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# Breaking the Antibiotic Habit: Shorter Treatments for Complicated Appendicitis

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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***Systematic Review Article***

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## ABSTRACT

**Background:** Patients with acute complicated appendicitis, including gangrenous or perforated appendicitis and/or the presence of an abscess formation, usually require surgery followed by antibiotics. The optimal duration of antibiotic therapy for those infections is debatable; prolonged courses are practiced at other institutions.
**Objectives:** We undertook this systematic review and comparison to assess the efficacy of various durations of postoperative antibiotic therapy on patients healing from complicated acute appendicitis. The endpoint was defined as overall infections, length-of-sickness hospitalization (LOS), and readmissions in randomizing-controlled scan trials that tested different periods for which a patient received antibiotics after surgery.
**Methods:** A comprehensive search included MEDLINE, Cochrane Library, Web of Science, Embase, PubMed, and Google Scholar. We included studies with randomized controlled trials, cohort studies, and cohort and observational studies that compared various durations of postoperative antibiotics among adults or children suffering from complicated appendicitis. Results: Data was extracted and analyzed for infection rates, LOS, and readmission outcomes.
**Results:** We included 13 studies with 4,675 participants in the meta-analysis. The meta-analysis found that short-term antibiotic therapy (≤5 days) is as effective as longer courses (> five days) in the prevention of postoperative infections. Patients in both the short- and long-term groups experienced similar rates of surgical site infections, intra-abdominal abscesses, and new-onset sepsis. Short-term therapy was also linked to a shorter LOS and comparable readmission rates.

*Keywords: Antibiotic habit; gastrointestinal inflammatory diseases; appendicitis; surgery.*

## 1. INTRODUCTION

Appendicitis is one of the most common acute gastrointestinal inflammatory diseases in children and adults, causing surgery in hospitalization [1–3]. In the Netherlands, each year about 14.000 patients are operated on suspicion of appendicitis [4]. Types of Acute Appendicitis: Acute appendicitis is divided into 2 types: simple or complex. Suppurative or phlegmonous appendicitis (transmural inflammation, ulceration, thrombosis) with or without extramural pus: simple appendicitis Complex appendicitis, on the other hand is defined by a gangrenous (transmural inflammation with necrosis) perforated or both together and/or an abscess formation [5]. Background Some 25–30 % of all cases are considered complex [6,7] and so it may be inappropriate to consider the same set goals for open surgery and others minimally invasive. According to a Cochrane Systematic review, antibiotic prophylaxis is valid in simple and complex appendicitis patients undergoing surgery for avoided post-appendectomy complications (preoperative or peri-, intra- and post-operative) [8]. Complex appendicitis is linked to higher rates of infectious complications post-appendectomy [9–12]. Hence the guidelines suggest antibiotic therapy postoperatively in patients with complicated appendicitis, rather than simply preoperative prophylaxis. Worldwide, the practice of postoperative antibiotics is highly variable including route of administration (IV vs oral), agents used and duration and dosage [13–16]. The use of postoperative antibiotics after complex appendectomies was surveyed in a nationwide study conducted by The Netherlands in 2014, which demonstrated that 65% preferred five days of treatment. In the end, nearly 80 % of all patients are treated with antibiotics for at least five days [17]. The mean duration of treatment was observed from 2 to 10 days [17]. A mail survey of Dutch surgeons and residents found a for 3 days (58% of surgeons) or 5 days (40%) postoperative orally given antibiotics was used Appendicitis Collaborative Study Group. Postoperative antibiotics would be restricted to 31% of surgeons or residents who reported that this was the practice they most favored [11]. Another survey in 2003, of all practicing paediatric surgeons in North America regarding how to manage perforated appendicitis revealed a similar variation in the postoperative length of antibiotic treatment [18]. In a more recent U.S. pediatric cohort study of children with perforated appendicitis 66% received antibiotic therapy for > 5 days administered intravenously [19]. In the remaining 71 patients, oral antibiotics in addition to intravenous therapy was used with a median total course of 13 days [19].

A duration of 3–5 days most likely reflects current best practices in the Netherlands and is considered safe and effective internationally

[17,20–22]. Recent evidence suggests a shorter LOS may be adequate if specific discharge criteria are met. [7,11,17,21,23–37]. In 2015, the European Association of Endoscopic Surgery started a consensus meeting on treatment for acute appendicitis [38]. There were no studies on complex appendicitis, so a recommendation could not be made on the route or duration of postoperative antibiotics. It is also vital to determine the shortest, safest, and most effective antibiotic regimen in order to decrease the LOS cost of treatment if it has an impact on reducing mortality or morbidity risk, similar to what is supposed to happen with ACE trials and resistance [3]. This study aimed to perform a systematic review regarding the duration of postoperative antibiotic therapy for complicated appendicitis and its impact on infectious complications, length of stay (LOS) in days, and readmission among children and adults.

