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Laparoscopic Heller myotomy versus peroral endoscopic myotomy in children with esophageal achalasia: a systematic review and meta-analysis

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Abstract

Background Currently, laparoscopic Heller myotomy (LHM) and peroral endoscopic myotomy (POEM) are the best treatment modalities for esophageal achalasia in children. The purpose of this systematic review and meta-analysis is to compare the efficacy of LHM and POEM.

Methods A systematic literature search was performed in PubMed/Medline, Google Scholar and Web of Science for original articles comparing LHM and POEM. All articles were analyzed with respect to operation duration, length of hospital stay, pre- and postoperative Eckardt score (ES), and pre- and postoperative lower esophageal sphincter (LES) pressure.

Results A total of 32 articles, reporting on 800 children, were selected and reviewed. Because of missing diagnostic values of ES and LES in the LHM group, the meta-analysis was limited to the POEM results. According to the random-effects model, the mean ES difference between pre- and post-operation was 4.387 (95% confidence interval [CI] 3.799-4.974), significantly different to zero (z=14.64, P<0.001), while the mean LES pressure difference was 3.63 mmHg mmHg (95%CI 2247-3.879), significantly different to zero (z=7.36, P<0.001). Operation duration was 130.15 min (95%CI 62.59-197.71) for the LHM method and 83.64 min (95%CI 55.14-112.14) for POEM. The pooled estimate of length of hospital stay was 3.4 days (95%CI 2.6-4.44) and it was comparable between the 2 methods.

Conclusions POEM has positive outcomes regarding ES and LES pressure pre- and postoperatively, as well as operation duration, while the length of hospitalization was comparable between POEM and LHM. Well-designed studies are warranted to further clarify differences between the 2 methods.

Keywords Lower esophageal sphincter pressure, operation time, outcome, length of hospitalization, Eckardt score

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Introduction

Esophageal achalasia (EA) is a rare disorder of the lower esophageal sphincter (LES) that leads to dysfunctional motility of the esophagus [1]. It is extremely rare in childhood, with an incidence of only 0.11/100,000 children annually [1]. The clinical presentation includes dysphagia to fluids and solids, vomiting, chest pain, regurgitation, recurrent episodes of chest infections due to aspiration, and weight loss [1]. Although in most cases is idiopathic, in some instances it may be associated with Trisomy 21, AAA syndrome (achalasia, alacrima, and adrenocorticotropic hormone insufficiency), Chagas disease, congenital hypoventilation syndrome,

glucocorticoid insufficiency, eosinophilic esophagitis, or familial dysautonomia [1].

The precise etiology of EA is still unclear, but it may be associated with autoimmunity, viral infection or neurodegeneration and other factors [1]. Combined diagnostic investigations are used to confirm the diagnosis of EA. A barium meal is used to rule out esophageal strictures and shows the delay in transition through the LES (bird-beak appearance) [2]. Esophagoscopy is used to preclude pseudo-achalasia, assess the esophageal wall and rule out esophagitis, *Trypanosoma cruzi*, malignancy, reflux esophagitis, and other causes of impaired esophageal motility [1]. However, high-resolution manometry or high-resolution impedance manometry (HRIM) is considered the gold standard method to demonstrate EA, by demonstrating patterns of esophageal contractility [2].

Although there are multiple modalities for the treatment of EA, surgery remains the most successful treatment of choice [1]. Currently, laparoscopic Heller myotomy (LHM) has become the gold standard in the treatment of EA [1]. However, more recently, a more attractive procedure, peroral esophageal myotomy (POEM) [3], has been proposed for the management of EA. POEM has been used in adults with excellent results [3], and has started to be adopted by pediatric surgeons and gastroenterologists [4]. As there is no curative treatment or any globalized consensus on 1 gold-standard intervention, the present study aimed to provide a systematic review and meta-analysis, comparing the reported results concerning the efficacy and outcomes of LHM and POEM for the treatment of EA in children.

Materials and methods

This meta-analysis adhered to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) statement (Appendix A) [5]. The protocol was registered with the International Prospective Register of Ongoing Systematic Reviews (PROSPERO), with registration number CRD42023389402.

Search strategy

We conducted a systematic search for articles concerning LHM and POEM for the treatment of EA in children in each of the following databases, covering a period from 1995 to December 31, 2023: PubMed, Google Scholar and Web of Science. Key terms used were: "achalasia esophagus", "children", "laparoscopic myotomy", "laparoscopic myotomy and fundoplication", "Heller myotomy", "peroral endoscopic myotomy", "per-oral endoscopic myotomy", and "POEM". The key terms were combined with the Boolean operators AND OR. The key words were used in all combinations to obtain the greatest number of articles. The literature search was restricted to the English language. Inclusion criteria were as follows: prospective observational and retrospective studies, randomized controlled trials, and case series with a minimum of 5 patients. Experimental studies, case reports, abstracts, reviews, editorials and comments were excluded. Articles were also excluded if they included less than 5 patients and a follow up less than 6 months. After the first screening, all the full text copies were reviewed independently by 2 authors (NZ and AA). When different articles were reported from the same author, only the study with the more recent data were reviewed.

Data extracted

The data extracted from each report included year of publication, type of publication, author, country, age (median, mean, range), patient sex, comorbidities, symptom duration, prior treatments, operative time, length of hospital stay, preoperative and postoperative objective evaluation of EA with Eckardt score (ES) [6], and LES pressure measured by manometry. Any disagreement in results was resolved through consensus. The collected data were recorded in a Microsoft Excel spreadsheet (Excel 2016, Microsoft Corporation).

Statistical analysis

The method used to compute the random-effects model was the DerSimonian and Laird method [7], a variation of the inverse variance method that incorporates an assumption that the different studies are estimating different, yet related, intervention effects. The publication bias (small study effect) was evaluated using Egger's test [8]. The analysis was conducted using StataCorp 2019 software (Stata v16 Base Reference Manual, College Station, TX: Stata Press) and the level of statistical significance was set at 0.05. Concerning the operation time and length of hospital stay, mean values and relevant standard deviations, when not available, were calculated from the median and the range using the methodology proposed by Luo *et al* and Wan *et al* [9,10], after checking the normality assumption [11]. A random-effects meta-analysis was applied to summarize results across studies. The analysis was stratified by method of operation. The meta-analysis was performed using Stata v16 software (StataCorp LP, College Station, TX).

