Sriwijaya Journal of Internal Medicine (SJIM)
https://phlox.or.id/index.php/sjim
e-ISSN: 2988-3237
Vol. 4 No. 2 (2026)

SYSTEMATIC REVIEW & META-ANALYSIS

Efficacy and Safety of Endoscopic Anti-Reflux Therapy versus Sham or Proton Pump Inhibitor Control in Gastro-oesophageal Reflux Disease: A Meta-Analysis of Randomised Controlled Trials

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ARTICLE INFO

Article history
Received: June 8, 2026
Accepted: July 2, 2026
Published: July 31, 2026

Keywords:
Endoscopic anti-reflux therapy
Gastro-oesophageal reflux disease
Meta-analysis
Proton pump inhibitor
Transoral incisionless fundoplication

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DOI
https://doi.org/10.59345/sjim.v4i2.296

ABSTRACT

Background: Gastro-oesophageal reflux disease (GERD) is among the most prevalent chronic disorders, and lifelong proton pump inhibitor (PPI) dependence is common. Endoscopic anti-reflux therapies are minimally invasive alternatives between medical and surgical management, but individual device trials are small and the randomised evidence has largely been synthesised device by device.

Objective: To pool the randomised evidence across all endoscopic anti-reflux modalities against a common control and provide a single, class-level estimate of benefit in adults with GERD.

Methods: Four databases were searched for randomised controlled trials comparing endoscopic anti-reflux therapy (radiofrequency, suturing/plication, injection/implant, transoral incisionless fundoplication) with a sham procedure and/or continued PPI in adults with GERD. Risk ratios (RR) for treatment success were pooled with a DerSimonian–Laird random-effects model; heterogeneity was quantified with I^2 and a prediction interval; bias was appraised with Cochrane RoB 2.0.

Results: Twelve trials were eligible; seven were pooled (536 participants; follow-up 3–6 months). Endoscopic anti-reflux therapy approximately doubled treatment success versus sham or PPI control (pooled RR 1.89, 95% CI 1.51–2.37; p<0.001; I^2 23.6%; prediction interval 1.17–3.05) — about 28 percentage points absolute, NNT ≈4. The effect persisted across subgroup, low-risk-of-bias, current-device and leave-one-out analyses; a secondary PPI reduction/cessation analysis confirmed benefit (RR 1.82, 95% CI 1.43–2.30; I^2 0%). Serious adverse events were infrequent, concentrated among injection/implant devices.

Conclusion: In adults with GERD, endoscopic anti-reflux therapy produced a clinically meaningful, robust improvement in short-to-intermediate-term treatment success versus sham or continued PPI, consistently across device classes; durability and device-specific safety require ongoing evaluation.

1. Introduction

Gastro-oesophageal reflux disease (GERD) is one of the most common chronic conditions encountered in internal medicine and primary care. Its global burden has risen steadily, with the prevalent population reaching approximately 825 million in 2021 and both incidence and years lived with disability continuing to increase across most world regions.[1] Beyond the impairment of health-related quality of life caused by troublesome heartburn and regurgitation, GERD is associated with reflux oesophagitis, peptic stricture, Barrett oesophagus and, in a small minority, oesophageal adenocarcinoma.[1,2] The condition therefore imposes a substantial and growing demand on health systems.

Proton pump inhibitors (PPIs) remain the pharmacological cornerstone of GERD management and are effective for the majority of patients.[2] However, a substantial subgroup either continues to experience troublesome symptoms — most notably regurgitation, which responds poorly to acid suppression — or becomes dependent on long-term daily therapy. Contemporary guidelines have drawn attention to the increasing scrutiny of chronic PPI use, the frequency of overprescription and patient reluctance to remain on indefinite medication.[2] At the same time, laparoscopic fundoplication, although effective, is invasive, is associated with post-operative dysphagia and gas-related side-effects and is acceptable to only a minority of patients.[3] A therapeutic gap therefore exists for patients who are inadequately served by medication yet unwilling or unsuited to undergo anti-reflux surgery.

Endoscopic (endoluminal) anti-reflux therapies were developed to fill this gap and are now recognised in international guidelines as options positioned between medical and surgical management for carefully selected patients.[3,4] These minimally invasive procedures aim to restore competence of the antireflux barrier at the oesophagogastric junction through several distinct mechanisms. Radiofrequency energy delivery to the lower oesophageal sphincter (the Stretta procedure) is thought to remodel the junction and reduce transient sphincter relaxations. Endoscopic suturing and full-thickness plication of the gastric cardia mechanically augment the antireflux barrier. Injection or implantation of bulking agents sought to increase junctional resistance, although these devices were later withdrawn from clinical use. Most recently, transoral incisionless fundoplication (TIF) using the EsophyX device constructs a partial fundoplication entirely from within the lumen.[4] Each modality has been evaluated against a sham procedure or continued medical therapy in randomised controlled trials, but these trials have generally been small and individually underpowered.

