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# Efficacy of intranasal corticosteroid sprays in relieving clinical signs of Eustachian tube dysfunction: a systematic review and meta-analysis of randomised, controlled trials

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**Review Article**

Tara J. Nibhanupudy takes responsibility for the integrity of the content of the paper

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## Abstract

**Objective.** Eustachian tube dysfunction is prevalent in both paediatric and adult populations. Current clinical guidelines recommend observation over topical intranasal corticosteroids for Eustachian tube dysfunction management, which remains controversial. This study aimed to systematically review randomised, controlled trials assessing topical intranasal corticosteroid efficacy in Eustachian tube dysfunction, and analyse effect through tympanometric normalisation.

**Methods.** PubMed, EMBASE, Web of Science and Cochrane Library databases were searched. All randomised, controlled trials assessing intranasal corticosteroids in adult or paediatric Eustachian tube dysfunction patients were included. A meta-analysis of proportions was used to evaluate tympanogram normalisation.

**Results.** Of 330 results, eight randomised, controlled trials met inclusion criteria and underwent qualitative data synthesis and risk-of-bias analysis. Meta-analysis of tympanometry data from four eligible trials ($n = 512$ ears) revealed no significant difference in tympanometric normalisation between intranasal corticosteroids and control (odds ratio 1.21, 95% confidence interval 0.65–2.24).

**Conclusion.** Study results do not strongly support intranasal corticosteroids for Eustachian tube dysfunction. Data were limited, emphasising the need for larger, higher quality, randomised, controlled trials.

## Introduction

Eustachian tube dysfunction refers to the failure of the Eustachian tube to adequately protect, ventilate, or drain secretions and pathogens away from the middle ear.[1,2] Insufficient drainage of the middle ear can result in otitis media with effusion (OME), defined as middle-ear fluid accumulation without signs or symptoms of acute infection.[3] An inability of the Eustachian tube to equilibrate pressures within the middle-ear space and the nasopharynx results in negative middle-ear pressure.[4–6] Signs of these common Eustachian tube dysfunction sequelae include middle-ear effusion, retraction or reduced mobility of the tympanic membrane, or a flat or left-shifted tympanogram.[2,6] Tympanometry is a highly sensitive (84–93 percent) tool for Eustachian tube dysfunction diagnosis.[7] Eustachian tube dysfunction is prevalent in both children and adults, particularly those of lower socioeconomic status.[8–11]

Reduction of oedema around the Eustachian tube opening through topical intranasal corticosteroids theoretically may improve the dysfunction.[11–17] Yet, conclusions from prior clinical trials of intranasal corticosteroids effects on Eustachian tube dysfunction have been conflicting, and it remains unclear whether patients without comorbid nasal symptoms would benefit from intranasal corticosteroids.[18,19] Current international guidelines for OME advise against pharmacological therapies as the risk-to-benefit ratio is uncertain, particularly in children.[3] Despite this, across specialties, intranasal corticosteroids remain one of the most prescribed treatments for Eustachian tube dysfunction patients, with or without additional nasal symptoms.[20]

Globally, management of Eustachian tube dysfunction continues to be controversial. To our knowledge, no systematic review and meta-analysis study has assessed randomised, controlled trials (RCTs) on the specific effects of intranasal corticosteroids in both paediatric and adult Eustachian tube dysfunction patients. The present study aims to (1) systematically review international literature for RCTs, evaluating the ability of intranasal corticosteroids to alleviate OME and negative middle-ear pressure in Eustachian tube dysfunction; and (2) conduct a meta-analysis of available data.

## Methods

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRIMSA') guidelines, a systematic review was undertaken for investigation of this topic. A protocol was produced and registered on PROSPERO (CRD42021264211).

### *Search strategy*

A standardised search query was created using the search items ("Eustachian Tube" or "Eustachian Tube Dysfunction") crossed with ("Flonase" or "Fluticasone" or ("Nasal steroid" AND "Administration, Intranasal")) within the following electronic databases: PubMed, EMBASE, Web of Science, and The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL)) (Appendix 1). Neither study design filters, nor date limitations were applied to the search. References of included studies were scanned to identify any additional relevant records.

### *Eligibility assessment*

Randomised, controlled trials assessing the effect of topical intranasal corticosteroid sprays on at least one of the stated primary outcomes in adult and children of any age clinically diagnosed with Eustachian tube dysfunction were included. As otitis media with effusion (OME) is a common complication of Eustachian tube dysfunction, clinical diagnoses of OME or middle-ear effusion were also accepted. No restrictions were set for control treatment. Studies that were non-RCTs, non-English, still unpublished, or that focused on the incorrect patient population (e.g. patulous Eustachian tube dysfunction, acute otitis media, rhinosinusitis) or incorrect intervention (e.g. orally administered corticosteroids) were excluded.