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Quality assessment of studies

Articles were evaluated for their quality using the MINORS index for non-randomized articles [12]. This tool includes 8 questions to estimate the quality of studies. The interpretation of each question is rated from 0 to 2 (0= not reported, 1= reported, 2= adequate). The best score for a study is 16. The ratings are given as "good", "fair" or "poor".

Results

Literature search and included studies

A total of 32 articles published between January 1999 and June 2023 were retrieved via the database search and were included in this meta-analysis [1,4,13-42] (Fig. 1).

Study characteristics and demographics

A summary of the characteristics of the eligible studies assessing the efficacy and outcome of LHM and POEM for EA is presented in Table 1. The total patient population included 800 children (female: 345, male/female: 1:0.73), aged 1-17 years. LHM was performed in 293 patients, and POEM in 507. The mean or median ages of patients participating in each eligible study are shown in Table 1. The majority of the studies were retrospective; there were only 2 prospective studies. Only 3 studies were comparative, as they compared 2 different intervention methods (myotomy, dilation, POEM), whereas the rest simply reported the results of a single method. For the comparative studies, we extracted the results of the different interventions and treated them as 2 separate studies. The evaluation of the intervention was conducted using the differences in the mean ES and the LES between pre- and post-operation. The ES is a simple symptom score (dysphagia, regurgitation, chest pain and weight loss), which was designed to quantify the response of symptoms to treatment [43]. The lower the mean ES and the lower the mean LES the better the results of the intervention.

Evaluation of ES in POEM

A total of 11 studies reported the mean ES difference pre- and postoperatively for the POEM procedure

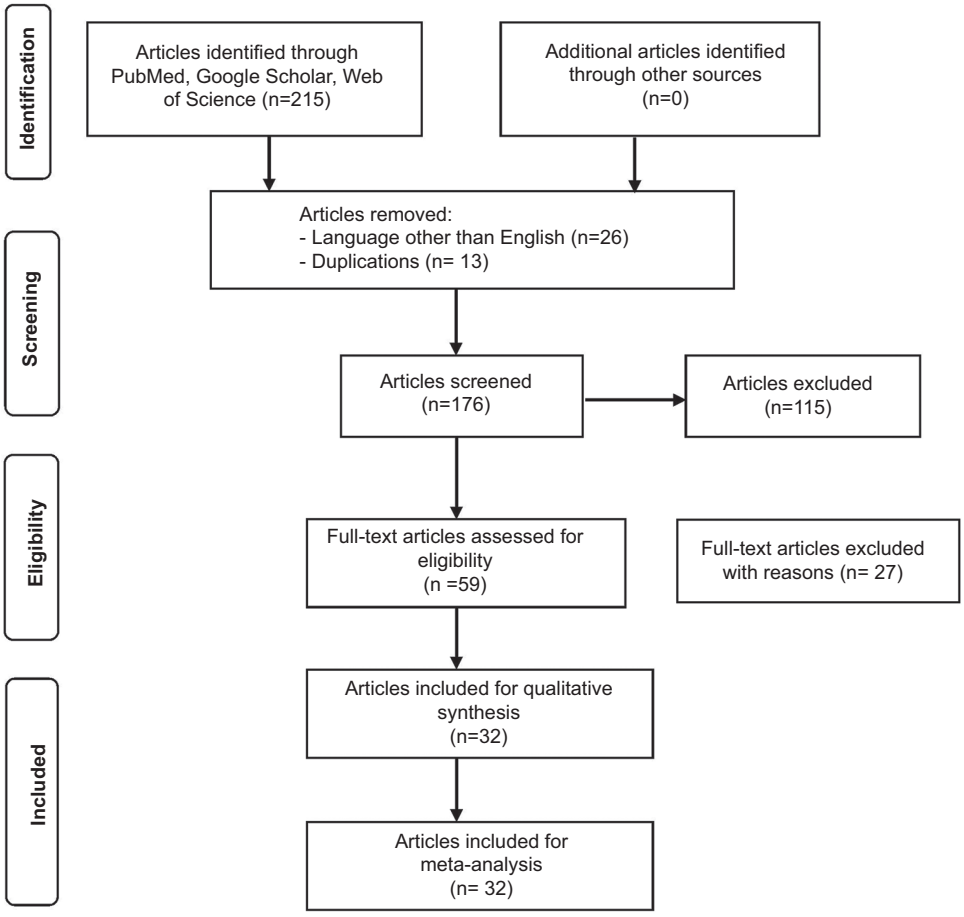

Figure 1 Flow chart showing the design of the systematic review

Table 1 Summary of characteristics of the included studies

Authors [ref.]	Year	Country	Study design	Number of patients (Female)	Age at intervention (years)
Waldhausen *et al* [13]	1999	USA	Retrospective	8 (5)	14.5 (11-17)
Esposito *et al* [14]	2000	Italy	Retrospective	8 (4)	6.3 (2-13)
Rothenberg *et al* [15]	2001	USA	Retrospective	9 (-)	12 (5-17)
Mehra *et al* [16]	2001	USA	Retrospective	22 (10)	11.3±3.4
Patti *et al* [17]	2002	USA	Retrospective	13 (7)	15 (6-17)
Mattioli *et al* [18]	2003	Italy	Retrospective	20 (6)	-
Paidas *et al* [19]	2007	USA	Retrospective	14 (6)	17 (11-19)
Garzi *et al* [20]	2007	Italy	Retrospective	12 (5)	11 (3.5-16)
Askegard-Gismann *et al* [21]	2009	Canada	Retrospective	26 (11)	15 (4-18)
Corda *et al* [22]	2010	UK	Retrospective	20 (7)	12 (5-15)
Tannuri *et al* [23]	2010	Brazil	Retrospective	15 (8)	12(9-17)
Esposito *et al* [24]	2013	Italy	Retrospective	31 (13)	ΔT.8.4
Alkhatrawi *et al* [26]	2013	Saudi Arabia	Retrospective	8 (4)	4.3 (1-13)
Pachl *et al* [25]	2014	UK	Retrospective	28 (15)	13 (3.2-17.4)
Franklin *et al* [1]	2014	USA	Retrospective	24 (11)	11 (5-18)
Chen *et al* [27]	2015	China	Prospective	27 (16)	13.8 (6-17)
Tang *et al* [28]	2015	China	Retrospective	5 (2)	ΔT: 15
Li *et al* [29]	2015	China	Retrospective	9 (5)	MT: 14.1
Caldaro *et al* [30]	2015	Italy	Retrospective	18 (10)	11.6 (2-17)
Petrosyan *et al* [42]	2016	USA	Retrospective	31 (20)	12.9 (5-18)
Tan *et al* [31]	2016	China	Retrospective	21 (11)	11.6 (2-17)
Altokhais *et al* [33]	2016	Saudi Arabia	Retrospective	6 (2)	14 (9-18)
Nabi *et al* [33]	2016	India	Retrospective	15 (6)	14 (9-16)
Grabowski *et al* [34]	2017	Poland	Retrospective	11 (4)	13 (6-17)
Miao *et al* [35]	2018	China	Retrospective	21 (12)	-
Choné *et al* [4]	2019	France	Retrospective	117 (48)	14.2±3.7
Liu *et al* [36]	2020	China	Retrospective	130 (48	9.7
Wood *et al* [37]	2020	USA	Prospective	21 (7)	11 (2-17)
Saez *et al* [38]	2021	Chile	Prospective	5 (1)	11 (2-17)
Petrosyan *et al* [39]	2022	USA	Retrospective	43 (16)	-
Peng *et al* [40]	2022	China	Retrospective	24 (10)	11 (2-17)
Nabi *et al* [41]	2022	India	Retrospective	38 (15)	14.7±3.3 (4-19)