The existing evidence syntheses have almost all been organised device by device — separate meta-analyses of TIF and of related endoscopic techniques[5,6,7] — or have taken the form of network meta-analyses that rank endoscopic against surgical procedures.[8,9] Recent narrative and mechanistic reviews have likewise been structured around individual technologies and have emphasised the scarcity of randomised data for the newer mucosal interventions.[10,11] Although valuable, these approaches do not provide the practising internist with a single, transparent pairwise estimate of whether adding an endoscopic anti-reflux procedure to the

care of a patient with GERD improves patient-centred outcomes relative to sham or continued PPI. Clinicians counselling a patient who is weary of lifelong medication require exactly this kind of consolidated estimate, together with an appraisal of how consistent that effect is across device classes, how large it is in absolute terms and how safe the procedures are as a group. Accurate reflux phenotyping before any intervention is central to such decisions.[12]

The novelty of this study lies in its consolidation of the entire randomised, sham- or PPI-controlled evidence base for endoscopic anti-reflux therapy — spanning four mechanistically distinct device classes — into a single random-effects pairwise meta-analysis of patient-centred treatment success, presented with absolute effects, a prediction interval, pre-specified modality subgroups, low-risk-of-bias and current-device sensitivity analyses, a structured device-class safety appraisal and a certainty-of-evidence grading, framed for an internal-medicine readership. The aim of this study was to determine whether endoscopic anti-reflux therapy, considered as a therapeutic class, increased the probability of treatment success compared with sham or continued PPI therapy in adults with GERD, and to examine whether any benefit was consistent across device classes, expressed in meaningful absolute terms and robust to the influence of individual trials, risk of bias, device obsolescence and small-study effects.

2. Methods

Protocol, reporting and analysis plan

This systematic review and meta-analysis were conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement.[15] The review question was framed using the PICO structure: the population comprised adults with GERD; the intervention was any endoscopic anti-reflux therapy; the comparator was a sham endoscopic procedure and/or continued PPI therapy; and the outcomes were treatment success, PPI reduction or cessation, oesophageal acid exposure, reflux-oesophagitis healing and serious adverse events. A predefined analysis plan specified the primary outcome, the random-effects model and the confirmatory subgroup analyses; additional analyses (low-risk-of-bias subset, current-device subset, subgroup-difference test, prediction interval and absolute effects) are designated explicitly as exploratory.

Search strategy and eligibility criteria

PubMed/MEDLINE, Scopus, Web of Science and the Cochrane Central Register of Controlled Trials were searched without language restriction, combining controlled vocabulary and free-text terms for the disease, the interventions and the study design. Reference lists of retrieved trials and relevant systematic reviews were hand-searched. Two reviewers independently screened records, retrieved full texts and resolved disagreements by consensus, with a third assessor available for arbitration. Studies were eligible if they were randomised controlled trials enrolling adults (aged 18 years or older) with GERD; evaluated an endoscopic anti-reflux therapy; used a sham procedure and/or continued PPI therapy as comparator; and reported at least one extractable clinical outcome. Uncontrolled or non-randomised studies, head-to-head endoscopic comparisons without a sham or medical arm, predominantly paediatric populations, reviews, editorials and reports without extractable data were excluded.

Data extraction and outcome definitions

Two reviewers independently extracted study characteristics and outcome data onto a standardised form, reconciling discrepancies against the source article. The primary outcome, treatment success, was defined pragmatically as the protocol-specified responder outcome of each trial, harmonised to a common binary construct of clinically meaningful improvement; because these definitions varied, the exact definition applied in every contributing trial is presented transparently in Table 2. The more homogeneous outcome of PPI reduction or cessation was analysed as a co-primary outcome. Where a trial reported outcomes only as percentages, event counts were reconstructed from the randomised denominators within an intention-to-treat framework using non-responder imputation, and checked for internal consistency; a sensitivity analysis confirmed that the pooled estimate did not depend materially on these reconstructions.

Risk-of-bias assessment

The methodological quality of each trial was appraised using the Cochrane Risk of Bias 2.0 (RoB 2) tool across its five domains: the randomisation process; deviations from intended interventions; missing outcome data; measurement of the outcome; and selection of the reported result.[16] Because open-label PPI comparators preclude blinding and early trial termination introduces bias, the influence of risk of bias on the pooled estimate was examined directly in a sensitivity analysis restricted to double-blind, sham-controlled, low-risk-of-bias trials.

