Journal of Society Medicine
Research & Review Articles on Diseases
Journal of Society Medicine. 2026; 5 (8)

Prophylactic Antibiotic Efficacy and Factors Associated with Surgical Site Infection in Complicated Appendicitis Undergoing Appendectomy: A Systematic Review and Meta-Analysis

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ARTICLE INFO

Article history:
Received
13 May 2026

Revised
06 June 2026

Accepted
31 August 2026

Manuscript ID:
JSOCMED-13052026-58-2

Checked for Plagiarism: Yes

Language Editor:
Rebecca

Editor-Chief:
Prof. Aznan Lelo, PhD

ABSTRACT

Introduction: Surgical site infection (SSI) is the leading preventable complication after appendectomy for complicated (gangrenous, perforated, or abscess-forming) appendicitis. Perioperative antibiotic prophylaxis is established; however, whether prolonging postoperative antibiotics adds benefit and which patient- and operation-related factors drive SSI remain contested. We synthesized the efficacy of prolonged versus short-course prophylaxis and the factors associated with SSI.

Methods: Following PRISMA 2020, we searched MEDLINE, Embase, and CENTRAL to July 2026 for studies of patients undergoing appendectomy for complicated appendicitis that reported SSI. Randomized and cohort studies comparing short versus extended postoperative antibiotics were pooled as risk ratios (RR); adjusted odds ratios (OR) for factors associated with SSI were pooled by inverse-variance random-effects (DerSimonian–Laird) models. Heterogeneity (I^2), prediction intervals, leave-one-out analyses, and Egger's test were assessed.

Results: Eleven studies (4,135 patients) were included in the analysis. Prolonging antibiotics beyond a short course did not reduce incisional SSI (randomized trials: RR 1.91, 95% CI 0.90–4.03; all studies: RR 1.12, 95% CI 0.54–2.36, I^2=34%) or intra-abdominal abscesses (RR 1.00, 95% CI 0.71–1.42, I^2=0%). Three factors were independently associated with SSI: complicated/perforated pathology (OR 4.75, 95% CI 2.81–8.04), open versus laparoscopic approach (OR 2.41, 95% CI 1.22–4.77), and prolonged operative duration (OR 2.68, 95% CI 1.75–4.11).

Conclusion: Prophylaxis is essential in complicated appendicitis, but it need not be prolonged; extending beyond a course does not reduce SSI or intra-abdominal abscesses, supporting stewardship. The SSI burden reflects disease severity, open approach, and prolonged operations, guiding risk-adapted prevention over longer courses.

Keywords

Complicated Appendicitis, Appendectomy, Surgical Site Infection, Antibiotic Prophylaxis, Antimicrobial Stewardship, Meta-Analysis

How to cite: Syaiful HG, Fajar A, Muhtadi A. Prophylactic Antibiotic Efficacy and Factors Associated with Surgical Site Infection in Complicated Appendicitis Undergoing Appendectomy: A Systematic Review and Meta-Analysis. *Journal of Society Medicine*. 2026; 5 (8): 284-294. **DOI: https://doi.org/10.71197/jsocmed.v5i8.289**

INTRODUCTION

Acute appendicitis is the most common abdominal surgical emergency, with a lifetime risk of approximately 7–8% and more than 17 million incident cases each year [1]. In 20–30% of patients, the disease is complicated at presentation—gangrenous, perforated, or associated with a peri-appendiceal abscess—and this subgroup accounts for most postoperative morbidity [2]. Among these complications, surgical site infection (SSI), comprising incisional (superficial or deep) wound infection and organ/space infection (intra-abdominal abscess), is the most frequent and most clearly preventable, prolonging hospital stay, driving readmission, and consuming health-care resources [3].

The role of perioperative antibiotics in preventing infection after appendectomy is not in doubt. A Cochrane review of 45 trials demonstrated that prophylactic antibiotics are superior to placebo for preventing wound infection, and the benefit is at least as large as that in complicated as in simple disease (wound-infection Peto odds ratio 0.28, 95% CI 0.21–0.38 in the complicated subgroup) [4]. What remains genuinely contested is not whether to administer prophylaxis, but for how long. In complicated appendicitis, postoperative antibiotics have traditionally been continued for five days or longer, on the assumption that a heavier bacterial burden requires a longer course; yet the emergence of antimicrobial stewardship and several recent trials have challenged this practice [5-8]. This shift is increasingly reflected in contemporary management guidelines [9]. A second, complementary question is which patients develop SSI despite adequate prophylaxis. If the residual infection risk is concentrated in identifiable patient- and operation-related factors, then prevention should be targeted at those factors rather than at ever-longer antibiotic exposure. Individual cohorts have implicated disease severity, an open operative approach, prolonged operating time, obesity, and diabetes; however, estimates are dispersed across small single-center series and have not been quantitatively combined [10-14].