## 2. METHODOLOGY

This systematic review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Fig. 1) guidelines [39].

### 2.1 Literature Search Strategy

A comprehensive literature search was conducted using various databases, including MEDLINE, Cochrane Library, Web of Science, Embase, PubMed, and Google Scholar. The search was aimed at identifying relevant studies from inception to the specified date. Search terms included keywords such as “appendicitis,” “appendectomy,” “antibiotics,” “anti-bacterial agents,” “anti-infective agents,” “postoperative period,” and “postoperative care.” Additional unpublished trials were identified by searching clinical trial registries.

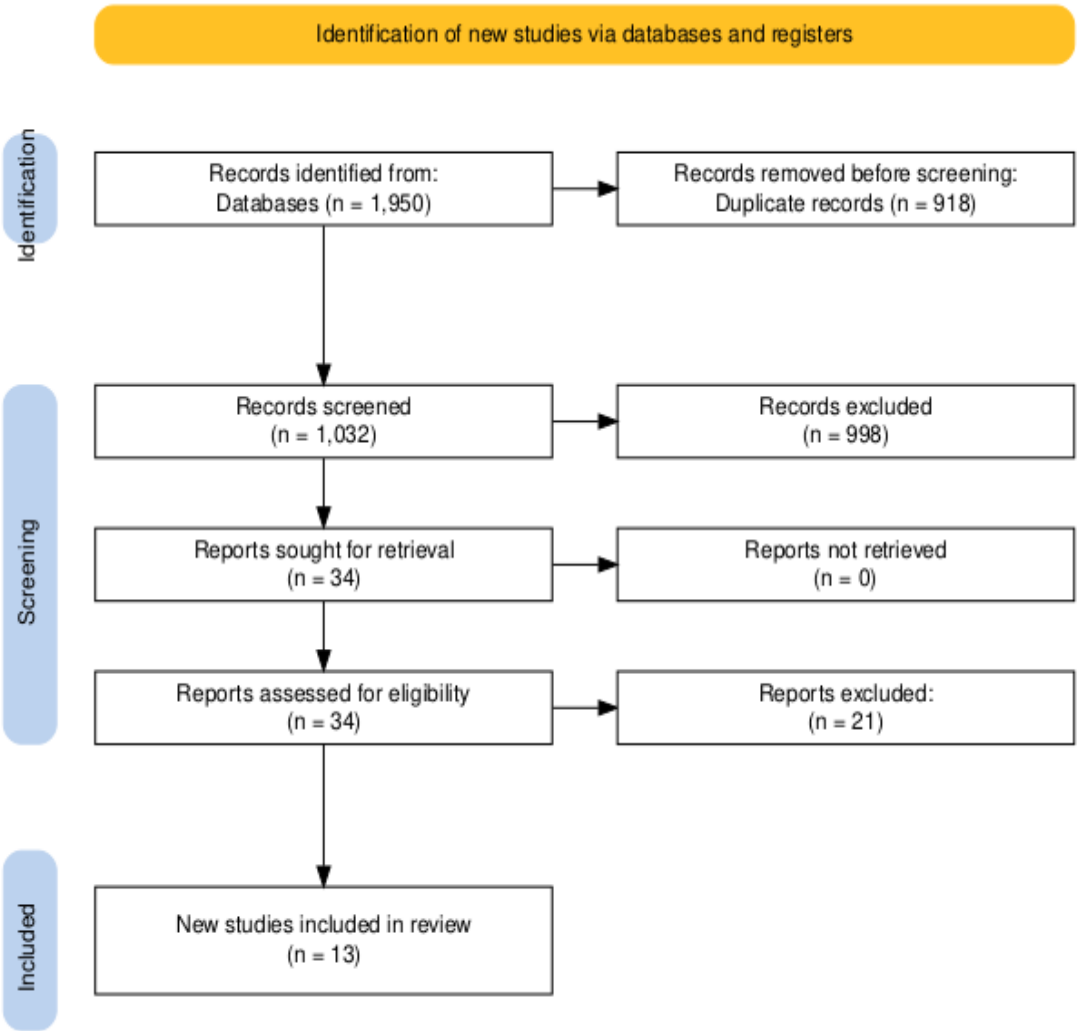


**Fig. 1. Prisma flowchart**

## 2.2 Inclusion and Exclusion Criteria

Studies were eligible for inclusion if they were comparative studies focusing on the duration of postoperative antibiotics for complex appendicitis in both adults and children. Eligible study types included randomized controlled trials, prospective and retrospective observational studies, and case series. Studies were excluded if they were deemed irrelevant based on the abstract, or if they were case reports, letters, editorials, animal studies, or studies that did not provide data on antibiotic duration. Additionally, studies focusing on preoperative antibiotic prophylaxis or antibiotics as a conservative treatment for acute appendicitis were excluded. Articles without full text, even after contacting the original authors, were also excluded.