Initial pooled results underwent screening for duplicates and title or abstract eligibility. Eligible papers underwent a full text review to yield the final included references. Records were managed within the software Zotero, version 6.0.13 (Corporation for Digital Scholarship, Vienna, Virginia, USA). Screening and eligibility assessment were performed independently in a blinded, standardised manner through the website application Rayyan by 2 reviewers (TN, CT) using standardised eligibility forms (Appendix 2).[21] Disagreements between reviewers were resolved by consensus. Consultation of third author was planned if warranted but was not found to be necessary.

### *Outcome measures*

Primary outcomes included changes in middle-ear fluid and negative middle-ear pressure severity (assessed through tympanometry and/or otoscopy), as well as Eustachian tube dysfunction symptomatology. Additional outcomes of interest included pure tone audiometry, adverse events, ability to delay procedural treatment, cost-effectiveness, quality of life (QoL) and nasopharyngoscopy, although analysis of these outcomes was not a requirement for study inclusion.

### *Data extraction*

A slightly modified version of Cochrane's data collection form for RCTs was piloted and used to extract data on these outcomes (Appendix 2). One review author (TN) extracted data from included studies, and a second author (CT) checked extracted data for accuracy. Data from studies with multiple publications were planned to be extracted into one form and reported as a single study. The extraction form structure included collection of general information on the study, as well as data on study methods, participant characteristics, comparison and intervention characteristics, description of study outcomes, and summary of data and analysis (Table 1).

### *Quantitative data synthesis and statistical analysis*

A meta-analysis was planned for one or more of the outcomes of interest, conditional on the clinical and methodological heterogeneity of included studies.[22] Narrative synthesis was to be implemented if extracted data was found to be overall insufficient for rigorous quantitative analysis.

Data was available from four RCTs to conduct a meta-analysis of proportions using R (version 4.1.3). The outcome measure was tympanogram normalisation, defined as proportion of study group (by ear) recovering completely on tympanometry (i.e. from Type B/C at baseline to Type A immediately upon completion of the intervention schedule).

Tympanometry data from 512 ears with baseline Eustachian tube dysfunction were pooled. A random-effects model was implemented based on the computed $I^2$ value for included studies ($I^2 = 53.8$ per cent [0.0 per cent; 84.7 per cent], moderate statistical heterogeneity). Comparison of normalisation rates between study arms was expressed as an odds ratio with 95 percent confidence interval (CI), where odds ratio >1 favours intranasal corticosteroids treatment over control intervention. Subgroup analyses were planned to assess intranasal corticosteroids impact on Eustachian tube dysfunction by characteristics such as intranasal corticosteroids type and dosage schedule, patient age, and patient comorbidities, however this was limited by the lack of available data. Due to significant heterogeneity in the collection and reporting of data for the other outcomes across the included references, a

**Table 1.** Structure of data extraction forms. Tailored from Cochrane's data collection form for randomized controlled trials. ETD = Eustachian tube dysfunction; OME = otitis media with effusion; MEE = middle-ear effusion; INCS = intranasal corticosteroids

| | |
|---|---|
| **General information** | Study author contact details<br>• Location of study |
| **Study methods** | • Aim and design<br>• Unit of analysis (subject vs. ear)<br>• Other analysis characteristics |
| **Study participant characteristics** | • Study inclusion and exclusion criteria<br>• Sample size, Baseline characteristics<br>• Diagnostic criteria for ETD/OME/MEE |
| **Intervention characteristics** | • INCS/Control type<br>• Administration method/scheduling<br>• Compliance |
| **Description of study outcomes** | • Definition and thresholds<br>• Measurement<br>• Person measuring/reporting |
| **Data and analysis** | • Data for each time point<br>• Withdrawals, Exclusions<br>• Statistical methods used<br>• Kev conclusions of studv authors |

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quantitative analysis was not feasible for other primary or additional outcomes of interest.

### Qualitative data synthesis

Narrative synthesis was employed to report the tympanometry data from additional included studies not eligible for quantitative analysis, for which collected data contained high methodological and clinical heterogeneity. For qualitative synthesis, a broader measure of treatment impact, tympanogram improvement, was reported. This outcome was defined as proportion of study group (by subject) found to experience any post-intervention improvement on tympanogram – either partial resolution (i.e. from Type B at baseline to Type C post-intervention) or complete resolution (i.e. from either Type B or C at baseline to Type A post-intervention).

### Quality assessment

A standard critical appraisal tool, the Cochrane revised risk-of-bias form for randomised trials[23], was used to assess for outcome-specific risk of bias in the tympanometry results of all eligible studies (Appendix 3). Randomisation process, deviations from intended interventions, missing outcome data, measurement of outcome, and selection of reported results were individually assessed. Disagreements were planned to be resolved by consensus, although was not found to be necessary. Risk-of-bias assessment results were summarised using the robvis tool.[24]

## Results

### Description of included studies

#### Study characteristics

Initial pooled results ($n = 330$) underwent title/abstract screening, and full reports were sought for potentially eligible papers ($n = 21$). Fifteen reports underwent full text review, as detailed in Figure 1. Based on study characteristics, eight RCTs were eligible for data synthesis (Figure 2). Study publication dates ranged from 1982 to 2020, and trials ranged in size from 59 to 217 participants. The majority of studies were conducted internationally ($n = 6$), while two studies were carried out within the United States. Four of the eight eligible studies, performed between 1982 and 2011 and randomising 312 subjects, reported data with clinical and methodological homogeneity that allowed for pooling and subsequent meta-analysis (highlighted in Figure 2).