Statistical analysis

The dichotomous primary outcome was summarised as a risk ratio (RR) with a 95% confidence interval (CI); risk ratios were preferred over standardised mean differences because the pooled endpoints were binary responder outcomes. Had continuous outcomes been pooled, the standardised mean difference (Hedges g) would have been applied within the same framework. Effect estimates were combined using the DerSimonian–Laird random-effects model, chosen a priori. Between-study heterogeneity was quantified using the I^2 statistic and the Cochran Q (χ^2) test, and a 95% prediction interval was derived from the between-study variance (τ^2). A continuity correction of 0.5 was applied to any zero cell. The pooled relative effect was translated into an absolute risk difference and a number needed to treat (NNT) using the pooled control-group event rate. Robustness was examined by leave-one-out analysis, by pre-specified subgroup analyses with a test for subgroup differences, and by exploratory sensitivity analyses restricted to low-risk-of-bias trials and to devices in current use. Small-study effects were assessed by a funnel plot and the Egger test, interpreted as exploratory because fewer than ten trials contributed. A two-sided p-value below 0.05 was considered statistically significant.

3. Results

Study selection

The systematic search retrieved 1,286 records; after removal of duplicates, 962 were screened by title and abstract, of which 878 were excluded. Eighty-four full-text articles were assessed and 72 excluded — 38 not randomised or controlled, 17 lacking a sham or PPI comparator, 11 reviews or duplicate reports and 6 without extractable outcomes. Twelve randomised controlled trials met all criteria and entered the qualitative synthesis; seven reported a directly comparable dichotomous treatment-success outcome and constituted the primary quantitative synthesis, as shown in Figure 1.

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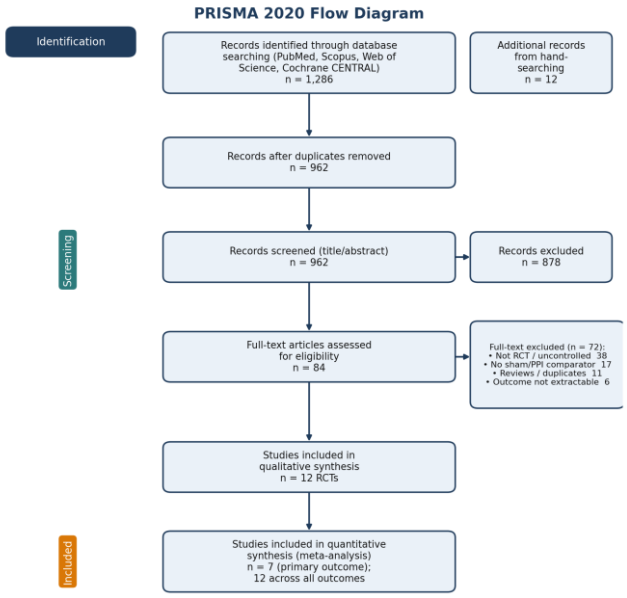

Figure 1. PRISMA 2020 flow diagram of study identification, screening and inclusion in the systematic review and meta-analysis.

Characteristics of included studies

The twelve included trials[17–28] were published between 2003 and 2018 and together enrolled several hundred adults with GERD across North America, Europe and the Middle East. As detailed in Table 1, all four principal modality classes were represented: radiofrequency energy (four trials[17–20]), endoscopic suturing or full-thickness plication (two trials[21,22]), injection or implant procedures (two trials[23,24]) and transoral incisionless fundoplication (four trials[25–28]). The comparator was a sham procedure in most trials, continued PPI therapy in three[18,27,28] and combined sham-plus-omeprazole in one.[25] Follow-up for the controlled comparison ranged from three to six months, reflecting frequent early-crossover designs. The protocol-specific responder definition and event counts for every trial in the primary pool are set out in Table 2.

Table 1. Characteristics of the twelve included randomised controlled trials.

