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Consensus statement

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The International Network on Oesophageal Atresia (INoEA) consensus guidelines on the transition of patients with oesophageal atresia–tracheoesophageal fistula

A list of authors and their affiliations appears at the end of the paper

Abstract

Oesophageal atresia–tracheoesophageal fistula (EA-TEF) is a common congenital digestive disease. Patients with EA-TEF face gastrointestinal, surgical, respiratory, otolaryngological, nutritional, psychological and quality of life issues in childhood, adolescence and adulthood. Although consensus guidelines exist for the management of gastrointestinal, nutritional, surgical and respiratory problems in childhood, a systematic approach to the care of these patients in adolescence, during transition to adulthood and in adulthood is currently lacking. The Transition Working Group of the International Network on Oesophageal Atresia (INoEA) was charged with the task of developing uniform evidence-based guidelines for the management of complications through the transition from adolescence into adulthood. Forty-two questions addressing the diagnosis, treatment and prognosis of gastrointestinal, surgical, respiratory, otolaryngological, nutritional, psychological and quality of life complications that patients with EA-TEF face during adolescence and after the transition to adulthood were formulated. A systematic literature search was performed based on which recommendations were made. All recommendations were discussed and finalized during consensus meetings, and the group members voted on each recommendation. Expert opinion was used when no randomized controlled trials were available to support the recommendation. The list of the 42 statements, all based on expert opinion, was voted on and agreed upon.

Sections

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Introduction

Oesophageal atresia–tracheoesophageal fistula (EA-TEF) is one of the most common digestive and respiratory malformations occurring in 1 in 2,400 to 4,500 births worldwide[1]. Since the first successful primary repair by Cameron Haight in 1941, postoperative outcomes have changed. Except for patients experiencing severe concomitant malformations, such as congenital heart disease, operative and perioperative care improvements have shifted the focus from mortality to morbidity and quality of life (QOL). EA-TEF is no longer just a neonatal surgical problem but a lifelong problem. Gastrointestinal, surgical, respiratory, otolaryngological, nutritional, psychological and QOL issues are prevalent not only in the first years of life but also in adolescence and adulthood[2–5]. Gastro-oesophageal reflux disease (GERD), peptic oesophagitis, gastric metaplasia and Barrett oesophagus, eosinophilic oesophagitis (EoE), anastomotic strictures, feeding disorders, dysphagia, and oesophageal dysmotility are the most frequent gastrointestinal long-term complications encountered in adolescents and adults[5,6]. Concerns in adults include oesophageal adenocarcinoma, squamous cell carcinoma and epidermoid carcinoma, which have been reported[6]. The common respiratory or otolaryngological complications encountered during this period include abnormalities in lung function, asthma, aspiration, recurrent chest infections and, in some cases, bronchiectasis[2]. Malnutrition and undernutrition can be seen in all age groups, as can psychological difficulties and impaired QOL. To date, although morbidity is well known and the need for careful multidisciplinary follow-up is highlighted, consensus evidence and expert opinion-based guidelines have only been published on the diagnosis and treatment of gastrointestinal, nutritional, surgical and respiratory complications in childhood[7–10]. There is currently a lack of a systematic approach to the care of these patients during adolescence and after the transition to adulthood. Hence, the International Network on Oesophageal Atresia (INoEA), which was formed in 2013, decided to help formulate clinical practice guidelines for the care of these patients during adolescence and after the transition to adulthood.

Methods

The project started in October 2019, when, under the auspices of INoEA, a working group consisting of selected members, including both paediatric and adult gastroenterologists, surgeons, respirologists, otolaryngologists, nutritionists, deglutologists, nurses, psychologists and a representative of patients with oesophageal atresia and parent support group in oesophageal atresia, was formed (Supplementary Box 1). The working group was formed by INoEA members in collaboration with the European Reference Network for Rare Inherited and Congenital (digestive and gastrointestinal) Anomalies and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition to look at formulating evidence-based clinical practice guidelines based on current knowledge for the evaluation and treatment of gastrointestinal, surgical, respiratory, otolaryngological, nutritional, psychological and QOL complications in adolescents and adults with EA-TEF. As a result, clinical questions were formulated to evaluate and treat these complications in adolescents and adults with EA-TEF (Box 1).

The questions were formulated by all members of the transition guidelines working group of INoEA after three online rounds of selection. The working group was subdivided into sub-specialities, including gastroenterology, surgery, respirology, otolaryngology, nutrition, psychology and QOL, whose members addressed the questions specific to their sub-speciality. Members of each of the sub-specialities included are listed in Supplementary Box 1. Each subgroup had a lead.

Questions were based on expert opinion owing to the lack of randomized control trials and meta-analysis in this field and answered using the results of systematic literature searches. Systematic literature searches were performed by M.W.D. and H.S., along with help from the lead of the Transition Working Group, U.K., with the help of a clinical librarian from database inception to January 2022. The Embase, MEDLINE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Clinical Trials, and PsycINFO databases were searched. Inclusion criteria were (1) systematic reviews, prospective or retrospective controlled studies, and prospective or retrospective cohort studies; (2) study population consisting of children 0–18 years of age and adults with oesophageal atresia; and (3) relevant papers obtained using the keywords "transition", "adolescence", "adulthood", "oesophageal", "oesophageal atresia", "tracheoesophageal fistula", "gastroesophageal reflux", "Barrett's oesophagus", "eosinophilic oesophagitis", "stricture", "fundoplication", "oesophageal replacement", "nutrition", "dysphagia", "gastrostomy", "asthma", "bronchiectasis", "quality of life", "oesophageal carcinoma" and "guidelines". Additional strategies for identifying studies included using the mentioned keywords to search in the reference lists of review articles and the included studies. Furthermore, all of the guideline committee members were asked to search the literature relevant to their assigned topics to possibly uncover further studies that the former search might have missed. After creating the initial reference list of review articles and studies, articles published before 1980, articles in languages other than English and French, animal studies, case reports with fewer than five patients, and abstracts presented only during conference proceedings were excluded. M.W.D., H.S. and U.K. systematically reviewed all the articles selected in the literature review and summarized the important findings in a tabular form. The summary tables of all the papers were sent to all the Transition Working Group members before they wrote their relevant sections.

Three consensus meetings were held in June of 2020, 2021 and 2022 to achieve consensus and formulate all recommendations. Each subgroup presented the recommendations or statements during the consensus meetings, wherein these were then discussed and modified according to the comments of the attendees. The consensus was formally achieved through the nominal group technique, a structured quantitative method. The group, consisting of members of all the subgroups, anonymously voted on each recommendation. A 9-point scale was used (1, strongly disagree; 9, fully agree), and votes were reported for each recommendation. It was decided in advance that consensus was reached if >75% of the working group members voted 6, 7, 8 or 9. After re-wording and/or modification, a consensus was reached for all of the recommendations for the questions (results of voting shown in Supplementary Table 1). A decision was also made to present algorithms and tables. The final draft of the guidelines was sent to all of the committee members for approval in 2022, and then critically reviewed by a multidisciplinary panel of members of the INoEA (see Acknowledgements).

Results

A list of 42 statements, all based on expert opinion, was voted on and agreed upon. These statements addressed the diagnosis, treatment and prognosis of gastrointestinal, surgical, respiratory, otolaryngological, nutritional, psychological and QOL complications that patients with EA-TEF faced during adolescence and after the transition to adulthood.

Box 1

Clinical questions for evaluation and treatment of complications in patients with EA-TEF

Gastroenterology

- Question 1: What are the common digestive symptoms in adolescents and adults with EA-TEF? What is the incidence and prevalence of GERD in adolescents and adults with EA-TEF?
- Question 2: What are the incidence, prevalence and causes of dysphagia (oropharyngeal and/or oesophageal) in adolescents and adults with EA-TEF?
- Question 3: What are the incidence and prevalence of oesophageal complications (peptic oesophagitis, eosinophilic oesophagitis, anastomotic and other strictures, mucosal bridge, and proximal pouch and diverticulum) in adolescents and adults with EA-TEF, and are there any predictive factors of these complications?
- Question 4: What are the incidence, prevalence and lifetime risks of Barrett oesophagus, including gastric and intestinal metaplasia and oesophageal adenocarcinoma and squamous cell carcinoma, in patients with EA-TEF?
- Question 5: How often should adult patients with stable EA-TEF be followed by adult gastroenterologists, and what surveillance should be performed for the timely diagnosis of Barrett oesophagus and oesophageal cancer in these patients?

Surgery

- Question 6: How to best investigate and treat adolescents and adults with persistent uncontrollable GERD, with or without previous fundoplication and other GERD surgery?
- Question 7: Which is the best surgical approach in adolescents and adults with EA-TEF with persistent uncontrollable GERD (MIS vs open surgery)? And what is the best approach for redo fundoplication?
- Question 8: How to best investigate and treat adolescents and adults with EA-TEF and persistent uncontrollable GERD with prior gastric pull-up or tube?
- Question 9: In adolescents and adults with EA-TEF with previous total oesophagogastric dissociation, is there a place for new gastric reconnection?
- Question 10: What is the best protocol for clinical follow-up and investigations in adolescents and adults with EA-TEF that underwent oesophageal substitution (with colon, jejunum, gastric pull-up or tube, or other strategies)?
- Question 11: Which is the best surgical strategy in adolescents and adults with EA-TEF with oesophageal substitution with a redundant and dilated colon?
- Question 12: After oesophageal substitution, many patients with EA-TEF have their own distal oesophagus left in place. Is there a need for surveillance of a residual oesophagus left in place, and what is the best strategy?

Respirology

- Question 13: How often should adult patients with stable EA-TEF be seen by respirologists, and how often should they have chest X-rays and pulmonary function tests?
- Question 14: What investigations should adult patients with EA-TEF have when experiencing worsening respiratory function or recurrent chest infections?
- Question 15: When should adult patients with EA-TEF be screened by CT scanning for bronchiectasis?
- Question 16: What are the indications for bronchoscopy in adults with EA-TEF?
- Question 17: What is the prevalence of asthma (as defined by national and international asthma guidelines) in adults with EA-TEF?
- Question 18: Are adults with EA-TEF at increased risk for lung cancer?
- Question 19: Is there a role for prophylactic antibiotics, such as azithromycin, in patients with EA-TEF with recurrent chest infections with or without bronchiectasis?
- Question 20: What is the best management (investigations and treatment) for patients with EA-TEF and chronic respiratory symptoms thought to be secondary to reflux?
- Question 21: Is there a role in the use of nebulized hypertonic saline, positive expiratory pressure technique and chest physiotherapy during acute respiratory exacerbation in the management of EA-TEF and chronic respiratory symptoms or complications at the time of transition?

