

Single-Dose Versus Prolonged or no Antibiotic Prophylaxis for Surgical Site Infection after Adult Appendectomy: A Systematic Review

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Abstract Background: Surgical site infection (SSI) remains a common complication following appendectomy. Although preoperative antibiotic prophylaxis is routinely recommended, it remains unclear whether continuing antibiotics postoperatively reduces SSI beyond a single preoperative dose, or whether prophylaxis can be omitted in low-risk patients, particularly in uncomplicated (non-perforated) appendicitis, where postoperative antibiotics serve no therapeutic role. This systematic review compared these strategies for preventing SSI in adults undergoing appendectomy. **Methods:** A systematic search of PubMed, Web of Science, the Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar was performed for studies published between January 2015 and December 2025. Studies involving adult patients undergoing open or laparoscopic appendectomy that evaluated preoperative antibiotic prophylaxis and reported SSI outcomes were eligible for inclusion. Randomized controlled trials and observational studies were included, whereas pediatric studies, case reports, editorials, conference abstracts, and studies evaluating antibiotics solely for therapeutic purposes were excluded. The review followed PRISMA 2020 guidelines. Risk of bias was assessed using RoB 2 for randomized trials, ROBINS-I for non-randomized studies, and the Newcastle–Ottawa Scale for cohort studies. Owing to heterogeneity in antibiotic regimens, comparators, and study designs, findings were synthesized narratively. The protocol was not registered. **Results:** Thirteen studies met the inclusion criteria. Given clinical and methodological heterogeneity, no meta-analysis was performed. Ten studies compared single-dose preoperative prophylaxis with prolonged postoperative antibiotic regimens, while three evaluated prophylaxis versus no prophylaxis in selected patient populations. Across studies, extending antibiotics into the postoperative period did not result in a consistent reduction in SSI compared with a single preoperative dose, irrespective of operative approach. Several studies reported increased healthcare costs, longer hospital stay, or greater antibiotic exposure with prolonged regimens. In the three studies evaluating omission of prophylaxis, all in highly selected populations, SSI rates did not differ significantly with or without prophylaxis; however, event numbers were small and the findings are not generalizable. **Conclusions:** In adults with uncomplicated or non-perforated appendicitis, limited evidence of variable quality suggests that a single preoperative dose may be adequate, as postoperative continuation did not consistently reduce SSI and may increase unnecessary antibiotic use. These findings should not be extrapolated to complicated appendicitis, and evidence supporting omission of prophylaxis is restricted to highly selected low-risk patients.

Key Words Appendectomy, Antibiotic Prophylaxis, Preoperative Antibiotics, Surgical Site Infection, Uncomplicated Appendicitis, Adult

INTRODUCTION

Appendectomy remains one of the most commonly performed emergency general surgical procedures

worldwide with an estimated lifetime risk of acute appendicitis of approximately 7–8% [1]. Despite advances

in operative technique and perioperative care, surgical site infection (SSI) remains one of the most common complications after appendectomy, with reported rates varying widely between studies and settings [2, 3]. SSIs following appendectomy are associated with prolonged hospital stay, increased readmission and reintervention rates, higher healthcare costs, and impaired patient quality of life [3].

The risk of postoperative infection is principally driven by bacterial contamination from the inflamed appendix and enteric flora, which provides a clear biological rationale for perioperative antimicrobial prophylaxis [4]. Although preoperative antibiotic administration has been shown to reduce wound infection rates in numerous trials and cohort studies, substantial heterogeneity exists in clinical practice regarding agent selection, dosing, timing, and duration of therapy [5, 6]. Some centres advocate a single preoperative dose while others favour extended postoperative courses, a variation that reflects both gaps in the evidence base and concerns about antimicrobial stewardship and emergent resistance [7].

The increasing adoption of laparoscopic appendectomy has further influenced SSI incidence and prophylactic considerations. Laparoscopy typically confers lower superficial wound infection rates than open approaches due to reduced tissue trauma and exposure; however, the core principles of antibiotic prophylaxis, including reducing bacterial inoculum and preventing contamination-related infection, remain applicable across operative modalities [8, 9]. The benefit of prophylactic antibiotics over no prophylaxis in appendectomy has been established by earlier evidence syntheses, most notably a Cochrane review demonstrating reduced wound infection and intra-abdominal abscess rates with prophylaxis [10]. For complicated appendicitis, in which postoperative antibiotics are given as treatment rather than prophylaxis, randomized trials have shown that short postoperative courses are as effective as longer ones [11, 12]. In contrast, in uncomplicated (non-perforated) appendicitis, the source of infection is removed at surgery and postoperative antibiotics serve no therapeutic purpose. In this setting, whether any postoperative continuation adds benefit beyond a single preoperative dose has been examined mainly in small individual trials and cohort studies, many published after the earlier reviews. More recently, several studies have also questioned whether prophylaxis is needed at all in highly selected low-risk patients. An updated synthesis of the evidence from the past decade, focusing on the duration of prophylaxis in adults rather than on its presence or absence, is therefore needed. Given the high global caseload of appendectomies and the largely preventable nature of many SSIs, a rigorous synthesis of the evidence regarding preoperative prophylactic antibiotics is necessary to inform practice, optimise patient outcomes, and promote prudent antibiotic use. Accordingly, this systematic review aimed to compare single-dose preoperative antibiotic prophylaxis with prolonged postoperative regimens for preventing surgical site infection

after appendectomy in adults, and to examine the evidence on omission of prophylaxis in selected low-risk patients.