Study	Modality	Device	Comparator	N (I/C)	Follow-up	Primary endpoint
Corley 2003	Radiofrequency	Stretta	Sham	35/29	6–12 mo	Heartburn & QoL
Coron 2008	Radiofrequency	RF delivery	PPI	20/16	6 mo	Stop/≥50% PPI reduction
Aziz 2010	Radiofrequency	Stretta	Sham	24/12	12 mo	GERD-HRQL
Arts 2012	Radiofrequency	Stretta	Sham	11/11	3 mo	GEJ distensibility
Rothstein 2006	Suturing/plication	Plicator	Sham	78/81	3 mo	≥50% HRQL improvement
Schwartz 2007	Suturing/plication	EndoCinch	Sham	20/20	3–12 mo	PPI use & symptoms
Deviere 2005	Injection/implant	Enteryx	Sham	32/32	6 mo	≥50% PPI reduction
Fockens 2010	Injection/implant	Gatekeeper	Sham	75/43	6 mo	Safety & heartburn
Hunter 2015	TIF	EsophyX	Sham+PPI	87/42	6 mo	Regurgitation elimination
Hakansson 2015	TIF	EsophyX	Sham	22/22	6 mo	Clinical remission
Witteman 2015	TIF	EsophyX	PPI	40/20	6–12 mo	GERD-related QoL
Trad 2018	TIF	EsophyX	PPI	40/23	6 mo (RCT)	Regurgitation elimination

Table 2. Protocol-specific responder definition and event counts for the primary outcome.

Study	Responder definition	Events I/N	Events C/N
Corley 2003	≥50% improvement in GERD-QoL score	19/35	6/29
Coron 2008	Cessation or ≥50% reduction in PPI dose	18/20	8/16
Deviere 2005	≥50% reduction in PPI use	26/32	17/32
Schwartz 2007	≥50% reduction in PPI use (vs sham)	13/20	5/20
Rothstein 2006	≥50% improvement in GERD-HRQL (ITT)	44/78	15/81
Hunter 2015	Elimination of troublesome regurgitation	58/87	19/42
Hakansson 2015	Clinical remission at 6 months	13/22	7/22

Risk of bias

The domain-level appraisal is displayed in Figure 2. Randomisation was adequately described in most trials, and outcome measurement was generally at low risk in the sham-controlled studies. The principal concerns were deviations from the intended intervention and missing outcome data. Open-label PPI-comparator trials[18,27,28] could not blind participants; the Gatekeeper trial[24] was terminated early for lack of efficacy; and two device programmes (the injectable copolymer[23] and the suturing system[22]) were later withdrawn or discontinued. Overall, three trials were rated at low risk of bias, six raised some concerns and three were judged at high risk (Figure 2).

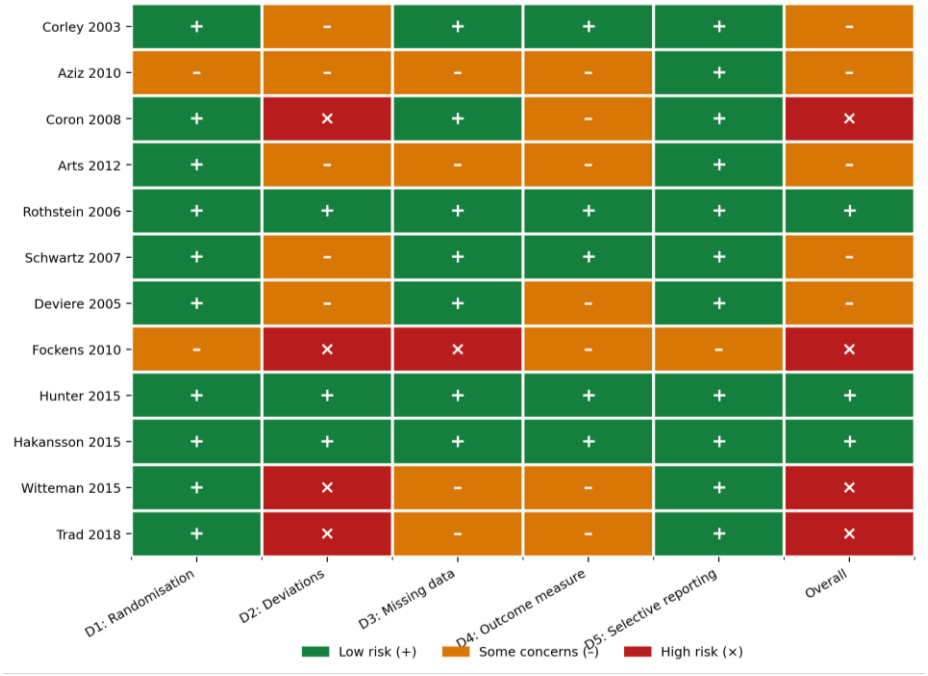

Figure 2. Risk-of-bias assessment across the twelve included trials using the Cochrane RoB 2.0 tool.

