

Antibiotics-First Strategy Versus Immediate Appendectomy for Uncomplicated Acute Appendicitis: A Narrative Review of Long-Term Recurrence and Outcomes

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1. Introduction

Acute appendicitis is among the most frequent surgical emergencies encountered globally, with an estimated lifetime risk of approximately 7–8%. Traditionally, appendectomy has been regarded as the definitive treatment because untreated appendicitis may progress to perforation, abscess formation, and diffuse peritonitis.

Historically, surgeons favored early operative intervention to minimize complications associated with delayed treatment. However, improvements in computed tomography (CT) imaging have enabled more accurate differentiation between uncomplicated and complicated appendicitis. This distinction has significantly influenced management strategies and introduced the possibility of non-operative treatment using antibiotics alone.

Over the past two decades, several randomized controlled trials and systematic reviews have evaluated conservative antibiotic therapy as an alternative to surgery in selected patients with uncomplicated appendicitis. The publication of the APPAC trial marked a major turning point by demonstrating that a large proportion of patients treated initially with antibiotics avoided appendectomy during follow-up. Subsequent trials, including the CODA trial, further expanded interest in non-operative management.

Despite growing acceptance of conservative treatment in selected cases, concerns remain regarding recurrence rates, treatment failure, missed complicated appendicitis, and long-term patient outcomes. The present review aims to summarize contemporary

evidence regarding antibiotics-first therapy compared with immediate appendectomy for uncomplicated acute appendicitis.

2. Methodology

A structured narrative review of the literature was performed using PubMed, Scopus, Google Scholar, and major surgical journals. Literature published between January 1995 and March 2026 was reviewed.

Search terms included:

- uncomplicated acute appendicitis
- appendectomy
- antibiotic therapy
- conservative management
- APPAC trial
- CODA trial
- recurrence
- laparoscopic appendectomy

Eligible studies included randomized controlled trials, systematic reviews, meta-analyses, cohort studies, and international guideline publications evaluating antibiotics-first management versus appendectomy in adults with CT-confirmed uncomplicated appendicitis.

Studies involving perforated appendicitis, pediatric-only populations, abscess formation, or non-English publications were excluded.

Preference was given to high-impact studies with long-term follow-up data, particularly randomized controlled trials and meta-analyses.

Study	Year	Key Findings
APPAC Trial	2015	Approximately 73% avoided surgery during first year
APPAC 5-Year Follow-up	2018	39.1% recurrence at 5 years
CODA Trial	2020	Antibiotics non-inferior in short-term outcomes
Vons et al.	2011	Higher recurrence with conservative treatment
Hansson et al.	2009	Antibiotics effective in selected patients

Table 1: Summary of Major Clinical Trials

2.1. Pathophysiology of Acute Appendicitis

Acute appendicitis typically develops following obstruction of the appendiceal lumen. Common causes include fecaliths, lymphoid hyperplasia, foreign bodies, parasites, and neoplasms. Luminal obstruction leads to increased intraluminal pressure, venous congestion, bacterial proliferation, ischemia, and progressive inflammation.

If untreated, inflammation may progress to gangrene, perforation, and generalized peritonitis. Modern surgical practice broadly categorizes appendicitis into uncomplicated and complicated disease.

Uncomplicated appendicitis refers to localized appendiceal inflammation without evidence of perforation, abscess, phlegmon, or generalized peritonitis. Complicated appendicitis includes perforation, diffuse contamination, abscess formation, or gangrenous appendicitis.

This distinction is clinically important because conservative antibiotic therapy is considered appropriate only in carefully selected patients with uncomplicated disease.

2.2. Defining Uncomplicated Appendicitis

Accurate diagnosis is essential when considering non-operative management. CT imaging remains the most reliable modality for diagnosing uncomplicated appendicitis in adults.

Typical CT findings include:

- Enlarged appendix greater than 6 mm in diameter
- Appendiceal wall thickening
- Periappendiceal fat stranding
- Localized inflammatory changes
- Features suggesting complicated appendicitis include:
 - Extraluminal air
 - Abscess formation
 - Perforation
 - Diffuse fluid collection
 - Phlegmon
 - Generalized peritonitis

The role of appendicolith remains controversial. Several studies have shown that patients with appendicolith have higher rates of treatment failure and recurrence following antibiotic therapy. Consequently, many clinicians consider appendicolith a relative

contraindication to non-operative management.

Ultrasonography may be useful in children and pregnant women; however, CT imaging demonstrates greater sensitivity and specificity in adult patients.

2.3. Antibiotics-First Strategy

Non-operative management generally involves intravenous antibiotics followed by oral antibiotic therapy. Most protocols target gram-negative and anaerobic organisms commonly associated with appendiceal infection.