METHODS

Search Strategy and Study Selection

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. Briefly, we searched PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and Google Scholar for studies published between 1 January 2015 and 31 December 2025, using combinations of terms related to adult patients, appendectomy, preoperative antibiotic prophylaxis and surgical site infection. These databases were selected to provide complementary coverage: PubMed for the core biomedical literature indexed in MEDLINE, CENTRAL for randomized and controlled trials, Web of Science for broad multidisciplinary coverage, and Google Scholar to capture studies published in regional journals that may not be indexed in the major databases. The full search strategies for each database are presented in the Supplementary Data 1.

Titles and abstracts were screened independently by two reviewers (TA and DA) to exclude irrelevant records. Full-text articles were then retrieved and assessed independently by the same two reviewers against the predefined eligibility criteria. Disagreements at either stage were resolved by discussion or by consultation with a third reviewer (AA). Screening was managed using EndNote.

Eligibility Criteria

We included studies of adult patients undergoing appendectomy (open or laparoscopic) that evaluated preoperative prophylactic antibiotics and reported surgical site infection outcomes. Eligible designs comprised randomized controlled trials, non-randomized comparative studies, cohort studies, and case-control studies. Systematic reviews and meta-analyses were not included as sources of data; however, their reference lists were screened to identify additional eligible primary studies. No additional eligible studies were identified through this process. Studies exclusively involving pediatric populations, those using antibiotics solely for therapeutic (rather than prophylactic) purposes, case reports, editorials, commentaries, conference abstracts without full text and non-English language publications were excluded.

Outcome Definition

The primary outcome was surgical site infection (SSI). SSI was accepted as defined by the individual studies, whether based on the Centers for Disease Control and Prevention (CDC) criteria, a wound grading system such as the Southampton wound score, or clinical diagnosis. All SSI types (superficial incisional, deep incisional, and organ/space) were eligible; when studies reported SSI types separately, the total number of SSIs was used where available. Because definitions and follow-up periods varied,

studies were considered comparable for narrative synthesis but not for statistical pooling, and the definition used by each study is reported in Table 1. Secondary outcomes, where reported, included length of hospital stay, antibiotic-related adverse events, and treatment costs.

Data Extraction

A standardised data extraction form was used to collect the following items: (1) study characteristics, including first author, publication year, country, and study design; (2) participant characteristics, including sample size in each intervention and comparator group, age, sex, and appendicitis severity (uncomplicated/non-perforated, complicated, or chronic); (3) operative approach (open or laparoscopic); (4) intervention and comparator details, including antibiotic agent(s), dose, route, timing of the preoperative dose relative to incision, and the number of doses and duration of any postoperative antibiotics; (5) outcome data, including the SSI definition or classification used, type of SSI (superficial, deep, or organ/space), number of SSI events in each group, reported effect estimates with 95% confidence intervals and P values, and the duration and method of SSI follow-up; and (6) secondary outcomes where reported, including length of hospital stay, antibiotic-related adverse events, and costs. Where multiple publications reported on the same study population, these were assessed for additional information and presented as a single study. Data were extracted independently by two reviewers (TA and DA) using this form, and discrepancies were resolved by discussion.

Risk of Bias Assessment

Randomized trials were assessed with RoB 2 [13], covering the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each study was judged as having low risk of bias, some concerns, or high risk of bias. The non-randomized comparative study was assessed with ROBINS-I [14], covering confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. The study was judged at low, moderate, serious, or critical risk of bias overall. Overall risk-of-bias judgements were derived using the algorithms recommended in the RoB 2 and ROBINS-I guidance [13, 14].

As for cohort studies, they were assessed with the Newcastle-Ottawa Scale [15], which allocates up to four stars for selection, two for comparability, and three for outcome (maximum nine). Star ratings were converted to good, fair, or poor quality using AHRQ thresholds [16]. Two reviewers (TA and DA) independently assessed risk of bias, with disagreements resolved by discussion. Tools were selected according to study design.

Data Synthesis

A meta-analysis was considered but not performed because of substantial clinical and methodological heterogeneity across the included studies. Specifically, the studies differed

in (1) antibiotic agents, including five different cephalosporins and co-amoxiclav-based regimens; (2) comparator regimens, which ranged from a single additional postoperative dose to a 5-day course, and in three studies no prophylaxis or placebo; (3) study populations, which included non-perforated, mixed-severity, and chronic appendicitis; (4) study designs, which included randomized trials, cohort studies, and a non-randomized comparative study; and (5) SSI definitions and follow-up methods. These differences are detailed in Table 1. Pooling such heterogeneous comparisons into a single estimate was judged likely to be misleading. A structured narrative synthesis was therefore performed in accordance with the Synthesis Without Meta-analysis (SWiM) reporting guideline [17]. Studies were grouped first by comparison (prophylaxis versus no prophylaxis; single-dose versus prolonged regimens) and then by operative approach (open versus laparoscopic). Within each group, findings were summarized according to the direction and magnitude of the difference in SSI rates, together with effect estimates and 95% confidence intervals where reported, rather than on statistical significance alone. Where studies differed in the direction or magnitude of effect, we examined whether the differences could be explained by population, operative approach, antibiotic regimen, study design, or risk of bias. For consistency across studies, risk ratios (RRs) with 95% confidence intervals were calculated from the reported event counts; effect estimates reported by the original authors are presented separately in Table 2.

