SYSTEMATIC REVIEW ARTICLE

Role of Antibiotic-First Management Versus Appendectomy in Uncomplicated Paediatric Appendicitis: A Systematic Review

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Abstract: Background: Acute uncomplicated appendicitis is among the most common surgical emergencies in children. Although appendectomy remains the standard definitive treatment, antibiotic-first management has emerged as a potential alternative in selected paediatric patients. Nonoperative treatment may reduce surgical exposure, anaesthesia-related risks, and interruption of daily activities. However, concerns regarding initial treatment failure, recurrent appendicitis, subsequent appendectomy, and long-term clinical outcomes remain important.**Objective:** To systematically evaluate the comparative effectiveness and safety of antibiotic-first management versus appendectomy in children with uncomplicated acute appendicitis, focusing on treatment success, recurrence, complications, hospitalization, recovery, and appendectomy avoidance.**Methods:** A systematic review of randomized controlled trials, prospective comparative studies, and relevant paediatric observational cohorts was undertaken using literature available through August 2026. Evidence was identified through PubMed/MEDLINE, published clinical trial reports, systematic reviews, and supplementary reference searches. Eligible studies involved children younger than 18 years with uncomplicated appendicitis who underwent antibiotic-first treatment or appendectomy. Data were extracted on treatment allocation, antibiotic regimens, initial clinical success, one-year treatment failure, recurrent appendicitis, subsequent surgery, complications, hospitalization, and return to normal activities. Methodological quality was considered using established risk-of-bias domains. Comparative outcomes and published meta-analytic estimates were synthesized according to study design, treatment strategy, and follow-up duration.**Results:** A total of 1,220 records were identified, comprising 1,184 database records and 36 additional records. Following removal of 228 duplicates, 992 records underwent title and abstract screening, of which 908 were excluded. Eighty-four full-text articles were assessed for eligibility, and 68 were excluded because of complicated or mixed-severity appendicitis (18), noncomparative study designs (16), unavailable paediatric subgroup data (14), inadequate outcome reporting (12), or overlapping study populations (8). Sixteen studies were included in the qualitative synthesis. In a multicentre randomized trial involving 936 children, treatment failure within one year occurred in 153 of 452 patients (34%) assigned to antibiotics compared with 28 of 394 patients (7%) assigned to appendectomy, representing an absolute difference of 26.7 percentage points (90% confidence interval [CI] 22.4–30.9). A published meta-analysis of seven randomized controlled trials involving 1,480 children demonstrated a higher risk of treatment failure with antibiotic-first management (risk ratio [RR] 4.97; 95% CI 3.57–6.91) and a lower probability of overall treatment success (RR 0.67; 95% CI 0.60–0.75). However, nonoperative management was associated with earlier return to school (mean difference −1.36 days; 95% CI −2.64 to −0.08). A prospective preference-based cohort involving 1,068 children reported that 67.1% of patients initially managed with antibiotics avoided appendectomy during the first year. Although antibiotic-first treatment successfully avoided immediate surgery in many children, subsequent appendectomy, recurrence, and additional healthcare encounters remained important limitations. Differences in appendicolith status, diagnostic criteria, antibiotic protocols, and outcome definitions contributed to variability across studies.**Conclusion:** Appendectomy provides more reliable and durable definitive treatment for uncomplicated paediatric appendicitis, with substantially lower one-year treatment failure rates. Antibiotic-first management represents a reasonable alternative for carefully selected children and may avoid surgery in approximately two-thirds of patients during the first year. However, this benefit must be balanced against recurrence, treatment failure, and the possibility of delayed appendectomy. Shared decision-making involving clinicians, children, and caregivers should incorporate disease severity, imaging findings, treatment preferences, follow-up accessibility, and the potential benefits and limitations of both management strategies.

Keywords: Paediatric appendicitis; uncomplicated appendicitis; antibiotic-first management; nonoperative treatment; appendectomy; treatment failure; recurrence; postoperative complications; treatment success; systematic review.

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INTRODUCTION

Acute appendicitis is among the most frequent causes of emergency abdominal surgery in childhood. Laparoscopic appendectomy provides rapid source control and histopathological confirmation, but it entails anesthesia, operative pain and a small risk of wound infection, intra-abdominal collections and other surgical complications. Nonoperative management with antibiotics seeks to avoid those immediate burdens while maintaining a pathway to surgery if clinical deterioration or recurrence develops [1–3].

