and management of OA/TOF-related feeding difficulties is supported.

2.4.1 Fear, anxiety, and trauma

Establishing oral feeding was clearly stressful for the parents who participated in this online discussion forum. Parents described increased levels of anxiety, from initial feeding attempts, through weaning onto pureed foods and then transitioning onto chewable foods. The data strikingly highlights that parents face anxiety at every mealtime or feed, an unavoidable event that occurs multiple times a day.

Recent work has demonstrated increased levels of anxiety generally in parents of children with OA/TOF (Le Gouez et al. 2016, Witt et al. 2019, Tan Tanny et al. 2021, Wallace et al. 2021), but there has been little exploration of anxiety related specifically to eating and drinking. Bevilacqua and colleagues (2020) identified that higher parental anxiety at mealtimes was associated with more frequent choking episodes in their child with OA/TOF. Wallace and colleagues included feeding difficulty, child age and OA complexity as co-variates in their questionnaire of parental anxiety in OA/TOF. Requiring speech and language therapy input for feeding difficulties (used as a proxy for having feeding difficulties), was the only child-related factor associated with higher levels of parental anxiety (Wallace et al.

2021). Since conducting the online forum, Wallace and colleagues have published further results arising from qualitative data obtained in their questionnaire study. Their themes of “anxiety, trauma and loss”, “isolated and unsupported” and “supported”, contained many similar findings to those in the current study. Persistent anxiety at mealtimes, as well as traumatic, life-threatening events were described (Wallace et al. 2022). They additionally reported feelings of loss and sadness, which were less clearly articulated in our results. They also used a parent support network for participant recruitment and thus the similarity of results may reflect that some of the same participants taking part in both research studies. However, it strengthens the findings that two projects, undertaken by researchers from different fields (psychology and speech and language therapy) and conducted entirely independent of each other, identified such similar themes.

Evidence from the general population and those with other chronic health conditions shows that mothers of children with feeding difficulties have elevated anxiety and stress, related to inadequate weight gain, feeling pressure to get the child to eat and not knowing how the child would develop in the future (Hewetson et al. 2009, Medoff-Cooper et al. 2010, Jones et al. 2013, Silverman et al. 2021, Lamm et al. 2022). However, parents of children with OA/TOF described the actual process of feeding the child as anxiety-inducing. They described experiencing or anticipating blue episodes or choking, creating fear at each mealtime. The unpredictable nature of feeding and the potential for an acute event, perceived as life-threatening, appeared to be an important factor in the sustained feelings of fear. Inconsistency or unpredictability are not reported in the literature as parent concerns in children with oro-pharyngeal dysphagia arising from neurological, cardiac, or gastroenterological conditions. Estrem and colleagues (2018) reported unpredictability at mealtimes with regard to how much a child would eat as a result of rigid feeding behaviours, such as those seen in children with avoidant/restrictive intake feeding disorders but not related to *how* the child might eat or whether there was a perceived immediate threat to life. This suggests that the anxiety experienced by parents of children with and without OA/TOF differs.

Several parents in the current study described themselves as experiencing post-traumatic stress responses, as opposed to generalised anxiety. Previous research identified that 59% of parents, and 69% of mothers, of children with OA/TOF (mean age 7 years) scored above the cut-off for post-traumatic stress disorder (PTSD) (Le Gouez et al. 2016). Assessment of PTSD requires identification of a trigger for the trauma. Le Gouez et al. (2016) used a tool specifically designed for use with parents of medically high-risk infants, i.e. the perinatal experiences are the trigger assessed with this tool. The presence of PTSD was not associated with severity of the neonatal course or OA/TOF sequalae/complexity at the time of assessment. Feeding was not used as a co-variate in the analysis. My results suggest that feeding experiences, the unpredictability and perceived life-threatening events have the potential to act as PTSD triggers, warranting further evaluation with a validated diagnostic tool to evaluate the frequency of feeding-related PTSD and the unique contribution feeding difficulties make when other confounding variables are controlled. There would also be value in determining if there are specific risk factors or triggers for the development of feeding-related PTSD, such as recurrent bolus obstruction/strictures or blue episodes.

The direction of any relationship between OA-related feeding difficulties and parental anxiety also remains unclear. Does having a child with more significant feeding difficulties cause increased anxiety/poorer parental quality of life, or are the feeding difficulties exacerbated by parents who are more anxious? Parents with higher levels of anxiety or depression may find it more difficult to read their child's feeding cues, provide appropriate mealtime structure and cope when presented with medical conditions that impair a child's ability to feed (Jones et al. 2013). Research undertaken with ex-preterm toddlers found mothers with higher anxiety or depression were more controlling and intrusive in their mealtime interactions, which hindered their child's attempts at independent feeding. This was combined with higher toddler distress, avoidance of eating and negative mealtime behaviours (Salvatori et al. 2015). Faugli et al (2005) analysed parent-child interaction using the Parent-Child Early Relational Assessment (PCERA) in a small

cohort of mothers in Norway. This tool uses video-taped interactions during play, feeding, a structured task and separation-reunion to evaluate the parent-child relationship (Faugli et al. 2005). They reported concern regarding the maternal physical contact, quality of maternal verbalisation and quality of infant eye contact during feeding. There was moderate concern with maternal initiation of social interaction and infant communication during feeding. There was mild concern regarding amount of maternal verbalisation and eye contact and infant expression of positive affect and cheerful mood during feeding. There was also mild concern regarding the mutual enthusiasm and enjoyment in interaction during feeding. All interaction measures were lower during feeding than in play. These data indicate that mothers focussed on the process of feeding to the detriment of interaction. It is not clear to what extent anxiety contributes to this altered interaction. A recent study found 42% of children with OA/TOF presented with a feeding disorder, displaying oppositional and aversive behaviours causing stressful mealtimes (Pham et al. 2022). It is unclear if earlier interactional difficulties may be contributing to these negative mealtime behaviours in later childhood. However, it is evident that assessment of the dyadic feeding relationship could provide valuable insight into the nature of OA/TOF-related feeding difficulties, providing opportunities for early intervention, to optimise caregiver and child quality of life. Further evaluation of the extent to which anxiety, depression or stress could impact on parent-child relationships and be a driver for or be driven by feeding difficulties is required.

There is potential that the relationship between PTSD and feeding difficulties is also bidirectional, i.e. PTSD triggered by perinatal experiences impacts on feeding outcome. This has not been investigated in OA/TOF but Pierrehumbert and colleagues investigated PTSD in parents of infants admitted to a neonatal unit and later feeding and sleeping outcomes (Pierrehumbert et al. 2003). They reported no correlation between feeding outcomes and *maternal* PTSD but did identify a partial correlation between *paternal* PTSD and feeding outcome (r 0.27, $p < .05$). The reasons for this were unclear. Caution is warranted given the small sample size; however,

the findings highlight the potential interaction between parent behaviour and feeding outcome.

Findings in the current study support the assertion that OA/TOF-related feeding issues are a significant contributor to raised parental anxiety and may trigger PTSD. Further research, using validated assessments of feeding ability, anxiety, and PTSD, is required to assess the strength of these potential associations and explore the contribution of feeding difficulties adjusting for other potentially confounding variables, such as type of OA, presence of co-morbidities, birth order and parent resilience.

2.4.2 Isolation and uncertainty

An increasing body of evidence indicates that parents of children with OA/TOF have reduced quality of life (Witt et al. 2019, Tan Tanny et al. 2021, Wallace et al. 2021). Alongside the potential for feeding-related anxiety and trauma to impact on quality of life, the online forum data indicated that parents experience social isolation due to a lack of confidence in others being able to feed their child, others not understanding the extent of the difficulties, avoiding social situations involving eating and not being able to rely on friends and family for support due to their lack of confidence in feeding the child. Social isolation resulting from caring for a child with feeding difficulties has been previously reported in studies which mirror many of the results in my study (Garro et al. 2005, Hewetson et al. 2009, Estrem et al. 2018, Tan et al. 2021, Lamm et al. 2022). This can include isolation from the other parent or family members/grandparents due to conflicting opinions as to how best to manage eating and drinking difficulties (Tan et al. 2021).

2.4.2.1 Family support

Having a good support system has been associated with better quality of life, well-being, and coping (Parrish 1997, Doty et al. 2014, Tan et al. 2021). Although feeding difficulties can create inter-family conflict, positive family functioning has been shown to mitigate feeding difficulties (Lamm et al. 2022). Estrem et al. (2018) highlighted that fathers were involved in supporting progression onto new food textures in children with selective

eating in ways that mothers felt unable to do. This partnership working was seen as valuable and supportive by some families in our research but was not widely reported.

In a clinical situation it can be easy to view feeding as the responsibility of one parent, often the mother. Identifying the feeding process as a family system is key to effectively managing difficulties (Parrish 1997). Engaging with family support was identified as a key component in a study of coping strategies employed by parents of children with chronic feeding difficulties (Garro 2004). Intervention at a family level, for example by facilitating a parent to share information with others, can help manage potential conflict regarding how best to support feeding, harness positive partnership working between parents and give confidence to the parent that others can care for their child, thus reducing feelings of isolation (Neille et al. 2021) .

2.4.2.2 Peer support

Several parents highlighted how beneficial they found support from an online community, specifically the TOFS (patient support group) Facebook page. The internet is now the most frequently accessed resource for parents seeking information (Doty et al. 2014). Researchers have identified that some parents value internet support from peers above that of professional support (Doty et al. 2014, Frey et al. 2022). This was evident in the present research, with some parents determining that the only useful support was that gained from other parents. Parents gain information but also valuable emotional support from online groups (Baum 2004). Sharing experiences has been found to be particularly valuable for parents of children with medical conditions (Han et al. 2001). Providing support to others by sharing one's own experience may benefit those sharing more than those receiving such support (Stehr 2023). A recent scoping review identified that parents who engaged with social media have higher perceptions of empowerment, social support, and self-efficacy (Frey et al. 2022). However, unfavourable outcomes from accessing online support have also been reported, including learning about "worst-case scenarios" resulting in increased levels of anxiety in those accessing support (Frey et al. 2022).

Participants in our research did not identify any negative outcomes of engaging in online support. However, the recruitment method (relying heavily on social media advertising) and use of the online forum method is likely to have biased participation to those familiar with, and potentially more positively engaged with, an online community. It is not clear whether this resulted in participants who were more or less anxious. Were participants those who were most anxious as a result of, or leading to their engagement with the Facebook forum, or were those recruited the most empowered, with highest levels of self-efficacy and therefore willing and able to share their experiences? It would be of value to further investigate feeding-related anxiety using multi-strand recruitment methods, including those accessing online support and those not accessing online support to evaluate the positive and negative impacts on parent well-being.

2.4.2.3 Professional support

Uncertainty as to where to get appropriate professional support was also evident and is mirrored in research conducted with mothers of children with feeding difficulties arising from other conditions (Tan et al. 2021). Parents described variable access to appropriate professional support, with reports of needing to "fight" to get the correct support and feeling like they were left to establish oral feeding alone. Service delivery in the UK for complex, rare conditions, such as OA/TOF, has been under scrutiny in recent years with calls for centralised, specialist centres where the child and family can access appropriate multi-disciplinary support to optimise outcome (Dingemann et al. 2020, Koumbourlis et al. 2020, Slater et al. 2021). As evidenced in non-OA/TOF populations, feeding outcome, including parental well-being, can be improved with appropriate access to specialist professional assessment and intervention and better parental understanding of the problem (Garro et al. 2005, Neille et al. 2021).

2.4.3 Limitations

This study used an asynchronous, online data collection method which facilitated participation from a larger number of parents than is typically delivered by qualitative research. There was excellent geographical

representation from the UK and 20% of responses were from outside the UK, indicating findings have international significance. While rich data were obtained, it is acknowledged that other qualitative methods, such as interviews, may have afforded greater depth of understanding.

Participants were overwhelmingly of white ethnicity and mothers. It has been noted previously that participants in online research are likely to have higher levels of education and income, although this type of demographic data was not collected in our study (Bartholomew et al. 2012). The lack of ethnicity and gender representation is likely due to the use of the patient support group for recruitment and Facebook for data collection. The participant demographics are likely to be representative of individuals most likely to access the patient support group and who are able and comfortable sharing their experiences on Facebook. As improved coping has been associated with communication with parents of children with the same problems [41], those not accessing the support group may not develop coping strategies as effectively and be at greater risk of poor outcome. Alternatively, those not accessing peer support may be coping well and not feel that support is required. My findings may therefore not be reflective of the experiences of those with different cultural expectations of parenting and feeding, those with limited literacy or English language skills or those who do not access patient support groups. My results may also not reflect the experiences of fathers. Quality of life research indicates that the impact on mothers and fathers differs (Boettcher et al. 2021). Therefore, specific exploration of fathers' experiences would be of value. Alternative qualitative methods, such as interviews which could employ purposive sampling targeting previous under-represented participants, would add valuable insights.

The recruitment strategy was raised by a reviewer during the publication process as a potential source of bias. The reviewer contended that due to this bias, the findings were ungeneralisable, representative of only those with high levels of anxiety or negative experiences. These concerns were published as a commentary alongside the paper (Jaffray 2022). This commentary, and my response can be found in Appendix 3. The response

acknowledges this potential source of bias but also argues that the value of qualitative research comes from purposively sampling those who are willing and able to share their experiences (Stewart et al. 2023). In the current research, use of a support group was a deliberate recruitment strategy, purposively chosen as a group who were likely to readily share information. From this, the richest, broadest information is obtained, developing an understanding of the breadth of experience. We argue that the aim of this qualitative research was not to estimate the prevalence of such experiences, nor quantify severity or evaluate associated variables but to describe the phenomenon itself in a richly detailed manner. The generalisability of the findings must therefore be considered through a qualitative, rather than quantitative, lens. We assert that findings should be considered generalisable if another parent considers the description of feeding difficulties "ring true" (known as naturalistic generalisability), or if a reader can intuitively apply this to their own experience (inferential generalisability) which are both indicated from feedback from members of the PPI group. Additionally, results may be considered generalisable if the findings can be used to generate a new concept (analytical transferability) (Smith 2018), as is the case with the model generated. Thus, the sampling methods are justified given the aim of the research.

The online forum ran in November-December 2020, at a time when the COVID pandemic restricted access to professional support. The experience of parents of children with OA/TOF was additionally explored within this online forum and the results were published and are provided in Appendix 4 (Stewart et al. 2021). We identified specific difficulties accessing services during this time, particularly community services. Many families described anxiety for their child's health at the beginning of the pandemic. For some this lessened as more was known about the disease and its impact on children, for others this changed into concern about the impact of "lockdown" on them and their children and for some high levels of anxiety about the disease itself remained. However, there were also benefits to health from not attending school or nursery, which allowed for optimal periods of health and development. The extent to which this impacted positively or negatively

on the experiences of feeding described in this study are difficult to quantify but are acknowledged.

2.5 Conclusions

This study describes the daily reality faced by parents of children with OA/TOF in establishing oral intake throughout early childhood and beyond. The impact of the feeding/swallowing difficulties reaches beyond the child's health and development to parental well-being and quality of life. The proposed feeding model, derived from these qualitative data, provides a framework to define the child and parent factors that interact to determine individual eating and drinking outcome at a family level. This model aims to define eating and drinking as a family system, recognising the impact of OA/TOF-related swallowing difficulties on the child and family. However, further research is required to explore and validate the relative contribution of each domain. This will be described in Chapter 6.

Chapter 3. Work package 1.2: Parent questionnaire

3.1 Introduction

Findings from the online forum indicate that OA/TOF-related feeding difficulties can have a negative impact on parent well-being. The findings indicated specific areas of concern: anxiety, post-traumatic stress disorder and generalised stress. A range of behaviours describing the child's feeding or swallowing difficulties were also identified, including coughing, choking, food refusal, gagging, going blue and prolonged mealtimes. Previous research has demonstrated that parent stress and anxiety can impact negatively on a child's mealtime behaviours and parent perception of a child's feeding skill, and that parent anxiety is mediated by child feeding abilities and co-morbidities (Fishbein et al. 2016, Silverman et al. 2021, Almaatani et al. 2023). Based on the findings from the online forum study and existing literature a bidirectional model of OA/TOF feeding difficulties as a parent/child dyadic process was proposed in Chapter 2.

Qualitative data have generated a theory of the phenomenon in question: children born with OA/TOF experience feeding and swallowing difficulties and their parents experience feelings of anxiety, isolation and stress associated with these difficulties, which both influence overall feeding-related QOL. However, qualitative study does not aim to determine the frequency of such experiences, nor does it test the proposed causal links or relations in the proposed theory (Strauss et al. 1998). The aim of work package 1.2 was to use quantitative methods to evaluate the concepts and relationships identified in the online forum.

3.2 Research questions:

1. What is the frequency and severity of parent-reported feeding difficulties in children born with OA/TOF?

2. How is feeding-related QOL impacted in families of children with OA/TOF?
3. Is feeding associated with anxiety and PTSD in parents of children with OA/TOF?
4. Which child- and parent-related factors explain variation in feeding outcome, feeding-related QOL, anxiety and PTSD?

3.3 Method

3.3.1 Study design

A cross-sectional, observational study using a questionnaire method was conducted. While a longitudinal study would be of benefit to understand how the age of the child and feeding development influence parent well-being, a cross-sectional design was chosen for pragmatic reasons, namely time and concern regarding potential participant attrition. Cross-sectional study also facilitated anonymous data collection.

Questionnaires are commonly used in health research, affording efficient collection of large volume data, in a standardised and structured manner facilitating statistical analysis (Schofield et al. 2013, Parahoo 2014). They are an accepted method for theory testing and development in mixed methods research (Mukumbang 2021). They have been used to collect data from parents in a numerous other studies concerning OA/TOF (Bergmann et al. 2022, Pham et al. 2022, Wallace et al. 2022). Questionnaire methods facilitate participation from a large number of individuals over a wide geographical area (Schofield et al. 2013). They allow participants to complete them at a time convenient to them, potentially over more than a single timepoint and anonymously (Schofield et al. 2013). These were all important factors in determining a questionnaire as the most appropriate method for this study.

Traditionally questionnaires were conducted either by post, telephone or face to face (Bowling et al. 2005). However, over the last 15 years, online methods have been increasingly popular (Regmi et al. 2016). With over 96%

of households in the UK having internet access (ONS2020) and latest figures indicating that 95% of the target participant population (adults aged 18-55) owned a smartphone, the ability to access online questionnaires is widespread (Uswitch 2024). Online methods provide advantages for data analysis and reduce the likelihood of non-response to specific questions, as participants can be "required" to provide an answer before moving on to the next question (Regmi et al. 2016). Surveys in my study were distributed online and by post. Mixed distribution has been cited as best practice, increasing response rates, and affording participant choice (Pulham et al. 2019, Lallukka et al. 2020).

3.3.2 Participants

The target participant group was parents of children aged 6 months-11 years born with OA/TOF, enabling evaluation during critical periods of oro-motor skill and independent eating and drinking development (Nicklaus 2020). The total number of potential families caring for a child with OA/TOF aged 6 months-11 years in the UK was estimated at 1360-1575 (based on an incidence of 130-150 new births a year (Burge et al. 2013). A pragmatic recruitment target of 200-235 (15%) was set.

3.3.2.1 Inclusion criteria

1. A parent or primary caregiver of a child aged 6 months--11 years born with OA/TOF

3.3.2.2 Exclusion criteria

1. Parents of children aged under 6 months or 12 years or over.

2. Parents of children without OA and/or TOF.

To optimise participation, parents without sufficient English were offered the opportunity to complete the questionnaire using a telephone interpreter. Parents without sufficient literacy were offered the opportunity to complete the questionnaire via telephone or video call with a member of the research team.

3.3.3 Recruitment

Recruiting sufficient numbers of participants is challenging in rare disease populations (Davies 2016). No centralised patient registry exists for OA/TOF in the UK. Neither is care centralised at specialist centres. This resulted in challenges accessing potential participants and subsequently influenced study design. To optimise recruitment, a multi-strand approach was adopted.

3.3.3.1 Route one: Direct invitation through Great Ormond Street Hospital electronic patient records (EPR) system

All children aged 6 months-11 years, with a diagnostic label of oesophageal atresia and/or tracheo-oesophageal fistula, were identified through the electronic patient records system and the surgical team's OA/TOF patient database at Great Ormond Street Hospital. An invitation to participate was initially sent electronically to parents through the patient portal (known as MyGOSH) for those families who had signed up to the portal. The invitation (Appendix 5) included a weblink and QR code link to the questionnaire, which included the participant information sheet (PIS), consent form and the questionnaire itself. A reminder was sent to all potential participants 6 weeks after initial invitation. To engage with families not using MyGOSH and to offer a choice of digital or paper completion methods, invitation letters and the questionnaire were also sent by post to all parents identified through the hospital records system. A stamped addressed envelope for return was included. Reminders were not sent by post.

3.3.3.2 Route two: Response to advertisement at healthcare facilities

Recruitment advertisements (Appendix 6) were distributed through speech and language therapist contacts at UK surgical centres, via London Paediatric Dysphagia Clinical Excellence Network and on Twitter. Clinicians were asked to display an advertisement poster and leaflets on appropriate wards and outpatient clinics. Interested participants gained access to the PIS, consent form and questionnaire using a QR code or typing in the web address.

3.3.3.3 Route three: Response to advertisement through TOFS charity

A recruitment advertisement (Appendix 6) was distributed electronically on the TOFS website, newsletter, and social media channels (Facebook and Twitter). Use of Facebook has been shown to be an effective recruitment method for online research, particularly for rare disease populations (Hausmann et al, 2022). Interested participants gained access to the PIS, consent form and questionnaire using a QR code or clicking a weblink. Unlike recruitment in route one, potential participants were not individually invited to take part, they responded to a generic advertisement, if interested.

The questionnaire was identical for each recruitment path but had different weblinks/QR codes to enable identification of recruitment pathway.

3.3.4 Consent

The front page of the questionnaire contained participant information (Appendix 7). Participants completing the online version provided electronic consent to participation prior to starting the main questionnaire. If participants answered no to any of the consent questions, they were taken to the finishing page and thanked for their time. Participants completing the questionnaire on paper provided written acknowledgement of their agreement to participate.

Due to the anonymous nature of the questionnaire, once submitted participants were unable to withdraw from the study. To minimise the impact of missing data, the online questionnaire was designed so that all questions had to be answered but partially complete questionnaires were visible. Partially completed questionnaires with over 80% completion were included in the final analysis.

3.3.5 Questionnaire design

The Smart Survey™ platform was used to create the online version of the questionnaire. Smart Survey™ is GDPR compliant and has a secure storage facility for anonymous data. The paper version of the questionnaire

was generated directly from the Smart Survey™ questionnaire with written guidance for question skipping, in place of electronic skip logic where appropriate.

The questionnaire consisted of bespoke questions and validated measures. It was designed with a mixed format, with questions organised into domains with least sensitive questions asked first to allow engagement with the survey before asking the most personal questions (Schofield et al. 2013). Participants answered questions about their child's eating and drinking before questions regarding the impact of any eating or drinking difficulties on their well-being. The questions were derived directly from the themes generated and variables identified during the online forum (Chapter 2). Where possible, validated tools were used to measure each theme or variable. Where no validated tool existed, bespoke questions were written. This process is outlined in Figure 3-1.

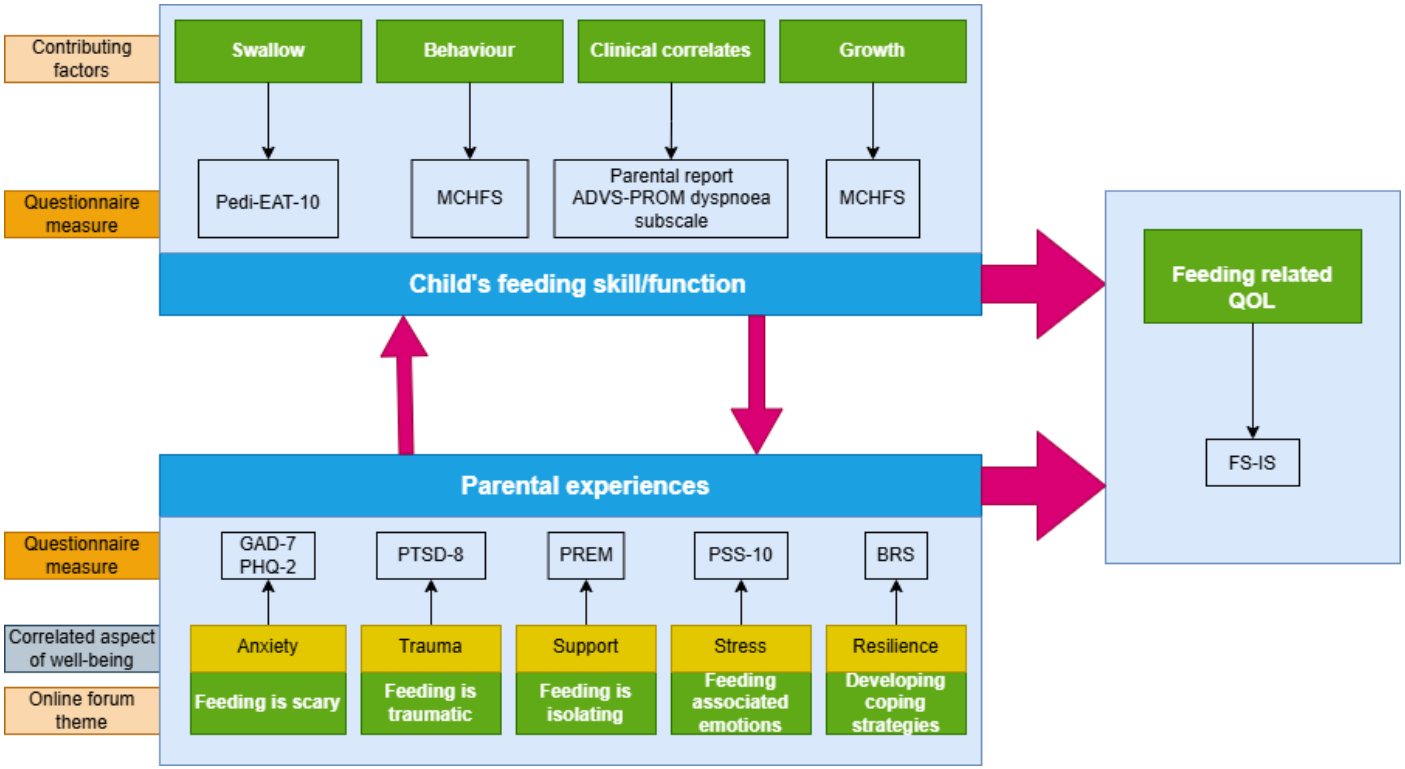


Figure 3-1. Schematic summary of questionnaire development.

Legend: MCHFS = Montreal Children's Hospital Feeding Scale, ADVS-PROM = Airway, Dyspnoea, Voice, Swallow-Patient Reported Outcome Measure, GAD-7 = Generalised anxiety disorder scale, PTSD-8 = Post-traumatic stress disorder scale, PREM = Patient-reported experience measure, PSS-10 = Perceived stress scale, BRS = Brief resilience scale, QOL = Quality of life, FSIS = Feeding-swallowing impact survey.

Use of the support group to facilitate recruitment ensured many parents could be invited to participate. However, as a result, all data collection needed to be parent reported. Medical and surgical data, collected from medical records, are likely to be more specific and detailed than that obtained from parent report (Davies 2016). However, this would require multiple site research and development approval and principal investigators to collect the data. Given the relatively small number of children treated for OA/TOF at any given hospital, the time involved in obtaining site specific approval and the lack of funding to support the time involved for PI participant identification and data collection, it was felt that the potential disadvantage of collecting parent reported medical history was outweighed by the benefit of accessing a larger cohort of potential respondents in an efficient manner. To optimise reliability of the medical history questions, these were written with the parent steering group. A full copy of the questionnaire is provided in Appendix 8. Validated measures were carefully considered for their demonstration of good psychometric properties, previous use with OA/TOF populations and brevity/ease of completion. Questions were predominantly closed questions to reduce cognitive burden and aid analysis (Schofield et al. 2013). Open text boxes were placed after particularly sensitive questions and at the end of the questionnaire to allow participants to expand on their answers, if they chose to.

3.3.5.1 Section 1: Demographic information

Data were collected on parent ethnicity, gender (child and parent), respondent relationship to the child, age (child and parent), household members, birth order and employment status.

3.3.5.2 Section 2: Medical information

Data were collected on gestational age, age at surgery, type of OA/TOF, need for dilatations, blue episodes, dyspnoea (ADVS-patient report outcome measure, described in 3.3.5.12) (Nouraei et al. 2017), cardiac comorbidity, syndrome diagnosis, upper airway abnormality, gastro-oesophageal reflux, growth and feeding method.

3.3.5.3 Swallow function: Pedi-EAT-10 (Serel Arslan et al. 2018)

The Pedi-EAT-10 is a 10-item, parent-completed screening tool for swallowing difficulties, adapted from the EAT-10 using literature review and expert consensus (Belafsky et al. 2008, Serel Arslan et al. 2018). Using a one-month recall period, parents rate each statement using a five-point Likert scale (0 = no problem, 4 = severe problem). The measure demonstrates excellent criterion validity with the penetration-aspiration scale ($r = .77$ for liquids ($p < .001$) and $r = .83$ for solids ($p < .001$), excellent test-retest reliability (ICC 0.983) and demonstrated known groups validity for a cohort of children with cerebral palsy with statistically significantly higher Pedi-EAT-10 scores seen in children with increasing severity of cerebral palsy (Soyer et al. 2017, Serel Arslan et al. 2018). Data from 51 children without swallowing difficulties indicates that a score of 4 or more indicates possible swallowing difficulty (Serel Arslan et al. 2018). The validity of the Pedi-EAT-10 to detect aspiration risk in children with OA/TOF has been investigated, reporting a sensitivity of 88%, specificity of 77%, positive predictive value of 22% and negative predictive value of 11% (Soyer et al. 2017). It has been used by two previous studies of children's swallowing in OA/TOF (Golonka et al. 2008, Soyer et al. 2017).

3.3.5.4 Feeding difficulty: Montreal Children's Hospital Feeding Scale (Ramsay et al. 2011)

The Montreal Children's Hospital Feeding Scale (MCHFS) is a 14-item, parent reported measure of feeding difficulties (Ramsay et al. 2011). It was designed to be a quick tool for identification of feeding difficulties in children aged 6 months-6 years. It covers child and parent domains of feeding: oro-motor skills, oro-sensory skills, appetite, parental worry, mealtime behaviour, mealtime strategies and family reaction to feeding difficulty. Items are rated using a seven-point Likert scale with anchor points at each end. Seven items are scored positive to negative, the other seven from negative to positive. A total score is obtained by reverse scoring the negative items and adding the values of each item. A threshold for "feeding difficulty" is provided

for each question. Cut-off scores for mild, moderate and severe feeding difficulties are given (Ramsay et al. 2011).

The tool demonstrates good test-retest reliability (ICC 0.85-0.92, *p* =<.001) (Ramsay et al. 2011, Rogers et al. 2018), good internal consistency, excellent construct validity with statistically significant differences in mean scores between a normative sample and clinical sample (Ramsay et al. 2011) and moderate-good criterion validity with subscales of the Child Eating Behaviour Questionnaire (r = -.44 - .67, *p*), the Feeding Interaction Scale (r = -.34, *p*.02) and the Comprehensive Feeding Practices Questionnaire (r = -.32 - .27, *p* <.05) (Rogers et al. 2018). The MCHFS has been used previously in four studies of children with OA/TOF (Baird et al. 2015, Menzies et al. 2017, Pham et al. 2022, Traini et al. 2022).

3.3.5.5 Feeding related quality of life: Feeding-Swallowing Impact Survey (Lefton-Greif et al. 2014)

The feeding-swallowing impact survey (FSIS) is an 18-item, parent-reported measure. It is divided into three subscales: daily activities (5 items), worry (7 items) and feeding difficulties (6 items), generating total and subscale scores. Using a one-month recall period, participants are asked “As a result of your child’s feeding/swallowing problems, how often have you had problems...?”. Participants rate each question using a 5-point Likert scale (1=never, 5=almost always). Total and subscale scores are generated by summing the scores and dividing by the number of scale items, generating mean scores out of five, or by summing the scores, generating a total score of 18-90, a daily activity score of 5-25, a worry score of 5-35 and a feeding score of 5-30 (Lefton-Greif et al. 2014) (Stewart et al 2024, under review).

Initial validation was undertaken with 164 children attending a tertiary feeding clinic. The tool demonstrated internal reliability (Cronbach’s alpha above 0.7 for total score and subscale scores). Construct validity was demonstrated with moderate correlation with the PEDS-QL Family Impact Module (Pearson correlation r=0.23-0.62). The tool demonstrated discriminant abilities with parents of children receiving tube feeding scoring significantly higher than

those orally fed on the “daily activities” subscale. Reference values generated from a UK community sample indicate that a score of 23 places a parent over the 75th percentile, demonstrating lower feeding-related quality of life (Stewart et al, under review). It has been used previously with parents of children with OA/TOF (Serel Arslan et al. 2020).

3.3.5.6 Parent anxiety: Generalised Anxiety Disorder assessment (Spitzer et al. 2006)

The GAD-7 is a robustly designed, widely used measure of anxiety, which aims to identify and assess severity of generalised anxiety disorders in adults. It is a seven-item, self-rated scale. Participants rate each statement using a four-point Likert scale reflecting symptom frequency over the last two weeks. Scores range from 7-28. Cut-off scores for mild, moderate and severe anxiety are provided. Authors suggest moderate or severe levels of anxiety require further investigation.

The GAD-7 demonstrates excellent internal consistency (Cronbach α= .92) and good test-retest reliability (ICC = .83). It demonstrates good construct validity, correlating well with the SF-20. It demonstrates weak-moderate correlation with disability days (r=.27) and health care access (r=.22) but moderate-strong correlation with symptom-related difficulties in activity and relationships (r=.63). There is good convergent validity with the Beck Anxiety Inventory (r=.72) and the anxiety subscale of the Symptom Checklist-90 (t=.74) (Spitzer et al. 2006).

Previous studies of anxiety in parents of children with OA/TOF have used the Hospital Anxiety and Depression Scale (Wallace et al. 2021), the State-Trait Anxiety inventory (Le Gouez et al. 2016, de Vos et al. 2024) and the PROMIS Anxiety scale (Tan Tanny et al. 2021). However ,the GAD-7 has been used widely in previous studies of anxiety in parents of children with a range of other health conditions, including respiratory conditions (Graziano et al. 2023), cancer (Gajda et al. 2024) and gastro-oesophageal reflux (Aizlewood et al. 2023). The GAD-7 was selected as it assesses anxiety only, which was the primary construct identified in the qualitative data. It is

also shorter than other screening tools, which was a particularly important consideration given the length of the whole questionnaire.

3.3.5.7 Parent depression-Patient Health Questionnaire-2 (Löwe et al. 2005)

The Patient Health Questionnaire-2 (PHQ-2) is a robust, widely used brief, 2-item measure which aims to screen for and monitor depression in adults. Participants rate two statements using a frequency Likert scale with a two-week recall period. A cut-off score of 3 or more demonstrates good sensitivity and specificity for a diagnosis of depression.

The tool demonstrates good construct validity, correlating with other measures of depression: Patient Health Questionnaire-9, Hospital Anxiety and Depression Scale, World Health Organisation 5-item Well-Being Index and Short Form Healthy Survey mental component (r=.67 - .87). It has good diagnostic accuracy, when compared to the gold standard Structured Clinical Interview and is sensitive to changes in depression severity (Löwe et al. 2005).

Previous studies of depression in parents of OA/TOF have used the Hospital Anxiety and Depression Scale (Wallace et al. 2021) and the PROMIS depression scale (Tan Tanny et al. 2021). The PHQ-2 was preferred in this study due to its ultra-brief nature.

3.3.5.8 Parent Stress: Perceived Stress Scale-10 (Cohen 1988)

The Perceived Stress Scale-10 (PSS-10) is a robust, widely used measure of perceived stress. The tool aims to determine how unpredictable, uncontrollable, and overloaded participants find their lives. Using a one-month recall period, participants rate each statement on a five-point frequency Likert scale. Statements are both positive and negative, therefore scoring requires reverse coding of positively framed questions. A total score out of 40 is obtained. Normative data provide mean scores and standard deviations for four different age groups (18-29, 30-44, 45-55 and 65 and over) (Cohen 1994).

Psychometric evaluation of the PSS-10 demonstrates good internal consistency (Cronbach's >.70) and good test-retest reliability (ICC >.70)(Lee 2012). The PSS-10 displays good criterion validity with moderate-strong correlation with a number of anxiety and depression scales (Lee 2012). Known groups validity has been demonstrated with several groups. Scores were significantly lower for young, white, married, employed, higher income parents who had a smaller number of children and parents without a child with a chronic illness (Lee 2012). Generalised stress has not been evaluated in OA/TOF previously but this tool has been used in previous research into the relationship between children's feeding difficulties and parent stress (Baker et al. 2023).

3.3.5.9 Parent trauma: Post Traumatic Stress Disorder-8 Scale(Hansen et al. 2010)

The Post Traumatic Stress Disorder-8 scale (PTSD-8) was designed as a short screening tool for PTSD. It has been used in numerous studies of PTSD in parents (Reid et al. 2020, Kara et al. 2021, Pontoppidan et al. 2022). Two previous studies of PTSD in parents of children with OA/TOF used the perinatal PTSD questionnaire (Le Gouez et al. 2016, de Vos et al. 2024). This tool examines PTSD arising from trauma occurring at or around the time of the child's birth. This was not the PTSD trigger for the current study. Therefore, a more general tool was chosen. Participants rated each item using a four-point frequency Likert scale (1= not at all, 4 = very often). The PTSD-8 comprises three subscales, pertaining to avoidance, intrusion and hypervigilance-the three constructs that form a diagnosis of PTSD. Participants were given instructions to specifically consider any traumatic event related to feeding when answering the questions. A diagnosis of PTSD is suspected if participants score at least three on any item in each of the three subscales. It is a simple scale that can be used by health professionals without prior knowledge of PTSD diagnosis (Andersen et al. 2018).

The tool demonstrates concurrent validity with a trauma symptom checklist (r = .58 - .78, p<.001). Test-retest reliability was good (r = .82, p<.001) (Hansen et al. 2010).

3.3.5.10 Parent Coping: Brief Resilience Scale (Smith et al. 2008)

The Brief Resilience Scale (BRS) is a six-item measure of an individual's ability to recover from stressful events. Participants rate each statement using a five-point agreement Likert scale (1 = strongly agree, 5 = strongly disagree). Three items are positively worded, three negatively. A total score is generated by reverse coding the negatively worded questions and summing the individual item scores. The total score can also be reported as a mean (Smith et al. 2008).

The BRS demonstrates moderate-good test-retest reliability (ICC .69 for one month, .62 for three-month retest). It demonstrates convergent validity with other resilience measures (r =.51- .59, p <.01), optimism (r =.45, p<.01) and purpose in life(r =.46, p<.01) and divergent validity with pessimism (r =-.40, p<.01) and alexithymia (difficulty experiencing, expressing and identifying emotions) (r =-.47, p<.01). The BRS also negatively correlates with perceived stress (r =-.60, p<.01), anxiety (r =-.46, p<.01), depression (r =-.41, p<.01), negative affect (r =-.34, p<.01) and physical symptoms (r =-.39, p<.01). The BRS had discriminant validity between those with and without a type D personality disorder and for women with and without a diagnosis of fibromyalgia (Smith et al. 2008).

The influence of parent resilience on parent well-being has not been previously explored in OA/TOF. The BRS has been used in other studies of parents in health research, including post-traumatic stress in parents of children admitted to intensive care (Rodriguez-Rey et al. 2018), and anxiety and depression in parents of children with moderate-severe disability (Rakap et al. 2024).

3.3.5.11 Support: patient reported experience measure.

A bespoke experience measure was designed to capture parent perception of the quality of feeding-related support provided by professionals. Parents rated each professional using a five-point scale of confidence in the advice provided (1 = extremely confident, 5 = not at all confident). If a participant

had not had support from that professional they were asked whether they felt they needed that support or not. There was also an overall satisfaction score, rated on a five-point rating scale (1 = very dissatisfied, 5 = very satisfied).

3.3.5.12 Airway-Dyspnoea-Voice-Swallowing Patient Reported Outcome Measure – dyspnoea subscale (ADVS)(Nouraei et al. 2017)

The ADVS PROM was designed as a patient reported measure of airway, dyspnoea, voice and swallowing for children with laryngotracheal stenosis and tracheobronchomalacia (Nouraei et al. 2017). Children with OA/TOF were included in the validation sample. It is a thirteen-item tool containing subscales for dyspnoea (5-item), voice (4-item) and swallowing (4-item). Statements are rated using a 6-point Likert scale for frequency (0=never, 5=all of the time). Only the dyspnoea subscale was used. The dyspnoea score is calculated by adding individual item scores and dividing by 2.5.

The dyspnoea subscale demonstrates good internal consistency (Cronbach-alpha 0.85). Construct validity is evidenced by correlation with Lanksy performance scale ($r = -0.68$; $P < 0.0001$) and PedsQL ($r = -0.57$; $P < 0.0001$). There were strong correlations between Myer–Cotton stenosis severity and dyspnoea scale and PROM score ($r = 0.68$; $P < 0.0001$) (Nouraei et al. 2017).

3.3.5.13 Questionnaire piloting

The questionnaire was piloted by the project parent steering group members (n=4). This informed wording of demographic and clinical variable questions, the time required for completion and overall readability/function of the questionnaire. The parents involved in the piloting determined that the questionnaire took 15-20 minutes to complete but did not feel that this was too lengthy or burdensome. Recruitment advertisements highlighted to potential participants that the questionnaire would take approximately 20 minutes to complete. Significant changes were made as a result of steering group feedback: addition of explanatory wording to clinical variable

questions, removal of items felt to be unreliable for parent report (such as laryngomalacia, tracheomalacia and dysmotility), removal of household income question as these were felt to be too intrusive, removal of questions related to the type of foods eaten according to the International Dysphagia Descriptors Standardisation Initiative framework as this was felt to be unreliable and minor alterations to question wording.

3.3.6 Data analysis

Online questionnaire raw data were downloaded directly from Smart Survey™ into Microsoft Excel and then transferred to SPSSv29 (IBM Corp, Chicago, Illinois, USA). Graphs and charts were created using GraphPad Prism (version 10.0.0 for Windows, GraphPad Software, Boston, Massachusetts USA, www.graphpad.com).

Categorical data were summarised using frequencies and percentages. Continuous data were summarised using means and standard deviations for normally distributed data and medians and interquartile ranges for skewed data.

Demographic and medical history were compared between those recruited via the patient support group and those recruited via the hospital using Chi^2 for categorical data, independent samples *t*-tests for normally distributed continuous data and Mann-Whitney-U for skewed continuous data. Distribution was assessed by visual inspection of Q-Q plots. All significance levels were set at 0.05.

Cronbach's alpha was used to assess the internal consistency of each tool for this population.

Spearman's correlation coefficients were calculated to explore the association between child and parent related factors and feeding-related QOL. Spearman's correlation was preferred to Pearson's correlation due to the categorical nature of many of the variables and skewed distribution of some continuous variables. This provided an exploratory overview which

helped inform development of multiple regression models. Significance was set at 0.05.

Multiple linear regression was used to determine predictor variables for: parent-reported feeding outcome, feeding-related QOL and parent well-being (anxiety and PTSD). To avoid over-fitting of the model and having too many variables for the sample size, predictor variables were chosen based on:

1. Statistically significant correlation (Spearman's rank correlation)
2. Clinically reasoned assumption of potential predictive value
3. Independence of variables (for example, depression and anxiety not included in the same model)

Dummy variables were created for nominal categorical variables with more than two categories. Ordinal variables were treated as continuous. Checks were made for test assumptions: distribution of residuals (visual inspection of dot plot), outliers (casewise diagnostics), leverage (leverage value and Cook's distance), multicollinearity (tolerance value) and normality (Q-Q plot).

3.3.6.1 Parent-reported feeding

The MCHFS was chosen as the dependent variable for feeding outcome as it provided a broader assessment of "feeding" difficulty than the Pedi-EAT-10. The MCHFS questions require a child to be attempting to eat or drink something by mouth. Therefore, parents of children who were fully tube fed did not answer these questions. To avoid omitting these children from the regression model, all fully tube fed children were assumed to have a severe feeding difficulty and were assigned a score of 71- the lowest total score in the severe feeding difficulty category.

3.3.6.2 Feeding-related QOL

Due to the large number of potential variables for the feeding-related QOL model, this was initially run as two models - one for child-related variables (for example, presence of strictures and severity of feeding difficulty) and one for parent-related variables (for example, parent anxiety level and

satisfaction with HCP support). Variables with statistically significant coefficients were then entered into a final feeding-related QOL model.

3.3.6.3 Parent well-being

Regression models were generated for parental anxiety and post-traumatic stress disorder. These were selected as they related most closely to the themes developed from the qualitative data and the feeding model.

3.4 Results

3.4.1 Response rate

One hundred and nine parents of children cared for at Great Ormond Street Hospital were invited to participate via the electronic patient portal (MyGOSH) and by post. A further 11 were invited by post only. Twenty-one parents returned postal questionnaires and 28 responses were received electronically, giving a total response rate of 49/120 (40.8%). Only one response was received from recruitment route two, direct advertisement at other healthcare facilities. This has been included in the results from the Great Ormond Street Hospital respondents. These participants will be known as the "hospital" group in all further analysis.

One hundred and twenty-five responses were received from those accessing the questionnaire via support group advertising. Data provided by the support group indicate that there are approximately 1500 parent members of children aged 6 months-11 years, indicating approximately 9% of eligible parent members participated. This group will be known as the "support group" participants in all further analysis.

In total, responses from 175 parents were included in the analysis.

3.4.2 Demographic characteristics

The demographic characteristics of all participants are presented in Table 3-1. The median age of all participants was 3 years (IQR 6). Participants in the support group had statistically significantly younger children than the

hospital group. Significantly more support group participants were from outside the UK. They were mainly from English-speaking countries with developed healthcare systems, comparable to the UK (USA n=3, Sweden n=1, South Africa n=2, Australia n=8, Middle East n=1, Italy n=1, Argentina n=1, Germany n=1, Hungary n=1, Ireland n=4, New Zealand n=1, Turkey n=1, Netherlands n=1). No participants asked for use of a telephone translator. In addition to child age, there were statistically significant differences in employment status, and parent age.

Table 3-1. Participant demographic characteristics

	TOFS n (%)	Hospital n (%)	All n (%)	Chi-^{2}
Place of residence				4.120 (p=.04)
UK	99 (79.2)	46 (92)	145 (82.9)	
Outside the UK	26 (20.8)	5 (8)	30 (17.1)	
Household				1.287 (p= .26)
One parent household	16 (12.9)	3 (6.7)	19 (11.2)	
Two parent household	108 (87.1)	42 (93.3)	150 (88.8)	
Employment				9.026 (p=.03)
Employed	87 (70.2)	33 (68.8)	120 (69.8)	
Self-employed	12 (9.7)	0 (0)	12 (7)	
Unemployed	9 (7.3)	9 (18.8)	18 (10.5)	
Unpaid work	16 (12.9)	6 (12.5)	22 (12.8)	
Partner employment				.053 (p=.82)
Employed	52 (53.1)	15 (55.6)	67 (53.6)	
Self-employed	46 (46.9)	12 (44.4)	58 (46.4)	
Unemployed	0 (0)	0 (0)	0 (0)	
Unpaid work	0 (0)	0 (0	0 (0)	
Parent gender				5.175 (p=.02)
Female	119 (96.7)	43 (87.8)	162 (94.2)	
Male	4 (3.3)	6 (12.2)	10 (5.8)	
Parent age				12.767 (p=.002)
Under 30	21 (16.8)	5 (19.2)	26 (14.9)	
30-39	73 (58.4)	18 (36.7)	91 (52.3)	
Over 40	31 (24.8)	26 (53.1)	57 (32.8)	
Number of children				.154 (.69)
1	52 (41.6)	18 (38.3)	70 (40.7)	
2 or more	73 (58.4)	29 (61.7)	102 (59.3)	
Child gender				1.635 (p=.20)
Male	83 (66.4)	15 (53.6)	98 (64.1)	
Female	42 (33.6)	13 (46.4)	55 (35.9)	
Child age Median (IQR)	4 (5)	6 (7)	4 (6)	3812.00 (p=.01)$^{\$}$

Comparison of demographic variables between participants recruited via TOFS support group and hospital sites. Chi^2 test for difference unless otherwise stated. $ = Mann-Whitney test. TOFS = support group. IQR = inter-quartile range.

3.4.3 Medical history

Parent-reported medical history is summarised in Table 3-2. There were significantly more children with type E (tracheo-oesophageal fistula only) in the hospital group (0.8% vs 10.2%). Overall, the cohort was representative of expected proportions of OA subtypes (expected prevalence: type A 7%, type B 2%, type C 86%, type D <1%, type E 4%) (Spitz 2007). Of those with OA and TOF, 9/156 (5.8%) were repaired more than a week post-birth.

A statistically significantly higher proportion of the support group participants reported an "unsafe swallow" (27.2% vs 10.2%). The median dyspnoea score was also significantly higher in the support group participants (6 vs 3). There were no other statistically significant differences.

Table 3-2. Parent-reported medical history.

	TOFS n (%)	**Hospital n (%)**	**All n (%)**	**Chi-^{2}**
OA type				8.085 (p=.016)^
OA and TOF (Type B/C/D)	116 (92.8)	42 (85.7)	158 (90.8)	
OA only (Type A)	8 (6.4)	2 (4.1)	10 (5.7)	
TOF only (Type E)	1 (0.8)	5 (10.2)	6 (3.4)	
Time of repair				.566 (p=.569)
Within a week of birth	111 (89.5)	41 (85.4)	152 (88.4)	
More than a week after birth	13 (10.5)	7 (14.6)	20 (11.6)	
Repair number				.385 (p=.536)
1	104 (83.2)	38 (79.2)	142 (82.1)	
2 or more	21 (16.8)	10 (20.8)	31 (17.9)	
Number of strictures				5.243 (p=.154)
None	32 (25.6)	15 (34.1)	47 (27.8)	
1-3	46 (36.8)	10 (22.7)	56 (33.1)	
4-6	24 (19.2)	6 (13.6)	30 (17.8)	
7 or more	23 (18.4)	13 (29.5)	36 (21.3)	

Time since last stricture				.116 (p=.733)
Within the last year	41 (44.1)	13 (40.6)	54 (43.2)	
More than a year ago	52 (55.9)	19 (59.4)	71 (56.8)	
Prematurity				.217 (p=.897)
≥ 37 weeks	77 (61.6)	31 (64.6)	108 (62.4)	
32-36 weeks	32 (25.6)	12 (25)	44 (25.4)	
28-31 weeks	16 (12.8)	5 (10.4)	21 (12.1)	
Syndrome				1.529 (p=.466)
None	91 (73.4)	32 (66.7)	123 (71.5)	
VACTERL	28 (22.6)	12 (25)	40 (23.3)	
Other	5 (4)	4 (8.3)	9 (5.2)	
Cardiac				3.099 (p=.078)
Yes	27 (22.1)	16 (35.6)	43 (25.7)	
No	95 (77.9)	29 (63.3)	124 (74.3)	
GOR treatment				1.197 (p=.274)
Yes	89 (71.8)	31 (63.3)	120 (69.4)	
No	35 (28.2)	18 (36.7)	53 (30.6)	
Blue episodes				.138 (p=.710)
Yes	69 (55.2)	28 (58.3)	97 (56.1)	
No	56 (44.8)	20 (41.7)	76 (43.9)	
VCP				.317 (p=.574)
Yes	17 (13.6)	5 (10.4)	22 (12.7)	
No	108 (86.4)	43 (89.6)	151 (87.3)	
Laryngeal cleft				1.735 (p=.188)
Yes	8 (6.4)	6 (12.5)	14 (8.1)	
No	117 (93.6)	42 (87.5)	159 (91.9)	
EOE				1.472 (p=.225)
Yes	6 (5)	0 (0)	6 (4.1)	
No	113 (95)	28 (100)	141 (95.9)	
Unsafe swallow				5.847 (p=.016)
Yes	34 (27.2)	5 (10.2)	39 (22.4)	
No	91 (72.8)	44 (32.6)	135 (77.6)	

Tube fed				.880 (p=.348)
Yes	25 (20)	13 (26.5)	38 (21.8)	
No	100 (80)	36 (73.5)	136 (78.2)	
Oral intake for tube fed children				.339 (p=.904)^
No oral	4 (3.2)	2 (4)	6 (3.4)	
Minimal oral	11 (8.8)	5 (10)	16 (9.1)	
Part oral	11 (8.8)	7 (14)	18 (10.3)	

Comparison of demographic variables between participants recruited via TOFS support group and hospital sites. Chi^2 test for difference unless otherwise stated. ^ Fisher's exact test. TOFS = support group, OA = oesophageal atresia, TOF = trachea-oesophageal fistula, GOR = gastro-oesophageal reflux, VCP = vocal cord palsy, EOE = eosinophilic oesophagitis. No oral intake defined as fully tube fed, minimal oral intake as small volumes for pleasure/enjoyment or therapeutic purposes but does not meet any nutritional requirements, part oral defined as oral intake which partially meets nutritional requirements.

3.4.4 Validated measures score summaries

3.4.4.1 Swallow function: Pedi-EAT-10

Responses on the Pedi-EAT-10 were provided by 167 (95.4%) parents. Internal consistency of the tool was excellent in this population (Cronbach's alpha .898). Parents of six fully tube fed children did not complete this measure. There were missing data from one participant. Fifty-four (32.3%) had no swallowing difficulties (Pedi-EAT-10 score of three or less), 113 (67.7%) had swallowing difficulties (Pedi-EAT-10 score of four or more). Data were not normally distributed; the median score was 8 (range 0-38, IQR 12) but to enable comparison with other studies the mean score is also reported: 9.14 (SD 8.20). Frequency of responses to each question are provided in Figure 3-2.

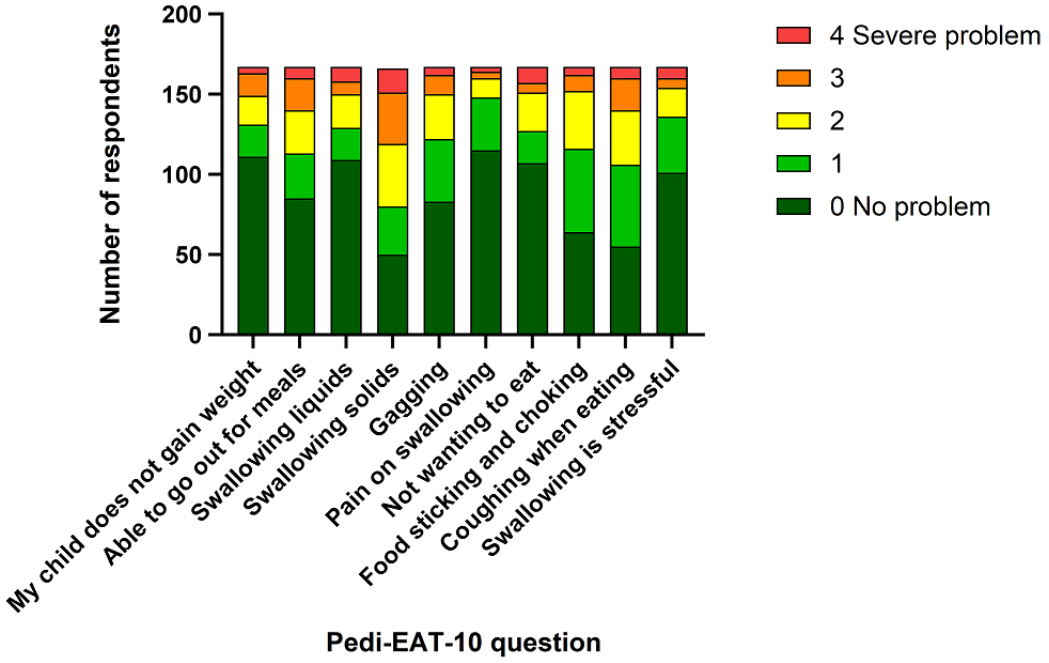


Figure 3-2. Frequency of responses to Pedi-EAT-10 questions.

Parents reported most difficulty with swallowing solids, food sticking and coughing when eating. The most frequently reported severe problems were swallowing solid foods (n=15, 9%); the child not wanting to eat (n=10, 6%) and swallowing liquids (n=9, 5.4%). The items most frequently reported as not being a problem were the child having pain on swallowing (n=115, 68.9%), the child not gaining weight (n=111, 66.5%) and swallowing liquids (n=109, 65.3%).

3.4.4.2 Montreal Children's Hospital Feeding Scale (MCHFS)

Responses were provided by 167 (95.4%) parents. Parents of six fully tube fed children did not complete this measure. On this measure, 106 (63.4%) scored as having no feeding difficulties, 20 (12%) had mild difficulties, 13 (7.8%) had moderate difficulties and 28 (16.8%) severe difficulties. The mean total score was 40.66 (SD 16.18). The frequency of responses to each question are provided in Table 3-3. Responses to negatively scored questions have been reverse scored, as per scoring guidelines.

Table 3-3. Frequency of responses to the Montreal Children's Hospital Feeding Scale.

	Rating response, n(%)							Feeding difficulty %	Mean (SD)
	1	2	3	4	5	6	7		
1. How do you find mealtimes with your child?	30 (18) Easy	21 (13)	31 (19)	30 (18)	36 (21)	9 (5)	10 (6) Very difficult	32	3.53 (1.75)
2. How worried are you about your child's eating?	21 (12) Not worried	28 (17)	21 (13)	23 (14)	38 (23)	20 (12)	16 (9) Very worried	58	3.92 (1.87)
3. How much appetite does your child have?	75 (46) Good appetite	17 (10)	18 (11)	20 (12)	14 (7)	17 (10)	6 (4) Never hungry	21	2.74 (1.95)
4. When does your child start refusing to eat during mealtimes?	53 (32) At the end	4 (2)	19 (11)	21 (13)	18 (11)	31 (18)	21 (13) At the beginning	31	3.74 (2.24)
5. How long to mealtimes take for your child (in minutes)?	12 (7) 1-10 min	37 (22) 11-20	50 (30) 21-30	36 (21) 31-40	21 (13) 41-50	6 (4) 51-60	5 (3) >60 min	41	3.33 (1.39)
6. How does your child behave during mealtimes?	57 (34) Behaves well	30 (18)	17 (10)	34 (20)	20 (12)	3 (2)	6 (4) Acts up, makes a big fuss	38	2.78 (1.71)
7. Does your child gag/spit/vomit certain types of food?	41 (24) Never	38 (23)	19 (12)	22 (13)	22 (13)	12 (7)	13 (8) Most of the time	52	3.20 (1.93)
8. Does your child hold food in his/her mouth without swallowing it?	66 (39) Never	36 (22)	17 (10)	14 (8)	11 (7)	18 (11)	5 (3) Most of the time	21	2.65 (1.87)
9. Do you have to follow your child around or use distraction so that your child will eat?	83 (50) Never	13 (8)	14 (8)	20 (5)	20 (12)	11 (7)	17 (10) Most of the time	29	2.83 (2.20)
10. Do you have to force your child to eat or drink?	82 (49) Never	24 (14)	22 (13)	11 (7)	11 (7)	11 (7)	5 (3) Most of the time	17	2.38 (1.78)
11. How are your child's chewing or sucking abilities?	87 (52)	22 (13)	25 (15)	12 (7)	10 (6)	3 (2)	8 (5)	35	

	Good						Very poor		2.26 (1.71)
12. How do you find your child's growth?	73 (44) Growing well	23 (14)	15 (9)	19 (11)	19 (11)	11 (7)	7 (4) Growing poorly	33	2.69 (1.91)
13. How does your child's feeding influence your relationship with him/her?	94 (56) Not at all	26 (16)	16 (9)	17 (10)	10 (6)	3 (2)	1 (1) Very negatively	19	2.02 (1.43)
14. How does your child's feeding influence your family relationships?	74 (45) Not at all	24 (15)	12 (7)	28 (16)	15 (8)	11 (7)	3 (2) Very negatively	40	2.59 (1.78)

Orange boxes are scores that meet the threshold for feeding difficulty.

To gain insight into the nature of the feeding difficulties, the MCHFS was examined at domain level. Results are summarised in Table 3-4.

Although internal consistency of the whole tool was good (Cronbach's alpha .883), domain-specific internal consistency ranged from poor to acceptable (Spiliotopoulou, 2009). Therefore, the nature of feeding difficulties was also examined at item level.

The most frequently reported feature of feeding difficulty was parent worry (58%). Of the mealtime characteristics, gagging/spitting/vomiting was most frequently reported (52%), followed by prolonged mealtimes (41%), challenging mealtime behaviour (38%) and chewing/sucking difficulties (34%). Results indicate that respondents perceived relationships with family members are more negatively impacted by feeding difficulties than the relationship with their child. Growth concerns were reported by 33% of parents.

Table 3-4. Feeding difficulty as defined by Montreal Children's Hospital Feeding Scale domains and internal consistency

Domain	Reaching threshold for feeding difficulty %	Cronbach's α
Oral motor		
Question 8	21	.63
Question 11	35	
Oral sensory		
Question 7	52	.44
Question 8	21	
Appetite		
Question 3	21	.59
Question 4	31	
Mealtime behaviours		
Question 6	38	.56
Question 8	21	
Parent concern		
Question 1	49	
Question 2	58	.67
Question 12	33	
Parent strategies		
Question 5	41	
Question 9	29	.59
Question 10	17	
Family reactions to feeding		
Question 13	19	.74
Question 14	40	

3.4.4.3 Feeding-swallowing impact survey (FSIS)

The FSIS was completed by 174 (99.4%) parents. Internal consistency of the tool in this population was excellent (Cronbach's alpha .944). Score summaries are provided in Table 3-5. Parents scored highest on the "worry" subscale and lowest on the "feeding" subscale.

Fifty-six (30.2%) parents reported "almost always" finding it hard to get help from others as they are scared to leave their child and 39 (22.4%) reported that others were reluctant to take care of their child due to fear when feeding them. Fifty-nine parents (33.9%) reported "almost always" worrying about their child's general health, 58 (33.3%) that their child will never eat like other

children and 57 (32.8%) that they aren't doing enough to help. Parents were least concerned about how to prepare foods appropriately.

Table 3-5. Total and subscale scores for the Feeding-Swallowing Impact Survey.

	Mean average item score (SD)	Mean summed score (SD)
Daily activities subscale	2.77 (1.26)	13.86 (6.32)
Worry subscale	3.02 (1.16)	21.11 (8.14)
Feeding subscale	1.95 (.98)	11.67 (5.89)
Total score	2.59 (1.02)	46.57 (18.36)

SD = standard deviation.

Compared with data generated from a UK community sample of children without swallow dysfunction, 85.6% of parents scored above the 75th centile and 74.1% scored above the 95th centile (Stewart et al, 2024, paper in preparation). Response frequencies for the community and OA samples are provided in Figure 3-3.