(Fig. 2, Supplementary Table 1). All studies demonstrated a higher mean preoperative ES compared to the postoperative value. According to the random-effects model, the summary preoperative to postoperative difference in mean ES for the POEM procedure was 4.387 (95% confidence interval [CI] 3.799-4.974), which was statistically significantly different to zero (z=14.64, P<0.001) (Fig. 2). According to the chi-square test for heterogeneity there was statistically significant heterogeneity (I^2=74%, chi-square=38.51, degrees of freedom (d.f.)=10, P<0.001) (Supplementary Table 1).

Evaluation of LES pressure in POEM

A total of 8 studies reported the mean LES pressure difference pre- and postoperatively for the POEM procedure (Fig. 3, Supplementary Table 2). All the studies demonstrated a higher preoperative mean LES pressure compared to the mean postoperative value. According to the result of the random-effects model the summary preoperative to postoperative difference in mean LES for the POEM procedure was 3.63 mmHg (95%CI 2.247-

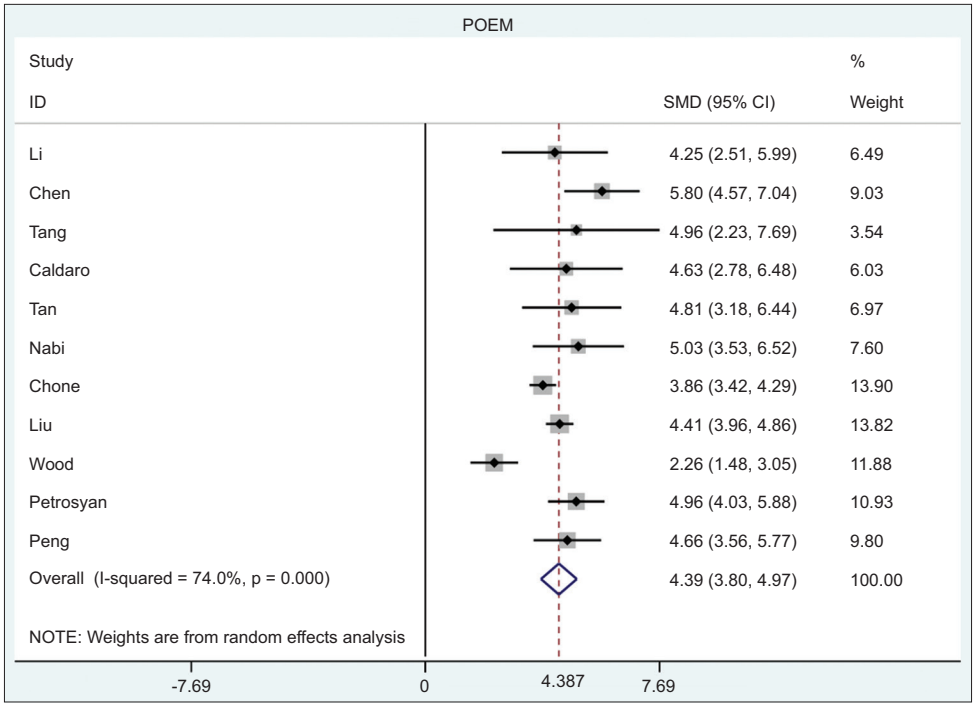

Figure 2 Forrest plot of mean Eckardt score difference, preoperatively and postoperatively, for the peroral endoscopic myotomy (POEM) procedure
SMD, standardized mean difference; CI, confidence interval