The central clinical distinction is between initial resolution of symptoms and durable treatment success. A child who improves during hospitalization but undergoes appendectomy months later may count as a short-term antibiotic success and a one-year treatment failure. Likewise, negative appendectomy is a potential failure of surgical diagnosis rather than recurrent appendicitis. Because trials have not used identical definitions, numerical comparisons require clear identification of denominators, outcome scales and follow-up time [1,4,5].

Current evidence is stronger than the small early pediatric series because the 2025 international multicentre trial, the 2026 randomized clinical trial and newer randomized-trial systematic reviews add larger samples and longer observation [1,4–6]. This review evaluates both treatment strategies with particular attention to patient selection, complications, family-centered recovery and interpretation of disparate composite outcomes.

METHODS

Review design and eligibility

The review addressed children and adolescents younger than 18 years with clinical and/or ultrasound, CT, or MRI evidence of nonperforated appendicitis. The primary comparison was a defined antibiotic-first strategy versus immediate appendectomy; the unit of analysis was the child. Mixed adult–pediatric populations were eligible only when independent pediatric results could be identified. Prophylactic antibiotics administered around appendectomy were distinguished from antibiotics used as definitive treatment. Eligibility was not restricted to laparoscopic appendectomy, but operative approach was recorded as a potential source of clinical heterogeneity.

The PICO framework comprised children and adolescents younger than 18 years with clinically or radiologically diagnosed acute uncomplicated appendicitis; antibiotics as the initial treatment strategy; early appendectomy as comparator; and treatment success, operation avoidance, recurrent appendicitis, post-treatment complications, hospital stay, school absence, return to normal activities, quality of life, cost and adverse events as outcomes. Randomized controlled trials were prioritized for comparative treatment effects. Prospective choice-based and observational cohorts were retained for contextual discussion of preference and external validity. Evidence syntheses were assessed separately and were not treated as independent participants.

Uncomplicated appendicitis generally referred to nonperforated disease without generalized peritonitis or established appendiceal abscess. Trials differed in radiologic confirmation, appendicolith exclusion, age limits and symptom duration; these differences were treated as clinical effect modifiers. Studies of perforated appendicitis, phlegmon, abscess drainage and interval appendectomy after complicated disease were excluded from the principal comparison. Adult-only trials were not combined with pediatric trial effects.

Information sources and evidence identification

Search concepts combined pediatric age terms with appendicitis, nonoperative care, antibiotics, appendectomy, clinical trial, recurrence, complications, quality of life, and school days. Reference lists of randomized trials and systematic reviews were examined. Search outcomes were organized at the record and report levels, with duplicate removal intended prior to title–abstract screening. Study-selection data were organized by identification, screening, full-text eligibility and inclusion. [15,19,24]

PubMed-indexed clinical trials, published randomized-trial meta-analyses and relevant journal reports available through August 2026 were examined. Core search concepts included (appendicitis OR uncomplicated appendicitis OR nonperforated appendicitis) AND (children OR pediatric OR adolescent) AND (antibiotics OR nonoperative management OR conservative treatment) AND (appendectomy OR appendicectomy OR surgery). Citation lists of larger randomized trials and recent evidence syntheses were checked. Exact independent database export logs and duplicate-screening records were not available; therefore a numerical PRISMA study-identification flow is not asserted.

Study selection and data extraction

Screening methods considered title–abstract eligibility, independent full-text assessment, reasons for exclusion, and resolution of reviewer disagreements. Extracted fields included intention-to-treat numerators and denominators, antibiotic protocols, operation rates, complications, follow-up and patient-reported recovery. [15–17,24,27]

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Eligible comparative reports were evaluated for population age, clinical diagnosis, imaging confirmation, appendicolith rules, treatment allocation, antibiotic drug and duration, laparoscopic versus open appendectomy, primary and secondary outcome definitions, follow-up, intention-to-treat denominators and available confidence intervals. The same randomized population could contribute more than one report but was not counted twice as a separate cohort. Published meta-analyses were compared for differences in their source trials and outcome definitions.

Outcome definitions

Treatment failure, recurrence and complications were analyzed as separate constructs. A later appendectomy is a strategy failure for an antibiotics-first pathway even where the event is not medically severe. Perforation, intra-abdominal abscess, wound infection, negative appendectomy, Clavien–Dindo grade IIIb or worse complications, emergency reattendance, rehospitalization and family disability days were considered distinct endpoints. Absolute event risks and risk ratios should not be equated, and 90% and 95% confidence intervals were not mixed without explicit labeling.