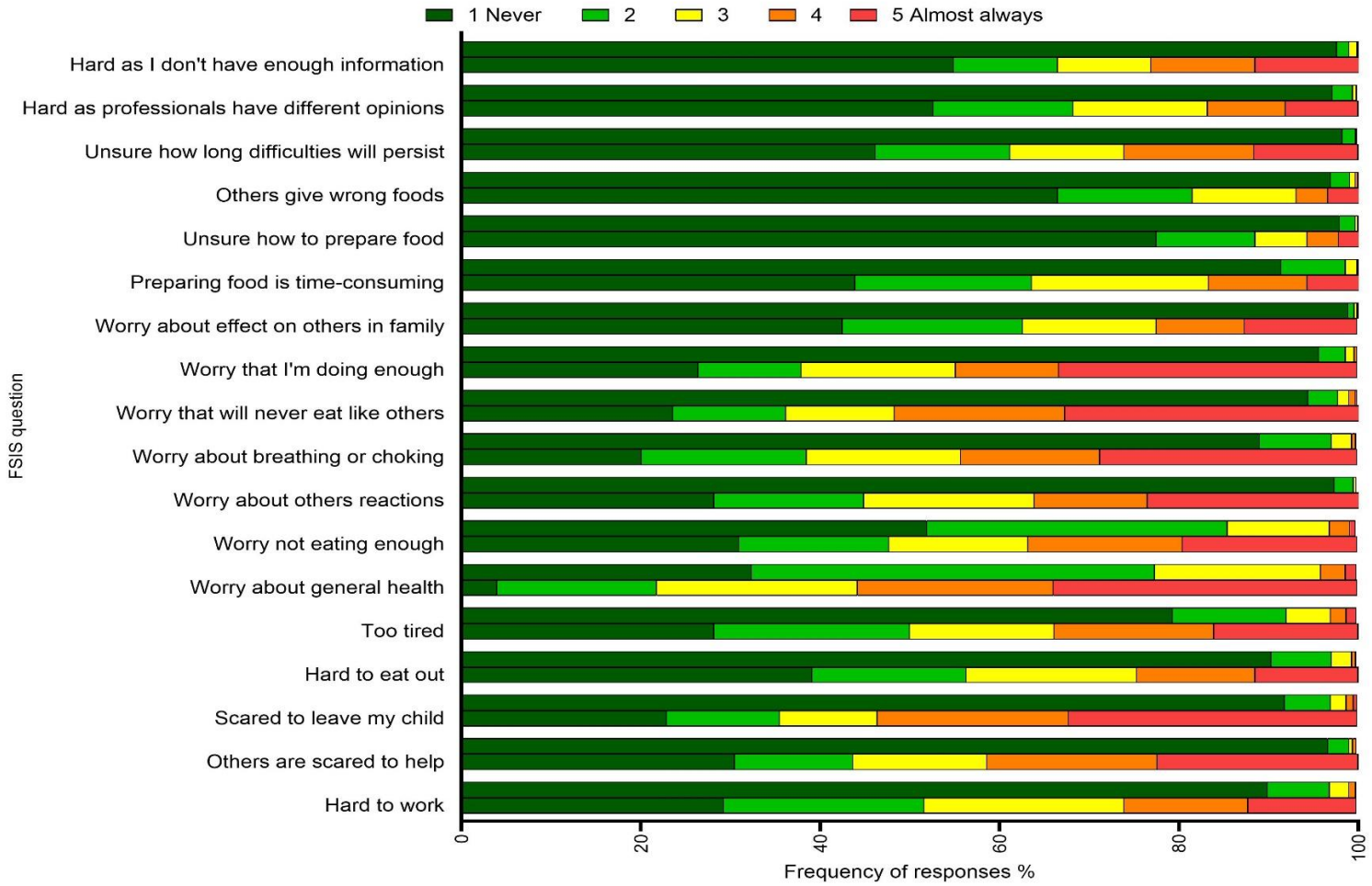


Figure 3-3. FSIS frequency of responses. Comparison of community (top bars) and OA (bottom bars) samples.

3.4.4.4 Generalised anxiety disorder-7 (GAD-7)

The GAD-7 was completed by 172 (98.3%) parents. Internal consistency was excellent (Cronbach's alpha .955). The mean score was 8.15 (SD 6.70). Sixty-eight (39.6%) had no anxiety (0-4), 44 (25.6%) scored as having mild anxiety (5-9), 23 (13.3%) scored as having moderate anxiety (10-14), and 37 (21.4%) with severe anxiety (15 or more). Further evaluation is recommended for those scoring 10 or greater, which is 34.7% of this cohort. The results are presented in Figure 3-4.

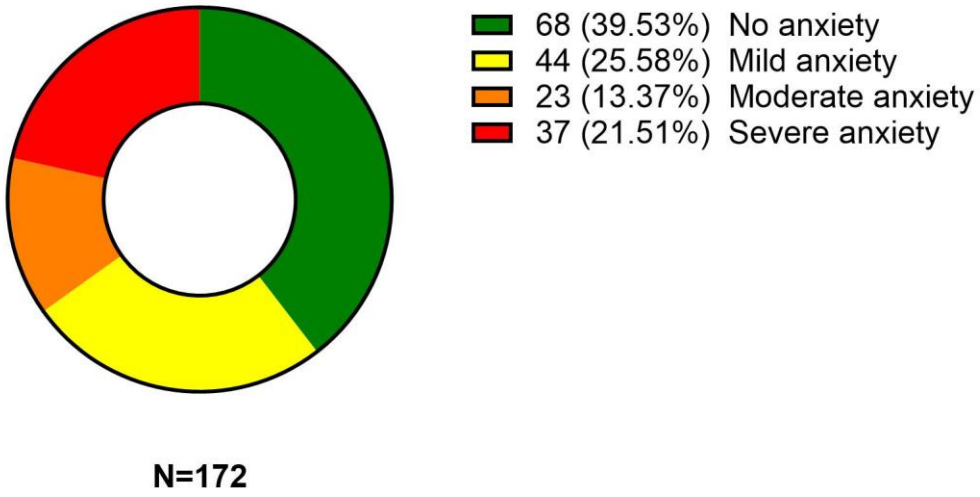


Figure 3-4. Results of the GAD-7 measure.

3.4.4.5 Patient Health Questionnaire-2 (PHQ-2)

The PHQ-2 was completed by 172 (98.3%) parents. Cronbach's alpha for the PHQ-2 was .899, indicating excellent internal consistency. The mean score was 1.59 (SD 1.91). One hundred and thirty participants (75.6%) scored less than three, indicating a diagnosis of depression is not likely and 42 (24.4%) scored three or greater, indicating a depressive disorder is likely.

3.4.4.6 Perceived stress scale-10 (PSS-10)

The PSS-10 was completed by 169 (95.4%) parents. Internal consistency of the PSS-10 was excellent in this cohort (Cronbach's alpha .885). The mean

score was 19.42 (SD 7.27). A comparison of mean scores with community cohorts from Sweden (Nordin et al. 2013) and the USA (Cohen 1994) is presented in Figure 3-5.

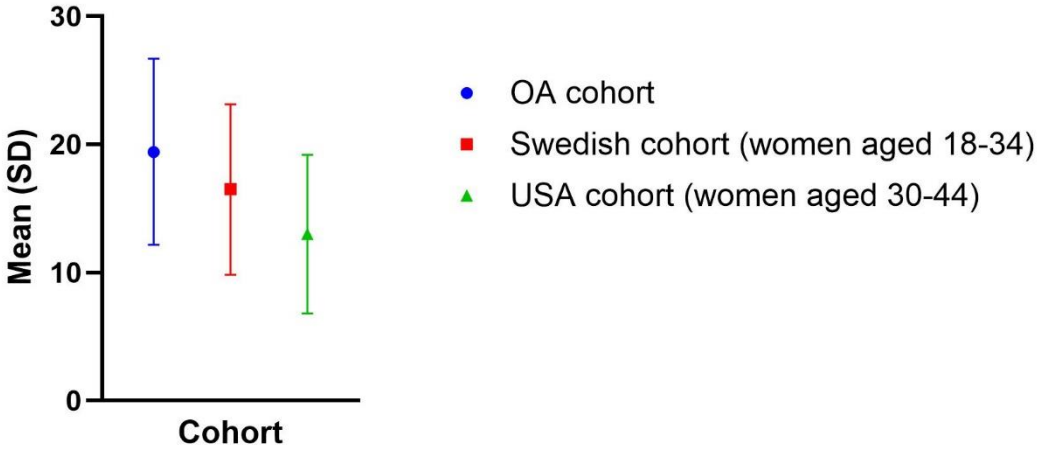


Figure 3-5. Mean and standard deviation scores on the Perceived Stress Scale.

3.4.4.7 Post-traumatic Stress Disorder-8 (PTSD-8)

The PTSD-8 was completed by 168 (96%) parents. Cronbach's alpha for this measure showed excellent internal consistency (.936). Frequency of those meeting the criteria for a diagnosis of post-traumatic stress disorder (PTSD) are presented in Table 3-6. The number of parents meeting the diagnostic criteria for 0, 1, 2 or 3 constructs are presented in Table 3-7.

Table 3-6. Frequency of diagnostic threshold for Post-Traumatic Stress Disorder diagnosis.

	Meeting diagnostic threshold n, (%)
Intrusion construct	113 (67.3)
Avoidance construct	80 (47.6)
Hypervigilance construct	87 (51.8)
PTSD diagnosis	64 (38.1)

PTSD = post-traumatic stress disorder

Table 3-7. Frequency of participants meeting diagnostic criteria by number of constructs.

Met diagnostic criteria	N (%)
For 0 constructs	47 (28.0)
For 1 construct	30 (17.9)
For 2 constructs	28(16.1)
For 3 constructs	64 (38.1)

3.4.4.8 Brief resilience scale (BRS)

The BRS was completed by 171 (97.7%) parents. Cronbach's alpha was .903, indicating excellent internal consistency. The mean total score was 19.14 (SD 5.32). The mean item score (total score/number of questions) was 3.19 (SD 1.08). Normative data are not available for a UK population. A mean item score of 3.19 equates to the 44.2 centile for women aged 30-39 or 51.8 centile for women aged 40-49, when compared to a German population sample (Kunzler et al. 2018).

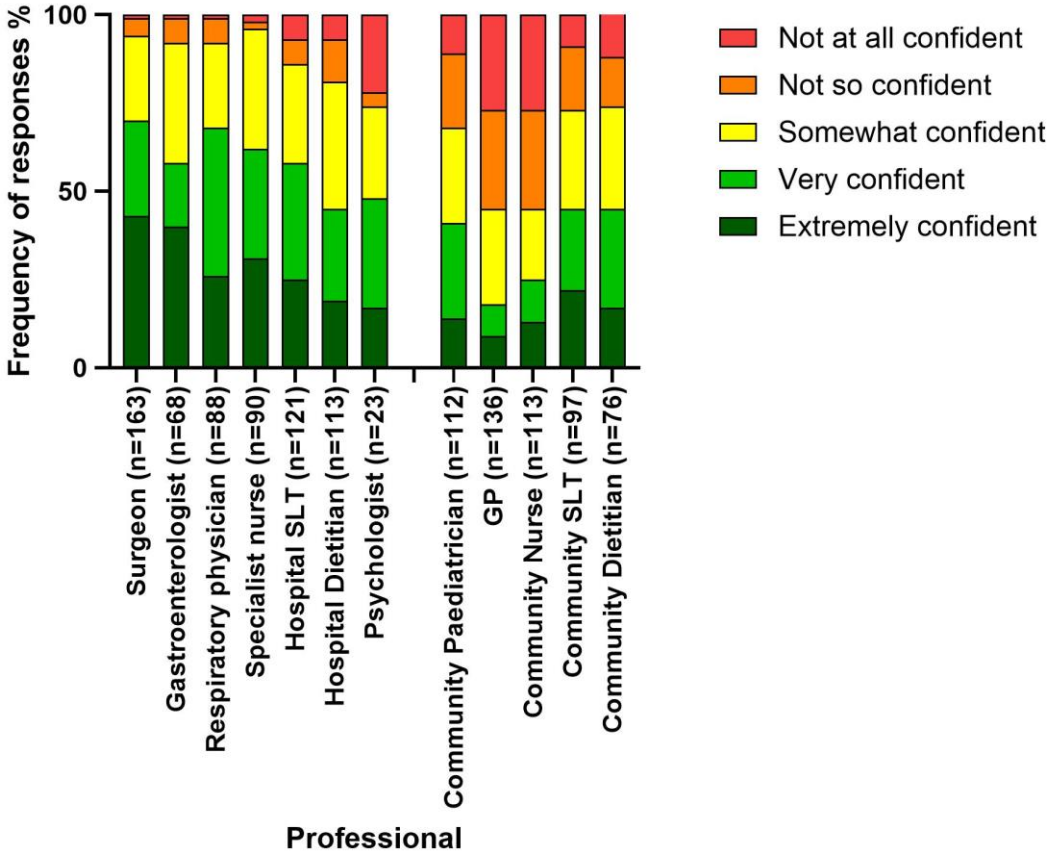
3.4.4.9 Professional support

One hundred and seventy-four (99.4%) completed the professional support questions. The mean overall satisfaction with professional support for feeding was 2.44 (SD 1.05). Frequency of responses are detailed in Table 3-8.

Table 3-8. Overall satisfaction with professional support for feeding.

	1 Very Satisfied (%)	2 Satisfied (%)	3 Neutral (%)	4 Dis-satisfied (%)	5 Very dis-satisfied (%)	Median (IQR)
Overall, how satisfied are you with the professional help you have been given with your child's feeding?	29 (16.7)	76 (43.7)	40 (23)	21 (12)	8 (4.6)	2 (1)

Advice regarding feeding was received from many different healthcare professionals. Confidence in the advice provided is detailed in Figure 3-6.



SLT = speech and language therapist. GP = general practitioner.

Figure 3-6. Confidence in professional advice provided

Respondents were most confident in the advice provided by their surgeon and respiratory physician, with 116 (71.1%) and 60 (68.1%) being very or extremely confident and 6 (3.7%) and 7 (7.9%) “not so” or “not at all” confident respectively. Eighteen (14.6%) respondents were “not so” or “not at all” confident with hospital SLT advice, 18.7% with hospital dietetic advice, 26% with psychologist advice, 27.9% with community SLT advice, 28.4% with community dietetic advice and 32.1% with community paediatrician

advice. Respondents were least confident in advice provided by community nurses (health visitor or school nurse) and GPs, with 53.9% and 55.1% respectively being “not so” or “not at all” confident.

As outlined in Table 3-9, there was considerable variation in the type of professional seen for feeding support. Advice for feeding was most widely accessed from a surgeon and least widely from a psychologist. Most frequently identified unmet need was for gastroenterology (26.7%) and psychology (21.1%) support.

Table 3-9. Frequency of access to healthcare professionals for feeding support.

	Seen (%)	Not seen, but no need (%)	Not seen, but would like to see (%)
Surgeon	163 (93.7)	6 (3.4)	5 (2.9)
Gastroenterologist	68 (39.5)	58 (33.7)	46 (26.7)
Respiratory physician	88 (51.2)	60 (34.9)	24 (14.0)
Specialist nurse	90 (52.3)	59 (34.3)	23 (13.4)
Hospital SLT	121 (70.3)	27 (15.7)	24 (14.0)
Hospital dietitian	113 (65.7)	33 (19.2)	26 (15.1)
Psychologist	23 (13.5)	112 (65.5)	36 (21.1)
Community paediatrician	112 (65.1)	41 (23.8)	19 (11.1)
GP	136 (79.1)	31 (18.0)	5 (2.9)
Community nurse	113 (66.1)	46 (26.9)	12 (7.0)
Community SLT	97 (56.4)	49 (28.5)	26 (15.1)
Community dietitian	76 (43.7)	64 (36.8)	34 (19.5)

SLT = Speech and Language Therapist, GP = General Practitioner

3.4.4.10 ADVS PROM-dyspnoea subscale

The ADVS was complete by 170 (97.1%). The dyspnoea subscale demonstrated excellent internal consistency in this population, with a Cronbach's Alpha of 0.84. The median score was 2 (IQR .2). Mean scores for a group of children undergoing diagnostic and therapeutic procedures at a single tertiary centre were 3.65 (SD 2.85) pre-procedure and 2.85 (SD 2.22) post-procedure (Nouraei et al. 2017).

3.4.5 Correlation

A summary of the statistically significant variables relating to feeding outcome (as determined by MCHFS), feeding-related QOL (as determined by FSIS), anxiety (as determined by GAD-7) and PTSD (as determined by PTSD-8) is provided in

Table 3-10. Birth order, living outside of the UK, ethnicity, employment status, number of surgical repairs, having a syndromic diagnosis, having a cardiac comorbidity, experiencing blue episodes, having a laryngeal cleft and have eosinophilic oesophagitis were not correlated with any of these outcomes. The MCHFS strongly correlated with the other measures of feeding: Pedi-EAT-10 (r=.76, p=<.001) and FSIS (r=.74, p=<.001).

Table 3-10. Summary of statistically significant correlations for outcomes of interest

	Feeding difficulty	Feeding-related QOL	Anxiety	PTSD
Child variables				
Child age	-.22**	-.35**	-.18*	-.18*
Child gender			-.17*	-.19*
Prematurity	.27**	.21*	-.155*	-.16*
Delayed repair	.19*			
Strictures	.16*	-.25**		
Dyspnoea	.46**	.49**	.41**	.41**
GOR	-.34**	-.36**	-.23*	-.23*
VCP	-.15*			
Unsafe swallow	-.25**			
Feeding difficulty		.72**	.49**	.48**
Parent variables				
Parent age	.17*	-.27**	.-.24**	-.26**
Parent gender			-.17*	-.19*
Anxiety	.49**	.67**		.69**
Depression	.42**	.62**	.80**	.60**
PTSD	.48**	.64**	.69**	
Stress	.48**	.59**	.68**	.65**
Resilience	.17**	-.32**	-.38**	-.49**
HCP support	.32**	.41**	.44**	.32**
One parent household		-.15*		
TOFS recruitment		-.21**	.27**	-.20*

Spearman's rank correlation. *p=<.05, **p=<.001. GOR = gastro-oesophageal reflux, VCP = vocal cord palsy, HCP = healthcare professional.

3.4.6 Factors associated with feeding difficulty

The linear regression model for feeding difficulty is detailed in Table 3-11. Test assumptions were met. The overall model was statistically significant, $F(12, 148)= 9.040$, (p=<.001) with an adjusted R^2 of 0.376. Regression coefficients can be found in Table 3-11. Dyspnoea, being born at 28-32 weeks' gestation, having had a stricture within the last year and parent anxiety were statistically significant contributors to feeding outcome assessed by MCHFS score.

Table 3-11. Multiple linear regression coefficients for feeding difficulty (Montreal Children's Hospital Feeding Scale)

MCHFS	***B***	**95% CI for *B***		***p* value**
		lower	**upper**	
One year increase in child age	-.022	-.764	.720	.954
Prematurity (4-7 weeks preterm)	.581	-4.456	5.617	.820
Prematurity (8-12 weeks preterm)	9.793	2.619	16.966	**.008**
One unit increase in dyspnoea PROM	.671	.181	1.160	**.008**
Repair <1 month post birth	-5.011	-11.956	1.935	.156
Stricture within the last year	7.390	2.859	13.039	**.011**
Stricture more than a year ago	-1.547	-7.189	4.095	.589
No comorbid cardiac condition	-1.328	-6.358	3.702	.603
No vocal cord palsy	-1.881	-8.209	4.447	.558
No report of unsafe swallow	-4.870	-10.151	.412	.070
Not receiving treatment for GOR	-4.887	-9.977	.202	.060
One unit increase on GAD-7 (parent anxiety)	.675	.319	1.031	**<.001**

B = regression coefficient. CI = confidence interval. PROM = parent/patient-reported outcome measure. GOR = gastro-oesophageal reflux. GAD-7 = measure of generalised anxiety disorder.

3.4.7 Factors associated with feeding-related QOL

Multiple linear regression test assumptions were met. The overall model was statistically significant, F (9, 148) = 33.807, (p=<.001) with an adjusted R^2 of 0.653. Regression coefficients can be found in Table 3-12. Child age, dyspnoea, any feeding difficulty, anxiety, PTSD and satisfaction with HCP support were independent predictors of feeding-related QOL. Being in a single parent household approached significance in the model.

Table 3-12. Multiple linear regression coefficients for feeding-related QOL (Feeding-Swallowing Impact Survey)

FSIS	***B***	**95% CI for *B***		***p* value**
		lower	**upper**	
One year increase in child age	-.796	-1.317	-.275	**.003**
One unit increase in dyspnoea PROM	.508	.124	.892	**.010**
Presence of mild feeding difficulties	9.556	3.917	15.195	**.001**
Presence of moderate feeding difficulties	15.251	8.546	21.956	**<.001**
Presence of severe feeding difficulties	10.085	4.809	15.361	**<.001**
One unit increase on GAD-7 (parent anxiety)	.517	.129	.904	**.009**
One unit increase on PTSD-7 (parent PTSD)	.733	.372	1.094	**<.001**
One unit decrease in satisfaction with HCP support	2.158	.310	4.005	**.022**
Single parent household	-5.538	-11.244	.167	.057

FSIS= Feeding-swallowing impact survey. *B* = regression coefficient. CI = confidence interval. PROM = parent/patient-reported outcome measure. PTSD = Post-traumatic stress disorder. HCP = Healthcare professional

3.4.8 Factors associated with parent anxiety

Multiple linear regression test assumptions were met. The overall model was statistically significant, F (14, 145) = 8.649, (p=<.001) with an adjusted R^2 of 0.402. Regression coefficients can be found in Table 3-13. Dyspnoea,

moderate prematurity, parent age under 30, resilience, satisfaction with HCP support and severe feeding difficulties were independent predictors of parent anxiety.

Table 3-13. Multiple linear regression coefficients for parent anxiety (GAD-7).

GAD-7	***B***	**95% CI for *B***		***p* value**
		lower	**upper**	
One year increase in child age	.150	.-.141	.440	.310
Prematurity (4-7 weeks preterm)	2.079	.079	4.080	**.042**
Prematurity (8-12 weeks preterm)	-.929	-3.836	1.978	.529
One unit increase in dyspnoea PROM	.271	.087	.455	**.004**
Parent age under 30 years	3.091	.229	5.953	**.034**
Parent age 30-39 years	1.882	0.211	3.975	.078
Not receiving GOR treatment	-.069	-1.980	1.842	.943
One unit increase in BRS (parent resilience)	-.308	-.475	-.142	**<.001**
One unit decrease in satisfaction with HCP support	1.528	.649	2.407	**<.001**
Male parent gender	-1.147	-4.815	2.520	.537
Recruitment via TOFS	-.767	-2.7888	1.254	.454
Presence of mild feeding difficulties	.255	-2.455	2.965	.853
Presence of moderate feeding difficulties	3.244	-.109	6.597	.058
Presence of severe feeding difficulties	3.921	1.321	6.521	**.003**

GAD-7 = Generalised anxiety disorders scale. CI = confidence interval. *B* = regression coefficient. PROM = parent/patient-reported outcome measure. BRS = brief resilience scale. TOFS = Patient support group. HCP = Healthcare professional. GOR = Gastro-oesophageal reflux.

3.4.9 Factors associated with PTSD

Multiple linear regression test assumptions were met. The overall model was statistically significant, F (14, 144) = 10.851, (p=<.001) with an adjusted R^2 of 0.466. Regression coefficients can be found in Table 3-14. Higher parent-reported dyspnoea scores, younger parent age, lower resilience, and

moderate and severe parent-reported feeding difficulties were independent predictors of parent PTSD. Having a child born very preterm approached significance in the model.

Table 3-14. Multiple linear regression coefficients for parent PTSD (PTSD-8).

PTSD-8	*B*	95% CI for *B*		*p* value
		lower	upper	
One year increase in child age	.233	-.069	.515	.133
Prematurity (4-7 weeks preterm)	1.139	-.879	3.156	.266
Prematurity (8-12 weeks preterm)	-2.856	-5.789	.077	.056
One unit increase in dyspnoea PROM	.377	.189	.564	**<.001**
Not receiving GOR treatment	-.266	-2.191	1.659	.785
One unit increase on BRS (parent resilience)	-.503	-.671	-.335	**<.001**
One unit decrease in satisfaction with HCP support	.566	-.320	1.452	.209
Male parent gender	-.954	-4.645	2.738	.610
Parent age under 30	4.476	1.559	7.394	**.003**
Parent age 30-39 years	2.644	.539	4.749	**.014**
Recruited via TOFS	.234	-1.831	2.300	.823
Presence of mild feeding difficulties	0.58	-2.718	2.834	.967
Presence of moderate feeding difficulties	4.812	1.439	8.185	**.005**
Presence of severe feeding difficulties	4.828	2.211	7.446	**<.001**

PTSD-8 = Post-traumatic stress disorder-8 questionnaire. CI = confidence interval. *B* = regression coefficient. PROM = patient/parent-reported outcome measure. BRS = brief resilience scale. HCP = Healthcare professional. GOR = Gastro-oesophageal reflux. TOFS = patient support group.

3.4.10 Summary of predictor variables

A summary of the statistically significant predictor variables is given in Table 3-15.

Table 3-15. Summary table of significant predictor variables for all linear regression models.

	Feeding difficulty	Feeding -related QOL	Parent anxiety	Parent PTSD
Child associated factors				
Increase in child age				
33-36 weeks gestation				
28-32 weeks gestation				
Increase in dyspnoea severity				
Delayed repair >1 month				
Stricture within a year				
Stricture over a year ago				
Mild feeding difficulties				
Moderate feeding difficulties				
Severe feeding difficulties				
Parent associated factors				
Parent age <30 years				
Parent age 30-39 years				
Increase in parent resilience				
Increase in parent anxiety				
Increase in parent PTSD				
Decrease in support satisfaction				

Green box = statistically significant variable indicating better outcome. Orange box = statistically significant variable indicating worse outcome. QOL = quality of life, PTSD = post-traumatic stress disorder, GOR = gastro-oesophageal reflux disease, TOFS = parent support group.

3.5 Discussion

This research builds upon the findings of the qualitative study (Chapter 2) through investigation of the frequency and severity of the phenomena described by parents and identification of explanatory variables. This discussion will explore the findings in relation to the existing literature on the topic. Results will be synthesised with the online forum in Chapter 6. The first three research questions will be considered in turn. The fourth (determining explanatory variables) will be addressed within each of the other questions.

3.5.1 What is the frequency, and severity of parent-reported feeding difficulties in children born with OA/TOF?

3.5.1.1 Frequency and severity of feeding difficulties

Providing quantitative confirmation for the presence and severity of feeding difficulties described in qualitative analysis of the online forum data, results from the MCHFS indicate that 63.4% of children have no parent-reported feeding difficulties, 12% mild, 7.8% moderate and 16.8% severe difficulties, with an additional 6 (3%) being fully tube fed. A recent study conducted in France in a cohort of 145 children aged 1-4 years (median 2.3 years) with OA/TOF also used the MCHFS and found 57.9% had no feeding difficulties, 15.2% had mild, 5.5% had moderate and 8.3% had severe difficulties. In this cohort a further 13.1% were tube fed (Pham et al. 2022). In Pham et al.'s study, all children requiring tube feeding were omitted from the percentage of children with mild/moderate/severe feeding difficulties. In the present study only children who were not having *any* oral intake were excluded. When the severe feeding difficulty and tube fed children are combined, frequency of moderate-severe feeding difficulties in the two cohorts is similar, at approximately 20%.

In contrast with these findings, Menzies et al (2020), identified no children with moderate or severe feeding difficulties and 15% with mild difficulties. This cohort was small (n=20) and recruited from a single centre MDT OA/TOF clinic. They excluded children with an OA repair over six months of age and those where introduction of solid food was delayed over one year. Thus, potentially those with more severe feeding difficulties were excluded from this sample, explaining some of the difference in reported frequency of feeding difficulties when compared to findings in the current study. An alternative explanation is that feeding concerns were addressed within the MDT clinic, resulting in better feeding outcomes.

3.5.1.2 Nature of feeding difficulties

Results from the MCHFS suggest that difficulties are not rooted in a specific domain, with varied frequency of items within each domain and similar

results across the domains. This may reflect the poor internal consistency of the MCHFS at domain level in this cohort.

Pham et al (2020) report frequency of mealtime characteristics for those with any severity of feeding difficulty (prolonged mealtimes, low appetite, oppositional/aversive behaviour, stressful mealtimes, oral hypersensitivity). However, these domains are different from those described by the authors of the tool (Ramsay et al. 2011). It is unclear which items were used to calculate these figures, making direct comparison difficult.

3.5.1.3 Factors associated with feeding outcome

Use of multiple linear regression facilitated exploration of potential explanatory variables associated with feeding outcome. This data builds on the rich descriptions of the feeding difficulties gathered in the online forum (Chapter 2).

Numerous factors correlated with MCHFS total score. On multivariable regression only being born 8-12 weeks preterm, dyspnoea, having a stricture within the last year and requiring GOR treatment were significant predictors of feeding outcome. This study did not find type of OA or having a delayed repair (both of which are associated with delayed introduction of oral feeding) were associated with feeding outcome. Evidence from other studies to determine the influence of OA type or delayed repair to date has been contradictory. In a small pilot study, Baird and colleagues (2015) reported higher MCHFS scores in children with non-type C OA. Yasuda and colleagues (2022) found long gap OA (typically type A OA) was associated with tube feeding dependence in univariate analysis, but non-significant in multivariable analysis. In a study using a bespoke, unvalidated telephone questionnaire, Bevilacqua and colleagues (2020) found long-gap OA was associated with the ability to self-feed at three years of age but was not associated with any other of the five feeding outcomes assessed. Consistent with findings in my study, Pham et al. (2022) did not find OA type associated with MCHFS score. There is a growing body of evidence to indicate that OA subtype alone, does not impact feeding outcome.

Results suggests that other factors causing disruption to feeding experience are more influential on feeding outcome than delayed introduction. Requiring a dilatation for stricture within the last year was associated with MCHFS score in multivariable regression. Supporting the assertion that strictures are related to feeding, Bevilacqua et al. (2020) reported the number of dilatations to be univariately associated with age at which foods are introduced. Yasuda and colleagues (2022) reported oesophageal anastomosis diameter was related to dependence on tube feeding. However, other studies have found no association between oesophageal abnormalities and feeding outcome (Menzies et al. 2017, Pham et al. 2022, Maybee et al. 2023). Differences may be due to the way in which data regarding strictures are collected. The present study found that strictures were associated with feeding if they had occurred in the last year, but not over a year. The number of strictures was not relevant. Other studies have reported total number of strictures/dilatation or the “ever” presence of strictures. Strictures result in an acute, rather than chronic disruption to feeding, and once dilatated, provide relief from bolus obstruction (Mahoney et al. 2017). Results study indicate that long-term disruption to feeding is not caused by strictures.

The need for GOR treatment was not statistically significantly associated with feeding outcome, although was nearing significance. Despite there being sound evidence for the negative impact of GOR on feeding behaviours and swallow in children (Mathisen et al. 1999, Sdravou et al. 2021), the specific impact of GOR on feeding in OA/TOF has received little attention and was not included as an independent variable in other studies of feeding outcome. In the current study, GOR was measured using a crude, dichotomous outcome of receiving current treatment. Future studies, using a validated measure of GOR and GOR symptoms, would be of value to further explore this relationship.

Much like GOR, breathing difficulties are known to impact on feeding in children (e.g. Jaffal et al. (2020)), yet have received little attention in empirical studies in OA/TOF to date. My study demonstrated that breathing difficulties (as identified by the parent-rated dyspnoea score) were

associated with the presence of feeding difficulties. Maybee and colleagues (2023), report a higher risk of dysphagia in children with tracheomalacia, and a higher risk in those with severe tracheomalacia than in those with mild or moderate disease. Further evidence for the significant impact of breathing difficulties on feeding outcome comes from Pham and colleagues (2022), who identified the need for inhaled corticosteroids as one of only two variables associated with feeding outcome in multivariable regression-the other being low weight. These findings all indicate that the impact of breathing on feeding and swallowing require greater consideration within this population than is currently afforded.

Younger age has previously been identified as being associated with higher prevalence of feeding difficulties (Coppens et al. 2016, Menzies et al. 2017, Maybee et al. 2023). While age was associated at a univariate level, it was not significant in multivariable regression in the current investigation. This indicates other factors (recency of strictures, GOR, breathing difficulties), that may be more prevalent in younger children, were driving the difference in outcome. This is valuable to understand in planning and delivery of services, suggesting that increased support in early years to address the underlying morbidities could optimise feeding outcome.

3.5.2 How is feeding-related QOL impacted in families of children with OA/TOF?

Compared to a community sample of UK parents without feeding difficulties, almost three quarters of parents of children with OA/TOF scored above the 95th centile on the FSIS, indicating that feeding-related QOL is greatly impacted for parents caring for a child with OA/TOF. This confirms findings from the online forum (Chapter 2). Cohort mean scores are similar to those reported by Serel Arslan et al (2020) who used a Turkish version of the FSIS in a study of 64 children aged 1-12 with OA/TOF.

Compared to other populations of children with feeding difficulties, total FSIS score was similar to those with moderate cerebral palsy (Mokhlesin et al. 2024), laryngeal cleft (Fracchia et al. 2017), mixed aetiology paediatric

feeding disorder (Simione et al. 2023) but higher than parents of children with Down syndrome (Serel Arslan 2022). They were lower than those of parents of children with severe cerebral palsy (Mokhlesin et al. 2024) and slightly lower than those for parents of autistic children with feeding disorder (Gent et al. 2024). In all populations parents score highest on the "worry" subtest, and lowest of the "feeding difficulties" subtest. Item level responses have not been reported in the literature to date, therefore it is not possible to determine whether there are population-specific areas of feeding-related QOL affected. However, these findings highlight the consistent impact on parents and underline the importance of addressing feeding and swallowing difficulties as a dyadic or family system. Focusing interventions only on the child fails to address important aspects of the feeding difficulty.

Results confirm findings of the online forum that feeding and swallowing difficulties impact parents beyond the mealtime itself and provide evidence to indicate that these issues are widespread. Nearly a quarter of respondents scored 4 or 5 (on a 5-point Likert scale) in a statement about it being hard to work. However, most frequently reported was the impact that the feeding difficulties had on access to childcare. Over 40% reported others were scared to look after their child, and over 50% reported that they were scared to leave their child (scoring 4 or 5). Not having easy access to childcare support adds to the burden of care and sense of isolation for parents. Feelings of isolation have been reported in previous research across feeding difficulties arising from varied aetiologies, including OA/TOF (Hewetson et al. 2009, Morton et al. 2019, Lamm et al. 2022, Wallace et al. 2022). Beyond determining whether parents lived in a single or two parent household, access to social support was not addressed in this questionnaire. Being in a single parent household was an independent predictor within the parent-factor regression model for FSIS but did not reach statistical significance in the final model, with a *p* value of .057. However, these findings, when considered with previous research, suggest that having good social support may be an important mediator for feeding-related QOL. Including discussion of the availability of social support in therapeutic conversations may identify an important area of need and highlight those who may benefit from closer

HCP support when navigating feeding challenges, such as at a new developmental milestone. Future research to evaluate the mediating value of social would be valuable.

3.5.2.1 Factors impacting feeding-related QOL

The questionnaire aimed to determine whether specific factors affected the degree to which feeding-related QOL was impacted, building on knowledge of the phenomena acquired from the online forum. Younger child age, breathing difficulties, severe feeding difficulties, younger parent age, higher parent anxiety, PTSD and satisfaction with HCP support were identified as independent predictors. Supporting the model proposed in Chapter 2, both child and parent variables influenced feeding-related QOL. These are novel findings within the field of OA/TOF, demonstrating the extent to which feeding-related QOL is impacted is dependent on a wide variety of factors.

Within other populations, Rama et al. (2022) identified weak-moderate correlations between higher socio-economic status, number of hospitalisations, severity of feeding/swallowing difficulty and FSIS score. Lefton-Greif et al. (2014) found no significant differences in scores between those from white and other ethnicities, above and below median income or between carers of children who were developmentally delayed or had typical development and no age group differences (<12 months, 12-18 months, >18 months). Severity of feeding difficulties was identified as the sole predictor of FSIS score for parents of autistic children (Gent, 2024).

Type of OA and time of repair were not associated with FSIS score in this study, contradicting work conducted in Turkey (Serel Arslan et al. 2020). The Turkish study consisted of 64 children, 43% of whom had isolated OA and 42% had delayed repair. They reported significantly worse scores in children with delayed repair and isolated OA/TOF. Compared to the Turkish cohort, children in the present study had better QOL than those with isolated OA and delayed repair but worse QOL than those with OA *and* TOF and early repair. Although representative of the population spread of OA type,

there were a smaller proportion of children with isolated OA and thus may have lacked power to demonstrate differences.

3.5.3 Is feeding associated with anxiety and PTSD in parents of children with OA/TOF?

3.5.3.1 Parent anxiety in OA/TOF

Results demonstrated that the mean anxiety score was in the “mild” category. This mirrors findings from an international support group survey study (Wallace et al. 2021) and a single centre prospective observational study (Tan Tanny et al. 2021). Supporting these findings is a cohort study (n=86) conducted in Canada using province level registry data, which found that levels of diagnosed anxiety disorder were not higher in mothers of children with OA/TOF than those without any gastro-intestinal abnormality (Urichuk et al. 2024). This would appear to contradict findings from the online forum, in which anxiety was identified as a major theme. However, nearly 35% of participants in this study had moderate or severe anxiety. Similarly, Wallace et al. (2021) found 44% of respondents presented with moderate-severe anxiety, indicating that while average scores are not raised, a considerable proportion of parents experience clinically relevant levels of anxiety. These proportions are higher than those reported in recent large UK cohort studies using the GAD-7 in which 9-24% of participants scored within the moderate-severe anxiety range (Kwong et al. 2021, Jia et al. 2022). These findings support the proposal that anxiety *is* raised for this population and warrants exploration of potential explanatory variables which may explain why some parents experience high anxiety, when others do not, including the specific role that feeding plays in increased anxiety which was so clearly described in the online forum.

Both the MCHFS and Pedi-EAT-10 had moderate-strong correlations with anxiety. Severe feeding difficulty (as determined by MCHFS score) was independently associated with anxiety in the multiple regression model. By using a validated measure of feeding difficulty, this evidence builds on that reported by Wallace et al. (2021) who used referral to Speech and Language

Therapy as a proxy for feeding difficulty to propose a relationship between feeding and parent anxiety.

Understanding the direction of the relationship between anxiety and feeding is of interest. High anxiety and increased stress are widely reported in parents caring for children with feeding difficulties associated with other underlying causes (Lefton-Greif et al. 2014, Silverman et al. 2021). There is evidence to show that increased levels of anxiety can negatively impact the child's mealtime behaviours and affect parent-child mealtime interaction (Faugli et al. 2008, Didehbani et al. 2011). In this study, regression analysis indicates that there is a bidirectional relationship; anxiety was an independent predictor of feeding difficulty, just as feeding difficulty was an independent predictor of anxiety. However, this relationship does not imply causation (Cohen et al. 2013). The model accounted for approximately 40% of score variation on the GAD-7, indicating there are likely to be other confounding factors that are unaccounted for. The plausibility of interplay between the two factors, however, is highlighted, along with the importance of assessing and treating feeding difficulties as a dyad, considering the parent as an integral part of the feeding outcome.

3.5.3.2 Feeding-related PTSD

Previous research has identified that parents of children with OA/TOF are at risk for PTSD (Le Gouez et al. 2016, de Vos et al. 2024). de Vos et al. (2024) found 33% of parents met the threshold for PTSD and Le Gouez et al. (2016) reported that 59% of parents met the threshold. Both these previous studies assessed PTSD with the presence of OA/TOF as the trigger.

de Vos et al. (2024) identified that parents of children under 6 months and those with major post-operative complications were at higher risk for PTSD. Le Gouez et al. (2016) found only a weak association between PTSD and age and no association with clinical variables. Feeding difficulties have not been previously considered as a trigger for PTSD in this population, however PTSD or PTSD-type symptoms were described by parents in the online forum (Chapter 2). Thus, feeding difficulties were determined as the trigger

for PTSD in the current study. Results showed that 38% of parents met the threshold for PTSD, similar to that reported by (de Vos et al. 2024).

Seventy-two percent of parents met the threshold for at least one construct of PTSD, the highest proportion being intrusion (67.8%). Intrusion symptoms involve reliving the traumatic event by way of distressing memories, flashbacks and distress (Staab et al. 2013). A high prevalence of intrusion symptoms has been previously reported in parents of children with congenital gastrointestinal conditions (including OA/TOF) (Roorda et al. 2022). Unlike other traumatic events, such as childbirth or hospital admission, parents experience the trigger of feeding-related PTSD multiple times a day, as they cannot avoid feeding their child. This highlights the importance of recognising when feeding events are triggering PTSD and ensuring parents access the appropriate psychological support.

As might be expected, parent-reported moderate and severe feeding difficulty (MCHFS score) were both associated with PTSD but not mild feeding difficulty. PTSD specifically related to feeding difficulty has not been investigated in OA/TOF or other conditions previously. It is not clear whether the nature of OA/TOF feeding difficulties, with the risk of acute bolus obstruction, places parents at a unique risk of developing a trauma response with feeding that is not seen in other populations with more chronic presentations and requires further exploration. However, it is evident that for this population, the risk of trauma should be recognised.

3.5.3.3 Parent factors associated with anxiety and PTSD

In the current study, younger parent age was associated with higher anxiety and PTSD scores. While parent age has not been included in any previous studies of PTSD, Wallace et al. (2021) also identified higher anxiety in parents under 30 years of age. Thus, there is a suggestion that younger parents may be more vulnerable to poorer mental health and should be highlighted for early monitoring and/or support.

Resilience, or the “ability to bounce back”, was assessed using the BRS (Smith et al. 2008). Resilience has previously been found to be protective for the development of psychopathology in parents of children admitted to intensive care (Rodriguez-Rey et al. 2018). It has also been identified as a mediator for anxiety in parents of children with disabilities (Rakap et al. 2024). In keeping with these findings, higher scores on the BRS were associated with lower anxiety levels and lower risk of PTSD.

The BRS measures personal agency-resilience within oneself (Windle et al. 2011). However, this is only one aspect of resilience and does not account for the resilience achieved through social support (Windle et al. 2011). Wallace et al. (2021) identified caring stress and support for caring were associated with anxiety scores. As previously discussed, social support was not explicitly included in my study, beyond identifying household make up (one or two parent households) and would be of value to include in future studies to determine its ability to mediate parental anxiety or the development of PTSD symptoms.

Satisfaction with HCP support was included and found to be an independent predictor of anxiety and feeding-related QOL but not PTSD. Those who reported greater satisfaction with the professional support received had lower level of anxiety and better QOL. Previous research has demonstrated how multidisciplinary input can positively impact parent anxiety around feeding difficulties in other populations (Greer et al. 2008, Silverman et al. 2021).

These association highlight the importance of ensuring access to the right support in a timely manner. It is widely recognised that OA/TOF is a complex, chronic condition requiring multi-disciplinary support (DeBoer et al. 2016, Dingemann et al. 2020, Platt et al. 2023). A recent position paper from the TOFS support group which calls for specialist, lifelong multi-disciplinary care, highlights that this is a priority for patients and their families (Slater et al. 2021).

Findings demonstrate the variability in access to and confidence in HCP feeding support and provide quantitative data to substantiate the challenges described in the online forum. While almost all had access to advice from a paediatric surgeon, under 40% had seen a paediatric gastroenterologist and only 13% a psychologist. Approximately 20% of parents identified a need for support from each of these professionals. Unmet need was evident within community and hospital dietetics, SLT, specialist nursing, respiratory and community paediatrics. Coordinated, multidisciplinary care has been shown to improve outcomes for children with OA/TOF, including reducing hospital admission, the number of post-repair procedures and length of stay, as well as having advantages for the family, such as reduced frequency of outpatient appointments (Platt et al. 2023).

Establishing multidisciplinary care aligns with the concept of service centralisation – that is, reducing the number of centres in which care is provided to improve outcomes in complex conditions. This results in a smaller number of centres caring for a larger volume of patients, building expertise within the whole multidisciplinary team (Dingemann et al. 2020). This approach may serve to address the needs of the families in this study, by ensuring equitable access to a highly specialist care team. However, care centralisation can come at a cost with reduced expertise in other centres and the benefits to surgical outcome in OA/TOF has been questioned (O'Connor et al. 2022). Care centralisation may also be detrimental to those living a long way from a specialist centre (Mungali 2005).

The “hub and spoke” model aims to address these issues, by having effective communication between a central, specialist “hub” and local “spokes”. Care is delivered at central, specialist centres while maintaining some intervention and care locally (Elrod et al. 2017). This has been effectively employed in a number of conditions in the UK, including cleft lip and palate, which is also a congenital condition requiring early surgical intervention with long-term, multi-disciplinary follow up (Scott et al. 2014). Within my study, participants reported lower confidence in community services than hospital-led services. In designing such a model of care, future

research should seek to understand what parents perceive as “good” care, and identify HCP needs, as has been carried out in other rare conditions (Wray et al. 2021, Ferreira et al. 2023).

3.5.3.4 Child factors associated with parent anxiety and PTSD

Results identified severity of dyspnoea as the only child factor predictive of higher anxiety and PTSD. Dyspnoea, reflecting chronic respiratory difficulties, has not been included as a potential contributor to anxiety or PTSD in previous OA/TOF research.

Within the qualitative data, blue episodes associated with feeding, that is acute respiratory difficulties, were often described as “traumatic” but were not associated with higher anxiety or risk of PTSD in the quantitative analysis. However, blue episodes were evaluated using a single item unvalidated question without any further explanation as to what constitutes a “blue episode”. This term may be too broad to identify those with significant or clinically relevant blue episodes and hence was not a good predictor. Further study with objective measures of respiratory and swallow function should be conducted to develop understanding of the relationship between acute and chronic breathing difficulties, anxiety and feeding.

Complexity of OA (including, type of OA, delayed repair, the need for more than one repair surgery, presence of co-morbidities and presence of strictures) was not associated with higher anxiety or presence of PTSD. Previous research supports the assertion that OA type or severity have limited influence on parental well-being outcome. Wallace et al. (2021), in their study of 240 parents found no difference in anxiety severity and OA complexity. Likewise, de Vos et al. (2024), in their study of 28 parents found no difference in anxiety level when comparing those with isolated OA and OA/TOF, and those who required additional surgeries or presented with major complications and those who did not. Tan Tanny et al. (2021) identified lower anxiety in those with isolated TOF, compared to those with OA and TOF or isolated OA, indicating reduced anxiety in those typically presumed to have the least complex clinical course. However, in keeping

with results from the present investigation, they found no association with any other markers of potential complexity (presence of multiple co-morbidities, dilatation or previous fundoplication). In the largest study of PTSD in OA/TOF to date, Le Gouez et al. (2016) found no child factors were associated with presence of parental PTSD. They included the need for complex surgery, prematurity (<34 weeks), length of stay, length of stay, neonatal severity score and the presence of severe sequalae at 2 years of age in the analysis.

3.5.4 Limitations

3.5.4.1 Parent-reported data

All measures in this study were parent-reported, without objective data with which to compare. MCHFS scores were moderately correlated with anxiety measures in this study. The potential for feeding outcome i.e. MCHFS scores, to reflect parent anxiety, rather than true function must be considered. Previous research comparing the MCHFS with an objective clinical measure of feeding found that parents were reliable reporters of their child's feeding difficulties and maintained objectivity (Rogers et al. 2018). The use of parent-reported data also limited the ability of the study to evaluate the potential causes of the outcomes reported. For example, oesophageal dysmotility is widely reported to impact feeding outcome (e.g. (Mahoney et al. 2017, Courbette et al. 2020), however it was not directly assessed. The Pedi-EAT-10 questionnaire aimed to provide a measure of swallow dysfunction. However, as highlighted by Duncan et al. (2021), it is not a reliable tool for differentiating the underlying cause of the swallowing difficulty. Although the Pedi-EAT-10 was included as a measure of *swallow* function, and the MCHFS as a measure of *feeding* difficulty, there is crossover between items within each questionnaire and thus they were not deemed to be independent. Therefore, swallow function per se was not included in the regression model. Future research using objective measures of swallow and feeding outcome would strengthen understanding of the complex interaction between anxiety and feeding.

3.5.4.2 Selection bias

To maximise sample size, participants were recruited through a patient support group (TOFS) and hospital sites. As discussed in Chapter 2, the decision to recruit via the support group has the potential for selection bias (those accessing the support group are not representative of, and may be systematically different to, all parents of children with OA/TOF) (Sedgwick 2013). While for qualitative methods this may be of less relevance, one of the aims of this study was to achieve statistical generalisability. Thus, selection bias is important to consider. However, the direction of the bias is difficult to determine. Are those accessing a support group those with greatest need and therefore are representing those for whom their child's difficulties are having the greatest impact-a key component of this research- or are those accessing the support group better supported, better informed and therefore less impacted than those not accessing peer support. Comparison of demographic and clinical characteristics of recruitment methods allowed for analysis of potential selection bias.

Previous research indicated that clinical characteristics of those recruited via online support groups and a clinical registry for children with rare rheumatological diseases were similar (Hausmann et al. 2022). However, in the present investigation, differences between groups existed, including age (younger child and parent age in the support group), OA type (fewer children with TOF only in the support group), parent gender (fewer males in the support group) and location (more living outside of the UK in the support group). Recruitment route was significantly correlated with numerous outcomes, including feeding-related QOL, parent anxiety and PTSD. However, recruitment route was a not a significant contributor in any regression model i.e. was not independently associated with any of the outcomes of interest. This suggests that although there were differences between those recruited via the support group and the hospital, it was other factors that were driving differences in outcome, rather than recruitment route explaining the differences.

3.5.4.3 Non-response bias

As with all questionnaire studies, non-response bias is also a potential source of bias (Sedgwick 2013). Non-response bias was not possible to calculate as no identifiable information was collected. However, this sample had approximately expected proportions of different types of OA/TOF, potentially more complex OA types were not over-represented (Spitz 2007). Sixty-five (35.7%) children were born before 37 weeks' gestation, which is higher than reported in a recent Canadian cohort study (20.8%) (Le-Nguyen et al. 2024) but comparable to French (35%) and Italian (36.4%) cohort studies (Sfeir et al. 2013, Cassina et al. 2016). Rates of VACTERL and congenital heart disease were also in line with other studies (Sfeir et al. 2013, Cassina et al. 2016). Thus, there is no evidence to suggest this cohort is over-representative of those with additional medical complexity.

3.5.4.4 Volunteer bias

Volunteer bias is also important to consider (Sedgwick 2013). The questionnaire was relatively long and required access to the internet. Although support for completion with translators or readers was advertised, no potential participants enquired about this support. It is acknowledged that limited socio-economic details were collected, as advised by the steering group, thus limiting the ability of this study to assess the impact of socio-economic factors on any of the assessed outcomes. The demographic details that were collected indicated that most participants were white, female, and employed, limiting the generalisability of findings outside of this demographic. While online methods have been shown to be effective for recruitment and participation (Hausmann et al. 2022), researchers have demonstrated that telephone questionnaires may help access wider socio-economic or more diverse samples (Lallukka et al. 2020). Investigating the impact on a more diverse sample, including fathers and those from under-represented socio-economic and ethnic groups, will be an important direction for future research.

3.5.5 Conclusion

This study provided evidence that approximately 20% of children with OA/TOF experience moderate-severe feeding difficulties. These impact on parent well-being, contributing to clinically significant generalised anxiety for 35% of parents. The study also provides the first reported evidence for feeding-triggered PTSD, which occurred in just under 40% of parents. The wide impact that feeding and swallowing difficulties have, beyond the mealtime itself, is further illustrated in this research. Evidence supports a complex, multidimensional picture of child and parent factors which interact to determine overall feeding QOL.

Chapter 4. Work package 2: Systematic review of oro-pharyngeal swallow and feeding characteristics in OA/TOF

4.1 Introduction

To gain a broader perspective, and determine prevalence, of feeding and swallowing characteristics a systematic review was undertaken. Comella et al. (2021) recently conducted a systematic review of oesophageal morbidity in OA/TOF, which included a broad review of "dysphagia". However, this work did not attempt to differentiate between oro-pharyngeal and oesophageal phase dysphagia, neither did it describe the specific features of the eating, drinking and swallowing difficulties.

4.1.1 Aim

Therefore, the aim of this work package was to:

Describe the characteristics of oro-pharyngeal swallow dysphagia and eating and drinking difficulties in those born with OA/TOF.

Research questions:

1. What are the characteristics of oro-pharyngeal swallowing impairment in OA/TOF as identified by instrumental assessment?

2. What are the characteristics of patient/carer reported eating and drinking difficulties in OA/TOF?

3. How are psychosocial aspects of eating and drinking impacted in individuals born with OA/TOF and their caregivers?

4.2 Methods

The study protocol was registered on PROSPERO (no. CRD42020207263.) and PRISMA guidelines followed. The protocol is provided in Appendix 9.

4.2.1 Mixed methods systematic review

A mixed method systematic review allows for inclusion of both qualitative and quantitative studies to generate a more complete synthesis (Stern et al. 2020). This method facilitates synthesis of data from different aspects of a single phenomenon, which was felt to be important for the topic under investigation. A key feature of mixed methods reviews is to integrate findings from qualitative and quantitative studies to identify confirmatory or contradictory data to create a greater breadth and depth of understanding than can be achieved from single paradigm evaluation (Stern et al. 2020).

4.2.2 Search strategy

The search strategy was developed with the guidance of a data information specialist at the Institute of Child Health library. The following search strategy was applied to MEDLINE: (Oesophageal Atresia/ OR Tracheoesophageal Fistula/ OR tracheoesophageal fistula OR tracheooesophgeal fistula OR trachea-esophageal fistula OR tracheo-oesophageal fistula OR oesophageal atresia OR esophageal atresia) AND (Deglutition/ OR exp Deglutition Disorders/ OR "Feeding and Eating Disorders of Childhood"/ OR Feeding Behaviour/ OR deglutition OR dysphagia OR feed* OR swallow*). Appropriate syntax alterations were made for searches in EMBASE, CINAHL, Pubmed, Scopus and Web of Science databases. The following databases were also searched: International Standardised Randomised Controlled Trials Number, clinicaltrials.gov. and Open Access Theses and Dissertations. Reference lists of included studies were hand searched. Inclusion/exclusion criteria are presented in Table 4-1.

.

Table 4-1. Inclusion/exclusion criteria

Inclusion criteria	Exclusion criteria
Empirical study of feeding or oro-pharyngeal swallowing function using instrumental (e.g. Videofluoroscopy) or non-instrumental (questionnaire) assessment, and/or, qualitative evaluation of feeding or swallowing outcome	Studies of oesophageal phase of swallowing (e.g. oesophageal manometry, pH impedance, gastric emptying, oesophageal/gastric endoscopy)
Includes participants with repaired congenital oesophageal atresia and/or tracheo-oesophageal fistula	Studies where OA/TOF is not reported separately i.e. cannot be distinguished from other conditions
Year of publication-1990-2020	Studies in which feeding/swallowing outcome has not been evaluated using an instrumental or validated non-instrumental tool or qualitative methods e.g., feeding outcome described as oral/non-oral only
Written in English language	Studies relating only to acquired tracheo-oesophageal fistula, such as button battery ingestion
Published in peer reviewed journal or grey literature (e.g. theses). Including: Ahead of Print, In-Process; Other Non-Indexed Citations	Review, opinion or commentary only
	Conference proceedings

4.2.3 Study selection

Searches were undertaken in January 2023 by AS and uploaded to Covidence (https://www.covidence.org/) for duplicate removal, screening and data extraction. Each article was screened (title/abstract) by two members of the team (AS plus one other member of the supervisory team). All studies rated “include” by at least one reviewer were included for full text screening, which was also conducted by two reviewers as above. Conflicts were resolved through consensus discussion at full text screening.

4.2.4 Data extraction

Data extraction was conducted by AS with 20% of all studies checked by another member of the supervisory team. Further checking by a second reviewer was not deemed necessary as no systematic errors were identified.

All studies were reviewed for any data relating to a characteristic of oro-pharyngeal swallow function or eating/drinking experience. Details of all the data extracted are provided in Table 4-2. Data were exported to Excel (Microsoft® Excel® for Microsoft 365 MSO (Version 2208 Build 16.0.15601.20818)) for analysis.

Table 4-2. Data extraction categories.

Authors
Date
Country
Title
Study design
Participant demographics: age at assessment, type of OA, age at repair, type of repair, co-morbidities
Inclusion/exclusion criteria
Participant recruitment
Sample size
Assessment type: instrumental, non-instrumental
Measurement tool used
Description of assessment results (e.g. Videofluoroscopy findings, questionnaire results, qualitative themes)
Prevalence of dysphagia or eating/drinking/mealtime characteristics
From qualitative studies “findings” were extracted: researcher themes or interpretations accompanied by illustrative quotes

To support consistent data extraction, definitions for swallow and mealtimes characteristics were used and are provided in Table 4-3.

Table 4-3. Swallow and mealtime characteristic definitions.

Aspiration	Food or drink entering the trachea during swallowing
Laryngeal penetration	Food or drink entering the laryngeal vestibule but remaining above or at the level of the vocal cords.
Oral stage dysfunction	Difficulty with preparing or transporting the bolus in the mouth
Pharyngeal residue	Food or drink remaining in the pharynx after swallowing
Nasal regurgitation	Food or drink entering the naso-pharynx or nasal cavity during swallowing
Delayed swallow initiation	Bolus dwelling in the pharynx prior to swallow initiation
Difficulty swallowing solids	Any reported difficulty swallowing any type of food
Difficulty swallowing liquids	Any reported difficulty swallowing liquids
Odynophagia	Pain on swallowing
Coughing/choking when eating	Reported coughing or choking *during* eating or drinking
Need for water	Any report of needing sips of fluid to aid bolus clearance when eating
Prolonged mealtimes	Any report of slow eating or feeding, mealtimes lasting over 30 minutes, slower to eat than peers.
Need for texture modification	Any report of avoiding certain food textures or altering food or drink texture to aid swallowing
Challenging mealtime behaviour	Parent report of excessive food refusal or selectivity, the need for distraction, difficulty sitting at a table or excessive passivity at mealtimes.
Avoiding eating with friends	Any action taken to avoid social aspects of eating or drinking
Increased parent anxiety	Any report of parent anxiety, worry or stress specifically at mealtimes

4.3 Quality assessment

The Mixed Methods Appraisal tool (MMAT) (Hong et al. 2018) was used to assess the quality and risk of bias of each paper. This tool was selected as it was designed

specifically for the purposes of assessing a mixed methods systematic review. It allows for a consistent approach to appraisal with a range of study designs. The MMAT consists of two screening questions, which are applied to all studies irrespective of design. The appropriate appraisal tool, consisting of a further five questions, is then selected depending on study design. Percentage of elements achieving a "yes" was used to assess overall study quality, alongside a narrative evaluation of the quality of included studies. As advised by the tool authors, the MMAT was not used to exclude studies of low methodological quality. Rather, it was used to report threats to quality overall.

4.4 Data synthesis

4.4.1 Quantitative

Prevalence ranges for each oro-pharyngeal swallow and eating/drinking/mealtime characteristic were calculated. Results from observational studies were included in a binary random effects DerSimonian-Laird meta-proportional analysis (proportion and 95% confidence interval) using Open Meta Analyst software (Wallace et al. 2012). To reduce the risk of selection bias, intervention studies were excluded from the prevalence meta-analysis.

Due to the inconsistent reporting of age and OA subtype, meta-analysis of these subgroups was not possible. Therefore, narrative synthesis was conducted to explore the impact of age and OA subtype/repair type on swallow/eating/drinking characteristics.

4.4.2 Qualitative

As per Joanna Briggs institute guidelines, qualitative data were synthesised using a meta-aggregation approach (Lockwood et al. 2015). Author interpretations ("findings") were aggregated into "categories" and an explanatory statement generated. Only findings that could be substantiated with data were deemed credible and included. Unsupported evidence was not included in the meta-aggregation.

4.4.3 Mixed methods synthesis

Where quantitative and qualitative data described the same phenomenon, a convergent segregated approach was used to synthesise data. In this approach separate quantitative and qualitative syntheses are conducted. Evidence from each synthesis is then integrated to generate greater depth of understanding. Integration involves juxtaposing the qualitative and quantitative syntheses – considering if results and findings complement or contradict. This can also be used to explain or contextualise findings to develop more robust practice recommendations (Stern et al. 2020).

4.5 Results

A total of 65 studies were included in this review. A PRISMA diagram outlining the study selection process is summarised in Figure 4-1.

A summary table of study types, populations and quality assessment is provided in Table 4-4 for all included studies. Most data were extracted from observational studies: case series (n=20), cross-sectional studies (n=37) and case report (n=1). There was one randomized control trial, one non-randomized trial, and one cohort study. There were two case control studies and three qualitative studies. Most studies were conducted in Europe (n=43), followed by North America (n=14), Australia (n=5) and Asia (n=2). One study was conducted in several countries. Thirty-six studies had fewer than 50 participants, 12 studies had 50-100 participants and 17 studies had over 100 participants. Forty-four studies reported repair type: all repair types (n=20), primary repair only (immediate or delayed) (n=22), oesophageal replacement only (n=2). Studies included participants of different age ranges: < 4 years (n=11), 0-18 years (n=27), >18 years (n=11). Fifteen studies included both children and adults of any age. One study did not report participant age.