Common antibiotic regimens include:

- Intravenous ertapenem followed by oral levofloxacin and metronidazole
- Ceftriaxone with metronidazole
- Piperacillin-tazobactam in selected cases

Patients are typically monitored clinically for:

- Fever
- Increasing abdominal pain
- Leukocytosis
- Signs of perforation
- Hemodynamic instability

Failure of conservative treatment usually necessitates urgent appendectomy.

2.4. Advantages of Conservative Management

2.4.1. Avoidance of Surgery

Antibiotic therapy allows selected patients to avoid anesthesia and operative intervention.

2.4.2. Reduced Immediate Complications

Several studies have reported lower short-term complication rates compared with surgery.

2.4.3. Faster Initial Recovery

Patients managed conservatively often experience shorter recovery periods and earlier return to routine activities.

2.4.4. Reduced Postoperative Morbidity

Non-operative treatment eliminates risks associated with surgical wounds, postoperative ileus, and anesthesia-related complications.

2.5. Limitations of Conservative Therapy

2.5.1. Risk of Recurrence

Recurrence remains the most significant limitation of antibiotic-

first management. Long-term studies have demonstrated that a proportion of patients eventually require appendectomy.

2.5.2. Initial Treatment Failure

Some patients fail to respond during the initial hospitalization and require urgent surgery.

2.5.3. Diagnostic Uncertainty

Conservative management may delay diagnosis of underlying appendiceal neoplasms or complicated disease.

2.5.4. Recurrent Hospital Visits

Patients treated non-operatively may require repeated imaging, emergency department visits, or rehospitalization.

2.6. Immediate Appendectomy

Appendectomy remains the definitive treatment for acute appendicitis. Laparoscopic appendectomy has largely replaced open surgery because of improved postoperative recovery and lower wound complication rates.

2.6.1. Advantages of Appendectomy

- Definitive treatment
- Elimination of recurrence risk
- Histopathological diagnosis
- Reduced long-term uncertainty
- Short hospital stay in uncomplicated cases

2.6.2. Disadvantages of Appendectomy

- Surgical site infection
- Postoperative pain
- Adhesion-related bowel obstruction
- Incisional hernia
- Anesthesia-related complications
- Although complication rates are generally low, surgery still carries inherent procedural risks.

2.7. Landmark Clinical Trials

2.7.1. The APPAC Trial

The Appendicitis Acuta (APPAC) trial remains one of the most influential studies evaluating antibiotic therapy for uncomplicated appendicitis.

In this multicenter randomized clinical trial conducted in Finland, 530 adult patients with CT-confirmed uncomplicated appendicitis were randomized to appendectomy or antibiotic therapy.

Key findings included:

- Approximately 73% of patients treated with antibiotics avoided surgery during the first year.
- Five-year follow-up demonstrated a cumulative recurrence rate of 39.1%.
- Most recurrent cases remained uncomplicated.
- Delayed appendectomy was not associated with significantly increased complications.

The APPAC trial demonstrated that antibiotics-first management may be a feasible alternative in selected patients.

2.7.2. The CODA Trial

The Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) trial further evaluated antibiotics-first management in a broader patient population.

The trial demonstrated that:

- Antibiotic therapy was non-inferior to surgery in short-term health status outcomes.
- Approximately 30% of patients treated with antibiotics underwent appendectomy within 90 days.
- Patients with appendicolith experienced higher complication and appendectomy rates.

The CODA trial highlighted the importance of shared decision-making and individualized treatment selection.

However, important limitations should be recognized. The study included patients with appendicolith, which may have increased treatment-failure rates compared with earlier trials. In addition, crossover between treatment groups and variability in antibiotic protocols may influence interpretation of long-term outcomes.

2.8. Long-Term Outcomes

2.8.1. Recurrence Rates

Long-term recurrence is the principal concern associated with conservative management.

Evidence from major studies demonstrates:

- Approximately 20–30% recurrence within 1 year
- Nearly 39% recurrence at 5 years in the APPAC trial

Despite recurrence risk, many patients prefer initial antibiotic therapy to avoid surgery.

2.8.2. Complications

Complication profiles differ significantly between conservative and surgical treatment strategies.

Several randomized trials and meta-analyses have demonstrated that patients treated initially with antibiotics generally experience fewer short-term complications compared with immediate surgery. Conservative treatment avoids operative trauma, anesthesia-related complications, postoperative wound infections, and procedure-associated morbidity during the initial hospitalization.