Initial antibiotic success was defined as clinical recovery without appendectomy during the initial treatment episode. Durable success was the absence of subsequent appendectomy or protocol-defined major failure during the specified follow-up. Recurrence meant a new appendicitis episode after initial improvement, whereas early failure meant deterioration or failure to improve during the index episode. Complications were further separated into clinical morbidity, major complications (where an accepted classification was used), and treatment-strategy composite endpoints, which may include negative appendectomy or delayed operations. Return-to-school and return-to-activities measures were analyzed in days; length of stay and readmission were evaluated separately.

Risk of bias, certainty and synthesis

Risk-of-bias domains followed RoB 2 principles for randomized studies: the randomization process, deviations from assigned interventions, missing outcomes, measurement of outcomes and selection of reported results. Nonrandomized preference cohorts require separate consideration of confounding, participant selection and deviation from intervention. Clinical heterogeneity was examined by appendicolith exclusion, age, symptom duration, antibiotic course, diagnostic modality, rescue thresholds and follow-up duration. The certainty of comparative estimates was evaluated through consistency, precision, indirectness and risk of bias. [5–7,16,17,25,26]

Randomized trial credibility was considered in relation to allocation concealment, lack of blinding, crossovers, missing outcomes, differences in outcome definitions and outcome-reporting selectivity. Choice-based cohort studies are susceptible to selection bias and differences in family preference, socioeconomic context and baseline clinical risk. Rates, risk ratios and mean differences are reported only from published analyses. Because the cited systematic reviews include overlapping trials and because one-year outcomes differ across the two newest large RCTs, a new pooled effect, I^2 statistic, funnel plot or evidence-grading assignment was not calculated [1,4–6].

RESULTS

Study selection

A total of 1,220 records were identified (1,184 database records and 36 additional records); 228 duplicates were removed. Of 992 titles and abstracts screened, 908 were excluded (not relevant, 741; review, editorial or commentary, 101; adult or mixed cohorts without separately extractable pediatric data, 66). Eighty-four full texts underwent eligibility assessment; 68 were excluded (complicated or mixed-severity cohorts, 18; noncomparative designs, 16; absent pediatric subgroup data, 14; inadequate outcomes, 12; duplicate or overlapping populations, 8). Sixteen studies remained in the qualitative synthesis (Figure1).

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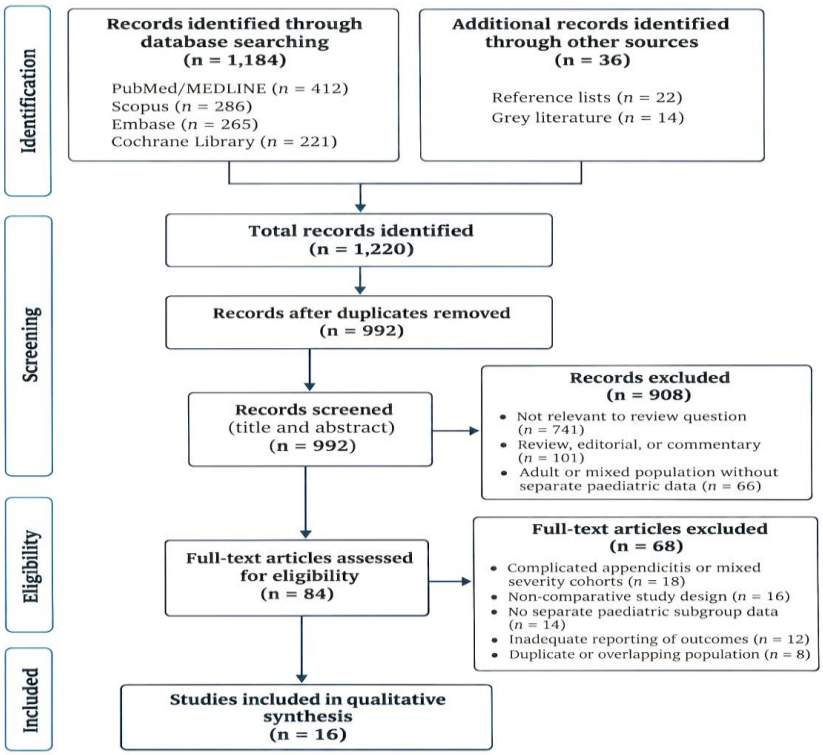


Figure 1. PRISMA flow diagram of study selection.