Figure 4-1. Study selection process

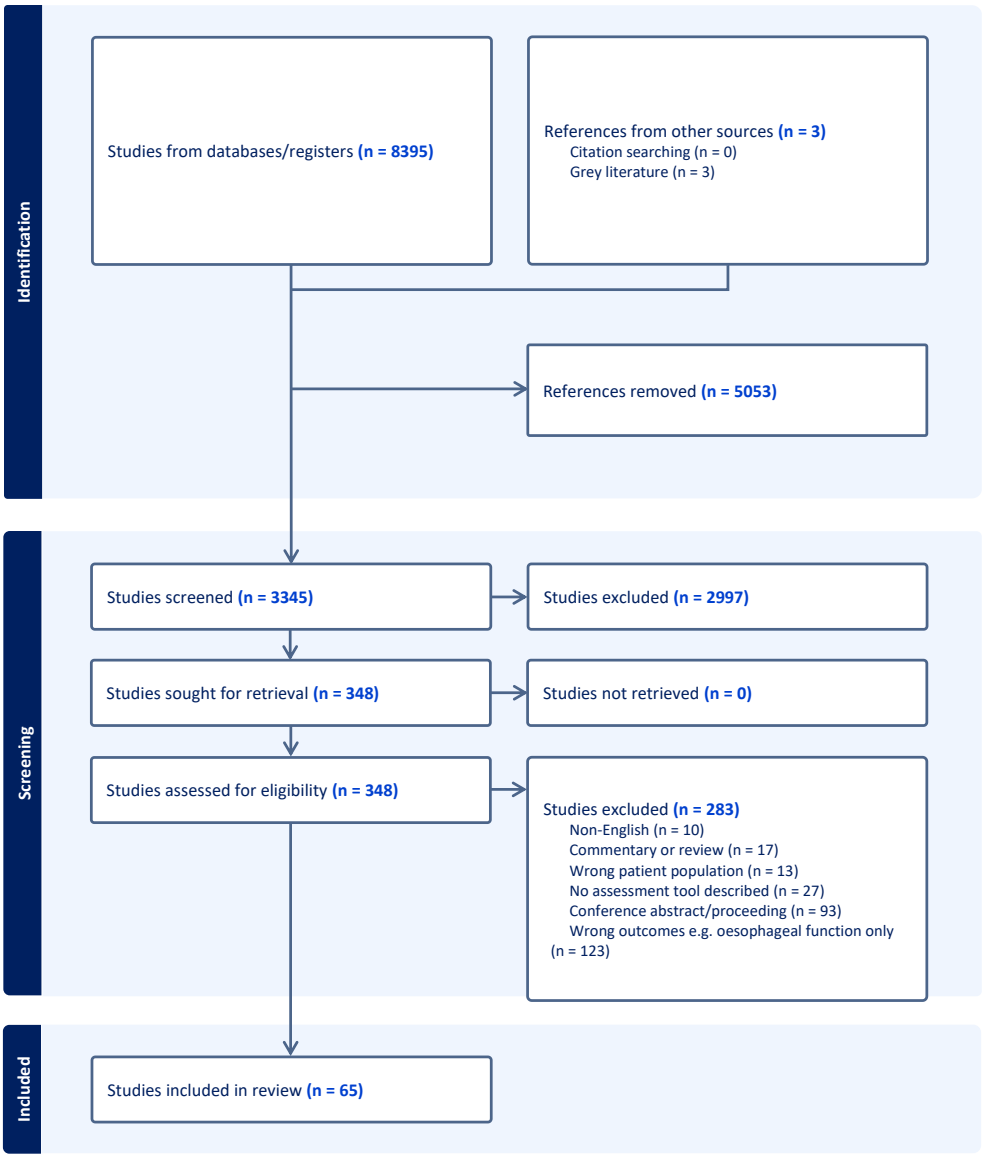


Table 4-4. Summary of study types, populations and quality assessment

Author and year	Country	Study type	Participant age	Repair type	Number of participants	Gross Type N					Type of assessment	MMAT
						A	B	C	D	E		
Maybee 2023	USA	Case series	<1 year; 1-4 years; 5-11 years; 11-18 years	NR	44	NR	NR	NR	NR	NR	Instrumental Non-instrumental	57%
Gibreel 2017	USA	Cross sectional	>18 years	Immediate primary; Oesophageal replacement; Delayed primary	46	4	1	40	0	1	Non-instrumental	100%
Demir 2017	Turkey	Case control	1-4 years	Immediate primary; Delayed primary	18	12	1	5	0	0	Instrumental	29%
Harrington 2021	USA	Case series	1-4 years	Delayed primary	45	39	12	7	0	0	Non-instrumental	86%
Thompson 2021	USA	Case series	1-4 years; 5-11 years	Oesophageal replacement	41	11	4	20	0	0	Non-instrumental	86%
DiNatale 2022	Switzerland	Cross sectional	5-11 years; 11-18 years; >18 years	Immediate primary; Oesophageal replacement; Delayed primary	30	5	0	25	0	0	Non-instrumental	43%
Bergmann 2022	Germany	Cross sectional	1-4 years; 5-11	Immediate primary;	44	6	1	36	NR	NR	Non-instrumental	43%

			years; 11-18 years	Delayed primary								
Puntis 1990	UK	Cross sectional	<1 year; 1-4 years; 5-11 years; 11-18 years; >18 years	Immediate primary; Oesophageal replacement	124	NR	NR	NR	NR	NR	Non-instrumental	55%
Cavallaro 1992	Italy	Cross sectional	1-4 years; 5-11 years	Immediate primary; Delayed primary	28	4	0	23	0	1	Non-instrumental	57%
Chetcuti 1993	Australia	Cross sectional	<1 year; 1-4 years; 5-11 years; 11-18 years; >18 years	Immediate primary; Oesophageal replacement; Delayed primary	334	16	6	290	0	22	Non-instrumental	14%
Ure 1995	Germany	Case series	>18 years	Oesophageal replacement	8	3	1	5	0	0	Non-instrumental	71%
Montgomery 1998	Sweden	Cross sectional	>18 years	NR	11	NR	NR	NR	NR	NR	Instrumental	57%
Krug 1999	Netherlands	Cross sectional	>18 years	Immediate primary; Delayed primary	39	NR	NR	NR	NR	NR	Non-instrumental	43%
Schier 2001	Germany	Cross sectional	5-11 years; 11-18 years; >18 years	Immediate primary; Oesophageal replacement; Delayed primary	128	14	9	93	6	0	Non-instrumental	57%

Hormann 2002	Austria	Case series	<1 year; 1-4 years; 5-11 years	NR	19	0	0	18	1	0	Instrumental	43%
Deurloo 2003	Netherlands	Cross sectional	>18 years	Immediate primary; Oesophageal replacement	38	1	0	39	0	0	Non-instrumental	86%
Deurloo 2005	Netherlands	Cross sectional	11-18 years; >18 years	NR	86	NR	NR	NR	NR	NR	Non-instrumental	71%
Cimador 2006	Italy	Case series	11-18 years	Immediate primary	15	0	0	15	0	0	Non-instrumental	43%
Taylor 2007	Australia	Cross sectional	>18 years	NR	132	NR	NR	NR	NR	NR	Non-instrumental	57%
Golonka 2008	Canada	Case series	<1 year	Delayed primary	4	2	1	1	0	0	Instrumental	29%
Frohlich 2008	Germany	Cross sectional	<1 year; 1-4 years; 5-11 years; 11-18 years; >18 years	NR	24	1	0	21	1	1	Non-instrumental	43%
Faugli 2008	Norway	Case control study	<1 year; 1-4 years	NR	37	NR	NR	NR	NR	NR	Non-instrumental	86%
Sistonen 2010	Finland	Cross sectional	>18 years	Immediate primary; Delayed primary	101	0	2	91	5	3	Non-instrumental	86%
Castilloux 2010	Canada	Cross sectional	1-4 years; 5-11 years	Immediate primary; Delayed primary	45	NR	NR	37	NR	NR	Non-instrumental	57%

Gatzinsky 2011	Sweden	Cross sectional	>18 years	Immediate primary; Oesophageal replacement; Delayed primary	73	3	1	69	1	5	Non-instrumental	86%
Legrand 2012	France	Cross sectional	5-11 years; 11-18 years	Immediate primary; Delayed primary	57	0	0	57	0	0	Non-instrumental	71%
Lemoine 2013	Canada	Case series	<1 year; 1-4 years; 5-11 years; 11-18 years	NR	40	5	0	35	0	0	Non-instrumental	43%
Baird 2015	Canada	Case series	<1 year; 1-4 years; 5-11 years	Immediate primary; Oesophageal replacement; Delayed primary	30	2	0	26	1	1	Non-instrumental	57%
Fraga 2015	USA	Case series	<1 year; 1-4 years; 5-11 years; 11-18 years	Immediate primary	22	0	0	19	0	3	Instrumental	71%
HuynhTrudeau 2015	Canada	Cross sectional	>18 years	Immediate primary; Oesophageal replacement	41	NR	NR	35	NR	NR	Non-instrumental	71%
Tan 2015	China	Case series	1-4 years; 5-11 years	NR	7	NR	NR	NR	NR	NR	Non-instrumental	71%

Yalcin 2015	Turkey	Case series	<1 year; 1-4 years; 5-11 years	Immediate primary; Delayed primary	32	3	0	26	2	1	Instrumental	43%
Presse 2016	Canada	Case series	>18 years	Immediate primary; Oesophageal replacement	37	6	0	31	0	0	Non-instrumental	71%
Coppens 2016	Netherlands	Case series	<1 year; 1-4 years; 5-11 years; 11-18 years	NR	111	9	1	86	6	6	Instrumental	71%
Barni 2019	Italy	Case report	<1 year	Immediate primary	1	0	0	1	0	0	Non-instrumental	50%
Menzies 2017	Australia	Case series	<1 year; 1-4 years; 5-11 years; 11-18 years	Immediate primary; Delayed primary	56	5	10	53	1	1	Non-instrumental	57%
Dellenmark-Blom 2019	Sweden	Cross sectional	1-4 years; 5-11 years; 11-18 years	Immediate primary; Oesophageal replacement; Delayed primary	116	NR	NR	NR	NR	NR	Non-instrumental	57%
Arslan 2020	Turkey	Non-randomised experimental study	1-4 years	Immediate primary; Oesophageal replacement; Delayed primary	20	9	0	11	0	0	Non-instrumental	43%

Dellenmark-Blom 2020	Sweden, Germany	Cross sectional	1-4 years; 5-11 years; 11-18 years	Immediate primary; Oesophageal replacement; Delayed primary	124	NR	NR	NR	NR	NR	Non-instrumental	71%
Serel Arslan 2020	Turkey	Cross sectional	1-4 years; 5-11 years; 11-18 years	Immediate primary; Oesophageal replacement; Delayed primary	64	28	0	36	0	0	Non-instrumental	57%
Bevilacqua 2020	Italy	Cross sectional	1-4 years	NR	51	6	2	43	0	0	Non-instrumental	43%
Birketvedt 2020	Norway	Cross sectional	11-18 years; >18 years	NR	68	3	0	58	4	3	Non-instrumental	71%
Menzies 2020	Australia	Cross sectional	1-4 years; 5-11 years	NR	20	NR	NR	1 9	NR	NR	Non-instrumental	57%
Ax 2021	Sweden	Cross sectional	1-4 years; 5-11 years; 11-18 years	NR	114	9	5	93	2	5	Non-instrumental	43%
Rabone 2021	UK	Cross sectional	>18 years	NR	92	NR	NR	54	NR	NR	Non-instrumental	100%
vanTuyllvan Serooskerken 2021	Netherlands	Case series	1-4 years; 5-11 years; 11-18 years	Delayed primary	11	6	5	0	0	0	Non-instrumental	86%
Pham 2022	France	Cross sectional	1-4 years	NR	145	7	NR	133	NR	NR	Non-instrumental	100%

Dellenmark-Blom 2022	Sweden, Germany	Cross sectional	1-4 years; 5-11 years; 11-18 years	Immediate primary ; Oesophageal replacement; Delayed primary	180	24	0	NR	NR	NR	Non-instrumental	71%
Dellenmark-Blom 2022	Sweden	Cross sectional	1-4 years; 5-11 years; 11-18 years	Delayed primary; Oesophageal replacement	30	12	8	10	0	0	Non-instrumental	86%
Traini 2022	Australia	Cross sectional	1-4 years; 5-11 years; 11-18 years	Immediate primary ; Delayed primary	21	NR	NR	14	NR	NR	Non-instrumental	71%
Celtik 2022	Turkey	Cross sectional	<1 year; 1-4 years; 5-11 years; 11-18 years	Immediate primary ; Oesophageal replacement	27	6	3	17	0	0	Instrumental	43%
Stewart 2022	UK	Qualitative research	<1 year; 1-4 years; 5-11 years; 11-18 years	Immediate primary; Delayed primary; Oesophageal replacement	127	3	NR	77	NR	4	Non-instrumental	100%
Wallace 2022	UK	Qualitative research	<1 year; 1-4 years; 5-11 years	NR	176	NR	NR	NR	NR	NR	Non-instrumental	100%
Capitanio 2021	Italy	Cross sectional	5-11 years; 11-18 years	NR	50	5	2	42	1	0	Non-instrumental	29%

Soyer 2022	Turkey	Case series	<1 year; 1-4 years	Immediate primary; Oesophageal replacement; Delayed primary	55	18	1	29	1	0	Instrumental	43%
Bourg 2022	France	Cohort study	5-11 years	Immediate primary; Oesophageal replacement; Delayed primary	93	NR	NR	NR	NR	NR	Non-instrumental	43%
Yasuda 2022	USA	Cross sectional	<1 year; 1-4 years; 5-11 years	Immediate primary; Delayed primary	330	NR	NR	NR	NR	NR	Non-instrumental	57%
Mikkelsen 2022	Norway	Cross sectional	11-18 years; >18 years	Immediate primary; Oesophageal replacement	68	3	0	58	4	3	Non-instrumental	100%
Leibovitch 2018	Isreal	Cross sectional	1-4 years; 5-11 years; 11-18 years; >18 years	NR	46	NR	NR	NR	NR	NR	Non-instrumental	43%
Baxter 2018	USA	Case series	1-4 years	NR	145	6	2	125	1	11	Non-instrumental	86%
Fung 2019	Canada	Case series	NR	NR	197	13	5	162	1	16	Instrumental	71%
Serel Arslan 2017	Turkey	Randomised controlled trial	<1 year; 1-4 years	Immediate primary; Delayed primary	24	8	0	16	0	0	Instrumental	57%

Soyer 2017	Turkey	Case series	1-4 years; 5-11 years	Immediate primary; Delayed primary	40	5	0	36	0	0	Instrumental	43%
Serel Arslan 2018	Turkey	Cross sectional	1-4 years; 5-11 years; 11-18 years	Immediate primary; Oesophageal replacement; Delayed primary	30	12	0	18	0	0	Non-instrumental	43%
Svoboda 2018	International	Cross sectional	<1 year; 1-4 years; 5-11 years; 11-18 years; >18 years	NR	928	176		742		9	Non-instrumental	57%

NR = Not reported

4.5.1 Quality assessment

Fifteen studies met over 80% of the MMAT criteria for their respective study design, indicating higher quality with lower risk of bias. Nineteen studies met less than 50% of the MMAT criteria, indicating lower quality or higher risk of bias. Quality assessment results are provided in Table 4-5. Analysis indicated selection bias as a frequent risk, typically as studies were conducted at specialist referral centres with higher than expected numbers of non-type C OA subtypes or non-consecutive case reporting. Quality was also impacted in a large number of studies due to use of unvalidated measurement tools.

Table 4-5. Quality assessment summary for all included studies.

Qualitative studies	**Are there clear research questions?**	**Do the collected data allow to address the research questions?**	**Is the qualitative approach appropriate to answer the research question?**	**Are the qualitative data collection methods adequate to address the research question?**	**Are the findings adequately derived from the data?**	**Is the interpretation of results sufficiently substantiated by data?**	**Is there coherence between qualitative data sources, collection, analysis and interpretation?**
Rabone 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Stewart 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wallace 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Quantitative descriptive studies	Are there clear research questions?	Do the collected data allow to address the research questions?	Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate?	Is the risk of nonresponse bias low?	Is the statistical analysis appropriate to answer the research question?
DiNatale 2022	Yes	Yes	Can't tell	Yes	No	No	No
Montgomery 1998	Yes	Yes	Can't tell	Can't tell	Yes	Can't tell	Yes
Hormann 2002	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell	Yes
Golonka 2008	No	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes
Frohlich 2008	Yes	Yes	Can't tell	Can't tell	Can't tell	No	Yes
Yalcin 2015	Yes	Yes	Can't tell	Can't tell	No	Can't tell	Yes
Dellenmark-Blom 2019	Yes	Yes	Can't tell	Can't tell	Yes	Can't tell	Yes
Dellenmark-Blom 2020	Yes	Yes	Can't tell	Yes	Can't tell	Yes	Yes

SerelArslan 2020	Yes	Yes	Can't tell	No	Yes	Can't tell	Yes
Bevilacqua 2020	Yes	Yes	Can't tell	Yes	No	Can't tell	No
Soyer 2022	Yes	Yes	Can't tell	No	No	Yes	No
Leibovitch 2018	Yes	Yes	Can't tell	Yes	No	Can't tell	No
Soyer 2017	Yes	Yes	Can't tell	Can't tell	Yes	Can't tell	Can't tell
SerelArslan 2018	Yes	Yes	Can't tell	No	Can't tell	Can't tell	Yes
Demir 2017	Yes	Yes	No	No	No	Can't tell	Can't tell
Lemoine 2013	Yes	Yes	No	Can't tell	Can't tell	No	Yes
Baird 2015	Yes	Yes	No	Yes	Yes	Can't tell	No
Puntis 1990	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes
Maybee 2023	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes
Gibreel 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Harrington 2021	Yes	Yes	Yes	Yes	No	Yes	Yes
Thompson 2021	Yes	Yes	Yes	Yes	No	Yes	Yes
Bergmann 2022	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell
Cavallaro 1992	Yes	Yes	Yes	Can't tell	No	Yes	No
Chetcuti 1993	No	No	Yes	Can't tell	No	Yes	No
Ure 1995	Yes	Yes	Yes	Can't tell	No	Yes	Yes
Krug 1999	Yes	Yes	Yes	Can't tell	No	Can't tell	No
Schier 2001	Yes	Yes	Yes	No	No	No	Yes
Deurloo 2003	Yes	Yes	Yes	Yes	No	Yes	Yes
Deurloo 2005	Yes	Yes	Yes	Can't tell	No	Yes	Yes
Cimador 2006	No	No	Yes	Can't tell	No	Yes	Yes
Taylor 2007	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes
Faugli 2008	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes
Sistonen 2010	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes
Castilloux 2010	Yes	Yes	Yes	Can't tell	No	Can't tell	Yes
Gatzinsky 2011	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes
Legrand 2012	Yes	Yes	Yes	Yes	No	Can't tell	Yes

Fraga 2015	Yes	Yes	Yes	No	Can't tell	Yes	Yes
Huynh 2015	Yes	Yes	Yes	Can't tell	No	Yes	Yes
Tan 2015	Yes	Yes	Yes	Yes	No	Can't tell	Yes
Presse 2016	Yes	Yes	Yes	No	No	Yes	Yes
Menzies 2017	Yes	Yes	Yes	No	No	No	Yes
Birketvedt 2020	Yes	Yes	Yes	Yes	No	Can't tell	Yes
Menzies 2020	Yes	Yes	Yes	Can't tell	Can't tell	No	Yes
Ax 2021	Yes	Yes	Yes	Yes	No	Yes	No
vanTuyllvan 2021	Yes	Yes	Yes	Yes	No	Yes	Yes
Pham 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Dellenmark-Blom 2022	Yes	Yes	Yes	Yes	No	Yes	Can't tell
Dellenmark-Blom 2022	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes
Traini 2022	Yes	Yes	Yes	No	Yes	Can't tell	Yes
Celtik 2022	Yes	Yes	Yes	No	No	No	Can't tell
Capitanio 2021	Yes	No	Yes	Can't tell	No	Can't tell	Can't tell
Bourg 2022	Yes	Yes	Yes	Can't tell	No	Can't tell	Can't tell
Yasuda 2022	Yes	Yes	Yes	No	Can't tell	Can't tell	Yes
Mikkelsen 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Baxter 2018	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes
Fung 2019	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes
Svoboda 2018	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes
Coppens 2016	Yes	Yes	Yes	Yes	No	No	Yes

Quantitative non-randomised studies	**Are there clear research questions?**	**Do the collected data allow to address the research questions?**	**Are the participants representative of the target population**	**Are measurements appropriate regarding both the outcome and intervention (or exposure)?**	**Are there complete outcome data?**	**Are the confounders accounted for in the design and analysis?**	**During the study period, is the intervention administered (or exposure occurred) as intended?**
Barni 2019	Yes	No	No	No	Yes	No	Yes
Arslan 2020	Yes	Yes	Can't tell	Can't tell	Yes	No	Can't tell
Quantitative randomised study design	Are there clear research questions?	Do the collected data allow to address the research questions?	Is randomization appropriately performed?	Are the groups comparable at baseline?	Are there complete outcome data?	Are outcome assessors blinded to the intervention provided?	Did the participant adhere to the assigned intervention?
Serel Arslan 2017	Yes	Yes	Can’t tell	Yes	Yes	Can’t tell	Can’t tell

4.6 Evidence synthesis

Studies are synthesised in four sections:

1) Characteristics and prevalence of oro-pharyngeal swallow impairment as assessed by instrumental assessment.

2) Characteristics and prevalence of swallow impairment as assessed by patient/parent report (non-instrumental assessment).

3) Characteristics and prevalence of eating and drinking adaptations (implied swallow impairment) as assessed by patient/parent report (non-instrumental assessment).

4) Characteristics and prevalence of the psychosocial impact of eating, drinking and swallowing difficulties.

4.7 Oro-pharyngeal swallow impairment (instrumental assessment)

Fifteen studies used instrumental assessment (videofluoroscopy n=12, fibreoptic evaluation of swallowing n=1, videomanometry n=1, oral pharyngeal motility study n=1) to characterise oro-pharyngeal swallow function. One paper included assessment of adults born with OA/TOF(Montgomery et al. 1998). Of the remaining 14, five only included children under 4 years of age. Prevalence ranges and pooled prevalence rates for each oro-pharyngeal swallow characteristic are provided in Table 4-6. One study presented swallow characteristics for a group of children undergoing intervention for pharyngeal dysphagia, these were not included in the pooled prevalence calculations (Serel Arslan et al. 2017).

Table 4-6. Prevalence range and pooled prevalence for oro-pharyngeal swallow characteristics from instrumental assessments.

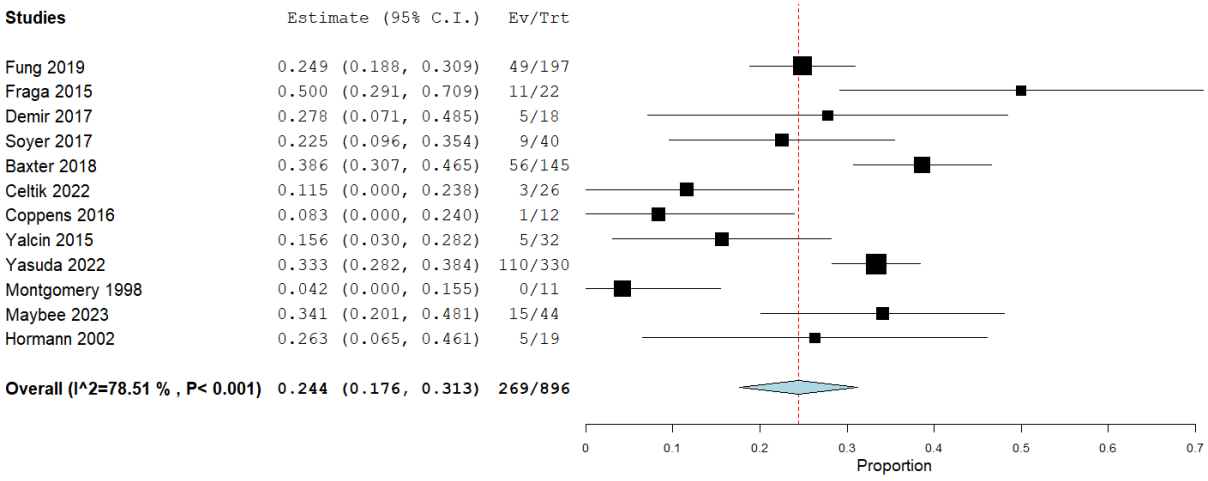
Characteristic (number of studies)	Total participants	Prevalence range	Pooled prevalence (95% CI)	Heterogeneity (I^2)
Aspiration (n=14)	896	0-1.00 all studies 0.8-0.45 case series only	0.24 (0.18, 0.31)	79% Substantial
Laryngeal penetration (n=9)	599	0-0.13	0.06 (0.01, 0.11)	76% Substantial
Oral stage dysfunction (n=6)	118	0-0.50	0.11 (0.02, 0.21)	66% Substantial
Pharyngeal residue (n=7)	188	0.05-0.38	0.13 (0.04, 0.21)	74% Substantial
Nasal regurgitation (n=4)	150	0.08-0.16	0.07 (0.00, 0.13)	63% Substantial
Delayed swallow initiation (n=4)	118	0.16-0.75	0.31 (0.11, 0.50)	85% Substantial
No pharyngeal deficit on VFSS (n=2)	177	0.39-0.72	0.55 (0.23, 0.87)	92% Substantial

Meta-proportional analysis conducted using binary random effects DerSimonian-Laerd.

Seven studies used categorical rating scales for various components of swallow physiology (Hormann et al. 2002, Yalcin et al. 2015, Coppens et al. 2016, Serel Arslan et al. 2017, Celtik et al. 2022, Soyer et al. 2022, Maybee et al. 2023). Six studies reported binary aspiration/no aspiration outcome only (Montgomery et al. 1998, Golonka et al. 2008, Fraga et al. 2015, Baxter et al. 2018, Fung et al. 2019, Yasuda et al. 2022). One videofluoroscopy study used quantitative methods to measure hyolaryngeal elevation (Demir et al. 2017). One study used low resolution manometry to quantify upper oesophageal sphincter pressures and timing, pharyngeal constriction, and bolus transit time (Montgomery et al. 1998).

The Penetration-Aspiration scale (PAS) (Rosenbek et al. 1996) was used in five studies as a validated measure of aspiration/penetration (Yalcin et al. 2015, Demir et al. 2017, Serel Arslan et al. 2017, Soyer et al. 2017, Soyer et al. 2022). Two studies reported median PAS scores (Serel Arslan et al. 2017, Soyer et al. 2022). One was the intervention study in which the median PAS was 8 (material enters the trachea with no attempt to clear) for liquids and 1.5 (no entry of material into the larynx or trachea) for solid foods (Serel Arslan et al. 2017). Soyer et al. (2022) used the PAS to report swallow characteristics in a single centre case series. Median PAS scores were 1 for all children, other than liquid swallows for children with delayed primary repair, where the median PAS was 2 (entry of material into the larynx with clearing). Other reported PAS scores were converted into percentage of aspiration or penetration and are included in Table 4-6. A forest plot details the pooled prevalence for aspiration in Figure 4-2.

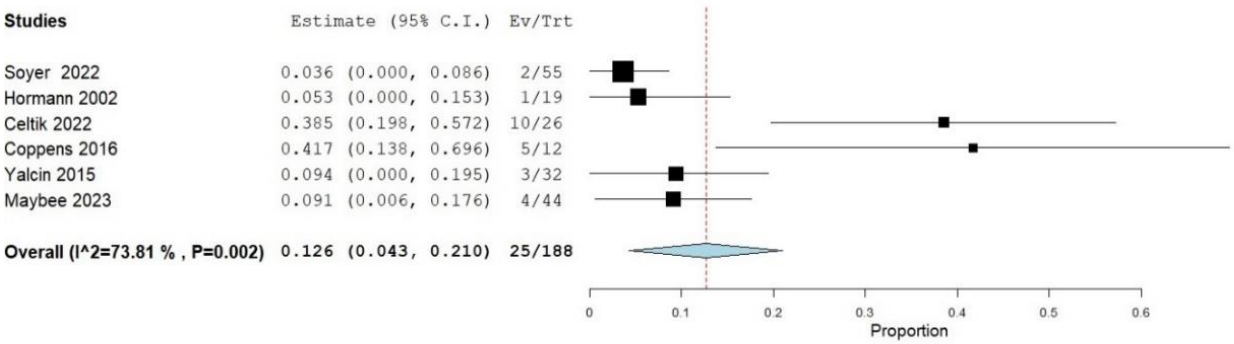
Figure 4-2. Forest plot for pooled prevalence of aspiration detected on instrumental assessment.



Two studies compared aspiration rates between repair or OA types. Celtik and colleagues reported that all children with aspiration in their cohort had long gap OA (Celtik et al. 2022). Soyer et al. (2022) reported more frequent aspiration of liquids for those with delayed primary repair, compared to those with oesophageal replacement and more frequent aspiration of “pudding” consistency for those with delayed primary repair, compared to those with early primary repair.

Seven studies reported rates of pharyngeal residue, four of which specified place of residue within the pharynx (Yalcin et al. 2015, Coppens et al. 2016, Serel Arslan et al. 2017, Soyer et al. 2022). Residue was reported in the valleculae, pyriform sinuses and on the pharyngeal wall i.e. throughout the pharynx. Celtik and colleagues reported significantly higher rates of residue in children born with long gap OA, compared to short gap OA (Celtik et al. 2022). Soyer and colleagues found no differences between those with primary repair and oesophageal replacement (Soyer et al. 2022). A forest plot detailing prevalence of residue is presented in Figure 4-3.

Figure 4-3. Forest plot for pooled prevalence of pharyngeal residue detected on instrumental assessment.



4.8 Patient/parent-reported eating and drinking difficulties (non-instrumental assessment)

4.8.1 Assessment tools

Forty-seven studies used non-instrumental methods. Twenty-three of these studies used validated assessment tools and twenty-four used author-generated assessment tools.

Validated assessment tools

Thirteen different validated or standardised tools were used across all studies. These are summarised in Table 4-7.

Table 4-7. Summary of validated assessment tools used in at least one included study.

Authors	Assessment tool	Summary of tool characteristics
Harrington et al. (2021) Thompson et al. (2021) Coppens et al. (2016) van Tuyll van Serooskerken et al. (2021) Celtik et al. (2022) Bourg et al. (2022) Yasuda et al. (2022) Baxter et al. (2018) Soyer et al. (2017)	Functional oral intake scale (Crary et al. 2005)	7-point, clinician-rated measure of oral and non-oral intake. Validated initially for adults with post-stroke dysphagia (Soyer et al. 2017, Harrington et al. 2021, van Tuyll van Serooskerken et al. 2021, Celtik et al. 2022). Author adapted versions (Coppens et al. 2016, Thompson et al. 2021, Yasuda et al. 2022) Paediatric adapted versions (Baxter et al. 2018, Bourg et al. 2022)
Barni et al. (2019) Birketvedt et al. (2020) Capitanio et al. (2021) Mikkelsen et al. (2022) Soyer et al. (2017)	EAT-10 (Belafsky et al. 2008)	10-item patient-reported screening tool, validated for adults with dysphagia. Components: swallowing impairment, swallowing-related QOL, weight gain (Capitanio et al. 2021, Mikkelsen et al. 2022) Validated paediatric version (Pedi-EAT-10) (Soyer et al. 2017, Barni et al. 2019) Author adapted version for OA (Birketvedt et al. 2020)

Gatzinsky et al. (2011) Yalcin et al. (2015) Traini et al. (2022) Soyer et al. (2017)	Dakkak dysphagia score (Dakkak et al. 1992)	Patient- or parent-rating of ability to swallow nine food/drink textures. Validated for use with adults.
Baird et al. (2015) Menzies et al. (2020) Pham et al. (2022) Traini et al. (2022)	Montreal children's hospital feeding scale (Ramsay et al. 2011)	18-item, parent-rated tool. Components: oro-motor function, mealtime length, mealtime behaviour and psychosocial impact. Validated in children 6 months-6 years.
Dellenmark-Blom et al. (2020) Dellenmark-Blom et al. (2022)	EA-QOL questionnaire (Dellenmark-Blom et al. 2017)	18-item, parent-rated tool (validated for children aged 2-7 years). Components: eating, physical health and treatment, social isolation and stress. 26-item parent or child-rated tool (validated for children aged 8-17 years). Components: eating, social relationships, body perception and health, wellbeing.
Serel Arslan et al. (2018)	Karaduman chewing performance scale (Serel Arslan et al. 2016)	5-point clinician-rated scale of chewing function. Validated children aged 2-15 years.
Serel Arslan et al. (2018)	International dysphagia diet standardisation initiative (Cichero et al. 2017)	7-point clinician-rated scale of food and drink texture descriptions. Validated for all ages.
Tan et al. (2015)	Atkinson swallow scale	5-point scale of ability to eat food/drink textures. Not clear if clinician or patient reported. Reliability/validity not reported.

Serel Arslan et al. (2020)	Turkish feeding-swallowing impact survey (Serel Arslan et al. 2018)	18-item parent-rated assessment of feeding-related quality of life. Validated for children aged 1-12.
Ax et al. (2021)	Oesophageal Atresia feeding survey	9-item parent-rated author developed assessment of strategies used to mitigate feeding difficulties. Used for children aged 2-17 years. Reliability/validity not reported.
Dellenmark-Blom et al. (2018)	Oesophageal Atresia coping questionnaire	9-item parent- or child-rated assessment of mealtime coping strategies. Condition-specific. Validated for children aged 2-17 years.
Bergmann et al. (2022)	pedsSWAL-QOL (Clayburgh et al. 2011)	32-item parent-rated assessment of swallowing-related quality of life. Adapted from adult tool. Reliability/validity not reported for paediatric version.
Gibreel et al. (2017)	Swallow dysfunction questionnaire	29-item patient-rated assessment of dysphagia. Components: ability to manage 5 food/drink consistencies, swallowing “habits”, eating/drinking quality of life. Validated for adults with OA.

4.9 Patient-/parent-reported characteristics of swallow impairment

Five patient or parent-reported characteristics related to swallow impairment were identified: difficulty swallowing solids, difficulty swallowing liquids, oral stage dysfunction, odynophagia and coughing when eating. Prevalence ranges and pooled prevalence rates for each swallowing characteristic are presented in Table 4-8.

Table 4-8. Prevalence ranges and pooled prevalence for patient-/parent-reported swallowing characteristics.

Characteristic (number of studies)	Total participants	Prevalence range	Pooled prevalence (95% CI)	Heterogeneity (I^2)
Difficulty swallowing food (n=14)	599	0.33-0.70	0.45 (0.36, 0.54)	82% Substantial
Difficulty swallowing liquids (n=8)	303	0.15-0.27	0.06 (0.02, 0.10)	60% Substantial
Oral stage dysfunction (n=3)	167	0.10-1.0 all studies 0.10-0.35 case series only	n/a	
Odynophagia (n=4)	111	0.13-0.73	0.30 (0.10, 0.50)	82% Substantial
Coughing or choking when eating (n=6)	390	0.15-0.45	0.22 (0.13, 0.31)	78% Substantial
No deficit (n=21)	2071	0.15-0.85	0.38 (0.28, 0.48)	95% Substantial

Meta-proportional analysis conducted using binary random effects DerSimonian-Laerd.

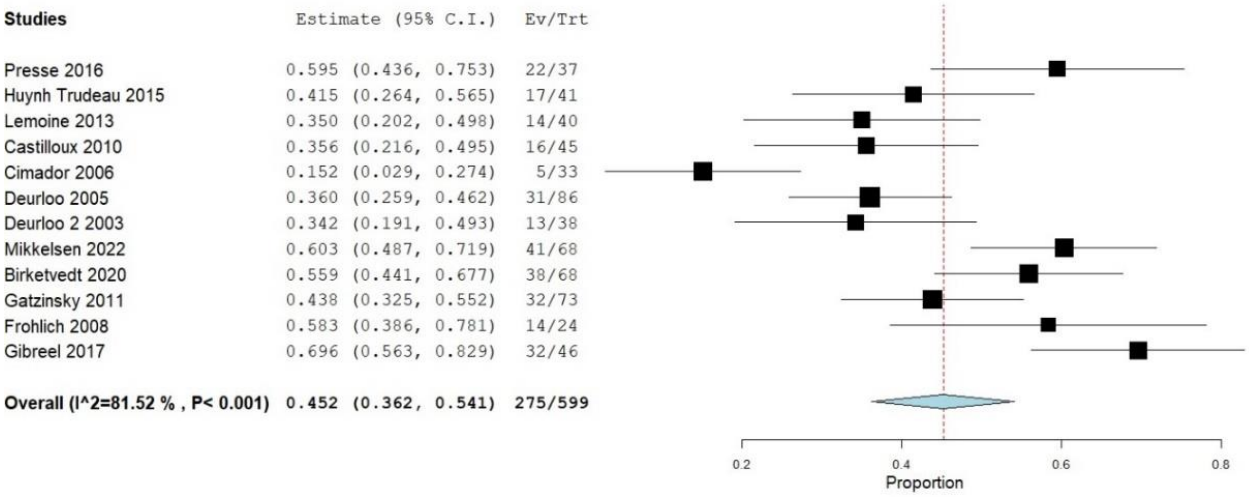
4.9.1 Difficulty swallowing food

Difficulty swallowing food was the most reported swallow characteristic, described in 14 studies. Figure 4-4 is a forest plot detailing the pooled prevalence. The highest rate (70%) was from a study of adults, of whom 85% had type C OA (Gibreel et al. 2017). Most studies included a wide range

of ages and all OA types. No studies reported “long gap”, oesophageal replacement or non-type C OA prevalence separately. Maybee and colleagues (Maybee et al. 2023) reported by age, identifying increasing prevalence of difficulty swallowing food throughout the first four years of life.

Five studies included only adult participants. Pooled prevalence rate for these studies was 0.50 (0.37, 0.62). Eight studies included only children. Pooled prevalence rate for these studies was 0.43 (0.34, 0.52).

Figure 4-4. Forest plot showing prevalence of patient/parent-reported difficulty swallowing food.



Four studies used Dakkak dysphagia score to assess difficulty with various food textures (Gatzinsky et al. 2011, Yalcin et al. 2015, Soyer et al. 2017, Traini et al. 2022). Median scores ranged from 4.5-12. Gatzinsky et al. (2011) reported increasing frequency of difficulty with increasing food texture . yogurt least reported, meat the most frequently reported as difficult to swallow. Two studies compared Dakkak scores between OA subtypes (Gatzinsky et al. 2011, Soyer et al. 2017). Both found significantly higher scores (more difficulty) in those with type A OA compared to type C OA. Soyer et al. (2017) reported higher scores for children with aspiration

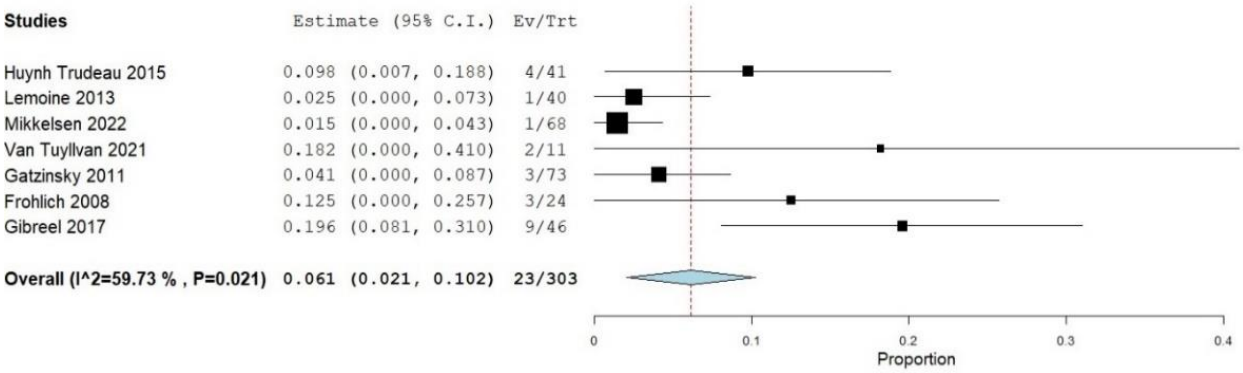
identified on VFSS compared to those without aspiration and those undergoing delayed OA repair compared to those with immediate repair.

Thirteen studies reported difficulty with specific food types. Meat was reported as difficult in 9/13 studies. Bread, rice and vegetables were also frequently reported as difficult to swallow.

4.9.2 Difficulty swallowing liquids

Eight studies reported prevalence of difficulty swallowing liquids (Frohlich et al. 2008, Gatzinsky et al. 2011, Lemoine et al. 2013, Huynh Trudeau et al. 2015, Gibreel et al. 2017, van Tuyll van Serooskerken et al. 2021, Mikkelsen et al. 2022, Maybee et al. 2023). Prevalence rates ranged from 1.5-27% (Table 4-8). A forest plot detailing the included studies is presented in Figure 4-5. In general, rates of swallowing liquids were lower than difficulty with solid foods. Gibreel et al. (2017) reported that 22% of adults had difficulty swallowing liquids but the frequency of difficulty was “rare” or “sometimes”. The highest prevalence of difficulty with liquids was reported by Maybee in children aged 0-6 months (27%), which reduced to 11% for those over 48 months. No studies reported difficulty by OA subtype or repair type.

Figure 4-5. Forest plot detailing prevalence of patient/parent-reported difficulty swallowing liquids.



4.9.3 Oral stage difficulties

Three studies reported the prevalence of oral stage difficulties using clinical observation (Serel Arslan et al. 2018, Arslan et al. 2020, Maybee et al. 2023). One was an intervention study in which all children were identified as having oral stage (chewing) difficulties (Arslan et al. 2020). Two retrospective case series reported prevalence rates of 10-35% (Serel Arslan et al. 2018, Maybee et al. 2023). Maybee and colleagues identified peak prevalence of oral stage difficulties at 24-48 months of age (35%). Serel Arslan and colleagues identified a significant correlation between time to starting oral feeding and chewing dysfunction, with mean time to starting oral feeding of 1 week for children without chewing disorder and 24 weeks for those with chewing disorder. There was no significant association between chewing function and repair type (Serel Arslan et al. 2018).

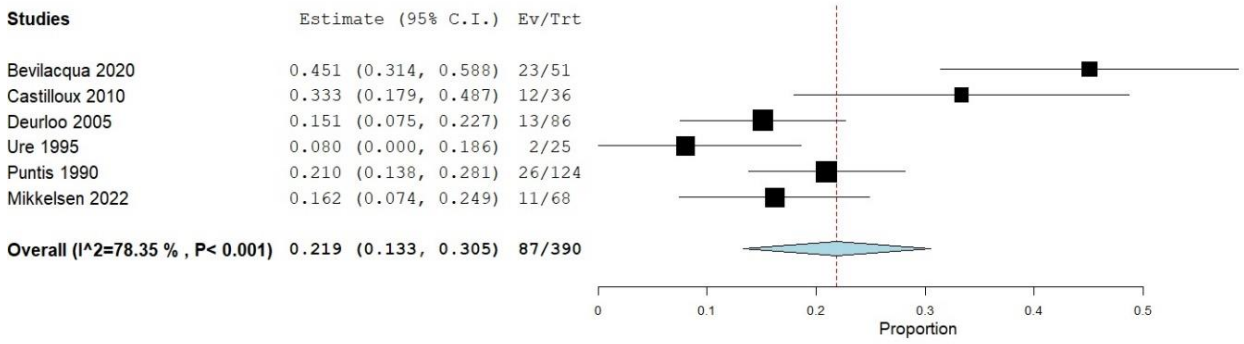
4.9.4 Odynophagia

Four studies reported odynophagia, with prevalence ranging between 13%-73% (Table 4-8). The study with the lowest reported rates included all ages (Frohlich et al. 2008), the highest included only adults (Montgomery et al. 1998). Pain was reported by 25% of adults who had undergone oesophageal replacement (Ure et al. 1995).

4.9.5 Coughing/choking

Six studies reported coughing or choking on eating/drinking, with prevalence ranging between 15-45% (Table 4-8 and Figure 4-6). The lowest rates were reported in a study of adolescents and adults (Deurloo et al. 2005), the highest in preschool-aged children (Bevilacqua et al. 2020). Puntis et al. (1990) differentiated between rates of coughing on food vs drink and by repair type. Coughing was most frequent on milk for children undergoing primary repair (32%). However, children requiring oesophagostomy coughed more frequently on solids (28%), than those with primary repair (16%).

Figure 4-6. Forest plot detailing pooled prevalence of patient-/parent-reported coughing with eating/drinking.



4.9.6 No deficit

Twenty-one studies reported no eating, drinking or swallowing difficulties using non-instrumental tools. Four studies reported results for those with long-gap OA (Harrington et al. 2021, Thompson et al. 2021, van Tuyll van Serooskerken et al. 2021, Bourg et al. 2022). There was no difference in prevalence comparing those reporting only long-gap OA (38% (95% CI 22-55%)) with those reporting mixed OA subtypes (38% (95% CI 28-48%)). Lowest rates of “no deficit” (15%) were reported in a study of adolescents and adults, 85% of whom had type C OA(Mikkelsen et al. 2022). Highest rates (85%) were reported in a study of children under 11 years of age, 95% of whom had type C OA (Menzies et al. 2020).

4.10 Patient-/parent-reported characteristics of eating and drinking adaptations

The most frequently reported alterations to eating and drinking were a need to drink water to clear food, eating slowly and food texture modification. Prevalence ranges and pooled prevalence rates are presented for these characteristics in Table 4-9.

Table 4-9. Prevalence range and pooled prevalence for patient-/parent-reported eating and drinking adaptations.

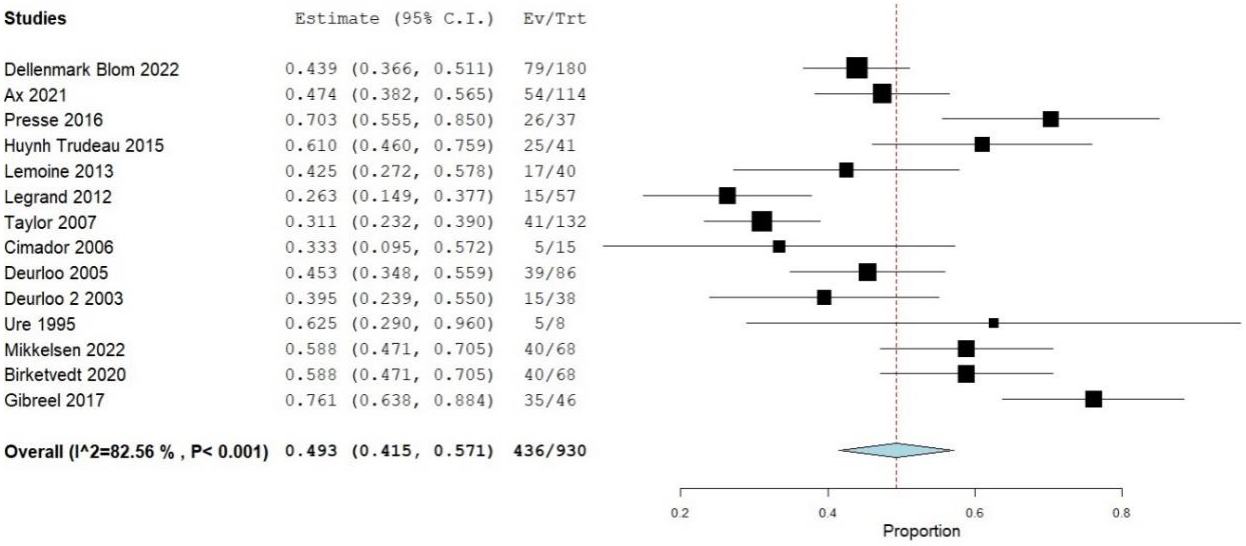
Characteristic (number of studies)	Total participants	Prevalence range	Pooled prevalence (95% CI)	Heterogeneity (I^2)
Need for water when eating (n=14)	930	0.31-0.75	0.49 (0.42, 0.57)	83% Substantial
Prolonged mealtimes/eating slowly (n=15)	1015	0.05-0.88	0.37 (0.28, 0.46)	91% Substantial
Need for texture modification (n=12)	753	0.05-0.54	0.28 (0.18, 0.38)	93% Substantial

Meta-proportional analysis conducted using binary random effects DerSimonian-Laerd.

4.10.1 Need for water to clear

Fourteen studies reported prevalence of using water to help clear food (Ure et al. 1995, Deurloo et al. 2003, Deurloo et al. 2005, Cimador et al. 2006, Taylor et al. 2007, Legrand et al. 2010, Lemoine et al. 2013, Huynh Trudeau et al. 2015, Presse et al. 2016, Gibreel et al. 2017, Birketvedt et al. 2020, Ax et al. 2021, Dellenmark-Blom et al. 2022, Mikkelsen et al. 2022), with rates ranging from 31% (Taylor et al. 2007)-75% (Gibreel et al. 2017). A forest plot detailing distribution and weighting is presented in Figure 4-7. Both the lowest and highest rates were reported in studies of adults. One study included only patients with long gap OA undergoing oesophageal replacement, reporting 5/8 participants (63%) using water to clear food (Ure et al. 1995). No other studies reported OA subtypes of repair type separately.

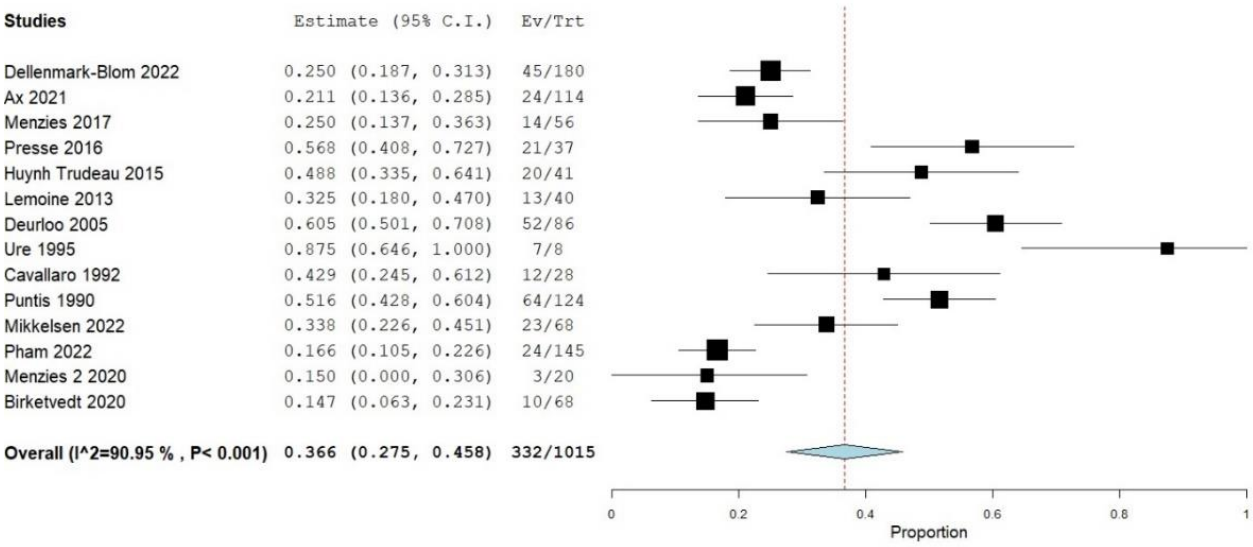
Figure 4-7. Forest plot detailing pooled prevalence of patient-/parent-reported need for water when eating.



4.10.2 Prolonged mealtimes

Fifteen studies reported the need to eat slowly or having prolonged feeds/mealtimes (Puntis et al. 1990, Cavallaro et al. 1992, Ure et al. 1995, Deurloo et al. 2003, Lemoine et al. 2013, Huynh Trudeau et al. 2015, Presse et al. 2016, Menzies et al. 2017, Birketvedt et al. 2020, Menzies et al. 2020, Ax et al. 2021, Dellenmark-Blom et al. 2022, Mikkelsen et al. 2022, Pham et al. 2022, Maybee et al. 2023). Prevalence ranged from 5-88%, as shown in Table 4-9 and the forest plot in Figure 4-8. The lowest prevalence was reported in children 0-6 months (Maybee et al. 2023), the highest by adults who had undergone oesophageal replacement (Ure et al. 1995). Puntis et al. (1990) reported those requiring oesophageal replacement separately from those undergoing primary anastomosis, identifying that mealtimes were less frequently prolonged in those undergoing oesophageal replacement than in those with primary repair (food only).

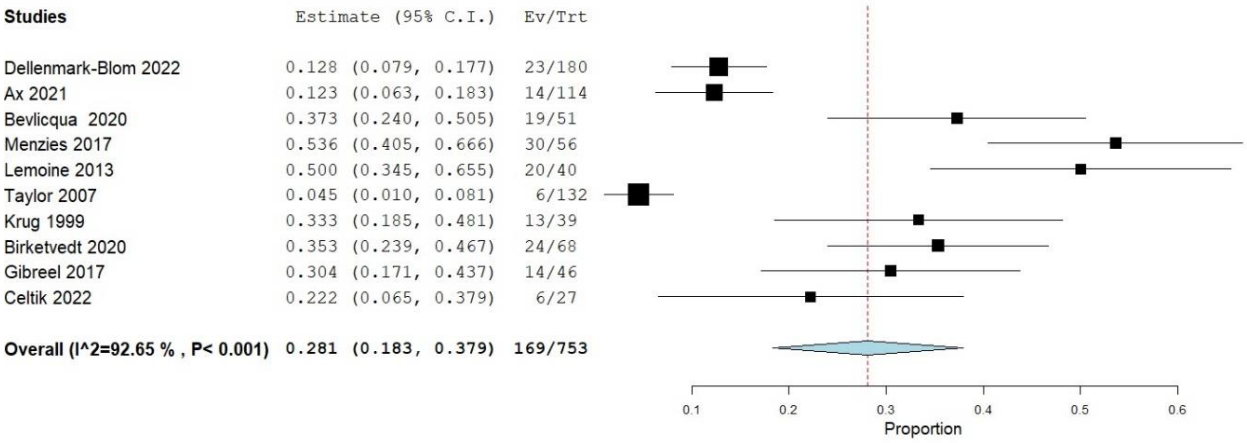
Figure 4-8. Forest plot detailed pooled prevalence of patient-/parent-reported prolonged mealtimes.



4.10.3 Texture modification

Twelve studies reported modification of food textures as a strategy to mitigate for swallowing difficulty (Krug et al. 1999, Taylor et al. 2007, Lemoine et al. 2013, Coppens et al. 2016, Gibreel et al. 2017, Menzies et al. 2017, Bevilacqua et al. 2020, Birketvedt et al. 2020, Ax et al. 2021, Celtik et al. 2022, Dellenmark-Blom et al. 2022, Maybee et al. 2023). As shown in Table 4-9 and Figure 4-9, prevalence ranged from 5% (Maybee et al. 2023)-54% (Menzies et al. 2017). The lowest rates were reported in children aged 0-6 months. Two studies included only adult participants, in which prevalence rates were 33%(Krug et al. 1999) and 30% (Gibreel et al. 2017). No studies reported OA subtypes or repair type separately.

Figure 4-9. Forest plot showing pooled prevalence of patient-/parent-reported need for texture modification.



4.11 Psychosocial aspects of eating and drinking

The psychosocial impact of eating and drinking difficulties for those born with OA/TOF and their parents/carers were described in studies using quantitative and qualitative methodologies, which are described separately and then synthesised.

4.11.1 Quantitative synthesis

Results from studies using quantitative methods are summarised in Table 4-10.

Table 4-10. Pooled prevalence of patient-/parent-reported psychosocial impacts to eating and drinking.

Characteristic (number of studies)	Total Participants	Prevalence range	Pooled prevalence (95% CI)	Heterogeneity (I^2)
Avoiding eating with friends (n=1)	68	0.09	n/a	n/a
Increased parent anxiety at mealtimes (n=3)	216	0.39-0.57	0.34 (0.13, 0.56)	88% Substantial
Challenging mealtime behaviour (n=4)	221	0.15-0.29	0.25 (0.19, 0.31)	0% Low

Meta-proportional analysis conducted using binary random effects DerSimonian-Laerd.

4.11.2 Eating and drinking-related quality of life (those born with OA)

Although a number of quantitative studies used tools which included items related to eating and drinking quality of life (QOL), only three papers reported specific results (Dellenmark-Blom et al. 2019, Dellenmark-Blom et al. 2022, Mikkelsen et al. 2022). Mikkelsen and colleagues reported 9% of adults born with OA/TOF avoided eating with friends because of their swallowing difficulties (Table 4-10). Dellenmark Blom (2019) noted that children with difficulty swallowing food more often avoided or expressed fear or worry about eating than those without difficulty (Dellenmark-Blom et al. 2019). Dellenmark Blom et al (2022) reported scores from a disease-specific QOL tool, identifying no statistically significant differences in eating subscale scores between those with long-gap (delayed repair) and short-gap OA (immediate repair) (Dellenmark-Blom et al. 2022).

4.11.3 Eating and drinking-related quality of life (family members)

Six studies reported some aspect of parental stress or anxiety at mealtimes using quantitative measures (Faugli et al. 2005, Menzies et al. 2017, Bevilacqua et al. 2020, Menzies et al. 2020, Bergmann et al. 2022, Pham et

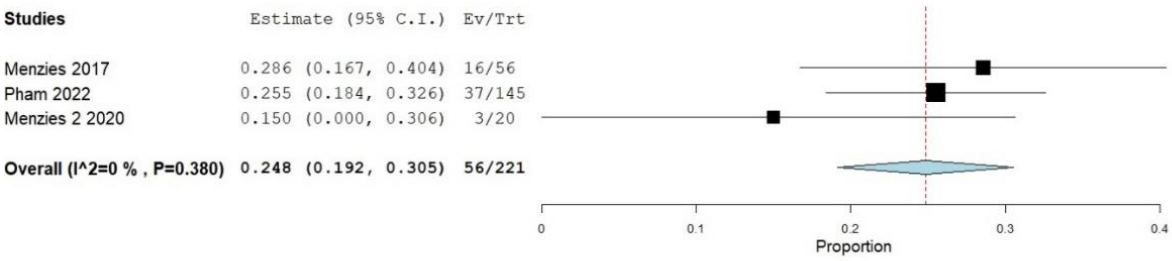
al. 2022). Frequent episodes of choking were associated with higher parental anxiety (Bevilacqua et al. 2020). Fear of choking was higher in parents of children under 5 years than over 5 years (Bergmann et al. 2022). Fear of choking resulted in parents not offering developmentally- or age-appropriate foods in 12/56 children (Menzies et al. 2017). Anxiety at feed times was found to negatively impact parent-child interaction (Faugli et al. 2005). Three studies reported prevalence rates for increased parent anxiety at mealtimes, generating a pooled prevalence rate of 34% (Table 4-10).

Four studies reported the impact of feeding or swallowing difficulties on family/parent quality of life more broadly using quantitative measures (Barni et al. 2019, Serel Arslan et al. 2020, Bergmann et al. 2022, Dellenmark-Blom et al. 2022). Dellenmark-Blom et al. (2022) found that a higher number of feeding difficulties was correlated with lower scores on the PedsQL family impact module. Using the Feeding-Swallowing Impact Survey (FSIS), Serel Arslan et al. (2020) identified significantly poorer feeding-related quality of life in those with isolated OA compared with OA/TOF and those with delayed repair compared to early repair. There were moderate-strong correlations between FSIS scores and time to start oral feeding. Bergmann et al. (2022) reported severe impact on swallowing-related quality of life in only 3/44 (7%) children born with OA with very or extremely low birth weight. Swallow-related quality of life was independent of OA type or surgery type (single vs staged repair).

4.11.4 Challenging mealtime behaviour

Four studies reported prevalence of extreme food selectivity or challenging mealtime behaviour (food refusal, distress) (Menzies et al. 2017, Menzies et al. 2020, Pham et al. 2022, Maybee et al. 2023). Prevalence range and pooled prevalence are detailed in Table 4-10 and the forest plot in Figure 4-10. The study conducted by Maybee et al was not included in the pooled prevalence as they reported by age group. Although three out of four studies included children of all ages, the mean age of participants was <4 years in all studies.

Figure 4-10. Forest plot detailing the pooled prevalence of parent-reported challenging mealtime behaviours.



4.11.5 Coping

Dellenmark-Blom (2019) and colleagues quantitatively investigated use of coping strategies during eating and drinking in children born with OA (Dellenmark-Blom et al. 2018). They identified nine different coping strategies, such as recognising responsibility ("I have learned what to do and can manage problems myself") and acceptance ("I am used to my situation and have adjusted to what I can eat"), used by 77% of children. Children aged 2-7 used a mean of six strategies, children aged 8-18 used a mean of 5 (when self-reported), or 6 (when parent-reported). These were more commonly employed by children who experienced difficulties swallowing food.

4.11.6 Qualitative synthesis

Three qualitative studies examined psychosocial aspects of eating and drinking (Rabone et al. 2021, Stewart et al. 2022, Wallace et al. 2022). All recruited using patient support groups. Two studies investigated experiences of parents of children born with OA/TOF (Stewart et al. 2022, Wallace et al. 2022). One investigated experiences of adults who had been born with OA/TOF (Rabone et al. 2021). Five categories were developed from aggregated data and are summarised below with illustrative quotes. It should be noted that the paper that arose from the online form (work package 1.1) is included in this evidence synthesis.

4.11.6.1 Fear and trauma associated with eating and drinking

Those born with OA/TOF and those caring for them experience anxiety and fear of coughing/choking when eating and drinking. For some, a trauma response is triggered.

“I constantly worry about eating if I don't have a drink nearby. Although I don't have as many symptoms as others might, it does cause me anxiety” (Rabone et al. 2021)

“It was terrifying. […] I was so scared she would get stuck and choke.”(Wallace et al. 2022)

“I think my first experience scarred me a little. Those earlier memories still haunt me and set me up to feel anxious about feeding…” (Stewart et al. 2022)

4.11.6.2 Isolation and a lack of support

Eating and drinking difficulties can cause those born with OA and those caring for them to avoid or have negative experiences in social situations. For parents a lack of support creates uncertainty about how to manage, increasing feelings of isolation.

"*I often avoid going out for meals or eating in crowded places due to worrying about how long it takes me to eat and having any issues in public. I also often feel as though friends and family may judge how slow I am at eating and I often become very anxious when eating in front of people.*" (Rabone et al. 2021)

“*I felt completely on my own and isolated. Very little support or advice…very much on my own fighting to do the best I could every day*” (Stewart et al. 2022)

“The hard thing was the sole responsibility: no one else would ever feed her or look after her without me as the choking frightened them.” (Wallace et al. 2022)

4.11.6.3 Being aware and grateful

Parents of children born with OA/TOF acknowledged that getting through difficult times with eating and drinking difficulties had made them grateful for progress, no matter how small.

“I never get tired of watching him eat. Little big steps….I'm surprised by what he can manage… I'm also surprised when he can't manage something that seems ok.”(Stewart et al. 2022)

“I would not change him for anything that has happened as it has taught me to never take anything for granted.” (Wallace et al. 2022)

4.11.6.4 Support to cope

Parents acknowledged the support systems that enabled them to develop ways to cope with eating and drinking difficulties. This included friends and family, support groups and professionals.

“I have a group of friends with babies around the same age and they are just wonderful while out and about.” (Stewart et al. 2022)

“The Facebook TEF support group was a lifeline during this time! So many food suggestions and encouragement was given.”(Wallace et al. 2022)

"I spent large parts of the day alone with baby and facing the fear of feeding […] without much support. Getting a SALT on board at this stage was probably more important for my mental welfare at this time than she realized." (Wallace et al. 2022)

4.11.6.5 Loss

Parents experienced feelings of loss of normal feeding experiences as a result of their child's eating and drinking difficulties.

"[Not being able to breastfeed her] *was hard for me because I felt that I had failed her. I did feel like her 'baby-hood' if you will, was stolen from her and I."* (Wallace et al. 2022)

4.11.7 Mixed methods synthesis

The available data from both quantitative and qualitative studies indicate that eating, drinking and swallowing difficulties have psychosocial impacts for those born with OA/TOF and those caring for them. Quantitative data indicate approximately 34% of parents experience mealtime anxiety. Qualitative data indicate that this arises from traumatic mealtime experiences, fear of choking, being unsure how to manage and feeling isolated. Quantitative data indicate that coping and resilience for individuals and parents/carers develops. Qualitative data expand this concept to show that this occurs through peer and professional support.

While qualitative data highlight that psychosocial aspects of eating and drinking are impacted by OA/TOF, there is very limited quantitative evidence, particularly for adults born with OA/TOF, limiting the ability to accurately determine their prevalence or the influence of medical/surgical factors on outcome (for example severity of swallow impairment or presence of gastro-oesophageal reflux).

4.12 Discussion

This systematic review aimed to summarise and synthesise the current evidence for the prevalence and nature of swallowing, eating and drinking difficulties, and their psychosocial impact for those born with OA/TOF. The main findings of this review are discussed under key headings of oropharyngeal dysphagia and psychosocial impact in keeping with the above-mentioned aims.