RESULTS

Study Selection

The database searches identified 707 records, of which 215 duplicates were removed. Of the 492 records screened by title and abstract, 329 were excluded, and 163 reports were sought for full-text retrieval. Of these, 51 could not be retrieved or were unavailable as full English-language publications, and 112 were assessed for eligibility. After excluding 99 reports (reasons shown in Figure 1), 13 studies were included in the review (Figure 1).

Study Characteristics

The 13 included studies [3-5,7,9,18-23] comprised ten randomized controlled trials, two cohort studies (one prospective and one retrospective), and one retrospective non-randomized comparative study. The studies were conducted across nine countries, including Iran, Nigeria, Spain, South Korea, Saudi Arabia, India, China, Pakistan, and Iraq. Most studies compared single-dose preoperative antibiotic prophylaxis with multiple-dose or postoperative antibiotic regimens, whereas a smaller number evaluated no-antibiotic strategies. The most frequently investigated prophylactic regimens consisted of cephalosporins combined with metronidazole, including cefazolin, cefuroxime, cefotaxime, ceftriaxone, and cefmetazole, as well as co-amoxiclav-based regimens. Antibiotics were generally administered intravenously within 30–60 minutes before skin incision or at induction of anesthesia.

Among the included studies, six evaluated laparoscopic appendectomies, six evaluated open appendectomies, and one included both surgical approaches. The mean participant age ranged from approximately 20.6 to 37.5 years. Sex distribution was reported in most studies and was generally balanced, with male participants comprising 27.4%–69.0% of the study populations. Most studies enrolled adults with uncomplicated or non-perforated appendicitis, while one study included patients with mixed appendicitis severity and another evaluated elective laparoscopic appendectomy for chronic appendicitis. Most studies assessed outcomes over a 30-day postoperative follow-up period using outpatient visits, hospital record review, telephone follow-up, or combinations of these methods, with several also performing evaluations at 48 hours, 72 hours, and 7 days. The characteristics of the included studies are summarized in Table 1.

Of the ten randomized controlled trials, nine were judged to have some concerns and one (Rafiq *et al.* [18]) to be at high risk of bias (Figure 2). Some concerns arose most often in the randomization process (eight trials), deviations from intended interventions (seven trials), measurement of the outcome (six trials), and selection of the reported result (eight trials). These reflected mainly insufficient reporting of allocation concealment, lack of blinding of participants and personnel, unblinded assessment of SSI, a partly subjective outcome, and the absence of a pre-specified protocol or analysis plan, respectively. Rafiq *et al.* was judged at high risk of bias because of deviations from the intended interventions and unblinded outcome assessment (domains 2 and 4). The non-randomized study [25] was judged at serious risk of bias using ROBINS-I because of confounding (Figure 3), as treatment allocation was determined retrospectively and baseline differences between groups were not adjusted for. Both cohort studies were of good methodological quality, with NOS scores of 9/9 [9] and 8/9 [24] (Table 3). When the two studies at high or serious risk of bias were set aside, the overall pattern of findings did not change: none of the remaining eight single-dose versus prolonged comparisons found a statistically significant difference in SSI, and their point estimates continued to fall on both sides of no effect.

Preoperative Antibiotic Prophylaxis Versus no Prophylaxis or Placebo

Three studies [9,20,21] evaluated whether prophylactic antibiotics could be omitted in selected appendectomy populations. SSI rates were low in all three, and none found a statistically significant difference between patients who did and did not receive prophylaxis; however, confidence intervals were wide, and the findings are limited to carefully selected patient populations.

Sánchez-Santana *et al.* reported SSI rates of 4.4% in patients who received prophylaxis and 5.2% in those with no prophylaxis recorded (RR 0.66, 95% CI 0.25–1.57; $p>0.05$) [9]. However, the authors attributed the absence of prophylaxis mainly to missing documentation rather than to

true omission, so this comparison may not reflect patients who genuinely received no prophylaxis. Dai *et al.* reported SSI rates of 5.8% with a single prophylactic dose and 5.6% with placebo in patients undergoing elective laparoscopic appendectomy for chronic appendicitis (OR 1.00, 95% CI 0.20–5.40; $p = 0.96$); with only six events in total, this trial could not exclude a clinically important effect in either direction [21]. He *et al.* reported infection rates of 0.6%, 0.7%, and 0.8% with no antibiotics, a single preoperative dose, and a 3-day regimen, respectively, following uncomplicated laparoscopic appendectomy ($p = 0.992$); the very low event rates limit the ability to detect small differences [20].

Single-Dose Preoperative Prophylaxis Versus Prolonged Antibiotic Regimens

Ten studies [3–5,7,18,19,22–25] compared single-dose preoperative prophylaxis with multiple-dose or postoperative antibiotic regimens. In all ten, patients had non-perforated or uncomplicated appendicitis, so postoperative antibiotics served as extended prophylaxis rather than as treatment of established infection; studies of therapeutic antibiotics for complicated appendicitis were excluded from this review. The duration of postoperative administration was 24 hours or less in eight studies [3,7,18,19,23,25] and longer than 24 hours in two, extending until discharge (mean 1.6 days) [24] or for 5 days orally [22]. None of the studies found a statistically significant difference in SSI between single-dose and extended regimens. However, most studies were small with few events, and the 95% confidence intervals were wide (Table 2), so these results cannot exclude a clinically relevant benefit or harm of extended administration. The direction of effect was also inconsistent, with point estimates favouring the single-dose regimen in some studies and the extended regimen in others.

