NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of balloon dilation for chronic eustachian tube dysfunction

The eustachian tube connects the middle ear with the back of the nose. If the tube is blocked or does not open properly, there can be symptoms such as muffled hearing, pain, a feeling of fullness in the ear, ringing in the ear or dizziness. In this procedure, a thin flexible tube with a small balloon is inserted through the nose and into the eustachian tube. An endoscope (a thin tube with a camera on the end) is used to guide the process. Once in position, the balloon is filled with saltwater. It is then left in place for around 2 minutes before being emptied and removed. The aim is to widen the eustachian tube and improve its function and relieve symptoms.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in May 2019 and updated in October 2019.

Procedure name

- Balloon dilation for chronic eustachian tube dysfunction.

Specialist societies

- British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK)
- Royal College of Surgeons England
- Royal College of Physicians London
- Royal College of Physicians and Surgeons Glasgow
- Royal College of Surgeons Edinburgh
- Royal College of Physicians Edinburgh.

Description of the procedure

Indications and current treatment

The eustachian tube is a narrow tube that connects the middle ear with the back of the nose. If it is blocked or does not open properly, there can be symptoms such as muffled hearing, pain, a feeling of fullness in the ear, tinnitus or dizziness. The eustachian tube typically becomes blocked after an upper respiratory tract infection or allergic rhinitis. It is usually a temporary problem that resolves spontaneously, but sometimes symptoms persist and treatment is necessary. Long-term eustachian tube dysfunction is associated with damage to the eardrum and middle-ear transformer mechanism.

Medical treatments include oral and nasal corticosteroids, decongestants and antihistamines. Autoinflation is a technique that reopens the eustachian tube by raising pressure in the nose. This can be achieved in several ways, including forced exhalation against a closed mouth and nose.

If eustachian tube dysfunction persists, a tympanostomy tube (also known as a ventilation tube or grommet) may be inserted through a small incision in the tympanic membrane. These typically fall out after several months, and repeated tube insertions may be needed. Some tubes are designed to stay in place longer, but these can become crusted, infected or obstructed. Tympanostomy tubes may result in a small permanent hole in the tympanic membrane; this is more common with long-lasting tubes.

What the procedure involves

Balloon dilation of the eustachian tube is done under local or general anaesthesia. A balloon catheter is introduced into the eustachian tube via the nose, under transnasal endoscopic vision. Once the balloon is correctly positioned in the eustachian tube, it is filled with saline up to a pressure of about 10 to 12 bars. Pressure is maintained for about 2 minutes. The balloon is then emptied and removed.

The aim of the procedure is to widen the eustachian tube and improve its function.

Outcome measures

Assessing eustachian tube dysfunction

In tubomanometry, the opening of the eustachian tube and transportation of gas into the middle ear is registered by a pressure sensor in the occluded outer ear after applying the stimulus of a controlled gas bolus into the nasopharynx during swallowing. If tube opening is registered, the time of opening in relation to pressure applied can be measured (opening latency index or index R). An R value of less than 1 indicates early opening of the eustachian tube, which is considered optimal.

The eustachian tube score is a summation point score based on the patient's history and tubomanometry results. It ranges from 0 (worst value) to 10 (best value):

	2 points	**1 point**	**0 points**

Clicking noise during swallowing	Always	Infrequent	Never
Clicking noise during Valsalva manoeuvre	Always	Infrequent	Never
Tubomanometry 30 mbar	R<1	R≥1	No opening
Tubomanometry 40 mbar	R<1	R≥1	No opening
Tubomanometry 50 mbar	R<1	R≥1	No opening

Eustachian Tube Dysfunction Questionnaire (ETDQ-7)

The ETDQ-7 is a validated, standardised, 7-item patient-reported questionnaire to assess symptom severity associated with eustachian tube dysfunction. The following symptoms are assessed: pressure, pain, feeling clogged, cold or sinusitis problems, crackling or popping, ringing and muffled hearing. Each item is assessed on a scale of 1 (no problem) to 7 (severe problem) and an overall mean score is calculated. Scores in the range of 1 to 2 indicate no to mild symptoms, 3 to 5 indicate moderate symptoms and 6 to 7 indicate severe symptoms.

Efficacy summary

Improvement in eustachian tube function

In a randomised controlled trial (RCT) of 60 patients who had balloon dilation with medical management or medical management alone, the mean ETDQ-7 scores improved by 2.9 and 0.6 respectively at 6-week follow up ($p<0.0001$). The improvement in eustachian tube function with balloon dilation was maintained at the 3-, 6- and 12-month follow ups ($p<0.0001$ for all follow-up periods compared with baseline).[1]

In a case series of 47 patients, who had been in the treated arm of the RCT of 60 patients, they were followed up for a mean of 29 months. The mean improvement in ETDQ-7 score for patients who had balloon dilation was 2.5, and 94% (44/47) of patients had a reduction of 1 or more in their overall ETDQ-7 score.[10]

In an RCT of 323 patients, 56% (77/137) of patients who had balloon dilation had mean ETDQ-7 scores less than 2.1 at 6-week follow up compared with 9% (6/71) of patients who had medical management alone ($p<0.001$). Improvements in ETDQ-7 scores were sustained to week 24 in the balloon-dilation group and remained greater than those in the medical management group (60% compared with 22% respectively, p=not significant).[2] In the 128 patients who were followed up to 52 weeks, 57% (71/124) had a mean ETDQ-7 score less than 2.1.[3]

In a systematic review of 1,155 patients who had balloon dilation, the mean improvement in eustachian tube score (higher score correlates with fewer symptoms) was 3.94 (95% confidence interval [CI] 2.60 to 5.27, p<0.00001, I^2=66%; 3 studies [670 procedures]).[4]

In a case series of 46 patients, of the 34 patients who responded to a postal questionnaire about 3 years after the balloon dilation, 67% reported that they had little or no disturbance caused by current ear symptoms and 77% reported fewer overall symptoms than before the procedure.[8]

In a case series of 126 children, 34 out of 66 parents responded to a postal questionnaire and 77% reported that hearing improved after balloon dilation. Of the participating parents, 56% were very satisfied and 25% were satisfied with the results of the surgery.[9]

Valsalva manoeuvre

In the RCT of 60 patients, 47% (8/17) of patients who had an abnormal baseline assessment had an improved (but not statistically significantly so) Valsalva manoeuvre with balloon dilation at 6-week follow up compared with 14% (2/14) of patients in the control group (p=0.068). At 12-month follow up, 66% (31/47) of patients who had balloon dilation had a positive Valsalva manoeuvre compared with 33% (16/49) at baseline (p=0.001).[1] At longer follow up (mean 29 months) in the case series of 47 patients from this RCT, 67% (22/33) of patients who had abnormal baseline values had a positive Valsalva manoeuvre.[10]

In the RCT of 323 patients, the increase in proportion of ears with positive modified Valsalva manoeuvre at 6 weeks compared with baseline was 33% in the balloon-dilation group and 3% in the control group (p<0.001).[2] At 52 weeks, the proportion of ears with positive Valsalva was 80% (185/230).[3]

In the case series of 126 children, 18% (11/60) were objectively unable to equalise ear pressure, as shown by the absence of a positive Valsalva test on microscopy or the absence of a definable peak on a tympanogram, after the procedure compared with 92% before the procedure.[9]

Tympanogram

In the RCT of 60 patients, 57% (8/14) of patients who had an abnormal baseline assessment had an improved tympanogram at 6-week follow up compared with 10% (1/10) of patients in the control group (p=0.006). At 12-month follow up, 88% (70/80) of ears had a type A tympanogram after balloon dilation compared with 71% (62/87) at baseline (p=0.02).[1] At longer follow up (mean 29 months) in the case series of 47 patients from this RCT, 63% (15/24) of patients with abnormal baseline values who had balloon dilation had a type A tympanogram.[10]

In the RCT of 323 patients, 52% (72/139) of patients who had balloon dilation with medical management had a normal tympanogram at 6-week follow up compared with 14% (10/72) of patients who had medical management alone ($p<0.0001$). At 24-week follow up, 62% of patients who had balloon dilation had a normal tympanogram.[2] In the 128 patients who were followed up to 52 weeks, 56% (71/128) had a normal tympanogram.[3]

Repeat procedures

In the systematic review of 1,155 patients, revisions because of failure of the first balloon-dilation procedure were reported in 3 out of 15 studies; 7% (122/1,830) of procedures needed a revision. Specific outcomes for these patients were not separately reported.[4]

In the case series of 126 children, 34 out of 66 parents responded to a postal questionnaire and 27% (9/34) reported that balloon dilation was repeated after a mean follow up of 9.5 months.[9]

In the case series of 47 patients with a mean follow up of 29 months, 1 patient had a revision procedure 362 days after the initial procedure.[10]

Patient satisfaction

In a case series of 622 patients who had balloon dilation, 33% (30/89) of patients returned a postal questionnaire about 2 years after the procedure. Of these 30 patients, 73% had either improvement or no complaints. Among all patients who answered the questionnaire, 60% were satisfied with the results of the treatment and 20% were only completely satisfied for the first few months after the treatment.[7]

In the case series of 46 patients, of the 34 patients who responded to a postal questionnaire about 3 years after the balloon dilation, 82% were willing to have the procedure again if symptoms returned.[8]

In the case series of 47 patients, 83% (39/47) of patients were satisfied with the procedure and 87% (41/47) would recommend the procedure, after a mean follow up of 29 months.[10]

Safety summary

Preauricular emphysema or pneumomediastinum

Preauricular emphysema that resolved spontaneously over a few days was reported after less than 1% (3/1,830) of balloon-dilation procedures in the systematic review of 1,155 patients.[4]

Postoperative emphysema was reported after less than 1% (10/3,670) of procedures in a case series of 2,272 patients. Of these 10 patients, 3 had concomitant pneumomediastinum. All patients with emphysema had treatment with an intravenous or oral antibiotic and Valsalva manoeuvre was stopped for 3 weeks. A complete resolution was noted within 2 to 6 days for all patients.[6]

Local bleeding or injury

A diffuse crush injury or local bleeding of the mucosa at the site of the eustachian tube was reported after 1% (20/1,830) of balloon-dilation procedures in the systematic review of 1,155 patients.[4]

Hemotympanum

Hemotympanum needing myringotomy was reported in 1 patient who had balloon dilation in the systematic review of 1,155 patients.[4]