#### Patient characteristics

All studies included patients with clinically diagnosed manifestations of Eustachian tube dysfunction. Most studies evaluated only children ($n = 7$), with varying age restrictions, while one study evaluated both children and adults.[25] The mean age of included patients ranged between 3.8 years[26] and 41.7 years.[25] In two of the eight studies, all[27] or nearly all (83.3 per cent)[28] paediatric patients had an additional comorbidity of adenoidal hypertrophy.

#### Intervention and control characteristics

Intranasal corticosteroid sprays assessed were mometasone,[26–29] beclomethasone[30–32] and triamcinolone acetonide.[25] Duration of treatment ranged from 4 weeks to 24 weeks. In the majority of the included RCTs, intranasal corticosteroid intervention was assessed alone in comparison to placebo.[25,27,29,31]

However, two of the included studies instead assessed intranasal corticosteroids in comparison to no treatment (with[30] or without[26] underlying co-intervention administered to both intervention and comparison groups). In another included study, two control groups were assessed – one group provided with no treatment and one group provided with a placebo nasal spray.[32] For this study, data were available only for both control groups combined; therefore, comparison data were extracted for both control groups (no treatment and placebo) in conjunction.

### Quantitative analysis of results – tympanometric normalisation

Tympanometry data from four of the included trials were eligible for meta-analysis of odds ratios for post-intervention rate of complete tympanometric normalisation by ear (Figure 3).[25,30–32]

In 512 pooled ears, there was no significant difference in the overall proportion of patients that recovered from type B/C tympanogram at baseline to type A tympanogram post intervention (odds ratio 1.21, 95 per cent confidence interval 0.65–2.24) when comparing Eustachian tube dysfunction patients receiving intranasal corticosteroids to those receiving control treatment. Tympanometry data obtained from included studies were not adequate for sub-group analysis.

### Qualitative synthesis of results

#### Tympanometric improvement

Eight RCTs were determined eligible for analysis through the systematic review screening. A qualitative analysis was conducted in which tympanometry data from all eight studies ($n = 771$ subjects) were compiled regardless of heterogeneity in data measurement and reporting (Figure 4).[26–32] Only five of the eight studies reported a statistical comparison between intranasal corticosteroids and controls for post-intervention tympanometric data.[26,27,29,31] Of these five studies, only one reported a significant difference (comparison between intranasal corticosteroids and placebo saline spray, $p = 0.0002$).[27] Qualitatively, it seemed that neither studies with the oldest participants[25] nor those with the youngest participants[5] found intranasal corticosteroids to be more effective in treating Eustachian tube dysfunction, at least in terms of tympanometric improvement.

#### Adverse events

Of the eight studies, six discussed adverse events that emerged during the course of treatment, while two did not discuss this outcome.[26,30] There were overall minimal differences in adverse events between intranasal corticosteroids and control groups.

#### Qualitative synthesis of additional outcomes

A number of studies discussed changes in reported symptoms,[25,27,29,32] otoscopy[28,30,32] and pure tone audiometry.[27,29,31] Very few studies reported on QoL,[28,29] cost-effectiveness[29] and nasopharyngoscopy.[28] No study contained discussion of the ability of intranasal corticosteroids to postpone or reduce the need for surgical management (e.g. tympanostomy tube placement).

### Risk-of-bias assessment

Risk-of-bias assessment was performed for the outcome of tympanometry across all included studies, using five domains