Otolaryngology

- Question 22: What are the prevalence and incidence of aspiration (direct and reflux) in adolescents and adults with EA-TEF, and how should it be investigated?
- Question 23: What is the incidence of recurrent TEF formation in adolescents and adults with EA-TEF?
- Question 24: What is the incidence of symptomatic unrepaired laryngeal clefts in adolescents and adults with EA-TEF?
- Question 25: What is the incidence of unilateral and bilateral vocal cord paralysis in adolescents and adults with EA-TEF, and what are the associated symptoms?
- Question 26: What are the incidence and prevalence of tracheomalacia or bronchomalacia in adolescents and adults with EA-TEF, what are the associated symptoms, and what is the best way to investigate this?
- Question 27: How often is vascular anomaly resulting in compression seen in adolescents and adults with EA-TEF, what are the presenting symptoms, and how should this be investigated and treated?
- Question 28: What percentage of adolescent and adult patients with EA-TEF are tracheostomy dependent, and why?
- Question 29: Should adolescents be routinely screened with laryngobronchoscopy for recurrent TEF, laryngeal cleft, tracheomalacia and aspiration at the time of transition, and how often should adult patients with stable EA-TEF be seen by adult otolaryngologists?

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Feeding and nutrition

- Question 30: What are the prevalence and incidence of malnutrition in adolescence and adulthood in patients with EA-TEF?
- Question 31: Are there any predictive factors for malnutrition in adolescents and adults with EA-TEF?
- Question 32: What are some of the therapeutic strategies to reduce the incidence of malnutrition in adolescents and adults with EA-TEF?
- Question 33: Which are the nutrients at risk in adolescents and adults with EA-TEF?
- Question 34: What is the role of dysphagia in the prevalence and incidence of feeding difficulties in adolescents and adults with EA-TEF, and is there a role of modified diets in improving feeding in these patients?
- Question 35: What is the role of GERD on feeding difficulties in adolescents and adults with EA-TEF?
- Question 36: What is the role of EoE on feeding difficulties in adolescents and adults with EA-TEF?
- Question 37: Should all adolescents be seen by a dietitian and deglutologist and routinely screened for nutritional deficiencies at the time of transition, and how often and when do adults with EA-TEF need to be routinely monitored by a dietitian and deglutologist?
- Question 38: What is the role of feeding difficulties and dysphagia on QOL outcomes in adolescents and adults with EA-TEF?
- Question 39: Does anxiety (parental and of the patients) have an effect on diet and feeding in adolescents and adults with EA-TEF?

Psychology and health-related QOL

- Question 40: What are the psychosocial needs of adolescent and adult patients with EA-TEF and their families during transition?
- Question 41: In what way does the health-related QOL develop over the course of childhood into adolescence and adulthood in patients with EA-TEF?
- Question 42: What are the main considerations in the optimal preparation of adolescent patients with EA-TEF and their parents for transition and transfer from paediatric to adult health care?

EA-TEF, oesophageal atresia–tracheoesophageal fistula; EoE, eosinophilic oesophagitis; GERD, gastro-oesophageal reflux disease; MIS, minimally invasive surgery; QOL, quality of life; TEF, tracheoesophageal fistula.

Gastroenterological complications in adolescents and adults with EA-TEF

Questions and recommendations on gastroenterological complications are respectively shown in Boxes 1 and 2.

1. Common digestive symptoms

In adult patients with oesophageal atresia, chronic gastrointestinal symptoms are common, whereas respiratory problems are less frequent. Despite the frequency of these gastrointestinal symptoms, most adults born with oesophageal atresia have become accustomed to living with some degree of dysphagia and reflux and often do not consider seeking medical attention, which can result in suboptimal management of GERD.

Eight case series reporting gastrointestinal symptoms in adult patients older than 18 years have been reported so far[11–18]. Only one controlled study compared 101 adult patients born between 1947 and 1985 who underwent surgery for oesophageal atresia with their native oesophagus (mean follow-up 36 years, range 22–57 years) with a randomly selected population of 287 control individuals without oesophageal atresia[12]. The prevalence of symptomatic GERD was significantly higher among patients than among controls (34% versus 8%; $P < 0.001$)[12]. Another case series found that GERD symptoms were reported by 63% of patients, and 25% of these had severe reflux symptoms, defined as occurring at least 3 days per week[11]. GERD symptoms in patients with oesophageal atresia also impaired QOL[19].

2. Prevalence and causes of dysphagia

Symptoms of dysphagia are extremely frequent and affect 39%[16] to 85%[12] of adults with EA-TEF; a significantly higher proportion than in control individuals (2%; $P < 0.001$)[12]. A prospective study using a disease-specific swallowing dysfunction questionnaire to assess swallowing dysfunction in 46 adults with repaired EA-TEF, with a follow-up of 40 years (age 18–63 years), confirmed the high prevalence of swallowing dysfunction (82%), worse with hard food consistencies (70%), and associated with frequently needing sips of liquids to facilitate swallowing (75%). A study in 81 adolescents with EA-TEF found similar figures, where dysphagia was found in 61% but did not influence QOL[20]. Although dysphagia is frequent and usually lifelong, patients do not spontaneously complain about it due to efficient coping strategies, that is, avoiding specific food consistency and flushing food with drinking water during meals, and resilience starting from early childhood[15,21].

The roles of dysmotility or residual stricture on reported dysphagia are not yet clear in adults. However, several causes can explain dysphagia (Box 3). Patients reporting dysphagia — especially when new onset or aggravated — should undergo endoscopic evaluation to exclude anastomotic stricture, EoE, Barrett oesophagus and even oesophageal cancer[22].

3. Prevalence and predictive factors of oesophageal complications

a. Peptic oesophagitis. The high incidence of GERD in patients with EA-TEF, coupled with abnormal oesophageal motility, which impairs normal acid clearance, renders these patients more prone to reflux and peptic oesophagitis. Studies of adult patients with oesophageal atresia have documented an incidence of endoscopic oesophagitis of 8–19% and a higher incidence of histological oesophagitis of 25–51%[12,15,17,23–26]. Studies of adolescents with oesophageal atresia have documented an incidence of endoscopic oesophagitis of 20–49.2% and of histological oesophagitis of 44.1–61.2%[27–30].

b. Eosinophilic oesophagitis. EoE is an increasingly recognized childhood disease. Cases of EoE occurring in patients with oesophageal atresia have been reported, with an incidence of up to 17%, although the exact prevalence of EoE in oesophageal atresia remains unknown in adults[31]. The prevalence of EoE was reported to be 9.5% in a prospective

study of 63 adolescents with oesophageal atresia[32]. Currently, there are no studies that have looked for or reported EoE in adult patients with EA-TEF.

c. Anastomotic and other strictures. Although anastomotic strictures have been reported in 18–60% of children with repaired oesophageal atresia, there is not much in the published literature about their prevalence in adolescents and adults with oesophageal atresia[7]. In a study of 101 adults with oesophageal atresia, anastomotic stricture was demonstrated in 8%[12]. Another study on 41 adults with oesophageal atresia showed that oesophageal stricture was detected in 7% of patients in a barium swallow[15].

d. Mucosal bridge and proximal pouch and diverticulum. There are only case reports of four children with oesophageal atresia with a mucosal bridge at the site of anastomotic repair, with the usual symptoms being dysphagia and food bolus impaction[33,34]. However, there is no published literature on the prevalence of mucosal bridge in adolescents and adults with oesophageal atresia. The only study in adult patients with oesophageal atresia to report on the proximal pouch and diverticulum is by Huynh-Trudeau et al., who report data on 41 patients, 13% of whom were found at endoscopy to have oesophageal diverticulum (proximal pouch)[15]. In a contrast study, diverticulum was seen in 14% of the same patients[15].

e. Oesophageal dysmotility. Oesophageal dysmotility is present to some degree in all patients with oesophageal atresia, with the aetiology being both congenital and iatrogenic. In a study of 101 adults with oesophageal atresia, manometry demonstrated non-propagating peristalsis in 80% of patients, with all changes being significantly worse in those with epithelial metaplasia ($P = 0.02$)[12]. Pedersen et al., using high-resolution manometry in 59 adolescents with oesophageal atresia, demonstrated oesophageal dysmotility in all patients, with 83.3% having no propagating swallows[27]. However, the contribution of

Box 2

Gastroenterology recommendations

Statement 1

In adults with EA-TEF, chronic symptoms of gastro-oesophageal reflux are common. However, since they might have become accustomed to living with these symptoms, they might not seek medical attention, which could contribute to suboptimal management of GERD.

Statement 2

Swallowing dysfunction is common in adults who underwent EA-TEF repair. Worsening dysphagia could be due to several different pathologies and should prompt investigations.

Statement 3

- Peptic oesophagitis: peptic and/or reflux oesophagitis persists well beyond infancy into adolescence and adulthood in patients with EA-TEF, and histological oesophagitis can be present even on a normal-appearing endoscopy. Thus, careful long-term evaluation for gastro-oesophageal reflux and its complications with endoscopy and biopsies is indicated following primary repair. There is currently no evidence about predictive factors predisposing to the development of reflux and/or peptic oesophagitis in adolescent and adult patients.
- EoE: there is currently limited evidence on the prevalence of EoE (>15 eosinophils per HPF plus symptoms of oesophageal dysfunction) in adolescents with EA-TEF, and there is no published evidence about its prevalence in adults. However, given the documented increased incidence of EoE in paediatric patients with EA-TEF, it is important to look for EoE with multiple biopsies during surveillance endoscopy at the time of transition and in adulthood in these patients.
- Anastomotic and other strictures: anastomotic strictures can occur beyond infancy in adolescents and adults with EA-TEF, and symptomatic patients should be investigated with contrast studies, endoscopy and biopsies. There is limited evidence that a history of anastomotic strictures can predict the occurrence of epithelial metaplasia.
- Mucosal bridge and proximal pouch: there is currently very limited information about the prevalence of mucosal bridge and proximal oesophageal pouch/diverticulum in adolescent and adult patients with EA-TEF.
- Dysmotility: oesophageal dysmotility persists beyond infancy in a majority of adolescent and adult patients with EA-TEF. It could be one of the causes of dysphagia in these patients. There is limited evidence that it might contribute to an increased risk of epithelial metaplasia in adult patients.

Statement 4

- The incidence of oesophageal gastric and intestinal metaplasia (Barrett oesophagus) is increased in adults with EA-TEF as compared with the general population.
- The real prevalence and incidence of oesophageal cancer (adenocarcinoma and squamous cell carcinoma) in adults with EA-TEF is unclear but oesophageal cancer remains a concern.