Among the six studies of open appendectomy, none found a statistically significant difference in SSI. Hosseini Khalifani *et al.* reported SSI rates of 5.9% with a single preoperative dose of cefazolin plus metronidazole and 3.8% with a four-dose 24-hour regimen ($p = 0.425$; RR 1.55, 95% CI 0.55–4.35), a difference that numerically favoured the extended regimen [3]. Brothor *et al.* reported SSI rates of 3.5% and 3.0% with single-dose and three-dose cefuroxime plus metronidazole, with one event in each group, while adverse events and treatment costs were greater in the multiple-dose group [7]. Shirah and Shirah, Rafiq *et al.*, Sadraei-Moosavi *et al.*, and Alammari *et al.* reported SSI rates of 7.2% vs 8.2%, 7.8% vs 9.1%, 1.3% vs 1.3%, and 6.7% vs 6.7% with single-dose and postoperative regimens, respectively; none of these differences was statistically significant [4,5,18,23]. Rafiq *et al.* additionally reported a significantly longer hospital stay among patients receiving postoperative antibiotics [18].

Among the four studies of laparoscopic appendectomy, none found a statistically significant difference in SSI. Choi *et al.* reported SSI rates of 4.0 and 6.0% in the single-dose

Table 1: Characteristics of the Included Studies

Author, year	Study design	Sample size, n (I / C)	Appendectomy type	Appendicitis severity	Antibiotic regimen	Comparison	SSI definition; follow-up
Hosseini Khalifani <i>et al.</i> [8]	RCT (double-blind)	136 / 158	Open (laparotomy)	Non-complicated suppurative appendicitis	Cefazolin 1 g + metronidazole 500 mg, IV, ~30 min pre-op	Single dose vs + 3 postop doses q6h (4 doses/24 h)	Clinical + pathological; 1 month
Brotobor <i>et al.</i> [7]	RCT	29 / 33	Open appendectomy (Lanz incision)	Uncomplicated (non-gangrenous, non-perforated)	Cefuroxime 1.5 g + metronidazole 500 mg, IV, at induction	Single dose vs + 2 postop doses at 8 h and 16 h	CDC; 30 days
Sánchez-Santana <i>et al.</i> [9]	Prospective cohort	664 / 266	Open (89%), Laparoscopic (10%), Abscess drainage (1%)	Mixed (all appendicitis types)	Amoxicillin-clavulanate 2 g (metronidazole + gentamicin if allergic), IV, 30–60 min pre-op	Prophylaxis vs no prophylaxis recorded	CDC; 30 days
Choi <i>et al.</i> [24]	Retrospective cohort	99 / 50	Laparoscopic (3-port technique)	Uncomplicated non-perforated (CT-confirmed)	2nd-generation cephalosporin (mainly cefbuperazone; dose NR), IV, median 53 min pre-op	Single dose vs continued postop until discharge (mean 1.6 days)	CDC; NR
Shirah and Shirah, [25]	Retrospective non-randomized comparative	237 / 245	Open appendectomy (grid-iron incision)	Non-perforated acute appendicitis	Cefazolin 1 g + metronidazole 500 mg, IV, 1 h pre-op	Single dose vs + 3 postop doses q8h	Clinical; 1 month
Rajput and Saxena, [23]	RCT	50 / 50	Laparoscopic appendectomy	Non-perforated appendicitis	Ceftriaxone 1 g + metronidazole 500 mg, IV, at induction	Single dose vs continued up to 24 h postop	Southampton score; 30 days
Bangaru <i>et al.</i> [22]	RCT	80 / 82	Laparoscopic (3-port technique)	Uncomplicated non-perforated acute appendicitis	Cefotaxime 1 g + metronidazole 500 mg, IV, 30 min pre-incision	Single dose vs + 1 IV dose, then oral antibiotics for 5 days	CDC; ≥30 days
Meena [19]	RCT	26 / 26	Laparoscopic appendectomy	Non-perforated appendicitis	Cefotaxime 1 g + metronidazole 100 mL, IV, at induction	Single dose vs + 3 postop doses at 8, 16, and 24 h	Southampton score; 7 days
He <i>et al.</i> [20]	RCT (single-center)	156 / 143 / 138 ^c	Laparoscopic appendectomy	Uncomplicated acute appendicitis (CT-confirmed)	Cefmetazole 1 g, IV, 30 min pre-incision	No antibiotics vs single dose vs single dose + 3 days postop	NR; NR
Dai <i>et al.</i> [21]	RCT (single-center, double-blind)	52 / 54	Laparoscopic appendectomy (3-trocar)	Chronic appendicitis (elective surgery)	Cefuroxime 1.5 g (clindamycin 0.9 g if allergic), IV, 30 min pre-op	Single dose vs placebo	CDC; 30 days
Rafiq <i>et al.</i> [18]	RCT	192 / 198	Open appendectomy (grid iron incision)	Non-perforated acute appendicitis	Cefuroxime + metronidazole (dose NR), IV, 30 min before induction	Single dose vs + 1 postop dose at 8 h	Clinical; 6 weeks
Sadraei-Moosavi <i>et al.</i> [5]	RCT	76 / 76	Open appendectomy (McBurney incision)	Non-perforated appendicitis	Ceftriaxone 1 g + metronidazole 500 mg, IV, pre-op (timing NR)	Single dose vs continued for 24 h postop	Clinical (US/CT for collections); 30 days
Alammar <i>et al.</i> [4]	RCT	120 / 120	Open appendectomy (McBurney point incision)	Non-perforated acute appendicitis	Ceftriaxone 1 g + metronidazole 500 mg, IV, 30 min pre-op	Single dose vs continued up to 24 h postop	Clinical; 30 days

