

## THE EFFICACY OF ANTIBIOTICS IN ACUTE APPENDICITIS TREATMENT : A COMPREHENSIVE SYSTEMATIC REVIEW

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### ABSTRACT

**Background:** Acute appendicitis has been the most common cause of lower abdominal pain leading to emergency visits worldwide. To avoid major complications, appendectomy has remained the standard treatment for uncomplicated acute appendicitis for over a century.

**The aim:** The aim of this study to show about the efficacy of antibiotics in acute appendicitis treatment.

**Methods:** By the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. This search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed, SagePub, and Scienedirect were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

**Result:** Five publications were found to be directly related to our ongoing systematic examination after a rigorous three-level screening approach. Subsequently, a comprehensive analysis of the complete text was conducted, and additional scrutiny was given to these articles.

**Conclusion:** The therapeutic effects of antibiotics and appendicectomy were comparable for the treatment of acute appendicitis.

**Keyword:** Appendicitis, acute, antibiotics, management, efficacy.

## INTRODUCTION

Acute appendicitis is inflammation of the vermiform appendix and remains the most common cause of the acute abdomen in young adults. The mainstay of treatment in most centres is an appendectomy, and, consequently, this is one of the most common operations performed on the acute abdomen. However, appendicitis can be notoriously difficult to diagnose, and there exists a negative appendectomy rate of 10%–20% despite the use of preoperative computed tomography (CT). In addition, as with all operations, postoperative complications exist, including wound infections, intra-abdominal abscesses, ileus and, in the longer term, adhesions. With this in mind, it is worth considering that the mainstay of treatment for other intra-abdominal inflammatory processes, such as diverticulitis, consists initially of conservative management with antibiotics.<sup>1,2</sup>

Acute appendicitis with the incidence of approximate 1/1000 person-years, which affect 8 million annually, is the most common reason for emergency abdominal surgery. The etiology of acute appendicitis is generally fecal residue or lymphoid tissue proliferation blocking the appendiceal lumen, resulting in high pressure in the lumen and damage to the integrity of the mucosa. Acute appendicitis is classified as either uncomplicated or complicated acute appendicitis. Though the definition of them varies among studies, generally the uncomplicated acute appendicitis may absence of perforation, abscess or peritonitis and may or may not include non-perforated gangrenous or a fecalith.<sup>3</sup>

Conservative treatment with antibiotics is an alternative choice for appendicitis; although the risk of failure is about 13% higher, but the risk of complications is lower. For instance, the odds of overall complications, bowel obstruction, and reoperation were 0.24 (95%CI: 0.13 to 0.44), 0.35 (95%CI: 0.17 to 0.71), and 0.17 (95%CI: 0.04 to 0.75) respectively, when compared to appendectomy. In addition, management might be more cost-effective with antibiotics than appendectomy.<sup>4</sup>

The perforation rate of 25% in patients with a history of pain of less than 24 h is not much lower than the 35% rate of perforation in patients with a history of over 48 h. These may indicate that uncomplicated and complicated appendicitis are distinct diseases. An alternative outcome is that the appendix becomes surrounded by a mass of omentum which walls the inflammatory process and prevents inflammation from spreading to the abdominal cavity (appendix mass), yet the resolution of the condition is delayed. If the appendix becomes walled off by the omentum but has perforated, an abscess will develop localized to the periappendiceal region in the right paracolic gutter or the subcecal area of the pelvis. However, there is no evidence to indicate the proportion of patients likely to develop diffuse sepsis because the antibiotic treatment alters the pattern of disease by replacing the risks of perforation with the lesser risk associated with surgery.<sup>5</sup>

In addition, there is interindividual variation between the host (patient) defense mechanisms and the disease. The indications for operative (surgery), nonoperative (antibiotics), or both in management are discussed. Laparoscopic appendectomy has become the gold standard of treatment, but nonoperative management with antibiotics may suffice in selected cases with uncomplicated appendicitis. The management of the appendix mass/abscess may entail an expedient appendectomy or a combination of conservative management and interval appendectomy.<sup>5</sup>