Statement 5

- Patients with stable EA-TEF should be reviewed by a gastroenterologist at least every 2 years between 18 and 34 years of age and annually from the age of 35 years onwards.
- Endoscopic surveillance with biopsy samples and narrow-band imaging, where available, should be performed every 5 years between 18 and 28 years of age, every 3 years between 28 and 40 years of age, every 2 years between 40 and 50 years of age, and annually onwards. Additional endoscopies are required in case of new or worsening symptoms and in accordance with the recommendations for existing Barrett oesophagus.

EA-TEF, oesophageal atresia–tracheoesophageal fistula; EoE, eosinophilic oesophagitis; GERD, gastro-oesophageal reflux disease; HPF, high-powered field.

Box 3

Causes of dysphagia in oesophageal atresia

Inflammatory
- Infectious oesophagitis (for example, candidiasis)
- Peptic oesophagitis and Barrett oesophagus
- Eosinophilic oesophagitis
- Oesophageal cancer
- Peptic stricture
- Post-fundoplication obstruction
- Mucosal bridge
- Vascular anomalies
- Anastomotic diverticulum
- Inlet patch

Anatomical
- Anastomotic stricture
- Congenital stenosis

Dysmotility
- Intrinsic
- Postoperative

oesophageal dysmotility to dysphagia symptoms and to an increased risk of epithelial metaplasia is currently unknown.

4. Risk of Barrett oesophagus, gastric and intestinal metaplasia, oesophageal cancer and squamous cell carcinoma

A systematic review summarized the prevalence of Barrett oesophagus in patients with EA-TEF[35]. Among long-term follow-up studies, the pooled prevalence of Barrett oesophagus was 5.0% (95% CI 4.5–5.6%, 317 of 6,282 patients) with a mean age of detection of 13.8 years (range 8 months to 56 years)[36]. Among these patients, gastric metaplasia was more common (227 patients), whereas intestinal metaplasia was found in a smaller proportion (54 patients). The prevalence of Barrett oesophagus among patients with oesophageal atresia was much higher than that in the general population, which is 0.5–2% in adults and 0.0024% in children[22,37]. Studies have not found a correlation between clinical symptomatology and the presence of Barrett oesophagus[16,38].

To date, worldwide, 14 cases of cancer have been reported in adult patients with EA-TEF, including 4 adenocarcinomas and 10 squamous cell carcinomas. The median age at diagnosis was 44 (mean 38, 19–47) years. Among them, only 3 had a documented Barrett oesophagus[35]. However, the true prevalence of oesophageal cancer is unclear as there are limited data on patients being followed into adulthood[35]. Sistonen et al. followed 272 patients from their surgical repair until a median age of 35 years and identified no cases of oesophageal cancer[39]. Another study estimated a 10-year oesophageal squamous cell carcinoma prevalence of 0.7% in adult patients with oesophageal atresia undergoing routine screening, which was 100 times higher than the prevalence in the general population[40].

5. Surveillance of patients with stable EA-TEF and timely diagnosis of Barrett oesophagus

Patients with stable EA-TEF should be reviewed by a gastroenterologist at least every 2 years between the ages of 18 and 34 years and yearly from the age of 35 years. Endoscopic surveillance with biopsy samples[41] and narrow-band imaging, when available, should be performed every 5 years between the ages of 18 and 28 years, every 3 years between 28 and 40 years, every 2 years between 40 and 50 years, and yearly thereafter. Additional endoscopies are required in case of new or worsening symptoms and according to the recommendations for existing Barrett oesophagus. Additional endoscopies are required in case of new or worsening symptoms. This careful surveillance is a comprehensive clinical and endoscopic screening system aiming to detect Barrett oesophagus, screen for oesophageal malignancy and start treatment early, when indicated. Patients must be informed about the need for this lifelong surveillance.

Surgery complications in adolescents and adults with EA-TEF

Questions and recommendations on surgical complications are respectively shown in Boxes 1 and 4.

6. Management of patients with persistent, uncontrollable GERD

GERD is a frequent finding in patients operated on for oesophageal atresia, ranging from 31% to 43% of patients[42]. There is, however, a lack of standardization on the definition of the disease and associated symptoms. Thus, the diagnosis must be confirmed before starting long-term anti-reflux treatment or planning surgery.

Oesophagitis can be detected in up to half of patients with oesophageal atresia who undergo oesophagogastroduodenoscopy[27]. Oesophagogastroduodenoscopy is useful to detect complications (for example, strictures or Barrett oesophagus) and associated conditions (for example, hiatal hernia, EoE)[43]. In the case of negative endoscopic findings, GERD must be objectively demonstrated using 24-h pH monitoring, which remains the gold standard in diagnosing GERD[44]. Moreover, as refluxes in infants and children are mainly weak or non-acidic, the association of symptoms with reflux episodes during multichannel intraluminal impedance and pH monitoring is recommended.

Barium swallow has a low sensitivity in detecting GERD[45] but it is necessary before surgical treatment of GERD to identify hiatus hernia, strictures or a short oesophagus. The test is also useful in failed anti-reflux surgery to help differentiate an obstructed fundoplication from one that has slipped or is loose[43].

Gastro-oesophageal scintigraphy has also been used for the diagnosis of GERD and evaluation of gastric emptying in these patients. There is insufficient evidence, however, to support the use of gastro-oesophageal scintigraphy in this context in patients with oesophageal atresia. Currently, no data exist on the predictive value of oesophageal manometry in diagnosing GERD or evaluating post-fundoplication complications in patients with oesophageal atresia[7]. Finally, endoluminal planimetry is a promising tool but there is currently no evidence of its real value in clinical practice.

7. The best surgical strategy for patients with persistent, uncontrollable GERD

Traditionally, open laparotomy has been used to perform fundoplication surgery but, nowadays, most groups prefer the laparoscopic approach. As far as the selection of the type of anti-reflux surgery in patients with oesophageal atresia is concerned, partial wraps might be associated with fewer adverse effects but with a higher failure rate than the complete Nissen fundoplication via laparoscopic surgery that, on the other side, might result in more dysphagia, retching, and gas or bloating. However, this observation is not supported by solid scientific data and, therefore, it is not possible to make a conclusive statement about the choice of fundoplication surgery in an EA-TEF cohort.

The laparoscopic approach has been demonstrated to be feasible, safe and effective also in revisional surgery after fundoplication surgery, both in the case of open and laparoscopic primary surgery. Oesophageal atresia repair often causes oesophageal shortening, especially in patients with long-gap atresia. Some surgeons, therefore, prefer to combine fundoplication surgery with some lengthening procedures (Collis gastroplasty), especially in children with previously failed fundoplication as this might decrease the GERD recurrence rate and could thus be considered if a primary repair fails.

Total oesophagogastric dissociation (TED) was proposed as a valid alternative to fundoplication and gastrostomy surgery to eliminate the risk of recurrence of GERD[46]. Originally proposed for children with neurological impairments, this operation has also been used in children with oesophageal atresia and severe reflux[47]. However, owing to its complication rate and long-term nutritional and metabolic complications, TED cannot be recommended as a first-line surgical treatment in children with refractory GERD[46,47].

8. Management of patients with persistent, uncontrollable GERD and prior gastric pull-up or tube

The most popular strategies for oesophageal substitution are the colon interposition and the gastric pull-up[48]. A direct consequence of a gastric pull-up is gastric and duodenal reflux, reported in 60–80% of patients[49,50]. Persistent reflux can lead to peptic oesophagitis, cicatricial strictures, Barrett oesophagus, and laryngeal or trachea-bronchial problems affecting the QOL of these patients[51–53]. Oesophagitis is a common finding in patients who underwent oesophageal substitution with gastric pull-up[54–56]. Endoscopic evaluation is paramount for the identification of oesophagitis or Barrett epithelium. The incidence of reflux oesophagitis seems to increase with time and, sometimes, there

Box 4

Surgical subgroup recommendations

Statement 6

- A correct diagnosis of GERD is mandatory before intensifying medical therapy or planning surgery. The diagnosis is based on the clinical context and the overall results of performed studies. MII-pH monitoring over 24 h is the best available tool for the diagnosis of GERD. Endoscopy should always be performed to rule out GERD complications, and a Barium swallow should be conducted to rule out anatomical gastro-oesophageal alterations, especially before surgery or after a failed fundoplication.
- Other tests (manometry, gastro-oesophageal scintigraphy and EndoFlip) might be useful prior to considering surgery but there is currently limited evidence about their role.

Statement 7

- The laparoscopic approach is nowadays the recommended surgical approach for anti-reflux surgery in patients with EA-TEF. The choice between total or partial fundoplication should be left to the preferences and expertise of surgeons.
- The laparoscopic approach is also possible in revisional surgery. However, the possibility of a 'short' oesophagus must be considered in patients with EA-TEF who failed a previous operation. The need for lengthening procedures of the oesophagus must be considered in these patients.
- Other complex procedures, such as total oesophageal dissociation or oesophageal resections, are not to be recommended as first-line surgery and must be evaluated on an individual patient basis.

Statement 8

Endoscopic surveillance with biopsy samples is mandatory. The proposed timing of endoscopies should be similar to what is recommended in statement 5 for patients with stable EA-TEF. MII-pH monitoring is recommended to assess the responsiveness to acid-suppressive medication. The best approach to manage persistent GERD is still controversial, with medical treatment being advocated as the first-line treatment.

Statement 9

Total oesophagogastric dissociation reversal is possible and indicated after gastrostomy weaning whenever good lung function is confirmed. The main indication is the development of severe nutritional or vitamin deficiencies. Endoscopic surveillance of the distal oesophagus is important.

Statement 10

Long-term follow-up of patients with EA-TEF who underwent oesophageal substitution is of paramount importance. Gastrointestinal complications need to be assessed through serial symptom evaluation and regular endoscopies. These patients are at the highest risk for poor respiratory outcomes and need close respiratory monitoring.

Statement 11

When a patient with EA-TEF colonic redundancy is asymptomatic, conservative treatment is advisable. Symptomatic patients should be extensively evaluated through endoscopy, contrast study, and CT or MRI scan. The surgical approach should be determined on an individual patient basis.

Statement 12

Due to the risk of chronic GERD in the residual distal oesophagus, endoscopic surveillance should be scheduled during follow-up. CT and/or MRI might be indicated in some patients. If Barrett epithelium is found in the distal oesophagus, endoscopic surveillance is indicated as well as a treatment similar to that for patients without EA-TEF.