RCT: Randomized Controlled Trial; I/C, Intervention/Comparison, IV: Intravenous, Pre-Op: Preoperative, Postop, Postoperative, SSI: Surgical Site Infection, CDC: Centers for Disease Control and Prevention, US: Ultrasound, CT: Computed Tomography, NR: Not Reported. ^cSample Sizes of the No-Antibiotic, Single-Dose, and 3-Day Groups, Respectively.

Table 2: Surgical Site Infection Outcomes of the Included Studies

Author, year	Comparison	SSI events, intervention, n (%)	SSI events, comparison, n (%)	Reported effect estimate; p value	RR (95% CI)
Prophylaxis vs no prophylaxis or placebo					
Sánchez-Santana <i>et al.</i> [9]	Prophylaxis vs no prophylaxis recorded	29 (4.4)	14 (5.2)	RR 0.66 (95% CI 0.25–1.57); p>0.05	0.83 (0.45–1.55) [†]
He <i>et al.</i> [20]	No antibiotics vs single dose vs single dose + 3 days postop	NR (0.6) ^b	NR (0.7) / NR (0.8) ^b	p = 0.992	NR
Dai <i>et al.</i> [21]	Single dose vs placebo	3 (5.8)	3 (5.6)	OR 1.00 (95% CI 0.20–5.40); p = 0.96	1.04 (0.22–4.91)
Single dose vs prolonged regimen: open appendectomy					
Hosseini Khalifani <i>et al.</i> [8]	Single dose vs 4 doses/24 h	8 (5.9)	6 (3.8)	p = 0.425	1.55 (0.55–4.35)

Table 2: Surgical Site Infection Outcomes of the Included Studies (Continue)

Author, year	Comparison	SSI events, intervention, n (%)	SSI events, comparison, n (%)	Reported effect estimate; p value	RR (95% CI)
Brotobor <i>et al.</i> [7]	Single dose vs 3 doses	1 (3.5)	1 (3.0)	p>0.05	1.14 (0.07–17.39)
Shirah and Shirah, [25]	Single dose vs 4 doses	17 (7.2)*	20 (8.2)*	p = 0.918	0.88 (0.47–1.64)
Rafiq <i>et al.</i> [18]	Single dose vs 2 doses	15 (7.8)	18 (9.1)	p = 0.65	0.86 (0.45–1.66)
Sadraei-Moosavi <i>et al.</i> [5]	Single dose vs continued for 24 h postop	1 (1.3)	1 (1.3)	NR (reported as not significant)	1.00 (0.06–15.70)
Alammar <i>et al.</i> [4]	Single dose vs continued up to 24 h postop	8 (6.7)	8 (6.7)	p = 0.886	1.00 (0.39–2.58)
Single dose vs prolonged regimen: laparoscopic appendectomy					
Choi <i>et al.</i> [24]	Single dose vs continued until discharge	4 (4.0)	3 (6.0)	p = 0.455	0.67 (0.16–2.89)
Rajput and Saxena, [23]	Single dose vs continued up to 24 h postop	3 (6.0) ^a	2 (4.0) ^a	p>0.05	1.50 (0.26–8.60)
Bangaru <i>et al.</i> [22]	Single dose vs + 1 IV dose, then oral for 5 days	2 (2.5)	3 (3.6)	p = 0.671	0.68 (0.12–3.98)
Meena, [19]	Single dose vs 4 doses/24 h	1 (3.8) ^a	1 (3.8) ^a	p = 1.000	1.00 (0.07–15.15)

SSI, surgical site infection; RR, risk ratio; OR, odds ratio; CI, confidence interval; IV, intravenous; postop, postoperative; NR, not reported. RR (95% CI): risk ratio of SSI (single dose vs comparator), calculated from reported event counts; RR < 1 favours single dose. ^aSSI reported as Southampton grade III wound infection. ^bNumber of SSI events not reported; percentages as reported by the authors. *The original study reported these SSI rates as 3.5% and 4.1%, calculated using the total study population (n = 482) as the denominator. To allow comparison with the other studies, we recalculated them using each group's own sample size: 17 of 237 patients (7.2%) in the single-dose group and 20 of 245 patients (8.2%) in the postoperative antibiotic group. †The absence of prophylaxis reflected missing documentation in most cases, according to the authors; the RR reported by the authors (0.66) differs from the RR calculated from event counts (0.83), possibly because of adjustment in the original analysis

Table 3: Assessment of Risk of Bias for Cohort Studies using the Newcastle–Ottawa Scale (NOS)