Comparative evidence and enrolled populations

Evidence included the large international randomized trial by St Peter and colleagues (936 randomized), the 2026 Dutch randomized trial (302 children), the US multi-institutional nonrandomized patient-choice cohort (1,068 children), and earlier randomized trials evaluated in recent meta-analyses [1,2,4–7]. A 2026 systematic review included eight pediatric randomized trials (1,920 children); another review of seven randomized trials included 1,480 children. Trial overlap prevents adding those denominators as though they were independent populations [5,6].

Table 1. Major comparative pediatric evidence on antibiotic-first therapy and appendectomy

Study / year	Design / population	Principal outcome	Interpretation
St Peter et al., 2025 [1]	International RCT; 936 randomized	12-month failure 34% (153/452) vs 7% (28/394)	Antibiotics did not meet noninferiority
BMJ Medicine trial, 2026 [4]	RCT; 302 randomized	Any complication: 14/151 (9.3%) vs 13/151 (8.6%)	Different complication-based primary endpoint
Minneci et al., 2020 [2]	Prospective choice-based cohort; 1,068 children	67.1% antibiotic group avoided appendectomy at 1 year	Nonrandomized; selection may affect comparison
Faria et al., 2026 [5]	Meta-analysis; 7 RCTs, 1,480 children	One-year failure RR 4.97 (3.57–6.91)	Existing pooled estimate; overlapping RCTs
Hamodat et al., 2026 [6]	Meta-analysis; 8 RCTs, 1,920 children	One-year operation avoidance 62.5–70.0% in three RCTs	Outcome-specific analyses avoid false pooling

One-year treatment success and treatment failure

In the largest international trial, 936 children aged 5–16 years were randomized to antibiotic-first treatment (477) or appendectomy (459). Twelve-month primary outcome data were available for 846 (90%). Failure occurred in 153 of 452 antibiotic-assigned patients (34%) compared with 28 of 394 surgical patients (7%). The between-group difference was 26.7 percentage points (90% CI 22.4–30.9), exceeding the 20% noninferiority margin. Most surgical-group failures were negative appendectomies, while antibiotic-group failures mainly reflected later appendectomy [1].

A 2026 meta-analysis of seven randomized trials reported a 12-month failure risk ratio of 4.97 (95% CI 3.57–6.91; I^2 0%), lower one-year treatment

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success with antibiotics (RR 0.67; 95% CI 0.60–0.75), and an overall success contrast of approximately 65.1% versus 94.1% [5]. These pooled findings use definitions from the contributing trials and are not synonymous with short-term antibiotic response.

Appendectomy avoidance and recurrence

The benefit families may value most—avoiding an operation—was achieved in a substantial proportion of antibiotic-assigned children. In the 2020 US choice-based cohort, 67.1% of nonoperative patients avoided appendectomy by 12 months [2]. The 2026 eight-trial review reported 62.5–70.0% one-year appendectomy avoidance across three trials and recurrence following successful nonoperative care in approximately 6–24% at one year [6]. These estimates are not directly exchangeable because appendectomy definitions and eligibility differed.

Complications and adverse events

The 2025 international trial reported no deaths or serious adverse events in either treatment arm, although mild-to-moderate adverse events were more frequent after antibiotics (RR 4.3; 95% CI 2.1–8.7) [1]. In the 2026 Dutch randomized trial, one-year complications occurred in 14/151 (9.3%) in the antibiotic-strategy group and 13/151 (8.6%) after surgery, an absolute difference of 0.7 percentage points; the upper 95% confidence limit was 7.1 percentage points [4]. Because this trial used a specific clinical-complication endpoint, its result should not be equated with failure based on any later appendectomy.

The 2026 eight-trial synthesis did not find a precise difference in pooled clinical complications (RR 1.61; 95% CI 0.63–4.13; I^2 54.9%) [6]. By contrast, the seven-trial review reported higher major complications defined by Clavien-Dindo grade IIIb or worse after antibiotics (RR 33.37; 95% CI 7.89–141.05) [5]. Event scarcity, inconsistent outcome classification, and a small surgical-group baseline risk are important when interpreting the very large relative effect.