EA-TEF, oesophageal atresia–tracheoesophageal fistula; GERD, gastro-oesophageal reflux disease; MII-pH, multichannel intraluminal impedance and pH.

is a replacement of oesophagitis areas with Barrett epithelium[50,55]. This observation increases the importance of endoscopic follow-up for the early identification of potentially malignant lesions. Indeed, da Rocha et al. recommended yearly endoscopic evaluation of both symptomatic and asymptomatic patients with EA-TEF[50]. The need for a lifelong follow-up is commonly accepted. Conservative treatment is usually successful, and surgery is only considered in case of persistent and progressively worsening symptoms[57,58].

9. New gastric reconnection in patients with previous TED

After TED, patients with EA-TEF can gradually start normal oral food intake and be weaned off the gastrostomy feeds, although this might result in nutritional and vitamin deficiencies owing to gastric transit exclusion[47]. Severe anaemia owing to impaired iron absorption has also been described[47]. As long as oral intake remains satisfactory, reversal seems unnecessary[47]. TED reversal is possible only when a thorough preoperative respiratory evaluation is performed to rule out gastro-oesophageal reflux-related complications. Intraoperatively, the Roux-en-Y can either be preserved or sacrificed. Maignan et al. described two paediatric patients with oesophageal atresia, with previous oesophagocoloplasty and TED, who effectively underwent oesophagogastric reconnection at the age of 12 and 10 years, with gastro-colonic anastomosis with posterior fundoplication[59].

10. The best protocol for clinical follow-up in patients that underwent oesophageal substitution

Short-term complications after oesophageal substitution mainly comprise anastomotic stenosis, leakage and dehiscence. These are usually diagnosed within standard postoperative follow-up before discharge. Less is known about long-term complications, both gastrointestinal and respiratory.

Gastro-colonic reflux is frequently reported in patients with oesophageal atresia who underwent colonic interposition[60], with histology of the neo-oesophagus confirming the presence of mild, chronic and non-specific inflammation[61]. However, a mismatch between endoscopic findings of inflammation and patient symptoms is commonly described, and dietary modifications combined with anti-reflux medications usually provide adequate symptom control[62]. Other complications involve peptic ulceration of the native oesophagus left in situ, redundancy of the colonic graft, lower junction stenosis and dumping syndrome[60–62].

Assessment of such complications should involve symptom evaluation and endoscopy[63]. Carcinomas of the interposed colonic segment and gastric metaplasia have been episodically described in adult patients with EA-TEF[40,60]. Therefore, periodic endoscopic surveillance is advisable to promptly detect and remove potentially malignant lesions[64]. Additionally, the height and weight of children with EA-TEF who underwent oesophageal substitution are usually lower compared with healthy individuals[62], suggesting that these patients might require an increased energy intake[65]. In addition, regular evaluation of the anastomosis should be considered as 20–40% of patients have strictures affecting normal oral consumption[60–62,65].

As for respiratory complications, chronic or recurrent cough, dyspnoea, and ventilatory disorders are most commonly described[66,67]. Furthermore, lung function impairment can occur from multiple micro-aspirations and subsequent chronic pulmonary inflammation. This impairment translates as low exercise capacity and lung volume, detectable in respiratory function tests[66,67]. Lastly, the development of a graft-respiratory fistula has been reported, frequently owing to the interposed organ ulceration[68,69]. This complication should be suspected in case of progressive respiratory symptoms and assessed via CT or MRI scans.

11. Surgical strategy for patients with oesophageal substitution and colonic redundancy

Colonic redundancy is one of the main complications after colonic interposition[70]. When redundancy is asymptomatic, expectant management is standard practice. In the case of symptomatic patients, a thorough preoperative investigation is paramount to assess anatomy, functional performance and vascularization of the transposed colon. Additionally, the surgical history of every patient needs to be considered and treatment should be tailored[70]. Several surgical approaches have been reported such as colonic conduit revision, colon–gastric disconnection with Roux-en-Y colon–jejunal anastomosis[47,71], resection and anti-mesenteric longitudinal tapering of the colonic segment, trans-hiatal colonic mobilization with anti-mesenteric tapering coloplasty, and reverse gastric tube oesophagoplasty[72]. Advantages of reverse gastric oesophagoplasty are the absence of an interposed organ between the oesophagus and stomach, excellent vascularization, and similar outcomes for subcutaneous, retrosternal or intrathoracic approaches.

12. Surveillance of and the best strategy for a residual oesophagus left in place

After oesophageal substitution, oesophagectomy is not always possible, and an oesophageal exclusion might be required. Mucous secretion from the excluded oesophageal cavity is usually a self-limiting process owing to mucosal gland atrophy[73]. However, between 2% and 8% of patients with mucocele can develop symptoms related to an infective process or a tracheal and bronchial compression with consequent respiratory distress, chest pain, cough, hiccoughs and dysphagia[74,75]. CT or MRI scans are considered the gold standard for symptom evaluation[76]. Surgical resection of the oesophagus can be difficult after a previous infection[77]. A few attempts of drainage have been described, which provided transient symptom relief but, in all patients, the mucocele recurred[78]. Other complications related to the excluded oesophagus involve leakage from the bypassed oesophagus, ulceration with fistula development and carcinoma of the oesophageal remnant[79–82]. Barrett oesophagus in the oesophageal stump can be an additional complication and endoscopic evaluation by retroflexion of the distal oesophageal stump is not always feasible.

Respiratory complications in adolescents and adults with EA-TEF

Questions and recommendations on respiratory complications are respectively shown in Boxes 1 and 5.

13. Respirological review of patients with stable EA-TEF

Patients with EA-TEF are at risk of respiratory morbidity their entire lives. A large, Finish, community-based study of 588 adults with EA-TEF reported that the proportion of patients with a history of pneumonia, bronchitis, persistent cough and wheezing were 56%, 70%, 31% and 33%, respectively. Compared with healthy individuals, bronchitis, cough and reduced respiratory-related QOL were more common in patients with EA-TEF[2,83]. Symptoms and lower respiratory tract infections (LRTI), although fairly common in adults, are more common in children[2]. A key complication is bronchiectasis, which is present in a substantial number of children; adult data are lacking[2]. Rates in children at referral centres, diagnosed by CT scanning, range from

Box 5

Respirology subgroup recommendations

Statement 13
We recommend that adult patients with EA-TEF should have routine follow-up with a respirologist and PFT at the time of transition. Subsequent regular follow-up and PFT can be individualized, although annual follow-up is recommended. More frequent follow-up is recommended in symptomatic patients. Consideration should also be given to annual chest X-rays.

Statement 14
Adult patients with EA-TEF with worsening respiratory status should be investigated for aspiration owing to oesophageal dysfunction, recurrent TEF and GERD as well as for tracheomalacia, laryngeal cleft, and classical asthma. Such testing could include a UGI series, bronchoscopy and upper endoscopy, pH-impedance testing, objective swallow assessment, and PFT with a bronchodilator response.

Statement 15
CT scan to rule out bronchiectasis should be considered for adult patients with EA-TEF and chronic cough, worsening PFT, and persistent CXR changes potentially owing to ongoing aspiration.

Statement 16
Indications for bronchoscopy in adult patients with EA-TEF include evaluating for tracheomalacia, determining whether recurrent TEF is present and obtaining lower airway cultures. Combined procedures, including upper endoscopy and, potentially, rigid laryngobronchoscopy, are encouraged.

Statement 17
Asthma symptoms can be due to aspiration and/or tracheomalacia rather than classical asthma. The precise prevalence of asthma in adults with EA-TEF remains unclear.

Statement 18
Lung cancer has been reported in one adult with likely uncontrolled aspiration; the incidence of lung cancers in adults with EA-TEF requires further research.

Statement 19
Chronic macrolide therapy has shown benefit in bronchiectasis owing to other causes and, therefore, might be beneficial in adult patients with EA-TEF and bronchiectasis but it has not been studied in these patients.

Statement 20
Adult patients with EA-TEF and respiratory symptoms due to GERD should be investigated with endoscopy and pH-impedance testing. When testing for GERD is negative, other causes should be investigated. Management in conjunction with a gastroenterologist is strongly recommended.

Statement 21
Adult patients with EA-TEF, clinically substantial tracheomalacia and recurrent or chronic lower respiratory tract infections may benefit from assisted airway clearance — particularly positive expiratory pressure therapy; the role of mucolytics, such as nebulized hypertonic saline, is currently unclear.

CXR, chest radiograph; EA-TEF, oesophageal atresia–tracheoesophageal fistula; GERD, gastro-oesophageal reflux disease; PFT, pulmonary function test; TEF, tracheoesophageal fistula; UGI, upper gastrointestinal.

17% to 31%[84–86]. Physician-diagnosed asthma was reported in 30% of 73 adults with EA-TEF[87]. However, asthma is atypical in this population and might be overdiagnosed. Asthma diagnosis correlates poorly with the presence of typical asthma symptoms, pulmonary function test (PFT) abnormalities or evidence of bronchial hyper-reactivity[86]. Atopy and allergy seem to be frequent in individuals with EA-TEF, and some people with EA-TEF and asthma have allergies, elevated exhaled nitric oxide, and bronchial hyper-reactivity[86]. In some patients, a false diagnosis of asthma was made in the absence of typical features[86]. Bronchial biopsy samples in children with EA-TEF showed inflammatory changes in two of three patients but were consistent with a diagnosis of bronchitis rather than asthma and correlated poorly with physician-diagnosed asthma[88].

PFT abnormalities are common in adults with EA-TEF. Roughly equal numbers of 28 adults with oesophageal atresia had obstructive or restrictive defects and about 11% had mixed defects[86]. About one-quarter to one-half of individuals with EA-TEF have normal lung function, and pulmonary function values for spirometry and total lung capacity generally fall in the low–normal range[2]. Small airway disease, as measured by lung clearance index, was abnormal in 70% of 28 adults but correlated poorly with symptoms[86].

Respiratory morbidity in this population almost certainly has multiple interacting causes. Tracheomalacia is present in the great majority of paediatric patients with EA-TEF but generally improves as airway cartilage stiffens. Tracheomalacia leads to a brassy cough typical of patients with EA-TEF and impedes mucociliary clearance, increasing the risk of LRTI[2]. Helpful investigations include forced inspiratory vital capacity curves during spirometry, dynamic CT imaging and flexible bronchoscopy[10]. Respiratory morbidity can be due to recurrent aspiration from any combination of oesophageal dysmotility, stricture or EoE, leading to food stasis and oropharyngeal aspiration, a recurrent TEF, or gastro-oesophageal reflux leading to aspiration[7]. Aspiration can also worsen tracheomalacia[2,10]. Anecdotally, spirometry and chest radiographs (CXRs) might assist with the early detection of aspiration, providing a rationale for regular monitoring. It has been postulated that atopy is more common in patients with EA-TEF owing to increased absorption of allergens from an abnormal alimentary tract[83].