Author, year	Selection				Comparability	Outcome			Total score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome was not present at start	Comparability of cohorts	Assessment of outcome	Follow-up long enough	Adequacy of follow-up	
Sánchez-Santana <i>et al.</i> [9]	★	★	★	★	★★	★	★	★	9/9
Choi <i>et al.</i> [24]	★	★	★	★	★	★	★	★	8/9

Each star (★) represents one point. Selection: maximum 4 stars; Comparability: maximum 2 stars; Outcome: maximum 3 stars. Quality was rated as good, fair, or poor using the AHRQ thresholds [16]; both studies were rated as good quality

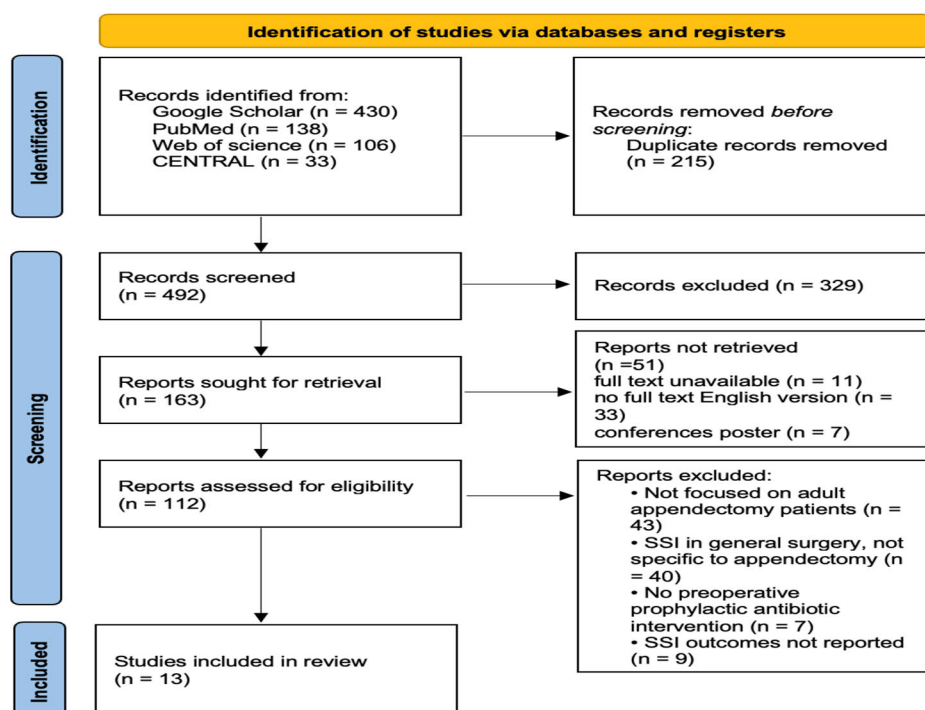


Figure 1: PRISMA 2020 Flow Diagram for the Selection of Studies

Study	D1	D2	D3	D4	D5	Overall
Hosseini Khalifani <i>et al.</i> , 2016						
Alammar <i>et al.</i> , 2023						
Sadraei-Moosavi <i>et al.</i> , 2017						
Brotobor <i>et al.</i> , 2025						
Rajput & Saxena, 2022						
Bangaru <i>et al.</i> , 2017						
Dai <i>et al.</i> , 2023						
Rafiq <i>et al.</i> , 2015						
He <i>et al.</i> , 2025						
Meena, 2023						

Domains:

D1: Bias arising from the randomization process.

D2: Bias due to deviations from intended intervention.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome.

D5: Bias in selection of the reported result.

Judgement

High

Some concerns

Low

Figure 2: Risk of Bias Assessment of Randomized Controlled Trials (RoB 2)

Study	D1	D2	D3	D4	D5	D6	D7	Overall
Shirah & Shirah (2016)								

Domains:

D1: Bias due to confounding.

D2: Bias due to selection of participants.

D3: Bias in classification of interventions.

D4: Bias due to deviations from intended interventions.

D5: Bias due to missing data.

D6: Bias in measurement of outcomes.

D7: Bias in selection of the reported result.

Judgement

Critical

Serious

Moderate

Low

Figure 3: Risk of Bias Assessment of the Non-Randomized Study (ROBINS-I)

and postoperative antibiotic groups (RR 0.67, 95% CI 0.16–2.89) [24], and Rajput and Saxena reported 6% and 4% (RR 1.50, 95% CI 0.26–8.60) [23]. Bangaru *et al.* reported SSI rates of 2.5% and 3.6% despite extending postoperative antibiotics orally for 5 days; all infections were superficial, and patients receiving single-dose prophylaxis had a shorter postoperative hospital stay [22]. Meena reported one SSI in each group (3.8% vs 3.8%; $p = 1.000$), with no significant difference in hospital stay [19].