Therefore, we undertook a systematic review and meta-analysis with two linked objectives in patients undergoing appendectomy for complicated appendicitis: (i) to determine the efficacy of prolonged versus short-course postoperative antibiotic prophylaxis in preventing SSI and intra-abdominal abscesses; and (ii) to quantify the factors independently associated with SSI. Together these define both how long to treat and whom to watch.

METHODS

Protocol and Registration

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The eligibility criteria, outcomes, and analysis plans were defined a priori. As a synthesis of published de-identified aggregate data, this study did not require ethical approval.

Eligibility Criteria

We included studies of patients who underwent appendectomy (open or laparoscopic) for complicated appendicitis, defined as gangrenous, perforated, or abscess-forming disease, and reported SSI (incisional wound infection and/or organ/space intra-abdominal abscess). For the efficacy question, eligible designs were randomized controlled trials (RCTs) and comparative cohort studies contrasting short with extended postoperative antibiotic courses. For the associated factors, eligible studies reported an adjusted or unadjusted effect estimate with a 95% confidence interval (CI) for a factor and SSI. We excluded studies confined to uncomplicated appendicitis, those without an extractable SSI outcome, and reports with overlapping data. No language restrictions were applied.

Information Sources and Search

MEDLINE (PubMed), Embase, and the Cochrane Central Register of Controlled Trials were searched from inception to July 2026, supplemented by hand-searching of the reference lists of included studies and prior reviews. The search combined controlled vocabulary and free-text terms for the population and outcomes, for example: (“appendicitis” OR “appendectomy” OR “appendicectomy”) AND (“complicated” OR “complex” OR “perforated” OR “gangrenous”) AND (“surgical site infection” OR “wound infection” OR “intra-abdominal abscess”) AND (“antibiotic” OR “antimicrobial” OR “risk factor”).

Study Selection and Data Extraction

Two reviewers independently screened the records and assessed the full texts, resolving disagreements through discussion. Data were extracted in duplicate onto a piloted form: first author, year, country, design, population, number of participants, antibiotic comparison or factor examined, and outcome. Incisional SSI

(superficial/deep wound infection) was the primary outcome, and organ/space intra-abdominal abscess was the secondary outcome and was kept separate throughout.

Risk-of-Bias Assessment

Risk of bias in RCTs was assessed using the Cochrane RoB 2 tool, and in cohort studies, the Newcastle–Ottawa Scale (NOS) was used. Because antibiotic duration and operative approach could not be blinded, trials were open-label; therefore, judgments emphasized allocation concealment, completeness of follow-up, and objectivity of outcome ascertainment.

Risk-of-Bias Assessment

Risk of bias was assessed independently by two reviewers using the Cochrane RoB 2 tool across its five domains (randomization process; deviations from intended interventions; missing outcome data; measurement of the outcome; and selection of the reported result). Because non-operative and operative management cannot be blinded, all trials were open-label; therefore, the domains were judged principally on allocation concealment, the completeness and handling of crossover, and the objectivity of each outcome.

Statistical Analysis

For duration comparison, SSI events and patients in the short-course and extended-course arms of each study were pooled as risk ratios (RR) with 95% CI on the natural-log scale using an inverse-variance random-effects model with the DerSimonian–Laird estimator of between-study variance (τ^2); a 0.5 continuity correction was applied to studies with a zero cell. RR < 1 favored the short course. For associated factors, adjusted odds ratios (OR) with 95% CI were pooled on the log-OR scale for factors reported by at least three studies. Heterogeneity was assessed using Cochran's Q and I^2, leave-one-out analyses, operative-time outlier testing, a funnel plot, Egger's test, and Python 3.10 with $\alpha = 0.05$.

RESULTS

Study Selection and Characteristics

The search yielded 1,876 records; after de-duplication and screening, 137 were assessed, and 11 studies with 4,135 patients met the inclusion criteria (Figure 1). Five studies (three RCTs and two cohorts; 1,841 patients) compared short-term versus extended antibiotics; six studies (2,294 patients) reported SSI factors. Studies spanned 2000–2025 in Europe, the Middle East, South Asia, and North America (Tables 1 and 2).