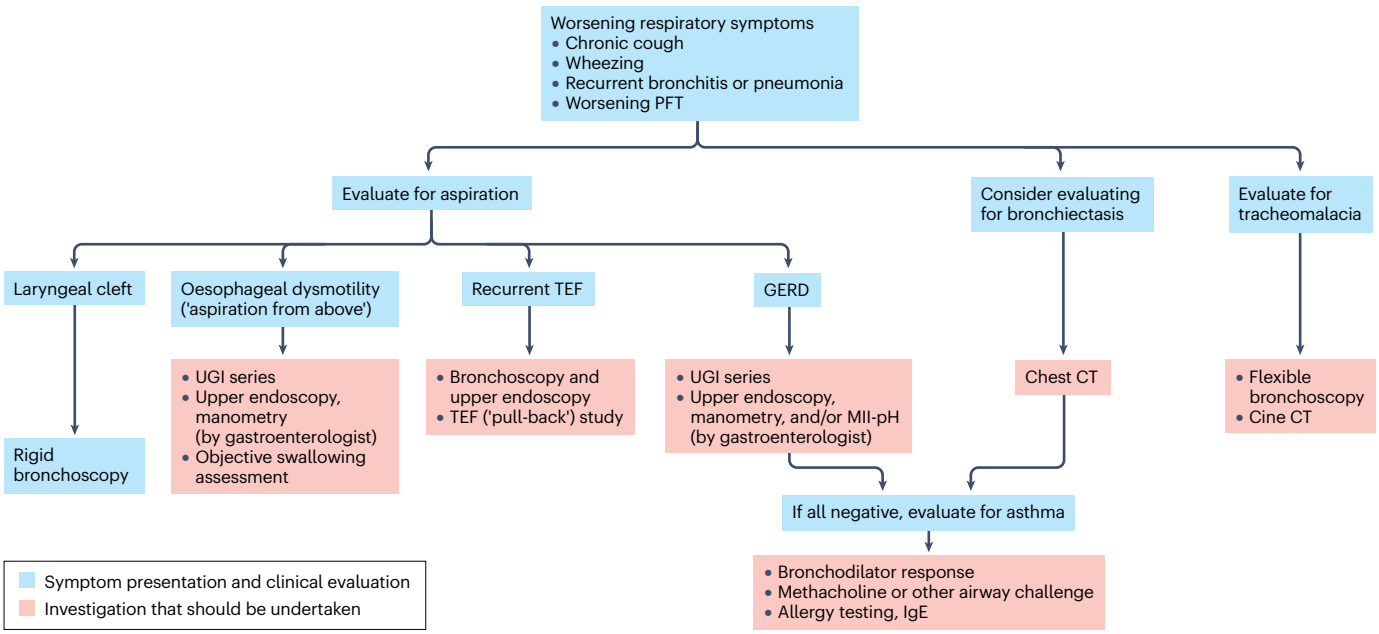

Fig. 1 | Algorithm for the investigation of oesophageal atresia–tracheoesophageal fistula in adult patients with worsening respiratory symptoms. Proposed algorithm to determine further respiratory investigations based on symptom presentation. Blue boxes denote symptom presentation and clinical evaluation. Arrows denote flow within the algorithm and decision-making process. Red boxes denote the investigation that should be undertaken in the clinical context described. GERD, gastro-oesophageal reflux disease; MII-pH, multichannel intraluminal impedance and pH; PFT, pulmonary function test; TEF, tracheoesophageal fistula; UGI, upper gastrointestinal.

Given high rates of morbidity, adult patients with EA-TEF should have regular follow-ups by a respiratory specialist (Supplementary Box 2) as recommended in the published EA-TEF respiratory care recommendations (TEF-RCR)[10]. In paediatric centres, this is often done in collaboration with a multidisciplinary team, including gastroenterologists, surgeons and otolaryngologists[4]. This is uncommon for adult EA-TEF care, and it is reasonable for either a respirologist or gastroenterologist to act as the gateway, with additional referral as indicated. Where the respirologist is the lead, access to a gastroenterologist for consultation is important. Follow-up should take place at least annually or more often if the patient has substantial symptoms or is unstable. Follow-up by the respirologist should include screening for respiratory symptoms and symptoms suggestive of aspiration risk (such as choking or reflux) and PFT. Annual CXR should be considered in patients with an increased aspiration risk. A CT scan should be considered when bronchiectasis is clinically suspected. The need for regular imaging in the EA-TEF cohort had a weak agreement among experts in their care recommendations for respiratory complications (TEF-RCR)[10].

14. Investigations during worsening respiratory function or recurrent chest infections

Adult patients with EA-TEF have a marked risk of LRTI; therefore, when infectious symptoms are present, a CXR and, possibly, a white blood cell count and sputum culture should be obtained. However, this lacked strong agreement in the TEF-RCR[10]. When there have been multiple radiographically confirmed cases of pneumonia, further investigation is recommended[10] (Box 5). Similarly, increasing respiratory symptoms or worsening PFT should prompt investigation for tracheomalacia and aspiration before assuming that the cause is asthma[2,10]. Aspiration should be assessed systemically, looking for swallowing dysfunction, recurrent TEF and GERD. Evaluation is best done in consultation with a gastroenterologist, and concurrent performance of bronchoscopy and upper endoscopy is helpful[2,10]. Investigations could include upper gastrointestinal series with a swallowing study by speech therapy, swallowing assessment at laryngoscopy and oesophageal motility studies. Evaluation, including diagnosis of GERD, is discussed in more detail elsewhere in this document. A recurrent TEF can be diagnosed by bronchoscopy and/or endoscopy with an injection of contrast or methylene blue into a retained pouch or other suspicious area but is often better diagnosed using an upper gastrointestinal 'pull-back' study whereby contrast is injected under pressure using catheters in the oesophagus, forcing contrast through a small TEF[10]. Particularly after aspiration has been excluded, testing for asthma may be considered, including spirometry, bronchodilator response, airway challenge testing and adjunctive allergy testing[86] (Fig. 1).

15. CT scanning for bronchiectasis

Bronchiectasis should be considered in the presence of a chronic wet (or moist) cough, chronic aspiration, worsening PFT or persistent atelectasis (particularly where there had been previous cases of pneumonia). CXRs lack sensitivity but can be suggestive and are occasionally diagnostic. CT is currently the most specific test[10].

16. Indications for bronchoscopy

Flexible bronchoscopy is helpful for the diagnosis of tracheomalacia, ideally during spontaneous breathing and cough. Bronchoscopy and broncho-alveolar lavage are used to obtain lower airway bacterial cultures. Pathogenic bacteria in the lower airways are strongly suggestive of chronic aspiration and should prompt further evaluation (see earlier)[10]. The value of lipid-laden macrophages and of other

potential broncho-alveolar lavage fluid markers of aspiration remains controversial[89]. Bronchoscopy might help identify a recurrent TEF as tracheal bronchus is common in patients with EA-TEF[2]. The TEF-RCR considered combined bronchoscopy and endoscopy to be the gold standard for the diagnosis of recurrent TEF[10]. Bronchoscopy might help evaluate a deep tracheal pouch, which is often present at the location of the original repair site and can have retained secretions[90]. Suspension micro-laryngoscopy to determine whether there is a concurrent small laryngeal cleft, vocal cord paresis or paralysis, or subglottic stenosis can be considered, although most patients are likely diagnosed in childhood[10].

17. Prevalence of asthma. In previous studies, 15% of 101 patients and 30% of 73 adults with EA-TEF have been diagnosed with asthma[83,87], although the actual prevalence of typical asthma is unclear (see earlier)[86,91].

18. Risk for lung cancer. To date, there has been only one case of pulmonary squamous cell carcinoma in a 19-year-old patient with oesophageal atresia, who likely had uncontrolled aspiration[92]. The role of lung cancer surveillance is unknown.

19. Prophylactic antibiotics in patients with EA-TEF with recurrent chest infections with or without bronchiectasis. There are no controlled trials in patients with EA-TEF and recurrent LRTI. Systematic reviews have suggested a role for oral antibiotics, such as azithromycin, and a small effect with inhaled antibiotics in adults with non-chest infection bronchiectasis with frequent exacerbations and for macrolides as anti-inflammatory treatment in chest infection-associated bronchiectasis. There was a strong agreement for macrolide administration in the TEF-RCR[10].

20. Best clinical management for a patient with EA-TEF with chronic respiratory symptoms thought to be secondary to reflux. Ideally, EA-TEF should be co-managed with a gastroenterologist, as discussed elsewhere in this document. In patients with GERD that are inadequately controlled medically, fundoplication might be necessary, but this can have adverse effects, as a tight fundoplication and oesophageal dysmotility can worsen aspiration. Some patients might require a 'loose' fundoplication. Fundoplications often loosen over time[7].

21. Nebulized hypertonic saline, PEP technique and chest physiotherapy during acute respiratory exacerbation at the time of transition. As tracheomalacia causes impaired mucociliary clearance, improving airway clearance is important during LRTI. Positive expiratory pressure (PEP) therapy is likely the optimal modality as it opens the malacic airways while promoting the removal of infected secretions[10]. It is possible to enhance PEP with the use of oscillating pressure techniques. Conventional percussion and postural drainage or physiotherapy vests have no obvious advantage over PEP techniques and have the disadvantage of not maintaining airways open; the value of adding oscillating pressure to PEP is unclear. Head-down percussion and postural drainage techniques promote GERD in patients with chest infections and should be avoided[93]. Nebulized hypertonic saline has been shown to have small benefits even in the absence of bronchiectasis in terms of improving lung function and sputum burden. Although the viscosity of sputum in patients with EA-TEF has not been measured, hypertonic saline could be helpful; there was weak consensus for this in the TEF-RCR[10].

Otolaryngological complications in adolescents and adults with EA-TEF

Questions and recommendations on otolaryngological complications are respectively shown in Boxes 1 and 6.

22. Aspiration

Patients with EA-TEF have an increased disposition to direct and reflux-related aspiration, which can be silent or result in symptoms and respiratory complications. Some compensation and resolution occur with growth by adolescence and adulthood to a variable degree. Contributing factors include (1) oesophageal dysfunction owing to dysmotility, GERD and delayed oesophageal clearance[94]; (2) post-surgical effects, including strictures, myenteric dysfunction, altered sensation, direct neural injury or traction of the recurrent laryngeal nerve[95]; (3) a recurrent fistula at the original repair site, a new lesion in a different location or a subtle communication missed during initial assessments[96]; (4) congenital or acquired co-existing gastrointestinal and/or airway pathology[97–99,100]; and (5) delayed oral-motor development and feeding difficulties that persist as adaptive and avoidant behaviours[101,102].