DISCUSSION

This systematic review evaluated prophylactic antibiotic strategies for preventing SSI after adult appendectomy. In

adults undergoing appendectomy for non-perforated or uncomplicated appendicitis, none of the ten studies comparing single-dose preoperative prophylaxis with prolonged regimens found a statistically significant reduction in SSI with postoperative continuation [3, 5, 7, 18, 19, 22–25]. SSI rates were low in both groups, and point estimates did not consistently favour either strategy, suggesting that postoperative continuation is unlikely to provide a large additional benefit in these lower-risk populations. However, because most studies were small, event numbers were low, and confidence intervals were wide, a smaller but clinically relevant effect cannot be excluded. This interpretation is further tempered by the risk

Factors Influencing Surgical Site Infection Following Adult Appendectomy

Classic fishbone diagram of multifactorial causes and prevention strategies

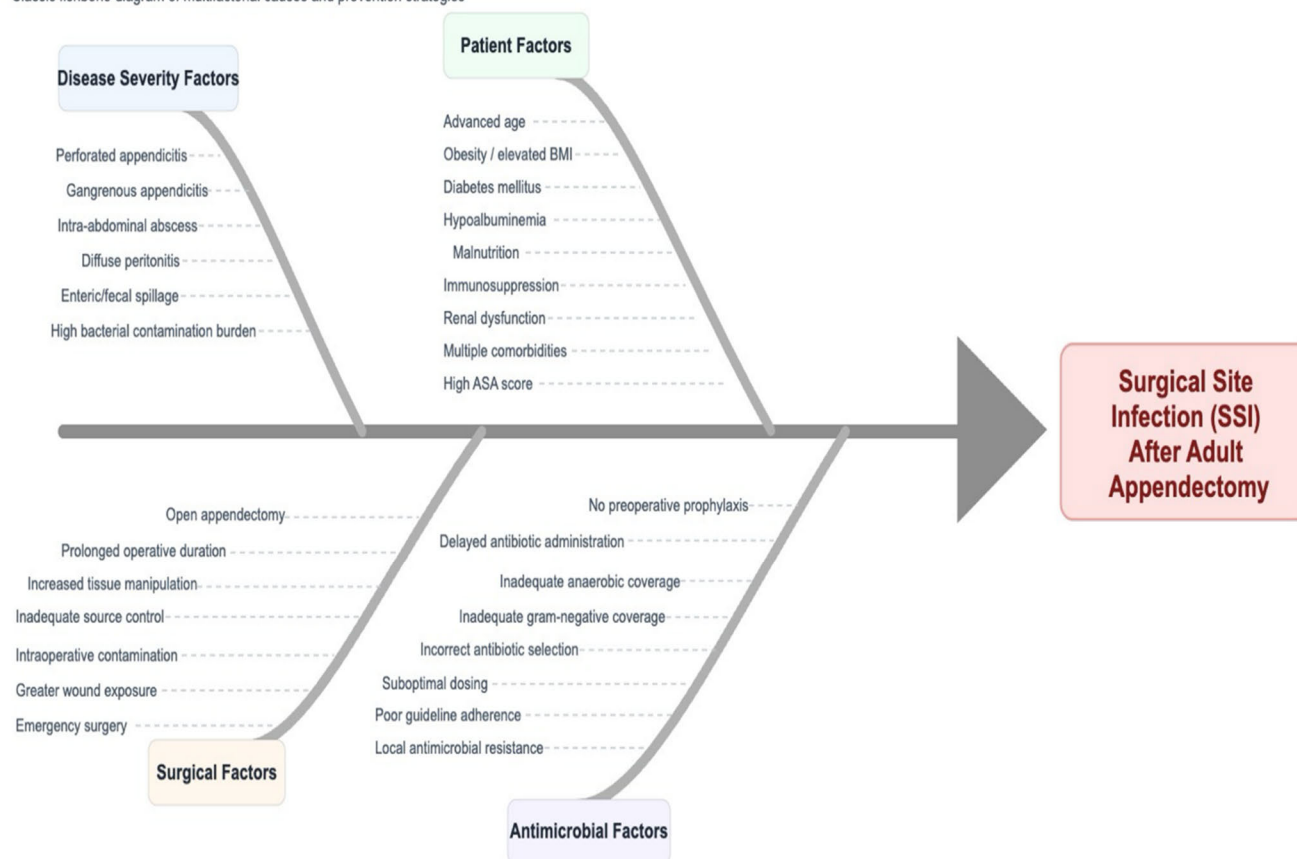


Figure 4: Factors Influencing Surgical Site Infection Following Adult Appendectomy

of bias of the evidence: nine of the ten randomized trials had some concerns, one was at high risk of bias, and the non-randomized study had a serious risk of bias, although the overall pattern of findings did not change when the latter two studies were set aside. Variation in SSI rates between studies is likely to reflect, at least in part, differences in patient selection, operative approach, study design, SSI definitions, and antibiotic protocols. Several studies also reported that extended regimens were associated with longer hospital stay, higher treatment costs, or more antibiotic-related adverse events [7,18,22,24].

The evidence on omitting prophylaxis altogether should be interpreted separately from the evidence on prophylaxis duration. Only three studies addressed this question, and all involved selected populations: patients undergoing laparoscopic appendectomy for uncomplicated acute appendicitis [20], patients undergoing elective laparoscopic appendectomy for chronic appendicitis [21], and a cohort in which the absence of prophylaxis mainly reflected missing documentation rather than planned omission [9]. Although none of these studies found a statistically significant increase in SSI without prophylaxis, event numbers were small and confidence intervals were wide. These findings therefore do not support omitting prophylaxis in routine practice and cannot be extended to patients with complicated appendicitis.