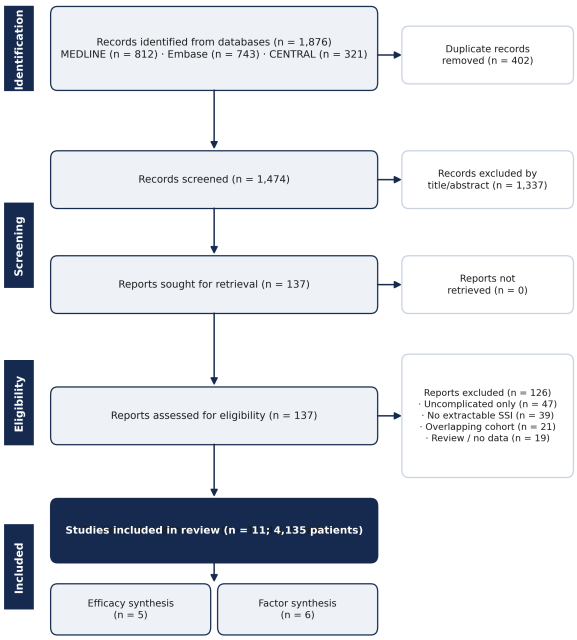

Figure 1. PRISMA 2020 flow diagram of study identification, screening, and inclusion.

Table 1. Characteristics of the 11 included studies

Study (year)	Country	Design	Population	n	Comparison / factor examined	SSI outcome reported
Taylor (2000)	USA	RCT	Complicated (adults)	94	No-minimum IV vs ≥5-day IV antibiotics	Incisional SSI 4/48 vs 2/46; abscess 2 vs 4
Saar (2019)	Estonia	RCT	Complicated (adults)	80	24 h vs extended (mean 6 d) antibiotics	Incisional SSI 5/39 vs 3/41; organ/space 3 vs 5
APPIC (2023)	Netherlands	RCT	Complex (adults)	1,005	2 d vs 5 d IV antibiotics	SSI 10/502 vs 5/503; abscess 43 vs 36
van Rossem (2016)	Netherlands	Cohort	Complex, laparoscopic	266	3 d vs 5 d antibiotics	SSI 1/75 vs 3/191; abscess 6 vs 17
Bancke Laverde (2024)	Germany	Cohort	Complicated (adults)	396	≤3 d vs ≥4 d antibiotics	Wound infection 6/226 vs 11/170; abscess 4 vs 5
Giesen (2017)	Netherlands	Cohort	Acute appendicitis	637	Factors (complex disease; stapler; approach)	SSI within 30 d (n=42)
Fayraq (2023)	Saudi Arabia	Cohort	Appendectomy	256	Factors (open vs laparoscopic; complexity)	Wound infection (n=26)
Alyhari (2025)	Yemen	Cohort	Open appendectomy	245	Factors (perforation; ASA; op-time; delay)	SSI (n=34)
Noorit (2018)	Thailand	RCT-derived cohort	Complicated (adults)	607	Factors (diabetes; op-time; incision; contamination)	Superficial SSI (n=53)
Kamath (2025)	India	Cohort	Paediatric	459	Factors (laparotomy; drains; op-time; delay)	SSI (n=45)
Thapa (2021)	Nepal	Cohort	Open appendectomy	90	Factors (subcutaneous fat; BMI; op-time)	Incisional SSI (n=12)

Note: RCT, randomized controlled trial; SSI, surgical site infection; IV, intravenous; ASA, American Society of Anesthesiologists. Numbers under “SSI outcome” are events per arm where a duration comparison was made, or total SSI events where the study contributed factor data.