To date, no consistent test for aspiration has been identified[89]. Events can be difficult to capture, especially if episodic. Chronic respiratory morbidity is used as an indirect indicator of aspiration though this might be confounded by other factors that affect respiratory clearance and airway inflammation. Patient-reported survey results and long-term reviews have identified an improvement but not complete resolution of dysphagia, food impaction, GERD symptoms, chest infections and regular antibiotic usage over time[102–105].

Investigations of oesophageal and/or gastro-oesophageal function (barium swallow, pH and multichannel intraluminal impedance studies, high-resolution manometry, oesophageal scintigraphy, radionuclide milk scans, upper gastrointestinal endoscopy with biopsy) are useful for understanding motility, GERD, strictures and oesophagitis but are less specific for aspiration[15,27]. Pull-back or pressure oesophagrams in a prone or semi-prone position identify H-type or recurrent TEFs[10] but are not widely used[106]. The predictive value of PFT, respiratory imaging modalities and flexible bronchoscopy with broncho-alveolar lavage for aspiration is inconsistent[27,89]. The importance of the presence of pepsin and bile acids in the airways is still under investigation. Lung biopsy is performed infrequently owing to its invasive nature[89].

23. Incidence of recurrent TEF formation

A recurrent TEF is estimated to occur in up to 5–14% of patients[94,96,107–109], although it can be as high as 20%[110]. Risk factors include previous anastomotic leak, congenital oesophageal stenosis[111], substantial oesophageal dysfunction and need for revision surgery[112]. The majority of recurrent TEF is in the same location as the original TEF repair. Less commonly, recurrent TEF can be acquired from oesophageal leaks (creating a new communication between the oesophagus and the pulmonary parenchyma, a segmental bronchus, or the trachea) or can be identified late even into adulthood (especially H-type fistulae or multiple fistulae), having been missed on original assessments[96,112–115]. A common feature for adult patients is a relative delay in diagnosis of TEF following the onset of symptoms, often for many months or years.

A recurrent TEF can be identified on contrast studies or chest CT but more commonly during bronchoscopy, which can be combined with simultaneous oesophageal endoscopy[10]. Positive pressure insufflation, dye or contrast, and gentle probing can assist with identification.

Box 6

Otolaryngology subgroup recommendations

Statement 22
The prevalence and incidence of aspiration (direct and reflux) in adolescents and adults with EA-TEF are unknown. Aspiration is likely to be a contributing factor to long-term morbidity but has been challenging to differentiate from other causes and difficult to objectively define and measure.

Statement 23
The incidence of recurrent TEF formation in adolescents and adults with EA-TEF is unknown. A high index of suspicion and a low threshold for investigation should be maintained when persistent respiratory symptoms are present, regardless of age and duration since the initial repair.

Statement 24
The incidence of symptomatic unrepaired laryngeal clefts in adolescents and adults with EA-TEF is unknown. Airway endoscopy is important to help identify co-existing or recurrent laryngotracheal abnormalities such as laryngeal clefts.

Statement 25
The incidence of vocal cord paralysis in adolescents and adults with EA-TEF is unknown. Investigation with laryngoscopy is important to consider, especially in those with persistent swallowing dysfunction and chronic respiratory symptoms.

Statement 26
The incidence and prevalence of tracheomalacia or bronchomalacia in adolescents and adults with EA-TEF are unknown. Respiratory symptoms tend to improve over time but might not completely resolve in adulthood and can be due to other factors in addition to residual tracheomalacia. Endoscopic airway assessment is the preferred modality to investigate tracheomalacia. The role of a CT scan in evaluating tracheomalacia requires further study.

Statement 27
The incidence of vascular anomaly resulting in compression in adolescents and adults with EA-TEF is unknown. An index of suspicion should be maintained for this diagnosis if respiratory and dysphagia symptoms persist over time, especially if there is a history of long-gap oesophageal atresia or congenital cardiac disease. If concerned, investigations should be undertaken.

Statement 28
The percentage of adolescent and adult patients with EA-TEF who are tracheostomy dependent is unknown. Decannulation of a tracheostomy can be achieved over time, but data regarding the persistent need for a tracheostomy in EA-TEF are lacking.

Statement 29
The high frequency of respiratory morbidity in this population justifies regular follow-up through to adulthood and an index of suspicion for co-existing unresolved, recurrent, new or missed laryngotracheal pathology. Clinical review and education at the time of transition in a multidisciplinary setting that includes otolaryngology might help identify those who would benefit from further investigation and follow-up.

EA-TEF, oesophageal atresia–tracheoesophageal fistula; TEF, tracheoesophageal fistula.

The site of the original defect in the posterior tracheal wall is usually recognizable; however, smaller openings might be obscured by airway secretions. In some situations, a blind-ending tracheal diverticulum or pouch is found rather than a recurrent TEF. This might contribute to reduced airway clearance, recurrent cases of pneumonia and atelectasis[90,115].

24. Incidence of symptomatic unrepaired laryngeal clefts

Laryngotracheal anomalies are a known association with EA-TEF[97,116,117]. Rates of secondary airway lesions have been reported to range from 20% to 40%[97,116–119] and can be as high as 62.6% in those requiring otolaryngology referral[97]. Risk factors include a lower gestational age, lower birthweight, genetic abnormalities and long-gap oesophageal atresia[118,119]. Laryngeal clefts are the second most common laryngotracheal lesion after tracheomalacia and have been reported to account for 3.6–12%[97,116–120] of the additional airway pathologies found in patients with EA-TEF. Benjamin–Inglis type 1 clefts are the most commonly identified, and the frequency decreases with the more extensive type of cleft[97,116]. Data regarding long-term swallowing outcomes and respiratory morbidity with respect to both repaired and unrepaired laryngeal clefts are currently lacking.

25. Incidence of unilateral and bilateral VCP and the associated symptoms

Vocal cord paralysis (VCP) in patients with EA-TEF is not well understood as the use of laryngoscopy is variable[121]. The incidence of congenital VCP is unknown and acquired VCP might be under-recognized and under-reported. An incidence ranging from 3% to 28% is reported for infants with EA-TEF[95,97,116,118,122–124]; however, less is known about adolescents and adults. The rate of postoperative VCP seems to be increased in TEF without oesophageal atresia (H-type or type E) and long-gap oesophageal atresia and lowest in type C. Additional risk factors include previous cervical oesophagostomy and anastomotic leakage[95,124]. VCP impairs vocal quality, airway patency and protection, swallowing function, and even sensation but presentation can be variable depending on the degree of dysfunction, acuity of onset and development of compensation. Symptoms from VCP, especially if unilateral or incomplete, might not be immediately recognized or may instead be attributed to

other factors. Bilateral VCP might need invasive intervention such as tracheostomy placement[95,97].

26. Tracheomalacia and associated symptoms

Tracheomalacia is the most frequently identified airway pathology in patients with EA-TEF, ranging from 37.4% to 89.2% of patients[97,116,118,125], and is known to persist after surgical repair. Specific data regarding bronchomalacia, either in isolation or combined with tracheomalacia, are lacking. A decreased incidence of tracheomalacia and lower respiratory morbidity are noted in patients with isolated oesophageal atresia[110,126].

The severity of tracheomalacia and symptomatology related to it is variable[116] and not always predicted by initial assessments[127]. Clinically substantial tracheomalacia naturally decreases with age and growth, with an estimated prevalence in adolescents and adults of 10–13%[91] and the most frequent respiratory symptoms being cough, choking, wheezing, shortness of breath and recurrent infection[110]. Bronchoscopy in the operating room enables assessment of the whole airway. Spontaneous respiration is critical as tracheomalacia can be underestimated by static assessment in a deeply anaesthetized patient. CT scanning techniques have been developed to analyse dynamic tracheal lumen size during inspiratory and end-expiratory manoeuvres and during passive breath holding under general anaesthesia[128,129]; however, the use is not widespread.

27. Vascular anomaly that results in compression: symptoms and clinical management

Intrathoracic vascular anomalies might be present in 18% of patients with EA-TEF and are substantially associated with long-gap oesophageal atresia[98,128,130,131] and severe cardiac malformations requiring surgery[1]. Patients with EA-TEF also have an increased incidence of anomalous aortic arch formation[98,131]. Dyspnoea, recurrent aspiration or cough might be the presentation in children owing to absent tracheal rigidity, whereas dysphagia is more typical in adulthood[98]. Symptoms are often non-specific, and some patients might be asymptomatic. An investigation is recommended prior to oesophageal stenting, oesophageal replacement surgery or when prolonged nasogastric tube use is being considered to prevent complications arising from a vascular lesion in the region[98].

An investigation can be undertaken with contrast swallow studies, laryngobronchoscopy, oesophagoscopy, echocardiography, contrast-enhanced chest CT or CT pulmonary angiogram with digital subtraction and three-dimensional image reconstruction[128]. Magnetic resonance angiography has not been extensively utilized to date.

28. Tracheostomy dependency

Studies about tracheostomy insertion during childhood and ongoing tracheostomy dependency into adolescence and adulthood in patients with EA-TEF are few owing to small numbers requiring the procedure. An incidence ranging from 5% to 23% has been described[97,118,119,122,132]. Tracheostomy is most commonly undertaken in the first year of life, especially if preterm, with a birthweight of <1.5 kg, medical complexity or if there are laryngotracheal abnormalities[122,132–134]. There are reports of successful decannulation[97]; however, long-term follow-up is often incomplete and scant details are available about the outcomes of those who are not decannulated.

29. Laryngobronchoscopy screening at time of transition in adolescents

Long-term studies show that patients with EA-TEF who are completely free from gastrointestinal or respiratory symptoms are in the minority[20,101,105,110]. Laryngotracheal diagnoses might have been previously detected with a variable degree of resolution or compensation, been asymptomatic, or potentially missed because of an overlapping symptom profile. Airway pathology can be difficult to identify during office assessment and might warrant laryngobronchoscopy to guide management and to enable vigilance during procedures that could be required in later years (for example, thyroidectomy or cardiac surgery where the recurrent laryngeal nerves can be at risk)[95]. During the transition, the role of otolaryngology in screening and long-term care might need to be considered. Patient education programmes can be beneficial to raise awareness of general and disease-specific dimensions to direct future care[135].

Feeding and nutrition in adolescents and adults with EA-TEF

Questions and recommendations on feeding and nutrition are respectively shown in Boxes 1 and 7.