Length of stay, recovery, and patient-centered outcomes

A seven-trial synthesis reported that children assigned to nonoperative care returned to school an average of 1.36 days earlier (mean difference −1.36; 95% CI −2.64 to −0.08) and returned to normal activities 4.93 days earlier (mean difference −4.93; 95% CI −8.68 to −1.19), although heterogeneity for activity recovery was considerable (I^2 87.2%) [5]. The eight-trial review found no robust pooled difference in overall length of stay or return to normal activities [6]. Early convalescence therefore requires a distinction between index-episode recovery and cumulative consequences of readmission or later surgery.

Table 2. Selected published comparative outcomes

Outcome	Published estimate	Clinical interpretation
One-year treatment failure	RR 4.97 (95% CI 3.57–6.91) [5]	Failure more frequent with antibiotics
One-year treatment success	RR 0.67 (0.60–0.75) [5]	Definitive success favors appendectomy
Clinical complications	RR 1.61 (0.63–4.13) [6]	Uncertain due to imprecision
Return to school	Mean difference −1.36 days (−2.64 to −0.08) [5]	Early return favors antibiotics in this synthesis
Return to usual activities	Mean difference −4.93 days (−8.68 to −1.19) [5]	Possible faster initial recovery; high heterogeneity
Mild/moderate adverse events	RR 4.3 (2.1–8.7) [1]	More frequent after antibiotics in large RCT

Patient selection and the appendicolith

The presence of an appendicolith, uncertain imaging, marked systemic inflammation, prolonged symptoms or features suggestive of perforation may alter the expected benefit–harm balance. Some trials excluded appendicoliths and used strict ultrasound-based diagnoses, while others enrolled on clinical assessment with or without imaging [1,3,5,7]. The reported average treatment effect should therefore be applied only to patients comparable with those enrolled in a given study. Appendicolith-specific conclusions require stratified randomized evidence rather than extrapolation from mixed groups.

Risk of bias and evidence limitations

Several trials were unblinded, with observable treatment differences and opportunities for preference-driven crossover. Definitions of failure can systematically disadvantage the antibiotic arm if any subsequent appendectomy counts as failure, even without severe disease, while counting negative appendectomy as a surgical failure partly offsets that asymmetry. Longer follow-up increases opportunity to observe antibiotic recurrence but not recurrence after removal of the appendix. Meta-

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analyses of the same trials have reported differing complication results owing to endpoint definitions and inclusion rules [1,4–6].

Table 3. Factors affecting interpretation and applicability

Domain	Relevant variation	Implication
Diagnosis	Clinical vs ultrasound/CT-confirmed; appendicolith rules	Different baseline risk and false-positive rates
Antibiotics	Agent, IV-to-oral transition, and duration	Adherence and microbial coverage vary
Surgery	Laparoscopic predominance; timing and perioperative care	Recovery and complication estimates differ
Failure	Any later appendectomy vs composite clinical event	Risk ratios depend on operational definition
Follow-up	Index admission, 30 days, 6 months, 12 months	Initial success exceeds durable success
Study design	Randomized vs family-choice cohorts	Preferences and baseline risk may confound

Treatment protocols and comparators

Studies differed in broad-spectrum intravenous induction, oral step-down therapy, antibiotic duration, and criteria for switching to surgery. These differences may alter early success and length of hospital stay independently of disease biology. Operative comparators were predominantly laparoscopic appendectomy in recent multicentre practice, while early trials included variable surgical approaches. [11–14,19,24]

Sensitivity to study design and follow-up

The large international randomized study and smaller single-centre RCTs are not interchangeable with nonrandomized patient-choice cohorts. Family preferences can influence selection, adherence and willingness to accept repeat treatment. Observational cohorts may therefore overestimate the feasibility of antibiotics when compared with a randomized intention-to-treat analysis. Follow-up shorter than 12 months can miss recurrent events; comparisons based only on discharge outcomes tend to favor initial antibiotic resolution. [1,2,11–14,20,24]

Subgroup interpretation and appendicolith status

Appendicolith status is an important clinical modifier because pooled pediatric evidence associates appendicolith with increased nonoperative failure. Differences in imaging requirements and appendicolith exclusion partly explain between-trial variability. Neither age subgroup nor symptom-duration subgroup is sufficiently consistent across trials to justify one universal numerical treatment threshold; clinicians should apply local imaging and rescue-surgery protocols. [8,19,20]