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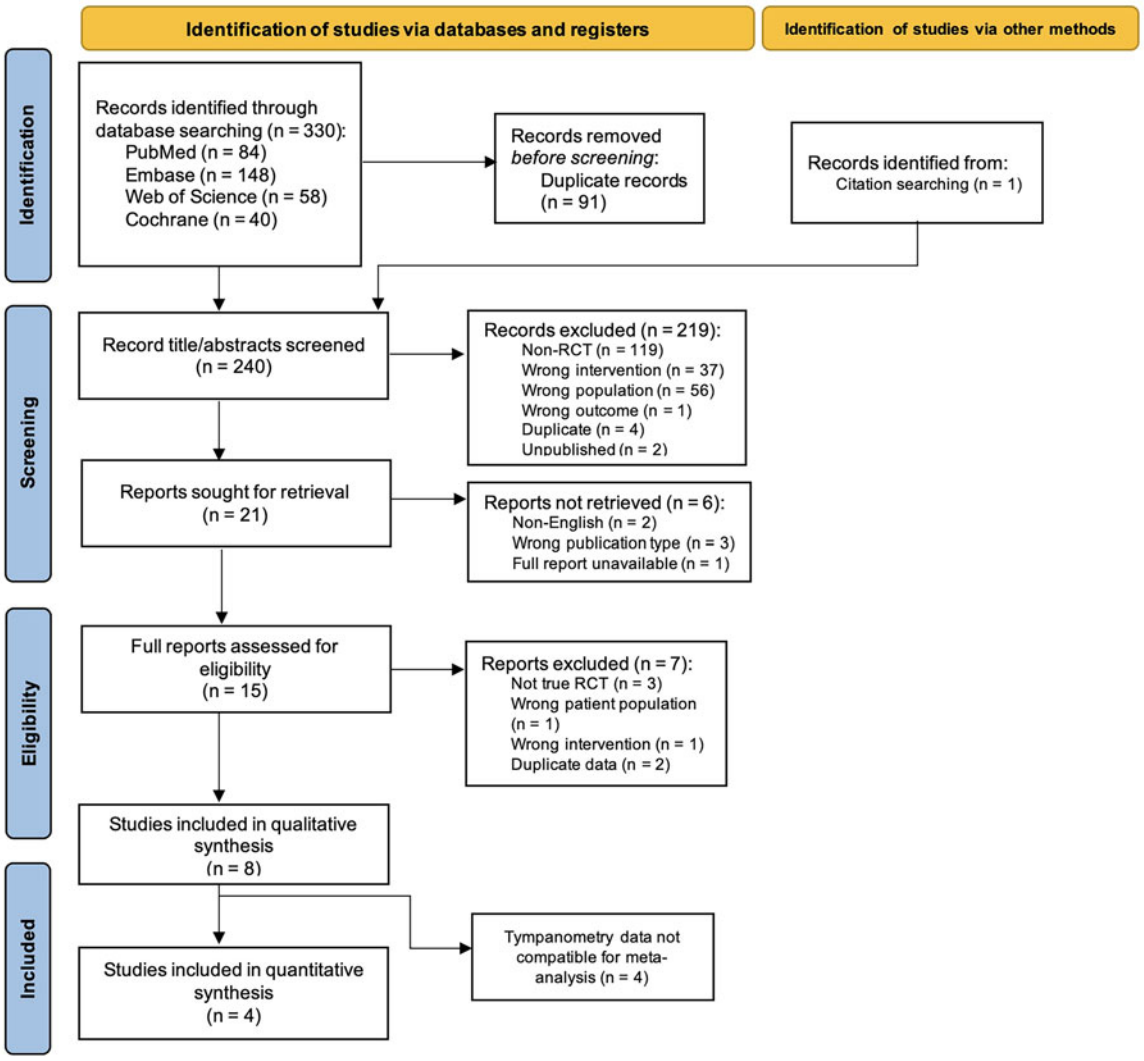


**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRIMSA') flow diagram used for identification of studies used; RCT = randomised, controlled trial.

**SUMMARY OF KEY STUDY CHARACTERISTICS**

| Study ID | Country | Participant Ages | Size | INCS type | Duration | Comparison | Outcomes Measured | Study Author Conclusion | RoB |
|---|---|---|---|---|---|---|---|---|---|
| Barati 2011 | Iran | Children, Age 1-10 | 92 | Beclomethasone* | 4 weeks | No treatment (Co-intervention: Antibiotic + Decongestant) | 1) Tympanogram normalization<br>2) Otoscopy<br>3) Reported symptoms (parent) | Effective | Some concerns |
| Bhargava 2014 | India | Children, Age 2-12 | 62 | Mometasone | 24 weeks | Placebo | 1) OME Resolution (Tympanometry, Otoscopy)<br>2) Reported symptoms<br>3) Audiometry | Effective | Low |
| Swain 2020 | India | Children, Age 5-10 | 96 | Mometasone | 12 weeks | Placebo | 1) OME Resolution (Tympanometry, Otoscopy)<br>2) Reported symptoms<br>3) Audiometry | Effective | Some concerns |
| Tracy 1998 | United States | Children, Age 3-11 | 59 | Beclomethasone* | 12 weeks | Placebo (Co-intervention: Antibiotic) | 1) Tympanogram normalisation<br>2) Otoscopy<br>3) Reported symptoms (parent) | Effective | Some concerns |
| Gluth 2011 | United States | Adults (≥18 years) Children (6-17 years) | 91 | Triamcinolone | 6 weeks | Placebo | 1) Tympanogram normalisation<br>2) Reported symptoms | Ineffective | Low |
| Lildholdt 1982 | Denmark | Children, Age 4-14 | 70 | Beclomethasone | 4 weeks | Placebo | 1) Tympanogram normalisation<br>2) Audiometry | Ineffective | High |
| Rahmati 2017 | Iran | Children, Age 2-6 | 84 | Mometasone | 4 weeks | No treatment | 1) Tympanogram normalisation | Ineffective | Some concerns |
| Williamson 2009 | United Kingdom | Children, Age 4-11 | 217 | Mometasone | 12 weeks | Placebo | 1) Tympanogram normalisation<br>2) Reported symptoms<br>3) Audiometry | Ineffective | Low |