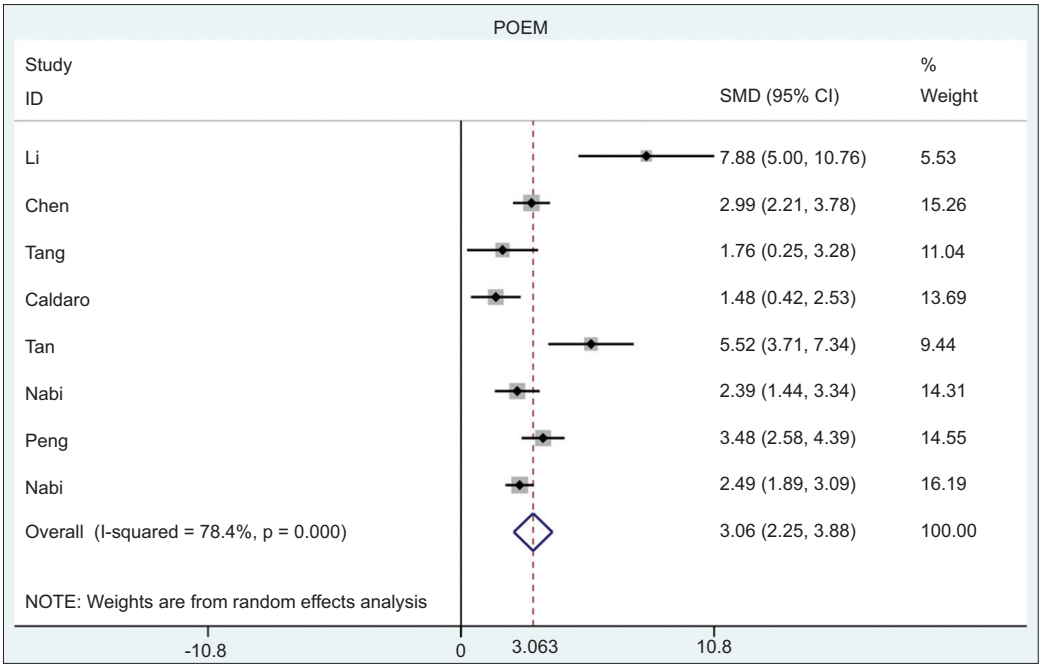

Figure 3 Forrest plot of mean lower esophageal sphincter (LES) pressure difference preoperatively and postoperatively for the peroral endoscopic myotomy (POEM) procedure
SMD, standardized mean difference; CI, confidence interval

3.879), which was statistically significantly different to zero (z=7.36, P<0.001) (Fig. 3). According to the chi-square test for heterogeneity there was statistically significant heterogeneity (I^2=78.4%, chi-square=31.47, d.f.=7, P<0.001) (Supplementary Table 2).

Evaluation of ES and LES pressure in LHM

A comparison of the different intervention methods (myotomy, dilation, POEM) was not performed, as there were very few studies that reported results for ES and LES when

myotomy or dilation was used. Consequently, the analysis in computing the summary effect of the differences in mean ES and LES pressure pre- and post- operatively was limited. In addition, the studies did not report adequate data to investigate the source of heterogeneity.

Evaluation of operation duration in LHM and POEM

A total of 7 studies reported the mean value and the standard deviation, and 3 more the median value and the range, of the operation duration. The pooled estimate of operation duration was 97.5 min (95%CI 79.2-115.7) (Fig. 4). Heterogeneity was very high (I^2=95%, τ^2=787.5). Significant heterogeneity was found among methods of operation (Q test P=0.014). The pooled estimate of operation duration was 130.2 min (95%CI 95.8-164.5) for the LHM method, compared with 82.5 min (95%CI 66.4, 98.6) for POEM (Supplementary Table 3).

Evaluation of length of hospital stay in LHM and POEM

The mean value and standard deviation for the length of hospital stay were reported in 10 studies, while the median and range were reported in 4 more studies. The pooled estimate of length of stay was 3.3 days (95%CI 2.6-3.9) (Fig. 5). Again, heterogeneity among studies was very high (I^2=97%, τ^2=1.15). There was no significant heterogeneity between methods in length of stay (Q test P=0.201). The pooled estimate of hospital stay was 2.8 days (95%CI 2.16-3.37) for the LHM method, compared with 3.6 days (95%CI 2.48-4.70) for POEM (Supplementary Table 4).

Evaluation of publication bias

Publication bias was assessed separately for both mean ES difference and mean LES pressure difference for the POEM procedure (Supplementary Figs. 1 and 2, Supplementary Tables 5 and 6). According to Egger's test, there was no statistically significant small-study effect for mean ES difference for POEM (P-value=0.452) (Supplementary Fig. 1 and Supplementary Table 5). On the other hand, according to Egger's test, there was a statistically significant small-study effect for mean LES pressure difference for POEM (P=0.001) (Supplementary Fig. 2 and Supplementary Table 6).

Funnel-plots for both operation duration and length of stay (Supplementary Figs. 3 and 4) display asymmetry, which could be related to publication bias. Egger's test for asymmetry was statistically significant for the operation duration (P=0.018), whereas for the length of stay it was not significant (P=0.214) (Supplementary Tables 7 and 8). One other possible reason for the asymmetry, apart from publication bias, was the fact that we could not use all available studies since not all of them reported mean values and standard deviations.

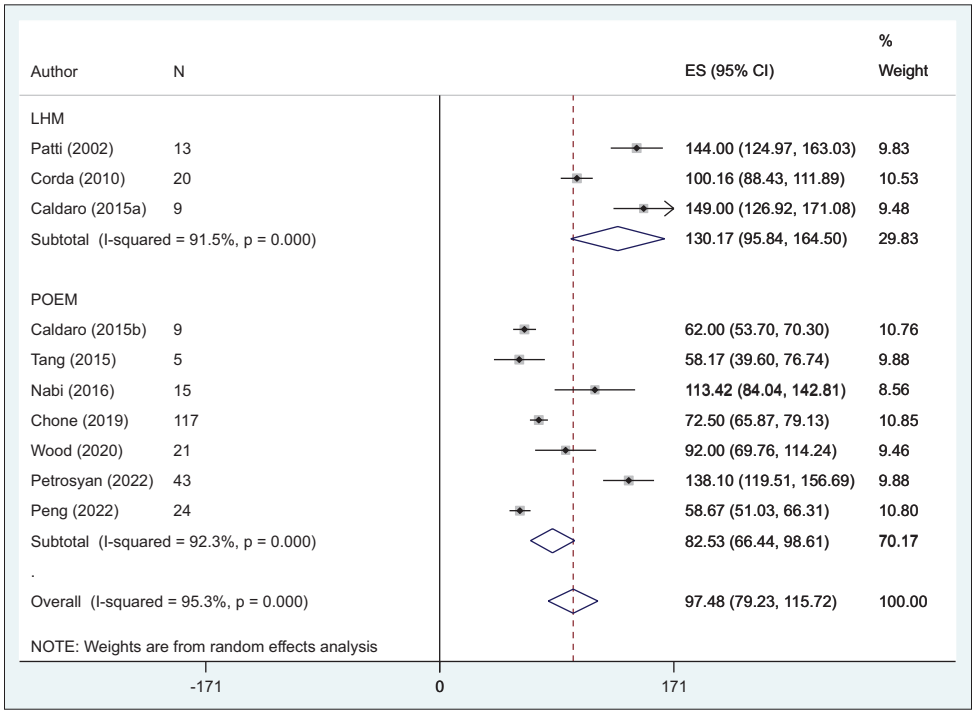

Figure 4 Forest plot of random-effects meta-analysis of the operation time (min) over all studies and by method of operation: laparoscopic Heller myotomy (LHM) vs. peroral endoscopic myotomy (POEM)
ES, Eckardt score; CI, confidence interval