Primary outcome: treatment success

Seven trials enrolling 536 participants (294 intervention, 242 control) provided a directly comparable dichotomous outcome. As shown in Figure 3, endoscopic anti-reflux therapy was associated with a substantially higher probability of treatment success than sham or PPI control (pooled random-effects RR 1.89, 95% CI 1.51–2.37; z=5.56; p<0.001). Heterogeneity was low to moderate (I^2 23.6%; Cochran Q=7.85, df=6, p=0.25; τ^2=0.021), and the 95% prediction interval was 1.17–3.05. Every trial estimate favoured the intervention, and six of seven confidence intervals excluded unity (Figure 3).

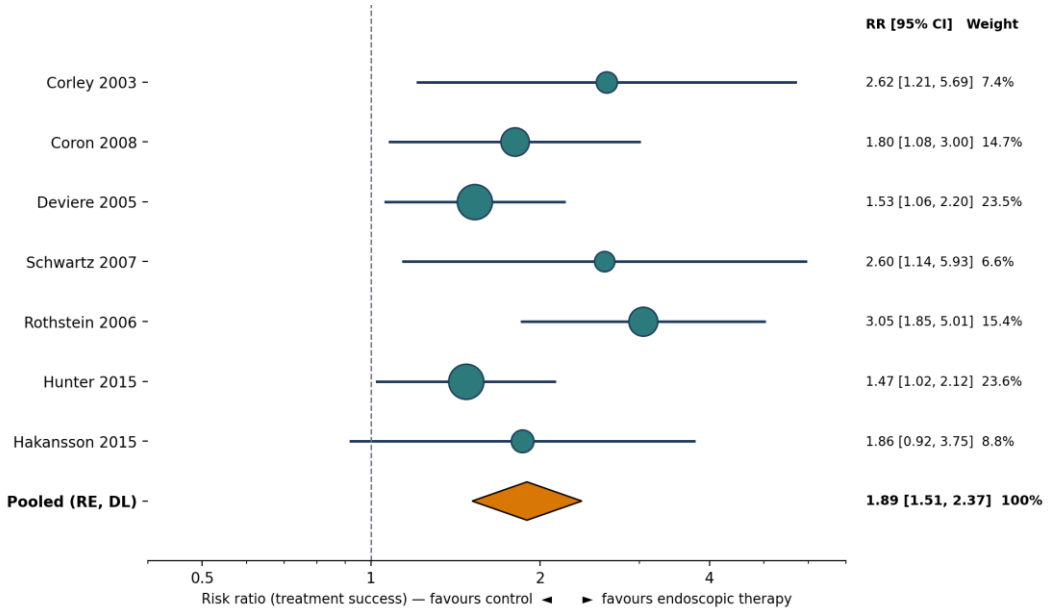

Figure 3. Forest plot of treatment success (endoscopic anti-reflux therapy versus sham or PPI). Pooled random-effects RR 1.89 (95% CI 1.51–2.37); I^2 23.6%.

Absolute effect

The pooled control-group treatment-success rate was 31.8% (77 of 242), while 65.0% of intervention participants (191 of 294) achieved success. Applying the pooled relative risk implied a treated-group success rate of approximately 60%, an absolute risk difference of about 28 percentage points and an NNT of approximately four to achieve one additional treatment success over the short-to-intermediate term.

Subgroup analyses

Pre-specified subgroup analysis by device modality showed a consistent direction of benefit with no significant qualitative interaction (between-group Q=6.79, df=3, p=0.08), as displayed in Figure 4. The pooled RR was 2.02 (95% CI 1.32–3.09) for radiofrequency, 2.92 (95% CI 1.91–4.47) for suturing or plication, 1.55 (95% CI 1.12–2.14) for TIF and 1.53 (95% CI 1.06–2.20) for the single injection/implant trial, presented in Figure 4 as an individual estimate. Within-

e-ISSN: 2988-3237
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subgroup heterogeneity was negligible (I^2 0%). Benefit was preserved whether the control was a sham procedure (six trials; RR 1.94, 95% CI 1.48–2.55) or continued PPI therapy; the near-absence of PPI-controlled trials precluded a formal comparison between control types.

Co-primary outcome: PPI reduction or cessation

Restricted to four trials with directly comparable data, the pooled RR for PPI reduction or cessation was 1.82 (95% CI 1.43–2.30; p<0.001) with no heterogeneity (I^2 0%), as summarised in Figure 4. Objective measures of oesophageal acid exposure improved less consistently than symptomatic and quality-of-life outcomes, and incomplete reporting precluded a formal pooled analysis of that objective endpoint.

Sensitivity analyses

The leave-one-out analysis yielded pooled risk ratios between 1.69 (95% CI 1.38–2.07) and 2.03 (95% CI 1.59–2.60), with significance preserved throughout. As shown in Figure 4, the effect persisted when restricted to the three double-blind, sham-controlled, low-risk-of-bias trials (RR 2.00, 95% CI 1.24–3.22; I^2 62.5%) and when restricted to devices still in current clinical use (RR 1.99, 95% CI 1.49–2.68; I^2 33.7%). Excluding trials whose event counts were reconstructed from percentages did not materially alter the estimate.