**Figure 2.** Qualitative summary of included study characteristics, including assessed risk of bias (RoB) grading for each study trial. The shaded studies in the Study ID column indicate the four studies for which tympanometry data was pooled for meta-analysis (Barati 2011, Gluth 2011, Lildholdt 1982, Tracy 1998). *Indicates INCS treatment administered as adjunct to co-intervention. INCS = intranasal corticosteroids; RoB = risk of bias; Barati 2011 = Barati et al., 2011;[30] Bhargava 2014 = Bhargava and Chakravarti, 2014;[28] Swain 2020 = Swain et al., 2020;[27] Tracy 1998 = Tracy et al., 1998;[32] Gluth 2011 = Gluth et al., 2011;[25] Lildholdt 1982 = Lildholdt and Kortholm, 1982;[31] Rahmati 2017 = Rahmati et al., 2017;[26] Williamson 2009 = Williamson et al., 2009.[29]

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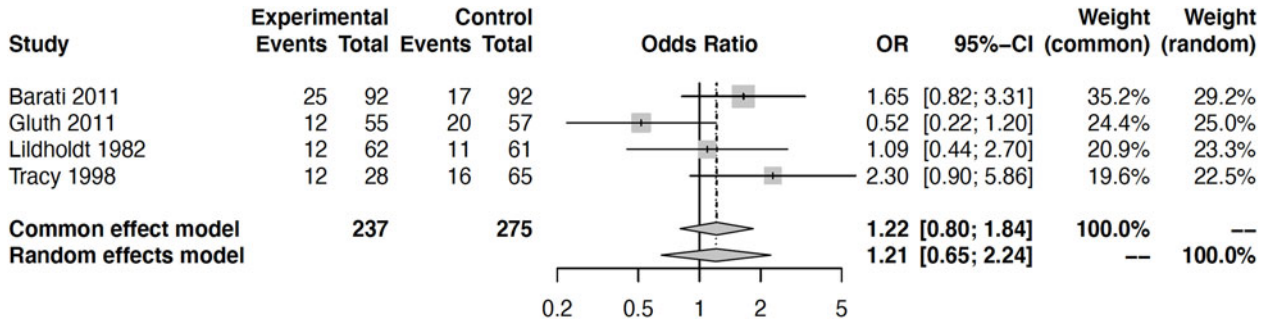


**Figure 3.** Meta-analysis of tympanometry data from four of the included trials; Pooled analysis of odds ratios (ORs) for proportion of study group participants with complete tympanogram normalization after course of treatment with INCS vs. control, presented with 95 percent confidence intervals. Tympanometric normalization, the outcome measure for ETD resolution, was defined as change in one ear from Type B/C (pathologic) to Type A (healthy) on tympanogram. Forest plot represents aggregated results of four included studies from the systematic review with similarly measured and reported tympanometric data. OR = odds ratio; 95%–CI = 95 per cent confidence interval. Barati 2011 = Barati et al., 2011;[30] Gluth 2011 = Gluth et al., 2011;[25] Lildholdt 1982 = Lildholdt and Kortholm, 1982;[31] Tracy 1998 = Tracy et al., 1998.[32]