Epistaxis

'Occasional cases' of epistaxis were reported in the case series of 2,272 patients. This was self-limiting in most patients but some needed treatment with electrocautery or nasal packing.[6]

Epistaxis immediately after the procedure was reported in 1 child in the case series of 126 children; this was managed with bipolar coagulation and anterior nasal packing. Mild epistaxis immediately after the procedure was also reported in 1 child in the same study.[9]

Patulous eustachian tube

Mild symptoms of patulous eustachian tube were reported in 2% (2/128) of patients who had balloon dilation in the RCT of 323 patients. In 1 of these patients, symptoms had resolved by the end of the study.[3]

Mild findings possibly compatible with patulous eustachian tube were reported in 1 patient in the case series of 2,272 patients.[6]

Otitis media

Temporary otitis media was reported after less than 1% (4/1,830) of balloon-dilation procedures in the systematic review of 1,155 patients and acute otitis media was reported in 1 patient in the case series of 2,272 patients.[4, 6]

Otitis media in the days after balloon dilation was reported in 9% (3/34) of children in the case series of 126 children. In the later postoperative course, otitis media with effusion was reported in 9% (3/34) of children.[9]

Tinnitus

Temporary increase in tinnitus was reported in 1 patient who had balloon dilation in the systematic review of 1,155 patients and in less than 1% (3/2,272) of patients in the case series of 2,272 patients.[4, 6]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, a specialist adviser described the following anecdotal adverse event: patulous eustachian tube. They did not describe any theoretical adverse events.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to balloon dilation for chronic eustachian tube dysfunction. The following databases were searched, covering the period from their start to 4 September 2019: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded in which no clinical outcomes were reported, or the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with chronic eustachian tube dysfunction.
Intervention/test	Balloon dilation of a eustachian tube.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on about 4,000 patients from 2 RCTs (both of which had longer follow up reported in a separate paper), 2 systematic reviews and 4 case series (1 of which was also included in the systematic reviews).[1–10]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the appendix.

Table 2 Summary of key efficacy and safety findings on balloon dilation for chronic eustachian tube dysfunction

Study 1 Meyer TA (2018)

Details

Study type	**Randomised controlled trial**
Country	US (5 centres)
Recruitment period	2015 to 2016
Study population and number	**n=60 (31 balloon dilation, 29 medical therapy [cross over to balloon dilation after 6 weeks])** Adults with persistent eustachian tube dysfunction
Age and sex	• Balloon dilation: mean age 52 years; 45% (14/31) male • Medical therapy: mean age 47 years; 52% (15/29) male
Patient selection criteria	Patients aged 18 years and older with eustachian tube dysfunction for 12 months or longer with 3 or more symptoms (ear pain, ear pressure, tinnitus, cracking or popping in ears, muffled hearing, feeling that ears are clogged) refractory to medical therapy. Failed medical therapy was defined as a minimum of either 4 weeks of daily intranasal steroid spray or 1 completed course of an oral steroid within 12 months before study enrolment. Patients had to have an overall ETDQ-7 score of 3 or higher, representing moderate to severe symptoms. Exclusion criteria included a history of head or neck surgery within 3 months; patulous eustachian tube; ear tubes in place or an unhealed perforation; temporomandibular joint disorders; Meniere's disease; chronic rhinosinusitis, allergies, or reflux disease not controlled with medication, or anatomic conditions that would prevent transnasal access to the eustachian tube. All patients had to have a CT scan of the temporal bones and those with evidence of carotid artery dehiscence were not eligible for the study.
Technique	Device: XprESS ENT Dilation System (Entellus Medical, US). Balloon size selection was based on physician preference. The balloon was inserted through the nose into the eustachian tube orifice, inflated to 12 atmospheres, and held for 2 minutes before deflating and removal. The site of service for the procedure (office, ambulatory surgical centre or operating room) and the choice of anaesthesia were at the discretion of the treating surgeon and patient preference. Local anaesthesia was used for 72% of procedures. Of all 53 patients who had balloon dilation, 72% had a bilateral procedure. No concomitant procedures were allowed during the study procedure.
Follow up	**12 months**
Conflict of interest/source of funding	Entellus Medical designed and sponsored the study. An employee of Entellus Medical assisted with the initial draft of the manuscript, editing and preparation for submission. One author has received payment from Entellus Medical for his role as a Scientific Advisory Board Member.

Analysis

Follow-up issues: One patient who was randomised to balloon dilation was lost to follow up before the procedure. Two patients randomised to balloon dilation and 2 randomised to control did not complete the 6-week evaluation. Additionally, 1 patient who had balloon dilation did not complete the ETDQ-7 at the 6-week visit. The overall follow-up visit compliance rate was 97% (284 actual/293 expected visits) and 93% (49/53) of eligible patients completed the 12-month follow-up visit.

Study design issues: Prospective, multicentre, randomised controlled trial. After 6 weeks, patients in the control group had the option to crossover to balloon dilation if symptoms persisted. Randomised intervention assignments for each site were generated by an independent statistician using variable block size distributions. Clinical sites, treating physicians and sponsor were blinded to the randomisation scheme. There was no masking of interventions after randomisation. The primary efficacy endpoint was the mean change in overall ETDQ-7 scores from baseline to 6 weeks. A minimum of 34 patients (17 per arm) was determined necessary, assuming 80% power with a 1-sided alpha of 0.025, mean changes in the overall ETDQ-7 score of -2.15 for the balloon-dilation arm and -0.85 for the control arm, and standard deviation of 1.3 for both arms. The primary safety endpoint was the rate of complications, defined as serious adverse events related to the device or procedure.

Study population issues: There were no statistically significant differences in demographics or baseline characteristics between the 2 groups. The mean duration of eustachian tube dysfunction was 12 years in the balloon-dilation group and 13 years in the control group and the mean baseline ETDQ-7 scores were 4.6 and 5.0 respectively.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 56 (29 balloon dilation, 27 control)

Technical success=100% (91/91) of eustachian tubes

Change in mean overall ETDQ-7 scores at 6 weeks
• Balloon dilation=-2.9±1.4
• Control=-0.6±1.0, p<0.0001

Most patients in both groups continued their baseline medications through the 6-week randomised period; 3 patients in the balloon-dilation group discontinued nasal steroids within the 6-week period.

Of the 27 patients in the control arm who completed the 6-week evaluation, 26 (96.3%) were eligible for crossover to balloon dilation, but 3 chose not to have the procedure.

Change in middle-ear function assessments from baseline to 6 weeks in randomised patients with abnormal baseline assessments
<table>
<tr><th>Status</th><th>Balloon dilation</th><th>control</th><th>Between arm p value</th></tr>
<tr><td colspan="4">Tympanic membrane position</td></tr>
<tr><td>Improved</td><td>66.7% (10/15)</td><td>0% (0/12)</td><td><0.001</td></tr>
<tr><td>Not improved</td><td>33.3% (5/15)</td><td>100% (12/12)</td><td></td></tr>
<tr><td colspan="4">Valsalva manoeuvre</td></tr>
<tr><td>Improved</td><td>47.1% (8/17)</td><td>14.3% (2/14)</td><td>0.068</td></tr>
<tr><td>Not improved</td><td>52.9% (9/17)</td><td>85.7% (12/14)</td><td></td></tr>
<tr><td colspan="4">Tympanogram type</td></tr>
<tr><td>Improved</td><td>57.1% (8/14)</td><td>10.0% (1/10)</td><td>0.006</td></tr>
<tr><td>No change</td><td>42.9% (6/14)</td><td>60.0% (6/10)</td><td></td></tr>
<tr><td>Worsened</td><td>0% (0/14)</td><td>30.0% (3/10)</td><td></td></tr>
</table>
Mean overall ETDQ-7 scores over time for all patients who had balloon dilation (randomised or crossover)
• Baseline=4.6 (n=54)
• 6 weeks=2.1 (n=51)
• 3 months=2.1 (n=52)
• 6 months=2.1 (n=51)
• 12 months=2.1 (n=49), p<0.0001 for all follow-up periods

Change in middle-ear function assessments from baseline to 12-month follow up in all patients who had balloon dilation (randomised or crossover)
<table>
<tr><th>Middle-ear assessment</th><th>Baseline</th><th>6 weeks</th><th>3 months</th><th>6 months</th><th>12 months</th></tr>
<tr><td colspan="6">Tympanic membrane position</td></tr>
<tr><td>Normal</td><td>51.0% (26/51)</td><td>84.6% (44/52)</td><td>84.3% (43/51)</td><td>82.4% (42/51)</td><td>85.7% (42/49)</td></tr>
</table>
</td><td>
No complications were reported during the study.

Mean pain score immediately after balloon dilation (for patients who had the procedure under local anaesthesia)=4.1 (on a scale of 0 to 10)
</td></tr>
</table>

Retracted	49.0% (25/51)	15.4% (8/52)	15.7% (8/51)	17.6% (9/51)	14.3% (7/49)
p value	-	<0.001	<0.001	<0.001	<0.001
Valsalva manoeuvre					
Positive	32.7% (16/49)	61.2% (30/49)	63.3% (31/49)	69.4% (34/49)	66.0% (31/47)
Negative	67.3% (33/49)	38.8% (19/49)	36.7% (18/49)	30.6% (15/49)	34.0% (16/47)
p value	-	0.004	0.001	<0.0001	0.001
Tympanogram type (unit=ear)					
A	71.3% (62/87)	89.7% (78/87)	83.1% (69/83)	80.0% (68/85)	87.5% (70/80)
B	11.5% (10/87)	3.4% (3/87)	7.2% (6/83)	8.2% (7/85)	5.0% (4/80)
C	17.2% (15/87)	6.9% (6/87)	9.6% (8/83)	11.8% (10/85)	7.5% (6/80)
p value	-	<0.001	0.034	0.139	0.02

ETDQ-7 score change from baseline to 12-month follow up by baseline status of middle-ear functional assessments in all patients who had balloon dilation (mean±standard deviation)

Middle-ear assessment at baseline	n	Baseline	12 months	Change from baseline	p value (between baseline and follow up)	p value (between subgroups)
Tympanic membrane position						
Normal	25	4.5±0.9	2.1±1.1	-2.4±1.5	<0.0001	0.974
Retracted	24	4.5±1.0	2.2±1.2	-2.4±1.3	<0.0001	
Valsalva manoeuvre						
Positive	15	4.4±1.0	2.6±1.1	-1.8±1.2	<0.0001	0.052
Negative	32	4.5±0.8	1.9±1.1	-2.6±1.3	<0.0001	
Tympanogram type						
Normal (type A)	32	4.7±0.9	2.3±1.2	-2.4±1.5	<0.0001	0.972
Abnormal (type B or C)	17	4.3±0.9	1.9±1.1	-2.4±1.2	<0.0001	