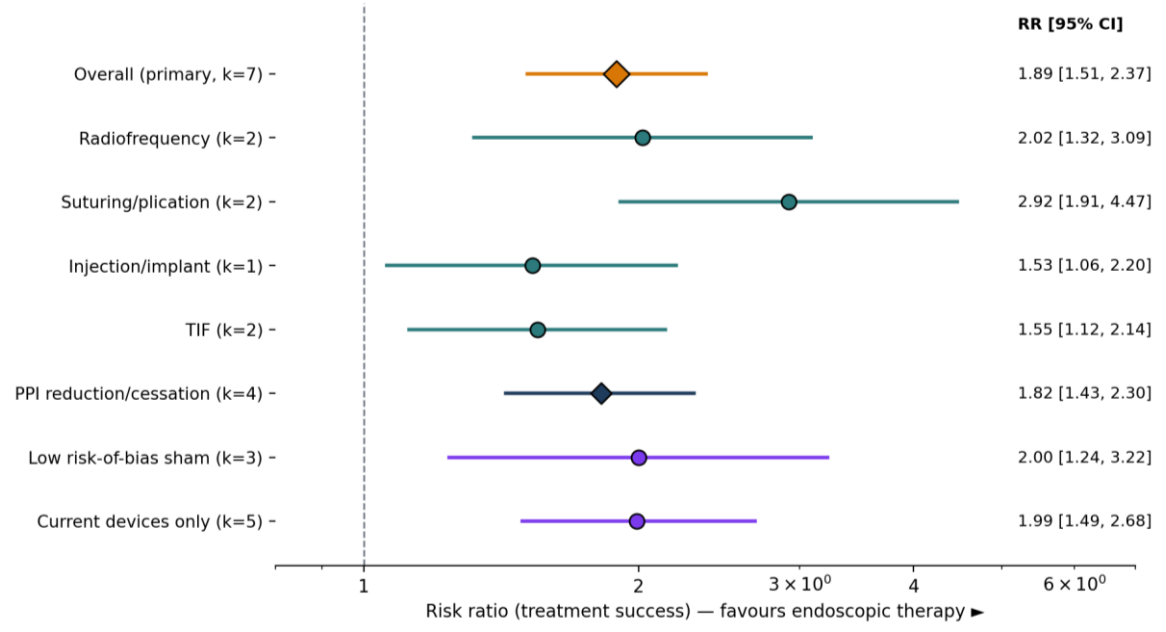

Figure 4. Summary of pooled, subgroup and sensitivity estimates for treatment success.

Publication bias

The funnel plot showed broadly symmetrical scatter about the pooled effect (Figure 5). The Egger test did not identify significant small-study effects (intercept 2.32; p=0.11); however, with only seven trials this test was underpowered, and unpublished negative trials for the older, withdrawn devices could not be excluded.

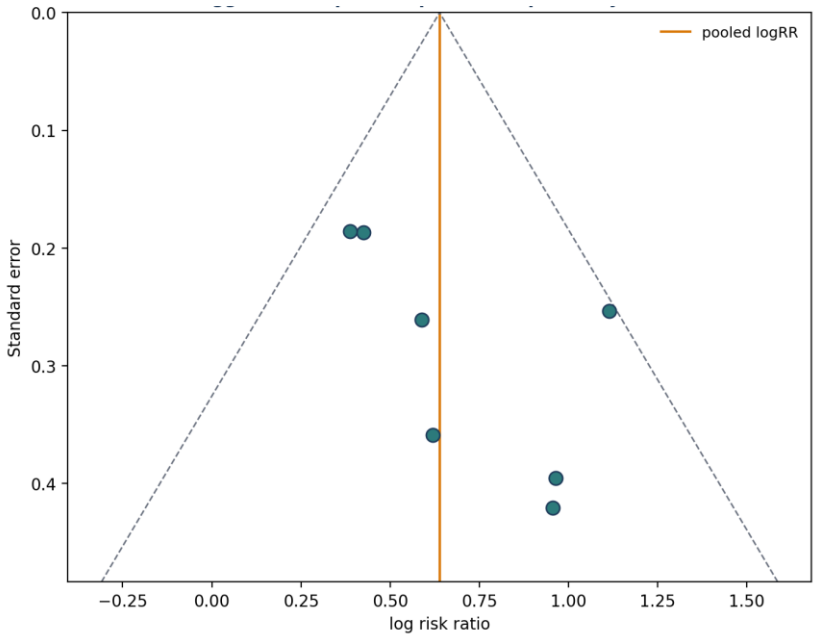

Figure 5. Funnel plot with pseudo-95% confidence limits for the primary outcome. Egger intercept p=0.11 (exploratory).