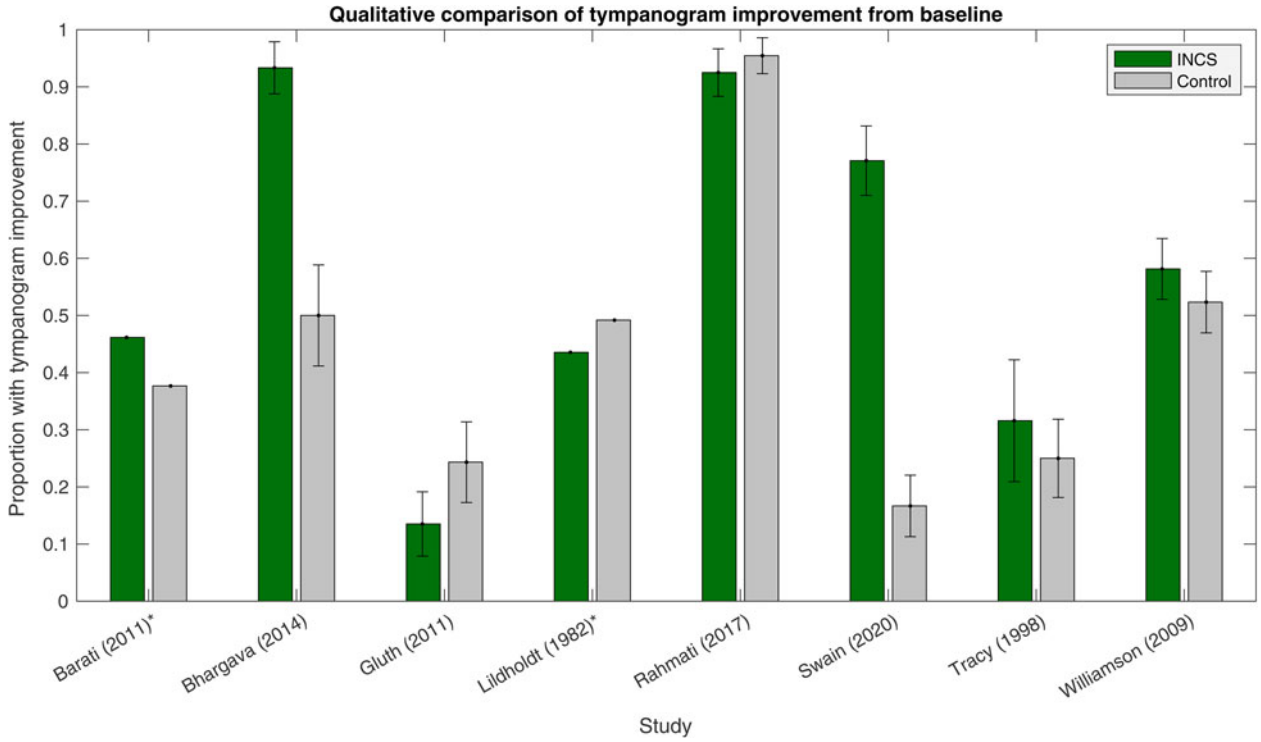


**Figure 4.** Comparing proportion of study group participants with any tympanogram improvement (by subject) after course of treatment. Improvement of tympanogram was used as the outcome measure for a qualitative analysis of ETD resolution, and included both partial resolution (change over the course of the intervention from tympanogram Type B to C) and complete resolution (change from tympanogram Type B to A or from Type C to A). Figure represents aggregated results of all eight studies deemed eligible for inclusion through systematic review. Error bars demonstrate 1 standard error (±68% CI around sample group proportion). *Marks studies collecting data with 'ears' as study unit (not independent points, standard error could not be calculated for this study data). INCS = intranasal corticosteroids; Barati (2011) = Barati et al., 2011;[30] Bhargava (2014) = Bhargava and Chakravarti, 2014;[28] Gluth (2011) = Gluth et al., 2011;[25] Lildholdt (1982) = Lildholdt and Kortholm, 1982;[31] Rahmati (2017) = Rahmati et al., 2017;[26] Swain (2020) = Swain et al., 2020;[27] Tracy (1998) = Tracy et al., 1998;[32] Williamson (2009) = Williamson et al., 2009.[29]

(Figure 5). Three studies were assessed as having a low risk of bias.[25,28,29] Five of the trials were found to have some concerns in the assignment of intervention (Domain 2), either due to a lack of specification about analysis on an intent-to-treat basis, or due to lack of clarity on the awareness of participants and outcome assessors regarding intervention allocation.[26,27,30–32] Of these five trials, one was found to be at high risk of bias due to missing outcome data beyond that accounted for by loss to follow-up[31] (Domain 3).

The remaining four trials were not found to have high-risk characteristics. However, due to the aforementioned concern, as well as additional concerns about the randomisation process and data reporting (Domains 1 and 5), these were judged as "some concerns" for bias.[26,27,30,32] Two of these four trials did not compare intranasal corticosteroids to placebos, and instead conducted a comparison to no treatment.[26,30] This may be of concern, as intranasal corticosteroids must be administered as a spray intranasally, and lack of treatment was likely an indicator to study participants and outcome assessors as to how the intervention was allocated. This poor allocation concealment may have compromised the benefits of randomisation for these trials, and potentially lowered reliability of each study's conclusions.

## Discussion

The aim of this study was to systematically review randomised, controlled trials evaluating the ability of intranasal