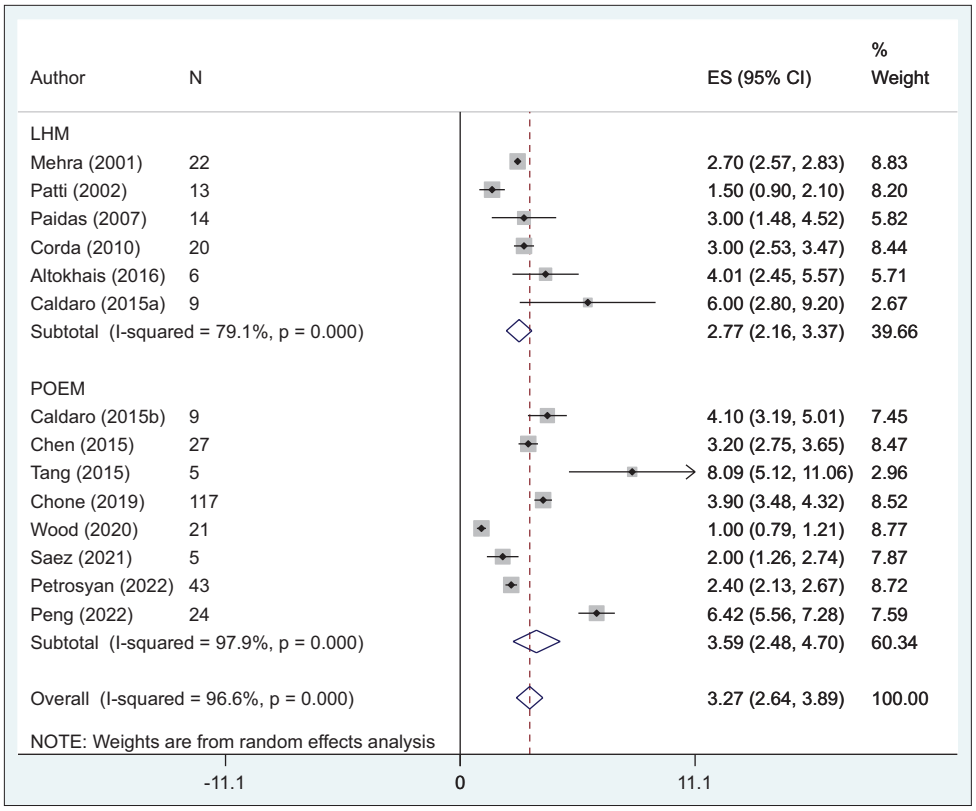

Figure 5 Forest plot of random-effects meta-analysis of the length of hospital stay (days) over all studies and by method of operation: laparoscopic Heller myotomy (LHM) vs. peroral endoscopic myotomy (POEM)
ES, Eckardt score; CI, confidence interval

Discussion

EA is a rare disorder in children and there are limited data regarding the effectiveness of current treatment methods. To our knowledge, this is the first systematic review with meta-analysis to evaluate the efficacy of the 2 most popular treatment modalities, POEM and LHM, in children, assessing the outcome in terms of the differences in mean ES and LES pressure from pre- to post-operation, in combination with perioperative characteristics such as operation duration and length of hospital stay. We chose to use these 2 parameters, as both ES and LES pressure have been proposed as objective tools for measuring the response to therapy [43].

Our results revealed that POEM, an established interventional method of treatment for EA in adults, is effective in children with EA, as all studies demonstrated a lower value of mean ES postoperatively compared to the mean value preoperatively, while the pooled mean reduction in ES was statistically significant. This indicates that the POEM procedure leads to the resolution of symptoms, improving the quality of life of pediatric patients. At the same time, this meta-analysis revealed that the duration of the POEM procedure is significantly shorter compared to LHM, whereas the length of hospitalization is similar for the 2 methods.

However, a comparison of the 2 treatment methods regarding the measurement of outcome using ES and LES was not possible, as the review of the current literature yielded very few studies that reported results of ES and LES pressure when LHM was performed. More specifically, only Waldhausen *et al* measured LES pressure pre- and postoperatively, reporting that it decreased significantly from >40 mmHg preoperatively to <6-10 mmHg after the procedure [13]. Notably, no study reported ES. This finding could potentially be attributed to the fact that ES is a scoring system initially developed for assessing the severity of symptoms in adults. The symptoms might differ in younger children, while their evaluation is probably more difficult in this age group. Future discussions could focus on the need for adapting or creating a separate ES for the pediatric population. As a result, we were not able to evaluate the reduction in mean ES and LES pressure postoperatively.

In contrast, other results of the current evaluation of these 2 methods for the management of pediatric EA, concerning the duration of the procedure and the length of hospitalization, were interesting. According to our meta-analysis, the LHM procedure takes longer (approximately 50 min more) than POEM, as POEM is a less invasive method compared to LHM. The operative duration of both methods was probably shorter when they were performed by

experienced hands. EA remains an extremely rare condition in children. In particular, POEM is a complex procedure, and is perhaps more difficult in a pediatric population with potentially high-risk complications, such as perforation and mediastinitis. Consequently, it should only be performed in children by experienced endoscopists with a knowledge of pediatric anatomy, advanced skills, and the ability to manage complications. As there is high heterogeneity regarding the management of pediatric achalasia among different centers worldwide, both procedures should be performed in high-volume experienced centers, in order to reduce complications and improve short- and long-term outcomes. Finally, the development of evidence-based global clinical guidelines is essential [3].

No significant difference in length of hospital stay was observed, as the pooled mean hospital stay of patients was approximately 3-4 days in both techniques. In contrast to our results, studies that have been carried out in adults demonstrate that POEM is associated with a shorter length of hospital stay compared to LHM [44]. This finding could potentially be attributed to the specific features of the pediatric population, to parental stress, and to surgeons and gastroenterologists choosing to continue hospitalization in order to monitor for postoperative complications, recurrent symptoms and adequate nutrition and physical growth, contributing to an increase in healthcare costs.