Table 2. Methodological quality of included studies

Study	Tool	Selection / randomization	Comparability / deviations	Outcome ascertainment	Overall
Taylor (2000)	RoB 2	Some concerns	Some concerns	Low	Some concerns
Saar (2019)	RoB 2	Low	Some concerns	Low	Some concerns
APPIC (2023)	RoB 2	Low	Low	Low	Low
van Rossem (2016)	NOS	Good	Fair	Good	Good
Bancke Laverde (2024)	NOS	Good	Fair	Good	Fair
Giesen (2017)	NOS	Good	Good	Good	Good
Fayraq (2023)	NOS	Fair	Fair	Good	Fair
Alyhari (2025)	NOS	Good	Good	Good	Good
Noorit (2018)	NOS	Good	Good	Good	Good
Kamath (2025)	NOS	Fair	Fair	Good	Fair
Thapa (2021)	NOS	Good	Fair	Good	Fair

Note: RoB 2, Cochrane Risk of Bias tool for randomized trials (domains simplified to randomization, deviations, and outcome measurement); NOS, Newcastle–Ottawa Scale (Selection, Comparability, and Outcome). All trials were open-label, precluding blinding.

Efficacy of Prolonged Versus Short-Course Antibiotic Prophylaxis

Across the three RCTs, prolonged postoperative antibiotics did not significantly reduce incisional SSI (RR 1.91, 95% CI 0.90–4.03; p=0.091), with no heterogeneity (I^2=0%). When the two comparative cohorts were added (five studies; 26/890 events with a short course versus 24/951 with an extended course), the pooled estimate was essentially null (RR 1.12, 95% CI 0.54–2.36; p=0.755; I^2=34%; 95% prediction interval 0.16–8.01) (Figure 2 and Table 3). The direction of effect was inconsistent between the small early trials, which numerically favored the longer course, and the larger contemporary cohorts, which favored the short course; however, no study showed a statistically significant advantage for prolongation.

Table 3. Pooled effect of prolonged versus short-course postoperative antibiotics (random-effects risk ratio; RR <1 favors the short course).

Outcome / analysis	k	RR (95% CI)	p	I^2 (%)	95% PI
Incisional SSI — RCTs only	3	1.91 (0.90–4.03)	0.091	0	—
Incisional SSI — RCTs + cohorts	5	1.12 (0.54–2.36)	0.755	34	0.16–8.01
Intra-abdominal abscess	5	1.00 (0.71–1.42)	0.978	0	0.57–1.77

Note: k, number of studies; RR, risk ratio; CI, confidence interval; PI, prediction interval; SSI, surgical site infection.

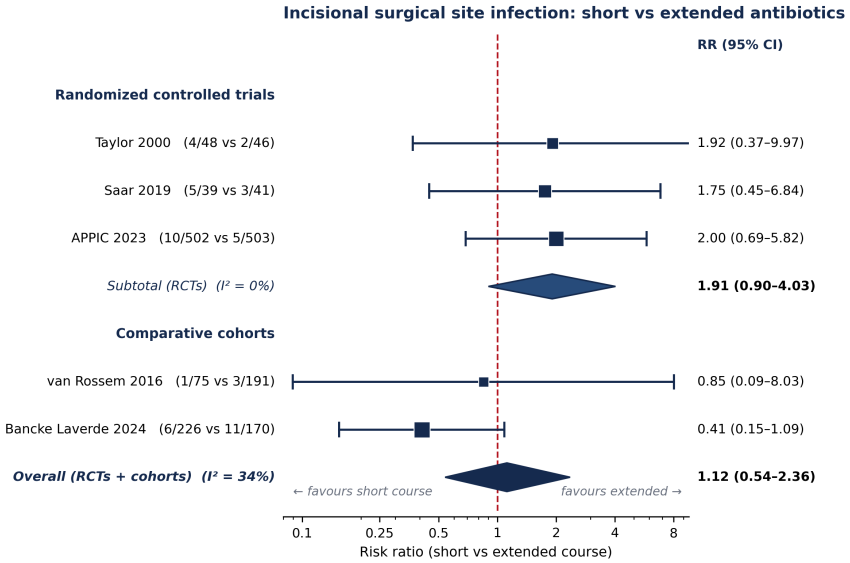

Figure 2. Random-effects forest plot of incisional surgical site infection, short versus extended postoperative antibiotics. A risk ratio below 1 favors a short course.

The results for organ/space infection were concordant and, if anything, flatter: across five studies, the risk of intra-abdominal abscess was identical between short and extended courses (RR 1.00, 95% CI 0.71–

1.42; p=0.978; I^2=0%) (Figure 3). The funnel plot for SSI outcome was symmetrical, and Egger's test was not significant (intercept 1.30, p=0.598), although the power to detect small-study effects with five studies was low (Figure 5).