30. Prevalence of malnutrition

Limited data on growth are currently available on adolescents and adults with EA-TEF. Most studies have evaluated growth in a mixed cohort of children and adolescents (aged 0–18 years) rather than data specific for the adolescent and adult population[20,26,102–104,136–139] (Supplementary Table 2). A study showed that 23.7% of 40 adults with EA-TEF had underweight[139]. Although a marked proportion of patients with EA-TEF are undernourished in their infancy, this seems to improve over time[102,138,140]. Interestingly, researchers reported healthy (18.5–24.9 kg/m^2) or above healthy (>25 kg/m^2) BMI in adult patients with EA-TEF[104], whereas another study on 928 patients with oesophageal atresia showed that 2% of patients had obesity, 15% had overweight, 62% had normal weight and 21% had underweight[103].

31. Predictive factors for malnutrition

Presse et al. found, in a study on 40 adult patients with EA-TEF, that those with underweight most likely also had underweight as adolescents and report postprandial fullness, the need to eat slowly, and have dysphagia, compared with patients with EA-TEF who were not malnourished[139]. Additionally, a history of failure to thrive persisting beyond 12 years of age appeared to impact BMI. In a study of 68 adolescents with EA-TEF, aged 13–20 years, stunting was associated with lower birthweight, longer hospital stay, history of gastrostomy feeding, more dilatations when under 12 months of age and greater dysphagia[136].

32. Therapeutic strategies to reduce malnutrition

Strategies to reduce the incidence of malnutrition in adolescent and adult patients with EA-TEF include teratment in a multidisciplinary clinic that includes a dietitian, deglutologist, gastroenterologist and respirologist. Some adolescents and adults with feeding difficulties or those who have increased energy requirements might need additional nutritional support with the help of oral high-energy, high-protein supplements or nasogastric or gastrostomy feeds to achieve adequate growth and nutrition. Patients with EA-TEF and an unsafe swallow owing to structural abnormalities or oropharyngeal dysphagia, in whom adequate oral intake is not possible or safe to achieve, might require enteral nutrition with nasogastric or gastrostomy feeds. A study evaluating longitudinal outcomes (3–37 years) in 109 adolescents and adults with EA-TEF reported the need for ongoing enteral nutrition via gastrostomy in 3.3% of the whole cohort[30].

Box 7

Feeding and nutrition subgroup recommendations

Statement 30
The prevalence of malnutrition decreases with age in patients with EA-TEF. The incidence of underweight in adolescent and adult patients with EA-TEF is increased, often due to digestive symptoms.

Statement 31
Predictive factors for malnutrition demonstrated in adolescent and adult patients with EA-TEF are a history of underweight when younger and swallowing difficulties.

Statement 32
Some of the therapeutic strategies to reduce the incidence of malnutrition in adolescent and adult patients with EA-TEF are follow-ups in a multidisciplinary clinic, monitoring of growth and nutrition, adapting and tailoring of textural quality of foods, supplemental enteral nutrition with feeding tubes and gastrostomy when indicated, and awareness of risk for eating disorders and psychosocial factors.

Statement 33
Studies have shown that foods most likely to be avoided in patients with EA-TEF are those that are non-soluble and difficult to eat, including red meat, fruit and vegetables. The nutrients that are at risk of being inadequate are iron, zinc, vitamin B_{12}, vitamin A, vitamin C, fibre and folate.

Statement 34
Dysphagia has a substantial effect on feeding and maintaining good nutritional status in adolescent and adult patients with EA-TEF. There are currently no data available on the efficacy of a modified diet in improving dysphagia and feeding in these patients.

Statement 35
Despite limited data on the effect of GERD on feeding, it is likely that GERD has an adverse effect on feeding and nutrition owing to symptoms and complications.

Statement 36
There are limited data on the prevalence of EoE in adolescents with EA-TEF, and there are currently no data on EoE in adults with oesophageal atresia. It is likely that EoE will result in symptoms of vomiting, dysphagia, and food bolus impaction and adversely affect feeding and nutrition, thereby highlighting the importance of evaluating symptomatic adolescent and adult patients with EA-TEF with endoscopy and biopsy.

Statement 37
All adolescents with EA-TEF should be seen at the time of transition by a dietitian and deglutologist and routinely screened for nutritional deficiencies and swallowing difficulties, particularly those with concerns regarding their growth and dietary intake. Adults with EA-TEF ideally should be monitored annually by a dietitian and deglutologist.

Statement 38
Based on limited evidence, feeding difficulties and dysphagia have an adverse outcome on the quality of life of adolescents and adults with EA-TEF.

Statement 39
Current evidence suggests that the majority of adolescents and adults with EA-TEF have concerns about meals owing to their own and parental anxiety, both in the presence and absence of pre-existing abnormalities, which has an adverse effect on feeding and eating. There is also evidence that a marked proportion of adolescents and adults with EA-TEF have disturbed eating habits and are at risk for the development of eating disorders.

EA-TEF, oesophageal atresia–tracheoesophageal fistula; EoE, eosinophilic oesophagitis; GERD, gastro-oesophageal reflux disease.

33. Nutrients at risk

Harder foods are often avoided by patients with EA-TEF as they are more difficult to swallow[21,101]. A study evaluating the nutritional status of 68 adolescent patients with EA-TEF found daily intake of energy to be below age-appropriate recommendations[136]. Nutrients that were most likely to be below the recommended dietary intake were iron, vitamin C and vitamin D.

34. The role of dysphagia in feeding difficulties and of modified diets for improving feeding

Children and adolescents with EA-TEF continue to experience dysphagia regardless of the number of years after surgical repair. In a study of 69 patients with EA-TEF, 45% had dysphagia at 5 years after surgical repair, 39% at 5–10 years and 48% at more than 10 years[141,142]. There are, however, limited data in the literature on the effect of dysphagia on feeding difficulties in adolescents and adults with EA-TEF. A study in which dysphagia was evaluated in 68 adolescents with EA-TEF using a modified eating assessment test questionnaire reported that more than two-thirds had symptoms of dysphagia[136]. Similar results were seen in a study on 40 adults with EA-TEF in which significantly ($P = 0.054$) more patients with underweight reported dysphagia (50% versus 14.3%)[139].

Although the use of modified diets has not yet systematically been studied in patients with EA-TEF, modification of the consistency of food or fluids, called texture-modified diets, is a commonly used management strategy in patients with oropharyngeal dysphagia and can help to reduce aspiration risk and thereby potentially improve oral feeding safety in patients with EA-TEF. It is vital to realize that diet modification can also negatively affect QOL as it could lead to dehydration, malnutrition and problematic post-aspiration airway clearance.

Additionally, substantial variability exists in modified diets[136,141]. Patients with EA-TEF most typically present with oesophageal dysphagia owing to the absence of or ineffective oesophageal contractility and, less commonly, with oropharyngeal dysphagia[7]. In patients with ineffective oesophageal motility, modified diets need to be prescribed with caution as increasing bolus consistency requires increased oesophageal contractility to clear the oesophagus, which might not be present in these patients and therefore might even worsen symptoms of dysphagia.

35. The role of GERD on feeding difficulties

GERD is a common complication after EA-TEF repair. A meta-analysis in patients with EA-TEF found a pooled prevalence of GERD of 40.2%[36]. GERD might not only result in loss of calories owing to vomiting but can also cause a fear of eating owing to chest pain and heartburn from reflux. Oral intake might also be compromised by reflux-related complications such as stricture, aspiration and worsening dysphagia owing to reflux oesophagitis. In a retrospective study conducted in 2002 with a sample size of 371 patients, a history of GERD was associated with height-for-age and weight-for-age (<5th percentile)[143]. Similarly, Legrand et al. reported that GERD was associated with decreased z scores for weight-for-height[20]. However, the association between growth and GERD was not seen in two other studies[138,144]. This might be owing to inconsistencies in the definition of GERD between studies.

36. The role of EoE on feeding difficulties

In the literature, most patients with EA-TEF and EoE are children and adolescents, with ages ranging from 8 months to 17 years. There are currently no data available on the incidence of EoE in adults with EA-TEF. In the study by Lardenois et al. including 63 adolescents with EA-TEF and EoE, 83% had dysphagia, 66% had a history of food impaction and 50% had feeding difficulties[32]. Vomiting and strictures that have an adverse effect on feeding and nutrition have also been reported in most studies evaluating EoE in patients with EA-TEF.

37. Dietary and nutritional management at the time of transition and in adulthood

Yearly clinical follow-ups in adulthood with standardized questionnaires are important to monitor gastrointestinal, respiratory and musculoskeletal symptoms of patients with EA-TEF[23]. Birketvedt et al. recommended a dietitian review for adolescents with EA-TEF as growth and feeding problems can persist[136]. In case of poor swallow safety and efficiency, a swallow evaluation by a deglutologist is advised.

38. The role of feeding difficulties and dysphagia on QOL

Although dysphagia is present from birth in patients with EA-TEF, patients learn to cope with the symptom and, unless prompted, do not report it as a problem[20]. Several studies focusing on paediatric patients with EA-TEF have shown that feeding difficulties and/or dysphagia have a negative effect on generic and condition-specific QOL[145]. In 8–17-year-olds, avoiding nutritional intake situations or expressing emotional concerns were associated with impaired eating QOL, even after adjusting for the influence of digestive symptoms[145].

When 18 teenagers aged 13–17 years with EA-TEF and their parents participated in focus groups and discussed the QOL of teenagers, experiences of 'eating and drinking' was the most commonly reported domain[146]. In a study on 97 adults with EA-TEF, those with dysphagia had reduced scores on general health (36-item short-form survey (SF-36)), physical component summary (SF-36) and physical well-being[147]. However, another study failed to identify a correlation between the physical component summary of SF-36 and self-reported dysphagia[13]. In both of these studies, the presence of dysphagia had a negative influence on the mental component summary of the SF-36. 'Swallowing total score' negatively correlated with the physical and mental components of the SF-36, indicating that greater swallowing total scores were associated with worse QOL[146,147].

39. The effect of anxiety on diet and feeding

Currently, there are sparse data in the available literature addressing the effect of parental and patient anxiety on feeding and diet in adolescents and adults with EA-TEF. Parents of 39 adolescents with EA-TEF reported that the most worrying period was feeding during infancy (48%), although this decreased as the child got older[148]. A study that examined long-term outcome data from 65 patients with EA-TEF 16 months to 20 years of age showed that patients whose parents tended to be anxious about feeding were more likely to develop moderate to severely disturbed eating habits, with 25% of all patients in the study having behavioural difficulties regarding food and eating[102].

Psychology and QOL in adolescents and adults with EA-TEF

Questions and recommendations on psychology and QOL are respectively shown in Boxes 1 and 8.