4.134.1 Oro-pharyngeal dysphagia

4.13.1 Determining prevalence

Pooled prevalence for aspiration caused by oro-pharyngeal dysphagia was 24%. This supports the assertion that, as discussed in the introductory chapter of this thesis, not all eating and drinking difficulties or aspiration-related respiratory disease in this population are caused by oesophageal dysfunction alone. However, current evidence is limited by a lack of natural history studies. Most data in this synthesis were generated by tertiary or referral centres, such as a research hospital or specialist aerodigestive clinic. Typically, investigation of oro-pharyngeal swallow function by instrumental assessment is initiated by symptom report or clinical observation prompting referral for videofluoroscopy. This selection bias is likely to have inflated reported prevalence of oro-pharyngeal swallowing difficulties. More accurate prevalence calculations requires either cohort studies in which all participants are assessed with instrumental assessment, or well-designed case series, in which the numbers of children in whom instrumental assessment was not provoked (and are therefore assumed to have no oro-pharyngeal dysphagia) are reported. The latter risks under-identification of impairment due to the limitations of observational swallow assessment or diagnosis from symptom report only, particularly given the challenge of differentiating oesophageal and pharyngeal stage swallow dysfunction (Duncan et al. 2018, Duncan et al. 2021).

4.13.2 Characteristics of oro-pharyngeal swallowing impairment

Most studies used videofluoroscopy to evaluate oro-pharyngeal swallow function and reported presence of aspiration/no aspiration as a binary outcome. A smaller number of reported features of swallow function using a categorical rating scale. None of the rating scales used demonstrated or considered reliability or validity, which must be noted as a limitation of the currently available evidence. As outlined in the introductory chapter, recent advances in the analysis of videofluoroscopy swallow studies could be used to provide more robust descriptions of swallow function. Miles et al. (2022) describe methods for reliably obtaining quantitative measures of pharyngeal

transit time, upper oesophageal sphincter opening, pharyngeal constriction, bolus clearance and coordination of airway closure. Standardised, valid and reliable categorical rating scales are now widely used to assess adults with dysphagia but have not been used in the OA/TOF population to date (Martin-Harris et al. 2008). Use of such methods in future studies would improve the quality of data available and our understanding thereof.

The more recent use of high-resolution manometry in the field of deglutition has significantly improved understanding of oesophageal motility patterns in those born with OA/TOF (Comella et al. 2021). As outlined in Chapter 1, this technology can also be used to assess pharyngeal function, providing quantitative assessment of velar and pharyngeal constriction, timing and efficiency of upper oesophageal sphincter opening and, when used with impedance, information regarding bolus flow (Omari et al. 2020). One study used low resolution manometry in adults born with OA, identifying altered timing of bolus transit through the pharynx (Montgomery et al. 1998). Ferris and colleagues used a cohort of children with OA/TOF without signs or symptoms of pharyngeal dysphagia to assess piecemeal deglutition in normal swallowing (Ferris et al. 2018). This demonstrates feasibility of use in this population but application to date has been limited. Use of this technology with a clinical cohort may improve understanding about the underlying aetiology of these oro-pharyngeal swallow patterns.

Despite the limitations, current evidence recognises the presence of oro-pharyngeal dysphagia. However, there is a significant evidence gap in understanding the mechanism underlying the impairment. Why do these children aspirate?

Structural airway abnormalities are common in this population and become apparent after extensive evaluation (Hall et al. 2013). Three studies in the current review examined the impact of upper airway structural abnormalities, reporting higher rates of oro-pharyngeal dysfunction in children with laryngeal cleft and vocal cord palsy (Fraga et al. 2015, Baxter et al. 2018, Fung et al. 2019). Demir et al. (2017) suggested incomplete hyoid movement caused by

a tethering effect may be an underlying cause of aspiration in this population. These are all plausible explanations for aspiration. However, this review also demonstrated that approximately 30% of children with OA have delayed swallow initiation, 12% present with post-swallow residue and 6% experience nasal regurgitation. It is unclear whether these features of oro-pharyngeal dysphagia can be explained by a structural airway abnormality, or whether there may be other mechanistic changes to swallow function occurring in this population. More specific evaluation to determine the underlying causes of altered swallow function may help to guide the development of more targeted treatment options.

Further evidence regarding the nature of eating, drinking and swallowing difficulties in this population was synthesised from symptom questionnaire or patient-/parent-report. These findings demonstrated a low prevalence of difficulty swallowing liquid (6%), compared to difficulty swallowing solid food (45%). This review also highlights the frequency with which adaptations to mealtimes and coping strategies are adopted by those with OA/TOF, the most frequent being adaptations which support the swallowing of food, rather than liquids. In their review of oesophageal morbidity, Comella et al. (2021), highlight the high levels of oesophageal dysmotility and gastro-oesophageal reflux, which provides a likely explanation for the difficulty with swallowing food. Yet, evidence from the current review highlights that oro-pharyngeal dysphagia is also present in a proportion of individuals with OA/TOF with potentially higher prevalence than might be expected from the parent-/patient-report of 6%.

One possible explanation for this is that the nature of dysphagia changes with time in those born with OA/TOF. Accurate subgroup analyses were not possible in either this review or that conducted by Comella et al. (2021). In the current review only one study explored prevalence of difficulty with liquid and food swallowing longitudinally, identifying reducing frequency of difficulty with liquids over the first two years of life, coupled with increasing difficulty with food (Maybee et al. 2023). It is also of interest to note that most studies of oro-pharyngeal instrumental assessment have been conducted in young

children. Given that instrumental assessment was generally a provoked assessment (i.e. evidence was from retrospective case series, rather than prospective cohort studies), it might be assumed that symptoms of oro-pharyngeal dysphagia present more frequently in younger children. This mismatch in instrumental assessment and patient-/parent-reported prevalence of difficulty with liquid swallowing may be attributable to a much wider range of ages included in the prevalence data acquired from patient-/parent-report than that from instrumental assessment. Understanding the true prevalence of oro-pharyngeal dysphagia and its relationship to age has important implications for service delivery, particularly for determining care pathways, the need for routine referral and assessment. Further study is therefore warranted.

4.14 Psychosocial impact

Evidence from both quantitative and qualitative data indicates that eating, drinking and swallowing difficulties in OA/TOF can have psychosocial, as well as health, impacts. This phenomenon has been more widely explored with parents/carers than for individuals born with OA/TOF. The development of a condition-specific QOL tool for children, which includes consideration of eating and drinking, has resulted in exploration of eating and drinking-related QOL (Dellenmark-Blom et al. 2017). However, relatively little is reported in the literature as to whether or how OA/TOF related swallow dysfunction impacts on eating and drinking-related QOL in adults. Evidence from the qualitative study included in this review suggests that adults born with OA/TOF experience anxiety related specifically to eating situations, which impact on their ability to enjoy meals out or social eating situations (Rabone et al. 2021). Several well-validated tools exist that specifically investigate these important aspects of QOL, such as the SWAL-QOL(McHorney et al. 2002) and MDADI (Chen et al. 2001), which could be adopted in clinical practice to ensure this important aspect of care is addressed, as well as a new condition-specific QOL tool (Ten Kate et al. 2023).

For children it is often parent QOL that is impacted by feeding difficulties (Silverman et al. 2021). Qualitative and quantitative evidence from the current review supports the findings from work package 1, demonstrating that eating and drinking-related QOL is significantly affected for parents of children with OA/TOF. Further integration of these findings will be presented in Chapter 6 (synthesis).

4.15 Limitations

Numerous conditions associated with swallow dysfunction and eating/drinking difficulties are known to co-occur with OA/TOF, such as cardiac abnormalities, structural airway abnormalities, gastro-oesophageal reflux, and prematurity. Likewise, numerous factors associated with OA subtype or repair type have the potential to impact on outcome. Subgroup analysis to assess the impact of OA subtype, repair type, co-morbidities, and the impact of late introduction to oral feeding on eating, drinking and swallowing outcomes was not possible due to varied reporting. As has been suggested previously, national, or international registries with prospectively collected data for a wide range of outcomes would be required to answer these questions (Comella et al. 2021).

4.16 Conclusions

This review suggests that prevalence of oral and pharyngeal phase swallowing difficulties may be as high as 24% in children with repaired OA/TOF. There is early evidence to suggest that oro-pharyngeal dysphagia may be more prevalent in young children. However further study, using more robust research designs, is required to determine its true prevalence and nature. In this population, swallowing difficulties present as altered eating and drinking behaviours, most commonly the need to drink water when eating (49%), prolonged mealtimes (37%) and the need to modify food or drink textures (28%) across the lifespan. Swallowing difficulties can impact on psychological well-being and quality of life, both for the individual and for parents/other family members. These aspects have been less widely

studied, particularly in adult populations, to date but should be included to ensure eating and drinking is considered holistically, rather than solely at an impairment level.

Chapter 5. Work package 3: Videofluoroscopic and manometric characterisation of swallow function in OA/TOF

5.1 Introduction

Chapter 2 and Chapter 3 provided insights into feeding difficulties associated with OA/TOF from a parent perspective. While providing insightful and important data, understanding the root cause of feeding difficulties - swallow function – requires examination of the physiology using other, direct methods of study.

5.1.1 Assessment of swallowing

As highlighted in the systematic review (Chapter 4), oro-pharyngeal or oesophageal impairment in OA/TOF can be identified using instrumental and non-instrumental (symptom report) methods. However, symptom report does not always align with physiological function, due to the differing ways in which an individual experiences and adapts to altered swallow physiology. Additionally, symptoms from different underlying impairments or diseases overlap (Wilkinson et al. 2021). Thus, symptom report does not differentiate underlying cause or specify physiological impairment (Duncan et al. 2021). Identification of underlying swallow impairment requires instrumental evaluation. An overview of swallow assessment methods is provided in Chapter 1. The study reported in this chapter employed videofluoroscopy and high-resolution impedance manometry to investigate swallow function.

5.1.1.1 Videofluoroscopy swallow study (VFSS)

Videofluoroscopy, also known as a modified barium swallow, is generally considered the “gold standard” for assessment of oral and pharyngeal swallowing in children. It is a dynamic, radiological assessment during which the oral cavity, pharynx, upper trachea and upper oesophagus are imaged during swallowing of a radiopaque contrast material using fluoroscopy

(Willging et al. 2019). Standardised presentation of a variety of food and fluid consistencies facilitates evaluation of swallow physiology.

Videofluoroscopy requires exposure to ionising radiation. Efforts must be made to ensure that exposure is as low as is reasonably achievable (the ALARA principle). Consequently, it is a time limited procedure (Ingleby et al. 2021). Radiation doses should also be minimised through use of pulsed fluoroscopy, judicious use of magnification, coning to avoid areas of high-density bone, such as the skull base, positioning close to the image detector and removal of unnecessary artefact from the images (Hiorns et al. 2006, Hong et al. 2021, Ingleby et al. 2021).

Videofluoroscopy analysis is done systematically to assess swallow physiology and bolus flow. The two broad analysis methods currently in use are: (1) categorical rating scales, (2) quantitative measures. However, until 2022, there were no validated methods for evaluating VFSS in children. Analysis used unvalidated, subjective rating scales, (Arvedson et al. 2017), or measures designed and validated for use with adults, for example the MBSImP (Martin-Harris et al. 2008). A version of the MBSImP is in development for use with bottle fed children, known as the BabyVFSSImP but at the time of writing was not available for use (Martin-Harris et al. 2020). The MBSImP tools rate 18 components of oral and pharyngeal swallowing using categorical scales. Training ensures 80% reliability is achieved prior to certified use.

Recently, Miles et al (2022), published a protocol for paediatric VFSS which included six validated, quantitative measures relating to the timing of bolus transit, coordination of airway closure with bolus transit, duration of hyoid elevation, bolus clearance and pharyngeal constriction ratios and maximum opening of the UOS. In addition to these objective measures, they recommend using three categorical descriptors for penetration/aspiration, bolus residue and naso-pharyngeal regurgitation. Further description of these measures can be found in 5.2.10.

Both analysis methods aim to identify features of swallow impairment that negatively impact on safety and/or efficiency of swallowing to guide intervention. As described in the systematic review, videofluoroscopy has been the most frequently reported modality for assessment of pharyngeal swallowing in OA/TOF to date. Existing data demonstrate signs of oro-pharyngeal dysphagia, including aspiration/penetration, post-swallow residue and delayed swallow initiation (Hormann et al. 2002, Yalcin et al. 2015, Yasuda et al. 2022). Structural abnormalities (vocal cord palsy and laryngeal cleft) have been identified as the mechanism for aspiration in some children (Fraga et al. 2015, Fung et al. 2019). However, the mechanism for aspiration/penetration or post-swallow residue remains unclear for those without structural impairment.

5.1.1.2 High-resolution impedance manometry

High resolution impedance manometry (HRIM) is recognised as the "gold standard" assessment of oesophageal motility (Yadlapati et al. 2021). With technological advances use of HRIM has been recognised as adding value to pharyngeal swallowing assessment, including in children, by providing a method of obtaining detailed information regarding swallow mechanics (Ferris et al. 2016, Omari et al. 2020).

Manometry involves insertion of a catheter containing pressure sensors at 1cm intervals into the nose, passing through the pharynx and oesophagus into the stomach. Over the last 15 years, impedance has been integrated within manometry catheters. Impedance assesses the bolus flow by evaluating resistance to electrical conductivity between two electrodes. Thus, as an electrically conductive bolus passes between the two impedance channels, resistance (impedance) drops. When impedance channels, typically spaced at 2cm intervals, are integrated with manometry sensors, information regarding bolus presence and flow is generated in conjunction with information regarding pressure. Pressure is generated from muscle contraction and distension during bolus flow within a confined area-such as the pharynx or oesophagus. Thus, HRIM is a pressure flow analysis tool (Omari 2023).

During HRIM, pressure data are transmitted to software which generates topography plots, also known as "Clouse" plots (

Figure 5-1). This facilitates intuitive interpretation of pressure waves (Pandolfino et al. 2009). Purpose designed software, such as Swallow Gateway ™, can generate semi-automatic analysis of these data. Use of this software generates numerous metrics which are designed to assess pharyngeal contractility and upper oesophageal sphincter function (Omari et al. 2020). These measures uniquely pinpoint areas of swallow impairment. Metrics applied in this study are discussed further in section 5.2.11.

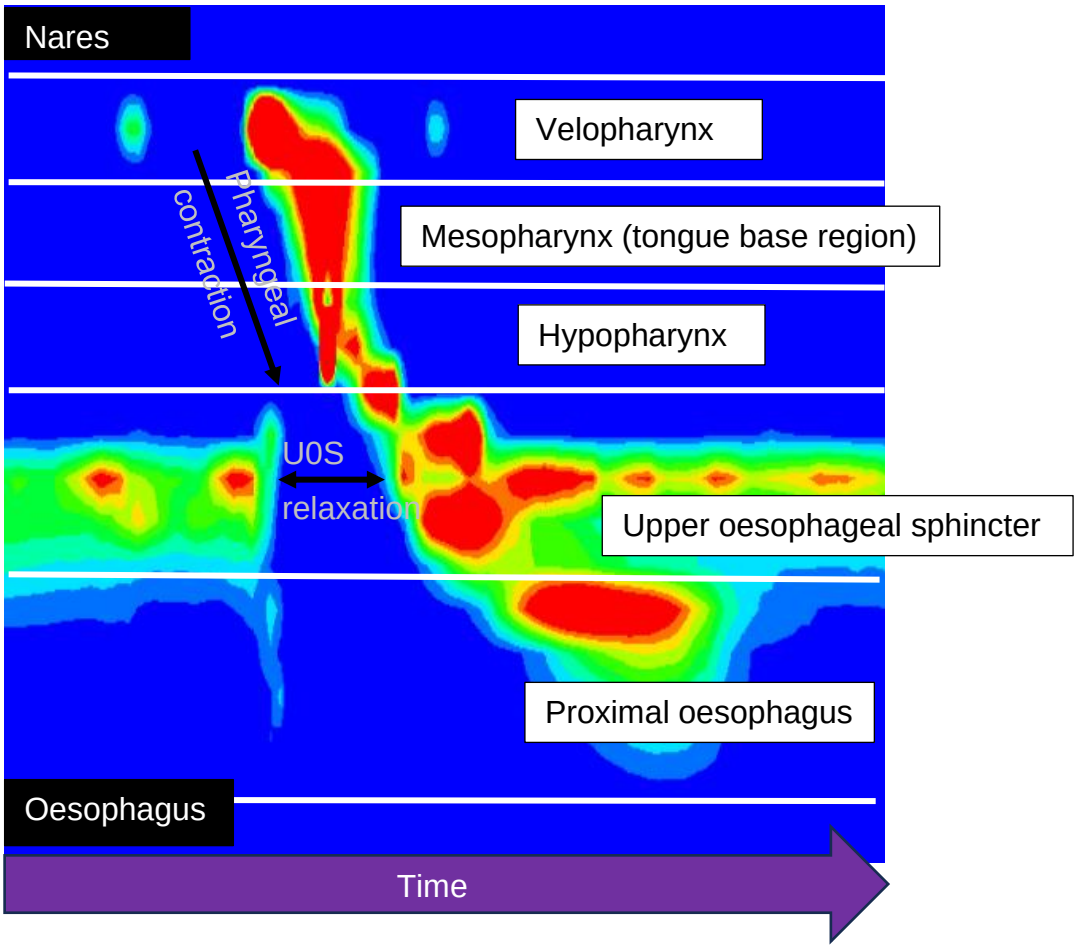


Figure 5-1. Example of a manometry topography (Clouse) plot indicating regions on interest visible on pharyngeal HRIM.

High resolution manometry has been applied to children with OA/TOF in the assessment of oesophageal function and has been determined as critical in

the evaluation of bolus clearance from the oesophagus (Rosen et al. 2018). Studies of oesophageal motility have reported abnormal distal contractile integral (DCI) in up to 100% of participants. Lemoine et al (2013) reported a case series of 40 children (mean age 8 years) in which 19 presented with weak motility and 21 with absent motility. Rayyan et al (2022) reported absent motility in 3/10, weak motility in 6/10 and normal motility in 1/10 infants (median age at assessment 62 days). Use of HRIM to assess pharyngeal function in children with OA/TOF is limited to one study, in which children with no known pharyngeal swallowing difficulties were used to evaluate typical piecemeal swallowing patterns (Ferris et al. 2018).

5.1.2 Aims and research questions

Primary aim:

To describe features of oral, pharyngeal, and oesophageal swallowing in children under one year of age with repaired OA/TOF using data from videofluoroscopy swallow study and high-resolution impedance manometry.

The specific research questions were:

1. What are the videofluoroscopic and manometric features of oral, pharyngeal, and oesophageal phases of swallowing?
2. What biomechanical swallow metrics are indicative of dysfunction in those with aspiration/laryngeal penetration/residue?
3. Is swallow function associated with functional feeding outcome at one year of age?

5.2 Methods

A prospective cohort study design was used to investigate swallow function in children born with OA/TOF in the first year of life. Longitudinal studies are appropriate for phenomena which are likely to change over time (Parahoo 2014), as is the case with feeding and swallowing given its developmental nature.

5.2.1 Ethical approval

The study was first approved by the London-Central Research Ethics Committee (20/LO/0098) and the Health Research Authority (IRAS ID: 262966) in March 2020 (Appendix 10). The approval process was then halted due to the COVID-19 pandemic. Delays to local research and development approval resulted in final approval being granted in December 2020. Due to slower than anticipated recruitment, a substantial ethics amendment was submitted in January 2022 and granted in April 2022 to allow for set-up of participant identification centres at four other surgical centres in London. Local research and development approval was obtained from St George's Hospital in June 2022 and the Evelina Children's Hospital in November 2022. Recruitment closed to all sites in July 2023.

5.2.2 Study sample

Inclusion and exclusion criteria are detailed in Table 5-1. An upper age limit of five months was chosen to capture swallow function before the introduction of weaning foods. Children were required to be able to take a minimum of 30mLs within one feed to increase the likelihood of completing a successful swallow assessment. Children undergoing oesophageal substitution repair due to long-gap atresia have a more complex clinical course and delayed introduction to oral feeding (Bourg et al. 2022) and were thus excluded to increase cohort homogeneity.

Table 5-1. Inclusion and exclusion criteria

Inclusion	Exclusion
Diagnosis of OA and/or TOF	Unrepaired OA and/or TOF
Under 5 months of age	Repair requiring gastric transposition/jejunal transposition or other non-primary repair
Undergone primary surgical repair	Fully tube fed
Orally feeding at least 30mLs at any one time	Requiring non-invasive ventilation

Consent from an adult with parental responsibility	Under a child protection order

OA = oesophageal atresia. TOF = tracheo-oesophageal fistula.

5.2.3 Participant recruitment

Potential participants were identified by the clinical care team and recruited by AS. The recruitment process for GOSH inpatients is presented in Figure 5-2. Study introductory leaflets and full participant information sheets (PIS) are provided in Appendix 11.

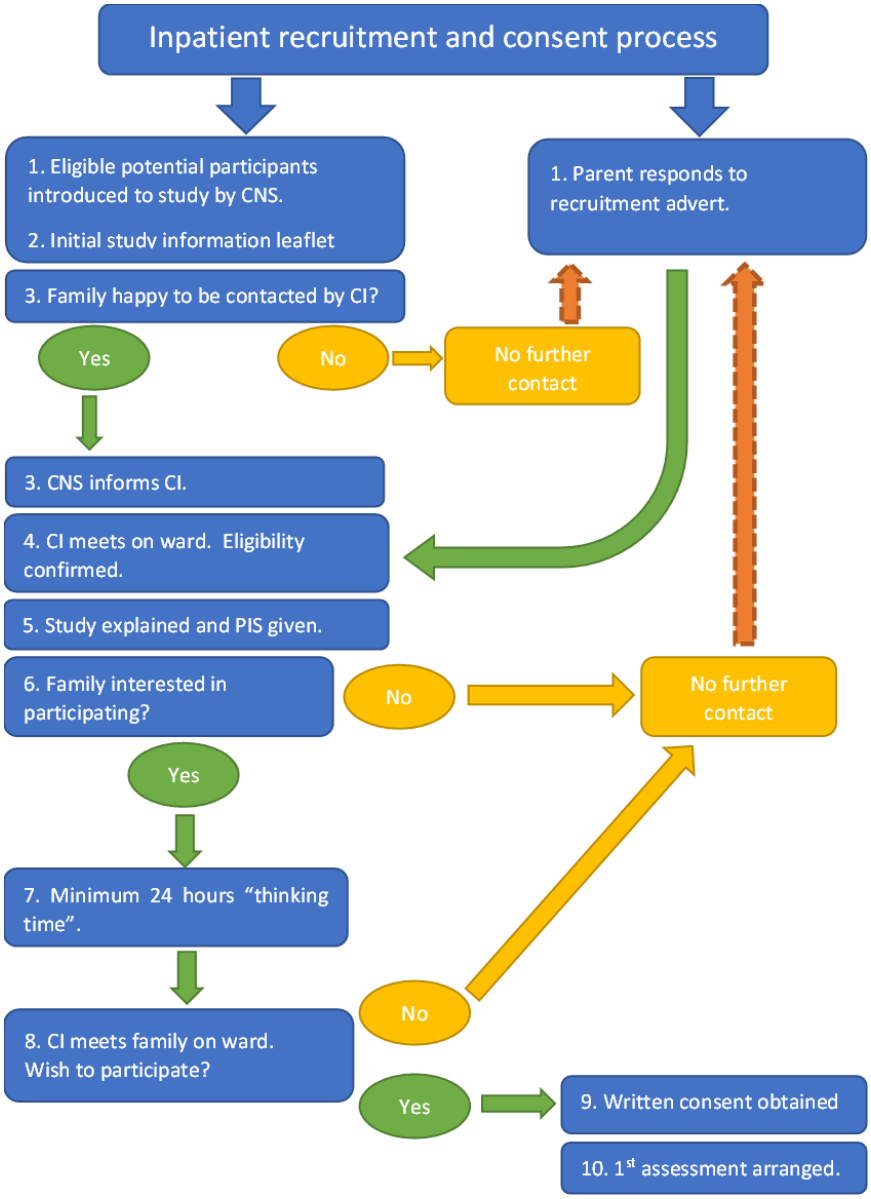


Figure 5-2. Inpatient recruitment process: Great Ormond Street Hospital

CNS = clinical nurse specialist. CI = chief investigator. PIS = participant information sheet.

5.2.3.1 Informed consent

Informed consent was obtained by the researcher prior to enrolment in the study. Participants were given a minimum of 24 hours after receipt of the PIS, before being contacted to determine study participation. If the family wished to proceed, written consent was sought from an adult with parental responsibility on behalf of their child. The consent form is provided in Appendix 11. An adult with parental responsibility was also required to consent to videofluoroscopy and high-resolution impedance manometry procedures at the time of the investigations, as is standard clinical practice.

5.2.3.2 Withdrawal from the study

Parents were able to withdraw their child from the study at any time. If parents withdrew after time 1 but prior to time 2 they were asked if they were happy to be contacted for data collection at time 3 as this did not involve direct swallow assessment. Any data collected prior to withdrawal was included in the final analysis.

5.2.4 Data collection

As detailed in Table 5-2, participants underwent assessment at three time points. The first two involved swallow assessment using VFSS and HRIM. The third involved parent report only.

Time 1 (aged 2-4 months) assessment of milk drinking. Early assessment is required to identify swallow dysfunction related to upper airway abnormalities or neonatal swallow dysfunction (Mahoney et al. 2017).

Time 2 (aged 8-10 months) assessment weaning foods and fluids. Developmental progression in oro-motor skill within the first six months of life enables introduction of solid foods (Arvedson 2006). Swallow physiology is

altered by food texture (Steele et al. 2015). Oesophageal phase abnormalities, as documented in individuals with OA/TOF, cause difficulties with food textures more commonly than liquid textures (Gibreel et al. 2017). Study of these developmental changes necessitated assessment at different time points in the process.

Time 3 (12 months) assessed feeding outcome through parental completion of a three-day food diary and a telephone review to provide detailed information regarding food textures and nutritional intake.

Table 5-2. Study visits and data collection schedule

Time point	Location	Assessment type				Outcomes		
		VFSS	HRIM	Parental feeding report	Food diary	CEDAS	Hospital admission	Chest infection
1. 2-4 months	Clinic visit	✓	✓	✓		✓	✓	✓
2. 8-10 months	Clinic visit	✓	✓	✓		✓	✓	✓
3. 12 months	Phone call			✓	✓	✓	✓	✓

VFSS = videofluoroscopy swallow study. HRIM = high resolution impedance manometry. CEDAS = children's eating and drinking activity scale. Chest infection defined as respiratory infection requiring antibiotics by parent report.

5.2.5 Videofluoroscopy procedure

5.2.5.1 Fluoroscopy equipment

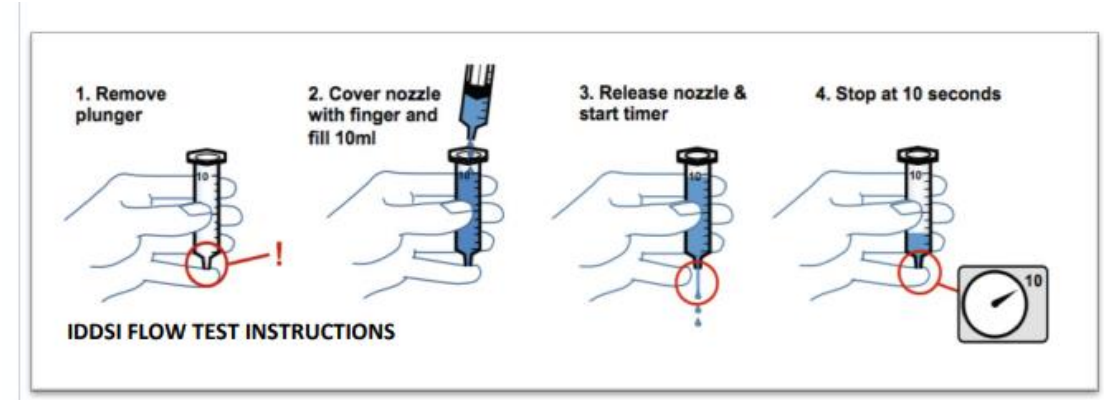
Videofluoroscopy swallow studies were all conducted using on a single-plane Siemens Artis Zee system installed 2006; (Siemens Healthineers AG, Siemensstr. 3, 91301. Forcheim, Germany) in the radiology department. All studies were completed by AS alongside a radiologist and radiographer and were reported in line with standard clinical care. Children sat in a Tumble Forms chair appropriate to the child's size, which attached to the fluoroscopy bed in an upright position, Figure 5-3, or were fed in an elevated side-lying position directly on the fluoroscopy bed if this was their usual feeding position. Oro-pharyngeal and oesophageal images were captured in the lateral position. If an anastomotic stricture was suspected on oesophageal screening, a barium swallow was conducted by the radiologist in supine, anterior-posterior position.

Figure 5-3. Videofluoroscopy swallow study set up

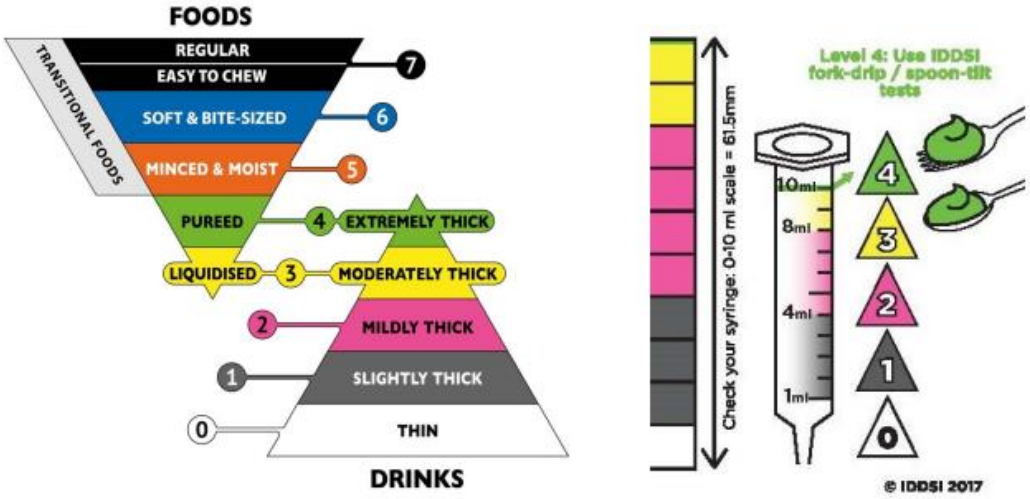
5.2.5.2 Contrast material

Parents provided their child's usual milk, feeding bottle and smooth pureed consistency food for use during the assessment in an effort to maximise participation (Hiorns et al. 2006). Barium sulfate contrast (E-Z-Paque 96% w/w or E-Z-HD 98% w/w, Bracco diagnostics) was mixed using a standardised recipe to achieve 30% w/v barium concentration (Barium Calculator – Swallowing Rehabilitation Research Lab (steeleswallowinglab.ca)). Barium concentration ranges from 20-40% w/v and should be optimised to ensure adequate image acquisition with the lowest barium concentration to maintain the desired fluid consistency and minimise taste disruption (Barbon et al. 2019). Locally completed review determined 30% w/v necessary for adequate imaging of liquid and puree consistencies, using this equipment in children. Fluids were flow tested according to International Dysphagia Diet Standardisation Initiative (IDDSI) guidelines to achieve a thin fluid (IDDSI 0) consistency (Cichero et al. 2017). This process is described in Figure 5-4. Pureed food was mixed with barium sulfate powder (E-Z-Paque 96% w/w or E-Z-HD 98% w/w, Bracco diagnostics) in a 2:1 ratio and IDDSI tested using the spoon tilt test (Cichero et al. 2017).

Figure 5-4. IDDSI testing procedure, framework and descriptors.



NOTE: Before use, check the nozzle is clear and free from any plastic residue or manufacturing defects that very occasionally occur.



IDDSI 2.0. | July 2019

5.2.5.3 Image capture

Fluoroscopy images were obtained at a pulse rate of 15/second and captured at a frame rate of 15/second. Determining the optimal pulse rate in paediatric fluoroscopy is a contentious issue, due to the need to balance rapid and complex movements which require high resolution imaging (high fluoroscopy rate) with the increase in radiation exposure that arises from

higher resolution images (Layly et al. 2020, Ingleby et al. 2021, Palmer et al. 2024). It is argued that to accurately rate components of swallowing, a pulse rate of 30/second is required (Bonilha et al. 2013, Miles et al. 2022). However, two studies conducted in children reported no difference in identification of aspiration/penetration when comparing studies conducted at 15 pulses/second with those at 30 pulses/second (Layly et al. 2020, Frakking et al. 2024). Palmer et al (2024) reported no statistically significant difference in timing measures on infant videofluoroscopy between those conducted at 30 pulses/second and 15 pulses/second. Therefore, given the inconclusive evidence in the literature and that standard clinical practice at this centre was to use 15 pulses/second, images were captured at 15 pulses and frames/second. Oesophageal screening was undertaken at 3 pulses/second in line with local guidelines.

Images were imported into the TIMS Medical Imaging Software (TIMS Review | Medical Imaging Software | TIMS Medical) for viewing. Images were additionally stored on the hospital Picture Archiving and Communication System (PACS) for clinical use and back-up in case of equipment failure.

5.2.5.4 Videofluoroscopy protocol

The videofluoroscopy protocol is detailed in Table 5-3. The protocol involved single bolus swallows and consecutive swallows. Previous research has demonstrated the value in interval screening to capture changes in swallow function over time while minimising radiation exposure and was therefore employed in this study (McGrattan et al. 2020). A published protocol for food consistencies in paediatric videofluoroscopy was not found. The bolus sizes were matched to those given in the HRIM protocol to allow for comparison. Children were fed by a parent at a pace directed by the child/parent. Bolus consistency and a maximum bolus size were controlled, however, the actual bolus size taken was determined by the volume taken by the child. The

order of each food/fluid challenge was determined by the child/parent, depending on what the parent felt would be most successful.

Table 5-3 Videofluoroscopy protocol

Aim	Number of swallows	Equipment	Consistency
Single bolus 0.5mls	X 5	Syringe with dummy	IDDSI 0
Consecutive sucking	Time 00:00 x 5 swallows Time 00:30 x 5 swallows Time 01:30 x 5 swallows Time 02:30 x 5 swallows	Own bottle	IDDSI 0
Oesophageal screen	x 5 swallows	Own bottle	IDDSI 0[1] IDDSI 4[2]
Single bolus 1ml	X 3	Spoon	IDDSI 4[2]
Single bolus 3ml	X 3	Spoon	IDDSI 4 [2]

[1]Time point 1 only, [2] Time point 2 only.

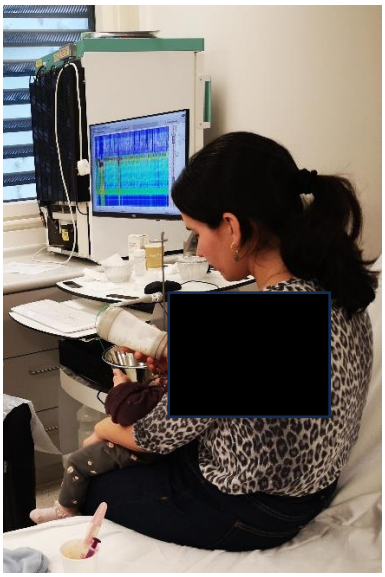
5.2.6 High resolution impedance manometry procedure

All HRIM procedures were conducted on the gastroenterology investigations unit, located on a short stay ward, at Great Ormond Street Hospital. Equipment was set up and checked by a staff nurse. Consent for the procedure was obtained by a consultant paediatric gastroenterologist who also inserted the catheter. A size 6 French, solid state, unidirectional, 25 pressure sensor with 12z impedance channel (13 ring) (Laborie, K62559-E1022D) catheter was used for all studies. The data were transmitted to the Medical Management System software (MMS) which provided the manometric recording by way of topography (Clouse) plots (Figure 5-5, image B). These data were then downloaded as a single ASCII file and

uploaded onto Swallow Gateway™. Swallow Gateway™ is a secure, GDPR-compliant, cloud-based software package which allows for detailed biomechanical analysis of impedance manometry data (Omari 2023).

Correct catheter placement was ensured by locating the upper and lower oesophageal sphincter following initial insertion. Where required, the catheter was adjusted to ensure sufficient pressure and impedance sensors were positioned in the pharynx. Pharyngeal and oesophageal metrics were obtained simultaneously, with the catheter capturing data from velum to stomach without re-siting. Parents were asked which was the easiest nostril for previous naso-gastric tube placement. The catheter was placed on the "easier" side if present. Anaesthetic lidocaine spray was added to gel lubricant which covered the tip of the catheter to aid passage through the nose. The child was held by a parent, or a nurse if the parent chose not to be present, for catheter placement. The catheter was secured to the child's cheek with tape. Distraction using music, video and toys was offered after catheter placement. A pacifier/dummy was offered if this was usually used by a child. Following catheter placement, the child was held in their natural feeding position by the parent, who sat on an examination table or chair (Figure 5-5).

Figure 5-5 High resolution impedance manometry positioning

A. B. 

A. Child feeding in mother's arms with HRIM catheter in situ. B. HRIM catheter linked to Medical Measurement Software (MMS) providing real time topography plot and impedance tracing.

5.2.7 HRIM protocol

There is no accepted protocol for pharyngeal or oesophageal HRIM in children under one year of age. The protocol used was based on that suggested by Rayyan (2020) following a body of work conducted on infants in a neonatal intensive care setting.

The assessment protocol is provided in Table 5-4. A 0.3mL single bolus was introduced due to the presence of piecemeal swallowing on 0.5mL boluses at time 1. To increase bolus conductivity, but minimise disruption to taste, 0.9% sodium chloride was added to all formula or expressed breastmilk and puree boluses in a 1:10 ratio. A child was given the opportunity to breastfed if they refused bottle drinking. To increase compliance the child's own milk (formula or expressed breastmilk) and bottle were used.

Table 5-4. High resolution impedance manometry protocol

	Aim	Time	Number of boluses	Equipment	Consistency
Time 1 and 2	No bolus	60 seconds			Resting pressures
	Single bolus 0.5mL	30 seconds between boluses	10	Syringe with dummy	IDDSI 0
	Sucking 10-15 seconds	60 seconds between sucking bursts	5	Own bottle	IDDSI 0
	Sucking ad lib		10 min	Own bottle	IDDSI 0
Time 2	Single bolus 1mL	30 seconds between boluses	5	Spoon	IDDSI 4
	Single bolus 3mL	30 seconds between boluses	5	Spoon	IDDSI 4
	No bolus	60 seconds			Resting pressure

IDDSI = International Dysphagia Diet Standardisation Initiative.

5.2.8 Videofluoroscopy swallow study analysis process

Videofluoroscopy images were analysed by the AS and an experienced speech and language therapist (MR). Videos were manually anonymised. AS was unblinded as the swallow studies had been reported for clinical purposes using standard local practice methods prior to analysis for research purposes. MR was blinded to previous VFSS outcome and history.

Each video was viewed independently by both assessors and a “worst” (highest) penetration/aspiration scale score assigned for each consistency. Any differences in scores were discussed and a consensus score agreed. Detailed analysis was undertaken for the swallow with the highest penetration/aspiration scale score for each consistency as recommended by Miles et al (2022).

For consistency of swallow selection where there was no aspiration or penetration, the best quality swallow from the final sucking burst or puree bolus was selected. This best image selection was judged to be in the most lateral position, with minimal movement artefact, a bolus size representative of most other swallows and good visualisation of the full oral cavity, pharynx, and upper oesophagus. If a good quality image was not available in the final sucking burst, the best quality swallow from the third sucking burst was selected.

All other pharyngeal measures were then made independently by each assessor with any differences in scores discussed immediately and a consensus score agreed. Oesophageal clearance ratings were made via consensus discussion only, due to the lack of validated or commonly used rating scale. Oesophageal stricture ratings were obtained from Radiology report on clinical systems, as this was deemed to be out of scope for Speech and Language Therapy practice. All ratings were recorded using pen and paper and transferred to an excel (Microsoft 365) spreadsheet.

5.2.9 Data analysis

5.2.10 Videofluoroscopy swallow metrics

As discussed in section 5.1.1, limited standardised analysis tools have been used in paediatric and infant VFSS in OA/TOF. Such tools have been relatively recently described in the literature and are acknowledged to be important developments in paediatric practice (Lefton-Greif et al. 2018, Dharmarathna et al. 2020). Therefore, swallows were analysed using a combination of categorical and quantitative methods to ensure that aspects of efficiency (bolus clearance) and safety (airway invasion) were assessed using the most robust and evidence-based methods available. Analysis methods are summarised in Table 5-5. The full level descriptors are provided in Appendix 12.

Table 5-5. Videofluoroscopy analysis methods

Name	Abbreviation	Definition	Rating	Reference values	Reference
Sucks per swallow	SpS	Number of sucks per swallow. Downward motion of the mandible to mandible returning to the neutral position is counted as one suck.	Total number of sucks per swallow	>3 sucks per swallow associated with increased aspiration risk.	Miles et al. (2022) McGrattan et al. (2017)
Nasopharyngeal regurgitation	NPR	Presence or absence of barium in the nasopharynx	Present/absent	Presence of NPR associated with increased risk of pharyngeal residue.	Miles et al. (2022)
Total pharyngeal transit time	TPT	Represents the total time of the bolus passage through the pharynx, from when the bolus head passes the posterior nasal spine to the time at which the bolus tail completely clears the PES. Measured in seconds	Recorded in seconds, to one hundredth of a second	TPT >0.5 seconds associated with increased aspiration risk of thin fluids.	Miles et al. (2022)

Coordination of airway closure with bolus transit	AirCl	Airway closure time in relation to bolus reaching PES. Coordination of airway closure with bolus transit. Measured in seconds	Recorded in seconds, to one hundredth of a second	Longer time to airway closure associated with increased aspiration risk of thin fluids. No cut-off reported.	Miles et al. (2022)
Bolus residue scale	BRS	Location of post-swallow bolus residue. Judged after the 1st swallow	6-point categorical scale (1-6)	Increased risk of aspiration in children with a score of 3 or more	Rommel et al. (2015)
Residue volume	ResVol	Volume of residue after initial swallow	5-point categorical scale (0-4)	Score of 2 or more indicates abnormality	Martin-Harris et al. (2008) Steele et al. (2019)
Penetration Aspiration Scale	PAS	Depth of airway invasion and response to airway invasion	8-point categorical scale (1-8)	Score of 3 or more indicates abnormality	Rosenbek et al. (1996)
Oesophageal clearance	n/a	Ability of oesophagus to propel and clear food or liquid from upper to lower	5-point categorical scale (0-4)	Score of 1 or more indicates abnormality	Martin-Harris et al. (2008)

		oesophagus and into the stomach.			
Stricture	n/a	The presence of anastomotic narrowing.	3-point categorical scale (1-3) 1 = no evidence of stricture 2 = narrowing /waisting visible but no bolus hold up. No immediate intervention required. 3 = stricture evident with bolus hold up. Intervention required.	Score of 2 or more indicates abnormality	Unvalidated, bespoke measure

n/a = not applicable

5.2.11 High resolution impedance manometry analysis

Data from HRIM studies were analysed in Swallow Gateway™ in conjunction with Prof Nathalie Rommel (NR) (Deglutologist, KU Leuven, Belgium). The analysis process involved:

1. Swallow identification: Bolus markers were cross-referenced with MMS to identify volume and consistency of each swallow.
2. Swallow selection: data from single bolus swallows were included if there were data from a minimum of three swallows for each bolus condition (volume and consistency) (Omari et al. 2020). For consecutive drinking (bottle or breastfeeding) the final swallow in the sequence was selected. There is no protocol to guide swallow selection for bottle or breastfeeding. In Swallow Gateway pharyngeal and oesophageal swallows are selected separately. During consecutive swallowing, oesophageal peristalsis is inhibited (Yadlapati et al. 2021). Swallow selection from the whole study topography plot is shown in Figure 5-6.
3. Landmark placement: swallow landmarks were manually assigned in accordance with Swallow Gateway guidance (Omari 2023). Pharyngeal landmarks: time of upper oesophageal sphincter relaxation, time of upper oesophageal sphincter contraction, position of velopharynx upper margin, position of hypopharynx upper margin, position of upper oesophageal sphincter apogee (at maximum laryngeal elevation), position of upper oesophageal sphincter distal margin. Oesophageal landmarks: position of the upper oesophageal sphincter distal margin, position of the oesophageal transition zone, position of the oesophago-gastric margin, position of the crural diaphragm, position of the stomach immediately below the oesophago-gastric junction high pressure zone, time of swallow onset (upper oesophageal sphincter relaxation), time of distal contraction at the transition zone, time of onset of distal contraction at the oesophago-gastric junction.

Figure 5-6. Swallow gateway swallow selection process

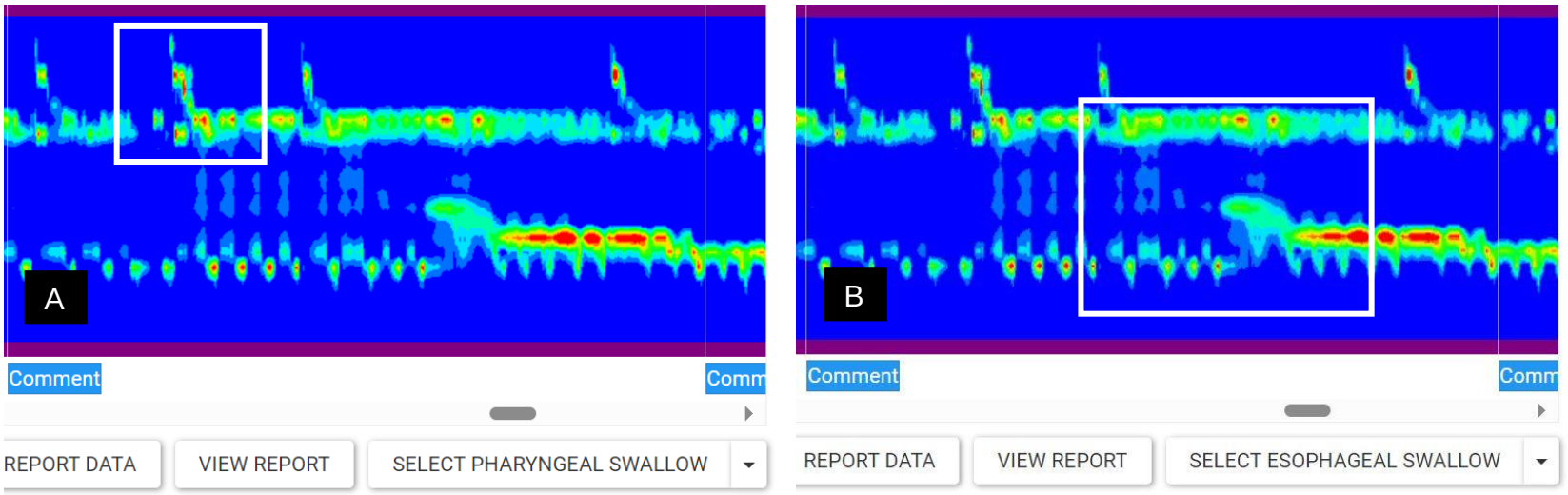


Image A white box = pharyngeal swallow selection. Image B white box = oesophageal swallow selection.

4. Metric acquisition: Metrics are automatically calculated by the Swallow Gateway™ software and were exported into Excel (Microsoft 365).

Swallow selection was conducted by AS. For piecemeal swallows impedance data were used to select the swallow with the largest volume (Ferris et al. 2018). Landmarks were placed by AS or NR. All landmark placements were checked for accuracy, adjusted if required and approved by NR.

5.2.12 HRIM swallow metrics

Four pharyngeal and two oesophageal swallow metrics were acquired from HRIM data, summarised in Table 5-6. Selected oesophageal metrics were those described in the Chicago Classification 4.0 and used to categorise participants by motility type and to report presence/absence of oesophago-gastric outflow obstruction (Yadlapati et al. 2021). Selected pharyngeal metrics were those recommended as a core outcome set by an expert working group (Omari et al. 2020).

Four measures within the core set were omitted: velopharyngeal contractile integral, mesopharyngeal contractile integral, hypopharyngeal contractile integral and hypopharyngeal intrabolus distension pressure. These measures all rely on accurate measurement within specific regions of the pharynx and are therefore dependent on the pharynx being of sufficient length. Given the fixed placement of pressure sensors at 1cm intervals in the manometry catheter, the infant pharynx is too short to allow for accurate regional contractility assessment or hypopharyngeal intrabolus pressure.

Table 5-6. Summary of HRIM derived swallow metrics

	Metric	Abbreviation	Definition	Measurement rating	Reference values	Reference
Pharyngeal	Pharyngeal contractile integral	PhCI	Measures contractile vigour from velo-pharynx to the upper margin of the upper oesophageal sphincter.	mmHg.s.cm		(Jadcherla et al. 2018, Omari et al. 2020)
Upper oesophageal sphincter	Upper oesophageal sphincter integrated relaxation pressure	UOS IRP	Measures the extent of upper oesophageal sphincter relaxation.	mmHg		(Omari et al. 2020, Damrongmanee et al. 2024)
	Upper oesophageal sphincter relaxation time	UOS RT	Measure the duration of upper oesophageal sphincter relaxation.	Milliseconds		(Omari et al. 2020)
	Upper oesophageal sphincter maximum admittance	UOS max ad	Measures the extent of upper oesophageal sphincter opening.	Millisiemens		(Omari et al. 2020)

Oesophageal	Distal contractile integral	DCI	Measures contractile vigour from the transition zone to the proximal margin of the oesophago-gastric junction.	mmHg.s.cm	Normal contractility 450 – 8000 Weak contractility 100 – 450 Absent contractility < 100	(Singendonk et al. 2020, Yadlapati et al. 2021)
	4 second integrated relaxation pressure	IRP4s	Measures the extent of lower oesophageal sphincter relaxation in relation to swallow onset.	mmHg	>25 indicates incomplete lower oesophageal sphincter relaxation	(Nikaki et al. 2016, Singendonk et al. 2020, Yadlapati et al. 2021)

mmHg = millimetres of mercury. mmHg.cm.s = millimetres of mercury multiplied by centimetres multiplied by seconds.

A lack of paediatric normative data, due to ethical issues arising from undertaking invasive procedures in healthy children, means that cut-off values for “normal” or “abnormal” pharyngeal metrics do not yet exist (Damrongmanee et al. 2024). Pharyngeal metrics are therefore reported but not defined as normal or abnormal.

5.2.12.1 Pharyngeal contractile integral

The pharyngeal contractile integral (PhCI) is a measure of swallowing “vigor”, which is the propulsive force required to move and clear the bolus from the pharynx (Jadcherla et al. 2018). It defines pressure over space and time, calculated by mean pressure x duration x length, reported in units of mmHg.s.cm (Omari et al. 2020). Pharyngeal contractile integral increases with bolus size (Ferris et al. 2021). It is also modulated by swallow type with higher PhCI seen in syringed boluses than during bottle feeding in infants (Jadcherla et al. 2018).

Clinical relevance has been demonstrated with increased risk of aspiration and dysphagia associated with lower PhCI in both adults and children (O'Rourke et al. 2017, Bayona et al. 2022, Omari et al. 2023, Damrongmanee et al. 2024). Although no cut-off values exist, Jadcherla and colleagues (2018) report mean values of 114 (SE 11) mmHg.s.cm for syringe boluses and 87 (SE 11) mmHg.s.cm during bottle feeding in a cohort of fully orally fed, thriving infants receiving “transitional” neonatal care.

5.2.12.2 Upper oesophageal sphincter integrated relaxation pressure

The UOS IRP quantifies the lowest non-consecutive 0.20 seconds of upper oesophageal sphincter pressure during relaxation measured in mmHg (Omari et al. 2020). Relaxation pressure is known to increase with bolus size and viscosity (Ferris et al. 2021).

Damrongmanee et al (2021) report significantly higher UOS 0.2s IRP in children (aged 11 months-18 years) with abnormal swallowing on VFSS than those with normal swallowing. High UOS IRP was identified in 5/6 children

with pharyngeal residue, supporting the assertion that reduced relaxation contributes to inadequate opening and thereby incomplete bolus clearance. They report a 5-95th percentile range of -7.98, 19.48 for those with normal VFSS. After adjusting for swallow dysfunction, UOS IRP was not affected by age. These figures were not used as cut-off values as the bolus size was significantly larger in the Damrongmanee cohort (5mL) compared to the current study (0.3mL), and as outlined above, UOS IRP increases with bolus size.

5.2.12.3 Upper oesophageal sphincter relaxation time

Upper oesophageal sphincter relaxation time (UOS RT) measures the duration that UOS pressure drops below 50% of baseline pressure or 35mmHG, whichever is lower. It is measured in units of seconds (Omari et al. 2020). In healthy adult swallowing, relaxation time is modulated by bolus volume and consistency, with relaxation time increasing with bolus size and decreasing with bolus viscosity (Ferris et al. 2021).

It is hypothesised that UOS RT that is insufficient for bolus size or consistency would result in obstructed bolus flow (Bayona et al. 2022). However, in clinical adult populations relaxation time was not identified as a reliable indicator of swallow impairment (Omari et al. 2023). Its relevance to infant swallowing has not previously been explored.

5.2.12.4 Upper oesophageal sphincter maximum admittance

Upper oesophageal sphincter maximum admittance (UOS MaxAd) is a measure of sphincter opening. It refers to the maximum admittance value recorded during bolus flow through the upper oesophageal sphincter, measured in units of millisiemens (mS). Low admittance values indicate lower reduced opening diameter and thus, lower than expected bolus flow through the upper oesophageal sphincter which, along with raised UOS IRP indicating reduced relaxation, is a marker of bolus obstruction (Omari et al. 2023).

Upper oesophageal sphincter maximum admittance increases with bolus size and viscosity, as well as bolus conductivity (Ferris et al. 2021). Comparison with other studies is reliant on these factors being equal. As very little research has been conducted in the age range used in this study, and any study where UOS MaxAd is reported has been conducted in older children taking larger boluses of undiluted 0.9% saline, this metric is difficult to compare. However, it is of value to report, to add to understanding of its relevance to swallow function in infants.

5.2.12.5 Distal contractile integral (DCI)

The primary aim of the DCI is to identify disorders of oesophageal motility. There are well-documented normal ranges. Normal DCI is between 450 – 8000 mmHg x s x cm. Weak contractility is 100 – 450 mmHg x s x cm. Absent contractility is below 100 mmHg x s x cm. Hypercontractility is over 8000 mmHg x s x cm (Yadlapati et al. 2021). These ranges apply to adults and children. The DCI is not affected by oesophageal length, and therefore age is not a confounding factor (Singendonk et al. 2020).

5.2.12.6 4 second integrated relaxation pressure (IRP4s)

The IRP4s metric is a measure of lower oesophageal sphincter relaxation. It is the mean of 4 seconds of maximum relaxation in a 10 second window which begins at the point of upper oesophageal relaxation. Stomach pressures are used as a reference point. This metric is a key indicator of obstruction at the level of the lower oesophageal sphincter. Higher than expected values indicate that there is insufficient relaxation of the lower oesophageal sphincter, which may inhibit bolus flow from the oesophagus to the stomach. Disorder at this level is commonly determined as an oesophago-gastric outflow obstruction (Yadlapati et al. 2021).

Cut-off values for abnormal IRP4s are documented in the Chicago Classification 4.0 (Yadlapati et al. 2021). IRP4s is known to be dependent on the specific equipment used, therefore cut-offs for abnormality should be determined by local assessment (Kahrilas et al. 2015). Establishing clear

cut-off values for IRP4s in children is also complicated by the impact of oesophageal length on this metric. Failure to account for oesophageal length would over-estimate abnormality as a shorter oesophagus is associated with higher IRP4s (Singendonk et al. 2020). A locally derived value of ≥25 mmHg was used as cut-off for normal value.

5.2.13 Feeding outcome

Feeding outcome was evaluated using the children's eating and drinking activity scale (Hanks et al. 2023). This six-point, categorical scale (Table 5-7), measures functional eating and drinking outcome in children aged 0-18. It primarily assesses activity level outcomes, according to the WHO-ICF framework (Organization 2007).

Table 5-7. Children's eating and drinking activity scale

CEDAS level	Descriptor
1	Tube use for all nutrition and hydration. Nothing by mouth. Non-nutritive sucking and/or mouthcare only.
2	Tube use for all nutrition and hydration. Oral intake offered for experience and/or pleasure only.
3	Tube use with consistent intake of food and/or drink. Oral intake partially meets nutrition and/or hydration needs.
4	Total oral intake but requires special preparation of drinks (IDDSI level 1-4) and/or food (IDDSI level 3-5, where not age-appropriate) and/or supplements needed for nutrition support.
5	Total oral intake but requiring special conditions (equipment/positioning/pacing/supervision) or food modification at IDDSI level 6-7 (where not age-appropriate) or food types/groups restricted by avoidance (where not age-appropriate) but without the need for supplements.
6	Total oral intake. Age-appropriate food and drink with no restrictions.

CEDAS = children's eating and drinking activity scale. IDDSI = International Dysphagia Diet Standardisation Initiative.

The tool was designed for prospective or retrospective use (Hanks et al. 2023).

Data from parent report of current feeding was used to assign a CEDAS at time one and two. A parent-completed three-day food diary and telephone interview were used to assign a CEDAS outcome at time point three.

5.2.14 Statistical analysis

5.2.14.1 Defining swallow function and feeding outcome

Cohort data were summarised using frequencies and percentages for categorical data and median, range and interquartile range for ordinal and continuous data. For consistency of reporting, all metrics were summarised using the median as most data were not normally distributed. Consequently, all inferential statistics were calculated using non-parametric methods.

Wilcoxon signed rank tests were used to assess differences between swallow metrics: a) at time 1 and time 2, b) between IDDSI 0 and IDDSI 4 consistencies and c) between single and consecutive swallow types. Test assumptions were met. Significance was set at <0.05.

5.2.14.2 Exploratory analysis of biomechanical swallow metrics

To generate hypotheses for potential biomechanical causes of aspiration/penetration and residue, metrics were categorised as functional or dysfunctional. Where accepted cut-off values existed, these were used to categorise a metric or outcome as dysfunctional. Where no accepted cut-off values exist, a value was considered potentially dysfunction if it was in the lowest performing quartile for this cohort Table 5-8.

Table 5-8. Determiners of dysfunction categorisation

Outcome	Determiner of dysfunction
Penetration/aspiration scale	≥3
Bolus residue scale	≥3
Residue volume	≥3
Sucks per swallow	≥4
Time to airway closure	Highest quartile
Pharyngeal contractile integral	Lowest quartile
UOS relaxation time	Lowest quartile
Maximum admittance	Lowest quartile
UOS integrated relaxation pressure	Highest quartile
LOS integrated relaxation pressure	Highest quartile
Distal contractile integral	100-449mmHg.cm.s = weak peristalsis <100mmHg.cm.s = absent peristalsis

UOS = upper oesophageal sphincter, LOS = lower oesophageal sphincter.

Inter-rater reliability

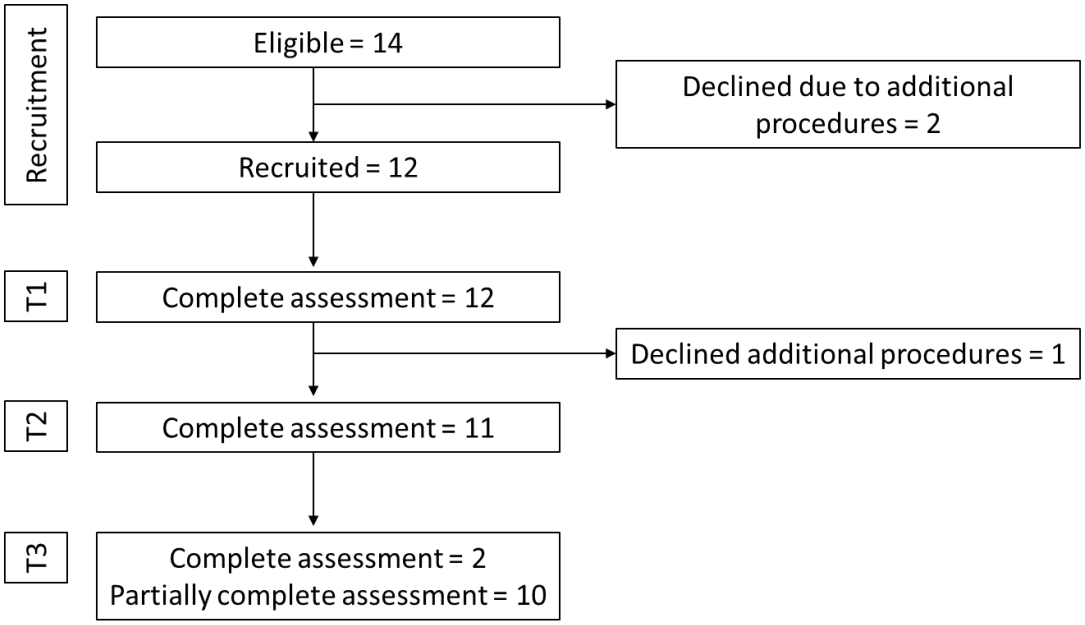
Inter-rater reliability for VFSS metrics were assessed using Cohen's Kappa for categorical variables and a two-way random, average measures, absolute agreement intraclass correlation coefficient for continuous variables. Cohen's kappa values of <0.20 were interpreted as poor reliability, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as good and 0.81-1.00 as very good (Altman 1990). ICC values less than 0.5 were interpreted as poor reliability, 0.5 to 0.75 moderate reliability, 0.75 to 0.9 good reliability, and values greater than 0.90 excellent reliability (Koo et al. 2016).

5.3 Result

5.3.1 Participants

Fourteen children were eligible and invited to participate, twelve children (86%) were recruited. Participation at each time point is presented in Figure 5-7.

Figure 5-7. Study participation flow chart



T1=time 1, T2=time 2, T3=time 3.

Demographic and medical history data are outlined in Table 5-9. All children had type C oesophageal atresia/tracheo-oesophageal fistula and underwent primary repair within the first three days of life. Children had a mean age of 3.89 months (SD 0.95) at time 1 VFSS and 3.96 months (SD 0.99) for time 1 HRIM. At time point 2, VFSS were carried out at a mean age of 9.55 months (SD 0.78) and HRIM at 9.55 months (SD (0.74). One child's family chose not to participate in the assessments at time point 2. Assessments were conducted on the same day for 9/12 and 9/11 at time 1 and 2, respectively. The largest gap between VFSS and HRIM was 35 days. The HRIM was delayed as a stricture requiring dilatation was identified on VFSS. Other

studies were conducted within 9 days of each other. This was due to scheduling difficulties or parent preference.

Table 5-9. Demographic and medical history information

	N	%
Female	7	58.3
Gestation		
≥ 37 weeks	7	58.3
35-<37 weeks	5	41.7
Cardiac abnormality	2	16.6
VACTERL	1	8.3
Other syndrome	1	8.3
Laryngeal cleft	1	8.3
Vocal cord palsy	0	0
Hospital readmission during study period	11	91.6
Respiratory cause	7	
Any dilation	5	41.6
More than 2 dilatations	2	16.6
Any other surgical procedure	5	41.6
Aortopexy	3	25.0
Fundoplication	1	8.3
Cardiac	1	8.3

Almost all (11/12) children had at least one hospital readmission during the study period. Seven children required admission for respiratory causes: blue episodes/tracheomalacia (n=3), long-stay viral infection (n=1), short-stay viral infection (n=3).