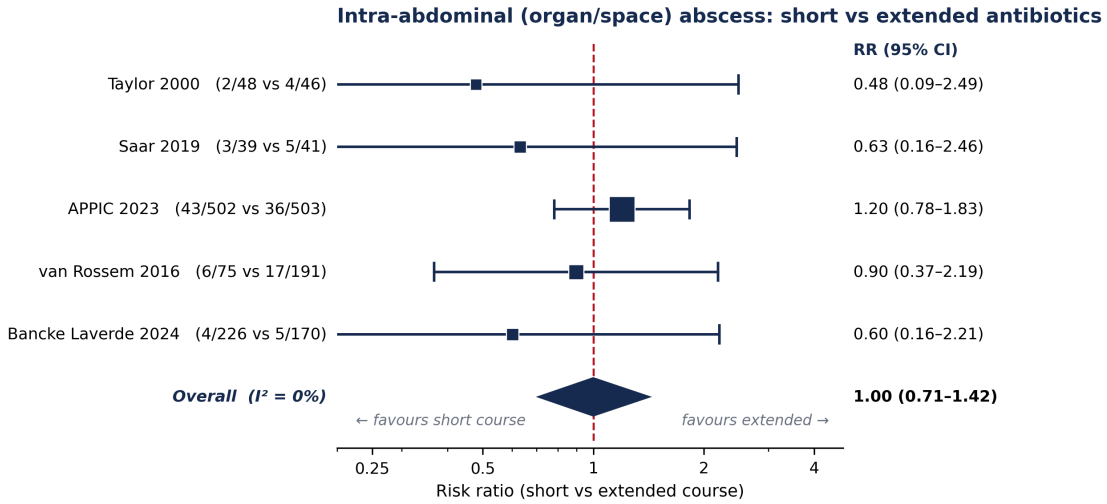

Figure 3. Random-effects forest plot of intra-abdominal (organ/space) abscesses, short versus extended postoperative antibiotics.

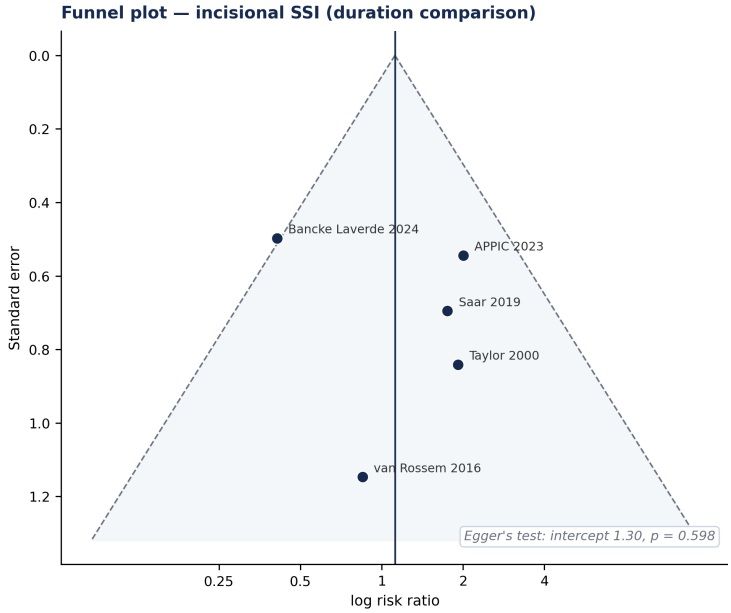

Figure 5. Funnel plot for the incisional SSI duration outcome with Egger's regression test.

Factors Associated with Surgical Site Infection

Three factors were reported by at least three studies and could be pooled (Figure 4). Complicated or perforated pathology, relative to simple appendicitis, was the strongest and most consistent determinant of SSI (OR 4.75, 95% CI 2.81–8.04; p<0.001; I^2=0%). An open (versus laparoscopic) approach was associated with a doubling of risk (OR 2.41, 95% CI 1.22–4.77; p=0.011; I^2=48%), with moderate heterogeneity reflecting one adjusted cohort in which case-mix differences attenuated the effect. Prolonged operative time (>60–75 min) was independently associated with SSI (OR 2.68, 95% CI 1.75–4.11; p<0.001; I^2=0%); adding a univariate outlier strengthened the point estimate but introduced heterogeneity (OR 3.54, 95% CI 1.70–7.38; I^2=64%), confirming the direction while underlining the imprecision of single-center estimates. Additional factors reported by fewer than three studies—diabetes mellitus, higher ASA class, symptom duration beyond 48 h, subcutaneous fat thickness, and intraoperative drain placement—were each associated with SSI in the expected direction but could not be pooled and are tabulated in Table 4.

