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Early vs Interval Appendectomy in Children With Complicated Appendicitis: A Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Non.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 October 2025 and was last updated on 22 October 2025.

INTRODUCTION

Review question / Objective To evaluate whether early appendectomy (EA) or initial non-operative management (NOM) with planned interval appendectomy (IA) leads to superior outcomes in children with complicated appendicitis, and whether the optimal approach depends on the presentation phenotype (appendiceal abscess/phlegmon vs diffuse perforation without abscess).

Rationale The timing of appendectomy in pediatric complicated appendicitis is controversial due to conflicting evidence in the literature. Previous studies that pooled different patient phenotypes (e.g. abscess/phlegmon vs diffuse peritonitis) have reported contradictory results. Notably, one randomized trial focusing on abscess/phlegmon cases found that initial non-operative treatment yielded outcomes similar or superior to early surgery, whereas another trial in diffuse perforation cases favored immediate appendectomy. These divergent findings imply that the optimal management may vary by clinical presentation, prompting this meta-analysis to synthesize the evidence and clarify the best approach for each subgroup.

Condition being studied Pediatric complicated appendicitis, defined as acute appendicitis with perforation leading to an abscess, phlegmon, or diffuse peritonitis. This condition represents a severe form of appendicitis in children, often requiring individualized management strategies.

METHODS

Search strategy The search strategy will utilize both controlled vocabulary and free-text keywords related to appendicitis and its complications (e.g., terms for perforated appendicitis, abscess, phlegmon) as well as terms for treatment timing (early appendectomy, interval appendectomy) in pediatric populations. The search will cover studies published from January 1995 through August

2025, ensuring a comprehensive capture of relevant literature.

Participant or population The review will focus on children (under 18 years of age) with complicated appendicitis. This includes pediatric patients who have perforated appendicitis accompanied by an abscess or phlegmon, or those with diffuse peritonitis resulting from appendiceal perforation.

Intervention Early appendectomy (EA) – prompt surgical removal of the appendix during the initial hospitalization for complicated appendicitis. In practice, this means an appendectomy performed as an emergency or urgent procedure soon after diagnosis, within the index admission.

Comparator Initial non-operative management (NOM) – treatment with antibiotic therapy (with or without percutaneous abscess drainage) during the initial presentation, followed by a planned interval appendectomy (IA) several weeks later after the acute infection has subsided. This two-stage approach allows the immediate inflammation to be controlled medically, with the appendectomy performed electively typically about 6–8 weeks after the initial episode.

Study designs to be included The review will include randomized controlled trials (RCTs) and comparative observational studies (such as prospective or retrospective cohort studies) that directly compare early appendectomy versus interval appendectomy in the target pediatric population. Case series or other non-comparative designs will not be included.

Eligibility criteria *Inclusion criteria: Studies involving pediatric patients (< 18 years) with complicated appendicitis that compare outcomes between early appendectomy and initial non-operative management with subsequent interval appendectomy.

*Exclusion criteria: Studies focusing solely on adult populations, single-arm or non-comparative case series/reports, and studies without extractable outcome data for the comparison of interest.

Information sources We will search multiple electronic databases, including PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL), for relevant studies from January 1995 to August 2025. In addition, the reference lists of relevant articles and prior reviews will be screened to identify any further eligible studies not captured by the database searches.

Main outcome(s) The primary outcome is the overall complication rate – defined as the occurrence of any post-treatment complication (a composite of clinically significant adverse events as reported in the individual studies).

Additional outcome(s) Secondary outcomes include: wound infection rates; intra-abdominal abscess formation after initial treatment; length of hospital stay (both the initial hospitalization and the total length of stay including any readmissions); unplanned readmissions; failure of initial NOM (i.e. the need for unplanned "rescue" appendectomy during the index admission); and the incidence of recurrent appendicitis in cases where an interval appendectomy was not performed.

Quality assessment / Risk of bias analysis Two reviewers will independently assess the risk of bias of each included study using appropriate standardized tools. For randomized trials, the Cochrane RoB 2 tool will be used, and for non-randomized comparative studies, the ROBINS-I tool will be used. Disagreements between reviewers will be resolved through discussion or by consulting a third reviewer. Additionally, the GRADE approach will be applied to rate the overall certainty of evidence for each key outcome.

Strategy of data synthesis We will perform a quantitative synthesis of data using meta-analysis. A random-effects model will be applied to account for possible between-study heterogeneity. For dichotomous outcomes, pooled risk ratios (or odds ratios, as appropriate) will be calculated using the Mantel–Haenszel method, and for continuous outcomes, pooled mean differences will be calculated using inverse-variance weighting; all pooled estimates will incorporate Knapp–Hartung adjustments for increased robustness in the presence of heterogeneity or a limited number of studies. Statistical heterogeneity will be evaluated with the I^2 statistic, and potential sources of heterogeneity will be explored via the prespecified subgroup analyses and, if data permit, meta-regression analyses (for example, examining effects of age or study design). We will also assess potential publication bias by inspecting funnel plots and using formal tests (e.g., Egger's test) when enough studies are available.

Subgroup analysis Yes – subgroup analyses are planned based on the appendicitis presentation phenotype of the patients. In particular, we will analyze outcomes separately for children who presented with an appendiceal abscess or phlegmon versus those who had a diffuse perforation without abscess. This stratification will

help determine if the relative benefits of early surgery versus interval management differ between children with contained abscess formations and those with more generalized contamination, as suggested by prior evidence.

Sensitivity analysis We will conduct sensitivity analyses to test the robustness of the meta-analysis findings. For example, we will re-run the analyses using an alternative random-effects model estimator (the Hartung–Knapp–Sidik–Jonkman method) to see if the results remain consistent under different statistical assumptions. We will also perform a quantitative bias analysis using E-value calculations, which assesses how strong an unmeasured confounder would need to be to nullify the observed effect sizes, thereby evaluating the robustness of conclusions against potential unmeasured confounding. These analyses will help ensure that the conclusions are not unduly influenced by model choices or residual biases.

Country(ies) involved Taiwan.

Keywords Complicated appendicitis; Early appendectomyInterval appendectomy; Non-operative management; Pediatric surgery; Meta-analy.

Contributions of each author

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