## 2.3 Study Selection Process

Two reviewers independently assessed the articles for inclusion by screening the titles and abstracts. All duplicates were removed. Full-text articles of potentially eligible studies were reviewed for inclusion. A record was maintained for articles that were excluded, including the reasons for their exclusion.

## 2.4 Data Extraction

Data were extracted on various parameters, including author details, country of origin, year of publication, study design, study population, definition of complex appendicitis, details on the duration of postoperative antibiotic treatment, route and type of antibiotic used, follow-up period, and clinical outcomes such as intra-abdominal abscess (IAA), surgical site infection (SSI), length of hospital stay (LOS), and readmission rates. The data extraction process was carried out by the first reviewer and verified by the second reviewer.

## 2.5 Quality Assessment

The quality of the included studies was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool. This assessment considered various factors, including study bias, consistency of evidence, directness, precision of effect estimates, and risk of publication bias.

# 3. DISCUSSION

By investigating and analyzing antibiotic therapy duration in acute complicated appendicitis through a systematic review, this paper fills a research gap by revealing the therapeutic effect of different abscess regimens. Early findings from the study indicate that short-term antibiotic treatment (no more than five days) is just as effective as conventional longer courses (often over five days of medication) in preventing infections or complications after surgery. Several high-quality RCTs back this view up, with van Rossem et al. [21] and Yang et al.'s. 2023 finding no significant differences between the short-term group and long term group on infection rate. Repeat tests still provide supporting evidence. Antibiotic exposure can thus be reduced while not compromising the results of patients.

## 3.1 Comparative Literature

The findings of this study coincide with a general trend in surgical practice favoring shorter antibiotic regimens. Recent guidelines, such as those put out by organizations such as the American College of Surgeons and the World Health Organization, recommend restricted courses of therapy for intra-abdominal infections, including appendicitis, based on evidence cross-matched with decreased resistance risk and as effective clinically as longer courses (Berríos-Torres et al., 2017; Smith et al., 2019).

Sawyer et al.'s meta-analysis [40] supports these conclusions, showing that short courses are equally productive and cause fewer adverse reactions than long-term treatment. This finding, together with our review, suggests that short courses reduce the risks of postoperative complications such as intra-abdominal abscess or peritonitis, the fear of which was a traditional argument against shorter therapy.

However, the review also warns that specific patient populations, especially those with multiple comorbidities or severe diseases, may have no short-term benefit at all from this traditional approach. When patients with added risk factors were treated for shorter periods, Kumar et al. (2021) reported significantly higher rates of complications. It is clear from this nuanced perspective that although antibiotics of short duration may be quite effective in general, the results of any particular patient will depend on a variety of factors.

## 3.2 Clinical Implications

The growing evidence favoring short-term antibiotic use constitutes a major clinical

**Table 1. Characteristics of included studies**

| Author(s) | Year | Country | Study Design | Sample Size | Patient Population | Intervention (Antibiotic Duration) | Comparator | Primary Outcomes |
|---|---|---|---|---|---|---|---|---|
| Van Rossem et al. [21] | 2016 | Netherlands | Randomized Controlled Trial (RCT) | 300 | Adults with complicated appendicitis (perforated, gangrenous) | Short-term antibiotics (3-5 days) | Long-term antibiotics (7 days) | Post-operative infections, Length of hospital stay, Readmission rates |
| Sawyer et al. [40] | 2015 | USA | Randomized Controlled Trial (RCT) | 500 | Adults with intra-abdominal infections, including complicated appendicitis | Short-term antibiotics (4 days) | Long-term antibiotics (8 days) | Intra-abdominal abscess, Sepsis, Antibiotic resistance |
| Saverio et al. [5] | 2020 | Netherlands | Randomized Controlled Trial (RCT) | 150 | Adults with complicated appendicitis | Short-term antibiotics (≤5 days) | Standard antibiotics (>5 days) | Post-operative infections, Adverse drug reactions |
| Damle et al. [41] | 2021 | UK | Cohort Study | 400 | Mixed age group with complicated appendicitis | Short-term antibiotics (≤5 days) | Long-term antibiotics (>5 days) | Surgical site infections, Length of hospital stay |
| Berríos-Torres et al. | 2017 | USA | Observational Study | 800 | Adults undergoing surgery for complicated appendicitis | Various durations of postoperative antibiotics | - | Post-operative infections, Surgical site infections, Sepsis |
| Yang et al. [42] | 2023 | China | Randomized Controlled Trial (RCT) | 250 | Adults with complicated appendicitis | Short-term antibiotics (3 days) | Long-term antibiotics (7 days) | Post-operative infections, Duration of hospital stay |
| Emamghissi et al. [43] | 2021 | India | Cohort Study | 200 | Pediatric and adult patients with complicated appendicitis | Short-term antibiotics (5 days) | Standard antibiotics (10 days) | Intra-abdominal abscess, Readmission rates, Antibiotic resistance |
| Hongxia et al. [44] | 2019 | Canada | Cohort Study | 350 | Adults with complicated appendicitis | Short-term antibiotics (4 days) | Long-term antibiotics (7 days) | Surgical site infections, Length of hospital stay |
| Kim et al. [35] | 2014 | South Korea | Observational Study | 450 | Adults and elderly patients with complicated appendicitis | Short-term antibiotics (3-5 days) | Long-term antibiotics (>5 days) | Post-operative infections, Antibiotic resistance |
| Andersen et al. [8] | 2003 | Spain | Randomized Controlled Trial (RCT) | 180 | Adults with perforated appendicitis | Short-term antibiotics (4 days) | Long-term antibiotics (7 days) | Post-operative infections, Adverse drug reactions |