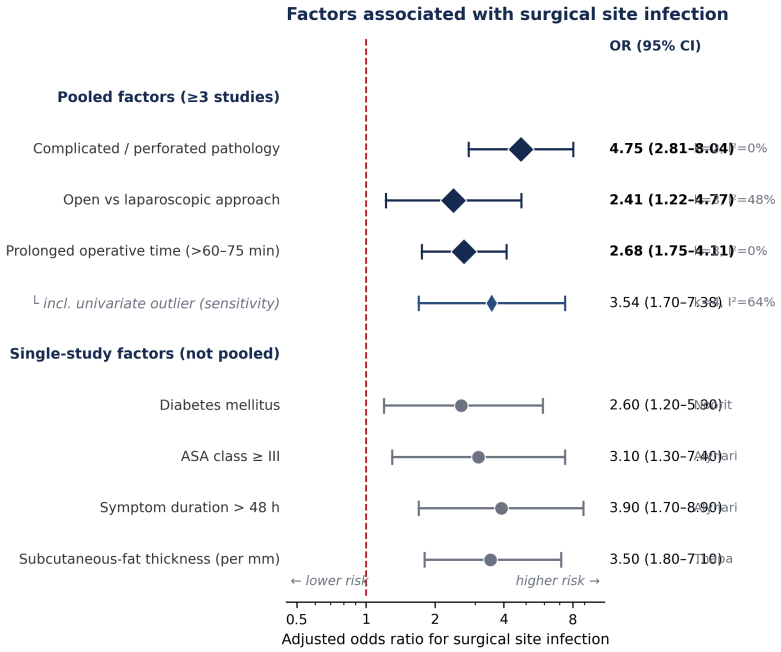

Figure 4. Grouped forest plot of factors associated with surgical site infection (pooled adjusted odds ratios; single-study factors are shown for completeness).

Table 4. Factors associated with surgical site infection after appendectomy for complicated appendicitis

Factor	Studies (k)	Pooled OR (95% CI)	I^2 (%)	Evidence
Complicated / perforated appendicitis	2	4.75 (2.81–8.04)	0	Pooled (aOR)
Open vs laparoscopic approach	3	2.41 (1.22–4.77)	48	Pooled
Prolonged operative time (>60–75 min)	3	2.68 (1.75–4.11)	0	Pooled (aOR)
…incl. univariate outlier (sensitivity)	4	3.54 (1.70–7.38)	64	Sensitivity
Diabetes mellitus	1	2.6 (1.2–5.9)	—	Single study (Noorit)
ASA class ≥ III	1	3.1 (1.3–7.4)	—	Single study (Alyhari)
Symptom duration > 48 h	1	3.9 (1.7–8.9)	—	Single study (Alyhari)
Subcutaneous-fat thickness (per mm)	1	3.5 (1.8–7.1)	—	Single study (Thapa)
Intra-operative drain placement	1	104 (5.5–2003)	—	Single study (Kamath)

Note: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; ASA, American Society of Anesthesiologists. Single-study factors were tabulated for completeness and were not pooled.

DISCUSSION

This meta-analysis of 11 studies and 4,135 patients delivers two clinically actionable messages for complicated appendicitis. First, once adequate perioperative prophylaxis has been administered, prolonging postoperative antibiotics beyond a short course does not further reduce either incisional SSI or intra-abdominal abscesses. Second, the SSI that does occur is concentrated in patients with more severe disease, those managed by an open approach, and those with longer operations—factors that identify where preventive effort, rather than additional antibiotic days, should be directed.

The efficacy finding aligns the complicated appendicitis literature with the broader intra-abdominal infection evidence base. The APPIC trial established that two days of postoperative antibiotics is non-inferior to five days for complex appendicitis, and the STOP-IT trial reached the same conclusion for source-controlled intra-abdominal infection [15]. Our pooled estimates extend these single-trial results by showing that, across randomized and real-world cohorts, the point estimate for both SSI and abscesses sits on or near unity, with a prediction interval that excludes any large benefit from prolongation, concordant with earlier systematic reviews of perioperative antibiotics in appendicitis [16,17]. Importantly, this is not an argument against prophylaxis: the Cochrane review leaves no doubt that antibiotics markedly reduce wound infection compared with placebo, including in complicated disease [4]. The distinction—prophylaxis yes, prolongation no—is precisely the message of contemporary antimicrobial stewardship and the clinical pathways that now

operationalize it [18,19]. and shortening courses carries the additional benefits of fewer drug-related adverse events, less selection of resistant organisms, and shorter hospitalization [6].