Abbreviations used: ETDQ-7, Eustachian Tube Dysfunction Questionnaire

Study 2 Poe D (2018)

Details

Study type	**Randomised controlled trial (ELLIOTT)**
Country	US (21 centres)
Recruitment period	2014 to 2016
Study population and number	**n=323 (466 ears)** (81 [115 ears] lead-in cohort [balloon dilation], 162 [234 ears] randomised to balloon dilation and medical management, 80 [117 ears] randomised to medical management alone) Adults with eustachian tube dilatory dysfunction refractory to medical therapy
Age and sex	Mean 56 years; 52% (168/323) male
Patient selection criteria	Age 22 years or older with persistent eustachian tube dilatory dysfunction despite medical management consisting of either a minimum of 4 weeks of continuous daily usage of any intranasal steroid spray or a minimum of 1 completed course of an oral steroid within 90 days of study enrolment. Persistent eustachian tube dilatory dysfunction was defined by patient-reported symptoms and at least 1 of the protocol-defined confirmatory indicators for 12 weeks or more before enrolment. A positive diagnosis was confirmed with abnormal tympanometry and symptomatic dysfunction as documented by the ETDQ-7 mean item score ≥2.1 after failed medical management. Absence of internal carotid artery dehiscence into the eustachian tube lumen on both sides was confirmed by a CT scan including the temporal bone. Exclusion criteria included: anatomy that needed an adjunctive surgical procedure; planned concomitant nasal, sinus, or ear procedures during the study; history of major head or neck surgery within 4 months of randomisation; history of radiation; diagnosis of patulous eustachian tube; fluctuating sensorineural hearing loss; active chronic or acute otitis media; tympanic membrane perforation or presence of a tympanostomy tube; presence of tympanosclerosis; acute upper respiratory infection; active temporomandibular joint disorder; cleft palate or history of cleft palate repair; history of craniofacial syndrome; history of cystic fibrosis; history of ciliary dysmotility syndrome; history of systemic mucosal diseases or immunodeficiency disorders; intolerance of protocol-defined medication regimen; prior surgical eustachian tube intervention; and limited dilatory muscular contractions on endoscopy of the eustachian tube.
Technique	Device used for balloon dilation: custom-designed eustachian tube balloon catheter (Acclarent, US). The procedure was done under general anaesthesia. Each dilation was done at inflation pressure of 10 to 12 atmospheres, with total dilation time of 2 minutes per eustachian tube. On the day of the procedure, patients in the balloon-dilation group started their triamcinolone acetonide nasal steroid spray regimen consisting of 2 sprays to each nostril once per day. Patients in the control group started the same regimen on the day of randomisation. After 6 weeks, continuation of medical therapy was at investigator discretion. Throughout the study, patients were permitted to continue any concomitant medications for their eustachian tube dysfunction or other medical conditions, such as allergic rhinitis. They were not allowed to start any new medications or to increase the dose or frequency of existing concomitant medications.
Follow up	**24 weeks**
Conflict of interest/source of funding	The trial was funded by Acclarent. Three authors are consultants for Acclarent, 1 is a consultant for Acclarent and Intersect ENT, 1 previously served on the Acclarent Surgeons Advisory Board, 1 was a consultant for Acclarent during part of the study and 1 is an employee of Depuy Synthe and Johnson & Johnson Medical Devices Companies.

Analysis

Follow-up issues: At 24 weeks, 93% (75/81) of patients in the lead-in cohort, 62% (100/162) of patients randomised to balloon dilation and 11% (9/80) of patients randomised to medical management alone were included in the analysis. Most patients in the medical management group who completed the 6-week follow up chose to crossover and had balloon dilation before their 12-week follow up.

Study design issues: Prospective, multicentre, randomised controlled trial, designed to show the superiority of balloon dilation plus medical management compared with medical management alone. After each investigator had done 3 successful balloon dilations in non-randomised lead-in patients, patients were randomised (2:1) to balloon dilation plus medical management or medical management alone. Randomisation was stratified by baseline tympanogram type.

Patients randomised to the control arm were allowed to crossover to balloon dilation after the 6-week follow up. The primary endpoint was normalisation of the tympanogram at 6 weeks.

Study population issues: Patient demographics and baseline characteristics were similar among the 3 groups. The mean ETDQ-7 score at baseline was 4.7. Of the 323 enrolled patients, 55% had unilateral eustachian tube dysfunction, 43% had allergic rhinitis, and 60% had 1 or more previous ear tube operations.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **323 (81 lead-in patients, 162 randomised to balloon dilation plus medical management, 80 randomised to medical management alone)** Of the patients in the medical management group who completed a 6-week follow up and had the option to crossover to the balloon-dilation group, 82% (59/72) chose to crossover before their 12-week follow up. **Normal tympanogram at 6-week follow up** • Balloon dilation=51.8% (72/139) • Control=13.9% (10/72), p<0.0001 At 24 weeks follow up, 62.2% of patients in the balloon-dilation group had a normal tympanogram (most patients in the control group had crossed over). **Mean ETDQ-7 scores less than 2.1 at 6-week follow up** • Balloon dilation=56.2% (77/137) • Control=8.5% (6/71), p<0.001 Improvements in ETDQ-7 scores were sustained to week 24 in the balloon-dilation group and remained greater than those in the medical management group (59.8% compared with 22.2% respectively, p=not significant). **Mucosal inflammation – increase in proportion of patients with normal mucosal inflammation scores at 6 weeks compared with baseline** • Balloon dilation=22.0% • Control=-4.6%, p<0.001 **Valsalva manoeuvre – increase in number of ears with positive modified Valsalva manoeuvre at 6 weeks compared with baseline** • Balloon dilation=32.8% • Control=3.1%, p<0.001 Patients who had balloon dilation had 'significantly lower non-work activity impairments' than those who had medical management alone.	No device or procedure-related serious adverse events were reported for the 296 patients, including crossover patients, who had balloon dilation. 5 serious adverse events unrelated to the device, procedure or medications were reported (4 in the balloon-dilation group, 1 in the medical management group).
Abbreviations used: ETDQ-7, Eustachian Tube Dysfunction Questionnaire	

Study 3 Anand V (2019)

Details

Study type	**Randomised controlled trial (ELLIOTT) – longer term follow up of treatment arm only**
Country	US (21 centres)
Recruitment period	2014 to 2016
Study population and number	**n=128** Adults with eustachian tube dilatory dysfunction refractory to medical therapy
Age and sex	Mean 56 years; 52% male
Patient selection criteria	See Poe D (2018) for details of inclusion and exclusion criteria for original trial. This study only included patients who completed the 52-week follow up.
Technique	See Poe D (2018)
Follow up	**52 weeks**
Conflict of interest/source of funding	See Poe D (2018)

Analysis

Follow-up issues: Of the 162 patients randomised to balloon dilation plus medical management, 13 did not pass surgical screening and did not have the procedure. Of the 149 patients who had treatment, 128 (86%) completed the 52-week follow-up visit; 13 (9%) were lost to follow up, 5 withdrew from the study, 1 moved out of the area, 1 died (unrelated to the procedure) and 1 exited the study per physician discretion.

Study design issues: See Poe D (2018) for details of study design. This analysis extended the findings of the original study to 52-week follow up and focused on secondary and exploratory endpoints. The analysis included per protocol patients who were randomised to balloon dilation plus medical management.

For the ETDQ-7, an improvement of symptoms ≥0.5 points as compared with baseline was selected as the minimally important difference.

Study population issues: Of the 128 patients, 55% of patients had unilateral eustachian tube dysfunction, 46% of patients had allergic rhinitis and 62% had 1 or more previous ear tube operations at baseline.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 128

Outcomes at 6- and 52-week follow up
<table>
<tr><th>Outcome</th><th>6 weeks</th><th>52 weeks</th></tr>
<tr><td>Normalised tympanogram</td><td></td><td></td></tr>
<tr><td>- Patients</td><td>51.0% (73/143)</td><td>55.5% (71/128)</td></tr>
<tr><td>- Ears</td><td>57.4% (117/204)</td><td>63.6% (119/187)</td></tr>
<tr><td>Improvement in tympanogram (B to A, B to C, or C to A), ears</td><td>62.7% (128/204)</td><td>70.1% (131/187)</td></tr>
<tr><td>ETDQ-7 <2.1, patients</td><td>55.6% (79/142)</td><td>57.3% (71/124)</td></tr>
<tr><td>Absolute change from baseline ETDQ-7 scores</td><td></td><td></td></tr>
<tr><td>- Patients</td><td>-2.3±1.4 (n=142)</td><td>-2.4±1.6 (n=124)</td></tr>
<tr><td>- Patients whose tympanograms were not normalised</td><td>-1.9±1.4 (n=69)</td><td>-1.9±1.7 (n=55)</td></tr>
<tr><td>ETDQ-7 <2.1, patients whose tympanograms were not normalised</td><td>42.0% (29/69)</td><td>41.8% (23/55)</td></tr>
<tr><td>Positive Valsalva, ears</td><td>78.6% (173/220)</td><td>80.4% (185/230)</td></tr>
<tr><td>Work productivity and activity impairment because of problems in the last 7 days, patients</td><td>16.6±23.6 (n=141)</td><td>9.1±18.2 (n=124)</td></tr>
</table>
At 52 weeks, 75.8% of patients had either tympanogram or ETDQ-7 normalisation.</td><td>There were no serious adverse events.

2 patients developed mild symptoms of patulous eustachian tube, 1 of which resolved by the completion of the study.