While antibiotic prophylaxis plays an important role in preventing postoperative infection, the development of SSI is multifactorial. Evidence from the included studies and the wider literature suggests that disease severity, patient characteristics, operative factors, and antimicrobial practices all contribute to postoperative infection risk. Figure 4 summarizes these interacting factors and illustrates how they collectively influence postoperative infection risk. Among the operative factors, laparoscopic appendectomy has been associated with lower wound infection rates than open appendectomy. One comparative study reported that wound infection in non-perforated appendicitis occurs in less than 5% to less than 10% of patients after open appendectomy and is even less frequent following laparoscopic appendectomy [22]. Disease severity is a major determinant of postoperative infection. A randomized controlled trial identified the pathological status of the appendix as an important contributing factor to SSI, demonstrating that wound infections occur more frequently in patients with perforated or gangrenous appendicitis than in those with non-perforated disease [19]. Similar findings were reported by another study, which documented baseline wound infection rates of less than 10% in non-perforated appendicitis compared with 15–20% in perforated appendicitis [23]. Patient-related factors may also contribute

to postoperative SSI. Increased subcutaneous fat thickness has been identified as a risk factor for incisional surgical site infection following appendectomy for acute appendicitis [7,26]. Although patient and operative characteristics modify the risk of SSI, these factors do not diminish the importance of appropriate antibiotic stewardship. Instead, they highlight that prophylactic antibiotics should be integrated into a broader perioperative strategy aimed at minimizing infection risk [27]. Current international guidelines reflect this approach.

Although they were not generated by this review, current guidelines are broadly consistent with its findings. The American Society of Health-System Pharmacists (ASHP) recommends administering prophylactic antibiotics before surgical incision and avoiding unnecessary postoperative continuation in uncomplicated cases [28], and the World Health Organization (WHO) recommends against prolonging surgical antibiotic prophylaxis after completion of the operation [29]. Similarly, the WARNING call to action emphasizes appropriate antibiotic selection and timely administration as part of antimicrobial stewardship [30].

Limitations

The main limitation is that most studies enrolled uncomplicated, non-perforated, chronic, or otherwise selected low-risk populations, which constrains the generalizability of the conclusions. Another limitation is that the very low SSI frequency across trials reduces power to detect small differences, so absence of statistical significance should not be interpreted as proof of complete equivalence in all settings. Study-specific limitations also temper interpretation, including observational design, incomplete adherence to prophylaxis protocols, non-power-based sampling in some reports, and the overall risk of bias of the included studies. Although the cohort studies demonstrated good methodological quality, most randomized controlled trials were judged as having some concerns in the RoB 2 assessment, one randomized trial was considered at high risk of bias, and the included non-randomized study had a serious risk of bias. These factors should be considered when interpreting the overall strength of the evidence. In addition, the review protocol was not prospectively registered, which increases the potential for undetected changes to the review methods and for selective reporting; however, the eligibility criteria, outcomes, and risk-of-bias methods were defined before screening began. In addition, SSI definitions and follow-up methods varied across studies, and several studies did not report organ/space infections separately, which may have led to under-ascertainment of deeper infections. Embase was not searched, so some relevant studies may have been missed, although this risk is partly reduced by the inclusion of CENTRAL, which incorporates trial records from Embase.

Implications for Practice and Future Research

According to the findings of this systematic review, single-dose preoperative antibiotic prophylaxis may be adequate for

most adults undergoing appendectomy for uncomplicated or non-perforated appendicitis. These implications should not be generalized to perforated appendicitis, periappendiceal abscess, diffuse peritonitis, or other complicated intra-abdominal infections, in which postoperative antibiotics are given as treatment rather than prophylaxis. Routine postoperative antibiotic administration did not consistently improve surgical site infection outcomes but was associated with greater antibiotic exposure, increased healthcare costs, longer hospital stay, and a higher burden of antibiotic-related adverse events in several studies [5,7,18,22]. Considering the growing concerns regarding antimicrobial resistance and the principles of antibiotic stewardship, limiting unnecessary postoperative antibiotic use may improve resource utilization while maintaining effective prevention of surgical site infection. This conclusion concerns the duration of prophylaxis; the current evidence does not support omitting preoperative prophylaxis outside highly selected patients or research settings.

Although no included study found a statistically significant benefit of prolonged prophylaxis, further well-designed randomized controlled trials with standardized antibiotic protocols and uniform definitions of surgical site infection are needed to strengthen the available evidence. Future research should also evaluate prophylactic strategies in higher-risk patient populations, including complicated appendicitis and patients with significant comorbidities, to determine whether the findings observed in uncomplicated appendicitis can be generalized to these groups.

CONCLUSIONS

Overall, the available evidence, which is limited by small study sizes, low event rates, and varying risk of bias, suggests that a single preoperative dose of prophylactic antibiotics may be adequate for most adults undergoing appendectomy for uncomplicated or non-perforated appendicitis. Extending antibiotics into the postoperative period did not produce a statistically significant reduction in surgical site infection in any included study and may increase healthcare costs, antibiotic exposure, and length of hospital stay.

Evidence on omitting prophylaxis altogether is separate and more limited. Three studies in highly selected populations found no statistically significant increase in SSI without prophylaxis, but these findings should not be extended to routine practice or to other patient groups. Further well-designed, adequately powered randomized controlled trials are needed to determine the optimal prophylactic strategy in higher-risk patients and to establish whether omission of prophylaxis can be safely adopted in routine clinical practice.

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