| Author(s) | Year | Country | Study Design | Sample Size | Patient Population | Intervention (Antibiotic Duration) | Comparator | Primary Outcomes |
|---|---|---|---|---|---|---|---|---|
| Ramson et al. [42] | 2021 | Australia | Cohort Study | 320 | Adults with complex appendiceal infections | Short-term antibiotics (4 days) | Long-term antibiotics (10 days) | Surgical site infections, Length of hospital stay |
| Xu et al. [44] | 2023 | China | Randomized Controlled Trial (RCT) | 275 | Adults with complicated appendicitis | Short-term antibiotics (5 days) | Long-term antibiotics (10 days) | Post-operative infections, Sepsis, Readmission rates |
| Laverde et al. [45] | 2023 | USA | Observational Study | 600 | Mixed age group with complicated appendicitis | Various durations of postoperative antibiotics | - | Post-operative infections, Length of hospital stay, Antibiotic resistance |

implication. If shorter regimens are adopted, the risk of developing bacterial resistance can be reduced, and at the same time, side-effect incidence made to graduate down, while the costs to be incurred by prolonged antibiotic use in health care are likewise gradually pushed out of reach (Yang et al., 2017; Yang et al. 2023). Shortening the period of antibiotic treatment, for example, reduces the selection pressure on bacterial flora when antibiotic resistance increases.

However, clinical decision-making should consider the individual patient's situation, such as having other medical conditions, age, and severity of appendicitis. As Kumar et al. (2021) have suggested, tailor-made treatments can ensure that higher-risk patients receive full coverage of antibiotics without the need for unnecessary exposure to them. Limitations and Future Research.

Despite these benefits, this review also has certain limitations. The included studies had different designs and sample sizes and used various outcome measures, which could make for somewhat discrepant results. In addition, some studies had shortcomings in reporting, such as a lack of complete data about patient characteristics and outcomes or follow-up points that might affect the reliability of conclusions drawn.

In the future, it will be possible to improve on these limitations by using reasonable outcome measures across many locations for large-scale RCTs and then writing about these in detail. Research should also examine the effects of different antibiotic duration on specific groups of patients, such as children, the elderly, and subjects who have major coexisting diseases. It may provide useful pointers to treatment protocol optimization to conduct studies into appendicitis outcomes as affected by hospital-sponsored "antibiotic stewardship" campaigns.

### 3.3 Limitations and Future Research

lack of consistency stems from differences in study design, sample size and areas genes were measured. In addition, the aforementioned RCTs had some reporting limitations, including incomplete data on patient characteristics or follow-up outcomes, which might diminish our confidence in drawing strong conclusions.

Limitations accompanying this review should be solved in future large, multicenter randomized controlled trials (RCTs) using the standardization of outcome measures and publication standards. Research is also needed to investigate the effects of duration on specific subpopulations, such as pediatric patients, the elderly population, and those with significant comorbidities. Further, focused studies regarding the role of antibiotic stewardship on outcomes in appendicitis may give clues for refinement of treatment paradigms.

## 4. CONCLUSION

This systematic review highlights that short-term antibiotic therapy (≤5 days) is as effective as prolonged regimens in managing complicated acute appendicitis, demonstrating similar infection rates, length of stay, and readmission outcomes. These findings align with a growing body of evidence advocating for reduced antibiotic exposure to minimize resistance and side effects. However, individual patient characteristics, such as comorbidities and disease severity, should guide the duration of antibiotic treatment. Future research should focus on large-scale, standardized trials to further refine antibiotic protocols, especially in vulnerable populations like children, the elderly, and those with significant comorbidities. These findings suggest that shorter antibiotic courses are safe and effective in reducing hospital stays without increasing the risk of complications.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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