5.3.2 Inter-rater reliability

Inter-rater reliability scores for all VFSS metrics are presented in Table 5-10 Total pharyngeal transit time had excellent reliability; airway closure, naso-

pharyngeal reflux, bolus residue scale and residue volume very good reliability; and the PAS and sucks per swallow good reliability.

Table 5-10. Inter-rater reliability for VFSS metrics

Metric	Inter-rater reliability
Penetration Aspiration Scale	**.759** [a]
Sucks per swallow	**.793** [a]
Nasopharyngeal reflux	**1.00** [a]
Bolus residue scale	**.941** [a]
Residue volume	**.884** [a]
Total Pharyngeal Transit time	**.992** [b]
Airway closure	**.879** [b]

[a] Cohen's kappa [b]Two-way random intraclass correlation coefficient. **Bold** = p <.001

5.3.3 Videofluoroscopic characteristics of swallowing

Videofluoroscopy metrics were obtained from consecutive swallow thin fluid (IDDSI 0) boluses in 12/12 (100%) of children at time point 1 and 8/11 (73%) at time point 2. Two children refused to bottle feed and one child was not offered thin fluids due to aspiration risk. Metrics were obtained from puree boluses (IDDSI 4) for 10/11 (91%) children. One child refused to eat any puree. Cohort median values by time point and consistency are presented in Table 5-11. Individual data are provided in Appendix 13.

Table 5-11 Median VFSS metrics

Metric	Time point	IDDSI level	Median	Minimum	Maximum	IQR
Penetration Aspiration Scale	1	0	1	1	4	1, 2
	2	0	2	1	8	1, 5
	2	4	1	1	8	1, 1
Bolus residue scale	1	0	1	1	3	1, 2
	2	0	2	1	2	1, 2
	2	4	2	1	4	1, 3
Residue volume	1	0	1	1	3	1, 2
	2	0	2	1	2	1, 2
	2	4	2	1	3	1, 3
Oesophageal clearance	1	0	3	1	3	2, 3
	2	4	3	2	3	2, 3
Sucks per swallow	1	0	3	1	5	2, 4
	2	0	3	1	5	2, 4
Total pharyngeal transit time	1	0	1.33	.53	2.67	1.02, 1.76
	2	0	1.09	.80	2.81	.90, 1.68
	2	4	1.56	.82	7.00	1.16, 2.37
Airway closure	1	0	.13	.07	1.33	.17, .32
	2	0	.38	.13	.66	.18, .58
	2	4	.15	.07	.34	.12, .21

IDDSI = International Dysphagia Diet Standardisation Initiative, IQR = interquartile range

5.3.3.1 Presence of aspiration and penetration

Five children (41.7%) presented with a PAS ≥3 indicating presence of aspiration or penetration. At time 1, 2/12 presented with laryngeal penetration (PAS 3-5). At time 2, 2/9 presented with laryngeal penetration to the level of the cords and 2/9 with aspiration (PAS 6-8). One child presented with laryngeal penetration only at time one. One child presented with laryngeal penetration at time one and aspiration at time two. All other children presented with aspiration or penetration at time two only.

Median PAS was higher at time 2, but the difference was not statistically significant (z = 1.28, *p* = .20). Only 1/10 children had a PAS ≥3 on IDDSI 4 consistency, compared to 2/12 on IDDSI 0 at time 1 and 3/8 on IDDSI 0 at time 2.

5.3.3.2 Bolus residue scale and residue volume

One child (out of 12) presented with post-swallow residue in a location other than the valleculae (indicating higher risk) on IDDSI 0 and 2/10 children for IDDSI 4 consistency. One child had residue greater than trace volume for IDDSI 0 and 3/10 for IDDSI 4. When observed in combination, one child had a residue location *and* volume score outside of the expected range i.e. residue lower than the valleculae and of a clinically significant volume.

Comparison on IDDSI 0 consistency revealed a statistically significant increase in median BRS between time 1 and time 2 (*z* = -2.52, *p* = .01) but not residue volume (*z* = .45, *p* = .66). However, values were within the "normal" range, indicating that bolus clearance difficulty was not a frequent feature of swallow function in this cohort.

5.3.3.3 Oesophageal clearance (VFSS)

Oesophageal clearance values were available for 11/12 children at time 1, assessed with IDDSI 0 consistency, and 9/10 children at time 2, assessed with IDDSI 4 consistency. Oesophageal retention was evident for 9/11 children at time 1. For 8/9 of these children, retrograde bolus movement was

seen. At time 2, oesophageal retention was seen in all children. Retrograde flow was visible in 6/9 children. Median values were the same at both time points.

One child at each time point was identified with an anastomotic stricture which required dilatation. This was identified on the oesophageal screen and confirmed with upper gastrointestinal swallow conducted at the time of the assessment. Onward referral to the surgical team was made immediately for appropriate management.

5.3.3.4 Sucks per swallow

A high suck swallow ratio, indicative of reduced efficiency at the oral phase, was present in 3/12 children. Two of these children had high values at both time points. One child had high values at time one only. At a cohort level, there was no difference in median sucks per swallow between time 1 and 2.

5.3.3.5 Nasopharyngeal regurgitation

Nasopharyngeal regurgitation was identified in 2/12 children at time 1 and 1/9 at time 2. No child presented with NPR on IDDSI 4 consistency.

5.3.3.6 Total pharyngeal transit time

All children presented with TPT scores above 0.5 seconds for IDDSI 0 consistency at both time points. Median values were significantly lower for IDDSI 0 consistency at time 2 (z = -2.52, p = .01), suggesting improved oral-pharyngeal efficiency and coordination between time points (Table 5-11).

5.3.3.7 Time to airway closure

Airway closure in relation to bolus head arrival at the pharyngo-oesophageal segment varied between 0.07 seconds (closure achieved in the next frame) and 1.33 seconds. No child achieved airway closure prior to the bolus head arriving at the pharyngo-oesophageal segment. Median time to airway closure increased significantly between time points (z = 2.38, p = .01), indicating higher risk of airway violation at time 2. Median time to airway

closure was significantly lower for IDDSI 4 than IDDSI 0 (z = 3.17, p = .005), (Table 5-11).

5.3.4 High resolution impedance manometric characteristics of swallowing

HRIM metrics were obtained from consecutive swallow boluses in 12/12 (100%) of children at time point 1 and 9/11 (82%) of children at time point 2. One child refused to bottle/breastfeed at time point 2 and one child was not offered a bottle/breastfeed due to aspiration risk from oro-pharyngeal dysphagia. Metrics were obtained from single swallow 0.3mL IDDSI 0 (thin fluid) boluses for 9/12 (75%) at time point 1 and 2/11 (18%) at time point 2. Metrics were obtained from 1mL IDDSI 4 (puree) boluses for 10/11 children (91%). One child refused. Data for all metrics are summarised in Table 5-12. Individual level data can be found in Appendix 13.

Table 5-12. HRIM metrics whole cohort median values

	Median		Minimum		Maximum		IQR	
	T1	T2	T1	T2	T1	T2	T1	T2
Pharyngeal contractile integral (mmHg.s.cm)								
IDDSI 0 consecutive	47.75	63.96	20.89	4.12	121.54	101.13	38.42, 93.55	42.98, 83.04
IDDSI 0 single	88.59		43.39		128.53		61.47, 130.16	
IDDSI 4		118.58		3.50		291.03		58.13, 147.83
Upper oesophageal sphincter relaxation time (s)								
IDDSI 0 consecutive	0.34	0.43*	0.17	0.34	0.56	0.70	.20, .46	.35, .56
IDDSI 0 single	0.30		0.22		0.49		.21, .40	
IDDSI 4		0.45		0.21		0.78		.29, .53
Upper oesophageal sphincter maximum admittance (mS)								
IDDSI 0 consecutive	1.29	1.33	0.65	0.82	2.24	1.77	1.17, 1.66	.98, 1.49
IDDSI 0 single	1.52		1.12		1.74		1.25, 1.76	
IDDSI 4		1.51		0.82		2.48		1.29, 1.91
Upper oesophageal sphincter integrated relaxation pressure (mmHg)								
IDDSI 0 consecutive	6.03	7.00	-4.23	-3.31	13.49	24.83	1.02, 8.97	1.40, 11.46
IDDSI 0 single	7.34		2.83		9.52		3.26, 11.68	
IDDSI 4		7.20		-4.01		23.74		3.14, 10.83
Distal contractile integral (mmHg.s.cm)								
IDDSI 0 consecutive	3.23	31.32	0.00	0.00	1095.64	610.32	.00, 107.41	1.24, 172.25
IDDSI 0 single	1.29		0.00		5.44		.00, 12.42	
IDDSI 4		18.12		0.00		502.68		.57, 99.26
Integrated relaxation pressure 4 seconds (mmHg)								
IDDSI 0 consecutive	6.59	24.40*	-3.49	7.50	17.11	33.50	2.58, 14.56	18.07, 27.06
IDDSI 0 single	14.76		5.25		28.12		6.41, 24.33	
IDDSI 4		18.70		3.04		68.66		8.15, 25.70

IDDSI = International Dysphagia Diet Standardisation Initiative. Consecutive = last swallow in consecutive feed. Single = median of 0.3mL single boluses.

Wilcoxon signed rank test, difference between time 1 and time 2 *p=<.05 (2-sided)

5.3.4.1 Pharyngeal contractile integral

There were no statistically significant differences in PhCI between IDDSI 0 continuous swallows at time 1 and 2 or between IDDSI 0 and IDDSI 4 consistencies (z = .42, p = .67, z = -1.18, p = .24). The PhCI was significantly higher in single swallows, compared to consecutive swallows (z = 2.31, p = .02).

5.3.4.2 Integrated relaxation pressure

There was no statistically significant difference in upper oesophageal sphincter IRP between time points (z = 1.23, p = .21) or consistency (z = .56, p = .58). Median values were lower, indicating greater relaxation, for single swallows compared to consecutive swallows, but this did not reach statistically significance (z = 1.78, p = .07).

One child presented with an IRP outside of the 5-95th percentile reported by Damrongmanee et al (2021), indicating potential obstruction of flow at the level of the upper oesophageal sphincter. This was evident on consecutive swallowing at time 2.

5.3.4.3 Upper oesophageal sphincter relaxation time

A statistically significant increase in UOS RT was seen at time 2 on consecutive IDDSI 0 swallows (z = 2.32, p = .02). Statistically significant differences were not observed between IDDSI 0 and 4 consistencies (z = -.53, p = .59) or single and consecutive swallows (z = 1.40, p = .16).

5.3.4.4 Upper oesophageal maximum admittance

There were no statistically significant differences in UOS max ad between time points (z = -.06, p = .95), bolus consistency (z = 1.33, p =.18) or single and consecutive swallows (z = -1.40, p = .16).

5.3.4.5 Distal contractile integral

Eight (out of 12) children presented with absent peristalsis (DCI < 100mmHg.s.cm) across all swallow types, consistencies and time points. Three children presented with a mixed presentation, with weak peristalsis (DCI 100-449 mmHg.s.cm) on consecutive swallows but absent peristalsis on single swallows. This was evident at time point 1 for two children and time point 2 for one child. One child had normal peristalsis on all trials except for single IDDSI 4 swallows at time point 2.

Median DCI fell into the absent peristalsis category for all swallow types, consistencies and time points. The DCI was statistically significantly lower for IDDSI 4 consistency, compared to IDDSI 0 (z= 2.10, p = .04) with an actual median difference of 22.67 mmHg. There was no statistically significant difference in DCI between time points (z = -.14, p = .89) or consecutive and single swallows (z = -.65, p = .51).

5.3.4.6 4 second integrated relaxation pressure

At time 1, 2/12 children had IRP4s values above the 25 mmHg cut-off value, indicating potentially obstructed flow through the LOS, evident only on single swallow boluses. At time 2, 5/11 children had high IRP4s. For 3/5, this was evident only on single swallows. For 1/5 it was evident on consecutive swallows only, for 1/5 on both swallow types. It should be noted that at time 2, single swallows were IDDSI 4 consistency, consecutive swallows were IDDSI 0. On consecutive swallowing, all but one child's IRP4s increased between time 1 and time 2.

Cohort median IRP4s were under the cut-off for all swallow types, consistencies and time points. Values were significantly higher for consecutive swallows, compared to single swallows (z = 2.29, p = .02) and at time 2 compared to time 1 (z = 2.55, p = .01). The median differences were both clinically relevant. Differences in consistency were not significant (z = -.70, p =.48).

5.3.5 Feeding outcome

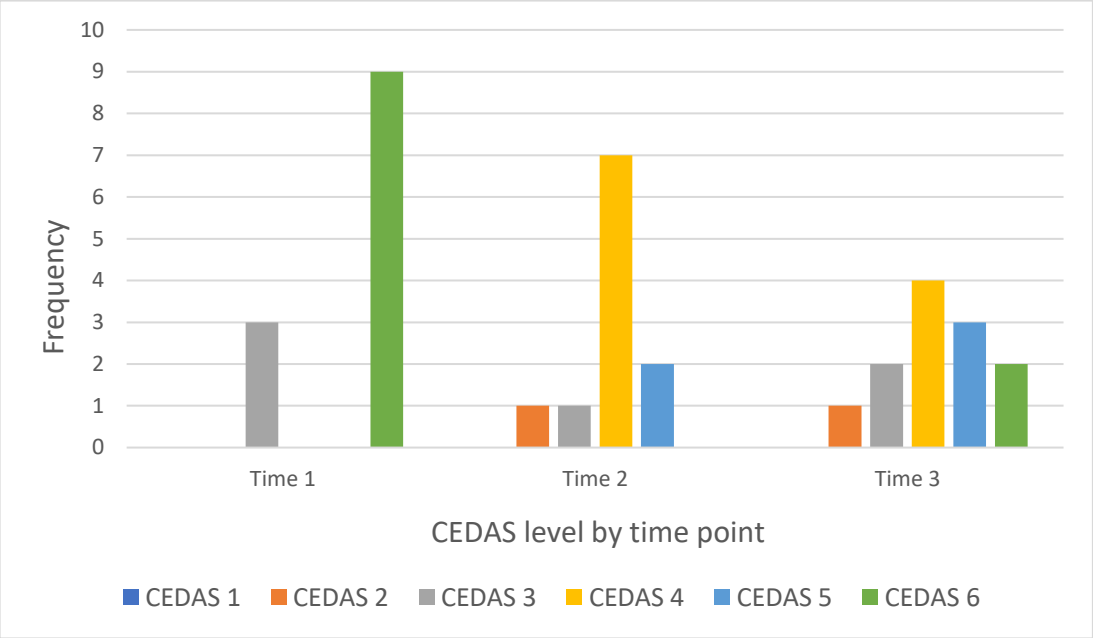
Only two parents completed the three-day food diary. Therefore, only information from telephone interviews was used to evaluate feeding outcome.

5.3.5.1 CEDAS

Median CEDAS scores were 6 (range 3-6) at time 1, 4 (range 2-5) at time 2 and 4 (range 2-6) at time 3. Frequency of CEDAS scores is presented in Figure 5-8. CEDAS levels reduced for all but one child between time points 1 and 2. This represents times pre- and post-introduction of solid/weaning foods. Between time 2 and 3, four children moved to a higher CEDAS level, five children remained at the same level and two children moved to a lower level. At time 3, 2/12 children had age-appropriate oral feeding (CEDAS 6), compared to 9/12 at time 1.

Four children required tube feeding, represented by CEDAS level 1-3. Two children were tube dependent for the duration of the study period. One child was tube fed only at time 1, one child only at time 3. All tube fed children received some oral intake alongside tube feeding at all time points.

Figure 5-8 CEDAS frequency by time point



CEDAS = Children's eating and drinking activity scale

5.3.6 Exploring causes of aspiration/penetration/residue

Table 5-13 shows individual level data for features of swallow impairment, biomechanical metrics and functional outcome. Outcomes or metrics indicative of dysfunction are coloured red. The overall picture is one of variation. No clear impairment pattern relates to functional outcome at 1 year of age. Every participant in this study exhibited swallow impairment at the oesophageal phase and 6/12 at the oral or pharyngeal phase.

Table 5-13. Summary of individual swallow impairment characteristics and functional feeding outcome.

	Symptom indicators of pharyngeal swallow dysfunction		Oral efficiency	Resp-swallow coord.	Pharynx contract	UOS function			LOS function	Motility status	Strictures	Outcome
ID	Aspiration/ Pene-tration	Post-swallow residue	SpS	Timing of airway closure	PhCI	UOS RT	Max ad	UOS IRP	IRP4s	DCI	Multiple strictures	One-year CEDAS
10	+	-	-	-	-	-	-	+	+	++	-	6
71	+	-	-	-	-	+	-	+	+	-	-	6
21^^	+	-		+	-	+	-	-	-	++	-	2
63^	+	-	+	+	-	+	-	-	-	++	+	4
18	+	+	-	-	-	-	-	-	-	+	-	5
19	-	-	-	-	+	-	-	+	-	+	-	5
25^	-	-	-	-					+	++	-	3
76	-	-	-	-	-	-	+	-	+	++	-	3
84^	-	-	-	+	-	-	-	-	-	++	+	5
11	-	-	+	+	-	-	-	-	-	++	-	4
12	-	-	-	+	-	-	-	-	-	++	-	4
26^	-	-	-	-	-	-	-	-	-	+	-	4

Assessment of IDDSI 0 at time 2, unless indicated. ^IDDSI 0 at time 1, ^^IDDSI 4 at time 2. Sps = sucks per swallow, PhCI = pharyngeal contractile integral, UOS RT = upper oesophageal sphincter relaxation time, Max ad = maximum admittance, UOS IRP = upper oesophageal sphincter integrated relaxation time, IRP4s = 4 second integrated relaxation pressure, DCI = distal contractile integral, CEDAS = children's eating and drinking activity scale, PAS = penetration-aspiration scale, BRS = bolus residue scale.

Impairment categorisation: Asp./pen.: + = PAS ≥3, - = PAS <3. Post-swallow residue: + = BRS >2 with residue volume >2, - = BRS 1-2. Oral efficiency: + =SpS = >3, - = SpS 1-3. Timing of airway closure, PhCI, UOS RT, Max ad: + = lowest quartile, UOS IRP, IRP4s: + = highest quartile. DCI: - = >450mmHg.cm.s (normal peristalsis), + = DCI 100-449mmHg.cm.s (weak peristalsis), ++ = DCI <100mmHg.cm.s (absent peristalsis). Multiple strictures: + = >2 strictures requiring dilatation in 1st year of life, - = 0-2 strictures requiring dilatation in 1st year of life.

In those with aspiration/penetration, no consistent pattern of biomechanical abnormality was identified. This suggests variability in the "cause" of aspiration. Three hypotheses are presented:

1. Incoordination of suck-swallow-breathe

Case 21 had prolonged time to airway closure and short UOS relaxation time, in the absence of prolonged total pharyngeal transit time, indicative of incoordination of respiration and swallow. Case 63 had high sucks per swallow with prolonged time to airway closure and short UOS relaxation time, indicative of inefficient sucking impacting on coordination of swallowing and respiration.

2. Upper oesophageal sphincter abnormality

Cases 10 and 71 presented with high UOS IRP, indicative of incomplete UOS relaxation, in the absence of any other low function oro-pharyngeal metric. This occurred in conjunction with high LOS IRP4s, indicative of incomplete LOS relaxation.

3. Undetected cause

Case 18 presented with no low function pharyngeal metrics compared to the cohort median but evidence of absent/weak oesophageal motility. This child was the only child with clinically significant post-swallow residue. Pharyngeal CI was close to the median, well above the 25th quartile, suggesting residue was not related to weak contractility.

5.4 Discussion

Study findings will be discussed in relation to the literature and their clinical implications considered. Results will be further synthesised with those of the other studies in Chapter 6.

5.4.1 Oro-pharyngeal dysphagia

Oro-pharyngeal dysphagia can be described as an impairment of swallow safety and/or efficiency which places an individual at risk of respiratory infection, suboptimal growth and weight gain, malnutrition and reduced quality of life (Arvedson 2006). Evidence from this study indicates that some degree of oro-pharyngeal impairment is a feature of dysphagia in approximately 40% of children under one year of age with early, primary repaired, type C OA/TOF.

5.4.1.1 Aspiration and laryngeal penetration

In the systematic review (Chapter 4), aspiration had a pooled prevalence of 0.24 (95% CI 0.18, 0.31) and penetration 0.06 (95% CI 0-0.13). Two children (16.6%) in this study presented with aspiration and three (25%) with penetration on VFSS. Aspiration and penetration events occurred more frequently on thin fluids than smooth puree.

Differences in reported prevalence may reflect differences in study methods. Most previous studies have high risk of selection bias, as only those with suspected aspiration risk are assessed using VFSS, thus over-estimating population prevalence of aspiration. Conversely, penetration is less easily identified from clinical report or observational assessment (Weir et al. 2009). It is less likely to provoke referral for instrumental assessment and would, therefore, be under-estimated in studies in which VFSS is conducted when clinical signs of impairment are identified. The use of VFSS in an unreferred population, some of whom were asymptomatic for oro-pharyngeal dysphagia, may therefore be more reflective of true population prevalence than previous studies. However, the small size of this study cohort prohibits firm conclusions to be drawn at a population level.

The pooled prevalence figure is based on children with all OA types. Two of the studies identified higher rates of aspiration for those with more complex subtypes (long gap or delayed primary repair) (Celtik et al. 2022, Soyer et al. 2022). The present study only included those with type C OA/TOF who

underwent primary repair. The lower frequency of aspiration may be a more accurate estimation of aspiration rates for this OA/TOF subtype.

However, of interest, one of the children for whom aspiration was identified was asymptomatic and would not have undergone VFSS evaluation based on clinical presentation. "Silent" (absence of a cough response) is widely acknowledged in children (Arvedson et al. 1994, Weir et al. 2011, Velayutham et al. 2018). However, it is not clear how commonly aspiration occurs in the absence of any other "red flags", such as non-specific respiratory events or suboptimal growth. To determine prevalence and significance of asymptomatic aspiration a larger study of symptomatic and asymptomatic children is required. While study of asymptomatic individuals is often precluded by ethical barriers, results from my study indicate inclusion of only symptomatic individuals may result in under-diagnosis of swallow impairment and aspiration risk.

Given the higher rate of penetration than previously reported, its clinical significance must be considered. Laryngeal penetration has previously been associated with an increased risk of aspiration (Friedman et al. 2000) and an increased risk of pneumonia (Gurberg et al. 2015). Intervention for laryngeal penetration, in the absence of aspiration on VFSS, has been associated with better feeding outcomes (Duncan et al. 2019). However, entry of contrast material above the level of the vocal cords is seen in healthy adult swallowing of thin liquids (Steele et al. 2019). No such data exist for children, due to ethical issues of conducting VFSS in those without known or suspected risk, raising questions as to whether laryngeal penetration is always associated with poorer outcomes, or whether a degree of laryngeal penetration is seen in healthy infant swallowing.

A recent paper by Miller and colleagues (2024), highlights that the depth and frequency of laryngeal penetration impacts on the likelihood that aspiration will occur. They identified that frequent penetration (>50% of swallows) resulted in aspiration later in the VFSS in 95% of cases. While laryngeal penetration to the level of the cords was more likely to lead to aspiration than

above cord penetration, in multiple regression analysis only frequency of events was statistically significant.

In the current study, depth of penetration was assessed using the PAS, and only penetration events reaching the vocal cords were determined as "abnormal" or higher risk. Frequency of events was not part of the analysis and would be important to include in future studies and in clinical practice to aid understanding of risk of laryngeal penetration and guide intervention.

5.4.1.2 Post-swallow residue

Residue was a low prevalence characteristic of oro-pharyngeal swallowing within the systematic review, with a pooled prevalence of 0.13 (95% CI 0.04, 0.21). Only one child in the current cohort presented with potentially clinically significant post-swallow residue supporting the assertion that difficulty with bolus clearance is not frequently present in children with OA/TOF. The findings contribute to understanding of bolus clearance by including a measure of residue volume, where previous studies have reported the presence/absence of residue and location only (Hormann et al. 2002, Yalcin et al. 2015, Coppens et al. 2016, Celtik et al. 2022, Soyer et al. 2022, Maybee et al. 2023). Possible causative mechanisms are considered in section 5.3.6.

5.4.1.3 Oral stage impairment

Oral stage impairment, defined as having more than 3 sucks per swallow, was evident in 25% of this cohort. As reported in the systematic review (Chapter 4), oral stage dysfunction has been previously reported in six studies using VFSS, generating a pooled prevalence of 0.11 (95% CI 0.02, 0.21) (Golonka et al. 2008, Yalcin et al. 2015, Coppens et al. 2016, Serel Arslan et al. 2017, Soyer et al. 2022, Maybee et al. 2023). A wide prevalence range (0-0.50) and the use of unvalidated, categorical rating scales in all previous studies make it difficult to ascertain whether oral stage difficulty is a true feature of swallow dysfunction in OA/TOF. The current study is the first to use a validated, quantitative measures of oral efficiency –

the number of sucks per swallow – for which a clinically relevant cut-off value exists (Miles et al. 2022).

Previous researchers have suggested that oro-motor dysfunction arises from delayed introduction to oral feeding (Serel Arslan et al. 2018, Soyer et al. 2022). Data regarding time to starting oral feeding were not collected in this study. However, all children underwent immediate, primary OA/TOF repair, and had established some oral feeding prior to recruitment and participation. It seems unlikely that the short delay between birth and commencing oral feeding post-surgery would be impacting sucking behaviour at 2-4 months of age.

Efficient sucking relies upon synchronicity of sucking with swallowing, respiration, and oesophageal clearance. Lau (2015) describes this process as a “nutritive sucking pathway” that allows for safe and efficient transport of milk from the oral cavity to the stomach. Sucking must be timed effectively with initiation of the central pattern generated movements of the pharyngeal swallow and a period of swallow apnoea during which the airway is closed to prevent bolus entry into the airway. While disruption of sucking patterns due to reduced coordination of respiration and swallow has been well-described, and may explain the inefficient suck behaviours identified in this population, Lau (2016) recognises the impact of reduced oesophageal bolus clearance on sucking behaviour has received far less attention than the influence of respiration. Given the evidence for poor motility and oesophageal clearance in this cohort, it may also be hypothesised that suck patterns are impacted by poor “downstream” clearance. While the inclusion of videofluoroscopy and HRIM in the current study has provided a unique opportunity to explore this phenomenon, inclusion of a larger dataset is required to confirm the hypothesis.

5.4.2 Exploration of biomechanical metrics

No single marker or pattern of impairment was identified to explain the presence of aspiration/penetration or post-swallow residue in this cohort. This is, perhaps, unsurprising given the complex neurophysiology of swallowing and its coordination with respiration. Recent research highlights the importance of the integration of all aspects of bolus acquisition, transport and swallow for functional feeding (Mayerl et al. 2020). Ferris et al. (2021) identify how swallow metrics are altered by bolus size and consistency, highlighting the important role that modulation of numerous aspects of swallow physiology plays in safe and efficient swallowing. These principles have been used to explore biomechanical swallow metrics as markers of dysfunction that are potentially causing aspiration/penetration or post-swallow residue.

5.4.2.1 Pharyngeal contractility

Pharyngeal contraction is a key component of pharyngeal swallowing during which pharyngeal constrictor muscles and the tongue generate sequential contractile forces behind the bolus to aid bolus transport through and clearance from the pharynx into the upper oesophagus (Willging et al. 2019). This was measured on HRIM using the PhCI metric. Cohort median PhCI was lower than that reported in other small studies of paediatric swallowing. Jadcherla et al. (2018) reported PhCI of 87 mmHg ± 11 in a group of healthy preterm infants during consecutive swallowing. This compares to 47.75 mmHg at time 1 and 63.96 mmHg at time 2 in the current study. However, low PhCI (as defined by being in the lowest quartile for this cohort) was not evident in any child with aspiration/penetration or post-swallow residue. Therefore, it is proposed that pharyngeal contractility was sufficient for the bolus size and consistency assessed and that abnormal pharyngeal contraction is not a feature of swallow dysfunction in this population. Alternative hypotheses were described in the results and will be discussed further in the following sections.

5.4.2.2 Incoordination of (suck)-swallow-breathe

Respiratory-swallow coordination relies upon prolonged expiration and shortened inspiration phases. Airway violation arises from an inability to modulate respiration, for example due to high resting respiratory rate, increased respiratory effort or reduced respiratory reserve, resulting in mistiming of airway closure in relation to bolus arrival in the pharynx (Mizuno et al. 2007, Lau 2015). Given the high rates of tracheomalacia observed in children with OA/TOF, respiratory compromise could feasibly be anticipated to impact on swallow coordination (Kovesi 2017, Porcaro et al. 2017). Previous research reported increased risk of dysphagia in children with tracheomalacia compared with those but did not attempt to explore this relationship further (Maybee et al. 2023).

Respiratory-swallow coordination was assessed using time to airway closure on videofluoroscopy, that is the time between arrival of the bolus at the proximal margin of the upper oesophageal sphincter and complete closure of the laryngeal vestibule (Miles et al. 2022). Two children with aspiration/penetration were found to have prolonged time to airway closure, indicating reduced coordination. The UOS relaxation time (RT) calculated on HRIM is a further swallow timing measure. Interestingly, both children additionally had short UOS RT, suggesting insufficient length of relaxation for the bolus size and consistency swallowed. UOS RT from HRIM was not reported in this age group in the literature reviewed as part of this thesis. While this metric has not been shown to be associated with aspiration risk in previous HRIM research conducted in adults (Omari et al. 2020), it may be of value in bottle fed infants, when sustained coordination of UOS relaxation with respiration is required, and may therefore be of greater importance to airway protection. This hypothesis requires further study with larger numbers of children.

5.4.2.3 Upper oesophageal sphincter abnormality

Two children presented with aspiration/penetration without evidence of suck-swallow-breathe incoordination. These children both presented with high

UOS integrated relaxation pressure (IRP), indicating incomplete sphincter relaxation. Damrongmanee and colleagues (2021) reported high IRP in 2/3 children with aspiration on VFSS, providing evidence to support the hypothesis that incomplete UOS relaxation is associated with aspiration risk.

Interestingly, the children in the current study also presented with high LOS IRP (IRP4s). In adults with achalasia, poor oesophageal relaxation (high IRP4s) correlated with high upper oesophageal relaxation pressures (Wauters et al. 2014, Baha et al. 2020). After treatment to improve lower oesophageal sphincter relaxation, upper sphincter pressures also reduced. It is proposed that high UOS pressures are compensating for poor oesophageal clearance, preventing retrograde movement of the bolus. The relationship between LOS and UOS has not been previously explored in OA/TOF or in children, in whom manometric evaluation has focussed either on the pharynx or oesophagus. The current study does not conclusively confirm a relationship between lower and upper oesophageal sphincter function but highlights an important area for future study of the mechanisms of pharyngeal dysphagia in this and other populations. Unlike other swallow assessments, HRIM provides an excellent method for evaluating swallow function from velum to stomach simultaneously and is therefore ideal for exploring this relationship further.

An alternative hypothesis is that high UOS IRP relates to anatomical differences. Laryngeal cleft is estimated to co-occur with OA/TOF in 3-19% of cases (Baxter et al. 2018, Londahl et al. 2018, Lejeune et al. 2021). Oro-pharyngeal dysphagia is common in children with laryngeal cleft but not all present with aspiration (Strychowsky et al. 2016). One child with high IRP was known to have an unrepaired cleft. It is possible that the raised IRP is signalling compensation of the UOS for altered anatomy. The relationship between UOS and laryngeal cleft has, as far as could be determined, not been previously examined. It presents an interesting topic of future research that may help to explain the variability seen in dysphagia presentation in those with laryngeal cleft.

5.4.2.4 Undetected cause

One child presented with laryngeal penetration and post-swallow residue on videofluoroscopy in the absence of any identified dysfunctional oro-pharyngeal metrics or known anatomical abnormality.

Although the current study provides a detailed exploration of swallow function, there were limitations to the HRIM analysis. One key metric not included is hypopharyngeal intrabolus pressure (hIBP). This measures pressure within a bolus as it passes through the pharyngo-oesophageal junction. Raised hIBP indicates that excess force has been exerted on the bolus as a result of insufficient distension, that is, insufficient upper oesophageal sphincter opening (Omari et al. 2022). However, this metric is measured on Swallow Gateway 1cm above the maximum height of the UOS. The average length of an adult pharynx is 13cm, compared to 3-4cm in a three month old child (Mittal 2011, Chuang et al. 2022). Thus, 1cm above the maximum height of the UOS in an infant is likely in the mid-pharynx, rather than the hypopharynx as in an adult. Adopting measurement of hIBP designed for adults, was found to give inaccurate measurement in this cohort and was not reported in the current study. The need to adapt some HRIM metrics to meet the specific needs of infants and children has been highlighted.

The inability to calculate hIBP within this study also prevented use of the swallow risk index (SRI). The SRI is a composite measure of swallow dysfunction which uses bolus presence time, intrabolus pressure, distension to contraction latency (a measure of timing of pharyngeal contraction in relation to bolus presence) and peak pharyngeal pressure to calculate a global measure of swallow dysfunction (Cheriyan et al. 2023). This measure highlights the integration, modulation and compensation of various aspects of swallow physiology in determining overall swallow safety and efficiency. Future study, which facilitates use of this measure in infant and paediatric research, may help identify alterations in swallow function that were not detected in the current study and add to our understanding of the interaction between different physiological elements.

5.4.2.5 The impact of age

Although a statistically significant increase in PAS scores was not identified, 2/12 (17%) of children presented with penetration at time 1 and none with aspiration, compared to 2/9 with penetration and 2/9 with aspiration (44%) at time 2. This potential increase in aspiration risk warrants exploration.

Infants were assessed at between 2-4 months of age and between 8-10 months of age during which physiological and anatomical development changes occur. Between approximately 3-6 months of age, sucking develops from being reflexive to volitional (Willging et al. 2019). Additionally, anatomical changes occur because of growth. This results in elongation of the pharynx, descent of the larynx and alterations to the angle of the oral-pharyngeal complex occurs as the tongue descends into the pharynx (Delaney et al. 2008). These anatomical changes create more space in the pharynx and reduce the protection afforded by high placement of the larynx (Delaney et al. 2008). This has the potential to increase difficulty with swallow-respiration coordination if underlying impairments, such as respiratory compromise, cannot be compensated for by changes in swallow function. It is hypothesised that these physiological and anatomical changes contribute to the increase in frequency of aspiration/penetration seen at time 2.

5.4.3 Oesophageal dysphagia

5.4.3.1 Oesophageal motility

In keeping with findings from previous research, all children were identified as having altered oesophageal motility on HRIM in this study (Comella et al. 2021). The predominant motility pattern was aperistalsis (66.6%) with the remaining children presenting with weak distal contractions. The proportion of reported motility patterns has varied in the literature to date. Data from the current study are congruent with Tong et al (2016) who reported aperistalsis in 5/8 (62.5%). Giorgio and colleagues (2011) report a slightly higher proportion, 7/9 (77.7%). Lower proportions of aperistalsis are reported by Lemoine et al (2013), 21/40 (52.5%), Rayyan et al (2022) 3/10 (30%) and

Courbette et al (2020), 4/16 (25%). Variation in reported proportions is likely in part related to small sample sizes in all studies.

The current study is the first to examine the impact of swallow type (consecutive or single) on peristalsis in children under 1 with OA. Inhibition of oesophageal peristalsis is expected during multiple swallowing, followed by augmented contraction (higher DCI compared to single swallows) at the end of repetitive swallowing (Yadlapati et al. 2021). Although there was no statistically significant difference in median DCI values, four children (25%) displayed improved motility patterns on consecutive swallows compared to single swallows.

Data to date have determined motility status from single swallows and have failed to accurately associate feeding presentation or symptoms with motility type (Comella et al. 2021). Findings in the current study indicate that differences in motility for texture and swallow type may further differentiate oesophageal motility. Future research should investigate if such differentiation improves correlation with symptoms and functional outcome. Further stratification of motility may help guide clinicians to provide more tailored support in the transition to solid food and the management of feeding difficulties. These findings also have relevance for the development of HRIM protocols for infants, which are currently lacking (Rosen et al. 2018). The presence of different patterns highlights the importance of including both food and drink and single and consecutive swallowing within a protocol.

5.4.3.2 Lower oesophageal sphincter function

According to the Chicago Classification, IRP4s is a measure of lower oesophageal sphincter relaxation. High IRP4s indicates incomplete relaxation and gastro-oesophago junction outflow obstruction (Yadlapati et al. 2021). A diagnostic threshold of ≥25 mmHg was applied in the current study.

Cohort median IRP4s did not reach the diagnostic threshold of ≥25 mmHg for incomplete lower oesophageal sphincter relaxation indicating that outflow

obstruction, unlike abnormal motility, is not universal in OA/TOF. However, there was considerable variation across bolus trials, with 7/12 children exhibiting above threshold IRP4s for at least one bolus type. No child consistently presented with above threshold IRP4s across single and consecutive swallows at both time points, although 2 presented with a consistent pattern at time 2. Possible explanations for this variability will be considered.

A recent study of 75 children with OA/TOF (median age 1.25 years, range 3 months – 17 years) identified no differences in IRP4s when compared with controls (n=80) (Tan Tanny et al. 2024). Mean IRP4s were within the normal range for IDDSI 0, 4 and 7 consistencies. In keeping with their findings, the current study also found no statistically significant difference between IDDSI 0 and 4 consistencies and median values were within the “normal” range. However, in addition to IRP4s they assessed LOS function using distension pressure during oesophageal emptying and bolus flow time. These novel metrics showed that there was evidence of obstructed flow at the oesophago-gastric junction. They, and others, argue that IRP4s is not a reliable measure of obstructed flow in isolation (Nikaki et al. 2016). They hypothesise that IRP4s is influenced by contact and intrabolus pressure. Lower oesophageal contractile vigor reduces bolus distension pressures, thereby reducing IRP4s. The higher IRP4s may be reflective of improved oesophageal contractility and bolus clearance. Thus, the variability across consistencies and consecutive/single swallows may be reflecting differences in the effectiveness of bolus clearance, rather than true differences in LOS relaxation. Tan Tanny et al (2024) suggest use of measures which combine manometric and impedance data to measure distension pressures and the related flow of the bolus through the oesophago-gastric junction to gain a more accurate diagnosis of true outflow obstruction. This may partly explain the inconsistent pattern of IRP4s values reported in the current study.

As well as varying with consistency and swallow type, IRP4s was significantly higher at time 2 than time 1. Repeated HRIM studies in term

infants under 1 year of age have not previously been reported. Might the difference in score demonstrate developmental progression?

It is acknowledged that lower oesophageal sphincter tone and control of relaxation are not fully developed at birth (Rolle et al. 2017). The lack of functional maturity is observed as easy vomiting and regurgitation in the first weeks after birth (Rosen et al. 2023). While sphincter tone is equal to that in adults by 3-6 weeks of age, control of relaxation is achieved between 6-12 months, at which point vomiting with feeding is almost entirely resolved (Rosen et al. 2023). The time points studied reflect a maturation period for the lower oesophageal sphincter. Thus, the increase in median IRP4s between time 1 and 2 may reflect typical development, rather than pathology.

Rayyan et al (2020) investigated development of oesophageal motility and lower oesophageal sphincter function in 10 preterm infants. Using HRIM, they assessed at weekly intervals between 34 and 37 weeks post-menstrual age. They identified an increase in IRP4s between time 1 and time 4 but hypothesise that this may not be related to maturing of vagal innervation and improved oesophageal propagation, but to the larger volume of oral intake at time 2. IRP4s is impacted by relaxation of the lower oesophageal sphincter but also by bolus distension of the lower oesophagus, which increases with larger volume, thereby increasing IRP4s.

The variability in IRP4s between swallow type and time, as well as the relationship between IRP4s and motility, highlight the challenge in using a single cut-off value to determine LOS obstruction that may benefit from intervention. As suggested by Tan Tanny et al. (2024), use of more accurate pressure-flow metrics across the LOS would be of benefit to understanding the prevalence and impact of oesophago-gastric outflow obstruction in this population.

5.4.4 Swallow characteristics and their association with feeding outcome

This study lacked power to statistically evaluate specific characteristics of swallow dysfunction with feeding outcome, however this relationship was explored using non-statistical methods. The “heatmap”, generated in section 5.3.6, highlights the variability of presentation, even within this relatively homogeneous cohort of term infants with type C OA/TOF. Previous studies have failed to explain symptoms or outcome using single “causes” of swallow impairment, such as oesophageal dysmotility (Tong et al. 2016, Courbette et al. 2020) or anastomotic stricture (Soyer et al. 2022). Evidence from the current study suggests that swallow impairment arises from oral stage dysfunction, pharyngeal dysfunction, oesophageal dysmotility and potentially gastro-oesophageal junction outflow obstruction but presentation is varied at an individual level. Thus, determining the specific contribution of one aspect, such as oesophageal dysmotility, is “muddied” by the presence of other aspects of swallow impairment. Overlapping symptomology for these different aspects of swallow make accurate differentiation difficult without thorough instrumental evaluation.

Variability may also be due to the choice of the CEDAS as an outcome tool. Although clinician rated, the CEDAS scores were assigned based on parent report of feeding, rather than direct observation. As demonstrated in Chapter 3, parent factors, such as anxiety and resilience, impact on the child’s feeding behaviour. While severity of the child’s feeding difficulty was shown to impact on parent anxiety, so too was parent anxiety shown to impact on feeding. As the CEDAS is based on what the child is doing functionally i.e. the type of foods that they are eating, it is dependent on the type of foods that they are offered. A more anxious parent is likely to give “easier” foods, which would result in a lower CEDAS score.

Functional outcome, such as the need for non-oral feeding is also determined by nutrition and growth parameters. The need for tube feeding, resulting in a lower CEDAS score, may be driven by insufficient oral feeding for growth, rather than concerns regarding swallow safety. This highlights the

interaction between parent and child factors on feeding outcome, and the multi-factorial determinants of feeding outcome which will be discussed further in Chapter 6.

5.4.5 Limitations

The main limitation to this study was the small number of children involved. Although this was designed as an exploratory study, recruited numbers were lower than planned. Recruitment from eligible participants was 85% and higher than anticipated. However, the number of eligible participants was lower than anticipated. Assessing the number of children who will be eligible is challenging in a rare disease, such as OA/TOF. Although the study involved those with the most common subtype, numbers do fluctuate year on year. Additionally, this study was due to commence in April 2020, at which point all research was paused due to the Covid-19 pandemic. This led to an 8-month delay in starting recruitment therefore reducing the time available for recruitment within the fellowship. It is not clear if the pandemic had any impact on the number of children born with OA/TOF or the distribution of cases across London hospitals. Efforts were made to increase numbers by setting up participant identification centres. However, ongoing impacts of the pandemic on research governance teams resulted in delays to obtaining site approvals which also limited the time available for recruiting.

The limited use of HRIM for pharyngeal assessment to date in this age group meant that there was no accepted way to select swallows from consecutive sucking. A decision was made to use a single swallow - the last in the suck burst - rather than the median value of multiple swallows, as was used to calculate metrics for single swallowed boluses. This allowed for concurrent evaluation of oesophageal and pharyngeal swallowing. Use of swallows earlier in the sequence result in inhibition of oesophageal peristalsis, potentially resulting in over-reporting of aperistalsis (Kahrilas et al. 2015). However, this is arguably at the expense of reliability.

During natural feeding, infants pause intermittently for catch up breathing. This results in more than one opportunity to select the last suck in a burst.

However, evidence from VFSS demonstrates that numerous aspects of swallowing change from the beginning of a feed to the end of the feed, including the number of sucks per swallow, timing of swallow onset and frequency of aspiration/penetration (McGrattan et al. 2020). The validity of selecting different swallows from different times within the feed to generate a median value for HRIM metrics is not known. Understanding how these metrics change during a feed and evaluating the validity of using a 'multiple swallows' approach to metric calculation are important areas for future research.

A further limitation arises from the lack of simultaneous VFSS and HRIM. Assessments were undertaken within a short timeframe of each other, thus mitigating for developmental changes. However, HRIM metrics have been used to hypothesise causes of aspiration/penetration where a child exhibits a *risk* of aspiration, as determined by performance on VFSS. Simultaneous assessment was not conducted due to the complex logistical arrangements required but would strengthen future studies of this nature.

5.4.6 Conclusions

This exploratory study has provided a rich data set which has given novel insights into swallow function in infants with type C OA/TOF, and to explore the use of pharyngeal HRIM. Results indicate that oro-pharyngeal dysphagia is not caused by ineffective pharyngeal contraction. There is evidence to support the hypothesis that coordination of the suck-swallow-breathe triad is impacted to the extent of causing increased aspiration risk in some children. There is early evidence to suggest reduced upper oesophageal sphincter relaxation, which is compensating for poor oesophageal clearance, may be contributing to aspiration risk in some children. This study confirms the presence of altered oesophageal motility in almost all children and indicates that lower oesophageal sphincter dysfunction may be causing additional issues with bolus obstruction for some children. This study highlights potential for quantitative analysis of VFSS and HRIM to describe biomechanical features of swallowing, elucidating underlying causes of dysphagia in OA/TOF .

Chapter 6. Synthesis

Integration of results from quantitative and qualitative studies is a key, distinguishing, feature of mixed methods methodology (Creswell et al. 2017). Data from different sources are first analysed individually, using processes appropriate to the methods used. These methods have been described and presented within each of the individual thesis chapters. The data from the quantitative and qualitative sources are then combined, contrasted and integrated to meet the overarching aim of the study (Creswell et al. 2017). Integration serves to offer insights or knowledge that cannot be generated when quantitative or qualitative data are analysed separately and can occur at multiple levels within a study (Moseholm et al. 2017). Within my thesis, integration at a *methods* level occurred when the results of the online forum (Chapter 2) were used to generate the questionnaire (Chapter 3). This type of integration is classified as *building*. This synthesis chapter will seek to *merge* findings from all four work packages to meet the overarching study aim:

- To characterise feeding and swallowing skills and difficulties in children with repaired OA/TOF.

Merging of data varies according to the core study design and is driven by the intent of integration. Within convergent study types, integration is intended to expand understanding, providing comprehensive, validated conclusions (Creswell et al. 2017). This is achieved by either comparing the data sets, or by transforming one of the data sets and conducting further analysis. Transformation may involve quantifying qualitative data or turning quantitative data into text descriptions (Fetters et al. 2013). Narrative or visual methods can be used to display the merged data (Creswell et al. 2017).

Within this thesis, data integration will be achieved by comparing the datasets, determining the ways in which results expand understanding of the

nature and prevalence of feeding difficulties in children with OA/TOF. This will be conducted using the “Paediatric Feeding Disorder” (PFD) framework (Table 1-3) and by revisiting, and revising, the dyadic model of feeding generated in section 2.3.9.

6.1 Characterising feeding in OA/TOF using the PFD framework

Results from each work package are summarised within the medical, feeding skill and psychosocial domains in Table 6-1, 6-2 and 6-3. Narrative synthesis identifies areas of congruence and discordance, to generate greater depth of understanding.

6.1.1 Medical domain

Data are congruent regarding the presence of cardiorespiratory compromise in some children with OA/TOF. Parents qualitatively identified events during feeding and mealtimes, including blue episodes and coughing. This is supported by quantitative evidence from validated questionnaires and instrumental assessment results from the systematic review and cohort study (evidence of aspiration). Evidence from the parent-reported questionnaire identified prevalence of swallow dysfunction of 67.7%. Evidence from the cohort study expands understanding by demonstrating that a smaller proportion of this swallow dysfunction results in aspiration due to oro-pharyngeal swallow dysfunction (16.7%).

Table 6-1. Comparison of study results by PFD Medical domain: Cardiorespiratory compromise during feeding or aspiration-related pneumonia

Work package 1.1 Online forum QUAL	Work package 1.2 Questionnaire QUAN	Work package 2 Systematic review QUAL+QUAN	Work package 3 Cohort study QUAN
<u>Parental description of:</u> • Blue episodes *"We had many many blue episodes"* • Gagging *"I hold my breath when he gags"* • Coughing/choking *"first choke on milk at 3 months old"*	<u>Pedi-EAT-10:</u> • 67.7% swallow dysfunction • 4.2% 'Severe problem' with coughing when eating • 5.4% 'Severe problem' Swallowing liquids takes extra effort • 9% 'Severe problem' Swallowing solids takes extra effort	<u>Pooled prevalence:</u> • Aspiration 0.24 (0.18, 0.31) • Coughing when eating 0.22 (0.13, 0.31) • No deficit 0.38 (0.28, 0.48)	<u>Videofluoroscopy:</u> • 2/12 (16.7%) aspiration • 3/12 (25%) laryngeal penetration • HRIM: • 12/12 (100%) Oesophageal dysmotility

QUAL = qualitative, QUAN = quantitative, HRIM = High-resolution impedance manometry.

6.1.2 Feeding skill domain

As evidenced in Table 6-2, congruence exists between qualitative and quantitative results with regard to the need for texture modification. Qualitatively, parents reported that their children were not reaching feeding milestones at the expected ages, resulting in them needing to modify the foods offered. This is reflected in evidence from the cohort study, in which only 2/12 infants were eating age-appropriate foods without modification or use of additional strategies at one year of age. Evidence from the systematic review expands knowledge of the frequency with which specific strategies are adopted, with approximately 50% of those with OA/TOF using a strategy or modification to support feeding, eating and drinking, most commonly using water to aid transit of food. It should be noted that these prevalence figures are from studies including children and adults. Nonetheless, results signal which strategies may be most effective to establish in children to limit the impact of swallow dysfunction.

Table 6-2 Comparison of study results by PFD Feeding skill domain: Need for texture/positioning/strategies modification

Work package 1.1 Online forum QUAL	Work package 1.2 Questionnaire QUAN	Work package 2 Systematic review QUAL+QUAN	Work package 3 Cohort study QUAN
Parental description of: • Not managing age-appropriate foods *"I feel like I'm not moving on…"* • Drinking water *"…often drinks continuously whilst eating."* • Small volumes *"Little bites small meals"* • Modifying texture *"…add water to food to loosen things up."*	MCHFS: • 41% mealtimes over 30 minutes	Pooled prevalence: • Need for water when eating 0.49 (0.42, 0.57) • Eating slowly 0.37 (0.28, 0.46) • Texture modification 0.28 (0.18, 0.38)	1-year CEDAS: • 10/12 (not managing age- appropriate foods)

QUAL = qualitative, QUAN = quantitative, CEDAS = Children's eating and drinking activity scale.

6.1.3 Psychosocial domain

Table 6-3 summarises the results of this thesis that concern the psychosocial domain of the PFD framework. Qualitative descriptions of psychosocial impact provided by parents and results from quantitative evaluation using validated measures support the assertion that psychosocial aspects of eating and drinking are impacted in OA/TOF. Qualitatively, parents described feelings of anxiety when feeding their children. Quantitative data determined that approximately one third of parents have moderate-severe anxiety and that having a child with severe feeding difficulties was associated with higher levels of anxiety in multivariable regression analysis. Some parents described feeding as a traumatic experience. Quantitative data identified that just over a third of parents met the criteria for post-traumatic stress disorder, when feeding difficulties were the trigger. Pooled prevalence from the systematic review also indicated that higher anxiety was evident in approximately one third of parents. These congruent data add validity and confidence to the assertion that feeding-related anxiety and trauma exist for around one in three parents. It should be noted that these figures are derived predominantly from mothers.

Isolation associated with feeding difficulties was described in qualitative data. One aspect that resulted in feelings of isolation was concern for, and from, others caring for their child because of feeding difficulties. Quantitative evidence was congruent with this phenomenon with, again, around one third of parents reporting that finding others to help care for their child was challenging. Avoidance of social occasions involving eating and drinking was also described by parents qualitatively. Quantitatively, 50% of parents reported this was ‘no problem’ and 4.2% reported this was a ‘severe problem’. Integrating these findings indicates that occasions such as eating out in restaurants or at family events are problematic, but parents employ strategies so that such activity can still be undertaken, remaining only a severe problem for a small proportion.

Food selectivity, “disruptive” mealtime behaviour and food aversion are also components of the psychosocial domain. There is some discordance

between results from qualitative and quantitative studies regarding this being a feature of feeding difficulties for children with OA/TOF. Food refusal was one of the clinical presentations identified by parents, but was not identified as a "theme", (i.e. was not a primary feature of mealtimes for many parents). Food selectivity was reported as specific food avoidance to prevent food sticking, rather than sensory difficulties, aversion, or rigidity. Quantitative results from the questionnaire and systematic review work packages indicate, however, that food refusal and challenging behaviour are a feature of mealtimes for 25-33% of children. This discordance may reflect the extent to which parents see this as challenging. Although on the MCHFS 38% of responses met the criteria for "feeding difficulty" when asked about their child's mealtime behaviour, only 6% rated it at the two highest points on the Likert scale. Likewise, 4.2% rated "My child does not like to eat" as a severe problem on the Pedi-EAT-10. Thus, it may only be a key feature of feeding for a small number, hence it was not identified in the qualitative themes. Indeed, several parents reported qualitatively that they were proud of their child's positive attitude towards eating, despite their challenges with swallowing.

Parental use of maladaptive strategies to mitigate for feeding difficulties, such as forcing their child to eat or excessive need for distraction at mealtimes, is also a feature of the psychosocial domain of PFD. Discordance exists for this element. These features were not reported within the qualitative data but were evident in the questionnaire study with 17% reporting use of force and 29% distraction to such a degree as to be deemed "problematic". This discordance may have arisen because of the open forum in which parents participated in the qualitative data collection – responses were visible on the Facebook group to all. If parents perceived the use of force or distraction as negative, they may not have felt able to share these experiences. Alternatively, it may be reflective of the way in which the questions were asked.

Table 6-3 Comparison of study results by PFD Psychosocial domain: Feeding aversion, stress and distress, disruptive behaviour, food selectivity, use of inappropriate strategies

Work package 1.1 **Online forum** **QUAL**	**Work package 1.2** **Questionnaire** **QUAN**	**Work package 2** **Systematic review** **QUAL+QUAN**
<u>Parental description of:</u> • Anxiety *"I'm always scared"* • Trauma *"The most horrifying moment of my entire life"* • Isolation *"I felt completely on my own"*	<u>Pedi-EAT-10:</u> • 4.2% 'severe problem' going out for meals • 4.2% 'severe problem' swallowing is stressful • 6% 'severe problem' child does not want to eat <u>MCHFS</u>: • 32% mealtimes are difficult • 58% worried about child's eating • 31% food refusal • 29% require distraction • 17% use force feeding • 19% negative impact on parent-child relationship • 40% negative impact on family relationships <u>FS-IS:</u> • 74.1% >95th centile	<u>Pooled prevalence:</u> • Increased parental anxiety 0.34 (0.13, 0.56) • Challenging mealtime behavior 0.25 (0.19, 0.31) <u>QUAL themes:</u> • Fear and trauma associated with eating *"It was terrifying"* • Isolation and a lack of support

	• 30.2% ‘almost always’ scared to leave child • 22.4% ‘almost always’ others scared to care for child • 33.3% ‘almost always’ worry about not doing enough to help <u>GAD-7:</u> • 34.7% parents have moderate/severe anxiety <u>PTSD-8:</u> • 38.1% met criteria for feeding-triggered PTSD	*“The hard thing was the sole responsibility”*

QUAL = qualitative, QUAN = quantitative, MCHFS = Montreal Children’s Hospital feeding scale, FS-IS = Feeding/swallowing impact survey, GAD-7 = Generalised anxiety scale, PTSD-8 = Post-traumatic stress disorder scale.

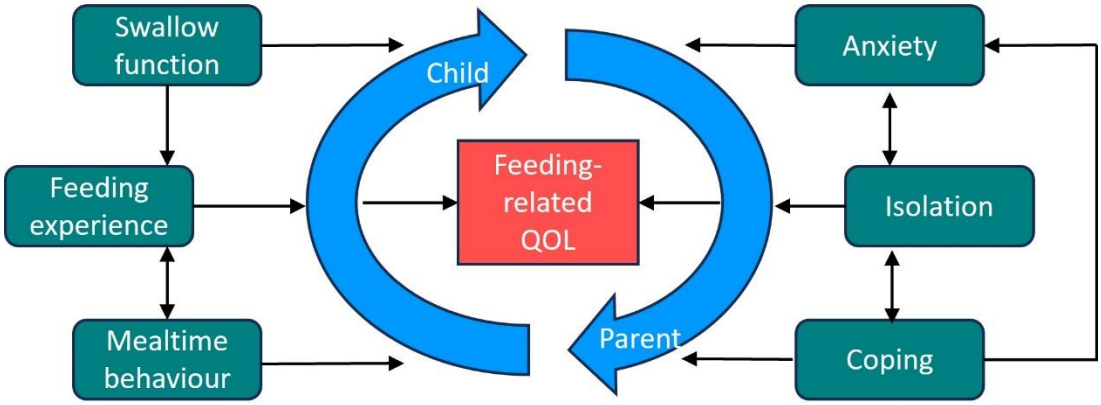
Use of both qualitative and quantitative methods in this study has allowed for a more complete picture of feeding and swallowing difficulties in OA/TOF to be generated. For the majority, swallow dysfunction arising from oesophageal abnormality with or without additional oro-pharyngeal impairment drives the use of adaptive mealtime strategies and modifications, evident in the feeding skill domain. Swallow abnormalities can result in unpredictable coughing, “choking”, bolus obstruction and blue episodes. These can cause parental anxiety and trauma. For a smaller number, food refusal and aversion exist alongside swallow dysfunction. Some parents adopt maladaptive mealtime strategies, such as force or excessive distraction. The degree to which these strategies exacerbate food refusal and aversion remains uncertain.

Although the framework acknowledges that impairment in one domain can impact another, it does not afford the opportunity to recognise how this occurs. By revisiting the dyadic model of feeding generated in Chapter 2, it is hoped that some of these relationships will be illuminated, generating further insight.

6.2 Characterisation using the model of OA/TOF feeding

The model of OA/TOF feeding generated using the qualitative data (parent experiences) is presented in Figure 6-1. The model highlights the dyadic nature of feeding, explicitly representing three child and three parent factors that potentially impact on feeding outcome. These components will be discussed in turn, referencing the additional data generated within this thesis and revisions proposed.

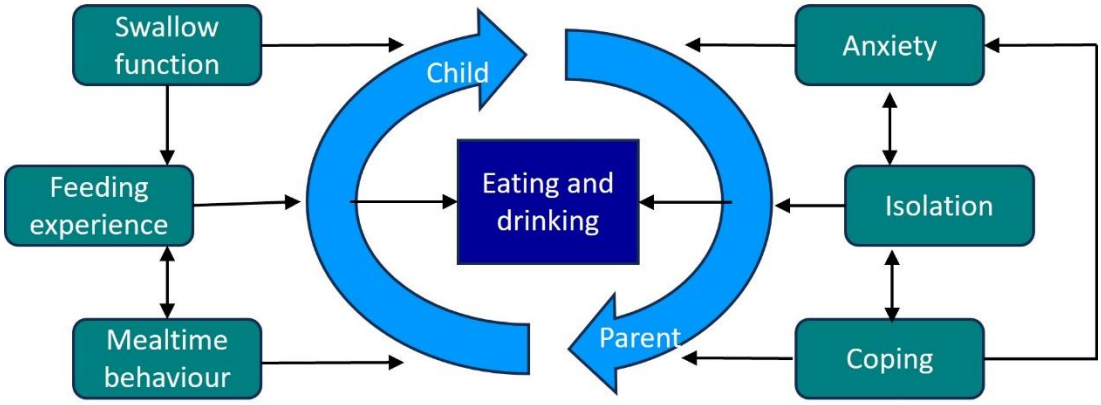
Figure 6-1. Feeding model proposed from online forum data



6.2.1 Feeding-related QOL

Within the initial model the overall outcome, the central box within the model, was named “feeding-related QOL”. On reflection, this is a restrictive term, focusing on one element – that of QOL. While clearly of central importance to outcome, using this term fails to capture all aspects of the mealtime experience for both child and parent. Thus, the term “eating and drinking” is proposed. This encapsulates all aspects: swallowing, mealtimes and psychosocial impacts and is of relevance to both the child and the parent. Additionally, it does not use the term “feeding”. Feeding is often associated with bottle or breast- “feeding” and is not usually used when talking about eating food or drinking from a cup. However, when an infant is bottle- or breast-feeding, “drinking” is still an appropriate term. Therefore, the model describes the factors influencing eating and drinking outcome in those born with OA/TOF.

Figure 6-2. Model updated to reflect change to overall outcome.

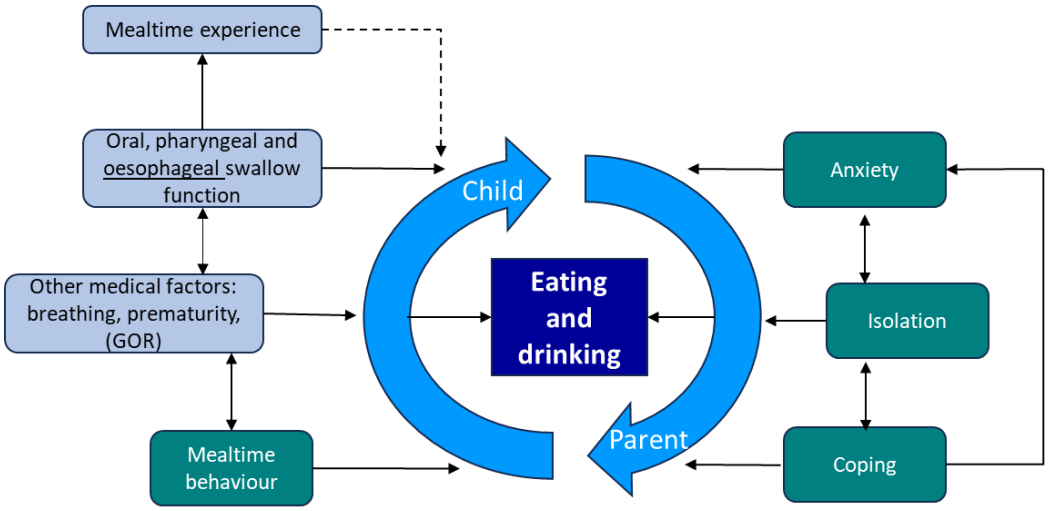


6.2.2 Swallow function

Within the initial model, swallow function encapsulated any medical condition that had the potential to impact on swallow function, including oro-pharyngeal swallow function, oesophageal function, gastro-oesophageal reflux and tracheomalacia. Evidence from work package three (cohort study) supports the inclusion of swallow function as a determinant of eating and drinking outcome. Oral, pharyngeal, and oesophageal swallow function were all shown to be impacted. No single pattern of impairment was associated with better or worse outcome. Hence in the revised model, swallow function is explicitly stated as “oral, pharyngeal and oesophageal swallow function”. The oesophageal phase is emphasised as this was impaired for all children in work package three (cohort study).

Other medical factors are now represented by a separate box in the updated model (Figure 6-3). Evidence from the multivariable regression analysis in work package one (questionnaire) indicated that breathing and prematurity were both independently associated with eating and drinking outcome. Evidence from work package three (cohort study) indicated that breathing difficulties may directly impact swallow coordination. Additionally, aspiration, which can have an impact on respiration, is a feature of oro-pharyngeal dysphagia in some children. Thus, the relationship between other medical factors and swallow function is bidirectional, graphically acknowledged within the model. Gastro-oesophageal reflux (GOR) is included but in parentheses to indicate a degree of uncertainty. Evidence from work package one did not indicate that GOR independently affected eating and drinking. However, the method used to assess GOR was unvalidated and therefore cannot be determined as reliable. Additionally, there is evidence from the literature to indicate that absent oesophageal motility is associated with more severe GOR but the impact on eating and drinking is uncertain. Understanding how and to what extent GOR impacts eating and drinking outcome is an important area for future study.