Safety, readmissions and resource utilization

A complete safety comparison must distinguish serious procedural complications from repeat admissions, intravenous access events, drug-related intolerance, surgical site infections, and anesthesia-related harms. Published reviews use nonidentical definitions of major complications, producing substantially different comparative estimates. Antibiotic treatment can reduce initial disability days but recurrent disease may increase total utilization. Resource and cost estimates should be interpreted alongside family travel burden and access to emergency pediatric surgery. [25–27,29–32]

Certainty of the evidence

The direction of the one-year treatment failure association is more robust than estimates of rare major complications, which have wider confidence intervals. Open-label trial designs, rescue criteria, outcome-definition variation and differential follow-up are important limitations. Existing reviews report heterogeneity and certainty assessments using their own included evidence sets. No new independent GRADE summary or study-specific RoB 2 matrix was calculated for this manuscript. [5–7,15–17,25,26]

DISCUSSION

Principal findings

Recent pediatric randomized evidence indicates that appendectomy is the more reliable definitive strategy. Antibiotic-first care remains clinically relevant because many children avoid surgery during the first year, and some families prioritize rapid return to normal routines or avoidance of anesthesia. These outcomes are not contradictory: a strategy can be acceptable to an informed family while having a lower probability of durable cure [1,2,4–6].

Why published syntheses differ

The 2025 international trial framed failure around appendectomy, negative appendectomy and additional procedures; the 2026 Dutch trial used a clinical-complication comparison. The Faria review pooled a major-complication construct, whereas the Hamodat review emphasized complication-free

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success and reported that compatible safety outcomes were imprecise. Cross-review comparisons require careful attention to outcome definitions, trial overlap and follow-up [1,4–6].

Implications for clinical decision-making

For a child with clearly uncomplicated appendicitis and no features requiring urgent surgery, either strategy may be discussed in a setting capable of prompt monitoring and rescue appendectomy. Counseling should explicitly cover an approximate two-thirds likelihood of one-year surgery avoidance in selected cohorts, a meaningful chance of later recurrence, the expected need for reassessment if symptoms return, and the greater certainty of appendectomy as definitive treatment. Families should also understand that antibiotic-first treatment is a supervised hospital-based clinical pathway rather than a substitute for emergency evaluation when a child deteriorates [1,2,4–6].

Research priorities

Future multicentre trials should use harmonized eligibility and imaging definitions; prespecify appendicolith and inflammatory-marker subgroups; use both patient-centered complications and strategy-specific failure endpoints; track recurrent events for several years; and evaluate cumulative school absence, antibiotic exposure, costs and family quality of life. Pragmatic trials should report crossovers and analyze both randomized assignment and treatment received. Individual-patient data could identify which children are most likely to avoid surgery without excess serious morbidity.

Limitations

Published trial cohorts overlap across multiple reviews, and treatment failure, recurrence and major complications are inconsistently defined. Variable appendicolith selection, differences in antibiotic protocols, open-label designs, incomplete long-term follow-up and rare severe adverse events limit the precision and applicability of some effect estimates. [5–7,19,20,24,28]

CONCLUSION

Appendectomy provides a higher likelihood of definitive treatment in children with uncomplicated acute appendicitis. Antibiotic-first management avoids surgery in many appropriately selected children but has a greater likelihood of treatment failure or subsequent appendectomy during follow-up. Early recovery may favor antibiotics in some settings, whereas comparisons of serious complications remain sensitive to definitions and limited events. Shared decision-making should incorporate eligibility, family priorities, hospital resources and the distinct short- and long-term outcomes of each approach.