So far, because of the low incidence of achalasia in the pediatric population, there are limited data available on the efficacy of POEM in children. The first systematic review and meta-analysis addressing the effectiveness of this promising treatment modality for pediatric achalasia was conducted by Lee *et al*, who demonstrated that POEM was efficacious and safe for treating achalasia in children, with a significant mean decrease in both ES and LES pressure after the procedure, by 6.88 points and 20.73 mmHg, respectively [45]. However, their findings were limited by the small total number of patients (n=142), and by the inclusion of non-randomized trials and low-quality studies. Recently, Zhong *et al* performed a systematic review and meta-analysis in order to evaluate the utility of this novel endoscopic technique in pediatric patients [46]. They reported that clinical success was achieved in the majority of children, with a significant mean reduction in ES and LES pressure following POEM, by 6.76 points and 19.38 mmHg, respectively [46]. However, this review included only observational studies and POEM was not compared with alternative therapeutic methods. Nabi *et al* carried out the most recent systematic review and meta-analysis that aimed to explore the clinical outcomes of POEM for pediatric achalasia [47]. Similarly, this study supported the claim that POEM is an effective intervention in children with achalasia, while the pooled mean reduction in ES was 6.71 post-POEM [47]. Overall, the results of these meta-analyses are consistent with our findings, demonstrating the efficacy of this minimally invasive procedure that could provide long-term symptom resolution in young patients.

Given that the published comparative data are insufficient to determine the ideal management of pediatric achalasia, our current knowledge of treatment algorithms is largely based on the adult literature. Although a treatment strategy for achalasia in pediatric patients remains a challenge, experience from adult studies can help and guide clinicians in treatment selection, according to relevant clinical factors. In general, based on network meta-analyses in adults, POEM and LHM have comparable efficacy and similar clinical success for the management of achalasia [48-50]. In 2 recent systematic reviews and meta-analyses, both POEM and LHM had greater efficacy than pneumatic dilation, but neither was significantly superior to the other [49,50]. In the same context, Shiu *et al* reported that POEM demonstrated similar results to LHM, and suggested that POEM with an anterior or posterior approach, and LHM with Dor or Toupet fundoplication, are the best initial treatments for achalasia [48].

A strength of our study is the systematic, comprehensive and detailed approach to evaluating POEM and LHM outcomes, based on ES and LES pressure pre- and postoperatively, as well as perioperative characteristics such as operative duration and length of hospitalization, all in accordance with the PRISMA reporting guidelines and following a predefined registered protocol. Moreover, the majority of the eligible studies had a low overall risk of bias and applicability concerns. Nevertheless, there are also study limitations to consider. First, the quality of meta-analyses will always be determined by the quality of the individual studies included in the analysis. The majority of the individual included studies were retrospective, while only 3 were prospective. As result, there is a lack of high-quality data available in the literature and there are no randomized controlled trials. Moreover, there are limited data for LHM, making it impossible to compare the 2 methods. The high heterogeneity regarding ES and LES pressure between the studies was probably associated with the varying design of the studies, the internal protocols, and the postoperative follow up of each institution.

In the present study, a comparison of the 2 most popular and effective methods for EA treatment in children, regarding their impact on ES and LES, was not possible, because of the inappropriate design of previous studies focusing on the LHM procedure. Therefore, our meta-analysis was restricted to the POEM method, which showed positive outcomes regarding ES and LES pressure pre- and postoperatively. On the other hand, this study demonstrates that POEM's mean procedure duration is shorter than that of LHM, while the length of hospital stay is similar. We highlight the need for carrying out well-designed studies with homogeneous use of objective diagnostic tools and long-term follow up of pediatric patients with EA, so as to further clarify the differences between the 2 methods.

Summary Box

What is already known:

- Esophageal achalasia (EA) is a rare disorder among the pediatric population
- Laparoscopic Heller myotomy (LHM) is the gold standard in the treatment of EA
- Peroral esophageal myotomy (POEM) has been recently introduced in children for the treatment of EA

What the new findings are:

- This is the first meta-analysis to evaluate the efficacy of the 2 most popular treatment modalities, POEM and LHM, in children
- POEM has positive outcomes regarding Eckardt score and lower esophageal sphincter pressure pre- and postoperatively
- POEM's mean procedure duration is shorter than that of LHM, while the length of hospital stay is similar

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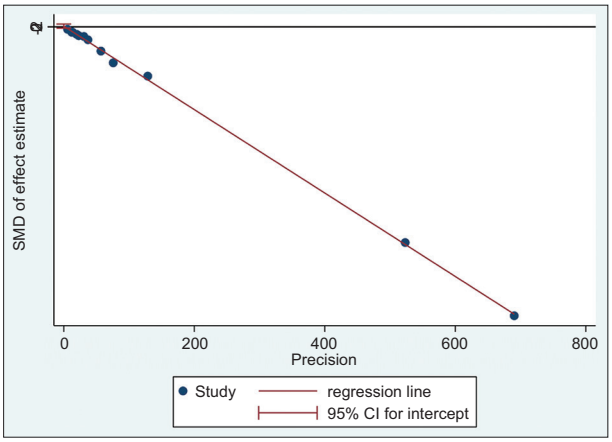
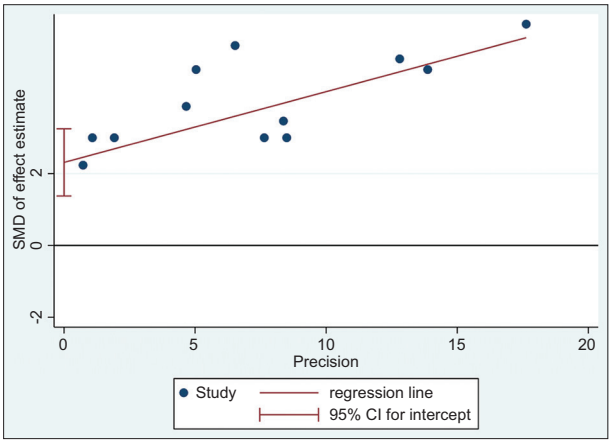
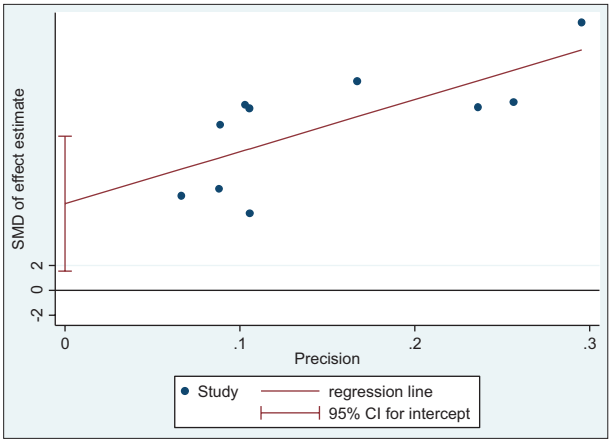
Supplementary material