## METHODS

### Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

### Criteria for Eligibility

For the purpose of this literature review, we compare and contrast the efficacy of antibiotics in acute appendicitis treatment. It is possible to accomplish this by researching of the efficacy of antibiotics in acute appendicitis treatment. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about the efficacy of antibiotics in acute appendicitis treatment. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

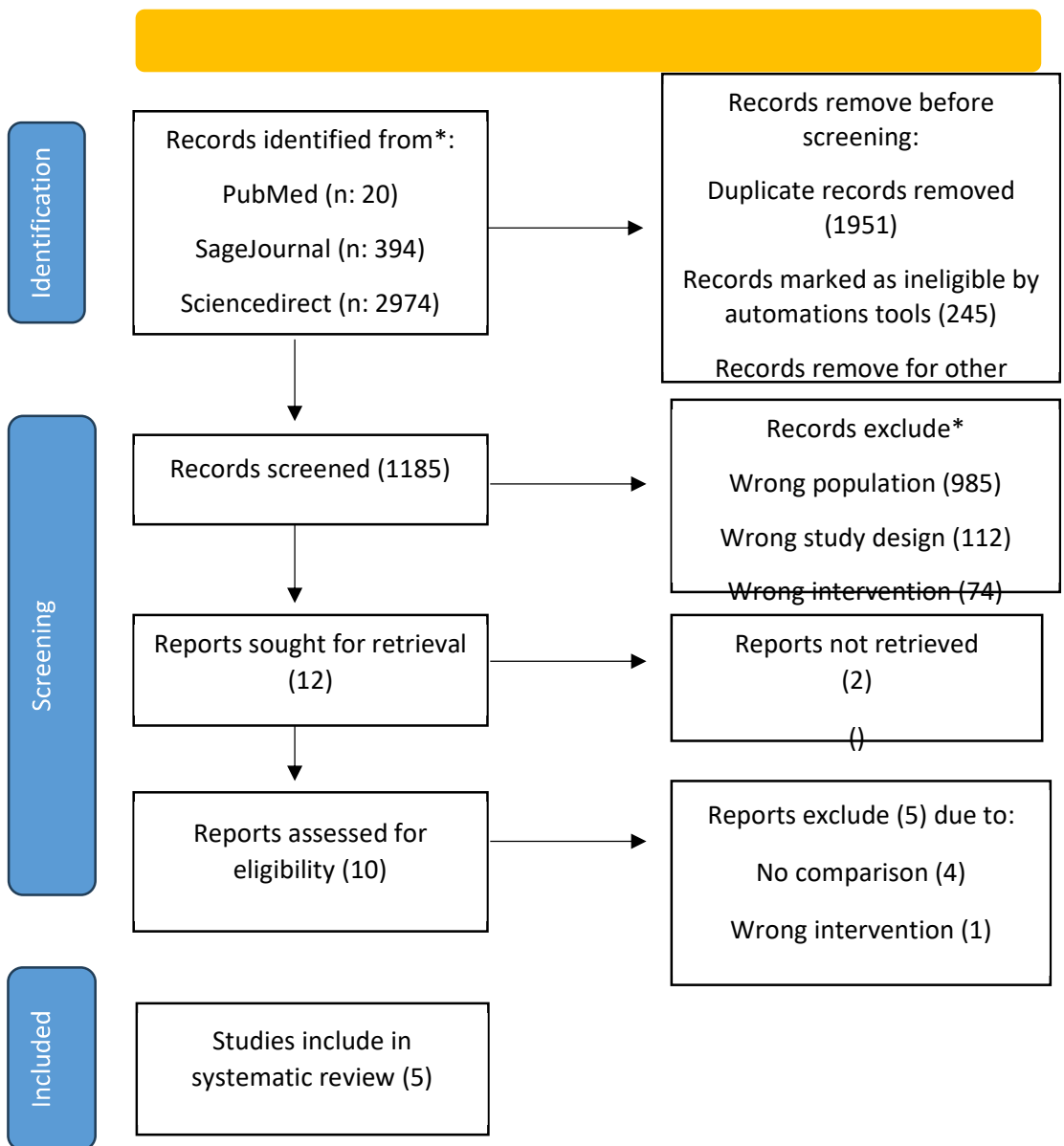
### Search Strategy

We used "the efficacy of antibiotics in acute appendicitis treatment." as keywords. The search for studies to be included in the systematic review was carried out using the PubMed, SagePub, and Scencedirect databases by inputting the words: ("*Appendicitis*"[MeSH Subheading] OR "*Antibiotics*"[All Fields] OR "*Efficacy*" [All Fields]) AND ("*management*"[All

Fields] OR " Treatment"[All Fields]) AND ("Teraphy"[All Fields]) OR ("Outcomes" [All Fields])) used in searching the literature.

**Data retrieval**

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and cannot have been seen anywhere else.



**Figure 1. Article search flowchart**

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

**Quality Assessment and Data Synthesis**

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable

for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

**RESULT**

Using reputable resources like Science Direct, PubMed, and SagePub, our research team first gathered 3388 publications. A thorough three-level screening strategy was used to identify only five papers as directly relevant to our ongoing systematic evaluation. Next, a thorough study of the entire text and further examination of these articles were selected. Table 1 compiles the literature that was analyzed for this analysis in order to make it easier to view.