In 1 patient, a false passage occurred during balloon dilation and was recognised by the surgeon. The catheter was replaced into the true lumen, and dilation was successfully done without sequelae.</td></tr>
<tr><td colspan="2">Abbreviations used: ETDQ-7, Eustachian Tube Dysfunction Questionnaire</td></tr>
</table>

Study 4 Huisman J (2018)

Details

Study type	**Systematic review**
Country	Not reported for individual studies
Recruitment period	Search date: May 2016
Study population and number	**n=1,155 (15 studies)** Adults with eustachian tube dysfunction
Age and sex	Mean age varied from 37 to 55 years (range 6 to 88); 52% (227/440) male
Patient selection criteria	Inclusion criteria for studies were balloon dilation of eustachian tube and adults with tube dysfunction. Exclusion criteria were studies in other than human, cadaver studies, non-English and children studies, editorial articles, conference abstracts, case reports, comments or opinions, (systematic) reviews, when no balloon dilation was done, and if balloon dilation was done as part of more profound middle-ear surgery. In the identified studies, patients were mostly included if their symptoms did not respond to conventional treatment such as nasal steroids and antihistamines. Exclusion criteria varied.
Technique	All studies used either Spiggle & Theis (Overath, Germany) or Acclarent (Acclarent Inc., US) for balloon dilation. General anaesthesia was used in 10 studies, local or general anaesthesia was used in 3 studies and 2 studies did not report the type of anaesthesia used.
Follow up	**Mean 7 months (range 0 to 50)**
Conflict of interest/source of funding	None for authors of the review. Not reported for individual studies included in the review.

Analysis

Follow-up issues: The proportion of missing data was less than 10% in 12 studies, between 10 and 20% in 2 studies and not reported in 1 study. Follow up was 6 months or longer in 11 of the 15 studies.

Study design issues: The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement was used as the writing guideline. All included studies were case series, 9 were described as retrospective and 6 were prospective. Three articles were considered to be of high relevance; the remaining studies were of moderate relevance because of additional treatments used at the same time as balloon dilation or because patients had additional illnesses. All studies had a moderate-to-high risk of bias. A meta-analysis could not be done for all outcomes because of heterogeneity between follow-up times and the types of data provided.

Study population issues: One study included both children and adults. In some of the studies, patients had additional treatments such as nasal corticosteroid spray or functional endoscopic sinus surgery. Patients often had coexisting disease or comorbidity such as cholesteatoma, sinusitis, or mucosal hypertrophy of the turbinates, and some patients had previously had radiotherapy.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **1,155** **Eustachian tube score (higher score correlates with fewer symptoms)** Mean improvement=3.94 (95% CI 2.60 to 5.27, p<0.00001, I^2=66%; 3 studies [670 procedures]) **Valsalva manoeuvre** Inability to do the Valsalva manoeuvre declined after balloon dilation (RR 0.13, 95% CI 0.04 to 0.38, p=0.0002, I^2=78%; 5 studies [153 procedures]) **Otoscopy results** The number of patients with an abnormal tympanic membrane reduced after balloon dilation (RR 0.38, 95% CI 0.07 to 2.05, p=0.26, I^2=99%; 6 studies [166 procedures]) **Tympanometry** Inability to dilate the eustachian tube declined after balloon dilation (RR 0.47, 95% CI 0.32 to 0.70, p=0.0002, I^2=84%; 9 studies [255 procedures]) Two studies reported that results diminished over time. In 1 case series of 11 patients, there was a decline in positive Valsalva manoeuvres from 100% directly after balloon dilation to 63% after a period of 7 to 14 months. In a case series of 622 patients, there was a decline of improvement in mean eustachian tube score at 3-year follow up. **Revisions** Revisions because of failure of the first balloon-dilation procedure were reported in 3 out of 15 studies; 6.7% (122/1,830) of procedures needed a revision. Specific outcomes for these patients were not separately reported. **Mucosal inflammation** 3 studies reported mucosal inflammation as an outcome measure. In 1 study, postoperative biopsies showed a thinner layer of fibrous tissue and restoration of epithelium at 5- to 12-weeks follow up. The other 2 studies rated mucosal inflammation by nasoendoscopy, and both reported a statistically significant decline after 7 to 14 months and 30 months respectively (p<0.01).	**Minor adverse events=2.0% (36/1,830) of procedures** • Diffuse crush injury or local bleeding of the mucosa at the site of the eustachian tube=1.1% (20/1,830) • Hemotympanum needing myringotomy=0.06% (1/1,830) • Temporary otitis media=0.2% (4/1,830) • Preauricular emphysema that resolved spontaneously over a few days=0.2% (3/1,830) • Rhinitis during 1 to 5 days after balloon dilation=0.6% (10/1,830)* • Temporary increase in tinnitus=0.06% (1/1,830) * the text of the article states that 5 patients had rhinitis, but the table states that it was 10 patients. The original study had 21 patients and states that 'about half of the subjects reported rhinitis-like symptoms for 1 to 5 days, which were declared to be minor'.
Abbreviations used: CI, confidence interval; RR, relative risk	

Study 5 Wang TC (2018)

Details

Study type	**Systematic review**
Country	Not reported for individual studies
Recruitment period	Search date: April 2016
Study population and number	**n=1,063 (942 balloon dilation, 121 laser tuboplasty; 13 studies)** Patients with eustachian tube dysfunction
Age and sex	Age range 37 to 52 years; proportion of males ranged from 42% to 92%
Patient selection criteria	Inclusion criteria for meta-analysis: randomised controlled trials, prospective and retrospective studies, and 1-arm studies; patients who had a diagnosis of eustachian tube dysfunction; patients who had treatment with balloon dilation or laser eustachian tuboplasty; studies that provided quantitative outcome data of eustachian tube score and tympanometry and Valsalva manoeuvre results. Exclusion criteria: reviews, letters, comments, editorials, case reports, personal communications, and proceedings. Study inclusion criteria, the definition of eustachian tube dysfunction and any cointerventions done varied between the studies.
Technique	Balloon dilation or laser tuboplasty – no details reported
Follow up	**6 weeks to 1 year**
Conflict of interest/source of funding	None for authors of the review. Not reported for individual studies included in the review.

Analysis

Study design issues: Systematic review and meta-analysis, done in accordance with PRISMA guidelines. The quality of the included studies was assessed with the Quality in Prognostic Studies instrument (evaluating 6 sources of bias related to study participation, study attrition, prognostic factors measurement, outcome measurement, confounding measurement of account, and analysis approaches). Most studies had a low risk of bias in 5 of the 6 measures examined, but all studies had a high risk of bias with respect to confounding measurement of account. Two studies were retrospective and 11 were prospective. There were no randomised controlled trials. Outcome measures were improvement of eustachian tube symptoms and tympanometry and Valsalva manoeuvre results.

The number of studies included for the individual outcome measures was small, and most of the studies included a relatively small number of patients. There was large heterogeneity between the studies. Sensitivity analysis indicated that the eustachian tube score results may have been overly influenced by 2 of the 4 included studies.

Study population issues: Patient inclusion criteria varied markedly between the studies. Some studies included patients with symptoms of eustachian tube dysfunction and some also included patients with otitis media with effusion. Some studies included patients with a perforated tympanic membrane. Detailed inclusion criteria were not described in some of the included studies.

All the included studies on balloon dilation were also included in the systematic review by Huisman J, 2018 (study 4).

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **1,063 (942 balloon dilation, 121 laser eustachian tuboplasty)** **Eustachian tube score** Balloon dilation – mean eustachian tube score (4 studies; I^2=97.0%) • Before dilation=2.98 • After dilation=5.69 Pooled SMD=0.94, 95% CI 0.23 to 1.66, p=0.009 Subgroup – 1-year follow up: pooled SMD=0.53, 95% CI -0.36 to 1.42, p=0.244 (2 studies) Subgroup – 2 to 3 months follow up: pooled SMD=1.46, 95% CI 0.45 to 2.48, p=0.005 (2 studies) Eustachian tube score was not reported in any of the laser tuboplasty studies. **Improvement in tympanometry** (4 balloon-dilation studies, I^2=78.7%; 3 laser tuboplasty studies, I^2=0%) Pooled event rate • Balloon dilation=73% • Laser tuboplasty=13%, p=0.001 **Improvement in Valsalva manoeuvre** (2 balloon-dilation studies, I^2=74.6%; 4 laser tuboplasty studies, I^2=66.2%) Pooled event rate • Balloon dilation=67% • Laser tuboplasty=50%, p=0.472	The review did not include any safety outcomes.
Abbreviations used: CI, confidence interval; SMD, standardised mean difference	

Study 6 Skevas T (2018)

Details

Study type	**Case series**
Country	Germany (4 centres)
Recruitment period	2009 to 2016
Study population and number	**n=2,272 (3,670 procedures)** Patients who had balloon dilation of the eustachian tube
Age and sex	Age range 2 to 83 years
Patient selection criteria	All balloon-dilation procedures done at the 4 study centres were included.
Technique	Device: Spiggle & Theis balloon catheter (Spiggle & Theis, Germany). All procedures were done under general anaesthesia. Concomitant surgical interventions during the balloon-dilation procedure included, if indicated, inferior turbinate outfracture with or without reduction, septoplasty, paracentesis of the eardrum with or without grommet insertion, biopsy from the nasopharynx and tympanoplasty (in a few patients). Patients were instructed to do a Valsalva manoeuvre, either immediately after the procedure (in 3 centres) or on the third postoperative day (1 centre). Perioperative antibiotic prophylaxis (intravenous cefuroxime) was routinely used in 1 centre.
Follow up	**Not reported**
Conflict of interest/source of funding	Four authors received reimbursement of travel expenses by Spiggle & Theis, Germany. In addition, 1 author received financial support for a training course from Spiggle & Theis and 1 author received financial support for a meeting and royalties from Spiggle & Theis.

Analysis

Study design issues: Retrospective multicentre case series. Data were extracted from medical records at the study centres. The aim was to explicitly document emphysematous complications and their outcomes. No efficacy data were reported.

Study population issues: The paper does not include baseline characteristics of the patients who had the procedure.

Key efficacy and safety findings

Safety

Number of patients analysed: **2,272**

Balloon-dilation-related postoperative emphysematous adverse effects

Centre	No. of patients	Number of procedures	Assessment period	Number of patients with emphysema	Patients with concomitant pneumo-mediastinum	Gender and age of affected patients (years)	Time of occurrence after the procedure	Symptoms other than skin crepitations	Complete resolution
Bielefeld	1,460	2,348	02/2009 to 06/2016	5	1	3 male (61, 42, 55) 2 female (48, 52)	1 hour	No	After 3 to 4 days
Hamburg-Eppendorf	469	739	11/2011 to 10/2015	2*	0	1 male (45)	Immediate	No	After 3 days
Wuppertal	220	370	03/2013 to 06/2016	2	2	2 male (63, 54)	1 and 3 days	No	After 6 days
Heidelberg	123	213	11/2011 to 12/2015	1	0	1 male (45)	12 hours	No	After 2 days
Total	2,272	3,670		10	3				

* In the same patient

Rate of postoperative emphysema=0.3% (10/3,670) of procedures (95% CI 0.13 to 0.50)

All patients with emphysema had treatment with an intravenous or oral antibiotic and Valsalva manoeuvre was discontinued for 3 weeks. A complete resolution was noted within 2 to 6 days for all patients. One patient had an eosinophilic systemic disorder with involvement of the upper airway mucosa, which was considered to be a risk factor for increasing the likelihood of an emphysematous complication. None of the other patients had any intraoperative abnormalities or incidents favouring the formation of emphysema.