40. Psychosocial needs of patients and their families during transition

During adolescence, physical, psychological, social and environmental changes occur, and this life period is associated with the developmental task of increasing autonomy, personal identity, social maturity and sexuality, and decision-making about lifestyle, health, education and vocation[149]. Limited research on the psychosocial functioning in adolescents and adults with EA-TEF has shown that they adjust well[150] but that there are risk groups for worse psychosocial functioning, namely those with more than one oesophageal dilatation, low birthweight and a distressed parent and/or family[150]. Findings regarding cognitive functioning and neurodevelopment in individuals with EA-TEF are limited and conflicting; hence, further research on such long-term outcomes is required[151–154]. Generally, adolescents with a chronic illness risk developing mental health disorders[155–159], which can affect disease management[155]. In paediatric patients with EA-TEF, risk factors for internalizing or behavioural problems include concomitant anomalies, young child age and low parental educational level[160]. Post-traumatic stress in adolescents with EA-TEF is associated with the number of days on a ventilator during neonatal hospital admission and digestive morbidity at follow-up[161]. The level of mental health in adolescents with EA-TEF is a main predictor of generic health-related QOL[161].

It has been suggested that the congenital nature of EA-TEF is beneficial to the adaptation of these individuals[19,162–166] but the evidence is limited. Children with EA-TEF use various coping strategies, which are often adopted at an early age[145,146]. In terms of eating strategies, indicating independence and acceptance, these become more common as the patient grows older. Acceptance of having feeding difficulties and imitating their peers with eating is associated with better QOL in relation to eating, whereas the use of disengagement coping is associated with worse QOL[145]. Adults with EA-TEF have reported gaining positive meaning from their stressful experiences, leading to increased resilience, empathy for others and gratitude[166].

Box 8

Psychology and QOL subgroup recommendations

Statement 40

We recommend that the psychological needs of adolescents and adults with EA-TEF and their parents be considered during transition with regard to the following.

- The developmental stage of adolescence and its potential effects on clinical relationships and the ability and willingness of adolescents to make medical treatment decisions.
- Resilience strategies for problems related to the function of the oesophagus and lungs (swallowing, gastro-oesophageal reflux, eating-related problems and respiratory morbidity).
- The mental health of adolescents and adults and their parents during the transition process, and to engage relevant psychological interventions if required.

Statement 41

We recommend, to gain a comprehensive understanding and strengthen the QOL of patients with EA-TEF throughout life, the following.

- Generic and condition-specific instruments with sound validity and reliability for patients should form part of routine follow-up care over time, enabling the provision of targeted supports and interventions to maintain or improve QOL.
- There should be a measurement model available to assess shared condition-specific QOL outcomes across adolescence into young adulthood for use in research and clinical practice.
- Adolescent health-related QOL be assessed prior to transfer from paediatric to adult care and, with patient consent, shared with receiving adult health services to enable relevant support, thereby facilitating the provision of optimal holistic adult care.
- During transition, health-care providers should offer special attention to care for the QOL of adolescents in relation to eating.

Statement 42

We recommend that optimal transition preparation of adolescents with EA-TEF and their parents comprises the following.

- A youth and family-centred, strength-based transition planning approach that enables adolescents to contribute to decision-making.
- Targeted and individualized education to increase patient knowledge of EA-TEF, including risk factors, and that this process continues in adult health-care services.
- Active development of adolescent health-care self-management skills, as developmentally appropriate, with dedicated support for parents to enable the change in role from health-care manager to health-care guide.
- Holistic care to meet the medical, educational, vocational and psychosocial needs of adolescents with EA-TEF.
- Appointment of a transition lead or 'champion' to facilitate coordinated care across both the paediatric and adult health-care settings.
- Engagement in conjoint systems involving both the paediatric and adult health-care teams to ensure supported and seamless transfer of care.

EA-TEF, oesophageal atresia–tracheoesophageal fistula; QOL, quality of life.

Parents of paediatric patients with EA-TEF have an increased risk of developing post-traumatic stress disorders[167], impaired mental health[168], anxiety[169] and depression[164]. Their anxiety and depression might be associated with child feeding problems, younger age of parents, perceived lack of care support and financial worries[169]. The risk for developing impaired mental health is also increased in parents of children with EA-TEF and with low income[150,167,168]. In this patient group, family functioning is similar to the general population[156] but child feeding problems, associated anomalies[170], and emotional and behavioural problems[171] might negatively affect family functioning.

Brief cognitive behaviour therapy might be an effective way to access treatment for anxiety in adolescents with chronic health conditions, and parenting interventions for disruptive behaviours might be effective in adolescents. There is currently insufficient evidence for psychologically effective treatment options for comorbid mental health disorders in adolescents with chronic health conditions[155] and for eating and swallowing-related problems in the context of EA-TEF[172,173].

41. Development of QOL from childhood to adolescence and adulthood in patients with EA-TEF

Most QOL studies of patients with EA-TEF are cross-sectional, with varying quality, assessment methods and findings, limiting knowledge of how QOL develops over the life course[165,174]. In cross-sectional studies of children with EA-TEF, findings on whether patient age influences QOL are differently reported[102,175,176]. In a longitudinal study on 110 patients with EA-TEF, their general health-related QOL was lower than that of healthy peers at 8 years but was normalized at 12 years[177]. In another longitudinal study on 62 patients with EA-TEF, the physical health-related QOL scores trended up, whereas the psychosocial health-related QOL scores decreased into adolescence so that the mean level at 20 years of age was lower than in healthy individuals[178]. This was not found in a cross-sectional health-related QOL study of 68 adolescents with EA-TEF[161]. Condition-specific QOL domains of importance to paediatric patients with EA-TEF aged 8–17 years, initially identified using focus groups with patients and their parents[146,179], relate to their eating, social relationships, body perception, health and well-being[180,181]. Another study found that QOL consequences in adolescents with EA-TEF were mainly related to eating[102]. Interestingly, in EA-TEF, there is good parent–child agreement in the ratings of child QOL[160,182].

Adults with EA-TEF have reported comparable physical QOL levels with healthy participants[13,21,183] and impaired general or physical health symptoms[147,162,164,184]. Four of these studies[162,164,184] considered patients with complex or complicated EA-TEF, including those with oesophageal replacement with colon[162,184], jejunum or gastric pull-up[63], patients who

had delayed anastomosis, and those with recurrent strictures requiring >10 dilatations[164]. In adults with EA-TEF, dysphagia might negatively influence general health or physical health-related QOL[19,21]; however, this was not shown in all studies[13]. Adults with EA-TEF had similar mental health symptoms compared with healthy participants using the SF-36 (refs. 13,21,147,183) but 23% of 90 adults with complex or complicated oesophageal atresia reported signs of depression[164]. Some studies[11] but not all[13,19] show that swallowing difficulties in adults with EA-TEF negatively influence mental health or well-being[21,147].

According to symptom-specific QOL assessments related to respiratory symptoms[21] and the gastrointestinal tract[162,164,184], adults with EA-TEF have QOL impairments compared with healthy individuals[164,184] but not compared with those with primary repair of oesophageal atresia[49,162]. A focus group study of 15 adults with EA-TEF from the Netherlands[177] and an online survey with 92 adults with oesophageal atresia from 11 different territories[166] both showed that a main problem experienced related to dysphagia and effect on eating, including psychological distress, challenges to dining out or restricted eating in the evening[177,166]. Adults with EA-TEF also described limitations in life owing to poor exercise capacity[177] and experiences of stigma related to others commenting on their EA-TEF, restricted openness about EA-TEF and social withdrawal[166,177]. The patients addressed a lack of knowledge and understanding about EA-TEF among health-care professionals[166,166,177]. Further, their dissatisfaction might be due to their surgical scars[147,166,177,183] or disfigured and/or winged scapula[183]. Such results have led to the development of a condition-specific QOL instrument for adults with EA-TEF[174].

42. Optimal preparation of adolescents and their parents for transition to adult health care

The transition of health care refers to the purposeful, planned shift from paediatric health care to receiving primary and speciality adult-oriented care that addresses the medical, psychosocial, educational and vocational needs of adolescents and young adults with chronic physical and medical conditions[185,186]. In patients with EA-TEF, one prospective intervention study on 29 patients has shown that, after the implementation of a 2-day transition educational programme, adolescents with EA-TEF had better levels of knowledge about their condition and high levels of satisfaction with the programme[135]. The issue of low health literacy and knowledge about risk factors in adolescents with chronic medical conditions is well documented in other comparable patient cohorts[187–189]. Readiness to transfer is challenged by adolescents lacking the necessary self-management skills to navigate the adult health-care setting[190] and enabling adolescents to negotiate the independence and interdependence course with parents[191]. The parental role is integral in supporting adolescent transition readiness[192–194]. Deficits in patient perceptions of health-care management and medication adherence might also impede transition readiness and health-care satisfaction[195]. With health-care transition support, adolescent patients can develop increased autonomy, motivation to manage their own health care and possess more positive attitudes towards transition[196,197]. Furthermore, a youth-centred strength-based focus and involving adolescents in transition planning and decision-making are essential[185,198].

The inclusion of targeted, holistic supports within transition programmes to address the educational, vocational and psychosocial needs of patients is important[197,199]. Patients with EA-TEF achieve more favourable outcomes (developmental milestones and less risky behaviours) compared with other disease groups[200]. However, it has been shown that paediatric patients with chronic illness as a whole experience lower academic achievement trajectories than their healthy peers owing to increased school absences, greater disengagement from school[201], the effect of disease treatment, and altered expectations of teachers and parents[202].

If the transfer from paediatric to adult health care is not managed well, it might result in care gaps and loss of follow-up[203–205]. A number of transition consensus statements highlight the importance of appointing a transition to facilitate coordinated care across both sites and conjoint transfer processes and collaboration between paediatric and adult health-care providers to enable a successful handover[197,199,206–208].

Conclusion

Dramatic improvement in neonatal care and paediatric surgery has been observed over the past 20 years, enabling most patients with EA-TEF to survive through adulthood. EA-TEF is no more a paediatric disease but an adult disease with chronic problems. Severe complications that were not observed in the past because only a few patients reached adulthood are now a concern. The transition from adolescence to adult medicine is, therefore, a new challenge. Transition is a critical period where the risk of poor compliance and loss of follow-up is high. This risk should be anticipated, and a good transition requires training and preparation of the adolescent and family and a multidisciplinary team. This Consensus Statement will hopefully contribute to improved care and outcomes for adolescent and adult patients with EA-TEF.

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Competing interests
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Additional information
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Consensus statement

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