**Table 1. The literature include in this study**

Author	Origin	Method	Sample Size	Result
Akbar, HF et al., 2022 <sup>6</sup>	Qatar	This was a single hospital based retrospective, cross-sectional study from Jan 2015 to May 2020.	182	One hundred eighty-two cases of uncomplicated acute appendicitis were included and managed conservatively, of which 52.2% were males while 47.8% were females. The median age of the patients was 26 years. Conservative treatment was successful in 26.2% of the patients, with a recurrence of 5.5% in the six-month follow-up period. The mean number of days of hospital stay was three days in patients treated with conservative or surgical treatment.
Picard, C et al., 2023 <sup>7</sup>	France	Cross-sectional study in a single medical centre.	104	A follow-up consultation was conducted for 102 patients, in a mean time span of 2 weeks after discharge from hospital. The follow-up CRP was ≤5 mg/L in 97% of cases (80/82 patients). The follow-up ultrasound was pathological (diameter>6 mm, infiltration, effusion) in 9% (n=9) of the 100 patients for whom data were available. Ultrasound monitoring has been implemented because it was a new service protocol but patient management has not changed even if the ultrasound was pathological (diameter>6 mm, infiltration, effusion) for 9 patients at 15 days of follow-up. No significant link was identified between having a pathological abdominal ultrasound at day 15 and recurrence of appendicitis. In our population, 14.4% patients had surgery (15/104) following a recurrence of the appendicitis in the 2 years after the antibiotic therapy. The median time for surgical treatment was at 82 days after the first day of the initial