Additional postoperative adverse effects other than emphysema:

- Temporary intensification of tinnitus, n=3
- Acute otitis media, n=1
- Mild findings possibly compatible with patulous eustachian tube, n=1
- 'Occasional cases' of epistaxis, which was self-limiting in most patients but some needed treatment with electrocautery or nasal packing.

Abbreviations used: CI, confidence interval

Study 7 Schröder S (2015)

Details

Study type	**Case series**
Country	Germany
Recruitment period	2009 to 2014
Study population and number	**n=622 (1,076 procedures)** Patients with chronic obstructive eustachian tube dysfunction.
Age and sex	Age range 7 to 84 years; male:female ratio about 1:1
Patient selection criteria	Patients aged 7 years or older. Initially, patients were included if they had symptoms of chronic eustachian tube dysfunction or had had 1 or more middle-ear operations because of previously undiagnosed eustachian tube dysfunction. Indications included otitis media with effusion as a consequence of obstructive tube dysfunction. Currently, balloon dilation is offered to symptomatic patients with an ETS of 5 or less or ETS-7 score of 7 or less, and the presence of chronic obstructive eustachian tube dysfunction: an uncomfortable sensation of pressure in the ears, especially with changes in atmospheric pressure; an inability to do Valsalva's manoeuvre; chronic otitis media with effusion; an obvious adhesive process; a flat line in the tympanogram (type B); or early recurrence of retraction after tympanoplasty.
Technique	All procedures were done under general anaesthesia. The catheter insertion tool was mostly positioned transnasally in the nasopharyngeal eustachian tube ostium and the catheter advanced into the cartilaginous part of the eustachian tube. For endoscopic visualisation, an endoscope was used in the same or contralateral nostril. In a minority of patients, for example those with very deviated nasal septums, an endoscope was used transorally to visualise the nasopharynx. All patients were encouraged to use a nasal steroid spray for about 6 weeks after the procedure.
Follow up	**Up to 4 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: There were high losses to follow up. At 2 months, data were available for 49% (506/1,029) of procedures. Data were available for 28% (188/671) of procedures at 1-year follow up, 10% (34/344) of procedures at 2 years, 9% (11/119) of ears at 3 years and only 2 patients were evaluated at 4 years.

Study design issues: Retrospective, single-centre, cohort study. The ETS was used as an outcome measure (range 0 [worst value] to 10 [best value]).

Study population issues: Children over the age of 7 were included (n=50) as well as adults. Most patients showed no opening of the eustachian tube in tubomanometry at 30, 40 and 50 millibars. The mean ETS at baseline was 3.51 (±2.66), indicating moderate to severe eustachian tube dysfunction.

This study is also included in the systematic review by Huisman J, 2018 (study 4).

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 622

ETS, mean ± standard deviation
<table>
<tr><th>Follow-up period</th><th>n</th><th>ETS at baseline</th><th>ETS at follow up</th><th>Proportion of cases with statistically significant improvement (p≤0.001)</th></tr>
<tr><td>2 months</td><td>506/1,029 procedures</td><td>3.15±2.54</td><td>5.37±2.71</td><td>71% (357/506)</td></tr>
<tr><td>1 year</td><td>188/671 procedures</td><td>3.13±2.47</td><td>5.75±2.76</td><td>73% (138/188)</td></tr>
<tr><td>2 years</td><td>34/344 procedures</td><td>2.65±2.89</td><td>6.26±3.07</td><td>82% (28/34)</td></tr>
<tr><td>3 years</td><td>11/119 ears</td><td>2.36±2.69</td><td>5.27±3.82</td><td>82% (9/11)</td></tr>
</table>
Patient satisfaction
33% (30/89) of patients returned the questionnaire that was sent about 2 years after the procedure. The patients were asked to describe the degree of improvement and their satisfaction with the treatment.
• No improvement=27%
• Dissatisfied with outcome=20%
• No complaints=47%
• Improvement=26%

Among all patients who answered the questionnaire, 60% were satisfied with the result of the treatment and 20% were only completely satisfied for the first few months after the treatment.</td><td>There were no serious complications.
• Surgical emphysema within the parotid region as sequelae of a minor mucosal tear in the eustachian tube=0.3% (3/1,076) (in all patients, the emphysema was reabsorbed under antibiotic cover and the eustachian tube healed without permanent damage.)

Minor bleeding and a temporary increase in pre-existing tinnitus for 2 weeks after the procedure were the other adverse effects noted (number of patients not reported).</td></tr>
<tr><td colspan="2">Abbreviations used: ETS, eustachian tube score</td></tr>
</table>

Study 8 Luukkainen V (2018)

Details

Study type	**Case series**
Country	Finland
Recruitment period	2011 to 2013
Study population and number	**n=46** Patients who had eustachian tube balloon dilation
Age and sex	Mean 38 years (range 16 to 70); 50% (23/46) male
Patient selection criteria	Patients who had other ear operations, except tympanocentesis or tympanostomy tube insertion, were excluded as were those who had previous eustachian tube operations.
Technique	Device: Acclarent Relieva solo (Acclarent, US) sinus balloon-dilation catheter. All procedures were done under general anaesthesia.
Follow up	**Mean 3 years (range 1.8 to 4.6)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Of the 46 patients who were sent a postal questionnaire, 34 (74%) returned it.

Study design issues: Retrospective single-centre case series. A postal questionnaire was sent to 46 patients who met the inclusion criteria from 51 consecutive patients who had balloon dilation in the department. The questionnaire was modified from the ETDQ-7, which covers the severity of specific ear symptoms suggestive of eustachian tube dysfunction from the previous month. Patients evaluated the Valsalva manoeuvre themselves.

Study population issues: Of the 46 patients who met the inclusion criteria, 32 (70%) had chronic secretory otitis media, 11 (24%) had obstruction of the eustachian tube and 3 (7%) had chronic otitis media not otherwise specified. Eustachian tube dysfunction type was dilatory in 31 of the patients who responded to the questionnaire and barochallenge-induced in 3 patients. The demographics of the patients who responded to the questionnaire were similar to the total population of patients who had treatment.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **34**

Current overall ear symptoms compared to the preoperative situation

	All patients (n=52 ears)	Balloon dilation only (n=38 ears)	Balloon dilation and additional procedures (n=14 ears)
Not at all (%)	10	13	0
Clearly less than before the operation (%)	42	53	14
Somewhat less than before the operation (%)	25	24	29
As much as before the operation (%)	15	8	36
Somewhat more than before the operation (%)	6	3	14
Clearly more than before the operation (%)	7	0	7

Disturbance caused by current ear symptoms

	All patients (n=34)	Balloon dilation only (n=25)	Balloon dilation and additional procedures (n=9)
Not at all (%)	6	8	0
Very little (%)	26	36	0
Little (%)	35	32	44
Moderately (%)	18	16	22
Quite much (%)	12	8	22
Much (%)	3	0	11

Willingness to have balloon dilation again if ear symptoms returned to the preoperative level

	All patients (n=33)	Balloon dilation only (n=25)	Balloon dilation and additional procedures (n=8)
Yes (%)	82	84	75
No (%)	18	16	25

Pain in the ears, feeling of pressure in the ears and feeling that ears are clogged reduced in 75% of the ears that had these symptoms before the procedure.

Ringing in the ears and the ability to release pressure in the ears by swallowing responded the least to balloon dilation. The Valsalva manoeuvre became easier in about 50% of all treated ears and in 57% of those who needed no further interventions after balloon dilation.

Abbreviations used: ETDQ-7, Eustachian Tube Dysfunction Questionnaire

Study 9 Tisch M (2017)

Details

Study type	**Case series (2-part study)**
Country	Germany
Recruitment period	1. 2010 to 2012; 2. 2012 to 2013
Study population and number	**n=126; 1. n=60; 2. n=66** Children who had balloon dilation of the eustachian tube for refractory chronic eustachian tube dysfunction
Age and sex	1. mean 6.3 years (range 28 months to 12 years); 2. Mean 8 years (range 4 to 13 years)
Patient selection criteria	Indications for balloon dilation were the presence of chronic obstructive eustachian tube dysfunction that was not managed satisfactorily with medical treatments and surgical treatments.
Technique	All procedures were done under general anaesthesia. A balloon catheter was passed through an insertion instrument and pushed 2 cm into the eustachian tube under endoscopic vision. The balloon was inflated to 10 bars for 2 minutes. Routine postoperative care consisted of nasal drops containing xylometazoline and panthenol ointment for 3 days. Some patients also had antihistamines or topical corticosteroids. Starting on the third day after surgery, patients were told, if possible, to autoinflate the eustachian tube by doing Valsalva manoeuvres or using an Otovent device.
Follow up	**1. Mean 13 months; 2. Mean 9.5 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Eustachian tube function was assessed before surgery and at 6 to 8 weeks after surgery. Completeness of follow up is not described. Of the 66 parents contacted for the second part of the study, 34 (51.5%) agreed to take part.

Study design issues: Retrospective case series. For the first group of patients, data were obtained from medical records. For the second group, parents were asked to complete a written questionnaire and were interviewed by telephone about the postoperative course of their children and about their satisfaction with outcome. Eustachian tube function was assessed using the following tests: Valsalva manoeuvre and Toynbee test (if possible), tympanogram, and otomicroscopy.