Figure 6-3. Model updated to reflect change to swallow function, medical factors and feeding experience.



6.2.3 Feeding experience

Within the initial model feeding experience related to any potentially negative experience the child had at mealtimes, such as coughing, gagging, periods of tube feeding and delayed introduction to oral feeding. Although these factors were described by parents in the qualitative study, there was no evidence from any of the quantitative studies to indicate that these factors determined eating and drinking outcome, beyond the presence of the swallow impairment itself. For example, delayed introduction to oral feeding because of long-gap OA and delayed repair was not a significant predictor of eating and drinking outcome in work package one (questionnaire). On the strength of the descriptions from parents the influence of swallow impairment on the feeding experience has been retained in the model but renamed as “mealtime experience” to better represent children of all ages (Figure 6-3). A solid line from the “swallow function” box highlights that these experiences arise from altered swallow physiology and a dotted line to the “child” supports their role as an antecedent factor impacting eating and drinking outcome.

6.2.4 Mealtime behaviours

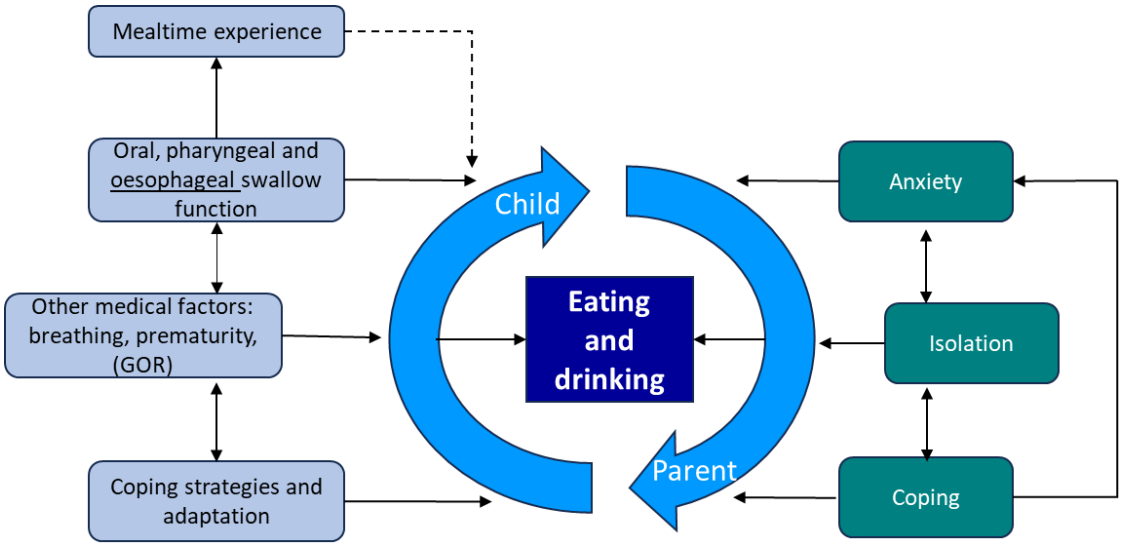
The mealtime behaviours component, which included factors such as food refusal, prolonged mealtimes, “challenging” behaviour, has also been removed from the model. Evidence from this study indicated that these should be determined as components of eating and drinking outcome i.e. are

behaviours that arise from swallow dysfunction in this population, rather than being factors that independently affect eating and drinking outcome. In the revised model such factors are viewed as part of the overall, central phenomenon of eating and drinking (the central box). Additionally, it is acknowledged that parent factors can influence these behaviours, for example by use of maladaptive strategies, and therefore they should not be represented as a “child” factor.

6.2.5 Coping strategies and adaptations

The component of coping strategies and adaptations is a new addition to the model (Figure 6-4). Evidence from work package two (systematic review) highlighted how mealtime adaptations are frequently employed by those with OA/TOF. Qualitative data also support this assertion, with parents describing how their child learned how to deal with the limitations imposed by altered swallow function, ultimately learning adaptive strategies, such as having frequent sips of water while eating, which impact positively on eating and drinking outcome.

Figure 6-4. Model updated to reflect inclusion of coping strategies.

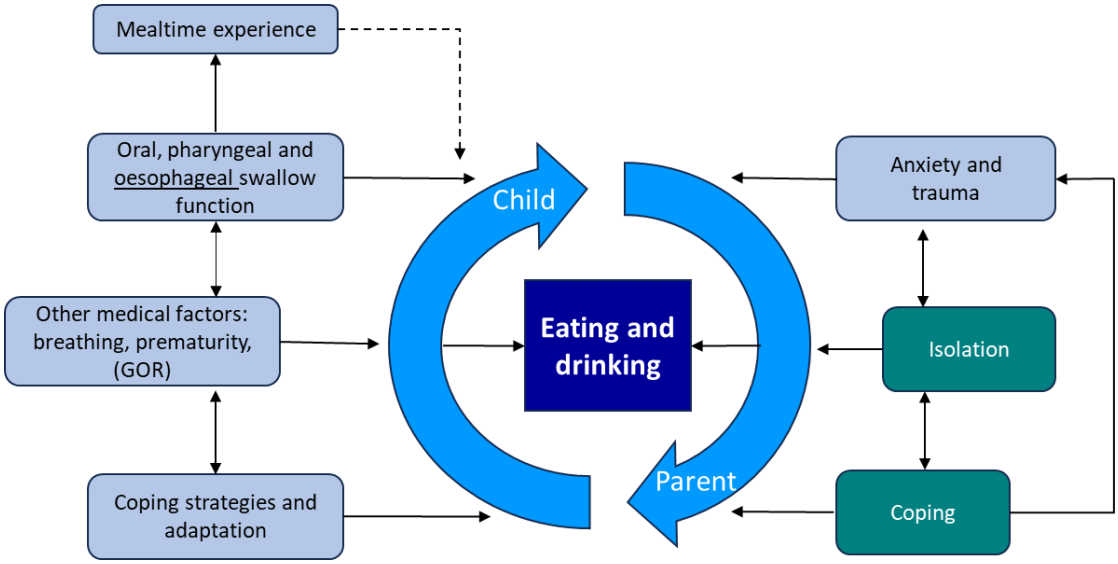


6.2.6 Parent anxiety

Multivariable regression conducted in work package one (questionnaire) identified parental anxiety as an independent predictor of feeding difficulties, supporting inclusion within the model. Evidence from work package three

(systematic review) also supports the assertion that a proportion of parents experience increased mealtime anxiety. Post-traumatic stress disorder was not included as an independent variable within the initial model due to its close correlation with anxiety. However, as feeding-triggered PTSD was identified in 38% of participants in this study it was felt to be an important factor to explicitly express within the model. Therefore, the "anxiety" component has been changed to "anxiety and trauma" (Figure 6-5). The bidirectional nature of the anxiety-eating and drinking relationship is captured by the two large circular arrows.

Figure 6-5. Model updated to reflect change to anxiety

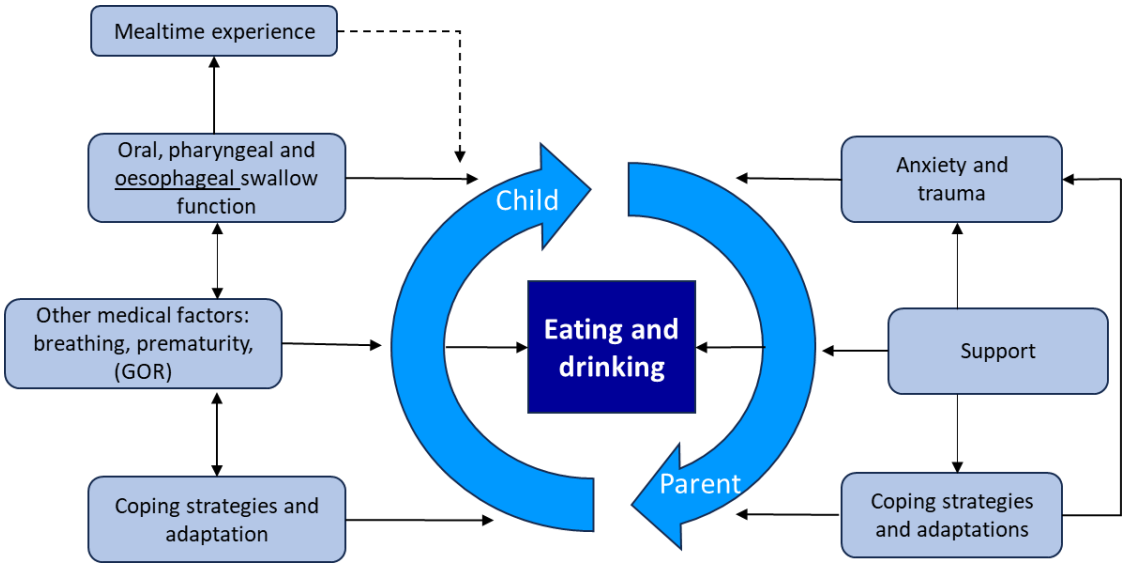


6.2.7 Isolation

The impact of isolation was evaluated in work package one (questionnaire) through assessment of parent perceived professional support. A perception of better support was an independent predictor of better feeding-related QOL and lower parental anxiety, supporting inclusion within the model. As shown in Figure 6-6, this has been renamed "support" as its absence underlies feelings of isolation, and is a potentially modifiable concept, and thus important for intervention. A uni-directional arrow is included from "support" to "anxiety and trauma" and "coping" to acknowledge the mediating role support can play in the development of anxiety and coping strategies. It should be noted that within the qualitative data parents described the importance of support from professionals but also friends and family, and the

feelings of isolation when this support was not present. Support outside of that from professionals was not included in work package one (questionnaire), and as such is highlighted as an important area for future research. Support encompassing all types of professional and social support is retained in the model due to findings from the qualitative data.

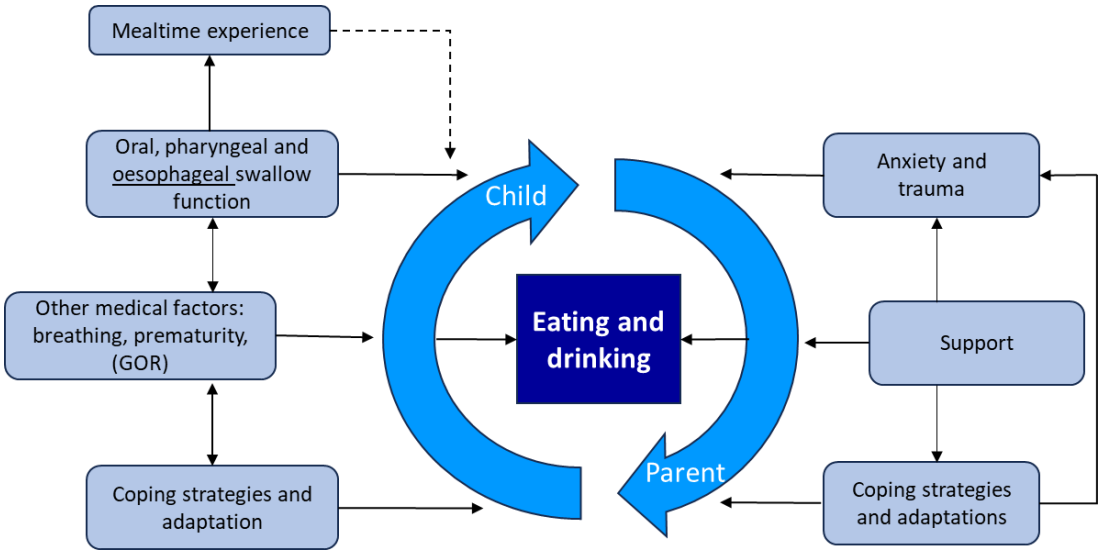
Figure 6-6. Model updated to reflect inclusion of support.



6.2.8 Coping

The "coping" component has been renamed "coping strategies and adaptations" to mirror this concept in the child part of the model, as depicted in Figure 6-7. In work package one (questionnaire) the role of coping was assessed using the concept of resilience – how easily one can "bounce back". Greater resilience was correlated with better feeding-related QOL but not with the presence of feeding difficulties per se. Being better able to bounce back from difficult situations mitigated some of the *impact* of the child's feeding and swallowing difficulties on QOL. Likewise, resilience mitigated parental anxiety and PTSD in multivariable regression – represented by a unidirectional arrow from "coping strategies and adaptation" to "anxiety and trauma". The role that having good support plays in the development of coping abilities was not expressly evaluated quantitatively but was identified qualitatively. A unidirectional arrow from "support" to "coping strategies and adaptation" reflects this finding in the model.

Figure 6-7. Final model depicting factors associated with eating and drinking outcome in oesophageal atresia/tracheo-oesophageal fistula.



6.2.9 Summary of the eating and drinking in OA/TOF model

This model (Figure 6-7) illustrates how multi-dimensional factors combine and interact to determine eating and drinking outcome in children with OA/TOF. It highlights the importance of viewing eating and drinking as a dyadic phenomenon, with parent and child factors influencing each other and overall outcome. It incorporates the concept of eating and drinking-related QOL as an important component of outcome, alongside those of safe and efficient eating and drinking for nutritional adequacy. The clinical implications are discussed in the following section.

6.3 The impact of COVID-19

This PhD commenced in 2019 and was therefore significantly impacted by the pandemic. Delays to recruitment and the approvals process, particularly research and development site approval, have already been discussed. The potential impact on families with regard to their experience of accessing healthcare, social support and the additional worry that living through a pandemic with a vulnerable child has also been discussed, with a further paper written with evidence generated in the online forum (Appendix 4). This may have influenced results by increasing participant anxiety, resulting in greater impact of, or to, feeding difficulties. The impact will likely never be

truly understood but the context of conducting this research during a pandemic is acknowledged as a potential limitation of the findings.

Completing this PhD during the pandemic period also impacted me, with additional childcare responsibilities (including home-schooling!) which generated time pressures, particularly during year two. I formally paused my studies and returned to clinical work April to June 2020 and extended my fellowship by three months as a result. In addition to the clinical work, I was involved in producing workforce guidance with the RCSLT. While valuable experience, it did create an additional workload.

6.4 Clinical implications

6.4.1 Multi-disciplinary assessment is essential

There are numerous international consensus guidelines written to guide the care of children with OA/TOF, written from the perspective of Gastroenterology, Respiratory and Surgical care (Krishnan et al. 2016, Dingemann et al. 2020, Koumbourlis et al. 2020, Dingemann et al. 2021). All have relevance to, but are not designed to capture aspects of, feeding and swallowing. The patient support group TOFS recently published a position statement urging review of service provision to ensure specialist, multi-disciplinary care is available to all (Slater et al. 2021). Evidence from work package 1 (questionnaire), highlighted inequity in access to different professionals in the UK, with access to gastroenterology and psychology support particularly limited. Findings in this thesis provide further evidence for the multi-dimensional nature and prevalence of eating and drinking difficulties in this population and thus strengthen the argument for multi-disciplinary care.

6.4.2 Addressing parental anxiety and trauma

Evidence from this study underlines how parental anxiety and trauma can develop from early feeding experiences and should form an essential part of the feeding/swallowing assessment. Early supportive care, ensuring the first experiences of feeding are positive and that support is available for all during

the critical phases of weaning onto family foods, may be of benefit in the prevention of severe anxiety and post-traumatic stress disorder. Recent evidence from a pilot study using a Family Integrated Care model, in which parents are supported to be optimally involved in their child's care throughout their hospital admission, has been shown to reduce parental anxiety in a cohort of medically complex infants, including those with OA/TOF (Ansari et al. 2023). Empowering parents, giving them confidence to develop coping strategies and adaptations has the potential to address the challenges of isolation and anxiety identified in this thesis. The frequency with which anxiety and PTSD were identified supports routine screening of parent mental health, so that appropriate care, including onward referral or signposting, is provided. Work in this thesis underlines the bidirectional nature of anxiety and feeding difficulties in this population. Professionals involved in supporting the child should consider whether intervention should specifically target parent anxiety, trauma, and isolation to optimise the child's eating and drinking.

6.4.3 Routine evaluation of oro-pharyngeal dysphagia in children with OA/TOF

Work in this thesis highlighted the presence of asymptomatic, "silent" aspiration and laryngeal penetration in a small number of children. This finding would only be identified on direct visualisation of the swallow using instrumental methods, such as videofluoroscopy or fibreoptic evaluation of swallowing (Arvedson 2008). There is, therefore, an argument for routine pharyngeal assessment in all children with OA/TOF in a bid to prevent future respiratory damage resulting from chronic aspiration. However, this risks over-diagnosis and unnecessary intervention. Coon et al (2016) highlighted negative outcomes for treatment of dysphagia in some infants suggestive of over-diagnosis. Yet, bronchiectasis and chronic cough are reported in OA/TOF and are more common in those with abnormal findings on VFSS (DeBoer et al. 2016, Maybee et al. 2023). Larger studies, with longer follow-up periods, would aid risk stratification and identify those who may benefit from intervention. Evidence from this study, however, currently supports

having a low threshold for instrumental oro-pharyngeal swallow evaluation in the presence of any respiratory or feeding “red flags”.

6.4.4 Use of pharyngeal HRIM in the assessment of swallowing in OA/TOF

Pharyngeal HRIM has advantages over more widely used instrumental approaches to swallow evaluation in children. It is non-radiological, allows for prolonged assessment of a complete feed, the child can be fed in their natural feeding position by a parent, and it does not require use of contrast material. While further study of the use of direct breastfeeding is required for use of impedance, manometric evaluation can be successfully achieved in breastfed infants. Perhaps most important is the role that HRIM plays in understanding the function of the upper oesophageal sphincter. Recent advances in VFSS analysis have provided a method for quantitatively calculating opening of the UOS, which may identify limited opening (Miles et al. 2022). However, reduced opening can be due to inadequate relaxation of the crico-pharyngeus, poor distensibility, or weak pharyngeal contraction resulting in inadequate hyolaryngeal traction (Jacob et al. 1989). Pharyngeal HRIM provides unique information differentiating relaxation, opening and contractility which aids diagnosis and informs intervention planning (Omari et al. 2023).

Evidence from this thesis indicates that oro-pharyngeal dysphagia in this cohort of children was not caused by weak pharyngeal contractility. There was indication of potential upper oesophageal sphincter abnormality, which warrants further use of HRIM in a research context to determine whether this is a feature of swallowing in larger numbers and to establish clinical relevance, to ultimately guide intervention.

6.5 Future research

Gaps in the research and further questions that have arisen from the work undertaken within this PhD have been highlighted throughout the thesis. The following section describes key research priorities.

1. Developing use of HRIM

Work conducted as part of this PhD has contributed to evidence demonstrating that HRIM is feasible in a paediatric population. It also serves to demonstrate how it could be used, in conjunction with existing measures, to determine the mechanisms that underlie a presentation of dysphagia. Understanding this brings potential to develop impairment phenotypes and determine how different components of swallowing interact, compensate, and modulate in functional and dysfunctional swallowing. Thus, interventions that are specific to the underlying mechanism, could be developed that target (re)habilitation of the swallow itself. This would be a significant step forward in the treatment of swallow dysfunction, which at present relies largely on compensatory strategies (such as texture modification, positioning changes or non-oral feeding methods). However, there are currently several barriers to its use, particularly in children.

A recent systematic review highlighted the variety of catheter type, bolus size, manufacturer and analysis software used in the literature to date and emphasised the importance of standardising protocols to obtain valid, reliable, and comparable data (Walters et al. 2024). To date, no agreed protocol exists for conducting oesophageal or pharyngeal HRIM in children who are too young to accept the volumes prescribed for adults. Evidence from this thesis indicates that for children under 1 year of age, data from breast- or bottle-feeding or spoon feeding are more consistently obtained than syringed single bolus swallows. It also highlights the need for paediatric specific analysis tools, to allow for a wider range of swallow metrics to be accurately obtained. Developing an international network of professionals and experts by experience to develop a protocol and analysis methods specific to the needs of children would increase the yield from future studies by facilitating comparison of data and meta-analyses.

Development of an international network could also have a broader shared goal of moving forward use of HRIM as a clinical tool. Acquiring normative data with which to compare and interpret data from clinical populations would

be highly beneficial. However, achieving this is challenging due to ethical barriers associated with catheter insertion in healthy children. Therefore, sustained expert conversation and consensus is likely to be the best way to develop further understanding of the interpretation of HRIM metrics, their relevance to function, potential phenotyping of swallow impairment and subsequent intervention development.

2. Developing family interventions for eating and drinking difficulties in OA/TOF

Evidence reported in this thesis provides a theoretical model to explain the multi-faceted nature of eating and drinking difficulties experience by those with OA/TOF, including the psychosocial impact on them and their families. This can be used as the foundation for the evaluation of existing treatments and the development of novel interventions aimed at improving eating and drinking. One such treatment strategy has recently been described by Tollne and colleagues (Tollne et al. 2024, Tollne et al. 2024). This team utilise an innovative process for sham feeding a child with long-gap OA at home, while they await surgical repair. The intervention addresses both child and parent factors, by enabling development of oral and pharyngeal swallowing skills, and responsive feeding through adapted feeding techniques. This process facilitates discharge home, as opposed to awaiting surgery in a hospital environment. Qualitative study shows parents are empowered by the intervention, which reduces anxiety around feeding, promotes feelings of being well-supported and supports parents to continue to adapt feeding to meet the needs of their individual circumstances (Tollne et al. 2024). This intervention is only suitable for those with delayed repair/long gap OA.

The model presented in this thesis can be used as a foundation for the development of other interventions that similarly aim to address multiple aspects of eating and drinking and provides a framework for outcome measurement. One area of need identified is targeted support for moving children from a liquid diet onto family foods. An intervention co-designed with parents, integrating knowledge of swallow (dys)function with effective coping

strategies/adaptations for the child and parent with outcome evaluation including factors relating to parent anxiety and confidence, as well as factors relating directly to the child's eating and drinking skill, is an example of how the model can be used in the design of future interventions and their evaluation.

Another priority for research is the development and evaluation of an intervention to address symptoms of PTSD. Access to psychology services may be essential for some but is unlikely to be universally available. Lloyd et al. (2021) outline an innovative parent group intervention which is designed to empower parents, help them develop problem-solving skills and manage their own mental health for parents of children with neurodisability. Exploring parent acceptability, prior to developing such a programme designed specifically for parents of children with OA/TOF, would be an important first step for future research.

A further gap in understanding is the relative contribution that parent anxiety plays in the development and maintenance of eating and drinking difficulties. Evidence from work package 1 (questionnaire) identified parent anxiety as a predictor of feeding outcome and feeding outcome as a predictor of parent anxiety. Thus, a bidirectional relationship is proposed. However, the current study relied on parent report for feeding difficulty. A prospective observational study using an objective measure of feeding difficulty, such as direct mealtime observation, alongside validated measures of anxiety would help answer this question and strengthen understanding. Continuing to develop understanding of this complex phenomenon will facilitate development of interventions, provide evidence for the development of care pathways, and improve outcomes.

6.6 Overall conclusion

This thesis presents an in-depth study of OA/TOF, providing data to understand the nature and prevalence of eating and drinking difficulties. Data indicate that oro-pharyngeal dysphagia is present in approximately 25%

of children under one year of age. Exploratory, data-driven hypotheses are proposed for the underlying mechanisms of these oro-pharyngeal impairments: respiratory-swallow coordination and upper oesophageal sphincter abnormality with intact pharyngeal contractility. Results indicate that swallow function alone does not determine eating and drinking outcome. Other biological factors including prematurity and respiratory status influence the severity of eating and drinking difficulties. Data are also presented that highlight how parental mental health can be impacted by caring for a child with OA/TOF associated feeding difficulties. Findings suggest that approximately 40% of parents may experience PTSD related to their child's feeding and/or present with moderate-severe anxiety. Parental anxiety may play a significant role in the development or maintenance of severe eating and drinking difficulties. The complex interaction of biological, psychological, and social factors should be central to the assessment and treatment of swallowing, eating and drinking difficulties in OA/TOF.

Chapter 7. References

Aizlewood, E. G., F. W. Jones and R. M. Whatmough (2023). "Paediatric gastroesophageal reflux disease and parental mental health: Prevalence and predictors." Clin Child Psychol Psychiatry **28**(3): 1024-1037.

Allemang, B., K. Sitter and G. Dimitropoulos (2022). "Pragmatism as a paradigm for patient-oriented research." Health Expect **25**(1): 38-47.

Almaatani, D., A. Zurbau, F. Khoshnevisan, R. H. J. Bandsma, T. A. Khan, J. L. Sievenpiper and M. Van Den Heuvel (2023). "The association between parents' stress and parental feeding practices and feeding styles: Systematic review and meta-analysis of observational studies." Matern Child Nutr **19**(1): e13448.

Almog, A. and A. Zani (2022). "Postoperative complications and long-term outcomes of Tracheoesophageal Fistula repair." Current Challenges in Thoracic Surgery **4**.

Altman, D. G. (1990). Practical statistics for medical research, Chapman and Hall/CRC.

Andersen, T. E., M. Hansen, S. L. Ravn, R. Seehuus, M. Nielsen and H. B. Vaegter (2018). "Validation of the PTSD-8 Scale in Chronic Pain Patients." Pain Med **19**(7): 1365-1372.

Ansari, N. S., L. S. Franck, C. Tomlinson, A. Colucci and K. O'Brien (2023). "A pilot study of family-integrated care (FICare) in critically Ill preterm and term infants in the Nicu: FICare Plus." Children **10**(8): 1337.

Arslan, S. S., N. Demir, A. A. Karaduman, F. C. Tanyel and T. Soyer (2020). "The functional chewing training for chewing dysfunction in children with repaired EA-TEF." Journal of pediatric surgery **55**(4): 635-638.

Arvedson, J., M. Lefton-Greif, D. Reigstad and L. Brodsky (2020). Clinical swallowing and feeding assessment, Plural Publishing San Diego, CA.

Arvedson, J., B. Rogers, G. Buck, P. Smart and M. Msall (1994). "Silent aspiration prominent in children with dysphagia." International journal of pediatric otorhinolaryngology **28**(2-3): 173-181.

Arvedson, J. C. (2006). "Swallowing and feeding in infants and young children." GI Motility online.

Arvedson, J. C. (2008). "Assessment of pediatric dysphagia and feeding disorders: clinical and instrumental approaches." Developmental disabilities research reviews **14**(2): 118-127.

Arvedson, J. C. and M. A. Lefton-Greif (2017). "Instrumental Assessment of Pediatric Dysphagia." Semin Speech Lang **38**(2): 135-146.

Ax, S. O., K. Abrahamsson, V. Gatzinsky, L. Jonsson and M. Dellenmark-Blom (2021). "Parent-Reported Feeding Difficulties among Children Born with Esophageal Atresia: Prevalence and Early Risk Factors." Eur J Pediatr Surg **31**(1): 69-75.

Baha, S., E. Sibel, D. Duygu, K. Ezgi, K. Tayfun and B. Serhat (2020). "Oropharyngeal swallowing functions are impaired in patients with naive-achalasia." European Archives of Oto-Rhino-Laryngology **277**: 1219-1226.

Baird, R., D. Levesque, R. Birnbaum and M. Ramsay (2015). "A pilot investigation of feeding problems in children with esophageal atresia." Dis Esophagus **28**(3): 224-228.

Bajwa, S. A., F. Toro and A. Kasi (2023). Physiology, esophagus. StatPearls [Internet], StatPearls Publishing.

Baker, L. N., D. O. Witherspoon, J. S. Nicholson and A. J. Fuglestad (2023). "The roles of child temperament, parent stress, and parenting style in family mealtimes." Appetite **188**: 106758.

Barbon, C. E. and C. M. Steele (2019). "Characterizing the flow of thickened barium and non-barium liquid recipes using the IDDSI flow test." Dysphagia **34**(1): 73-79.

Barni, A., D. Zecchillo, S. Uberti and S. Ratti (2019). "Osteopathic Manipulative Treatment in a Paediatric Patient with Oesophageal Atresia and Tracheo-Oesophageal Fistula." Case reports in gastroenterology **13**(1): 178-184.

Bartholomew, M. K., S. J. Schoppe-Sullivan, Glassman, M., , C. M. Kamp Dush and J. M. Sullivan (2012). "New parents' Facebook use at the transition to parenthood. , 61(3), pp.455-469." Family relations **61**(3): 455-469.

Baum, L. S. (2004). "Internet parent support groups for primary caregivers of a child with special health care needs." Pediatric nursing **30**(5).

Baxter, K. J., L. M. Baxter, A. M. Landry, M. L. Wulkan and A. M. Bhatia (2018). "Structural airway abnormalities contribute to dysphagia in children with esophageal atresia and tracheoesophageal fistula." Journal of Pediatric Surgery **53**(9): 1655-1659.

Bayona, H. H. G., N. Pizzorni, J. Tack, A. Goeleven, T. Omari and N. Rommel (2022). "Accuracy of high-resolution pharyngeal manometry metrics for predicting aspiration and residue in oropharyngeal dysphagia patients with poor pharyngeal contractility." Dysphagia **37**(6): 1560-1575.

Belafsky, P. C., D. A. Mouadeb, C. J. Rees, J. C. Pryor, G. N. Postma, J. Allen and R. J. Leonard (2008). "Validity and reliability of the Eating Assessment Tool (EAT-10)." Annals of Otology, Rhinology & Laryngology **117**(12): 919-924.

Benjamin, B. and A. Inglis (1989). "Minor congenital laryngeal clefts: diagnosis and classification." Annals of Otology, Rhinology & Laryngology **98**(6): 417-420.

Bergeron, M., A. P. Cohen and R. T. Cotton (2017). "The Management of Cyanotic Spells in Children with Oesophageal Atresia." Front Pediatr **5**: 106.

Bergmann, S., L. A. Ritz, A. Widenmann-Grolig, S. Jechalke, D. von Schweinitz, J. Hubertus and E. Lurz (2022). "Swallowing-related quality of life in children with oesophageal atresia: a national cohort study." European journal of pediatrics((Bergmann, von Schweinitz) Department of Paediatric Surgery, Dr. von Hauner Children's Hospital, University Hospital, LMU Munich, Munich, Germany(Ritz) Sana Klinikum Lichtenberg, Berlin, Germany(Widenmann-Grolig, Jechalke) Patient Support Group KEKS e.V.).

Berlin, K. S., W. H. Davies, D. J. Lobato and A. H. Silverman (2009). "A Biopsychosocial Model of Normative and Problematic Pediatric Feeding." Children's Health Care **38**(4): 263-282.

Bevilacqua, F., B. Ragni, A. Conforti, S. Gentile, A. Zaccara, A. Dotta, P. Bagolan and L. Aite (2020). "Fixed the gap, solved the problem? Eating skills in esophageal atresia patients at 3 years." Dis Esophagus **33**(1).

Birketvedt, K., A. Mikkelsen, L. L. Klingen, C. Henriksen, I. B. Helland and R. Emblem (2020). "Nutritional Status in Adolescents with Esophageal Atresia." The Journal of pediatrics **218**(jlz, 0375410): 130-137.

Boettcher, J., M. Boettcher, S. Wiegand-Grefe and H. Zapf (2021). "Being the Pillar for Children with Rare Diseases-A Systematic Review on Parental Quality of Life." Int J Environ Res Public Health **18**(9).

Bonilha, H. S., J. Blair, B. Carnes, W. Huda, K. Humphries, K. McGrattan, Y. Michel and B. Martin-Harris (2013). "Preliminary investigation of the effect of pulse rate on judgments of swallowing impairment and treatment recommendations." Dysphagia **28**(4): 528-538.

Bourg, A., F. Gottrand, B. Parmentier, J. Thomas, A. Lehn, C. Piolat, A. Bonnard, R. Sfeir, J. Lienard, V. Rousseau, M. Pouzac, A. Liard, P. Buisson, A. Haffreingue, L. David, S. Branchereau, V. Carcauzon, N. Kalfa, M.-D. Leclair, H. Lardy, S. Irtan, F. Varlet, T. Gelas, D. Potop and M. Auger-Hunault (2022). "Outcome of long gap esophageal atresia at 6 years: A prospective case control cohort study." Journal of pediatric surgery(jmj, 0052631).

Bowling, A. and S. Ebrahim (2005). Handbook of health research methods: investigation, measurement and analysis. UK, McGraw-Hill Education.

Braun, V. and V. Clarke (2019). "Reflecting on reflexive thematic analysis." Qualitative Research in Sport, Exercise and Health **11**(4): 589-597.

Braun, V. and V. Clarke (2020). "Can I use TA? Should I use TA? Should I not use TA? Comparing reflexive thematic analysis and other pattern-based

qualitative analytic approaches." Counselling and Psychotherapy Research **21**(1): 37-47.

Braun, V. and V. Clarke (2022). Thematic analysis: a practical guide. London, Sage.

Burge, D., K. Shah, P. Spark, N. Shenker, M. Pierce, J. Kurinczuk, E. Draper, P. Johnson and M. Knight (2013). "Contemporary management and outcomes for infants born with oesophageal atresia." Journal of British Surgery **100**(4): 515-521.

Capitanio, M., R. Guana, S. Garofalo, F. Scottoni, M. G. Cortese, C. Marchetti and F. Gennari (2021). "Quality of life and long-term results in patients operated on for Esophageal Atresia." Minerva pediatrics(101777303).

Carbo, A. I., M. Brown and N. Nakrour (2021). "Fluoroscopic swallowing examination: radiologic findings and analysis of their causes and pathophysiologic mechanisms." Radiographics **41**(6): 1733-1749.

Cassina, M., M. Ruol, R. Pertile, P. Midrio, S. Piffer, V. Vicenzi, M. Saugo, C. F. Stocco, P. Gamba and M. Clementi (2016). "Prevalence, characteristics, and survival of children with esophageal atresia: A 32-year population-based study including 1,417,724 consecutive newborns." Birth Defects Research Part A: Clinical and Molecular Teratology **106**(7): 542-548.

Castilloux, J., D. Bouron-Dal Soglio and C. Faure (2010). "Endoscopic assessment of children with esophageal atresia: Lack of relationship of esophagitis and esophageal metaplasia to symptomatology." Canadian journal of gastroenterology = Journal canadien de gastroenterologie **24**(5): 312-316.

Cavallaro, S., A. Pineschi, G. Freni, M. G. Cortese and T. Bardini (1992). "Feeding troubles following delayed primary repair of esophageal atresia." European journal of pediatric surgery : official journal of Austrian Association of Pediatric Surgery ... [et al] = Zeitschrift fur Kinderchirurgie **2**(2): 73-77.

Celtik, U., S. Eyigor, E. Divarci, B. Sezgin, Z. Dokumcu, C. Ozcan, K. Ozturk and A. Erdener (2022). "Fiberoptic endoscopic evaluation of swallowing (FEES) study: the first report in children to evaluate the oropharyngeal dysphagia after esophageal atresia repair." Pediatric surgery international **38**(9): 1227-1233.

Chen, A. Y., R. Frankowski, J. Bishop-Leone, T. Hebert, S. Leyk, J. Lewin and H. Goepfert (2001). "The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the MD Anderson dysphagia inventory." Archives of Otolaryngology–Head & Neck Surgery **127**(7): 870-876.

Cheriyan, S. S., M. S. Schar, C. M. Woods, S. Bihari, C. Cock, T. Athanasiadis, T. I. Omari and E. H. Ooi (2023). "Swallowing biomechanics in

tracheostomised critically ill patients compared to age-and gender-matched healthy controls." Critical Care and Resuscitation **25**(2): 97-105.

Chuang, Y. J., S. J. Hwang, K. A. Buhr, C. A. Miller, G. D. Avey, B. H. Story and H. K. Vorperian (2022). "Anatomic development of the upper airway during the first five years of life: A three-dimensional imaging study." PloS one **17**(3): e0264981.

Cichero, J. A., P. Lam, C. M. Steele, B. Hanson, J. Chen, R. O. Dantas, J. Duivestein, J. Kayashita, C. Lecko, J. Murray, M. Pillay, L. Riquelme and S. Stanschus (2017). "Development of International Terminology and Definitions for Texture-Modified Foods and Thickened Fluids Used in Dysphagia Management: The IDDSI Framework." Dysphagia **32**(2): 293-314.

Cimador, M., M. Carta, M. R. Di Pace, G. Natale, A. Castiglione, M. Sergio, G. Corsello and E. De Grazia (2006). "Primary repair in esophageal atresia. The results of long term follow-up." Minerva pediatrica **58**(1): 9-13.

Clayburgh, D., H. Milczuk, S. Gorsek, N. Sinden, K. Bowman and C. MacArthur (2011). "Efficacy of tonsillectomy for pediatric patients with Dysphagia and tonsillar hypertrophy." Archives of Otolaryngology–Head & Neck Surgery **137**(12): 1197-1202.

Cohen, J., P. Cohen, S. G. West and L. S. Aiken (2013). Applied multiple regression/correlation analysis for the behavioral sciences, Routledge.

Cohen, S. (1988). "Perceived stress in a probability sample of the United States."

Cohen, S. (1994). Perceived Stress Scale.

Comella, A., S. P. Tan Tanny, J. M. Hutson, T. I. Omari, W. J. Teague, R. M. Nataraja and S. K. King (2021). "Esophageal morbidity in patients following repair of esophageal atresia: A systematic review." J Pediatr Surg **56**(9): 1555-1563.

Connor, M. J., L. R. Springford, V. V. Kapetanakis and S. Giuliani (2015). "Esophageal atresia and transitional care--step 1: a systematic review and meta-analysis of the literature to define the prevalence of chronic long-term problems." Am J Surg **209**(4): 747-759.

Cook, I. J., W. J. Dodds, R. O. Dantas, B. Massey, M. Kern, I. Lang, J. Brasseur and W. Hogan (1989). "Opening mechanisms of the human upper esophageal sphincter." American Journal of Physiology-Gastrointestinal and Liver Physiology **257**(5): G748-G759.

Coppens, C. H., L. van den Engel-Hoek, H. Scharbatke, S. A. F. de Groot and J. M. T. Draaisma (2016). "Dysphagia in children with repaired oesophageal atresia." Eur J Pediatr **175**(9): 1209-1217.

Courbette, O., T. Omari, A. Aspirot and C. Faure (2020). "Characterization of Esophageal Motility in Children With Operated Esophageal Atresia Using

High-resolution Impedance Manometry and Pressure Flow Analysis." J Pediatr Gastroenterol Nutr **71**(3): 304-309.

Crary, M. A., G. D. Mann and M. E. Groher (2005). "Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients." Arch Phys Med Rehabil **86**(8): 1516-1520.

Creswell, J. W. and V. L. P. Clark (2017). Designing and conducting mixed methods research, Sage publications.

Dakkak, M. and J. R. Bennett (1992). "A new dysphagia score with objective validation." Journal of clinical gastroenterology **14**(2): 99-100.

Damrongmanee, A., K. El-Chammas, L. Fei, H. Zang, N. Santucci and A. Kaul (2021). "Pharyngeal and upper esophageal sphincter motor dynamics during swallow in children." Neurogastroenterology & Motility **33**(2): e13962.

Damrongmanee, A., K. El-Chammas, N. Santucci, L. Fei and A. Kaul (2024). "Characterization of pharyngeal contractile integral using pharyngeal manometry in children." Journal of pediatric gastroenterology and nutrition.

Davies, W. (2016). "Insights into rare diseases from social media surveys." Orphanet J Rare Dis **11**(1): 151.

de Vos, C., L. van Wyk, D. Sidler and P. Goussard (2024). "Anxiety and post-traumatic stress disorder in parents of chidlren born with esophageal atresia." Pediatric Respiratory Journal **2**(2): 64-71.

DeBoer, E. M., J. D. Prager, A. G. Ruiz, E. L. Jensen, R. R. Deterding, J. A. Friedlander and J. Soden (2016). "Multidisciplinary care of children with repaired esophageal atresia and tracheoesophageal fistula." Pediatric pulmonology **51**(6): 576-581.

Delaney, A. L. and J. C. Arvedson (2008). "Development of swallowing and feeding: prenatal through first year of life." Developmental disabilities research reviews **14**(2): 105-117.

Dellenmark-Blom, M., K. Abrahamsson, J. Dingemann, S. Witt, C. Dingemann, L. Jonsson, V. Gatzinsky, M. Bullinger, B. M. Ure, J. E. Chaplin and J. H. Quitmann (2022). "Factors of family impact in a Swedish-German cohort of children born with esophageal atresia." Orphanet journal of rare diseases **17**(1): 207.

Dellenmark-Blom, M., K. Abrahamsson, J. Quitmann, R. Sommer, S. Witt, J. Dingemann, S. Flieder, L. Jönsson, V. Gatzinsky and M. Bullinger (2017). "Development and pilot-testing of a condition-specific instrument to assess the quality-of-life in children and adolescents born with esophageal atresia." Dis Esophagus **30**(7): 1-9.

Dellenmark-Blom, M., J. E. Chaplin, L. Jonsson, V. Gatzinsky and K. Abrahamsson (2018). "The relationship of coping, digestive symptoms and Eating-Quality-of-Life among children with oesophageal atresia: Findings

from the Swedish OA-QOL©-study." Journal of Pediatric Gastroenterology and Nutrition **66**(Supplement 2): 931.

Dellenmark-Blom, M., J. E. Chaplin, J. H. Quitmann, L. Jonsson, V. Gatzinsky, J. Dingemann and K. Abrahamsson (2019). "The prevalence and role of coping strategies in the nutritional intake of children born with esophageal atresia: a condition-specific approach." Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus **32**(7).

Dellenmark-Blom, M., S. Orno Ax, E. Ost, J. F. Svensson, A.-M. Kassa, L. Jonsson, K. Abrahamsson, V. Gatzinsky, P. Stenstrom, A. Tollne, E. Omling and H. Engstrand Lilja (2022). "Postoperative morbidity and health-related quality of life in children with delayed reconstruction of esophageal atresia: a nationwide Swedish study." Orphanet journal of rare diseases **17**(1): 239.

Dellenmark-Blom, M., J. Quitmann, J. Dingemann, S. Witt, B. M. Ure, M. Bullinger, L. Jonsson, V. Gatzinsky and C. Dingemann (2020). "Clinical Factors Affecting Condition-Specific Quality-of-Life Domains in Pediatric Patients after Repair of Esophageal Atresia: The Swedish-German EA-QOL Study." Eur J Pediatr Surg **30**(1): 96-103.

Demir, N., T. Soyer, S. Serel Arslan, S. Yalcin, A. A. Karaduman and F. C. Tanyel (2017). "Alterations in hypolaryngeal elevation after esophageal anastomosis: A possible mechanism for airway aspiration." Dysphagia **32**(1): 152.

Deurloo, J. A., S. Ekkelkamp, J. F. W. M. Bartelsman, F. J. W. Ten Kate, M. Schoorl, H. A. Heij and D. C. Aronson (2003). "Gastroesophageal reflux: prevalence in adults older than 28 years after correction of esophageal atresia." Annals of surgery **238**(5): 686-689.

Deurloo, J. A., S. Ekkelkamp, J. A. J. M. Taminiau, C. M. F. Kneepkens, F. W. J. ten Kate, J. F. W. M. Bartelsman, D. A. Legemate and D. C. Aronson (2005). "Esophagitis and Barrett esophagus after correction of esophageal atresia." Journal of pediatric surgery **40**(8): 1227-1231.

Dharmarathna, I., A. Miles and J. Allen (2020). "Twenty years of quantitative instrumental measures of swallowing in children: a systematic review." Eur J Pediatr **179**(2): 203-223.

Di Pace, M. R., A. M. Caruso, P. Catalano, A. Casuccio and E. De Grazia (2011). "Evaluation of esophageal motility using multichannel intraluminal impedance in healthy children and children with gastroesophageal reflux." Journal of pediatric gastroenterology and nutrition **52**(1): 26-30.

Didehbani, N., K. Kelly, L. Austin and A. Wiechmann (2011). "Role of parental stress on pediatric feeding disorders." Children's Health Care **40**(2): 85-100.

Dimitrov, G., M. Aumar, A. Duhamel, M. Wanneveich and F. Gottrand (2024). "Proton pump inhibitors in esophageal atresia: A systematic review and

meta-analysis." Journal of Pediatric Gastroenterology and Nutrition **78**(3): 457-470.

Dingemann, C., S. Eaton, G. Aksnes, P. Bagolan, K. M. Cross, P. De Coppi, J. Fruithof, P. Gamba, I. Goldschmidt, F. Gottrand, S. Pirr, L. Rasmussen, R. Sfeir, G. Slater, J. Suominen, J. F. Svensson, J. M. Thorup, S. Tytgat, D. C. van der Zee, L. Wessel, A. Widenmann-Grolig, R. Wijnen, W. Zetterquist and B. M. Ure (2021). "ERNICA Consensus Conference on the Management of Patients with Long-Gap Esophageal Atresia: Perioperative, Surgical, and Long-Term Management." Eur J Pediatr Surg **31**(3): 214-225.

Dingemann, C., S. Eaton, G. Aksnes, P. Bagolan, K. M. Cross, P. De Coppi, J. Fruithof, P. Gamba, S. Husby, A. Koivusalo, L. Rasmussen, R. Sfeir, G. Slater, J. F. Svensson, D. C. Van der Zee, L. M. Wessel, A. Widenmann-Grolig, R. Wijnen and B. M. Ure (2020). "ERNICA Consensus Conference on the Management of Patients with Esophageal Atresia and Tracheoesophageal Fistula: Follow-up and Framework." Eur J Pediatr Surg **30**(6): 475-482.

Dodrill, P. and M. M. Gosa (2015). "Pediatric Dysphagia: Physiology, Assessment, and Management." Ann Nutr Metab **66 Suppl 5**: 24-31.

Doty, J. L. and J. Dworkin (2014). "Online Social Support for Parents: A Critical Review." Marriage & Family Review **50**(2): 174-198.

Duncan, D. R., C. DiFilippo, M. Kane, M. Lurie, M. E. McSweeney and R. L. Rosen (2021). "Overlapping Symptoms of Gastroesophageal Reflux and Aspiration Highlight the Limitations of Validated Questionnaires." J Pediatr Gastroenterol Nutr **72**(3): 372-377.

Duncan, D. R., K. Larson, K. Davidson, K. May, R. Rahbar and R. L. Rosen (2019). "Feeding Interventions Are Associated With Improved Outcomes in Children With Laryngeal Penetration." J Pediatr Gastroenterol Nutr **68**(2): 218-224.

Duncan, D. R., P. D. Mitchell, K. Larson and R. L. Rosen (2018). "Presenting signs and symptoms do not predict aspiration risk in children." The Journal of pediatrics **201**: 141-146.

Elrod, J. K. and J. L. Fortenberry (2017). "The hub-and-spoke organization design: an avenue for serving patients well." BMC health services research **17**: 25-33.

Estrem, H. H., B. F. Pados, J. Park, K. A. Knafl and S. M. Thoyre (2017). "Feeding problems in infancy and early childhood: evolutionary concept analysis." Journal of advanced nursing **73**(1): 56-70.

Estrem, H. H., S. M. Thoyre, K. A. Knafl, B. Frisk Pados and M. Van Riper (2018). ""It's a Long-Term Process": Description of Daily Family Life When a Child Has a Feeding Disorder." J Pediatr Health Care **32**(4): 340-347.

Faugli, A., G. Aamodt, K. Bjornland, R. Emblem and T. H. Diseth (2005). "Assessment of early mother-child relation in infants with oesophageal atresia." Nordic journal of psychiatry **59**(6): 498-503.

Faugli, A., R. Emblem, M. Veenstra, K. Bjornland and T. H. Diseth (2008). "Does esophageal atresia influence the mother-infant interaction?" Journal of pediatric surgery **43**(10): 1796-1801.

Faure, C. and F. Righini Grunder (2017). "Dysmotility in Esophageal Atresia: Pathophysiology, Characterization, and Treatment." Front Pediatr **5**: 130.

Ferreira, R. L., I. J. B. do Nascimento, V. I. A. de Almeida, V. R. L. de Oliveira, L. G. Marangne, F. dos Santos Gameleira, T. R. C. Dutra, D. de Oliveira Santos, M. P. D. Afonso and P. E. A. Dos Santos (2023). "The utilisation of primary health care system concepts positively impacts the assistance of patients with rare diseases despite limited knowledge and experience by health care professionals: A qualitative synopsis of the evidence including approximately 78 000 individuals." Journal of Global Health **13**.

Ferris, L., S. Doeltgen, C. Cock, N. Rommel, M. Schar, S. Carrión, I. Scholten and T. Omari (2021). "Modulation of pharyngeal swallowing by bolus volume and viscosity." American Journal of Physiology-Gastrointestinal and Liver Physiology **320**(1): G43-G53.

Ferris, L., S. King, L. McCall, N. Rommel, I. Scholten, W. Teague, S. Doeltgen and T. Omari (2018). "Piecemeal Deglutition and the Implications for Pressure Impedance Dysphagia Assessment in Pediatrics." Journal of pediatric gastroenterology and nutrition **67**(6): 713-719.

Ferris, L., N. Rommel, S. Doeltgen, I. Scholten, S. Kritas, R. Abu-Assi, L. McCall, G. Seiboth, K. Lowe and D. Moore (2016). "Pressure-flow analysis for the assessment of pediatric oropharyngeal dysphagia." The Journal of pediatrics **177**: 279-285. e271.

Fetters, M. D., L. A. Curry and J. W. Creswell (2013). "Achieving integration in mixed methods designs—principles and practices." Health services research **48**(6pt2): 2134-2156.

Fetters, M. D. and D. Freshwater (2015). Publishing a methodological mixed methods research article, Sage Publications Sage CA: Los Angeles, CA. **9:** 203-213.

Fischer, J., J. Balleisen, J. Holzki, G. Cernaianu, M. Alejandre Alcazar and M. Dubbers (2020). "Tracheoscopic Findings and Their Impact on Respiratory Symptoms in Children with Esophageal Atresia." Eur J Pediatr Surg **30**(4): 371-377.

Fishbein, M., K. Benton and W. Struthers (2016). "Mealtime Disruption and Caregiver Stress in Referrals to an Outpatient Feeding Clinic." JPEN J Parenter Enteral Nutr **40**(5): 636-645.

Fracchia, M. S., G. Diercks, A. Yamasaki, C. Hersh, S. Hardy, M. Hartnick and C. Hartnick (2017). "Assessment of the feeding Swallowing Impact Survey as a quality of life measure in children with laryngeal cleft before and after repair." Int J Pediatr Otorhinolaryngol **99**: 73-77.

Fraga, J. C., E. A. Adil, A. Kacprowicz, M. L. Skinner, R. Jennings, C. Lillehei and R. Rahbar (2015). "The association between laryngeal cleft and tracheoesophageal fistula: myth or reality?" The Laryngoscope **125**(2): 469-474.

Fraga, J. C., R. W. Jennings and P. C. Kim (2016). "Pediatric tracheomalacia." Semin Pediatr Surg **25**(3): 156-164.

Frakking, T. T., M. David, A. B. Chang, A. Sarikwal, S. Humphries, S. Day and K. A. Weir (2024). "Influence of frame rate in detecting oropharyngeal aspiration in paediatric videofluoroscopic swallow studies–An observational study." European Journal of Radiology **170**: 111275.

Frey, E., C. Bonfiglioli, M. Brunner and J. Frawley (2022). "Parents' Use of Social Media as a Health Information Source for Their Children: A Scoping Review." Acad Pediatr **22**(4): 526-539.

Friedman, B. and J. B. Frazier (2000). "Deep laryngeal penetration as a predictor of aspiration." Dysphagia **15**: 153-158.

Frohlich, T., S. Otto, P. Weber, D. Pilic, A. Schmidt-Choudhury, T. G. Wenzl and H. Kohler (2008). "Combined esophageal multichannel intraluminal impedance and pH monitoring after repair of esophageal atresia." Journal of pediatric gastroenterology and nutrition **47**(4): 443-449.

Fung, S. W., E. Lapidus-Krol, M. Chiang, E. M. Fallon, B. Haliburton, E. J. Propst and P. P. Chiu (2019). "Vocal cord dysfunction following esophageal atresia and tracheoesophageal fistula (EA/TEF) repair." Journal of Pediatric Surgery **54**(8): 1551-1556.

Gajda, J., C. Johns and T. Zimmermann (2024). "Impact of pediatric cancer on parents' relationships." Eur J Oncol Nurs **69**: 102514.

Garand, K. L., G. McCullough, M. Crary, J. C. Arvedson and P. Dodrill (2020). "Assessment across the life span: The clinical swallow evaluation." American Journal of Speech-Language Pathology **29**(2S): 919-933.

Garro, A. (2004). "Coping patterns in mothers/caregivers of children with chronic feeding problems." J Pediatr Health Care **18**(3): 138-144.

Garro, A., S. K. Thurman, M. E. Kerwin and J. P. Ducette (2005). "Parent/caregiver stress during pediatric hospitalization for chronic feeding problems." J Pediatr Nurs **20**(4): 268-275.

Gatzinsky, V., L. Jonsson, C. Johansson, G. Gothberg, U. Sillen and L. G. Friberg (2011). "Dysphagia in adults operated on for esophageal atresia--use of a symptom score to evaluate correlated factors." European journal of

pediatric surgery : official journal of Austrian Association of Pediatric Surgery ... [et al] = Zeitschrift fur Kinderchirurgie **21**(2): 94-98.

Gent, V., J. Marshall, K. A. Weir and D. Trembath (2024). "Investigating the impact of autistic children's feeding difficulties on caregivers." Child: Care, Health and Development **50**(1): e13218.

Gibreel, W., B. Zendejas, R. M. Antiel, G. Fasen, C. R. Moir and A. E. Zarroug (2017). "Swallowing Dysfunction and Quality of Life in Adults With Surgically Corrected Esophageal Atresia/Tracheoesophageal Fistula as Infants: Forty Years of Follow-up." Annals of surgery **266**(2): 305-310.

Giorgio, V., P. Karanika, K. J. Lindley, F. Boccellari, N. Thapar, J. Curry and O. Borrelli (2011). "Esophageal pressure topography features in childrenwith repaired esophageal atresia and tracheo-esophageal fistula." Digestive and Liver Disease **43**(SUPPL. 5): S426-S427.

Goday, P. S., S. Y. Huh, A. Silverman, C. T. Lukens, P. Dodrill, S. S. Cohen, A. L. Delaney, M. B. Feuling, R. J. Noel, E. Gisel, A. Kenzer, D. B. Kessler, O. Kraus de Camargo, J. Browne and J. A. Phalen (2019). "Pediatric Feeding Disorder: Consensus Definition and Conceptual Framework." J Pediatr Gastroenterol Nutr **68**(1): 124-129.

Goldani, H. A., A. Staiano, O. Borrelli, N. Thapar and K. J. Lindley (2010). "Pediatric esophageal high-resolution manometry: utility of a standardized protocol and size-adjusted pressure topography parameters." Official journal of the American College of Gastroenterology| ACG **105**(2): 460-467.

Goldman-Yassen, A. E., J. Gross, I. Novak, E. Poletto, J. S. Kim, J. K. Son and T. L. Levin (2019). "Identification of clinical parameters to increase the diagnostic yield of the non-emergent upper gastrointestinal series in pediatric outpatients." Pediatric radiology **49**: 162-167.

Golonka, N. R. and A. H. Hayashi (2008). "Early "sham" feeding of neonates promotes oral feeding after delayed primary repair of major congenital esophageal anomalies." American journal of surgery **195**(5): 659-662.

Graziano, S., N. Ullmann, R. Rusciano, A. Allegorico, F. Boldrini, L. Rosito, A. L. Quittner, R. Cutrera and P. Tabarini (2023). "Comparison of mental health in individuals with primary ciliary dyskinesia, cystic fibrosis, and parent caregivers." Respiratory Medicine **207**: 107095.

Greer, A. J., C. S. Gulotta, E. A. Masler and R. B. Laud (2008). "Caregiver stress and outcomes of children with pediatric feeding disorders treated in an intensive interdisciplinary program." J Pediatr Psychol **33**(6): 612-620.

Gurberg, J., R. Birnbaum and S. J. Daniel (2015). "Laryngeal penetration on videofluoroscopic swallowing study is associated with increased pneumonia in children." International journal of pediatric otorhinolaryngology **79**(11): 1827-1830.

Hall, N. J., M. Wyatt, J. I. Curry and E. M. Kiely (2013). "A standardised investigative strategy prior to revisional oesophageal surgery in children: High incidence of unexpected findings." Journal of Pediatric Surgery **48**(11): 2241-2246.

Han, H.-R. and A. E. Belcher (2001). "Computer-mediated support group use among parents of children with cancer–an exploratory study." Comput Nurs **19**(1): 27-33.

Hanks, E., A. Stewart, C. K. Au-Yeung, E. Johnson and C. H. Smith (2023). "Consensus on level descriptors for a functional children's eating and drinking activity scale." Developmental Medicine & Child Neurology **65**(9): 1199-1205.

Hansen, M., T. E. Andersen, C. Armour, A. Elklit, S. Palic and T. Mackrill (2010). "PTSD-8: A Short PTSD Inventory." Clinical Practice and Epidemiology in Mental Health **6**(1): 101-108.

Harrington, A. W., J. Riebold, K. Hernandez, S. J. Staffa, J. W. Meisner, D. Zurakowski, R. Jennings, T. Hamilton and B. Zendejas (2022). "Feeding and growth outcomes in infants with type C esophageal atresia who undergo early primary repair." The Journal of Pediatrics **241**: 77-82. e71.

Harrington, A. W., J. Riebold, K. Hernandez, S. J. Staffa, W. J. Svetanoff, D. Zurakowski, T. Hamilton, R. Jennings, N. M. Mehta and B. Zendejas (2021). "Nutrition delivery and growth outcomes in infants with long-gap esophageal atresia who undergo the Foker process." Journal of Pediatric Surgery **56**(12): 2133-2139.

Hausmann, J. S., J. Vizcaino-Riveros, A. C. Marin, M. Minegishi, R. Cox, M. L. Chang, L. E. Schanberg, M. Natter, E. R. Weitzman and C. L. R. Investigators (2022). "Feasibility and efficacy of online strategies to Recruit Parents of Children with Rheumatic Diseases for Research." ACR Open Rheumatology **4**(5): 410-416.

Hesse-Biber, S. N. and R. B. Johnson (2015). The Oxford handbook of multimethod and mixed methods research inquiry, Oxford University Press.

Hewetson, R. and S. Singh (2009). "The lived experience of mothers of children with chronic feeding and/or swallowing difficulties." Dysphagia **24**(3): 322-332.

Hiorns, M. P. and M. M. Ryan (2006). "Current practice in paediatric videofluoroscopy." Pediatric radiology **36**: 911-919.

Hong, J. Y., N. K. Hwang, G. Lee, J. S. Park and Y. J. Jung (2021). "Radiation Safety in Videofluoroscopic Swallowing Study: Systematic Review." Dysphagia **36**(1): 73-82.

Hong, Q. N., P. Pluye, S. Fàbregues, G. Bartlett, F. Boardman, M. Cargo, P. Dagenais, M.-P. Gagnon, F. Griffiths and B. Nicolau (2018). "Mixed methods appraisal tool (MMAT), version 2018." Registration of copyright **1148552**(10).

Hormann, M., P. Pokieser, M. Scharitzer, W. Pumberger, M. Memarsadeghi, B. Partik and O. Ekberg (2002). "Videofluoroscopy of deglutition in children after repair of esophageal atresia." Acta radiologica (Stockholm, Sweden : 1987) **43**(5): 507-510.

Hseu, A., T. Recko, R. Jennings and R. Nuss (2015). "Upper Airway Anomalies in Congenital Tracheoesophageal Fistula and Esophageal Atresia Patients." Ann Otol Rhinol Laryngol **124**(10): 808-813.

Hua, K., S. Yang, Y. Zhang, Y. Zhao, Y. Gu, S. Li, J. Liao and J. Huang (2020). "Thoracoscopic surgery for recurrent tracheoesophageal fistula after esophageal atresia repair." Diseases of the Esophagus **33**(9): doaa023.

Huynh Trudeau, V., S. Maynard, T. Terzic, G. Soucy and M. Bouin (2015). "Dysphagia among adult patients who underwent surgery for esophageal atresia at birth." Canadian journal of gastroenterology & hepatology **29**(2): 91-94.

Ingleby, H. R., H. S. Bonilha and C. M. Steele (2021). "A tutorial on diagnostic benefit and radiation risk in videofluoroscopic swallowing studies." Dysphagia: 1-26.

Ioannides, A. S. and A. J. Copp (2009). "Embryology of oesophageal atresia." Semin Pediatr Surg **18**(1): 2-11.

Jadcherla, S. R., V. Prabhakar, K. A. Hasenstab, S. Nawaz, J. Das, M. Kern, G. Balasubramanian and R. Shaker (2018). "Defining pharyngeal contractile integral during high-resolution manometry in neonates: a neuromotor marker of pharyngeal vigor." Pediatric research **84**(3): 341-347.

Jaffal, H., A. Isaac, W. Johannsen, S. Campbell and H. G. El-Hakim (2020). "The prevalence of swallowing dysfunction in children with laryngomalacia: a systematic review." International journal of pediatric otorhinolaryngology **139**: 110464.

Jaffray, B. (2022). "Invited commentary on Stewart A, et al.: Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula: A hard sample to swallow." Journal of Pediatric Surgery **57**(12): 800.

Jia, R., K. Ayling, T. Chalder, A. Massey, N. Gasteiger, E. Broadbent, C. Coupland and K. Vedhara (2022). "The prevalence, incidence, prognosis and risk factors for symptoms of depression and anxiety in a UK cohort during the COVID-19 pandemic." BJPsych open **8**(2): e64.

Jones, C. J. and R. Bryant-Waugh (2013). "The relationship between child-feeding problems and maternal mental health: a selective review." Advances in Eating Disorders **1**(2): 119-133.

Kahrilas, P. J., A. J. Bredenoord, M. Fox, C. P. Gyawali, S. Roman, A. J. Smout, J. E. Pandolfino and I. H. R. M. W. Group (2015). "The Chicago

Classification of esophageal motility disorders, v3. 0." Neurogastroenterology & Motility **27**(2): 160-174.

Kara, B. H. and J. Stuart (2021). "The direct and indirect effects of parental trauma on child adjustment for resettled refugees in Australia." International Journal of Migration, Health and Social Care **17**(4): 474-486.

Kim, H. I., S. J. Hong, J. P. Han, J. Y. Seo, K. H. Hwang, H. J. Maeng, T. H. Lee and J. S. Lee (2013). "Specific movement of esophagus during transient lower esophageal sphincter relaxation in gastroesophageal reflux disease." Journal of Neurogastroenterology and motility **19**(3): 332.

Kim, J.-J. (2023). GERD Pathogenesis and Essential Anatomic Knowledge for Antireflux Surgery. Laparoscopic Antireflux Surgery, Springer**:** 7-13.

Ko, D., C. Lee, J. K. Youn, H.-B. Yang and H.-Y. Kim (2020). "Do children with esophageal atresia show worse growth outcomes?" Advances in Pediatric Surgery **26**(2): 54-60.

Koo, T. K. and M. Y. Li (2016). "A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research." J Chiropr Med **15**(2): 155-163.