				hospitalisation (IQR: 55–233). None of the patients who underwent an operation because of a recurrence presented with complicated appendicitis. There were no cases of abscess, peritonitis nor plastron in the 15 patients who were operated on in our study. All the anatomopathological results concluded to the diagnosis of appendicitis.
<b>Salminen, P et al., 2022<sup>8</sup></b>	Finland	A double-blind, placebo-controlled, superiority RCT in adults with CT-confirmed uncomplicated acute appendicitis was designed to compare placebo with antibiotics (intravenous ertapenem followed by oral levofloxacin and metronidazole).	72	From May 2017 to September 2020, 72 patients with a mean(s.d.) age of 37.5 (11.1) years were recruited at five hospitals. Six were excluded after randomization (5 early consent withdrawals, 1 randomization protocol violation), 35 were assigned to receive antibiotics, and 31 to receive placebo. Enrolment challenges (including hospital pharmacy resources in an acute-care surgery setting) meant that only the lowest sample size of three predefined scenarios was achieved. The 10-day treatment success rate was 87 (95 per cent c.i. 75 to 99) per cent for placebo and 97 (92 to 100) per cent for antibiotics. This clinical difference of 10 (90 per cent c.i. -0.9 to 21) per cent was not statistically different for the primary outcome (1-sided $P = 0.142$ ), and secondary outcomes were similar.
<b>CODA., 2020<sup>9</sup></b>	UK	We conducted a pragmatic, nonblinded, noninferiority, randomized trial comparing antibiotic therapy (10-day course) with appendectomy in patients with appendicitis at 25 U.S. centers.	1552	In total, 1552 adults (414 with an appendicolith) underwent randomization; 776 were assigned to receive antibiotics (47% of whom were not hospitalized for the index treatment) and 776 to undergo appendectomy (96% of whom underwent a laparoscopic procedure). Antibiotics were noninferior to appendectomy on the basis of 30-day EQ-5D scores (mean difference, 0.01 points; 95% confidence interval [CI], -0.001 to 0.03). In the antibiotics group, 29% had undergone appendectomy by 90 days, including 41% of those with an appendicolith and 25% of those without an appendicolith. Complications were more common in the antibiotics group than in the appendectomy group (8.1 vs.

				3.5 per 100 participants; rate ratio, 2.28; 95% CI, 1.30 to 3.98); the higher rate in the antibiotics group could be attributed to those with an appendicolith (20.2 vs. 3.6 per 100 participants; rate ratio, 5.69; 95% CI, 2.11 to 15.38) and not to those without an appendicolith (3.7 vs. 3.5 per 100 participants; rate ratio, 1.05; 95% CI, 0.45 to 2.43). The rate of serious adverse events was 4.0 per 100 participants in the antibiotics group and 3.0 per 100 participants in the appendectomy group (rate ratio, 1.29; 95% CI, 0.67 to 2.50).
<b>Steiner, Zvi et al., 2018<sup>10</sup></b>	Israel	Non-randomized, prospective cohort study included all children admitted between 2014 and 2016, with clinical and laboratory tests suspicious for AUA.	362	Nineteen children, did not respond to the conservative antibiotic treatment (CAT) regimen, had continuous or deteriorating abdominal pain or tenderness and underwent appendectomy 1–2 days after admission. Histology examination revealed two gangrenous appendices without perforation, but with appendicolith; 12 with inflamed appendices, 3 with mild acute subsiding appendicitis with lymphoid hyperplasia, 1 with appendicolith without inflammatory changes, and 1 florid lymphoid hyperplasia with enterobius vermicularis. The antibiotic management protocol was successfully completed by 343 children who were discharged home without operation.

Akbar, HF et al (2022)<sup>6</sup> showed conservative management is no doubt gaining ground, and a lot of centers are inclined towards non-operative management; therefore, further randomized controlled trials and meta-analyses should be carried out on the matter for a more conclusive verdict.

Picard,C et al (2023)<sup>7</sup> showed NOT with a narrowed antibiotic therapy using amoxicillin-clavulanic acid appears to be an effective alternative to surgical intervention for AUA in children with regard to local bacteriological epidemiology. Narrowed antibiotic therapy by amoxicillin/clavulanic acid presents satisfactory results and limits the risk of developing antibiotic resistance compared with antibiotics with a broader spectrum. Our results also lead us to conclude that this treatment does not induce a risk of aggravation or complications for the patients. These results should be confirmed by larger studies.

Salminen, P et al (2022)<sup>8</sup> showed the lack of antibiotic superiority statistically suggests that a non-inferiority trial against placebo is warranted in adults with CT-confirmed mild appendicitis.

CODA (2020)<sup>9</sup> showed for the treatment of appendicitis, antibiotics were noninferior to appendectomy on the basis of results of a standard health-status measure. In the antibiotics group, nearly 3 in 10 participants had undergone appendectomy by 90 days. Participants with an appendicolith were at a higher risk for appendectomy and for complications than those without an appendicolith.