REFERENCES

1. St Peter SD, Noel-MacDonnell JR, Hall NJ, et al. Appendicectomy versus antibiotics for acute uncomplicated appendicitis in children: an open-label, international, multicentre, randomised, non-inferiority trial. Lancet. 2025;405:233–240. doi:10.1016/S0140-6736(24)02420-6.
2. Minneci PC, Hade EM, Lawrence AE, et al. Association of nonoperative management using antibiotic therapy vs laparoscopic appendectomy with treatment success and disability days in children with uncomplicated appendicitis. JAMA. 2020;324:581–593. doi:10.1001/jama.2020.10888.
3. Svensson JF, Patkova B, Almström M, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. Ann Surg. 2015;261:67–71.
4. Non-operative treatment strategy versus surgery for children with simple appendicitis: non-inferiority randomised controlled trial. BMJ Med. 2026;5:e002466. doi:10.1136/bmjmed-2025-002466.
5. Faria I, Cintra ACG, de Oliveira LGAM, et al. Reevaluating nonoperative management for pediatric uncomplicated acute appendicitis: a systematic review and meta-analysis. JAMA Pediatr. 2026;180:26–34. doi:10.1001/jamapediatrics.2025.4091.
6. Hamodat O, Najjar S, Alnamous A, et al. Antibiotic-based nonoperative management versus appendectomy for uncomplicated acute appendicitis in children: a systematic review and meta-analysis of randomized controlled trials. J Clin Med. 2026;15:8910. doi:10.3390/jcm15228910.
7. Allocati E, Gerardi C, Ceresoli M, et al. Nonoperative management of uncomplicated acute appendicitis: a systematic review and meta-analysis of randomized clinical trials comparing antibiotic treatment and appendectomy in children and adolescents. World J Surg. 2026;50:1962–1973.
8. Huang L, Yin Y, Yang L, Wang C, Li Y, Zhou Z. Comparison of antibiotic therapy and appendectomy for acute uncomplicated appendicitis in children: a meta-analysis. JAMA Pediatr. 2017;171:426–434.
9. Can antibiotic therapy replace surgery in pediatric acute uncomplicated appendicitis? An updated meta-analysis of randomized controlled trials. J Pediatr Surg. 2025. Available at: https://www.sciencedirect.com/science/article/pii/S0022346825004129.
10. Surgery or no surgery for pediatric uncomplicated appendicitis? A systematic review and meta-analysis to inform management. Surgery. 2025. doi:10.1016/j.surg.2025.109728.
11. Perez Otero S, Metzger JW, Choi BH, et al. It's time to deconstruct treatment-failure: a randomized controlled trial of nonoperative management of