Koumbourlis, A. C., Y. Belessis, M. Cataletto, R. Cutrera, E. DeBoer, M. Kazachkov, S. Laberge, J. Popler, F. Porcaro and T. Kovesi (2020). "Care recommendations for the respiratory complications of esophageal atresia-tracheoesophageal fistula." Pediatr Pulmonol **55**(10): 2713-2729.

Kovesi, T. (2017). "Aspiration Risk and Respiratory Complications in Patients with Esophageal Atresia." Front Pediatr **5**: 62.

Kovesi, T., F. Porcaro, F. Petreschi, M. Trozzi, S. Bottero and R. Cutrera (2018). "Vocal cord paralysis appears to be an acquired lesion in children with repaired esophageal atresia/tracheoesophageal fistula." Int J Pediatr Otorhinolaryngol **112**: 45-47.

Koziarkiewicz, M., A. Taczalska, I. Jasinska-Jaskula, H. Grochulska-Cerska and A. Piaseczna-Piotrowska (2015). "Long-term complications of congenital esophageal atresia–single institution experience." Indian pediatrics **52**: 499-501.

Krishnan, U., H. Mousa, L. Dall'Oglio, N. Homaira, R. Rosen, C. Faure and F. Gottrand (2016). "ESPGHAN-NASPGHAN Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Esophageal Atresia-Tracheoesophageal Fistula." J Pediatr Gastroenterol Nutr **63**(5): 550-570.

Krug, E., J. H. Bergmeijer, J. Dees, R. de Krijger, W. J. Mooi and F. W. Hazebroek (1999). "Gastroesophageal reflux and Barrett's esophagus in adults born with esophageal atresia." The American journal of gastroenterology **94**(10): 2825-2828.

Kunzler, A. M., A. Chmitorz, C. Bagusat, A. J. Kaluza, I. Hoffmann, M. Schafer, O. Quiring, T. Rigotti, R. Kalisch, O. Tuscher, A. G. Franke, R. van Dick and K. Lieb (2018). "Construct Validity and Population-Based Norms of the German Brief Resilience Scale (BRS)." Eur J Health Psychol **25**(3): 107-117.

Kwong, A. S., R. M. Pearson, M. J. Adams, K. Northstone, K. Tilling, D. Smith, C. Fawns-Ritchie, H. Bould, N. Warne and S. Zammit (2021). "Mental health before and during the COVID-19 pandemic in two longitudinal UK population cohorts." The British journal of psychiatry **218**(6): 334-343.

Lal, D. R., S. K. Gadepalli, C. D. Downard, D. J. Ostlie, P. C. Minneci, R. M. Swedler, T. H. Chelius, L. Cassidy, C. T. Rapp, D. Billmire, S. Bruch, R. C. Burns, K. J. Deans, M. E. Fallat, J. D. Fraser, J. Grabowski, F. Hebel, M. A. Helmrath, R. B. Hirschl, R. Kabre, J. Kohler, M. P. Landman, C. M. Leys, G. Z. Mak, J. Raque, B. Rymeski, J. M. Saito, S. D. St Peter, D. von Allmen, B. W. Warner, T. T. Sato and C. Midwest Pediatric Surgery (2018). "Challenging surgical dogma in the management of proximal esophageal atresia with distal tracheoesophageal fistula: Outcomes from the Midwest Pediatric Surgery Consortium." J Pediatr Surg **53**(7): 1267-1272.

Lallukka, T., O. Pietilainen, S. Jappinen, M. Laaksonen, J. Lahti and O. Rahkonen (2020). "Factors associated with health survey response among young employees: a register-based study using online, mailed and telephone interview data collection methods." BMC Public Health **20**(1): 184.

Lamm, K., I. Kristensson Hallstrom and K. Landgren (2022). "Parents' experiences of living with a child with Paediatric Feeding Disorder: An interview study in Sweden." Scand J Caring Sci.

Lanzoni, G., C. Sembenini, S. Gastaldo, L. Leonardi, V. P. Bentivoglio, G. Faggian, L. Bosa, P. Gaio and M. Cananzi (2022). "Esophageal dysphagia in children: state of the art and proposal for a symptom-based diagnostic approach." Frontiers in Pediatrics **10**: 885308.

Lau, C. (2015). "Development of suck and swallow mechanisms in infants." Annals of Nutrition and Metabolism **66**(Suppl. 5): 7-14.

Lau, C. (2016). "Development of infant oral feeding skills: what do we know?" The American journal of clinical nutrition **103**(2): 616S-621S.

Layly, J., F. Marmouset, G. Chassagnon, P. Bertrand, D. Sirinelli, J.-P. Cottier and B. Morel (2020). "Can we reduce frame rate to 15 images per second in pediatric videofluoroscopic swallow studies?" Dysphagia **35**: 296-300.

Le-Nguyen, A., E. K. Landry, P. Jantchou, C. Daoust, N. Piche, A. Aspirot and C. Faure (2024). "Outcomes of Premature Infants With Type C Esophageal Atresia." J Pediatr Surg.

Le Gouez, M., L. Alvarez, V. Rousseau, P. Hubert, V. Abadie, A. Lapillonne and E. Kermorvant-Duchemin (2016). "Posttraumatic Stress Reactions in Parents of Children Esophageal Atresia." PLoS One **11**(3): e0150760.

Lee, E. H. (2012). "Review of the psychometric evidence of the perceived stress scale." Asian Nurs Res (Korean Soc Nurs Sci) **6**(4): 121-127.

Lefton-Greif, M. A., K. E. McGrattan, K. A. Carson, J. M. Pinto, J. M. Wright and B. Martin-Harris (2018). "First Steps Towards Development of an Instrument for the Reproducible Quantification of Oropharyngeal Swallow Physiology in Bottle-Fed Children." Dysphagia **33**(1): 76-82.

Lefton-Greif, M. A., S. O. Okelo, J. M. Wright, J. M. Collaco, S. A. McGrath-Morrow and M. N. Eakin (2014). "Impact of children's feeding/swallowing problems: validation of a new caregiver instrument." Dysphagia **29**(6): 671-677.

Legrand, C., L. Michaud, D. Neut, R. Sfeir, C. Thumerelle, M. Bonnevalle, D. Turck and F. Gottrand (2010). "Long term outcome of children with esophageal atresia." Journal of Pediatric Gastroenterology and Nutrition **50**(SUPPL. 2): E133-E134.

Legrand, C., L. Michaud, J. Salleron, D. Neut, R. Sfeir, C. Thumerelle, M. Bonnevalle, D. Turck and F. Gottrand (2012). "Long-term outcome of children with oesophageal atresia type III." Archives of disease in childhood **97**(9): 808-811.

Lejeune, S., R. Sfeir, V. Rousseau, A. Bonnard, T. Gelas, M. Aumar, N. Panait, P.-Y. Rabattu, S. Irtan and V. Fouquet (2021). "Esophageal atresia and respiratory morbidity." Pediatrics **148**(3).

Lemoine, C., A. Aspirot, G. Le Henaff, H. Piloquet, D. Levesque and C. Faure (2013). "Characterization of esophageal motility following esophageal atresia repair using high-resolution esophageal manometry." Journal of pediatric gastroenterology and nutrition **56**(6): 609-614.

Lévesque, D., R. Baird and J.-M. Laberge (2013). "Refractory strictures post-esophageal atresia repair: what are the alternatives?" Diseases of the Esophagus **26**(4): 382-387.

Lindahl, H. and R. Rintala (1995). "Long-term complications in cases of isolated esophageal atresia treated with esophageal anastomosis." Journal of pediatric surgery **30**(8): 1222-1223.

Lloyd, J., G. Bjornstad, A. Borek, B. Cuffe-Fuller, M. Fredlund, A. McDonald, M. Tarrant, V. Berry, K. Wilkinson and S. Mitchell (2021). "Healthy Parent Carers programme: mixed methods process evaluation and refinement of a health promotion intervention." BMJ open **11**(8): e045570.

Lockwood, C., Z. Munn and K. Porritt (2015). "Qualitative research synthesis: methodological guidance for systematic reviewers utilizing meta-aggregation." JBI Evidence Implementation **13**(3): 179-187.

Londahl, M., A. L. Irace, K. Kawai, N. D. Dombrowski, R. Jennings and R. Rahbar (2018). "Prevalence of Laryngeal Cleft in Pediatric Patients With Esophageal Atresia." JAMA **144**(2): 164-168.

Löwe, B., K. Kroenke and K. Gräfe (2005). "Detecting and monitoring depression with a two-item questionnaire (PHQ-2)." Journal of Psychosomatic Research **58**(2): 163-171.

Mahoney, L. and R. Rosen (2017). "Feeding Problems and Their Underlying Mechanisms in the Esophageal Atresia-Tracheoesophageal Fistula Patient." Front Pediatr **5**: 127.

Manikam, R. and J. A. Perman (2000). "Pediatric feeding disorders." Journal of clinical gastroenterology **30**(1): 34-46.

Martin-Harris, B., M. B. Brodsky, Y. Michel, D. O. Castell, M. Schleicher, J. Sandidge, R. Maxwell and J. Blair (2008). "MBS measurement tool for swallow impairment--MBSImp: establishing a standard." Dysphagia **23**(4): 392-405.

Martin-Harris, B., K. A. Carson, J. M. Pinto and M. A. Lefton-Greif (2020). "BaByVFSSImP© a novel measurement tool for videofluoroscopic assessment of swallowing impairment in bottle-fed babies: establishing a standard." Dysphagia **35**: 90-98.

Mathisen, B., L. Worrall, J. Masel, C. Wall and R. Shepherd (1999). "Feeding problems in infants with gastro-oesophageal reflux disease: a controlled study." Journal of paediatrics and child health **35**(2): 163-169.

Maxwell, J. A., M. Chmiel and S. E. Rogers (2015). Designing integration in multimethod and mixed methods research. The Oxford handbook of multimethod and mixed methods reasearch inquiry. S. N. Hesse-Biber and R. B. Johnson. Oxford, Oxford University Press**:** 223-229.

Maybee, J., J. Deck, E. Jensen, A. Ruiz, S. Kinder and E. DeBoer (2023). "Feeding and Swallowing Characteristics of Children With Esophageal Atresia and Tracheoesophageal Fistula." Journal of Pediatric Gastroenterology and Nutrition **76**(3).

Mayerl, C. J., C. E. Edmonds, E. A. Catchpole, A. M. Myrla, F. D. Gould, L. E. Bond, B. M. Stricklen and R. Z. German (2020). "Sucking versus swallowing coordination, integration, and performance in preterm and term infants." Journal of Applied Physiology **129**(6): 1383-1392.

McGrattan, K. E., H. McGhee, A. DeToma, E. G. Hill, S. C. Zyblewski, M. Lefton-Greif, L. Halstead, S. M. Bradley and B. Martin-Harris (2017). "Dysphagia in infants with single ventricle anatomy following stage 1 palliation: Physiologic correlates and response to treatment." Congenit Heart Dis **12**(3): 382-388.

McGrattan, K. E., H. C. McGhee, K. L. McKelvey, C. S. Clemmens, E. G. Hill, A. DeToma, J. G. Hill, C. E. Simmons and B. Martin-Harris (2020).

"Capturing infant swallow impairment on videofluoroscopy: timing matters." Pediatric radiology **50**: 199-206.

McHorney, C. A., J. Robbins, K. Lomax, J. C. Rosenbek, K. Chignell, A. E. Kramer and D. Earl Bricker (2002). "The SWAL–QOL and SWAL–CARE outcomes tool for oropharyngeal dysphagia in adults: III. Documentation of reliability and validity." Dysphagia **17**: 97-114.

Medoff-Cooper, B., M. Naim, D. Torowicz and A. Mott (2010). "Feeding, growth, and nutrition in children with congenitally malformed hearts." Cardiol Young **20 Suppl 3**: 149-153.

Menzies, J. and J. Hughes (2020). "Parental feeding concerns of infants and young children with oesophageal atresia." Journal of paediatrics and child health **56**(11): 1791-1794.

Menzies, J., J. Hughes, S. Leach, Y. Belessis and U. Krishnan (2017). "Prevalence of Malnutrition and Feeding Difficulties in Children With Esophageal Atresia." Journal of pediatric gastroenterology and nutrition **64**(4): e100-e105.

Mikkelsen, A., U. I. Moinichen, H. M. Reims, K. Grzyb, L. Aabakken, L. Morkrid, H. Ijsselstijn and R. Emblem (2022). "Clinical variables as indicative factors for endoscopy in adolescents with esophageal atresia." Journal of pediatric surgery(jmj, 0052631).

Miles, A., I. Dharmarathna, L. Fuller, M. Jardine and J. Allen (2022). "Developing a protocol for quantitative analysis of liquid swallowing in children." American Journal of Speech-Language Pathology **31**(3): 1244-1263.

Miller, A. J. (2008). "The neurobiology of swallowing and dysphagia." Developmental disabilities research reviews **14**(2): 77-86.

Miller, A. L., C. K. Miller, L. Fei, Q. Sun, J. P. Willging, A. de Alarcon and S. P. Pentiuk (2024). "Predictive Value of Laryngeal Penetration to Aspiration in a Cohort of Pediatric Patients." Dysphagia **39**(1): 33-42.

Miller, C. K., J. Reynolds, L. N. Kelchner, D. Scarborough, S. Langmore and M. Gosa (2023). "Tutorial on clinical practice for use of the fiberoptic endoscopic evaluation of swallowing procedure with pediatric populations: part 2." American Journal of Speech-Language Pathology **32**(1): 55-82.

Miller, C. K. and J. P. Willging (2020). "Fiberoptic endoscopic evaluation of swallowing in infants and children: protocol, safety, and clinical efficacy: 25 years of experience." Annals of Otology, Rhinology & Laryngology **129**(5): 469-481.

Mittal, R. (2011). "Motor function of the pharynx, esophagus, and its sphincters."

Mizuno, K., Y. Nishida, M. Taki, S. Hibino, M. Murase, M. Sakurai and K. Itabashi (2007). "Infants with bronchopulmonary dysplasia suckle with weak pressures to maintain breathing during feeding." Pediatrics **120**(4): e1035-e1042.

Mokhlesin, M., A. Ebadi, F. Yadegari and Z. S. Ghoreishi (2024). "Translation and Psychometric Properties of the Persian Version of the Feeding/Swallowing Impact Survey in Iranian Mothers." Folia Phoniatr Logop **76**(1): 22-29.

Montgomery, M., H. Witt, R. Kuylenstierna and B. Frenckner (1998). "Swallowing disorders after esophageal atresia evaluated with videomanometry." Journal of pediatric surgery **33**(8): 1219-1223.

Morgan, D. L. (2013). Integrating qualitative and quantitative methods: A pragmatic approach, Sage publications.

Morton, K., L. Marino, J. Pappachan and A. Darlington (2019). "Feeding difficulties in young paediatric intensive care survivors: a scoping review." Clinical nutrition ESPEN **30**: 1-9.

Moseholm, E. and M. D. Fetters (2017). "Conceptual models to guide integration during analysis in convergent mixed methods studies." Methodological Innovations **10**(2): 2059799117703118.

Mukumbang, F. C. (2021). "Retroductive Theorizing: A Contribution of Critical Realism to Mixed Methods Research." Journal of Mixed Methods Research **17**(1): 93-114.

Mungali, I. (2005). "Trend towards centralisation of hospital services, and its effect on access to care for rural and remote communities in the UK." Rural and Remote Health **5**(2): 1-8.

Neille, J. and G. Selikson (2021). ""I was always struggling": Caregivers' experiences of transitioning a child from oral to long-term non-oral feeding at an out-patient hospital clinic in South Africa." Child Care Health Dev **47**(5): 705-712.

Neubauer, B. E., C. T. Witkop and L. Varpio (2019). "How phenomenology can help us learn from the experiences of others." Perspect Med Educ **8**(2): 90-97.

Nicklaus, S. (2020). "Eating and drinking in childhood." Handbook of Eating and Drinking: Interdisciplinary Perspectives: 391-412.

Nikaki, K., J. L. S. Ooi and D. Sifrim (2016). "Chicago classification of esophageal motility disorders: applications and limits in adults and pediatric patients with esophageal symptoms." Current gastroenterology reports **18**: 1-14.

Nordin, M. and S. Nordin (2013). "Psychometric evaluation and normative data of the Swedish version of the 10-item perceived stress scale." Scand J Psychol **54**(6): 502-507.

Nouraei, S. A., E. Makmur, A. Dias, C. R. Butler, R. Nandi, M. J. Elliott and R. Hewitt (2017). "Validation of the Airway-Dyspnoea-Voice-Swallow (ADVS) scale and Patient-Reported Outcome Measure (PROM) as disease-specific instruments in paediatric laryngotracheal stenosis." Clin Otolaryngol **42**(2): 283-294.

Nurminen, P., A. Koivusalo, M. Hukkinen and M. Pakarinen (2019). "Pneumonia after Repair of Esophageal Atresia-Incidence and Main Risk Factors." Eur J Pediatr Surg **29**(6): 504-509.

O'Connor, E. and B. Jaffray (2022). "Surgeon-Level Variation in Outcome following Esophageal Atresia Repair Is Not Explained by Volume." European Journal of Pediatric Surgery **32**(02): 160-169.

O'Rourke, A., K. Humphries, A. Lazar and B. Martin-Harris (2017). "The pharyngeal contractile integral is a useful indicator of pharyngeal swallowing impairment." Neurogastroenterology & Motility **29**(12): e13144.

Omari, T. (2023). Swallow Gateway for High Resolution Pharyngeal and Esophageal Manometry. . Flinders online learning, Flinders Univeristy.

Omari, T., C. Cock, P. Wu, M. M. Szczesniak, M. Schar, J. Tack and N. Rommel (2023). "Using high resolution manometry impedance to diagnose upper esophageal sphincter and pharyngeal motor disorders." Neurogastroenterology & Motility **35**(1): e14461.

Omari, T., N. Rommel, T. Jan, M. Szczesniak, P. Wu, M. Schar, S. Doeltgen and C. Cock (2022). "Transient hypopharyngeal intrabolus pressurization patterns: Clinically relevant or normal variant?" Neurogastroenterology & Motility **34**(6): e14276.

Omari, T., A. Snel, C. Barnett, G. Davidson, R. Haslam and J. Dent (1999). "Measurement of upper esophageal sphincter tone and relaxation during swallowing in premature infants." American Journal of Physiology-Gastrointestinal and Liver Physiology **277**(4): G862-G866.

Omari, T. I., M. Ciucci, K. Gozdzikowska, E. Hernandez, K. Hutcheson, C. Jones, J. Maclean, N. Nativ-Zeltzer, E. Plowman, N. Rogus-Pulia, N. Rommel and A. O'Rourke (2020). "High-Resolution Pharyngeal Manometry and Impedance: Protocols and Metrics-Recommendations of a High-Resolution Pharyngeal Manometry International Working Group." Dysphagia **35**(2): 281-295.

Omari, T. I. and U. Krishnan (2020). "What is the role of high-resolution oesophageal manometry in paediatrics?" Journal of Paediatrics and Child Health **56**(11): 1754-1759.

Organization, W. H. (2007). International Classification of Functioning, Disability, and Health: Children & Youth Version: ICF-CY, World Health Organization.

Palmer, P. M., A. H. Padilla, S. C. Murray, M. Rashidi, A. Martinez-Fisher and T. Winter (2024). "The Impact of Videofluoroscopic Pulse Rate on Duration and Kinematic Measures in Infants and Adults with Feeding and Swallowing Disorders." Dysphagia: 1-14.

Pandolfino, J. E. and W. J. Bulsiewicz (2009). "Evaluation of esophageal motor disorders in the era of high-resolution manometry and intraluminal impedance." Current gastroenterology reports **11**(3): 182-189.

Parahoo, K. (2014). Nursing research: principles, process and issues, Bloomsbury Publishing.

Parrish, M. (1997). "Family adaptation to a child's feeding and swallowing disorder: a social work perspective." Seminars in Speech and Language **18**(1): 71-78.

Pavithran, J., I. V. Puthiyottil, M. Narayan, S. Vidhyadharan, J. R. Menon and S. Iyer (2019). "Observations from a pediatric dysphagia clinic: Characteristics of children at risk of aspiration pneumonia." Laryngoscope **129**(11): 2614-2618.

Pedersen, R. N., S. Markow, S. Kruse-Andersen, N. Qvist, T. P. Hansen, O. Gerke, R. G. Nielsen, L. Rasmussen and S. Husby (2013). "Esophageal atresia: gastroesophageal functional follow-up in 5-15 year old children." Journal of pediatric surgery **48**(12): 2487-2495.

Pham, A., E. Ecochard-Dugelay, A. Bonnard, E. Le Roux, T. Gelas, V. Rousseau, N. Thomassin, I. Cabon-Boudard, A. Nicolas, A. Guinot, J. Rebeuh, A. Le Mandat, D. D. Djeddi, V. Fouquet, A. Boucharny, S. Irtan, J. Lemale, A. Comte, L. Bridoux-Henno, C. Dupont-Lucas, G. Dimitrov, A. Turquet, C. Borderon, C. Pelatan, E. Chaillou Legault, C. Jung, S. Willot, L. Montalva, D. Mitanchez, F. Gottrand and M. Bellaiche (2022). "Feeding disorders in children with oesophageal atresia: a cross-sectional study." Arch Dis Child **107**(1): 52-58.

Pierrehumbert, B., A. Nicole, C. Muller-Nix, M. Forcada-Guex and F. Ansermet (2003). "Parental post-traumatic reactions after premature birth: implications for sleeping and eating problems in the infant." Archives of Disease in Childhood-Fetal and Neonatal Edition **88**(5): 400-404.

Pizzorni, N., S. Rocca, A. Eplite, M. Monticelli, S. Rama, F. Mozzanica, L. Scarponi and A. Schindler (2024). "Fiberoptic endoscopic evaluation of swallowing (FEES) in pediatrics: A systematic review." International Journal of Pediatric Otorhinolaryngology: 111983.

Platt, J. M., A. Nettel-Aguirre, C. L. Bjornson, I. Mitchell, K. Davis and J. M. Bailey (2023). "Multidisciplinary coordination of care for children with

esophageal atresia and tracheoesophageal fistula." Journal of Child Health Care: 13674935231174503.

Pontoppidan, M., M. Thorsager, M. Friis-Hansen, A. Slade and L. S. Sadler (2022). "Minding the Baby versus usual care: study protocol for a quasi-cluster-randomized controlled study in Denmark of an early interdisciplinary home-visiting intervention for families at increased risk for adversity." Trials **23**(1): 529.

Porcaro, F., L. Valfre, L. R. Aufiero, L. Dall'Oglio, P. De Angelis, A. Villani, P. Bagolan, S. Bottero and R. Cutrera (2017). "Respiratory problems in children with esophageal atresia and tracheoesophageal fistula." Ital J Pediatr **43**(1): 77.

Presse, N., J. Taillefer, S. Maynard and M. Bouin (2016). "Insufficient Body Weight of Adults Born With Esophageal Atresia." Journal of pediatric gastroenterology and nutrition **62**(3): 469-473.

Pulham, R. A., J. Wray, Y. Feinstein, K. Brown, C. Pierce, S. Nadel, N. Pathan, E. Garralda and P. Ramnarayan (2019). "Feasibility and acceptability of methods to collect follow-up information from parents 12 months after their child's emergency admission to pediatric intensive care." Pediatric Critical Care Medicine **20**(4): e199-e207.

Puntis, J. W., D. G. Ritson, C. E. Holden and R. G. Buick (1990). "Growth and feeding problems after repair of oesophageal atresia." Archives of disease in childhood **65**(1): 84-88.

Rabone, C. and V. Wallace (2021). "A thematic analysis exploring the psychological well-being of adults born with esophageal atresia." Journal of psychosomatic research **145**(0376333, juv): 110474.

Rakap, S. and M. Vural-Batik (2024). "Mitigating the impact of family burden on psychological health in parents of children with special needs: Buffering effects of resilience and social support." Journal of Applied Research in Intellectual Disabilities **37**(1): e13179.

Rama, C. G., F. B. Bernardes, M. A. Lefton-Greif, D. S. Levy and V. L. Bosa (2022). "Translation, cultural adaptation, reliability, and validity evidence of the Feeding/Swallowing Impact Survey (FS–IS) to Brazilian Portuguese." Dysphagia: 1-12.

Ramsay, M., C. Martel, M. Porporino and C. Zygmuntowicz (2011). "The Montreal Children's Hospital Feeding Scale: A brief bilingual screening tool for identifying feeding problems." Paediatrics & child health **16**(3): 147-e117.

Rayyan, M. (2020). Characterizing the esophageal function of infants in the NICU. Doctor in Biomedical Sciences, KU Leuven.

Rayyan, M., M. Embrechts, H. Van Veer, R. Aerts, I. Hoffman, M. Proesmans, K. Allegaert, G. Naulaers and N. Rommel (2019). "Neonatal

factors predictive for respiratory and gastro-intestinal morbidity after esophageal atresia repair." Pediatr Neonatol **60**(3): 261-269.

Rayyan, M., T. Omari, V. Cossey, K. Allegaert and N. Rommel (2022). "Characterizing Esophageal Motility in Neonatal Intensive Care Unit Patients Using High Resolution Manometry." Frontiers in Pediatrics **10**: 806072.

Rayyan, M., T. Omari, G. Naulaers, R. Aerts, K. Allegaert and N. Rommel (2020). "Maturation of esophageal motility and esophagogastric junction in preterm infants." Neonatology **117**(4): 495-503.

Re, G. L., F. Vernuccio, M. Di Vittorio, L. Scopelliti, A. Di Piazza, M. Terranova, D. Picone, C. Tudisca and S. Salerno (2019). "Swallowing evaluation with videofluoroscopy in the paediatric population." Acta Otorhinolaryngologica Italica **39**(5): 279.

Regmi, P. R., E. Waithaka, A. Paudyal, P. Simkhada and E. van Teijilingen (2016). "Guide to the design and application of online quesitonnaire surveys." Nepal Journal of Epidemiology **6**(4): 640-644.

Reid, K. and D. Berle (2020). "Parental trajectories of PTSD and child adjustment: Findings from the Building a New Life in Australia study." American Journal of Orthopsychiatry **90**(2): 288.

Reilly, S., D. Skuse, B. Mathisen and D. Wolke (1995). "The objective rating of oral-motor functions during feeding." Dysphagia **10**: 177-191.

Rodriguez-Rey, R., J. Alonso-Tapia and G. Colville (2018). "Prediction of parental posttraumatic stress, anxiety and depression after a child's critical hospitalization." J Crit Care **45**: 149-155.

Rogers, S., M. Ramsay and J. Blissett (2018). "The Montreal Children's Hospital Feeding Scale: Relationships with parental report of child eating behaviours and observed feeding interactions." Appetite **125**: 201-209.

Rolle, U. and A. J. Burns (2017). "Vascular, Neurological and Functional Development of the Oesophagus." Esophageal and Gastric Disorders in Infancy and Childhood: 73-76.

Romeo, G., B. Zuccarello, F. Proietto and C. Romeo (1987). "Disorders of the esophageal motor activity in atresia of the esophagus." Journal of pediatric surgery **22**(2): 120-124.

Rommel, N., C. Borgers, D. Van Beckevoort, A. Goeleven, E. Dejaeger and T. I. Omari (2015). "Bolus residue scale: an easy-to-use and reliable videofluoroscopic analysis tool to score bolus residue in patients with dysphagia." International journal of otolaryngology **2015**.

Roorda, D., A. Van Der Steeg, M. Van Dijk, J. Derikx, R. Gorter, J. Rotteveel, J. van Goudoever, L. van Heurn, J. Oosterlaan and L. Haverman (2022). "Distress and post-traumatic stress in parents of patients with congenital

gastrointestinal malformations: a cross-sectional cohort study." Orphanet Journal of Rare Diseases **17**(1): 353.

Rosen, R., J. M. Garza, N. Tipnis and S. Nurko (2018). "An ANMS-NASPGHAN consensus document on esophageal and antroduodenal manometry in children." Neurogastroenterology & Motility **30**(3): e13239.

Rosen, R., Y. Vandenplas, M. Singendonk, M. Cabana, C. DiLorenzo, F. Gottrand, S. Gupta, M. Langendam, A. Staiano and N. Thapar (2018). "Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition." Journal of pediatric gastroenterology and nutrition **66**(3): 516-554.

Rosen, R. D. and R. Winters (2023). Physiology, Lower Esophageal Sphincter, StatPearls Publishing, Treasure Island (FL).

Rosenbek, J. C., J. A. Robbins, E. B. Roecker, J. L. Coyle and J. L. Wood (1996). "A penetration-aspiration scale." Dysphagia **11**: 93-98.

Sadreameli, S. C. and S. A. McGrath-Morrow (2016). "Respiratory Care of Infants and Children with Congenital Tracheo-Oesophageal Fistula and Oesophageal Atresia." Paediatr Respir Rev **17**: 16-23.

Salvatori, P., F. Andrei, E. Neri, I. Chirico and E. Trombini (2015). "Pattern of mother-child feeding interactions in preterm and term dyads at 18 and 24 months." Front Psychol **6**: 1245.

Satter, E. (1990). "The feeding relationship: problems and interventions." The Journal of pediatrics **117**(2): S181-S189.

Schier, F., S. Korn and E. Michel (2001). "Experiences of a parent support group with the long-term consequences of esophageal atresia." Journal of pediatric surgery **36**(4): 605-610.

Schofield, M. J. and C. Forrester-Knauss (2013). Surveys and questionnaires in health research. South Melbourne, Victoria, Australia, Oxford University Press.

Scott, J. K., S. D. Leary, A. R. Ness, J. R. Sandy, M. Persson, N. Kilpatrick and A. E. Waylen (2014). "Centralization of services for children born with orofacial clefts in the United Kingdom: a cross-sectional survey." The Cleft Palate-Craniofacial Journal **51**(5): 102-109.

Sdravou, K., E. Emmanouilidou-Fotoulaki, A. Printza, E. Andreoulakis, S. Beropouli, G. Makris and M. Fotoulaki (2021). Factors associated with feeding problems in young children with gastrointestinal diseases. Healthcare, MDPI.

Sedgwick, P. (2013). "Questionnaire surveys: sources of bias." Bmj **347**.

Serel Arslan, S. (2022). "Swallowing Related Problems of Toddlers with Down Syndrome." J Dev Phys Disabil: 1-11.

Serel Arslan, S., N. Demir, A. Barak Dolgun and A. Karaduman (2016). "Development of a new instrument for determining the level of chewing function in children." Journal of oral rehabilitation **43**(7): 488-495.

Serel Arslan, S., N. Demir, A. A. Karaduman and P. C. Belafsky (2018). "The Pediatric Version of the Eating Assessment Tool: a caregiver administered dyphagia-specific outcome instrument for children." Disabil Rehabil **40**(17): 2088-2092.

Serel Arslan, S., N. Demir, A. A. Karaduman, F. C. Tanyel and T. Soyer (2018). "Chewing Function in Children with Repaired Esophageal Atresia-Tracheoesophageal Fistula." Eur J Pediatr Surg **28**(6): 534-538.

Serel Arslan, S., N. Demir, A. A. Karaduman, F. C. Tanyel and T. Soyer (2020). "Assessment of the Concerns of Caregivers of Children with Repaired Esophageal Atresia-Tracheoesophageal Fistula Related to Feeding-Swallowing Difficulties." Dysphagia **35**(3): 438-442.

Serel Arslan, S., H. E. Kılınç, Ö. F. Yaşaroğlu, Ö. İnal, N. Demir and A. A. Karaduman (2018). "Reliability and validity of the Turkish version of the Feeding/Swallowing Impact Survey." Journal of Developmental and Physical Disabilities **30**: 723-733.

Serel Arslan, S., T. Soyer, N. Demir, S. Yalcin, A. Karaduman, I. Karnak and F. C. Tanyel (2017). "Effect of Swallowing Rehabilitation Protocol on Swallowing Function in Patients with Esophageal Atresia and/or Tracheoesophageal Fistula." European Journal of Pediatric Surgery **27**(6): 526-532.

Sfeir, R., A. Bonnard, N. Khen-Dunlop, F. Auber, T. Gelas, L. Michaud, G. Podevin, A. Breton, V. Fouquet, C. Piolat, J. L. Lemelle, T. Petit, F. Lavrand, F. Becmeur, M. L. Polimerol, J. L. Michel, F. Elbaz, E. Habonimana, H. Allal, E. Lopez, H. Lardy, M. Morineau, C. Pelatan, T. Merrot, P. Delagausie, P. de Vries, G. Levard, P. Buisson, E. Sapin, O. Jaby, C. Borderon, D. Weil, S. Gueiss, D. Aubert, A. Echaieb, L. Fourcade, J. Breaud, C. Laplace, M. Pouzac, A. Duhamel and F. Gottrand (2013). "Esophageal atresia: data from a national cohort." J Pediatr Surg **48**(8): 1664-1669.

Sharp, W. G., A. Silverman, J. C. Arvedson, N. F. Bandstra, E. Clawson, R. C. Berry, B. O. McElhanon, A. M. Kozlowski, M. Katz and V. M. Volkert (2022). "Toward better understanding of pediatric feeding disorder: a proposed framework for patient characterization." Journal of pediatric gastroenterology and nutrition **75**(3): 351-355.

Sheppard, J. J., R. Hochman and C. Baer (2014). "The dysphagia disorder survey: validation of an assessment for swallowing and feeding function in developmental disability." Research in developmental disabilities **35**(5): 929-942.

Shieh, H. F. and R. W. Jennings (2017). Long-gap esophageal atresia. Seminars in pediatric surgery, Elsevier.

Silverman, A. H., G. Erato and P. Goday (2021). "The relationship between chronic paediatric feeding disorders and caregiver stress." J Child Health Care **25**(1): 69-80.

Simione, M., S. Harshman, C. E. Cooper-Vince, K. Daigle, J. Sorbo, K. Kuhlthau and L. Fiechtner (2023). "Examining Health Conditions, Impairments, and Quality of Life for Pediatric Feeding Disorders." Dysphagia **38**(1): 220-226.

Singendonk, M., S. Kritas, C. Cock, L. Ferris, L. McCall, N. Rommel, M. Van Wijk, M. Benninga, D. Moore and T. Omari (2014). "Applying the Chicago Classification criteria of esophageal motility to a pediatric cohort: effects of patient age and size." Neurogastroenterology & Motility **26**(9): 1333-1341.

Singendonk, M. M., L. F. Ferris, L. McCall, G. Seiboth, K. Lowe, D. Moore, P. Hammond, R. Couper, R. Abu-Assi and C. Cock (2020). "High-resolution esophageal manometry in pediatrics: Effect of esophageal length on diagnostic measures." Neurogastroenterology & Motility **32**(1): e13721.

Singh, S. and S. Hamdy (2005). "The upper oesophageal sphincter." Neurogastroenterology & Motility **17**: 3-12.

Sintusek, P., M. Mutalib and N. Thapar (2023). "Gastroesophageal reflux disease in children: What's new right now?" World Journal of Gastrointestinal Endoscopy **15**(3): 84.

Slater, G. and J. Faulkner. (2021). "Towards a holistic model for the treatment of oesophageal atresia." from https://tofs.org.uk/wp-content/uploads/2022/01/TOWARDS-A-HOLISTIC-MODEL-FOR-THE-TREATMENT-OF-OESOPHAGEAL-ATRESIA-final.pdf.

Smith, B. (2018). "Generalizability in qualitative research: Misunderstandings, opportunities and recommendations for the sport and exercise sciences." Qualitative research in sport, exercise and health **10**(1): 137-149.

Smith, B. W., J. Dalen, K. Wiggins, E. Tooley, P. Christopher and J. Bernard (2008). "The brief resilience scale: assessing the ability to bounce back." Int J Behav Med **15**(3): 194-200.

Smith, J. A. (2015). Qualitative psychology: A practical guide to research methods, Sage Publications.

Soyer, T., S. S. Arslan, O. Boybeyi, N. Demir and F. C. Tanyel (2022). "The Role of Oral Feeding Time and Sham Feeding on Oropharyngeal Swallowing Functions in Children with Esophageal Atresia." Dysphagia(8610856, dyy).

Soyer, T., O. Boybeyi, S. Serel Arslan, N. Demir, U. E. Arslan, F. C. Tanyel and S. Kiran (2022). "The cause of dysphagia in patients with esophageal

atresia: a systematic review and meta-analysis." Pediatric surgery international **38**: 1341-1348.

Soyer, T., S. Yalcin, S. S. Arslan, N. Demir and F. C. Tanyel (2017). "Pediatric Eating Assessment Tool-10 as an indicator to predict aspiration in children with esophageal atresia." Journal of Pediatric Surgery **52**(10): 1576-1579.

Sparre, S., G. Zachariassen, S. Husby and K. G. Holm (2022). "Breastfeeding and growth in infants with abdominal wall defects and oesophageal atresia-a prospective case-control study." Journal of Pediatric Gastroenterology and Nutrition **74**(2 Supplement 2): 962-963.

Spitz, L. (2007). "Oesophageal atresia." Orphanet J Rare Dis **2**: 24.

Spitzer, R. L., K. Kroenke, J. B. W. Williams and B. Lowe (2006). "A brief measure for assessing generalized anxiety disorder. The GAD-7." Archives of Internal Medicine **166**(10): 1092-1097.

Staab, J. P., C. S. Fullerton and R. Ursano (2013). A critical look at PTSD: Constructs, concepts, epidemiology, and implications. Response to Disaster, Routledge**:** 101-128.

statistics, O. f. n. (2020). Internet access households and individuals, Great Britain

Steele, C. M., W. A. Alsanei, S. Ayanikalath, C. E. Barbon, J. Chen, J. A. Cichero, K. Coutts, R. O. Dantas, J. Duivestein, L. Giosa, B. Hanson, P. Lam, C. Lecko, C. Leigh, A. Nagy, A. M. Namasivayam, W. V. Nascimento, I. Odendaal, C. H. Smith and H. Wang (2015). "The influence of food texture and liquid consistency modification on swallowing physiology and function: a systematic review." Dysphagia **30**(1): 2-26.

Steele, C. M., M. Peladeau-Pigeon, C. A. Barbon, B. T. Guida, A. M. Namasivayam-MacDonald, W. V. Nascimento, S. Smaoui, M. S. Tapson, T. J. Valenzano and A. A. Waito (2019). Reference values for healthy swallowing across the range from thin to extremely thick liquids, ASHA.

Stehr, P. (2023). "The benefits of supporting others online – How online communication shapes the provision of support and its relationship with wellbeing." Computers in Human Behavior **140**.

Stern, C., L. Lizarondo, J. Carrier, C. Godfrey, K. Rieger, S. Salmond, J. Apostolo, P. Kirkpatrick and H. Loveday (2020). "Methodological guidance for the conduct of mixed methods systematic reviews." JBI Evid Synth **18**(10): 2108-2118.

Stewart, A., C. H. Smith, S. Eaton, P. De Coppi and J. Wray (2021). "COVID-19 pandemic experiences of parents caring for children with oesophageal atresia/tracheo-oesophageal fistula." BMJ Paediatr Open **5**(1): e001077.

Stewart, A., C. H. Smith, R. Govender, S. Eaton, P. De Coppi and J. Wray (2022). "Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula." Journal of pediatric surgery **57**(12): 792-799.

Stewart, A., C. H. Smith, R. Govender, S. Eaton, P. De Coppi and J. Wray (2023). "Qualitative research: A different option on the menu." Journal of Pediatric Surgery **58**(4): 782-783.

Strauss, A. and J. Corbin (1998). "Basics of qualitative research techniques."

Strychowsky, J. E., P. Dodrill, E. Moritz, J. Perez and R. Rahbar (2016). "Swallowing dysfunction among patients with laryngeal cleft: more than just aspiration?" International journal of pediatric otorhinolaryngology **82**: 38-42.

Sundler, A. J., E. Lindberg, C. Nilsson and L. Palmer (2019). "Qualitative thematic analysis based on descriptive phenomenology." Nurs Open **6**(3): 733-739.

Svoboda, E., J. Fruithof, A. Widenmann-Grolig, G. Slater, F. Armand, B. Warner, S. Eaton, P. De Coppi and E. Hannon (2018). "A patient led, international study of long term outcomes of esophageal atresia: EAT 1." Journal of Pediatric Surgery **53**(4): 610-615.

Tambucci, R., G. Angelino, P. De Angelis, F. Torroni, T. Caldaro, V. Balassone, A. C. Contini, E. Romeo, F. Rea, S. Faraci, G. Federici di Abriola and L. Dall'Oglio (2017). "Anastomotic Strictures after Esophageal Atresia Repair: Incidence, Investigations, and Management, Including Treatment of Refractory and Recurrent Strictures." Front Pediatr **5**: 120.

Tan, J., N. Cocks and M. Claessen (2021). "Mothers' perspectives of support for their child with feeding/swallowing disorders." Speech, Language and Hearing **25**(1): 17-28.

Tan Tanny, S. P., N. D. Senior, A. Comella, L. McCall, J. M. Hutson, S. Finch, M. Safe, W. J. Teague, T. I. Omari and S. K. King (2024). "Esophago-gastric junction findings on high resolution impedance manometry in children with esophageal atresia." Journal of Pediatric Gastroenterology and Nutrition.

Tan Tanny, S. P., M. Trajanovska, F. Muscara, J. M. Hutson, S. Hearps, T. I. Omari, W. J. Teague and S. K. King (2021). "Quality of Life Outcomes in Primary Caregivers of Children with Esophageal Atresia." J Pediatr **238**: 80-86 e83.

Tan, Y., J. Zhang, J. Zhou, T. Duan and D. Liu (2015). "Endoscopic Incision for the Treatment of Refractory Esophageal Anastomotic Strictures in Children." Journal of pediatric gastroenterology and nutrition **61**(3): 319-322.

Tanaka, N., K. Nohara, A. Ueda, T. Katayama, M. Ushio, N. Fujii and T. Sakai (2019). "Effect of aspiration on the lungs in children: a comparison using chest computed tomography findings." BMC Pediatr **19**(1): 162.

Tang, T. C., S. T. Leach and U. Krishnan (2024). "Proton pump inhibitors, antibiotics, and atopy increase the risk of eosinophilic esophagitis in children with esophageal atresia." Journal of Pediatric Gastroenterology and Nutrition.

Taylor, A. C. F., K. J. Breen, A. Auldist, A. Catto-Smith, T. Clarnette, J. Crameri, R. Taylor, S. Nagarajah, J. Brady and K. Stokes (2007). "Gastroesophageal reflux and related pathology in adults who were born with esophageal atresia: a long-term follow-up study." Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association **5**(6): 702-706.

Teague, W. J. and J. Karpelowsky (2016). "Surgical management of oesophageal atresia." Paediatric respiratory reviews **19**: 10-15.

Ten Kate, C. A., N. M. Teunissen, J. van Rosmalen, L. S. Kamphuis, M. P. van Wijk, M. Joosten, E. S. van Tuyll van Serooskerken, R. Wijnen, H. IJsselstijn and A. B. Rietman (2023). "Development and validation of a condition-specific quality of life instrument for adults with esophageal atresia: the SQEA questionnaire." Diseases of the Esophagus **36**(6): doac088.

Thompson, K., B. Zendejas, W. J. Svetanoff, B. Labow, A. Taghinia, O. Ganor, M. Manfredi, P. Ngo, C. J. Smithers, T. E. Hamilton and R. W. Jennings (2021). "Evolution, lessons learned, and contemporary outcomes of esophageal replacement with jejunum for children." Surgery (United States) **170**(1): 114-125.

Titgemeyer, S. C. and C. P. Schaaf (2022). "Facebook Support Groups for Pediatric Rare Diseases: Cross-Sectional Study to Investigate Opportunities, Limitations, and Privacy Concerns." JMIR Pediatr Parent **5**(1): e31411.

Tollne, A., T. Nilsson, J. F. Svensson, M. Almström and E. Öst (2024). "Parents' experiences of sham feeding their child with esophageal atresia at home while awaiting reconstructive surgery. A qualitative interview study." Pediatric Surgery International **40**(1): 61.

Tollne, A., E. Öst, T. Nilsson, M. Almström and J. F. Svensson (2024). "Parents caring and sham-feeding their child born with Esophageal atresia at home while waiting for reconstructive surgery." Pediatric Surgery International **40**(1): 257.

Tomaselli, V., M. Volpi, C. Dell'Agnola, M. Bini, A. Rossi and A. Indriolo (2003). "Long-term evaluation of esophageal function in patients treated at birth for esophageal atresia." Pediatric surgery international **19**: 40-43.

Tong, S., K.-a. Mallitt and U. Krishnan (2016). "Evaluation of gastroesophageal reflux by combined multichannel intraluminal impedance and pH monitoring and esophageal motility patterns in children with esophageal atresia." European Journal of Pediatric Surgery **26**(04): 322-331.

Torres-Silva, C. A. (2018). "Chronic Pulmonary Aspiration in Children: Diagnosis and Management." CURRENT PROBLEMS IN PEDIATRIC AND ADOLESCENT HEALTH CARE **48**(3): 74-81.

Traini, I., S. Y. Chan, J. Menzies, J. Hughes, M. J. Coffey, T. Katz, I. R. McKay, C. Y. Ooi, S. T. Leach and U. Krishnan (2022). "Evaluating the Dietary Intake of Children With Esophageal Atresia: A Prospective, Controlled, Observational Study." Journal of pediatric gastroenterology and nutrition **75**(2): 221-226.

Traini, I., J. Menzies, J. Hughes, S. T. Leach and U. Krishnan (2020). "Oesophageal atresia: The growth gap." World J Gastroenterol **26**(12): 1262-1272.

Ure, B. M., E. Slany, E. P. Eypasch, M. Gharib, A. M. Holschneider and H. Troidl (1995). "Long-term functional results and quality of life after colon interposition for long-gap oesophageal atresia." European journal of pediatric surgery : official journal of Austrian Association of Pediatric Surgery ... [et al] = Zeitschrift fur Kinderchirurgie **5**(4): 206-210.

Urichuk, M., C. Singh, A. Zrinyi, S. A. L. Min and R. Keijzer (2024). "Mental Health Outcomes of Mothers of Children With Congenital Gastrointestinal Anomalies Are Similar to Control Mothers: A Longitudinal Retrospective Cohort Study." Journal of Pediatric Surgery.

Uswitch. (2024). "UK mobile phone statistics, 2023." Retrieved 26 Feb 2024, from https://www.uswitch.com/mobiles/studies/mobile-statistics/#:~:text=A%20breakdown%20of%20UK%20age,80%25%20aged%2065%20and%20above.

Van der Zee, D. C., P. Bagolan, C. Faure, F. Gottrand, R. Jennings, J.-M. Laberge, M. H. Martinez Ferro, B. Parmentier, R. Sfeir and W. Teague (2017). "Position paper of INoEA working group on long-gap esophageal atresia: for better care." Frontiers in pediatrics **5**: 63.

Van Lennep, M., U. Krishnan, R. Saoji and M. P. Van Wijk (2019). "Fundoplications in patients born with esophageal atresia: Preoperative workup and evaluation of postoperative symptoms." Diseases of the Esophagus **32**(Supplement 1): 37.

van Lennep, M., M. M. J. Singendonk, L. Dall'Oglio, F. Gottrand, U. Krishnan, S. W. J. Terheggen-Lagro, T. I. Omari, M. A. Benninga and M. P. van Wijk (2019). "Oesophageal atresia." Nat Rev Dis Primers **5**(1): 26.

van Tuyll van Serooskerken, E. S., M. Y. A. Lindeboom, J. W. Verweij, D. C. van der Zee and S. H. A. J. Tytgat (2021). "Childhood outcome after correction of long-gap esophageal atresia by thoracoscopic external traction technique." Journal of pediatric surgery **56**(10): 1745-1751.

van Wijk, M., F. Knuppe, T. Omari, J. de Jong and M. Benninga (2013). "Evaluation of gastroesophageal function and mechanisms underlying gastroesophageal reflux in infants and adults born with esophageal atresia." Journal of pediatric surgery **48**(12): 2496-2505.

Velayutham, P., A. L. Irace, K. Kawai, P. Dodrill, J. Perez, M. Londahl, L. Mundy, N. D. Dombrowski and R. Rahbar (2018). "Silent aspiration: who is at risk?" The Laryngoscope **128**(8): 1952-1957.

Vergouwe, F. W., M. Spoel, N. W. van Beelen, S. J. Gischler, R. M. Wijnen, J. van Rosmalen and H. IJsselstijn (2017). "Longitudinal evaluation of growth in oesophageal atresia patients up to 12 years." Archives of Disease in Childhood-Fetal and Neonatal Edition **102**(5): F417-F422.

Wallace, B. C., I. J. Dahabreh, T. A. Trikalinos, J. Lau, P. Trow and C. H. Schmid (2012). "Closing the gap between methodologists and end-users: R as a computational back-end." Journal of statistical software **49**: 1-15.

Wallace, V., K. Honkalampi and M. Korhonen (2022). "Fear, isolation and the importance of support: A qualitative study of parents' experiences of feeding a child born with esophageal atresia." Journal of pediatric nursing **67**(jns, 8607529): e9-e15.

Wallace, V., K. Honkalampi and E. Sheils (2021). "Anxiety and Depression in Parents of Children Born with Esophageal Atresia: An International Online Survey Study." J Pediatr Nurs **60**: 77-82.

Wallis, C., E. Alexopoulou, J. L. Antón-Pacheco, J. M. Bhatt, A. Bush, A. B. Chang, A.-M. Charatsi, C. Coleman, J. Depiazzi and K. Douros (2019). "ERS statement on tracheomalacia and bronchomalacia in children." European Respiratory Journal **54**(3).

Wauters, L., L. Van Oudenhove, M. Selleslagh, T. Vanuytsel, G. Boeckxstaens, J. Tack, T. Omari and N. Rommel (2014). "Balloon dilation of the esophago-gastric junction affects lower and upper esophageal sphincter function in achalasia." Neurogastroenterology & Motility **26**(1): 69-76.

Weir, K., S. McMahon, L. Barry, I. B. Masters and A. Chang (2009). "Clinical signs and symptoms of oropharyngeal aspiration and dysphagia in children." European Respiratory Journal **33**(3): 604-611.

Weir, K., S. McMahon, L. Barry, R. Ware, I. B. Masters and A. B. Chang (2007). "Oropharyngeal aspiration and pneumonia in children." Pediatr Pulmonol **42**(11): 1024-1031.

Weir, K. A., S. McMahon, S. Taylor and A. B. Chang (2011). "Oropharyngeal aspiration and silent aspiration in children." Chest **140**(3): 589-597.

Wilkinson, J. M., D. C. Codipilly and R. P. Wilfahrt (2021). "Dysphagia: evaluation and collaborative management." American family physician **103**(2): 97-106.

Willging, J. P., C. K. Miller and A. P. Cohen (2019). Pediatric dysphagia: Etiologies, diagnosis, and management, Plural Publishing.

Windle, G., K. M. Bennett and J. Noyes (2011). "A methodological review of resilience measurement scales." Health and Quality of Life Outcomes **9**(1): 1-18.

Witt, S., M. Dellenmark-Blom, J. Dingemann, C. Dingemann, B. M. Ure, B. Gomez, M. Bullinger and J. Quitmann (2019). "Quality of Life in Parents of Children Born with Esophageal Atresia." Eur J Pediatr Surg **29**(4): 371-377.

Wray, J., K. Brown, J. Tregay, S. Crowe, R. Knowles, K. Bull and F. Gibson (2018). "Parents' Experiences of Caring for Their Child at the Time of Discharge After Cardiac Surgery and During the Postdischarge Period: Qualitative Study Using an Online Forum." J Med Internet Res **20**(5): e155.

Wray, J., H. Sugarman, L. Davis, C. Butler, D. McIntyre and R. Hewitt (2021). "Improving community-based care for children with a rare condition: The example of long-segment congenital tracheal stenosis and perceptions of health professionals, parents and teachers." International Journal of Pediatric Otorhinolaryngology **143**: 110651.

Yadlapati, R., P. J. Kahrilas, M. R. Fox, A. J. Bredenoord, C. P. Gyawali, S. Roman, A. Babaei, R. K. Mittal, N. Rommel and E. Savarino (2021). "Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©." Neurogastroenterology and motility **33**(1): e14058.

Yalcin, S., N. Demir, S. Serel, T. Soyer and F. C. Tanyel (2015). "The evaluation of deglutition with videofluoroscopy after repair of esophageal atresia and/or tracheoesophageal fistula." Journal of pediatric surgery **50**(11): 1823-1827.

Yasuda, J. L., G. N. Taslitsky, S. J. Staffa, P. D. Ngo, J. Meisner, S. Mohammed, T. Hamilton, B. Zendejas and M. A. Manfredi (2022). "Predictors of enteral tube dependence in pediatric esophageal atresia." Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus(cr5, 8809160).

Zang, J., S. Kiehn, T. Flugel, J. C. Koseki, A. Niessen, S. H. Kim, C. Pflug and J. C. Nienstedt (2022). "Implementation of Pediatric Flexible-Endoscopic Evaluation of Swallowing: A Systematic Review and Recommendations for Future Research." Dysphagia **37**(6): 1822-1838.

Zerbib, F. and T. Omari (2015). "Oesophageal dysphagia: manifestations and diagnosis." Nature reviews Gastroenterology & hepatology **12**(6): 322-331.

Chapter 8. Appendices

Appendix 1. Online forum standard operating procedure

SaFE | Swallowing, Feeding & Eating in children born with OA/TOF

SaFE Standard Operating Procedure: Online Discussion Forum

Aims

An online discussion forum will be established with support from TOFS, the OA/TOF support group, in an attempt to access a wider range of opinions and experiences relating to the parent/carer perceptions of:

1. The impact that COVID-19 has had on the TOFS community.

a) Access to services
b) Access to education
c) Health impacts

2. The impact that OA/TOF related feeding difficulties have on parental well-being.

a) When establishing oral feeding
b) During mealtimes
c) During transition periods e.g. starting nursery, school, gaining independence

Participants

The online forums will be targeted at parents of children born with OA/TOF. A participant information sheet will be provided to ensure parents are fully aware of the purpose of the research, confidentiality and how the results will be used to help them decide whether to take part.

Method:

We will set up a research specific, private Facebook group. We will generate a list of questions, part 1 related to COVID, part 2 related to feeding difficulties. Parents or carers of children with OA/TOF will be invited to participate in an online discussion, sharing their own experiences in response to a set of questions generated by the research team. Questions will be posed 1 at a time. Parents can choose to answer as many or as few questions as they wish. Parents will be asked to provide basic information regarding the age of their child, their relationship to the child, the type of OA and how they are currently fed. This will be used to describe the group characteristics only. Participants would be made aware that the forum is for research purposes and that information they provide will be analysed anonymously. They will need to confirm their consent to this when applying to join the group by agreeing with the following statements:

"I understand that I will provide basic personal information to allow the research team to know who took part in the forum but that they will not be able to identify me by name.

I understand that all my responses will be analysed anonymously. The results of the study will be reported for the forum discussion as a whole and I will not be identified in any report or publication.

I understand that the results of the study will be published and shared with professionals at conferences and in journals and a summary of the results will be available on the TOFS website and shared in the CHEW newsletter.

I understand that information I give in relation to this project in any online posts may be anonymised and directly quoted in publications and presentations."

The Facebook group will be moderated by an individual independent of the research team. They will send anonymised transcripts of the data to the research team. We anticipate that the process will take approximately 3 months.

Roles and responsibilities:

Moderator:

- Support set up of the FaceBook group
- Accept new participants.
- Ensure the group abide by the "rules" (as they would for the TOFS FaceBook group)
- Post new questions. This will involve monitoring activity on the forum and posting questions as they feel is appropriate.
- Send anonymised transcripts to the research team at weekly intervals.
- Send anonymised demographic information to the research team.

The moderator will be paid £750 for their time.

Research team:

- Set up the FaceBook group in collaboration with the moderator.
- Generate the list of questions, with support from the PPI group.
- Analyse the anonymised data.
- Produce summarised findings.
- Disseminate the research findings.

TOFS:

- Support recruitment of the research through advertisement.
- Support dissemination of the research findings.

Analysis and dissemination

The research team will collate online forum responses and undertake a thematic analysis. All data analysis will be conducted by the research team. The results of the study will be published and shared with professionals at conferences and in journals. We will produce summaries of the research for dissemination through social media and TOFS. The results of the study will be reported for the forum discussion as a whole and no individual will be identified in any report or publication. A representative from TOFS will be invited to co-author any publications. TOFS will be acknowledged in all disseminated materials.

Practical set-up of the online forum
The forum will be set up as a separate private group on Facebook that can be accessed through the TOFS facebook page and website. A link to the group will enable further advertising through the research team's network, including twitter. A link to participant information will be made available and potential participants will be encouraged to read this information before joining the forum.

Non-users of Facebook
Recognising the need and importance of being inclusive, it is acknowledged that there may be some groups of potential participants who are less likely to use Facebook or engage with an online forum. Hearing the views of anyone who wants to participate is important, so if there are individuals who want to express their views but do not want to access the online forums they will be able to answer the questions via email.

Registering to take part:
When someone registers their interest in contributing to the online forum they will be asked for some basic demographic information: their age, gender, relationship to the individual with OA/TOF (e.g. parent, patient), ethnicity, age of the child with OA/TOF, location (broad geographical areas), type of OA/TOF, if known and how their child is fed (tube or oral). Forum participants will be given some brief information re: forum conduct and what to do if they are adversely affected by any of the discussion topics. People will be able to join part-way through the forum and will be given the opportunity to read and comment on earlier questions/posts.

Confidentiality:
As the forum will be run through Facebook, forum participants will post responses using their own names (or Facebook name). This personally identifiable information with only be visible to other forum participants and the forum moderators. This is consistent with the method used by other charities for previous research. Forum posts will be sent to the research team weekly - or more frequently if there is a high volume of activity - by the moderators in an anonymised form. The research team will have access to demographic information only about forum participants, and in an anonymous form that does not link to forum posts.

Data protection:
Anonymised transcripts and non-identifiable demographic information will be stored on a password protected computer or encrypted USB. Access will only be granted to members of the research team. Research data will be held for 5 years after project completion.

Moderation/monitoring of the forum:
The moderator would typically view the forum twice per day – once in the morning and once at the end of the day – or more frequently if there is a high volume of activity. Moderators will respond to forum participants on the forum thread as appropriate to keep discussions on topic, to introduce new discussion topics or to ask probing questions in response to previous posts to generate further posts on the same topic or to clarify existing responses. The moderator can contact the research team at any point if they require more information or assistance.

Managing upsetting or offensive forum posts:
The moderator will follow TOFS policies to manage upsetting, offensive or inappropriate forum posts. Participants will be given clear guidance about acceptable forum conduct. Offensive/inappropriate forum posts will be removed in a clear and transparent

way. If a post has to be removed from the forum the moderator will state the reason why and the poster will be invited to repost their comment in a way that it is keeping with the forum policy. If a forum participant repeatedly posts offensive or inappropriate comments on the forum and has been unresponsive to feedback their access to the forum page can be revoked.

What to do if you have concerns about the wellbeing of a forum participant:
Due to the sensitive nature of the discussion topics some forum participants may become distressed or make forum posts that cause moderators to have concerns about their wellbeing. Information about who to contact if forum participants wish to seek support (including contact information for the charity helplines) will be made available in a visible area on the forum page and the moderator should signpost participants as they usually would if they contact them asking for support.

Handling a complaint
It is likely that any complaints will come directly through to TOFS in the first instance or through the forum itself. All complaints should be documented including how it was handled and what the outcome was. <u>This information should be fed back to the research team as soon as possible.</u>

If the complaint relates to the research project:

- Try to ascertain the nature of the complaint and see whether there is anything you can do to rectify the issue in the first instance.

- Ask the participant if they would like to speak to a member of the research team in person and supply contact details for:
    - The Chief Investigators ([redacted] – alex.stewart@gosh.nhs.uk)
    - One of the co-investigators (Jo Wray – [redacted])

- Ask the participant if they would like to speak to someone external to the research team and supply contact details for:
    - The NHS complaints procedure
    - The local Research Ethics Committee

The nature of the complaint should be documented and any action take on the tracker form

If the complaint is unrelated to the research project:

- Encourage the participant to speak directly to the person(s) involved or a senior member of their healthcare team if their complaint relates to their/their child's/other family member's treatment for OA/TOF

- If the participant expresses a reluctance to do so, encourage them to contact their local independent complaints resource (PALS) or go through the NHS complaints procedure

- Document the nature of the complaint and any action taken

Study research staff and collaborators are strongly discouraged from becoming involved in non-research complaints when working on the project. This may cause confusion and delay in getting assistance for the participant and could compromise the researcher's role.

Appendix 2. Online forum participant information sheet

SaFE | Swallowing, Feeding & Eating in children born with OA/TOF

tofs supporting those born unable to swallow

NHS Great Ormond Street Hospital for Children NHS Foundation Trust

UCL

FUNDED BY NIHR | National Institute for Health Research

Information sheet: SaFE online forum

What is SaFE and who is involved?

SaFE is a PhD project being carried out by Alexandra Stewart, a speech and language therapist, alongside a team of researchers at Great Ormond Street Hospital and University College London. The aim is to better understand the swallowing and feeding difficulties that children born with OA and/or TOF experience. This part of the project aims to understand how these feeding and swallowing difficulties impact on parents or carers. Given the extraordinary times we are currently experiencing, we thought it would also be useful to explore the impact that the COVID-19 pandemic is having on those effected by OA/TOF.

What would I be doing if I take part?

We will use a forum on Facebook to gather some preliminary information from parents and carers about their experiences of feeding their child. This information will be used to develop a questionnaire that will further explore these issues. Participants for the questionnaire part of the research will be recruited separately. We will also ask you about the impact that OA/TOF-related issues relating to the COVID -19 pandemic have had on you and your child.

We have developed a set of questions, in collaboration with a project steering group, which you are invited to answer. This is a discussion forum so you are encouraged to read other people's responses and think about whether this has also been your experience or how your experience was different. There are no right or wrong answers. We are very interested in everybody's opinion. It does not matter if your experience is the same or different to other people. You do not have to answer all the questions. You can post multiple responses to each question. You can give as much or as little information as you wish.

If you do not wish to take part in the Facebook forum you can answer the questions by email, by emailing safestudy.tof.oa@gmail.com.

In order to take part you will need to provide some basic information about yourself: your child's age and the type of OA/TOF he or she child has, your gender, your relationship to the child with OA/TOF, the general area that you live and your ethnicity (if you know). This is to make sure that we understand who has taken part in the research. This information will not be linked to your responses.

How is the forum being managed?
The discussion group will be moderated by one of the TOFS Facebook moderators. They will accept new participants to the forum, pose questions and ensure that any posts are appropriate. Offensive or inappropriate posts will be removed and the poster asked to repost in an appropriate manner. The moderator may remove a participant who makes repeated offensive posts.

How is the information I provide going to be used?
The moderator will anonymise all the posts and send a transcript to the research team for analysis. The results of the study will be published and shared with professionals, for example, at conferences and in journals. Results will also be summarised and shared with parents, for example in the TOFS newsletter. The results of the study will be reported for the forum discussion as a whole and no individual will be identified in any report or publication. However, individual quotes may be used anonymously.

The information will be used by the SaFE project team to design a questionnaire so that we can explore the impact on parents and carers in greater depth. We hope that this information will help professionals and others supporting people effected by OA/TOF provide the most useful support and deliver effective services.

How will my data be kept safe?
We ask that you do not share the name of your child or any other individual involved in your child's care. Please do not share any photographs on this forum.