Steiner, Zvi et al (2018)<sup>10</sup> showed the feasibility and safety of conservative management of AUA in children. A rigorous diagnostic plan with strict inclusion and exclusion criteria was used, leading to an approximately 85% success rate of CAT instead of appendectomy. The CAT does not compete with surgery or make appendectomy obsolete. It is a safe alternative in selected suitable cases and can spare appendectomy.

## DISCUSSION

Acute appendicitis is the most common cause of abdominal pain in emergency departments. The lifetime risk of acute appendicitis in males is 8.6 and 6.7% in females with recent meta-analysis showing an increasing trend in the incidence of appendicitis in the newly industrialised countries. Appendectomy has unquestionably been the standard treatment for acute appendicitis for over a century with more than 300,000 appendectomies performed annually in the United States. Although appendectomy is generally well tolerated, it is a major surgical intervention and can be associated with postoperative morbidity. Recently, an increasing amount of evidence has been reported showing that the majority of patients with uncomplicated acute appendicitis may be treated with antibiotics alone instead of surgery.<sup>8,11</sup>

Acute appendicitis is a clinical diagnosis based on history, physical examination, laboratory investigations, and imaging. The diagnosis is established in approximately 90% of patients presenting with classic symptoms of appendicitis, which include migratory pain to the right lower quadrant, vague periumbilical pain, low-grade fever, anorexia, nausea, and vomiting. Although historically appendectomy is the goal standard treatment for acute appendicitis, recently, there has been a marked increase in using broad-spectrum antibiotics as a safe primary approach for patients with uncomplicated acute appendicitis who wish to avoid surgery and the potential postoperative complications.<sup>12</sup>

It is widely believed that acute appendicitis always results in perforation. This belief has persisted since Fitz's initial explanation of the connection between McBurney's report on reduced death from pelvic infections following an appendectomy, and the appendix that an urgent appendectomy is required upon appendicitis diagnosis stems from this line of reasoning. Fitz and McCurney were published 40 years before antibiotics were widely accessible. Minimal invasive treatment is effective and safe, as demonstrated in several randomized clinical trials (RCTs), with a success rate ranging from 63-85%. Such trials have been the subject of meta-analyses and thorough reviews, with positive results. However, because children have unique anatomical and pathophysiologic characteristics, the clinical picture of acute appendicitis in pediatric patients differs from that in adults, making treatment choices for children more challenging.<sup>13,14</sup>

Efficacy rates were higher in the appendectomy group. Nevertheless, the antibiotics-only group maintained an efficacy rate greater than 70% at one-year follow-up. Risk factors that decreased the efficacy in medical management included the presence of appendicolith, neoplasm, appendiceal dilatation, peri-appendiceal fluid collection, higher mean temperature, CRP, and bilirubin. Complications were more frequent and significant in the surgery group. These included complications related to anaesthesia, surgical site infections, damage to nearby structures, and pulmonary embolism. Despite several years of follow-up and disease recurrences, higher financial costs were observed in surgically treated patients compared to the antibiotics-only group.<sup>15</sup>

During the 1950s, an initial non-operative approach for acute appendicitis was attempted, but it was not generally accepted at the time. Appendicitis complicated by appendicular abscess/phlegmon may be managed with antibiotics and non-operative strategies with reduced complication rates compared to surgery, like other acute inflammatory intestinal conditions – i.e. diverticulitis and enterocolitis. In this sense, antibiotic therapy may be associated with reduced costs of treatment, avoiding operation and its consequent complications. However, the use of antibiotics alone as primary therapy for uncomplicated acute appendicitis is still being assessed, and studies have shown conflicting results so far.<sup>12</sup>

## CONCLUSION

In conclusion, the therapeutic effects of antibiotics and appendectomy were comparable for the treatment of acute appendicitis. Therefore, we recommend that more individuals are considered for antibiotic therapy instead of surgery.

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