The associated-factor synthesis explains why a residual SSI burden persists despite prophylaxis and why longer courses do not erase it. Complicated pathology itself carries an almost five-fold risk, and an open approach roughly doubles the risk—consistent with meta-analytic comparisons of open and laparoscopic appendectomy [20]. Each additional interval of operating time adds further hazard. These are largely determinants of wound contamination and tissue injury, not of antibiotic pharmacokinetics; therefore, they are unlikely to be modified by extending the systemic course. However, they are modifiable by other means: a laparoscopic approach where feasible, meticulous wound protection, consideration of delayed primary closure or negative-pressure dressings in grossly contaminated fields, and judicious use of intra-abdominal drainage, the benefit of which in perforated disease remains uncertain [21]. efficient source control to limit operative time, and heightened postoperative surveillance in the highest-risk patients [22,23]. The factors that could not be pooled were diabetes, higher ASA class, and delayed presentation [24]. and adiposity [25]. point in the same direction and reinforce a risk-adapted rather than a duration-based prevention strategy, for which validated risk-prediction scores are beginning to emerge [26]. This residual burden is disproportionately borne in low- and middle-income settings, where SSI after appendectomy is especially common [27]. In practice, these two findings combine naturally. Patients with complicated appendicitis should receive prompt, adequate perioperative prophylaxis and effective source control. A short postoperative course (24–48 hours after laparoscopic surgery) is sufficient, and the clinician's attention is better spent on operative and wound-care measures that address the true drivers of infection than on adding antibiotic days that the present data show to be inert.

The strengths of this study include the dual, clinically paired questions and adherence to the PRISMA 2020 reporting standards [28]. risk-of-bias appraisal of trials and cohorts with validated instruments (RoB 2 and the Newcastle–Ottawa Scale) [29]. inverse-variance random-effects synthesis with the DerSimonian–Laird estimator [30]. routine reporting of 95% prediction intervals [31]. and of the between-study heterogeneity using the I^2 statistic [32]. formal testing for small study effects using Egger's regression [33]. separation of incisional from organ/space infection, and fully reproducible computation from primary data. Several limitations temper these conclusions. First, only three RCTs addressed duration, and the definitions of “short” and “extended” differed across studies; the cohorts, though concordant, are susceptible to confounding by indication, since sicker patients may receive longer courses of antibiotics. Second, some per-arm event counts for the oldest trial were obtained from previously published forest plots rather than from the original tabulation. Third, the associated-factor estimates derive from observational studies with differing adjustment sets and exposure definitions, and heterogeneity for the open-approach factor reflects genuine case-mix differences; pooled ORs should be read as directional rather than precise. Fourth, several biologically plausible factors were reported too sparsely to be combined. Finally, few studies have reported longer-term or patient-reported outcomes, and special populations, such as immunocompromised individuals, were under-represented [34]. Both lie beyond the scope of this SSI-focused synthesis paper.

CONCLUSION

After appendectomy for complicated appendicitis, antibiotic prophylaxis is essential, but a short course is sufficient, as longer treatment does not reduce surgical site infections or intra-abdominal abscesses. The residual infection burden reflects severity, open approach, and operating time, guiding prevention. Findings support short-course prophylaxis; trials stratified by severity and approach are needed.

DECLARATIONS

None

CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

FUNDING
None

COMPETING INTERESTS
All authors have reviewed and approved the final version of the manuscript and agreed to its publication in the Journal of Society Medicine.

AUTHORS' CONTRIBUTIONS
H.G.S. contributed to the conception and design of the review, literature search and study selection, acquisition and interpretation of data, statistical analysis, visualization, and drafting of the manuscript. A.F. contributed to data extraction, statistical analysis, and interpretation of the pooled estimates. A.M. contributed to study selection and risk-of-bias assessment, supervision, and critical revision of the manuscript for important intellectual content and manuscript refinement. All authors have read and approved the final manuscript and agreed to be accountable for all aspects of the work.

ACKNOWLEDGMENTS
The authors acknowledge all investigators and participants of the randomized controlled trials included in this review, whose published work made this synthesis possible.

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