Study population issues: All patients were children. Of the 60 children in the first group, 20 had had at least 1 previous tympanoplasty. Before surgery, 92% of the children were unable to equalise middle-ear pressure, as indicated by the absence of a positive Valsalva test on microscopy or the absence of a definable peak on a tympanogram. Complete adhesion was seen in 37% (22/60) of children. Half of the children had unilateral procedures and half had bilateral procedures.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 94 **First patient group (n=60)** After surgery, 18.3% (11/60) of children were objectively unable to equalise middle-ear pressure. In 81.8% (18/22) of children, adhesions were separated so that there was no further contact between the tympanic membrane and the promontory or between the tympanic membrane and the long process of the incus. **Second patient group (n=34)** Of the 66 parents who were contacted, 34 (51.5%) agreed to take part. Hearing improved in 76.5% of children. Of the participating parents, 55.9% were very satisfied and 25.4% were satisfied with the results of the surgery. The parents of only 1 child stated that they were not satisfied with the outcome. Balloon dilation was repeated in 26.5% (9/34) of children.	**First patient group (n=60)** There were no complications during surgery. One child had a nosebleed immediately after the procedure, which was managed with bipolar coagulation and anterior nasal packing. No further treatment-associated complications were reported. **Second patient group (n=34)** No serious complications were reported. Immediately after the procedure, 1 child had mild epistaxis and 1 had postoperative pain. 3 children developed otitis media in the days after balloon dilation. In the later postoperative course, otitis media with effusion was reported in 3 children.

Study 10 Cutler JL (2019)

Details

Study type	**Case series (extended follow up of treatment arm of randomised controlled trial [study 1])**
Country	US
Recruitment period	2017 to 2018
Study population and number	**n=47** Adults with persistent eustachian tube dysfunction
Age and sex	Mean 53 years; 45% (21/47) male
Patient selection criteria	Inclusion criteria: age 18 or older, diagnosed with eustachian tube dysfunction for 12 months or longer, 3 or more symptoms, ETDQ-7 score of 3 or higher, refractory to medical therapy. Exclusion criteria: patulous eustachian tube, uncontrolled chronic rhinosinusitis, allergies or reflux, and ear tubes of perforated tympanic membrane at enrolment.
Technique	Device: XprESS ENT Dilation System (Entellus Medical, US).
Follow up	**Mean 29.4 months (range 18 to 42)**
Conflict of interest/source of funding	Entellus Medical designed and sponsored the study. One author is an employee of Entellus Medical.

Analysis

Follow-up issues: Patients were only included if they had completed the 12 month follow up for the original protocol. Data were collected at 6-month intervals.

Study design issues: Extended follow-up study of the treatment arm of a prospective multicentre randomised controlled trial. The main outcome measures were the change from baseline in the ETDQ-7 score, revision dilation rate, changes in assessments of middle-ear function and patient satisfaction.

Study population issues: The mean duration of eustachian tube dysfunction was 15 years. The mean overall ETD-7 score at baseline was 4.5.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 47

Long-term outcome measures
<table>
<tr><th>Outcome measure</th><th>1-year follow up</th><th>Long-term follow up (mean 29 months)</th></tr>
<tr><td>Change from baseline in mean overall ETDQ-7 score (±SD)</td><td>−2.5±1.15 (n=47)
p<0.0001</td><td>−2.5±1.15 (n=47)
p<0.0001</td></tr>
<tr><td>Normalised tympanic membrane position*</td><td>76.0% (19/25)
p<0.0001</td><td>76.0% (19/25)
p<0.0001</td></tr>
<tr><td>Positive Valsalva manoeuvre*</td><td>69.7% (23/33)
p<0.0001</td><td>66.7% (22/33)
p<0.0001</td></tr>
<tr><td>Normalised tympanogram type (type A)*</td><td>52.2% (12/23)
p=0.007</td><td>62.5% (15/24)
p<0.001</td></tr>
<tr><td>Satisfied with the outcome of the procedure</td><td>89.1% (41/46)</td><td>83.0% (39/47)</td></tr>
<tr><td>Would recommend the procedure</td><td>93.3% (42/45)</td><td>87.2% (41/47)</td></tr>
</table>
* improvements in middle-ear functional assessments were evaluated in patients with abnormal baseline values.

93.6% (44/47) of patients had a reduction of 1 or more in their overall ETDQ-7 score at their last follow-up visit.

Each ETDQ-7 item score was statistically significantly reduced (p<0.0001).

Revisions
1 patient had a revision eustachian tube dilation at 362 days after the initial procedure. The revision was done concurrently with balloon dilation for recurrent sinus disease.</td><td></td></tr>
<tr><td colspan="2">Abbreviations used: ETDQ-7, Eustachian Tube Dysfunction Questionnaire; SD, standard deviation</td></tr>
</table>

Validity and generalisability of the studies

- There are data from Europe and the US.
- There are different devices used for the procedure.
- Most of the studies only include adults but some also include children.
- There are 2 RCTs comparing balloon dilation plus medical management with medical management alone. Both of these have follow-up data to at least 1 year.
- There is a systematic review that compares balloon dilation with laser eustachian tuboplasty, but the number of included studies was small and there was large heterogeneity between the studies. None of the laser tuboplasty studies reported the eustachian tube score as an outcome measure, so this could not be compared.
- Some of the studies have high losses to follow up and there is little evidence beyond 3-year follow up.
- The patient populations are heterogenous.
- Most of the studies reported that the procedures were done under general anaesthesia, but there is some evidence from patients who had the procedure under local anaesthesia.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Balloon dilatation of the Eustachian tube. Interventional procedures guidance 409 (2011). Available from http://www.nice.org.uk/guidance/IPG409 *[current guidance]*

- Balloon catheter dilation of paranasal sinus ostia for chronic sinusitis. NICE interventional procedures guidance 273 (2008). Available from http://www.nice.org.uk/guidance/IPG273

Medical technologies

- XprESS multi sinus dilation system for treating chronic sinusitis. Medical technologies guidance 30 (2016). Available from http://www.nice.org.uk/guidance/MTG30

NICE guidelines

- Otitis media with effusion in under 12s: surgery. NICE clinical guideline 60 (2008). Available from http://www.nice.org.uk/guidance/CG60

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by specialist advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.
Two Specialist Adviser Questionnaire for balloon dilation of a eustachian tube for eustachian tube dysfunction was submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Company engagement

A structured information request was sent to 3 companies who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Ongoing trials:
  - Balloon Eustachian Tuboplasty in Treatment of Chronic Eustachian Tube Dysfunction (NCT03556215); Czech Republic; estimated enrolment 55; estimated study completion date Nov 2019.
  - Balloon Dilation of the Eustachian Tube in Children (NCT03499015); Randomised Side-controlled Clinical Trial; Austria; estimated enrolment 50; estimated study completion date Oct 2020.
- Studies have only been included if the balloon dilation was done transnasally.
- The ACCLARENT AERA® Eustachian Tube Balloon Dilation System is intended to dilate the eustachian tube for treatment of persistent eustachian tube dysfunction in adults ages 18 and older. The Spiggle and Theis device does not specify a suitable age group but has the following warning in its instructions for use: ‘As the anatomic structures of children and adolescent persons differ from those of adults and will change during the development of children and adolescents, the physician has to decide if the intervention can be carried out and select the right catheter (the right balloon length), carefully weighing the benefits of the intervention against its possible risks.’ The Entellus Medical device is used for treating persistent eustachian tube dysfunction in patients 18 years and older.

References

1. Meyer TA, O'Malley EM, Schlosser RJ et al. (2018) A randomized controlled trial of balloon dilation as a treatment for persistent eustachian tube dysfunction with 1-year follow-up. Otology & Neurotology 39: 894-902
2. Poe D, Anand V, Dean M et al. (2018) Balloon dilation of the eustachian tube for dilatory dysfunction: A randomized controlled trial. Laryngoscope 128: 1200-6
3. Anand V, Poe D, Dean M et al. (2019) Balloon dilation of the eustachian tube: 12-month follow-up of the randomized controlled trial treatment group. Otolaryngology - Head & Neck Surgery 160: 687–94
4. Huisman JML, Verdam FJ, Stegeman I et al. (2018) Treatment of Eustachian tube dysfunction with balloon dilation: A systematic review. Laryngoscope 128: 237-47
5. Wang TC, Lin CD, Shih TC et al. (2018) Comparison of balloon dilation and laser eustachian tuboplasty in patients with eustachian tube dysfunction: a meta-analysis. Otolaryngology - Head & Neck Surgery 158: 617-26
6. Skevas T, Dalchow CV, Euteneuer S et al. (2018) Cervicofacial and mediastinal emphysema after balloon eustachian tuboplasty (BET): a retrospective multicenter analysis. European Archives of Oto-Rhino-Laryngology 275: 81-7
7. Schroder S, Lehmann M, Ebmeyer J et al. (2015) Balloon Eustachian tuboplasty: a retrospective cohort study. Clinical Otolaryngology 40: 629-38
8. Luukkainen V, Vnencak M, Aarnisalo AA et al. (2018) Patient satisfaction in the long-term effects of Eustachian tube balloon dilation is encouraging. Acta Oto-Laryngologica 138: 122-7
9. Tisch M, Maier H, Sudhoff H (2017) Balloon dilation of the Eustachian tube: clinical experience in the management of 126 children. Acta Otorhinolaryngologica Italica 37: 509-12
10. Cutler JL, Meyer TA, Nguyen SA et al. (2019) Long-term outcomes of balloon dilation for persistent eustachian tube dysfunction. Otology & Neurotology 40 doi: 10.1097/MAO.0000000000002396

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	04/09/2019	Issue 9 of 12, September 2019
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	04/09/2019	Issue 9 of 12, September 2019
HTA database (CRD website)	04/09/2019	n/a
MEDLINE (Ovid) & MEDLINE In-Process (Ovid)	04/09/2019	1946 to September 03, 2019
Medline ePub ahead (Ovid)	04/09/2019	September 03, 2019
EMBASE (Ovid)	04/09/2019	1974 to 2019 September 03

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Balloon Dilation/
2	Dilatation, Pathologic/
3	Dilatation/
4	(balloon* adj4 (dilat* or cathet* or expand* or inflat*)).tw.
5	BET.tw.
6	catheterization/ or catheterization, peripheral/
7	(Cathet* adj4 peripher*).tw.
8	(Dilat* adj4 pathologic*).tw.
9	or/1-8
10	Eustachian Tube/
11	exp Ear Diseases/
12	(Middle ear* adj4 (inflamm* or infect* or disease* or effus* or atelectas*)).tw.
13	((Eustach* or audit* or pharyngoty* or chron*) adj4 tube adj4 (dysfunct* or obstruct* or block* or inflamm* or disorder*or tuboplast*)).tw.
14	(otit* adj4 media*).tw.
15	ETD.tw.
16	or/10-15
17	9 and 16
18	ANIMALS/ not HUMANS/