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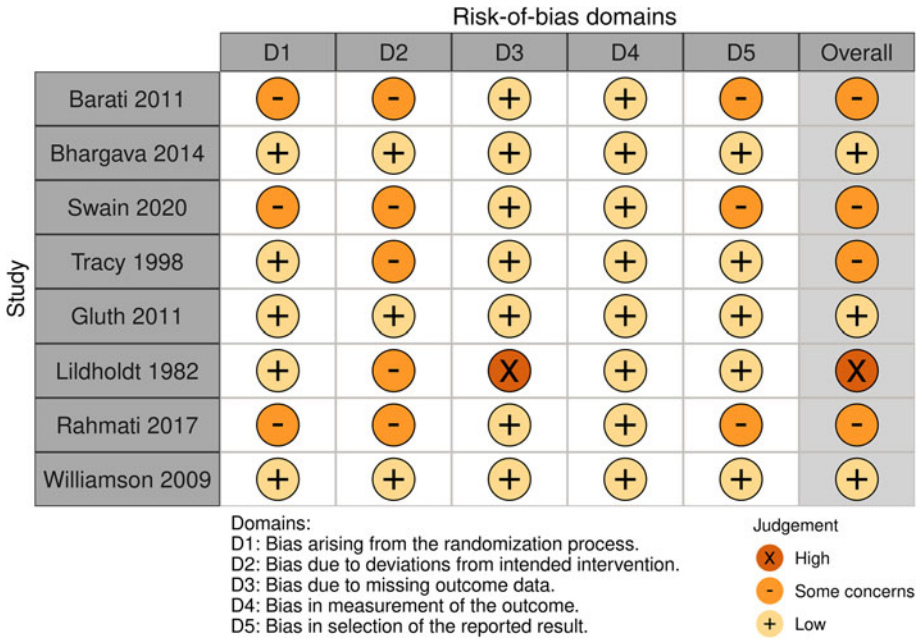


**Figure 5.** Risk of Bias assessment of included studies, performed for the outcome of tympanometry using a revised Cochrane risk of bias tool for randomized trials (RoB 2). Judgement was made on five domains; three studies were assessed as low risk of bias[25,28,29] four studies as generating some concerns[26,27,30,32], and one study as high risk of bias.[31] Barati 2011 = Barati et al., 2011;[30] Bhargava 2014 = Bhargava and Chakravarti, 2014;[28] Swain 2020 = Swain et al., 2020;[27] Tracy 1998 = Tracy et al., 1998;[32] Gluth 2011 = Gluth et al., 2011;[25] Lildholdt 1982 = Lildholdt and Kortholm, 1982;[31] Rahmati 2017 = Rahmati et al., 2017;[26] Williamson 2009 = Williamson et al., 2009.[29]

corticosteroids to alleviate clinical signs (OME, negative middle-ear pressure) in patients with Eustachian tube dysfunction and conduct a meta-analysis of available data. Study results do not provide supportive evidence for the use of intranasal corticosteroids to reverse sequelae of Eustachian tube dysfunction in children and adults. On the basis of complete tympanometric normalisation, neither intranasal corticosteroids nor control interventions were favoured to a statistically significant degree when pooling tympanometric data from Eustachian tube dysfunction patients in four RCTs.[25,30–32]

Corticosteroids also failed to demonstrate benefit for treatment of Eustachian tube dysfunction sequelae in previous systematic reviews and meta-analyses.[1,33,34] However, two of these studies focused on treatment of only adult Eustachian tube dysfunction patients (≥ 18 years old;[1] ≥ 16 years old[33]), and assessed a wide range of medical management types, with very little data compiled specifically regarding intranasal corticosteroids efficacy alone. The third of these previous studies assessed the use of steroids in children (≤ 12 years old) diagnosed with OME, however the majority of outcome data characterised oral steroid treatment rather than intranasal corticosteroids.[34]

Based on these data, current clinical guidelines have recommended against medical management for Eustachian tube dysfunction. Continued observation is recommended instead, with tympanostomy tube placement for at-risk patients (unilateral or bilateral OME persisting for ≥ 3 months and/or type B tympanogram).[3]

Generally, conservative medical management reduces both risk and cost relative to procedural treatments. However, previous data have shown that intranasal corticosteroids are one of two medical management strategies with the highest adult Eustachian tube dysfunction-associated direct costs.[20] All studies except one[26] demonstrated less than ideal rates of spontaneous resolution in the control group (16.7–52.3 per cent), despite evaluation over long periods of time (up to 24 weeks).[28] In paediatric patients, Eustachian tube dysfunction persistence without treatment can interfere with behavioural development and impairments in learning, language and speech.[3,9,35] Given that intranasal corticosteroids are not definitively effective, an investigation of alternative interventions is warranted.

Compared to intranasal corticosteroids, a one-time tympanostomy tube placement may be more effective for Eustachian tube dysfunction, as it requires no daily action and is more resistant to variability in compliance. For many patients, tympanostomy tube placement may only require a brief outpatient procedure. Notably, one of the senior authors performs myringotomy as an anecdotal predictor of response to tympanostomy. Additional interventions such as Eustachian tube insufflation and Eustachian tube balloon dilatation may also be effective, however more conclusive data are needed on these options.

Of note, this study primarily focused on studies of patients without comorbid nasal symptoms. Patients experiencing nasal symptoms presumably would benefit from use of intranasal corticosteroids to treat their comorbid nasal condition, but the decision to start intranasal corticosteroids is less clear for patients without comorbid symptoms. Therefore, while there may be an association with nasal comorbidities and Eustachian tube dysfunction, a strength of this study is that it may better address patients who experience Eustachian tube dysfunction without comorbid nasal symptoms.