As the forum will be run through Facebook, you will post responses using your name (or Facebook name). This personally identifiable information with only be visible to other forum participants and the forum moderator. Your anonymised demographic information and responses will be sent to the research team and stored on a password protected computer or encrypted USB drive. Your information will not be shared with anyone else. The Facebook group will be a closed (private) group and access will be granted by the moderator. The research team will not have access to the forum group. The group will be archived after the transcripts have been received by the research team. The anonymised transcripts will be kept for 5 years after the end of the project.

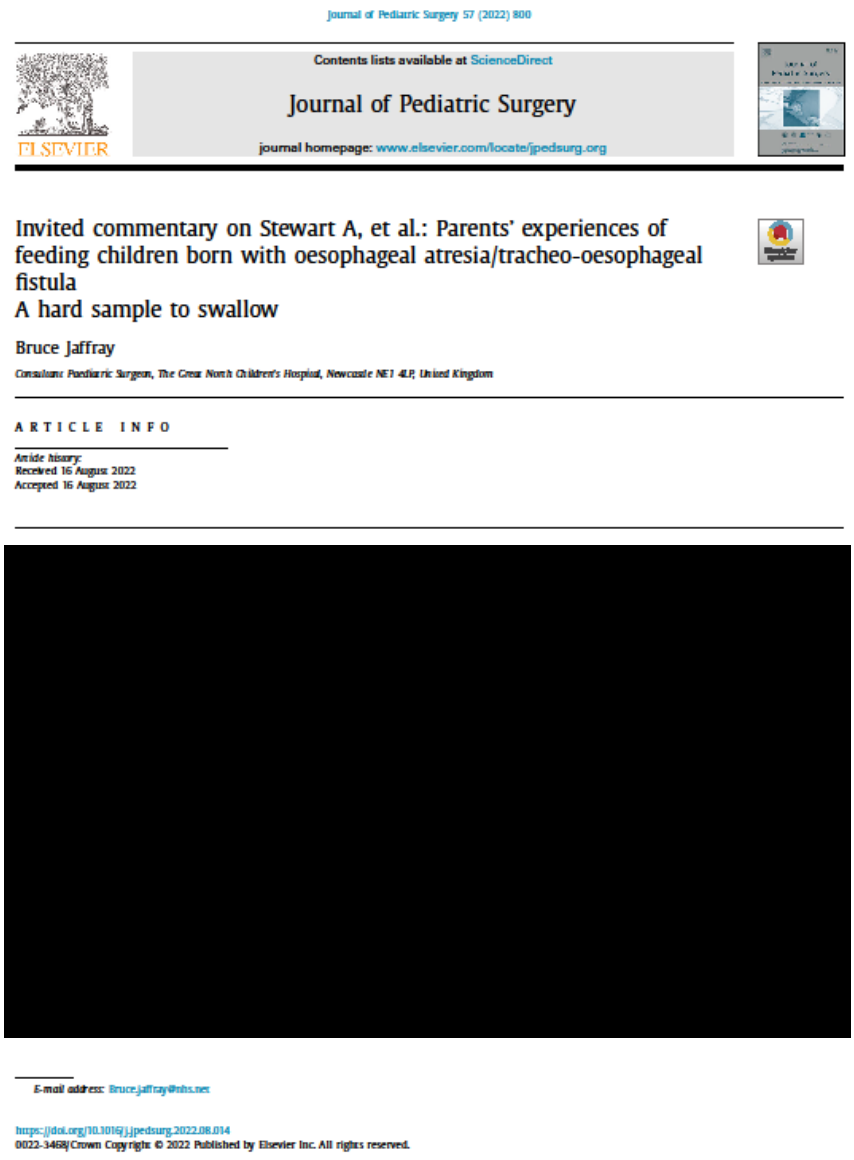
Who is funding this project?
SaFE is being funded by the National Institute for Health Research. It has been reviewed and approved by the Central London Ethics committee.

Any questions?
If you have any questions please contact the lead researcher, Alex Stewart, on [redacted].

If you want to take part please click on this link or https://www.facebook.com/groups/safestudy.onlineforum or head to the TOFS facebook page and follow the link to the "Safe study online forum group". You will be asked to complete some demographic questions. You will then be granted access to the forum by the moderator. You are free to stop taking part at any time.

Appendix 3. Letters to the editor

Double click on the image to be directed to a readable PDF.



Journal of Pediatric Surgery 57 (2022) 800

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Invited commentary on Stewart A, et al.: Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula
A hard sample to swallow

Bruce Jaffray

Consultant Paediatric Surgeon, The Great North Children's Hospital, Newcastle NE1 4LP, United Kingdom

ARTICLE INFO

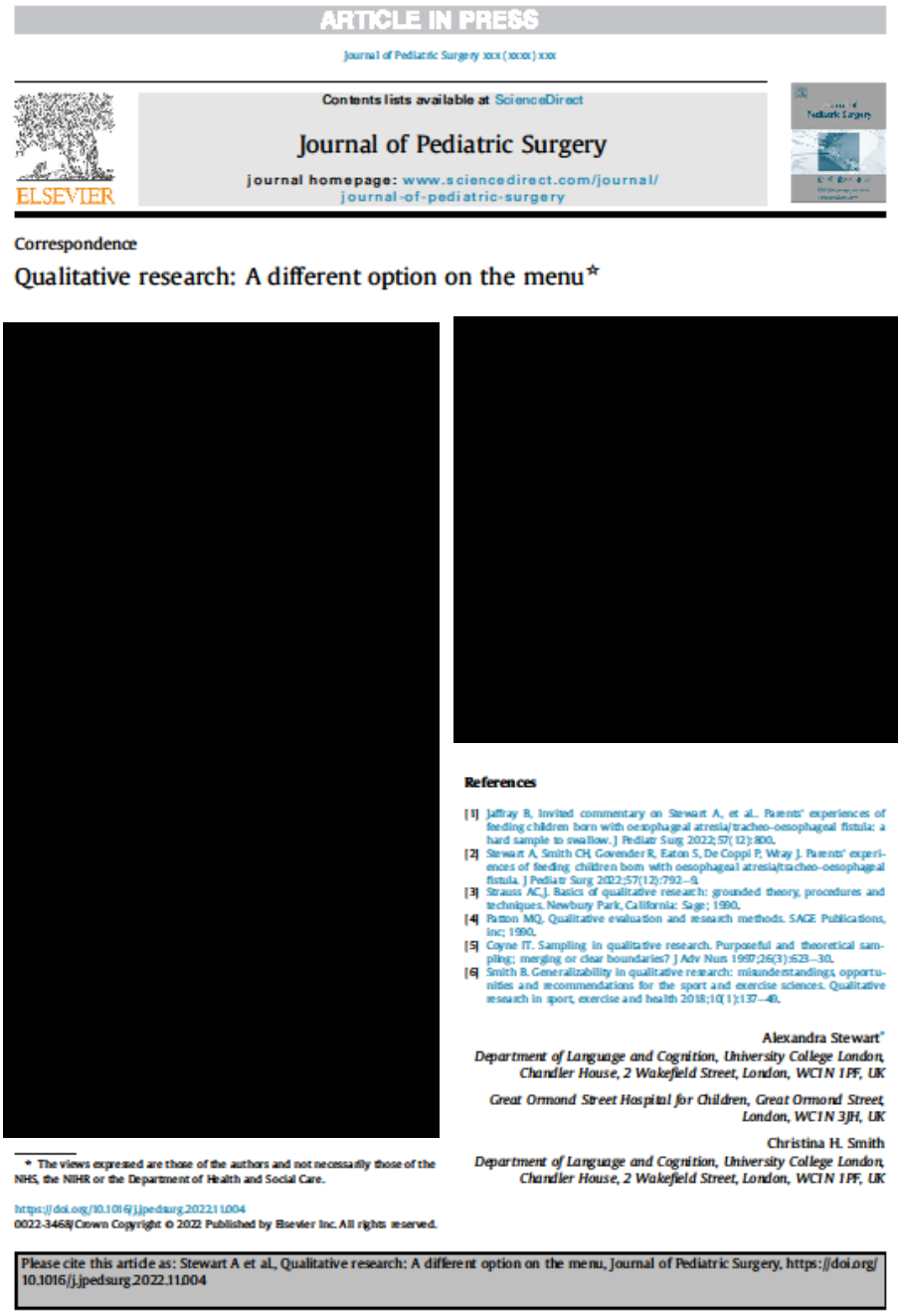
Article history:
Received 16 August 2022
Accepted 16 August 2022

[redacted]

E-mail address: Bruce.jaffray@nhs.net

https://doi.org/10.1016/j.jpedsurg.2022.08.014

Double click on the image to be directed to a readable PDF.



ARTICLE IN PRESS

Journal of Pediatric Surgery xxx (xxxx) xxx

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.sciencedirect.com/journal/journal-of-pediatric-surgery

Correspondence

Qualitative research: A different option on the menu*

[redacted]

[redacted]

References

[1] Jaffray B. Invited commentary on Stewart A, et al., Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula: a hard sample to swallow. J Pediatr Surg 2022;57(12):800.
[2] Stewart A, Smith CH, Govender R, Eaton S, De Coppi P, Wray J. Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula. J Pediatr Surg 2022;57(12):792–9.
[3] Strauss AC,J. Basics of qualitative research: grounded theory, procedures and techniques. Newbury Park, California: Sage; 1990.
[4] Patton MQ. Qualitative evaluation and research methods. SAGE Publications, Inc; 1990.
[5] Coyne IT. Sampling in qualitative research. Purposeful and theoretical sampling; merging or clear boundaries? J Adv Nurs 1997;26(3):623–30.
[6] Smith B. Generalizability in qualitative research: misunderstandings, opportunities and recommendations for the sport and exercise sciences. Qualitative research in sport, exercise and health 2018;10(1):137–49.

Alexandra Stewart*
Department of Language and Cognition, University College London, Chandler House, 2 Wakefield Street, London, WC1N 1PF, UK
Great Ormond Street Hospital for Children, Great Ormond Street, London, WC1N 3JH, UK
Christina H. Smith
Department of Language and Cognition, University College London, Chandler House, 2 Wakefield Street, London, WC1N 1PF, UK

* The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

https://doi.org/10.1016/j.jpedsurg.2022.11.004
0022-3468/

Please cite this article as: Stewart A et al., Qualitative research: A different option on the menu, Journal of Pediatric Surgery, https://doi.org/10.1016/j.jpedsurg.2022.11.004

Appendix 4. Pandemic experiences of caring for a child with OA/TOF

Double click on the image below for a link to the full paper.

Open access Original research

BMJ Paediatrics Open

COVID-19 pandemic experiences of parents caring for children with oesophageal atresia/tracheo-oesophageal fistula

Alexandra Stewart,[1,2] Christina H Smith,[2] Simon Eaton,[3] Paolo De Coppi,[3,4] Jo Wray[5]

To cite: Stewart A, Smith CH, Eaton S, *et al*. COVID-19 pandemic experiences of parents caring for children with oesophageal atresia/tracheo-oesophageal fistula. *BMJ Paediatrics Open* 2021;5:e001077. doi:10.1136/bmjpo-2021-001077

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjpo-2021-001077).

Received 1 March 2021
Revised 27 April 2021
Accepted 5 May 2021

For numbered affiliations see end of article.

Correspondence to
Ms Alexandra Stewart; alex.stewart@gosh.nhs.uk

ABSTRACT

Purpose The COVID-19 pandemic has resulted in a global health crisis of unparalleled magnitude. The direct risk to the health of children is low. However, disease-containment measures have society-wide impacts. This study explored the pandemic experiences of parents of children with oesophageal atresia/tracheo-oesophageal fistula (OA/TOF) in the UK.

Design A phenomenological approach underpinned use of an asynchronous online forum method, in collaboration with a patient support group. Data were evaluated using thematic analysis.

Results The online forum ran between 7 November and 18 December 2020 with 109 participants.

Pandemic experiences were divided into themes relating to healthcare and disease containment. Participants described positive experiences with remote healthcare but identified limitations. Delays and cancellations led to escalation of care to an emergency level, slower developmental progress and feelings of being abandoned by services. Inpatient care was perceived as safe but caring alone was emotionally and practically challenging. Disease containment themes revealed anxiety regarding health risks, 'collateral' damage to well-being because of isolation, and an impact on finances and employment. Parents described a transition from worry about direct health risks to concern about the impact of isolation on socialisation and development. A process of risk–benefit analysis led some to transition to a more 'normal life', while others continued to isolate. Benefits to their child's health from isolation were reported.

Conclusions Parents' experiences of caring for a child with OA/TOF during the pandemic were varied. Rapid adoption of telehealth has demonstrated the enormous potential of remote healthcare delivery but requires refinement to meet the needs of the individual. Future pandemic planning should aim to retain community healthcare services to avoid escalation of care to an emergency, manage chronic and developmental concerns, and support parental well-being. Accurate and consistent disease-specific information is highly valued by parents. Third sector organisations are ideally positioned to support this.

What is known about the subject?

- Direct health risk to children from COVID-19 is low but there is a high risk of 'collateral' damage from strategies required to contain the virus.
- Patient support groups can be powerful allies in providing accurate and consistent messages, that is particularly useful to those with rare diseases.
- Social media can facilitate rapid and effective data collection in a rare disease cohort.

What this study adds?

- A parent perspective of the impact of pandemic-related reduction in healthcare provision and use of telehealth, highlighting areas of need for pandemic and post-pandemic service delivery.
- An insight into parents' experiences and decision-making surrounding disease-containment measures which highlights the variation, even within a single, rare disease.
- Isolation has resulted in exceptionally low exposure to usual childhood infections resulting in improved health for children with oesophageal atresia/tracheo-oesophageal fistula.

INTRODUCTION

The emergence of SARS-CoV-2 brought about the largest global health crisis for a generation.

Although it is now suggested that children are approximately 50% less likely to be infected than adults, account for 1%–5% of cases worldwide[1 2] and rarely experience severe disease,[3] early data indicated that 'high-risk' groups for severe disease existed.[4] As a result, children deemed 'extremely clinically vulnerable' were advised to 'shield', avoiding all contact with others to minimise their risk of being infected.

One group of vulnerable children are those born with oesophageal atresia/tracheo-oesophageal fistula (OA/TOF). A rare, congenital abnormality, OA/TOF occurs in approximately 1/3500 live births in the UK that results in a blind-ending oesophageal

Appendix 5. Questionnaire – electronic patient portal invitation to participate

Dear

We would like to invite you to take part in a research project called the SaFE study (Swallowing, feeding and eating in children born with oesophageal atresia/tracheo-oesophageal fistula). The project aims to understand feeding and swallowing in this group of children so that we can improve the care provided in hospitals and other healthcare settings.

SaFE is made up of three different projects. You may already have been involved with or heard about one of the other projects. In this part of the study, we are using a questionnaire to look at how your child's eating/drinking affects you as a parent. We are inviting all parents of children aged 6 months-11 years old born with oesophageal atresia (OA) and/or tracheo-oesophageal fistula (TOF) to take part. We'd be interested to hear from mothers and fathers, but please complete separate questionnaires. The questionnaire takes about 20 minutes to complete.

To find out more information and to complete the questionnaire please either click on the link or scan the QR code below.

https://www.smartsurvey.co.uk/s/W8RVVF/

Thank you very much for considering taking part. If you have any questions, please contact Alex Stewart (lead researcher) on [redacted], or you can message through the myGOSH app.

An important note! We are working with the TOFS charity to let families who are not treated at Great Ormond Street Hospital know about the project. You may see a link to the questionnaire on their website or Facebook page. The questionnaires are the same so there is no need to complete both. Thank you!

Appendix 6. Questionnaire recruitment adverts

Click on the image for high resolution version.

Appendix 7. Questionnaire consent and participant information sheet

I have read and understood the information above	Yes No
I confirm that I am the parent of a child aged 6 months-11years who was born with oesophageal atresia and/or tracheo-oesophageal fistula (OA/TOF)	Yes No
I understand that completing this questionnaire is voluntary and my child's care will not be affected by my decision to take part or not.	Yes No
I understand that the questionnaire is anonymous but that I will need to give basic details about myself and my child.	Yes No
I understand that the questionnaire will ask about my child's feeding and my well-being.	Yes No
I understand that once I submit my answers I will not be able to withdraw from the study as the researchers will not be able to identify which answers are mine.	Yes No
I understand that the results of the study will be shared, including in a medical journal, at medical conferences and through the TOFS charity.	Yes No
I wish to take part in the study	Yes No

We would like to invite you to take part in a research study exploring Swallowing, Feeding and Eating in children born with oesophageal atresia/tracheo-oesophageal fistula, called the SaFE study for short.

Before you decide whether you would like your child to take part, it is important that you understand why the research is being done and what it would involve. Please take time to read this information carefully. Discuss it with family and friends if you wish.

You are free to decide whether or not to take part. The care you receive from the hospital or at home will not be affected if you choose not to take part. Please ask if there is anything that is not clear or if you would like more information. If you, or a family member would like an interpreter or someone to read the questions to help you take part, please contact us ([redacted]) and we would be happy to arrange this.

SaFE is a PhD project being carried out by Alex Stewart, a speech and language therapist, alongside a team of researchers at Great Ormond Street Hospital and University College London. It is supported by "TOFS", the support group for those born with oesophageal atresia and tracheo-oesophageal fistula and their families.

You may know that in November/December 2020 we carried out an online forum on Facebook. Many thanks if you took part. We have looked at everything that what said and now want to understand some parts in more detail using a questionnaire. The questionnaire focuses on how OA/TOF feeding difficulties affects parents. Research has already shown that caring for a child with OA/TOF can be anxiety-provoking. We would like to understand how much of a part feeding difficulties play in this. We hope that understanding the full extent of what families are dealing with will help health professionals provide the best possible care.

What does taking part in the study involve?

This part of the SaFE study involves completing a questionnaire. You can complete it online, or there is a paper version if you prefer. We will ask you to provide some details about you and your child, including: your age, where in the UK you live, your

ethnicity, the type of OA/TOF your child has and some basic medical information.

The questionnaire will take about 20 minutes to complete.

Why have I been invited to take part?

You have been invited because you are the parent of a child born with OA/TOF who has been treated at Great Ormond Street Hospital. We would very much like all parents of children over 6 months old and under 12 years old to take part in the study. We would really like mothers and fathers to take part, but please complete separate questionnaires.

What are the possible benefits of taking part?

We don't think there will be any immediate benefits to you if you take part. However, you will be helping health professionals to understand the whole impact of OA/TOF feeding difficulties. This will mean that we can improve care for families who have a child born with OA/TOF in the future.

What are the possible disadvantages of taking part?

You may find thinking about the effects of your child's feeding difficulties upsetting. If you do, please speak to someone about how it has made you feel. This may be a family member, friend or one of the TOFS TLC members. But if you are still worried, please speak to a health professional about your concerns. There are many places to get support and help.

Do I have to take part?

No. It is totally up to you whether to take part or not. Your decision won't effect the care your child is given.

What if I decide I no longer want to take part?

You may choose not the complete the questionnaire. However, as we do not know who has completed each questionnaire, once it is submitted we will not be able to withdraw your responses.

What will happen to the results of this study?

The project will be presented at national and/or international medical conferences. Results will be shared with the OA/TOF community, with the support of the TOFS charity and the international EAT federation (a group of international OA/TOF support groups which includes the UK TOFS charity). They will be published in a medical journal and included in a publicly available PhD thesis.
All information will be shared anonymously. Neither you nor your child will ever be able to be identified.

Who is organising and funding this study?
The lead researcher on this project is Alex Stewart, an experienced Speech and Language Therapist working at Great Ormond Street Hospital. The research team includes Professor De Coppi (Consultant Paediatric Surgeon at Great Ormond Street Hospital), Professor Jo Wray (a Psychologist) and Dr Christina Smith (a Speech and Language Therapist).
The project has been funded by the National Institute of Health Research.

How have patients and the public been involved in this study?
10 parents of children born with OA/TOF were involved in designing the project. 4 parents are closely involved in delivering the project. They have been involved in thinking about the risks/benefits, how best to ask families to be involved and how best to carry out the project. Please ask if you would like to talk to one of these parents about the project. They would be very happy to answer questions from a parent's perspective.

Who has reviewed this study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. This study has been reviewed and given a favourable ethical opinion for conduct in the NHS by the London-Central Research Ethics Committee. It has also been approved by the Research Department at Great Ormond Street Hospital.

I'm interested in taking part, what should I do?
Please continue to complete the questionnaire. You can save it and finish it later if you need to. If you would like to be sent a paper copy with a stamped addressed

envelope to return it in, please contact Alex Stewart by phone or email.

If you have any further questions please contact Alex Stewart on: [redacted].

Appendix 8. Work package 1.1 questionnaire

Double click on the image below for a copy of the full questionnaire.

Understanding the impact of feeding difficulties in children with OA/TOF

We would like to invite you to take part in a research study exploring Swallowing, Feeding and Eating in children born with oesophageal atresia/trache-oesophageal fistula, called the SaFE study for short.

Before you decide whether you would like your child to take part, it is important that you understand why the research is being done and what it would involve. Please take time to read this information carefully. Discuss it with family and friends if you wish.

You are free to decide whether or not to take part. The care you receive from the hospital or at home will not be affected if you choose not to take part. Please ask if there is anything that is not clear or if you would like more information. If you, or a family member would like an interpreter or someone to read the questions to help you take part, please contact us [redacted] and we would be happy to arrange this.

SaFE is a PhD project being carried out by Alex Stewart, a speech and language therapist, alongside a team of researchers at Great Ormond Street Hospital and University College London. It is supported by "TOFS", the support group for those born with oesophageal atresia and trache-oeosphageal fistula and their families.

You may know that in November/December 2020 we carried out an online forum on Facebook. Many thanks if you took part. We have looked at everything that what said and now want to understand some parts in more detail using a questionnaire. The questionnaire focuses on how OA/TOF feeding difficulties affects parents. Research has already shown that caring for a child with OA/TOF can be anxiety-provoking. We would like to understand how much of a part feeding difficulties play in this. We hope that understanding the full extent of what families are dealing with will help health professionals provide the best possible care.

What does taking part in the study involve?
This part of the SaFE study involves completing a questionnaire. You can complete it online, or there is a paper version if you prefer. We will ask you to provide some details about you and your child, including: your age, where in the UK you live, your ethnicity, the type of OA/TOF your child has and some basic medical information.

The questionnaire will take about 20 minutes to complete.

Why have I been invited to take part?
You have been invited because you are the parent of a child born with OA/TOF who has been treated at Great Ormond Street Hospital. We would very much like all parents of children over 6 months old and under 12 years old to take part in the study. We would really like mothers and fathers to take part, but please complete separate questionnaires.

What are the possible benefits of taking part?
We don't think there will be any immediate benefits to you if you take part. However, you will be helping health professionals to understand the whole impact of OA/TOF feeding difficulties. This will mean that we can improve care for families who have a child born with OA/TOF in the future.

Appendix 9. Systematic review protocol

Protocol for systematic review of the literature

The characteristics of feeding and oro-pharyngeal swallowing difficulties associated with repaired OA/TOF: a systematic review.

Identification 1a Identify the report as a protocol of a systematic review

Update 1b If the protocol is for an update of a previous systematic review, identify as such

Registration 2 If registered, provide the name of the registry (e.g., PROSPERO) and registration number

Authors

Contact 3a Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author

Contributions 3b Describe contributions of protocol authors and identify the guarantor of the review

Amendments 4 If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments

Support

Sources 5a Indicate sources of financial or other support for the review

Sponsor 5b Provide name for the review funder and/or sponsor

Role of sponsor/funder 5c Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol

INTRODUCTION

Rationale 6 Describe the rationale for the review in the context of what is already known

Approximately 150 babies a year are born in the UK with oesophageal atresia and/or tracheo-oesophageal atresia. Oesophageal atresia occurs when the oesophagus (food pipe) fails to join up during early foetal development. Tracheo-oesophageal fistula describes an abnormal connection that forms between the oesophagus and trachea (windpipe). When the baby feeds, milk cannot pass into the stomach but can pass into the lungs.

Surgery is needed within the first few days of life and is extremely successful, with 90-95% of babies surviving. However, approximately 50-80% of babies will have ongoing feeding or swallowing difficulties resulting in choking, chest infections and pneumonia. They can also lead to food refusal, distress at mealtimes and parental anxiety.

This review aims to synthesise the current literature describing the exact nature of the feeding and swallowing difficulties and the risk factors for developing difficulties.

Objectives 7 Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)

- To describe the characteristics of feeding difficulties in individuals with repaired OA/TOF.
- To describe the characteristics of oro-pharyngeal swallowing difficulties in individuals with repaired OA/TOF.

P – Individuals born with OA/TOF

I – Undergoing instrumental or non-instrumental assessment of oro-pharyngeal swallowing/feeding

C –

O – Presenting with a feeding or swallowing difficulty

T (timing) – Any time following surgical repair

S (setting) – Reported in any hospital or community care setting

METHODS

Eligibility criteria 8 Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review

Inclusion criteria:

- Empirical study of feeding or oro-pharyngeal swallowing function using instrumental or non-instrumental (questionnaire) assessment, and/or, qualitative evaluation of feeding or swallowing outcome
- Includes participants with repaired congenital oesophageal atresia and/or tracheo-oesophageal fistula
- Year of publication-1990-2020
- Written in English language
- Published in peer reviewed journal or grey literature (e.g. thesis). Including: Ahead of Print, In-Process; Other Non-Indexed Citations.

Exclusion criteria:

- Studies of oesophageal phase of swallowing (e.g. oesophageal manometry, pH impedance, gastric emptying, oesophageal/gastric endoscopy)
- Review, opinion or commentary only
- Studies where OA/TOF is not reported separately i.e. cannot be distinguished from other conditions
- Studies in which feeding/swallowing outcome has not been evaluated using an instrumental or non-instrumental tool or qualitative methods e.g., feeding outcome described as oral/non-oral only.
- Studies relating only to acquired tracheo-oesophageal fistula, such as button battery ingestion.
- Conference proceedings.

Information sources 9 Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage

- MEDLINE, EMBASE, CINAHL, Pubmed, Scopus, Web of Science databases
- ISRCTN and clinicaltrials.gov
- Open Access Theses and Dissertations, NDLTD databases
- Hand searching of reference lists for included studies
-

Search strategy 10 Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

For MEDLINE:
- (Oesophageal Atresia/ OR Tracheoesophageal Fistula/ OR tracheoesophageal fistula OR tracheooesophageal fistula OR trachea-esophageal fistula OR tracheo-oesophageal fistula OR oesophageal atresia OR esophageal atresia) AND (Deglutition/ OR exp Deglutition Disorders/ OR "Feeding and Eating Disorders of

Childhood"/ OR Feeding Behaviour/ OR deglutition OR dysphagia OR feed* OR swallow*)

- Limits: English language, 1990-

Study records

Data management 11a Describe the mechanism(s) that will be used to manage records and data throughout the review.

Covidence will be used to manage records and data throughout the review.

Where the facility exists, searches will be saved within each database. Search results will be exported to EndNote. Results will be uploaded to Covidence for screening and data extraction.

Selection process 11b State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)

The CI will undertake all searches and remove duplicates. Results will be independently screened using the title and abstract by the CI and a 2nd researcher. Those identified as potentially applicable will undergo full text review and eligibility assessment by the CI and a 2nd researcher. Disagreement will be resolved through consensus discussion between the 2 reviewing researchers and a 3rd researcher not involved in the eligibility assessment.

Meta-analysis will be conducted where sufficient homogeneity of assessment method exists (such as reporting of aspiration on videofluoroscopy).

Data collection process 11c Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators

Data will be extracted by the CI using Covidence and exported to Excel or other appropriate software tool for statistical analysis as required.

Data items 12 List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications

An excel spreadsheet will be created to summarise:

- Authors
- Date
- Publication
- Country
- Title
- Study design
- Participant demographics: age at assessment, type of OA/TOF, age at repair, type of repair
- Inclusion/exclusion criteria
- Participant selection (consecutive/non-consecutive/referred population)
- Sample size
- Assessment type (e.g. videofluoroscopy, parent reported questionnaire, notes review)
- Outcome measures used
- Assessment of clinically relevant endpoint (e.g. parent/patient reported measure)
- Description of assessment results by OA/TOF type (e.g. videofluoroscopy findings, questionnaire results, qualitative themes)
- Statistical analysis method
- Prevalence of dysphagia or feeding difficulty characteristics
- Reported risk factors (e.g. vocal cord palsy, GORD, cardiac comorbidities)

Outcomes and prioritization 13 List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale

Primary outcomes:

- Components of physiological impairment at oral or pharyngeal stages of swallowing from instrumental swallow assessment
- Components of feeding difficulties reported, including child and parent factors

Secondary outcomes:

- Identification of risk factors for dysphagia or feeding difficulty
- Growth (height, weight)

Risk of bias in individual studies 14 Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis

Quality assessment will be conducted at study level using the appropriate Joanna Briggs Institute tool for each type of study design. All studies, regardless of quality will be included in a narrative synthesis. Studies of 'good' quality will be considered for inclusion in quantitative synthesis, where heterogeneity of assessment method allows.

Data

Synthesis 15a Describe criteria under which study data will be quantitatively synthesized

Quantitative synthesis is not anticipated due to the small number of studies conducted and heterogeneity of assessment methods and reported time points

used within this field. Where more than three studies exist, using sufficiently homogenous assessment and reporting methods for dysphagia or feeding characteristics, meta-analysis will be conducted.

15b If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I2, Kendall's tau)

If possible, pooled prevalence estimates will be calculated for dysphagia characteristics. This will be conducted by pooling prevalence estimates from individual studies and transforming into log odds. Log odds will be transformed back into the original scale. To account for heterogeneity a random effects model will be used.

15c Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)

It is not anticipated that numbers will be sufficiently large for subgroup analysis. However, if possible, sub analysis of pooled prevalence estimates by OA/TOF type will be conducted.

15d If quantitative synthesis is not appropriate, describe the type of summary planned

Data will be summarised using narrative synthesis of: oro-pharyngeal dysphagia and feeding difficulty characteristics. Prevalence ranges will be provided.

Meta-bias(es) 16 Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)

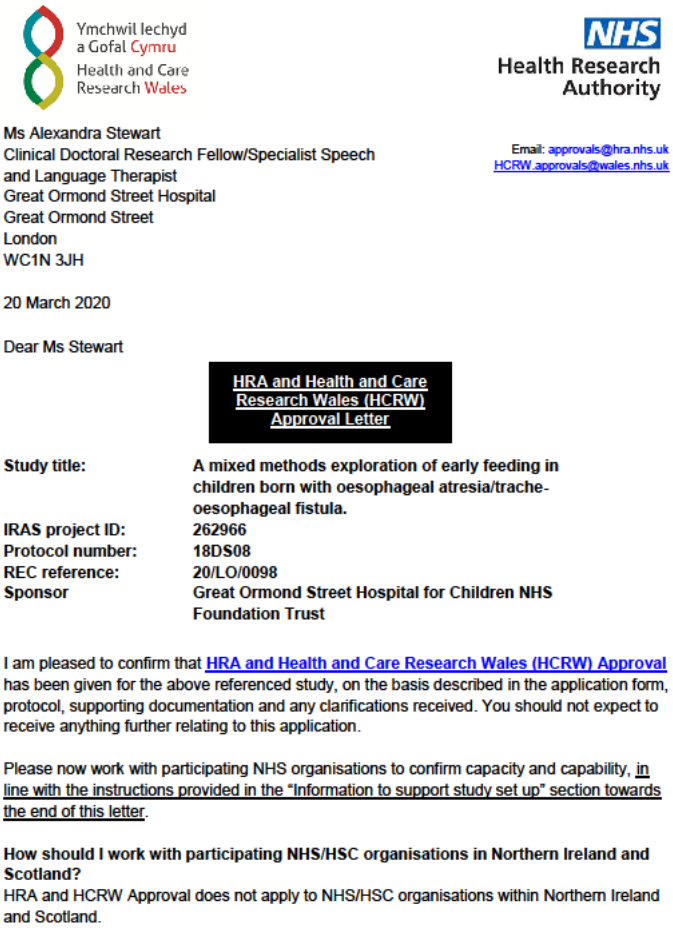
No planned assessment of meta-bias.

Confidence in cumulative evidence 17 Describe how the strength of the body of evidence will be assessed (e.g., GRADE)

Risk of bias will be assessed from the quality assessment conducted as part of the review. Separate analysis will not be conducted as there is no appropriate tool for use in non-intervention/epidemiological studies.

Appendix 10. Health research authority and research ethics committee approvals

Double click on the image to be directed to a full, readable version.



Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Ms Alexandra Stewart
Clinical Doctoral Research Fellow/Specialist Speech and Language Therapist
Great Ormond Street Hospital
Great Ormond Street
London
WC1N 3JH

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

20 March 2020

Dear Ms Stewart

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**A mixed methods exploration of early feeding in children born with oesophageal atresia/trache-oesophageal fistula.**
IRAS project ID:	**262966**
Protocol number:	**18DS08**
REC reference:	**20/LO/0098**
Sponsor	**Great Ormond Street Hospital for Children NHS Foundation Trust**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

Double click on the image to be directed to a full, readable version.

NHS
Health Research Authority

London - Central Research Ethics Committee
3rd Floor, Barlow House
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0207 104 8171

20 March 2020

Ms Alexandra Stewart
Great Ormond Street Hospital for Children
Great Ormond Street
London
WC1N 3JH

Dear Ms Stewart

Study title:	**A mixed methods exploration of early feeding in children born with oesophageal atresia/trache-oesophageal fistula.**
REC reference:	**20/LO/0098**
Protocol number:	**18DS08**
IRAS project ID:	**262966**

Thank you for your response. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 06 February 2020

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Other [HRA HCRW assessment response]	1	27 February 2020
Other [REC response letter]	1	03 March 2020
Participant information sheet (PIS) [PIS]	2	19 February 2020
Research protocol or project proposal [Protocol]	2	27 February 2020
Sample diary card/patient card [Food diary]	2	30 January 2020

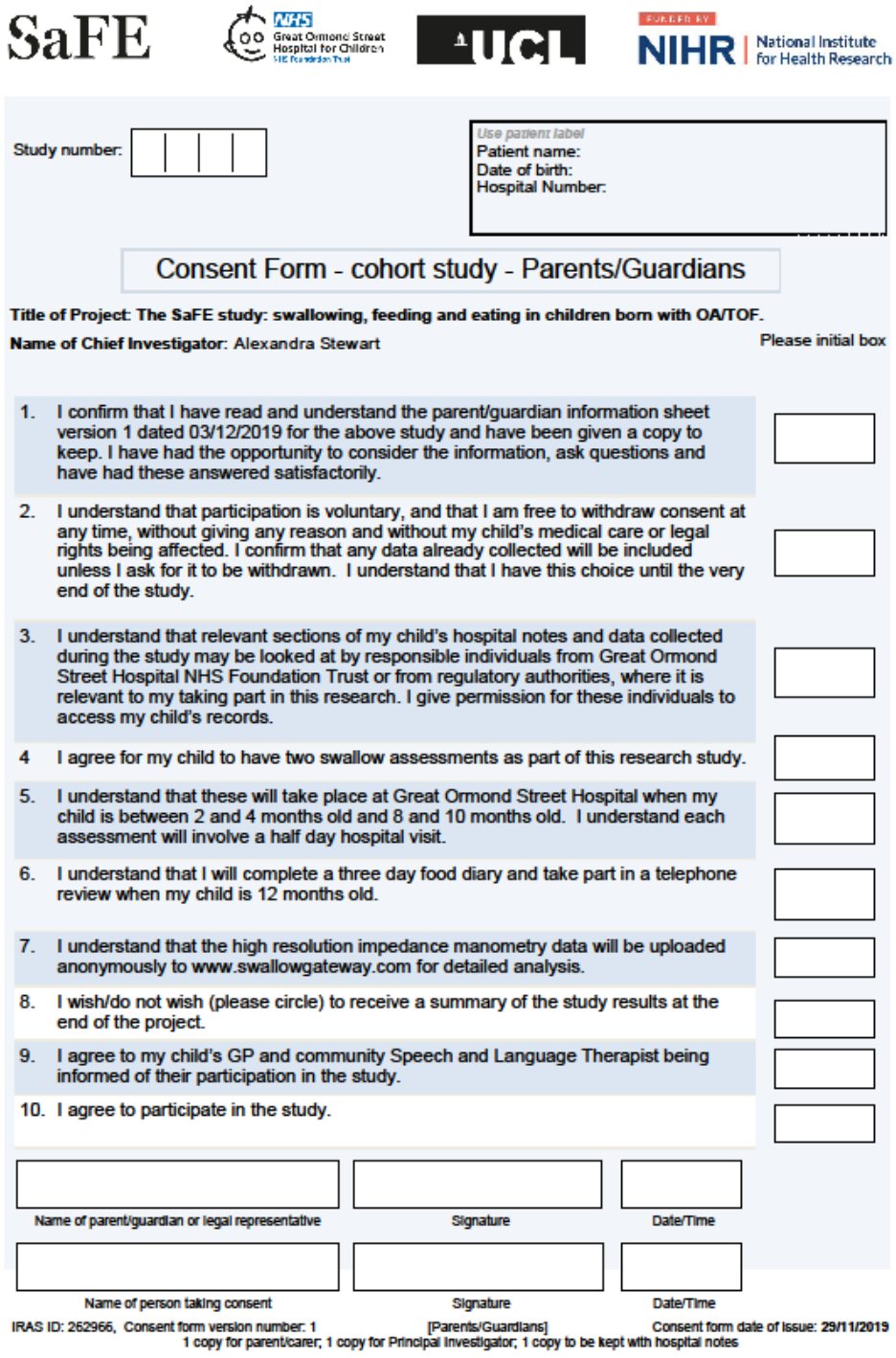
Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Recruitment advert (cohort study)]	1	29 November 2019
Copies of advertisement materials for research participants [Work package 2 (online forum) advert wording]	1	29 October 2019
Copies of advertisement materials for research participants	1	29 November 2019

Appendix 11. Work package 3 – cohort study – consent and participant information sheet

Double click on the image to be directed to readable version



SaFE

Great Ormond Street Hospital for Children NHS Foundation Trust

UCL

FUNDED BY NIHR | National Institute for Health Research

Study number: | | |

Use patient label
Patient name:
Date of birth:
Hospital Number:

Consent Form - cohort study - Parents/Guardians

Title of Project: The SaFE study: swallowing, feeding and eating in children born with OA/TOF.

Name of Chief Investigator: Alexandra Stewart

Please initial box

1. I confirm that I have read and understand the parent/guardian information sheet version 1 dated 03/12/2019 for the above study and have been given a copy to keep. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that participation is voluntary, and that I am free to withdraw consent at any time, without giving any reason and without my child's medical care or legal rights being affected. I confirm that any data already collected will be included unless I ask for it to be withdrawn. I understand that I have this choice until the very end of the study. ☐
3. I understand that relevant sections of my child's hospital notes and data collected during the study may be looked at by responsible individuals from Great Ormond Street Hospital NHS Foundation Trust or from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to access my child's records. ☐
4. I agree for my child to have two swallow assessments as part of this research study. ☐
5. I understand that these will take place at Great Ormond Street Hospital when my child is between 2 and 4 months old and 8 and 10 months old. I understand each assessment will involve a half day hospital visit. ☐
6. I understand that I will complete a three day food diary and take part in a telephone review when my child is 12 months old. ☐
7. I understand that the high resolution impedance manometry data will be uploaded anonymously to www.swallowgateway.com for detailed analysis. ☐
8. I wish/do not wish (please circle) to receive a summary of the study results at the end of the project. ☐
9. I agree to my child's GP and community Speech and Language Therapist being informed of their participation in the study. ☐
10. I agree to participate in the study. ☐

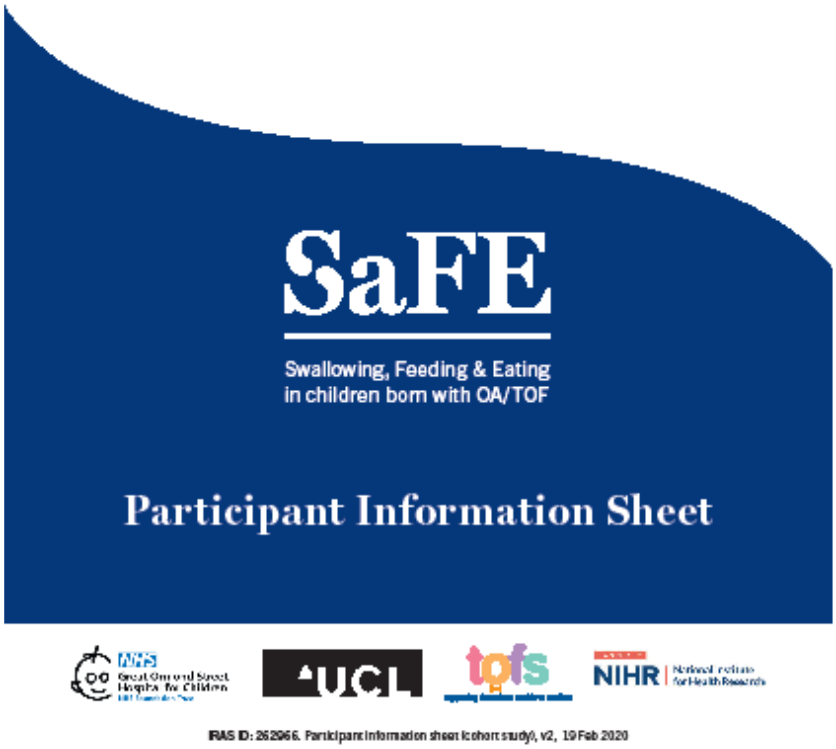
Name of parent/guardian or legal representative	Signature	Date/Time

Name of person taking consent	Signature	Date/Time

IRAS ID: 262966, Consent form version number: 1 [Parents/Guardians] Consent form date of issue: 29/11/2019

1 copy for parent/carer; 1 copy for Principal Investigator; 1 copy to be kept with hospital notes

Double click on the image to be directed to a full, readable version.



Appendix 12. Videofluoroscopy scoring definitions

Name	Rating	Definition	Reference
Suck swallow ratio (SSR)	1 2 3 4 5 or more	Number of sucks per swallow. Downward motion of the mandible to mandible returning to the neutral position is counted as one suck. The total number of sucks per swallow is counted.	(Miles et al. 2022) (McGrattan et al. 2020)
Nasopharyngeal reflux	Present or absent	Presence or absence of barium in the nasopharynx	(Miles et al. 2022)
Total pharyngeal transit time	In milliseconds	Represents the total time of the bolus passage through the pharynx, from when the bolus head passes the posterior nasal spine to the time at which the bolus tail completely clears the PES	(Miles et al. 2022)
Coordination of airway closure with bolus transit	In milliseconds	Airway closure time in relation to bolus reaching PES. Coordination of airway closure with bolus transit.	(Miles et al. 2022)
Bolus residue scale (BRS)	1 = no residue 2 = residue in valleculae 3 = residue in posterior pharyngeal wall or pyriform sinuses 4 = residue in valleculae and posterior pharyngeal wall or pyriform sinuses 5 = residue in posterior pharyngeal wall and pyriform sinuses 6 = residue in valleculae and posterior pharyngeal wall and pyriform sinuses	Location of post-swallow bolus residue. Judged after the 1st swallow	(Rommel et al. 2015)
Residue volume	1 = No residue 2 = Trace residue 3 = Residue collection 4 = Majority residue	Volume of residue after initial swallow	MBSImP training resources

	5 = No bolus clearance		
Penetration Aspiration Scale (PAS)	1 = material does not enter the airway 2 = material enters the airway, remains above the vocal folds, and is ejected from the airway 3 = material enters the airway, remains above the vocal folds, and is not ejected from the airway 4 = material enters the airway, contacts the vocal folds, and is ejected from the airway 5 = material enters the airway, contacts the vocal folds, and is not ejected from the airway 6 = material enters the airway, passes below the vocal folds, and is ejected from the airway 7 = material enters the airway, passes below the vocal folds, and is not ejected from the airway despite effort 8 = material enters the airway, passes below the vocal folds, and no effort is made to eject	Depth of airway invasion	(Rosenbek et al. 1996)
Oesophageal	1 = complete clearance, oesophageal coating 2 = oesophageal retention 3 = oesophageal retention with retrograde flow below PES 4 = oesophageal retention with retrograde flow through PES 5 = minimal to no oesophageal clearance	Ability of oesophagus to propel food or liquid bolus from upper to lower oesophagus and into the stomach.	MBSImP training resources
Stricture	1 = no evidence of stricture 2 = narrowing/waisting visible but no bolus hold up. No immediate intervention required.	Determined from radiology report and medical note review	Unvalidated. Needed for description of outcomes and done to ensure manometry catheter OK

	3 = stricture evident with bolus hold up. Intervention required.		to pass. Manometry delayed if dilatation required.

Appendix 13. Individual swallow metrics results

Individual swallow metric results

Table 1. IDDSI 0 individual videofluoroscopy results

	Time	PAS	Suck per swallow	NPR	TPT	Airway closure	BRS	Residue volume	Oes. clearance
10	1	1	2	0	1.333	0.200	1	1	3
	2	3	2	0	0.882	0.176	1	1	
11	1	1	5	0	1.943	0.201	1	1	1
	2	2	5	0	2.814	0.603	2	2	
12	1	1	3	0	1.765	0.294	1	1	3
	2	2	3	0	1.688	0.656	2	2	
18	1	2	4	0	2.667	1.330	2	2	3
	2	5	3	0	1.118	0.353	1	1	
19	1	2	2	1	1.133	0.133	2	2	1
	2	1	3	0	1.667	0.133	2	2	
21	1	1	1	0	0.533	0.067	2	2	3
25	1	1	2	0	0.660	0.070	1	1	
26	1	1	3	1	1.600	0.133	3	2	3
63	1	4	5	0	1.733	0.333	2	3	3
	2	1	4	0	0.941	0.529	2	2	

71	1	3	2	0	1.067	0.133	1	1	
	2	8	1	1	0.800	0.200	1	1	
76	1	1	3	0	1.000	0.067	1	1	2
	2	2	2	0	1.059	0.412	2	2	
84	1	2	1	0	1.333	0.700	1	1	3

PAS = penetration aspiration scale, NPR = nasopharyngeal reflux, TPT = total pharyngeal transit time, BRS = bolus residue scale, Oes. Clearance = oesophageal clearance. Colour codes: PAS: green = 1, orange = 2, red = 3 and above, Sucks per swallow: green = 1 or 2, red = 3 or more, NPR: green = absent, red = present, TPT: red = > 0.5 seconds, BRS and residue volume: green = 1 or 2, red = 3 or more, Oes. Clearance: green = 1, red = 2 or more.

Table 2. IDDSI 4 individual videofluoroscopy results

ID	PAS	NPR	TPT	Airway closure	BRS	Residue volume	Oes. clearance
10	1	0	2.471	0.118	1	1	3
11	1	0	1.206	0.201	4	2	
12	1	0	1.875	0.250	2	2	2
18	1	0	0.824	0.118	4	3	2
19	1	0	1.333	0.133	2	2	3
21	8	0	1.005	0.335	2	2	3
63	1	0	1.353	0.176	2	3	2
71	1	0	7.000	0.067	1	1	3
76	1	0	1.765	0.176	2	3	3
84	1	0	2.333	0.133	1	1	3

PAS = penetration aspiration scale, NPR = nasopharyngeal reflux, TPT = total pharyngeal transit time, BRS = bolus residue scale, Oes. Clearance = oesophageal clearance. Colour codes: PAS: green = 1, orange = 2, red = 3 and above, Sucks per swallow: green = 1 or 2, red = 3 or more, NPR: green = absent, red = present, TPT: red = > 0.5 seconds, BRS and residue volume: green = 1 or 2, red = 3 or more, Oes. Clearance: green = 1, red = 2 or more.

Table 3. Individual high resolution manometry results

ID	Time	Swallow type	IDDSI level	Pharyngeal				Oesophageal	
				PhCI	UESRT	UES max ad	UES IRP	DCI	IRP4s
25	1	Consecutive	0	93.66	0.18	1.43	7.95	0.00	17.11
		Single 0.3ml	0	128.53	0.22	1.69	9.22	5.44	10.41
	2	Single 1ml	4	142.27	0.52	1.47	6.97	24.11	8.87
11	1	Consecutive	0	46.70	0.24	1.62	7.27	0.00	6.59
		Single 0.3ml	0	69.77	0.34	1.74	2.83	0.00	7.65
	2	Consecutive	0		0.37	1.12	-2.71	0.24	22.19
		Single 1ml	4		0.41	1.66	5.36	3.15	36.87
71	1	Consecutive	0	112.84	0.26	2.24	5.44	1095.64	1.05
		Single 0.3ml	0	169.46	0.29	2.20	6.01	614.13	25.23
	2	Consecutive	0	45.04	0.35	1.44	17.35	610.32	27.41
		Single 1ml	4	27.72	0.30	1.44	14.01	312.40	27.23
84	1	Consecutive	0	42.63	0.36	1.86	13.49	18.31	3.94
	2	Consecutive	0	73.39	0.45	1.50	-0.64	0.00	17.48
		Single 0.3ml	0	72.80	0.52	1.46	0.46	11.59	24.40
26	1	Consecutive	0	93.21	0.40	1.30	9.27	121.72	2.58
		Single 0.3ml	0	113.33	0.49	1.26	3.88	0.02	19.11
19	1	Consecutive	0	121.54	0.48	1.18	3.67	250.98	-3.49
		Single 0.3ml	0	91.31	0.23	1.27	9.19	3.96	5.25
	2	Consecutive	0	42.30	0.42	1.77	12.36	229.89	10.92

		Single 1ml	4	58.73	0.53	1.95	10.80	120.76	18.70

21	1	Consecutive	0	40.64	0.26	2.00	15.74	22.41	13.79
		Single 0.3ml	0	43.39	0.38	1.66	7.70	2.16	28.12
	2	Single 1ml	4	136.83	0.21	1.74	8.69	0.00	5.31
10	1	Consecutive	0	48.79	0.56	1.01	-4.23	0.00	5.61
		Single 0.3ml	0	86.51	0.39	1.12	9.52	0.00	6.09
	2	Consecutive	0	84.43	0.56	1.39	24.83	30.83	26.00
		Single 1ml	4	236.76	0.49	1.40	0.78	12.18	26.08
76	1	Consecutive	0	37.36	0.17	0.65	6.62	0.00	16.66
		Single 0.3ml	0	90.67	0.26	1.58	6.29	1.66	19.14
	2	Consecutive	0	101.13	0.67	0.82	6.73	0.00	30.42
		Single 1ml	4	127.08	0.54	1.39	3.62	0.08	6.68
18	1	Consecutive	0	31.66	0.49	1.23	0.14	0.00	14.56
		Single 0.3ml	0	54.59	0.24	1.45	6.99	0.91	27.53
	2	Consecutive	0	58.27	0.70	1.75	4.97	138.97	19.83
		Single 0.3ml	0	102.76	0.31	1.59	9.56	0.01	17.94
		Single 1ml	4	106.44	0.37	1.59	5.82	19.00	24.83
63	1	Consecutive	0	85.04	0.31	1.29	5.30	0.00	9.55
	2	Consecutive	0	93.36	0.37	1.04	1.32	31.81	7.50
		Single 1ml	4	49.45	0.34	1.45	5.42	5.12	26.40
12	1	Consecutive	0	20.89	0.19	1.17	8.07	64.48	13.83
	2	Consecutive	0	69.29	0.36	1.39	7.97	5.16	24.21
		Single 1ml	4	87.46	0.28	1.22	14.17	0.56	19.82

PhCI=Pharyngeal contractile integral, UES RT = Upper esophageal sphincter relaxation time, UES max ad = Upper esophageal sphincter maximum admittance, IRP = Integrated relaxation pressure, DCI = Distal contractile integral, IRP4s = Integrated relaxation pressure 4 seconds. DCI colour code: Green: > 450mmHg. Orange: 100-449mmHg, Red: <100mmHg. IRP4s colour code: Green = within normal range. Red = above normal value threshold. CEDAS = Children's eating and drinking activity scale. CEDAS colour code: Green = age-appropriate feeding. Orange = full oral feeding but not age appropriate. Red = tube feeding required. Consecutive swallow = last swallow in consecutive feed. Single swallow = median value 0.3mL single bolus.

Appendix 14. Outputs from doctoral fellowship period

Peer reviewed publications:

First/corresponding author

Stewart, A., & Burr, S. (2021). Thickened liquids: do they still have a place in the paediatric dysphagia toolkit?. Current Opinion in Otolaryngology & Head and Neck Surgery, 29(3), 194-199.

Stewart, A., Smith, C. H., Eaton, S., De Coppi, P., & Wray, J. (2021). COVID-19 pandemic experiences of parents caring for children with oesophageal atresia/tracheo-oesophageal fistula. BMJ Paediatrics Open, 5(1).

Stewart, A., Smith, C. H., Govender, R., Eaton, S., De Coppi, P., & Wray, J. (2022). Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula. Journal of pediatric surgery, 57(12), 792-799.

Hanks, E., Stewart, A., Au-Yeung, C. K., Johnson, E., & Smith, C. H. (2023). Consensus on level descriptors for a functional children's eating and drinking activity scale. Developmental Medicine & Child Neurology, 65(9), 1199-1205.

Stewart, A., Govender, R., Eaton, S., Smith, C. H., De Coppi, P., & Wray, J. (2024). The characteristics of eating, drinking and oro-pharyngeal swallowing difficulties associated with repaired oesophageal atresia/tracheo-oesophageal fistula: a systematic review and meta-proportional analysis. Orphanet Journal of Rare Diseases, 19(1), 253.

Contributing author:

Halfpenny, R., Stewart, A., Carter, A., Wyatt, M., Jephson, C., O'Dwyer, E., & Cavalli, L. (2021). Dysphonia and dysphagia consequences of paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS). International Journal of Pediatric Otorhinolaryngology, 148, 110823.

Halfpenny, R., Stewart, A., Kelly, P., Conway, E., & Smith, C. (2021). Dysphagia rehabilitation following acquired brain injury, including cerebral palsy, across the lifespan: a scoping review protocol. Systematic Reviews, 10, 1-7.

Weststrate, H., Stimpson, G., Thomas, L., Scoto, M., Johnson, E., Stewart, A., ... & Au-Yeung, C. K. (2022). Evolution of bulbar function in spinal muscular atrophy type 1 treated with nusinersen. Developmental Medicine & Child Neurology, 64(7), 907-914.

O'Connor, G., Marino, L. V., Tume, L. N., Stewart, A., Gates, S., Lanigan, J., ... & Kinsella, S. (2022). Research priorities for pediatric intensive care nutrition within the United Kingdom: a national institute of health research james Lind alliance priority setting partnership. Critical care explorations, 4(3), e0649.

Public engagement dissemination

TOFS support group

Research summary: Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula – TOFS | OA/TOF Support

Research Follow-up: Covid-19 impact on TOF families – TOFS | OA/TOF Support

Great Ormond Street Hospital

Learning from patients and families during a pandemic | Great Ormond Street Hospital

Conference presentations:

Invited speaker:

Stewart, A. Feeding and swallowing difficulties in oesophageal atresia/trachea-oesophageal fistula panel discussion. QUAD conference. 10-14 October 2022, Cincinnati, USA

Stewart, A. Clinical and videofluoroscopic evaluation of swallowing. ESPGHAN Winter motility meeting. 7-8 December 2022. Ashridge House, Hertfordshire, UK.

Stewart A. Feeding difficulties and dysphagia management: the role of Speech and Language Therapists. European Society of Gastroenterology, Hepatology and Nutrition Conference, Vienna, Austria, 17-20 May 2023

Stewart A. Integrating advances in paediatric dysphagia with family-centred care. Amrita Dysphagia Conference, Kochi, India, 25-27 October 2023

Stewart A. Eating, drinking and swallowing difficulties in OA/TOF: what does the research show? TOFS family conference, University College London Institute of Child Health, London,18 November 2023

Stewart A. How do you assess feeding problems in OA/TOF. Joint ERNICA-ESPGHAN meeting on oesophageal atresia, Wroclaw, Poland, 10 April 2024

Stewart A. The importance of holistic care in paediatric dysphagia: lessons learnt from a study of oesophageal atresia. European Society of Swallowing Disorders Congress, Muenster, Germany, 25-27 September 2024

Stewart A. Paediatric dysphagia pre-congress workshop. European Society of Swallowing Disorders Congress, Muenster, Germany, 25-27 September 2024

Accepted abstract:

Stewart A., Azam A., Johnson E., Smith C. A single centre, 10-year retrospective review of one-year feeding outcomes in children with a diagnosis of hypoplastic left heart syndrome. UK Swallowing Research Group conference, London, UK, February 2020, UKSRG conference, February 2020, London, UK (poster)

Livermore P, Bichard E, Brind J, Evans J, Handley S, Harniess P, Jewell T, Katchburian L, Kerr-Elliot T, Kim J, Nightingale R, Shkurka E, Simcock IC, Sipanoun P, and **Stewart, A.** The importance of peer-support for clinical academics at Great

Ormond Street Children's Hospital. GOSH conference, London, November 2020 (virtual conference)

Eaton J, Stewart A, Bennison R, Simcock IC. Videofluoroscopy swallow service: an allied health professional collaboration. GOSH conference, London, November 2020 (virtual conference)

Hanks, E., **Stewart, A**., Johnson, E., Smith, C. Gaining expert consensus on level descriptors of a paediatric functional oral intake scale (p-FOIS). UK Swallowing Research Group conference, 3-4 February 2022, London, UK. (poster)

Stewart, A., Smith, C. H., Govender, R., Eaton, S., De Coppi, P., & Wray, J. "Every feed I worry and prepare for the worst": Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula. QUAD conference, 10-14 October 2022, Cincinnati, USA. (oral)

Stewart A., Smith, C. H., Govender, R., Eaton, S., De Coppi, P., & Wray, J. Parents' experiences of feeding children born with oesophageal atresia/tracheo-oesophageal fistula. European Society of Swallowing Disorders, Toulouse, France, 30 November-2 December 2023. (oral)

Stewart A., Van Hoeve, E., Mustafa, A., Lefton-Greif, M., Smith, C. Generating UK normative data for the Feeding Swallowing Impact Survey. UK Swallowing Research Group conference. Birmingham, UK, 8-9 February 2024. (oral)

Stewart, A., Govender, R., Eaton, S., Smith, C. H., De Coppi, P., & Wray.J. The characteristics of eating, drinking and oro-pharyngeal swallowing difficulties associated with repaired oesophageal atresia/tracheo-oesophageal fistula: a systematic review and meta-proportional analysis. European Society of Swallowing Disorders Congress, Muenster, Germany, 25-27 September 2024. (oral)

Leadership roles:

1. Member of three working groups developing national guidelines with the Royal College of Speech and Language Therapists (Covid guidelines, use of thickened fluids and use of high-resolution manometry). I am co-lead author for the manometry guidelines.

2. Working group member for paediatric dysphagia national workforce development group (HEE/RCSLT)

3. Steering group member for priority setting partnership for nutrition in intensive care

4. Involvement in the development of a core outcome set for oesophageal atresia

5. Established a UK network for Speech and Language Therapists conducting research in paediatric dysphagia

6. Chair of a national network of Speech and Language Therapists working in paediatric dysphagia, including organisation of 12 study days

7. Scientific chair for UK Swallowing Research Group conference

8. Member of TOFS research advisory group

Supervision/mentoring:

1. Supervision of 3 PCAF mentees
2. Named clinical supervisor for 2 DCAF applications (awaiting outcome)
3. Supervisor for 4 UCL MSc projects

Appendix 15. Figure reprint permissions

Double click on the images for a readable version.

SPRINGER NATURE LICENSE
TERMS AND CONDITIONS

Nov 27, 2024

This Agreement between Alex Stewart ("You") and Springer Nature ("Springer Nature") consists of your license details and the terms and conditions provided by Springer Nature and Copyright Clearance Center.

License Number	5917130277242
License date	Nov 27, 2024
Licensed Content Publisher	Springer Nature
Licensed Content Publication	Nature Reviews Disease Primers
Licensed Content Title	Oesophageal atresia
Licensed Content Author	Marinde van Lennep et al
Licensed Content Date	Apr 18, 2019
Type of Use	Thesis/Dissertation
Requestor type	academic/university or research institute
Format	print and electronic
Portion	figures/tables/illustrations
Number of figures/tables/illustrations	1
Would you like a high resolution image with your order?	no

SPRINGER NATURE LICENSE
TERMS AND CONDITIONS

Nov 27, 2024

This Agreement between Alex Stewart ("You") and Springer Nature ("Springer Nature") consists of your license details and the terms and conditions provided by Springer Nature and Copyright Clearance Center.

License Number	5917010538578
License date	Nov 27, 2024
Licensed Content Publisher	Springer Nature
Licensed Content Publication	Springer eBook
Licensed Content Title	GERD Pathogenesis and Essential Anatomic Knowledge for Antireflux Surgery
Licensed Content Author	Jin-Jo Kim
Licensed Content Date	Jan 1, 2023
Type of Use	Thesis/Dissertation
Requestor type	academic/university or research institute
Format	print and electronic
Portion	figures/tables/illustrations
Number of figures/tables/illustrations	1
Will you be translating?	no
Circulation/distribution	1 - 29

JOHN WILEY AND SONS LICENSE
TERMS AND CONDITIONS

Nov 27, 2024

This Agreement between Alex Stewart ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

License Number	5917120827439
License date	Nov 27, 2024
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Pediatric Pulmonology
Licensed Content Title	Care recommendations for the respiratory complications of esophageal atresia-tracheoesophageal fistula
Licensed Content Author	Thomas Kovesi, Federica Porcaro, Jonathan Popler, et al
Licensed Content Date	Aug 7, 2020
Licensed Content Volume	55
Licensed Content Issue	10
Licensed Content Pages	17
Type of use	Dissertation/Thesis
Requestor type	University/Academic
Format	Print and electronic

Order Date	27-Nov-2024	**Type of Use**	Republish in a thesis/dissertation
Order License ID	1550384-1		
ISSN	1527-1323	**Publisher**	RADIOLOGICAL SOCIETY OF NORTH AMERICA, INC.
		Portion	Image/photo/illustration

LICENSED CONTENT

Publication Title	Radiographics	**Publication Type**	e-Journal
Article Title	Fluoroscopic Swallowing Examination: Radiologic Findings and Analysis of Their Causes and Pathophysiologic Mechanisms	**Start Page**	1733
		End Page	1749
		Issue	6
		Volume	41
Author / Editor	Radiological Society of North America.	**URL**	http://bibpurl.oclc.org/web/8257
Date	01/01/1981		
Language	English		
Country	United States of America		
Rightsholder	Radiological Society of North America		

REQUEST DETAILS

Portion Type	Image/photo/illustration	**Distribution**	U.K. and Commonwealth (excluding Canada)
Number of Images / Photos / Illustrations	1	**Translation**	Original language of publication
Format (select all that apply)	Electronic	**Copies for the Disabled?**	No
Who Will Republish the Content?	Academic institution	**Minor Editing Privileges?**	No
		Incidental Promotional Use?	No
Duration of Use	Life of current edition		
Lifetime Unit Quantity	Up to 499	**Currency**	GBP
Rights Requested	Main product		

NEW WORK DETAILS

Title	PhD thesis	**Institution Name**	Great Ormond Street Hospital
Instructor Name	Alex Stewart		
		Expected Presentation Date	2025-03-16

ADDITIONAL DETAILS