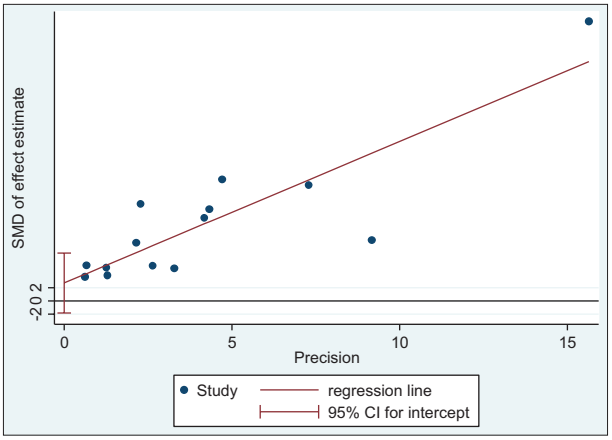
Supplementary Figure 1 Egger's test plot for mean Eckardt score difference for the peroral endoscopic myotomy (POEM) procedure
SMD, standardized mean difference; CI, confidence interval



Supplementary Figure 2 Egger's test plot for mean lower esophageal sphincter (LES) pressure difference for the peroral endoscopic myotomy (POEM) procedure
SMD, standardized mean difference; CI, confidence interval



Supplementary Figure 3 Egger's test plot for the operation duration (min) over all studies
SMD, standardized mean difference; CI, confidence interval



Supplementary Figure 4 Egger's test plot for the length of stay (days) over all studies
SMD, standardized mean difference; CI, confidence interval

Supplementary Table 1 Results of meta-analysis of difference in mean Eckardt score, preoperatively and postoperatively, for the peroral endoscopic myotomy (POEM) procedure

Study [ref.]	SMD	95%CI	% Weight
Li (2015) [29]	4.253	2.514-5.992	6.49
Chen (2015) [27]	5.804	4.568-7.041	9.03
Tang (2015) [28]	4.963	2.233-7.692	3.54
Caldaro (2015) [30]	4.631	2.779-6.482	6.03
Tan (2016) [31]	4.806	3.176-6.437	6.97
Nabi (2022) [47]	5.026	3.528-6.524	7.60
Chone (2019) [4]	3.859	3.424-4.294	13.90
Liu (2020) [36]	4.413	3.961-4.865	13.82
Wood (2020) [37]	2.263	1.481-3.046	11.88
Petrosyan (2022) [39]	4.956	4.027-5.885	10.93
Peng (2022) [40]	4.665	3.556-5.773	9.80
D+L pooled SMD	4.387	3.799-4.974	100.00

Heterogeneity Chi-squared=38.51 (d.f. = 10), P<0.001
I^2 (variation in SMD attributable to heterogeneity) = 74.0%
Estimate of between-study variance Tau-squared = 0.5969
Test of SMD=0, z=14.64, P<0.001
SMD, standardized mean difference; CI, confidence interval

Supplementary Table 2 Results of meta-analysis of difference in mean lower esophageal sphincter (LES) pressure, preoperatively and postoperatively, for the peroral endoscopic myotomy (POEM) procedure

Study [ref.]	SMD	95%CI	% Weight
Li (2015) [29]	7.876	4.995-10.758	5.53
Chen (2015) [27]	2.995	2.210-3.780	15.26
Tang (2015) [28]	1.765	0.254-3.276	11.04
Caldaro (2015) [30]	1.477	0.421-2.533	13.69
Tan (2016) [31]	5.525	3.707-7.343	9.44
Nabi (2016) [33]	2.388	1.438-3.338	14.31
Peng (2022) [40]	3.484	2.575-4.394	14.55
Nabi (2022) [47]]	2.491	1.888-3.094	16.19
D+L pooledSMD	3.063	2.247-3.879	100.00

Heterogeneity Chi-squared=32.47 (d.f. = 7) P=0.000
I-squared (variation in SMD attributable to heterogeneity) = 78.4%
Estimate of between-study variance Tau-squared = 0.9760
Test of SMD=0, z=7.36; P<0.001
SMD, standardized mean difference CI, confidence interval

Supplementary Table 3 Results of meta-analysis of mean operation duration (min) over all studies for laparoscopic Heller myotomy (LHM) vs. peroral endoscopic myotomy (POEM)

Method and Author [ref.]	Effect	95%CI	% Weight
LHM			
Patti (2002) [17]	144	124.974-163.026	9.83
Corda (2010) [22]	100.161	88.432-111.891	10.53
Caldaro (2015a) [30]	149	126.918-171.082	9.48
Subgroup, DL	*130.171*	*95.84-164.501*	*29.83*
POEM			
Caldaro (2015b) [30]	62	53.703-70.297	10.76
Tang (2015) [28]	58.17	39.596-76.744	9.88
Nabi (2016) [33]	113.423	84.038-142.808	8.56
Chone (2019) [4]	72.5	65.868-79.132	10.85
Wood (2020) [37]	92	69.76-114.24	9.46
Petrosyan (2022) [39]	138.1	119.509-156.691	9.88
Peng (2022) [40]	58.67	51.029-66.311	10.8
Subgroup, DL	*82.528*	*66.444-98.612*	*70.17*
Overall, DL	97.475	79.23-115.72	100

Cochran's Q statistics for heterogeneity

Measure	Value	df	P-value	I^2
LHM	23.62	2	0	91.50%
POEM	77.81	6	0	92.30%
Overall	192.78	9	0	95.30%
Between	6.07	1	0.014	