## Further discussion

### *Intranasal corticosteroids may be effective in paediatric Eustachian tube dysfunction with a primarily adenoidal pathogenesis*

In two of the four studies that reported intranasal corticosteroids to be an effective treatment, a significant proportion (all[27] or nearly all (83.3 per cent)[28]) of the paediatric patients had the additional comorbidity of adenoidal hypertrophy. While neither study was entered in the meta-analysis, the high rate of comorbid adenoid hypertrophy found in these studies may suggest a relationship between paediatric Eustachian tube dysfunction and adenoid hypertrophy. Adenoidal hypertrophy is the most common entity causing Eustachian tube obstruction in children, and inflammation of the adenoid pads is a theorised aetiology for Eustachian tube dysfunction.

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In children with nasal pathology, such as inflamed or enlarged adenoids, intranasal corticosteroid efficacy may be more related to reductions in adenoidal inflammation, which may improve Eustachian tube function.

### *Age does not seem to play a role in intranasal corticosteroid efficacy*

The mean age of included patients ranged between 3.8 years[26] and 41.7 years.[25] This includes paediatric patients on both sides of the threshold (around 7 years of age) for morphological maturity of the Eustachian tube, as well as adults.[36] Qualitatively, in terms of tympanometric improvement, it seemed that neither studies with the oldest participants[25] nor those with the youngest participants[26] found intranasal corticosteroids to be more effective in treating Eustachian tube dysfunction. Of note, RCTs assessing the effect of intranasal corticosteroids in Eustachian tube dysfunction in adults are scarce. Only one study including the adult population was found for inclusion in the systematic review, identifying a clear deficit in current clinical evidence around this problem.

### *Limitations*

Data regarding differences in adherence to the nasal spray regimen between placebo and intervention groups were only available for two of the eight included studies.[29,32] Intranasal corticosteroids are most effective when used consistently. Studies that reported on adherence found no significant difference between treatment groups. However, for other studies it is unknown how consistently the administration schedule was followed.

Additionally, it is unspecified how included Eustachian tube dysfunction patient diagnoses were distributed between acute (signs/symptoms < 3 months) versus chronic (signs/symptoms ≥ 3 months) for all included studies except one.[32] While management is similar between acute and chronic Eustachian tube dysfunction, patients with acute symptoms may have been more likely to self-resolve during treatment in both placebo and intervention groups.[2] The impact of this limitation was likely small in the context of this study, however may be important to keep in mind for future studies in this topic.

- Eustachian tube dysfunction is multifactorial and leads to insufficient drainage and pressure regulation of the middle-ear cavity, which can significantly affect quality of life in adult and paediatric populations
- Topical administration of anti-inflammatory corticosteroids is theorised to improve Eustachian tube dysfunction, however conclusions from prior clinical trials on the subject have been conflicting
- Current international guidelines advise against intranasal corticosteroids for Eustachian tube dysfunction and its common sequelae, yet many providers continue to prescribe intranasal corticosteroids for this condition
- To our knowledge, no systematic review and meta-analysis study has assessed randomised, controlled trials on the specific effects of intranasal corticosteroids in both paediatric and adult Eustachian tube dysfunction patients
- Current evidence on this topic is of mediocre quality and does not support the use of intranasal corticosteroids in Eustachian tube dysfunction

Overall, available data obtained through systematic review was small in quantity, extremely heterogenous, and on average mediocre in quality. This precluded any planned quantitative subgroup analysis and lessens the predictive power and generalisability of our findings. Trends in efficacy by study size, participant age distribution, intranasal corticosteroids type, and/or treatment duration were only able to be assessed qualitatively. Existing systematic review and meta-analyses, in conjunction with the current study, provide evidence that a significant gap remains in the literature. Larger, higher-quality RCTs are needed with thorough subgroup data collection to more rigorously address this still unresolved contention in Eustachian tube dysfunction medical management.

## Conclusions

Study results do not provide supportive evidence for the use of intranasal corticosteroids in Eustachian tube dysfunction. Neither intranasal corticosteroids nor control interventions were favoured to a statistically significant degree when pooling tympanometric normalisation rates from Eustachian tube dysfunction patients in four RCTs.[25,30–32] As study results do not provide supportive evidence for the use of intranasal corticosteroids in Eustachian tube dysfunction, current clinical recommendations of avoiding intranasal corticosteroids for treatment of Eustachian tube dysfunction sequela remain acceptable, and further investigation of alternative interventions is warranted.

The precise mechanism of action of intranasal corticosteroids on Eustachian tube dysfunction remains unclear. Larger, higher-quality randomised, controlled trials are needed to more rigorously identify potential variations in intranasal corticosteroids efficacy among Eustachian tube dysfunction patient subgroups. Authoritative clinical data is particularly lacking in the adult Eustachian tube dysfunction patient population as well as in comparing Eustachian tube dysfunction patients with comorbid nasal conditions (e.g., allergic and non-allergic rhinitis, inflammation of the adenoids) to those with alternative Eustachian tube dysfunction aetiologies.

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