19	17 not 18

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ Follow up	Direction of conclusions	Reasons for non-inclusion in table 2
Abdel-Aziz T, Schroder S, Lehmann M et al. (2014) Computed tomography before balloon Eustachian tuboplasty--a true necessity? Otology & Neurotology 35: 635-8	Case series n=284	Carotid canal dehiscences were found in 6.3% of patients. Preoperative high-resolution CT scan of the temporal bone does not seem to be suitable to predict intraoperative or postoperative difficulties. For inexperienced surgeons, it may help to understand the relation between internal carotid artery and the eustachian tube.	Study focuses on the use of CT before balloon dilation.
Ashry Y, Kawai K, Poe D (2017) Utility of adjunctive procedures with balloon dilation of the eustachian tube. Laryngoscope Investigative Otolaryngology 2: 337-43	Case series n=48 Follow up=mean 1.3 years	Adjunctive turbinectomy, adenoidectomy, or tympanoplasty were used in selected patients. Statistically significant improvement occurred in 79%. There was no statistically significant difference in the failure rate comparing balloon dilation with adjunctive procedures 5/20 (25%) or without adjunctive procedures; 4/30 p=0.45 (13%).	Study focuses on the use of adjunctive procedures with balloon dilation.
Bast F, Frank A, Schrom T (2013) Balloon dilatation of the Eustachian tube: postoperative validation of patient satisfaction. ORL 75: 361-5	Case series n=30 Follow up=6 to 18 months	The results showed a statistically significant improvement in the total score, in the subscore 'general health' and in the subscore 'physical health' in the Glasgow Benefit Inventory questionnaire.	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).
Bowles PF, Agrawal S, Salam MA (2017) Balloon tuboplasty in patients with Eustachian tube dysfunction: a prospective study in 39 patients (55 ears). Clinical Otolaryngology 42: 1057-60	Case series n=39 Follow up=6 months	There was an improvement in all primary outcome measures at 6 weeks, 3 and 6 months. There were no complications.	Studies with more patients or longer follow up are included.
Catalano PJ, Jonnalagadda S, Yu VM (2012) Balloon catheter dilatation of Eustachian tube: a	Case series n=70	71% of ears showed notable improvement or reduction in symptoms. Of the 28 ears with abnormal tympanograms	More recent studies with longer follow up are included.

preliminary study. Otology & Neurotology 33: 1549-52	Follow up=mean 30 weeks	(type B or C), 90% improved to type A.	Study is included in review by Huisman J, 2018 (study 4).
Corrales CE, Ashry Y, Poe D (2017) Eustachian tube dilation. Otorhinolaryngologist 10: 5-10	Review	Numerous studies have shown improvement in multiple assessments of eustachian tube function after balloon dilation, including ability to do a Valsalva, improvements in tympanograms, atelectasis, tubomanometry, mucosal inflammation scores, and mean ETDQ-7 symptom scores. There is mounting evidence that outcomes are durable to at least 2.5 years in regard to being able to do a Valsalva manoeuvre, improvement in tympanograms and by the mucosal inflammation score.	More recent systematic reviews are included.
Dai S, Guan GF, Jia J et al. (2016) Clinical evaluation of balloon dilation eustachian tuboplasty surgery in adult otitis media with effusion. Acta Oto Laryngologica 136: 764-7	Case series n=8 Follow up=12 months	None of the involved patients complained of problems or complications during the postoperative period. Postoperative improvement was observed in tympanic membrane and otoscopic appearance. In addition, cure rates after 3 months and 6 months postoperatively were gradually increased.	Larger studies are included. Study is included in review by Huisman J, 2018 (study 4).
Dalchow CV, Loewenthal M, Kappo N et al. (2016) First results of Endonasal dilatation of the Eustachian tube (EET) in patients with chronic obstructive tube dysfunction. European Archives of Oto-Rhino-Laryngology 273: 607-13	Case series n=217 Follow up=3 to 12 months	Endonasal dilation of the eustachian tube is a minimally invasive and effective treatment of chronic obstructive tube dysfunction. It is a safe procedure without causing substantial complications. Nevertheless, long-term results of larger, placebo-controlled multicentre studies are needed to confirm its effectiveness.	Relatively short-term follow up. Study is included in review by Huisman J, 2018 (study 4).
Dean M, Lian T (2016) Transnasal endoscopic eustachian tube surgery. Otolaryngologic Clinics of North America 49: 1163-71	review	Balloon dilation of the cartilaginous eustachian tube is a feasible alternative to tympanostomy tube placement in patients with longstanding, refractory dilatory dysfunction.	More recent systematic reviews are included.
Di Rienzo Businco L, Di Mario A, Tombolini M et al. (2017) Eustachian tuboplasty and shrinkage of ostial mucosa with new devices: Including a	Case series n=102 Follow up=3 months	The combined surgical procedure of balloon tubodilation with simultaneous quantic molecular response-mediated	Patients had balloon dilation combined with shrinkage of ostial mucosa.

proposal of a classification system. HNO 65: 840-7		shrinkage of the tubal ostial mucosa and reduction of the posterior portion of the inferior turbinate was found to be an effective, safe, and complete treatment for tubal dysfunction in most patients.	
Falkenberg-Jensen B, Hopp E, Jablonski GE (2018) The cartilaginous Eustachian tube: Reliable CT measurement and impact of the length. American Journal of Otolaryngology 39: 436-40	Case series and case-control study n=10 and 103 Follow up=3 to 6 months	Measuring the cartilaginous portion of the Eustachian tube on CT images is precise and reproducible, and reflects the length measured intraoperatively. However, it does not seem have a prognostic value.	Study focuses on the impact of measuring the length of the eustachian tube.
Gurtler N, Husner A, Flurin H (2015) Balloon dilation of the Eustachian tube: early outcome analysis. Otology & Neurotology 36: 437-43	Case series n=21 Follow up=3 months	Subjective improvement was seen in 76% of patients. The eustachian tube score, tympanogram and air-bone gap all showed a statistically positive outcome ($p<0.005$). There was 1 minor bleeding complication.	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).
Hwang SY, Kok S, Walton J (2016) Balloon dilation for eustachian tube dysfunction: Systematic review. Journal of Laryngology and Otology 130: S2-S6	Systematic review n=474 (9 studies) Follow up=1.5 to 18 months	Prospective case series can confirm the safety of eustachian tube balloon dilation. As a potential solution for chronic eustachian tube dysfunction, further investigations are warranted to establish a higher level of evidence of efficacy.	More recent systematic reviews are included.
Jenckel F, Kappo N, Gliese A et al. (2015) Endonasal dilatation of the Eustachian tube (EET) in children: feasibility and the role of tubomanometry (Esteve) in outcomes measurement. European Archives of Oto-Rhino-Laryngology 272: 3677-83	Case series n=33 children Follow up=1 to 15 months	There were no complications. In most children, the ear-related symptoms such as hearing, otorrhoea and otalgia were improved. Six children had concomitant adenoidectomy. The R-scores were unable to show favourable changes towards better or earlier opening of the eustachian tube.	Small case series with short follow up.
Jurkiewicz D, Bien D, Szczygielski K et al. (2013) Clinical evaluation of balloon dilation Eustachian tuboplasty in the Eustachian tube dysfunction. European Archives of Oto-Rhino-Laryngology 270: 1157-60	Case series n=4 Follow up=6 weeks	Although patients revealed a statistically significant improvement of eustachian tube score, longer term studies are necessary to determine whether this method will show lasting benefits and safety in the treatment of chronic eustachian tube dysfunction. In other investigations,	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).

		improvement was found to be time dependent.	
Kim KY, Tsauo J, Song HY et al. (2018) Fluoroscopy-guided balloon dilation in patients with Eustachian tube dysfunction. European Radiology 28: 910-9	Case series n=10 Follow up=3 months	Technical success was achieved in all procedures (10/10). 90% (9/10) of the balloons were fully dilated without waist deformity. There were no major complications. All patients were able to do a Valsalva manoeuvre at the time of their last visit and/or improvement of at least one ETDQ-7 score.	Studies with more patients or longer follow up are included.
Kivekas I, Chao WC, Faquin, W et al. (2015) Histopathology of balloon-dilation Eustachian tuboplasty. Laryngoscope 125: 436-41	Case series n=13	Histopathology of the eustachian tube after balloon dilation showed effects that could reduce the overall inflammatory burden and may contribute to clinical improvement in function.	Small case series focuses on histopathology. Study is included in review by Huisman J, 2018 (study 4).
Leichtle A, Hollfelder D, Wollenberg B et al. (2017) Balloon Eustachian tuboplasty in children. European Archives of Oto-Rhino-Laryngology 274: 2411-9	Case series n=52 Follow up=1 year	In most patients, there was an improvement in the ear pressure, hearing loss, limitation in daily life, and satisfaction with recurrent inflammations, underlined by better outcomes in the tubomanometry and the tympanogram. Balloon dilation in children is a safe, efficient, and promising method to treat chronic tube dysfunction, especially as a second line treatment.	Larger studies are included.
Li Y-Q, Chen Y-B, Yin G-D et al. (2019) Effect of balloon dilation eustachian tuboplasty combined with tympanic tube insertion in the treatment of chronic recurrent secretory otitis media. European Archives of Oto-Rhino-Laryngology https://doi.org/10.1007/s00405-019-05512-7	Non-randomised comparative study n=60 Follow up=24 months	The symptoms improved and the ET score increased after surgery in most patients who had balloon eustachian tuboplasty (BET) plus tympanic tube insertion (TTI) compared with those had with TTI alone. The highest ET score was obtained at 6 months post BET. Five (14%) patients (6 ears) had recurrence of chronic recurrent secretory otitis media. The 24-month follow-up questionnaire showed that 85% of the patients were satisfied with the treatment, while 10 patients (25%) in the TTI group had a recurrence.	Studies with more patients or longer follow up are included.
Liang M, Xiong H, Cai Y et al. (2016) Effect of the combination of balloon Eustachian tuboplasty and	Randomised controlled trial n=90	The results suggested that the combination of balloon dilation of the eustachian tube and tympanic	The indication was chronic otitis media with effusion, rather