CI, confidence interval; DL, DerSimonian and Laird method df, degrees of freedom

Supplementary Table 4 Results of meta-analysis of mean length of hospital stay (days) over all studies for laparoscopic Heller myotomy (LHM) vs. peroral endoscopic myotomy (POEM)

Method and Author [ref.]	Effect	95%CI	% Weight
LHM			
Mehra (2001) [16]	2.7	2.575-2.825	8.83
Patti (2002) [17]	1.5	0.902-2.098	8.2
Paidas (2007) [19]	3	1.481-4.519	5.82
Corda (2010) [22]	3	2.531-3.469	8.44
Altokhais (2016) [32]	4.011	2.45-5.572	5.71
Caldaro (2015a) [30]	6	2.799-9.201	2.67
Subgroup, DL	*2.767*	*2.163-3.371*	*39.66*
POEM			
Caldaro (2015b) [30]	4.1	3.185-5.015	7.45
Chen (2015) [27]	3.2	2.747-3.653	8.47
Tang (2015) [28]	8.089	5.118-11.061	2.96
Chone (2019) [4]	3.9	3.483-4.317	8.52
Wood (2020) [37]	1	0.786-1.214	8.77
Saez (2021) [38]	2	1.257-2.743	7.87
Petrosyan (2022) [39]	2.4	2.131-2.669	8.72
Peng (2022) [40]	6.42	5.56-7.28	7.59
Subgroup, DL	*3.59*	*2.482-4.699*	*60.34*
Overall, DL	3.268	2.642-3.893	100

Cochran's Q statistics for heterogeneity

Measure	Value	df	p-value	I^2
LHM	23.93	5	0	79.10%
POEM	330.13	7	0	97.90%
Overall	382.25	13	0	96.60%
Between	1.63	1	0.201	

CI, confidence interval; DL, DerSimonian and Laird method; df, degrees of freedom

Supplementary Table 5 Egger's test for small-study effect of mean Eckardt score difference for the peroral endoscopic myotomy (POEM) procedure

Number of studies=11			Root MSE=40.7			
Std_Eff	Coeff.	Std. Error	t	P-value	95% CI	
Slope	-6.679	0.055	-121.39	<0.001	-6.803	-6.554
Bias	11.501	14.643	0.79	0.452	-21.623	44.626

Test of H0: no small-study effects; p-value=0.452
MSE, mean squared error; Std_Eff, standardized effect; CI, confidence interval

Supplementary Table 6 Egger's test for small-study effect of mean lower esophageal sphincter (LES) pressure difference for the peroral endoscopic myotomy (POEM) procedure

Number of studies=8			Root MSE=0.606		
Std_Eff	Coeff.	Std. Error	t	P-value	95%CI
Slope	0.197	0.037	5.26	0.002	0.105-0.289
Bias	2.313	0.383	6.05	0.001	1.377-3.249

Test of H0: no small-study effects; P=0.001
MSE, mean squared error; Std_Eff, standardized effect CI, confidence interval

Supplementary Table 7 Egger's test for small-study effect of mean operative time (min) for laparoscopic Heller myotomy (LHM) vs. peroral endoscopic myotomy (POEM)

Number of studies=10			Root MSE=3.391		
Std_Eff	Coeff.	Std. Err.	t	P-value	95%CI
slope	41.668	13.738	3.03	0.016	9.989-73.347
bias	6.925	2.339	2.96	0.018	1.532-12.318

Test of H0: no small-study effects; P=0.018
MSE, mean squared error; Std_Eff, standardized effect; CI, confidence interval

Supplementary Table 8 Egger's test for small-study effect of mean length of hospital stay (days) for Laparoscopic Heller myotomy (LHM) vs. peroral endoscopic myotomy (POEM)

Number of studies=14			Root MSE=5.279		
Std_Eff	Coef.	Std. Err.	t	P-value	95%CI
slope	2.138	0.358	5.99	<0.001	1.361 to 2.916
bias	2.7139	2.070	1.31	0.214	-1.796 to 7.224

Test of H0: no small-study effects; P=0.214
MSE, mean squared error Std_Eff, standardized effect; CI, confidence interval

Appendix A PRISMA Statement Checklist 2020

Section and Topic	Item #	Checklist item	Location where item is reported
		TITLE	
Title	1	Identify the report as a literature review.	Page 1 of the main manuscript
		ABSTRACT	
Abstract	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings. See the PRISMA 2020 for Abstracts checklist for the complete list.	Page 2 of the main manuscript
		INTRODUCTION	
Rationale	3	Describe the rationale for the review in the context of existing knowledge, i.e., what is already known about your topic.	Page 3 of the main manuscript
Objectives	4	Provide an explicit statement of the objective (s) or question (s) the review addresses with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 3 of the main manuscript
		METHODS	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses with study characteristics (e.g., PICOS, length of follow up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 4 of the main manuscript
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4 of the main manuscript
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4 of the main manuscript

(*Contd...*)

Appendix A (*Continued*)

Section and Topic	Item #	Checklist item	Location where item is reported
Selection process	8	State the process for selecting studies (i.e., screening, eligibility). Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4 of the main manuscript
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool (s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 4 and 5 of the main manuscript
		RESULTS	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure S1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure S1
Study characteristics	17	Cite each included study and present its characteristics (e.g., study size, PICOS, follow up period).	Pages 5-6 of the main manuscript, Table S1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Pages 7-8 of the main manuscript, Suppl. Figures S2-S5, Suppl. Tables S4-S5
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimates and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Pages 6-7 of the main manuscript, Figures 1-4 and Suppl. Tables S1-S5
		DISCUSSION	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 8-9 of the main manuscript
	23b	Discuss any limitations of the evidence included in the review.	Pages 9-10 of the main manuscript
	23c	Discuss any limitations of the review processes used.	Pages 9-10 of the main manuscript
	23d	Discuss implications of the results for practice, policy, and future research.	Page 10 of the main manuscript
		OTHER INFORMATION	
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 11 of the main manuscript
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 11 of the main manuscript
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 11 of the main manuscript
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 11 of the main manuscript
Competing interests	26	Declare any competing interests of review authors.	Page 11 of the main manuscript
Availability of data, code, and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 11 of the main manuscript

Adapted from: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.doi: 10.1136/bmj.n71