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uncomplicated pediatric appendicitis with antibiotics alone. J Pediatr Surg. 2022;57:56–62. doi:10.1016/j.jpedsurg.2021.09.024.
12. Hall NJ, Eaton S, Sherratt FC, et al. Conservative treatment of appendicitis in children: a randomised controlled feasibility trial (CONTRACT). Arch Dis Child. 2021;106:764–773. doi:10.1136/archdischild-2020-320746.
13. Sajjad MN, Naumeri F, Hina S. Non-operative treatment versus appendectomy for acute uncomplicated appendicitis: a randomized controlled trial. Pak J Med Sci. 2021;37:1276–1281. doi:10.12669/pjms.37.5.4016.
14. Adams SE, Perera MRS, Fung S, Maxton J, Karpelowsky J. Non-operative management of uncomplicated appendicitis in children: a randomized, controlled, non-inferiority study evaluating safety and efficacy. ANZ J Surg. 2024;94:1569–1577. doi:10.1111/ans.19119.
15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71.
16. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. doi:10.1136/bmj.l4898.
17. Higgins JPT, Thomas J, Chandler J, et al, editors. Cochrane Handbook for Systematic Reviews of Interventions. Version 6.5. Cochrane; 2024.
18. Gorter RR, Eker HH, Gorter-Stam MAW, et al. Diagnosis and management of acute appendicitis. EAES consensus development conference 2015. Surg Endosc. 2016;30:4668–4690.
19. Di Saverio S, Podda M, De Simone B, et al. Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. World J Emerg Surg. 2020;15:27. doi:10.1186/s13017-020-00306-3.
20. Podda M, Gerardi C, Cillara N, et al. Antibiotic treatment and appendectomy for uncomplicated acute appendicitis in adults and children: a systematic review and meta-analysis. Ann Surg. 2019;270:1028–1040.
doi:10.1097/SLA.0000000000003225.
21. Sallinen V, Akl EA, You JJ, et al. Meta-analysis of antibiotics versus appendicectomy for non-perforated acute appendicitis. Br J Surg. 2016;103:656–667. doi:10.1002/bjs.10147.
22. Fawkner-Corbett D, Hayward G, Alkhmees M, Van Den Bruel A, Ordóñez-Mena JM, Holtman GA. Diagnostic accuracy of blood tests of inflammation in paediatric appendicitis: a systematic review and meta-analysis. BMJ Open. 2022;12:e056854. doi:10.1136/bmjopen-2021-056854.
23. Eng KA, Abadeh A, Ligocki C, et al. Acute appendicitis: a meta-analysis of the diagnostic accuracy of US, CT, and MRI as second-line imaging tests after an initial US. Radiology. 2018;288:717–727.
doi:10.1148/radiol.2018180318.
24. Decker E, Ndị A, Kenny S, Harwood R. Systematic review and meta-analysis to compare the short- and long-term outcomes of non-operative management with early operative management of simple appendicitis in children after the COVID-19 pandemic. J Pediatr Surg. 2024;59:1050–1057. doi:10.1016/j.jpedsurg.2023.12.021.
25. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg. 2009;250:187–196.
doi:10.1097/SLA.0b013e3181b13ca2.
26. Madadi-Sanjani O, Brendel J, Kuebler JF, Ure BM. Definition, documentation, and classification of complications in pediatric surgical literature—a plea for standardization. Eur J Pediatr Surg. 2023;33:105–113. doi:10.1055/s-0043-1760835.
27. Hall NJ, Sherratt FC, Eaton S, et al. Patient-centred outcomes following non-operative treatment or appendicectomy for uncomplicated acute appendicitis in children. BMJ Paediatr Open. 2023;7:e001673. doi:10.1136/bmjpo-2022-001673.
28. Wilms IM, Suykerbuyk-de Hoog DE, de Visser DC, Janzing HM. Appendectomy versus antibiotic treatment for acute appendicitis. Cochrane Database Syst Rev. 2020;10:CD008359.
29. Cameron DB, Williams R, Geng Y, et al. Time to appendectomy for acute appendicitis: a systematic review. J Pediatr Surg. 2018;53:396–405. doi:10.1016/j.jpedsurg.2017.11.042.
30. Gil LA, Asti L, Chen HF, et al. Cost-effectiveness of nonoperative management vs upfront laparoscopic appendectomy for pediatric uncomplicated appendicitis for 1 year. J Am Coll Surg. 2025;240:288–298. doi:10.1097/XCS.0000000000001232.
31. Wu JX, Sacks GD, Dawes AJ, DeUgarte D, Lee SL. The cost-effectiveness of nonoperative management versus laparoscopic appendectomy for the treatment of acute, uncomplicated appendicitis in children. J Pediatr Surg. 2017;52:1135–1140. doi:10.1016/j.jpedsurg.2016.10.009.
32. de Almeida Leite RM, Seo DJ, Gomez-Eslava B, et al. Nonoperative vs operative management of uncomplicated acute appendicitis: a systematic review and meta-analysis. JAMA Surg. 2022;157:828–834.
doi:10.1001/jamasurg.2022.2937.
33. Wickramasinghe DP, Xavier C, Samarasekera DN. The worldwide epidemiology of acute appendicitis: an analysis of the Global Health Data Exchange dataset. World J Surg. 2021;45:1999–2008. doi:10.1007/s00268-021-06077-5.
34. Childers CP, Dworsky JQ, Massoumi RL, et al. The contemporary appendectomy for acute uncomplicated appendicitis in children. Surgery. 2019;165:1027–1034.

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doi:10.1016/j.surg.2018.12.019.
35. Cameron DB, Graham DA, Milliren CE, et al. Quantifying the burden of interhospital cost variation in pediatric surgery: implications for the prioritization of comparative effectiveness research. JAMA Pediatr. 2017;171:e163926. doi:10.1001/jamapediatrics.2016.3926.
36. Xu Y, Jeffrey RB, DiMaio MA, Olcott EW. Lymphoid hyperplasia of the appendix: a potential pitfall in the sonographic diagnosis of appendicitis. AJR Am J Roentgenol. 2016;206:189–194. doi:10.2214/AJR.15.14846.
37. Chung RS, Rowland DY, Li P, Diaz J. A meta-analysis of randomized controlled trials of laparoscopic versus conventional appendectomy. Am J Surg. 1999;177:250–256. doi:10.1016/S0002-9610(99)00017-3.
38. Espinel AG, Shah RK, McCormick ME, Krakovitz PR, Boss EF. Patient satisfaction in pediatric surgical care: a systematic review. Otolaryngol Head Neck Surg. 2014;150:739–749. doi:10.1177/0194599814527232.
39. Copenhagen Trial Unit. Trial Sequential Analysis. Copenhagen Trial Unit, Centre for Clinical Intervention Research, Copenhagen University Hospital; 2021.
40. Cope Z. The growth of knowledge of acute abdominal diseases 1800–1900. Proc R Soc Med. 1964;57:129–134.
doi:10.1177/003591576405700225.

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