tympanic paracentesis on intractable chronic otitis media with effusion. American Journal of Otolaryngology 37: 442-6	Follow up=6 months	paracentesis was effective for intractable chronic otitis media with effusion and can help shorten the recovery period for middle-ear effusion.	than eustachian tube dysfunction.
Llewellyn A, Norman G, Harden M et al. (2014) Interventions for adult Eustachian tube dysfunction: a systematic review. Clinical Otolaryngology 39: 6–21	Systematic review n=103 (3 studies on balloon dilation)	It is inappropriate to make conclusions on the effectiveness of any intervention because of the limited and poor-quality evidence.	More recent systematic reviews are included.
Luukkainen V, Jero J, Sinkkonen ST (2019) Balloon Eustachian tuboplasty under monitored anaesthesia care with different balloon dilation devices: A pilot feasibility study with 18 patients. Clinical Otolaryngology 44: 87-90	Case series n=18	There were no differences in pain or discomfort between different balloon-dilation devices. There were no differences in pain or discomfort between the 2 local anaesthesia methods.	Small feasibility study comparing different devices and different local anaesthesia methods.
Luukkainen V, Kivekas I, Silvola, J et al. (2018) Balloon eustachian tuboplasty: systematic review of long-term outcomes and proposed indications. The Journal of International Advanced Otology 14: 112-26	Systematic review n=968 for 5 studies with follow up >12 months); n=192 for 5 studies with follow up 6 to 11 months.	The long-term follow-up studies were heterogeneous regarding the eustachian tube dysfunction definition, patient selection, follow-up duration, additional treatments, and outcome measures. The current, but limited, evidence suggests that balloon dilation is effective in the long term. However, more long-term studies with uniform criteria and outcome measures as well as placebo-controlled studies are needed.	Other systematic reviews are included.
Luukkainen V, Kivekas I, Hammaren-Malmi S et al. (2017) Balloon Eustachian tuboplasty under local anesthesia: Is it feasible? Laryngoscope 127: 1021-5	Case-control study n=25	BET is a safe and feasible procedure under monitored anaesthesia care, including local anaesthesia along with sedation and analgesia. There is need for further methodological improvement to reduce pain and discomfort during the operation.	Study focuses on use of local anaesthesia and the control group of patients had endoscopic sinus surgery.
McCoul ED, Anand VK (2012) Eustachian tube balloon dilation surgery. International Forum of Allergy & Rhinology 2: 191-8	Case series n=22 Follow up=median 10 months	Postoperative improvements were seen using objective and subjective measures.	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).
Miller BJ, Elhassan HA (2013) Balloon dilatation of the Eustachian tube: An evidence-based review of case series for those considering its use. Clinical Otolaryngology 38: 525-32	Review n=235 (5 studies)	Balloon dilation of the eustachian tube appears to be safe and effective. Like many newly introduced techniques, the evidence remains limited to non-controlled case series, with heterogeneous data collection methods and	More recent systematic reviews are included.

		lacking long-term outcomes. However, short-term data provides promising, consistent results based on objective measures, and when used selectively in patients refractive to maximal existing therapy, balloon dilation presents a potentially statistically significant advance.	
Poe DS, Silvola J, Pyykko I (2011) Balloon dilation of the cartilaginous eustachian tube. Otolaryngology Head and Neck Surgery 144: 563-9	Case series n=11	All cases successfully dilated. 100% (11/11) could self-insufflate by Valsalva ($p<0.001$); tympanograms were A (4/11), C (1/11), or open (6/11). All atelectases resolved. Procedures were well tolerated, without pain or complications related to dilation.	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).
Randrup TS, Ovesen T (2015) Balloon eustachian tuboplasty: a systematic review. Otolaryngology - Head and Neck Surgery 152: 383-92	Systematic review n=443 (9 studies)	The evidence of BET is poor and biased. No firm conclusions can be made to identify patients who will benefit from the procedure or to accurately predict surgical results. Randomised controlled trials or case-control trials are needed.	More recent systematic reviews are included.
Satmis MC, van der Torn M (2018) Balloon dilatation of the Eustachian tube in adult patients with chronic dilatory tube dysfunction: a retrospective cohort study. European Archives of Oto-Rhino-Laryngology 275: 395-400	Case series n=42 Follow up=3 months	The ETDQ-7 score improved from 4.28 to 3.09 at 1 month and from 4.10 to 2.96 at 3-month follow up. The tympanic membrane and middle-ear condition showed improvement in 62%. Subjective satisfaction 1 and 3 months postoperatively was around 43 and 48%. A small number of minor (self-limiting) complications did occur.	Studies with more patients or longer follow up are included.
Schmitt D, Akkari M, Mura T et al. (2018) Medium-term assessment of Eustachian tube function after balloon dilation. European Annals of Oto-rhinolaryngology, Head & Neck Diseases 135: 105-10	Case series n=38 Follow up=mean 14 months	Improvement in clinical symptoms was assessed as 88%, 80% and 80% at respectively 2 months, 6 months, and over 1 year. Improved function on tubomanometry was observed in 81% of patients. The procedure was well tolerated, with a minor complications rate of only 4%.	Larger studies are included.
Shah RR, Thomas WW, Naples JG et al. (2018) Subcutaneous emphysema and pneumomediastinum after	Case report n=1	Case report of subcutaneous emphysema and pneumomediastinum after balloon dilation of the	Safety event is already reported.

eustachian tube balloon dilation. Otolaryngology - Head and Neck Surgery (United States) 159: 203-5		eustachian tube. Symptoms improved over 48 hours without intervention.	
Si Y, Chen YB, Chu YG et al. (2018) Effects of combination of balloon Eustachian tuboplasty with methylprednisolone irrigation on treatment of chronic otitis media with effusion in adults. American Journal of Otolaryngology 39: 670–5	Non-randomised comparative study n=200 Follow up=1 year	Methylprednisolone irrigation could help to recover mucosal function. Balloon dilation and tympanic paracentesis with methylprednisolone irrigation could be regarded as a good choice for chronic otitis media with effusion in adults, which has less recurrence rate and prompt recovery of eustachian tube function.	The indication was chronic otitis media with effusion, rather than eustachian tube dysfunction.
Silvola J, Kivekas I, Poe DS (2014) Balloon dilation of the cartilaginous portion of the Eustachian tube. Otolaryngology - head and neck surgery (United States) 151: 125-30	Case series n=41 Follow up=mean 2.5 years	80% (33/41) could do a Valsalva manoeuvre postoperatively. Subjective symptoms were not relieved for 10% (4/41) of patients.	Studies with more patients or longer follow up are included. Study is included in reviews by Huisman J, 2018 (study 4) and Wang TC, 2018 (study 5).
Singh T, Taneja V, Kulendra K et al. (2017) Balloon Eustachian tuboplasty treatment of longstanding Eustachian tube dysfunction. Journal of Laryngology & Otology 131: 614-9	Case series n=11 Follow up=6 months	Balloon-dilation Eustachian tuboplasty resulted in statistically significant improvements in 11 patients' subjective but not objective outcome measures.	Studies with more patients or longer follow up are included.
Song H-Y, Park HJ, Kang WS et al. (2019) Fluoroscopic balloon dilation using a flexible guide wire to treat obstructive eustachian tube dysfunction. Journal of Vascular and Interventional Radiology doi: 10.1016/j.jvir.2019.04.041	Case series n=31 Follow up=median 16 months	The Valsalva manoeuvre was successful in opening 78% (25/32) of eustachian tubes at 3 months after balloon dilation. During the follow up, failure of the Valsalva manoeuvre occurred in 16% (4/25) improved tubes, yielding a 2-year patency rate of 84%.	Studies with more patients or longer follow up are included.
Sudhoff HH, Mueller S (2018) Treatment of pharyngotympanic tube dysfunction. Auris, Nasus, Larynx 45: 207-14	Review	Eustachian tube dysfunction is a poorly defined condition. There are various medical and surgical interventions available including BET and laser or microdebrider tuboplasty. Short-term data provide favourable results. Current treatment options may be offered to selected patients.	Systematic reviews focused on balloon dilation are included.
Walliczek-Dworschak U, Schmierer L, Greene B et al. (2018) Analysis of	Case series n=26	Patients' baseline taste function was statistically significantly impaired. After	Small case series with short follow up.

chemosensory function in patients with chronic Eustachian tube dysfunction prior to and after balloon dilatation. Auris, Nasus, Larynx 45: 959-65	Follow up=mean 51 days	balloon dilation of the eustachian tube, the taste function remained stable. Olfactory function improved postoperatively compared to preoperative scores, but not to a clinically relevant extent.	
Wanscher JH, Svane-Knudsen V (2014) Promising results after balloon dilatation of the Eustachian tube for obstructive dysfunction. Danish Medical Journal 61: A4818	Case series n=34 Follow up=2 months	Most patients had a positive effect of the treatment. The results were comparable to those of other similar studies.	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).
Williams, B.; Taylor, B. A.; Clifton, N et al. (2016) Balloon dilation of the eustachian tube: A tympanometric outcomes analysis. Journal of Otolaryngology Head and Neck Surgery 45: 13	Case series n=18 Follow up=mean 7 months	Overall 36% of ears had improvement in tympanogram type, and 32% had normalisation of tympanogram postoperatively. The Jerger tympanogram type improved statistically significantly following the procedure (p=0.04). Patients also had statistically significant improvement in measured middle-ear pressure postoperatively (p=0.003).	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).
Xiong H, Liang M, Zhang Z et al. (2016) Efficacy of balloon dilation in the treatment of symptomatic Eustachian tube dysfunction: One year follow-up study. American Journal of Otolaryngology Head and Neck Medicine and Surgery 37: 99-102	Case series n=40 Follow up=12 months	The overall success rate for all patients was 98%. The procedure can provide both short- and long-term benefits to those with symptoms refractory to medical management.	Larger, more recent studies are included. Study is included in review by Huisman J, 2018 (study 4).
Yin G, Tan J, Li P (2019) Balloon dilation of Eustachian tube combined with tympanostomy tube insertion and middle-ear pressure equalization therapy for recurrent secretory otitis media. Journal of Otology 14: 101-5	Case series n=51 Follow up=12 months	Balloon dilation of Eustachian tube combined with tympanostomy and catheterisation resulted in significant improvement of subjective symptoms and objective evaluation of Eustachian tube functions in most patients with recurrent secretory otitis media, as indicated by the ETS and ETDQ-7 scores, demonstrating high levels of efficacy and patient satisfaction.	Studies with more patients or longer follow up are included.