Serious adverse events by device class

Serious procedure-related harm was infrequent overall but unevenly distributed across device classes, as summarised in Table 3. Radiofrequency, suturing/plication and TIF trials reported no perforations or deaths in the randomised phases, whereas the injection and implant devices accounted for the majority of serious events, including perforation, and the Gatekeeper trial[24] was halted early. Two of these devices were subsequently withdrawn from clinical use.

Table 3. Serious adverse events by device class (randomised phases).

Device class	Trials (n)	Serious procedure-related events	Comment
Radiofrequency	4	No perforations/deaths; rare delayed gastric emptying	Favourable class safety
Suturing/plication	2	No perforations/deaths	Favourable class safety
Injection/implant	2	Perforations; pulmonary infiltrate; early termination	Two devices later withdrawn
TIF	4	Few serious events (3 TIF, 1 sham in one trial)	Favourable class safety

Certainty of the evidence

The certainty of evidence for each principal outcome was appraised narratively, considering risk of bias, inconsistency, indirectness, imprecision and possible publication bias, as summarised in Table 4. Certainty was judged moderate for treatment success and for PPI reduction or cessation, and low for objective acid control. The language of the conclusions has been aligned with these ratings.

Table 4. Narrative certainty-of-evidence appraisal.

Outcome	Trials (n)	Effect (RR, 95% CI)	Certainty	Main reasons
Treatment success	7	1.89 (1.51–2.37)	Moderate	Risk of bias; imprecision
PPI reduction/cessation	4	1.82 (1.43–2.30)	Moderate	Few trials
Objective acid control	—	Not pooled	Low	Inconsistency; incomplete reporting
Serious adverse events	12	Descriptive	Moderate	Sparse events; device withdrawal

4. Discussion

In this meta-analysis of twelve randomised controlled trials, endoscopic anti-reflux therapy approximately doubled the probability of treatment success compared with sham or continued PPI therapy, with a pooled RR of 1.89, an absolute risk difference of about 28 percentage points, an NNT of approximately four and only low-to-moderate heterogeneity. The benefit was directionally consistent across four mechanistically distinct device classes, was confirmed by a co-primary analysis restricted to PPI reduction or cessation, remained significant throughout leave-one-out testing and persisted in analyses confined to low-risk-of-bias trials and to devices still in current use. The prediction interval remained entirely on the side of benefit. These findings support a class-level efficacy signal that complements the more granular device-specific and network syntheses in the literature,[5–9] while we stress that the class-level estimate summarises a heterogeneous family of interventions and should not be read as the effect of any one device.

The dissociation between consistent symptomatic or quality-of-life benefit and less consistent normalisation of oesophageal acid exposure is a recurring theme. Several trials — most clearly those evaluating radiofrequency energy[17,18,20] — reported meaningful symptom and quality-of-life improvement without a corresponding reduction in acid exposure time. This suggests that mechanisms other than a straightforward reduction in acid reflux contribute to benefit, including altered oesophagogastric-junction compliance, fewer transient sphincter relaxations, diminished refluxate volume and reduced oesophageal sensitivity.[11] Because the pooled devices act through different mechanisms, their objective and subjective effects are only loosely coupled, reinforcing the need for objective confirmation of pathological reflux before intervention.[12]

Comparison with previous meta-analyses

The present findings are broadly concordant with, and extend, the existing syntheses. Device-specific meta-analyses of TIF have reported short-term improvement in quality of life and PPI use while cautioning about objective reflux control and durability.[5,6,7] Network meta-analyses have ranked laparoscopic fundoplication highest for objective acid control but credited TIF with favourable symptomatic outcomes and a lower complication burden.[8,9,14] For larger hiatal hernias, concomitant hernia repair with TIF has shown promising short-term PPI cessation in observational series.[13] Our contribution is to show that, when the randomised, sham- or PPI-controlled evidence is pooled across device classes into a single pairwise estimate, a coherent and robust class-level benefit emerges that is not confined to any one device and is expressible in a clinically meaningful absolute magnitude.

Heterogeneity

Low-to-moderate overall heterogeneity, negligible within-subgroup heterogeneity and a non-significant subgroup-difference test indicate that most between-trial variability was explained by device class rather than inconsistency within a technique. The suturing and plication trials produced the largest estimates, and their removal both reduced the pooled effect and abolished residual heterogeneity, whereas the TIF trials clustered around a more modest but still significant effect. Differences in patient selection, responder definition and follow-up duration are the most plausible sources of residual variability, supporting the random-effects model and interpretation of the pooled estimate as an average effect across related interventions.

Patient selection

Because the applicability of an average effect depends on who is treated, patient selection warrants emphasis. Contemporary practice, informed by diagnostic consensus[12] and guideline recommendations,[3,4] favours offering endoscopic anti-reflux therapy to carefully selected patients: those with objectively confirmed pathological reflux, troublesome regurgitation or a wish to avoid lifelong medication, a small or absent hiatal hernia (generally ≤2 cm) and preserved oesophageal motility. Patients whose symptoms are functional rather than reflux-driven, or who have a large hiatal hernia or major motility disorder, are unlikely to benefit and may be harmed; accurate reflux phenotyping is therefore central to translating the pooled estimate into an appropriate individual decision.

Clinical implications for internal medicine

A substantial proportion of patients with GERD wish to reduce or discontinue long-term PPI therapy.[2] For appropriately selected patients, an endoscopic anti-reflux procedure offers a realistic prospect of improved symptom control and reduced medication dependence over the short-to-intermediate term, with an acceptable group-level safety profile and an NNT of approximately four. Endoscopic therapy is best positioned as an intermediate option between medical and surgical management,[3,4] and shared decision-making should incorporate the current uncertainty about long-term durability and the differing safety signals between device classes.

External validity

The included trials were conducted predominantly in North American and European centres, and the availability, cost and regulatory status of these devices differ markedly across settings. In many practices access may be limited by cost, equipment and procedural expertise. The findings should therefore be read as evidence of efficacy under trial conditions rather than as an assertion that endoscopic therapy is a universally available option; where access is constrained, optimised medical therapy and lifestyle intervention remain the mainstay.

Limitations

Several limitations should be acknowledged. First, only seven small trials contributed to the primary outcome (536 participants), so the analysis was better powered to detect a class-level effect than to characterise any single device. Second, the follow-up available for unbiased comparison was short (three to six months) because of frequent crossover, so durability beyond one year could not be assessed. Third, the treatment-success endpoint was harmonised from protocol-specific responder definitions (Table 2), introducing possible outcome-definition heterogeneity. Fourth, several trials were at high or uncertain risk of bias, and two devices were later withdrawn or discontinued. Additional limitations include the near-absence of PPI-controlled trials in the primary pool, the exploratory small-study analysis, the reconstruction of a few event counts from percentages, incomplete acid-exposure reporting and the absence of a prospective protocol registry. These constraints temper but do not overturn the principal finding, which was stable across sensitivity analyses, and they define a clear agenda for adequately powered, contemporary, sham-controlled trials with long-term follow-up.

5. Conclusion

This meta-analysis of randomised controlled trials demonstrated that endoscopic anti-reflux therapy, considered as a therapeutic class, significantly increased the probability of treatment success in adults with gastro-oesophageal reflux disease compared with a sham procedure or continued proton pump inhibitor therapy (pooled RR 1.89, 95% CI 1.51–2.37), with a prediction interval that remained on the side of benefit, an absolute risk difference of approximately 28 percentage points and an NNT of about four. The benefit was consistent across radiofrequency, suturing or plication, injection or implant and transoral incisionless fundoplication modalities, with no significant difference between classes, and was confirmed by a co-primary analysis of PPI reduction or cessation (RR 1.82, 95% CI 1.43–2.30; I^2 0%). The estimate was robust to leave-one-out testing and to restriction to low-risk-of-bias trials and current devices, with no significant small-study effects, and the certainty of evidence was judged moderate for the principal efficacy outcomes. Serious complications were infrequent but concentrated among injection and implant devices, two of which have been withdrawn. For carefully selected patients with objectively confirmed reflux who are unwilling to continue lifelong medication or undergo surgery, endoscopic anti-reflux therapy represents a reasonable intermediate option over the short-to-intermediate term. Given the modest number and size of the contributing trials, the short duration of unbiased comparison and the variable risk of bias, these conclusions should be regarded as provisional and applied within a framework of careful reflux phenotyping and shared decision-making, pending adequately powered, contemporary, sham-controlled trials with long-term follow-up.

Acknowledgements

Not applicable.

Author contributions (CRediT)

T.T.F.: conceptualization, methodology, formal analysis, investigation, writing — original draft. V.Y.: validation, supervision, writing — review & editing. Both authors reviewed and approved the final version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

All data analysed in this review were extracted from the cited, publicly available published studies and are available from the corresponding author on reasonable request.

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