However, antibiotics-first management is associated with risks unique to non-operative therapy, including:

- Recurrent appendicitis
- Failure of initial antibiotic therapy
- Rehospitalization
- Requirement for delayed appendectomy
- Repeated imaging and follow-up visits
- Immediate appendectomy, although definitive, may result in surgical complications such as:
 - Surgical site infection
 - Intra-abdominal abscess
 - Postoperative ileus
 - Adhesion-related intestinal obstruction

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- Incisional hernia
 - Anesthesia-associated adverse events

The APPAC trial reported lower overall complication rates in the antibiotic group compared with the appendectomy group during long-term follow-up. Importantly, most recurrent episodes following conservative therapy remained uncomplicated and were successfully managed with delayed appendectomy when required.

Meta-analyses have also demonstrated that delayed appendectomy following recurrence does not appear to significantly increase the risk of perforation or major postoperative morbidity in appropriately selected patients.

2.8.3. Hospital Stay and Return to Normal Activity

Length of hospital stay varies between studies and treatment protocols. Some investigations have demonstrated comparable hospitalization durations between antibiotics-first therapy and laparoscopic appendectomy, whereas others report slightly shorter recovery times with conservative management.

Patients treated with antibiotics often resume routine activities earlier because they avoid postoperative pain and wound recovery. In contrast, laparoscopic appendectomy usually requires a brief postoperative recovery period despite minimally invasive techniques.

Return-to-work intervals are frequently shorter in conservatively managed patients during the initial treatment phase.

2.8.4. Patient Preference and Shared Decision-Making

Modern management of uncomplicated appendicitis increasingly emphasizes shared decision-making.

Some patients prefer antibiotic therapy to avoid surgery, anesthesia, postoperative pain, and recovery-related disruption. Others choose appendectomy because it offers definitive treatment with minimal risk of recurrence.

Effective counseling should include discussion regarding:

- Possibility of recurrence
- Potential need for delayed surgery
- Risks of operative intervention
- Expected recovery timelines
- Presence of appendicolith
- Individual comorbidities and lifestyle factors

The CODA trial significantly reinforced the importance of individualized patient-centered treatment selection.

2.9. Special Considerations

2.9.1. Elderly Patients

Older adults may present atypically and possess higher operative risk because of comorbid conditions. Conservative management may be considered selectively, although exclusion of malignancy remains important.

2.9.2. Pediatric Population

Although this review primarily focuses on adults, pediatric studies have also explored non-operative management. Results remain variable, and recurrence risk continues to be a concern in children.

2.9.3. Pregnant Patients

Diagnosis during pregnancy may be challenging because of altered anatomy and nonspecific symptoms. Surgical management generally remains preferred in many cases because delayed perforation may increase maternal and fetal complications.

2.9.4. Quality of Life

Short-term quality-of-life outcomes often favor conservative management because patients avoid surgery and recover more rapidly.

Long-term quality-of-life outcomes appear similar between both treatment strategies.

2.9.5. Cost-Effectiveness

Initial hospitalization costs may be lower with antibiotic therapy. However, recurrent admissions, repeated imaging, and delayed appendectomy can reduce long-term economic advantages.

Several studies suggest that overall cost differences between strategies may narrow over extended follow-up periods.

2.9.6. Role of Appendicolith

The presence of appendicolith has emerged as a significant predictor of treatment failure.

Studies demonstrate that appendicolith is associated with:

- Increased recurrence risk
- Higher perforation rates
- Greater likelihood of emergency appendectomy

Many surgeons therefore consider appendicolith an unfavorable feature for antibiotics-first management.

2.9.7. Current Guidelines

The World Society of Emergency Surgery (WSES) guidelines recognize antibiotic therapy as a safe alternative in selected patients with uncomplicated appendicitis.

The American College of Surgeons also supports shared decision-making while emphasizing appropriate patient selection and informed counseling.

Modern guidelines recommend:

- CT-confirmed uncomplicated appendicitis
- Careful exclusion of perforation or abscess
- Patient counseling regarding recurrence risk
- Individualized treatment planning

2.9.8. Future Perspectives

Future research is expected to focus on:

- Artificial intelligence-assisted imaging
- Biomarkers predicting recurrence
- Personalized treatment algorithms
- Outpatient antibiotic protocols
- Risk stratification models

Further long-term studies are required to identify patients most likely to benefit from non-operative management.

3. Conclusion

Management of uncomplicated acute appendicitis has evolved substantially over recent decades. Although appendectomy remains the definitive treatment with near-complete elimination of recurrence risk, contemporary evidence supports antibiotics-first therapy as a reasonable alternative in carefully selected patients.

The APPAC and CODA trials demonstrated that many patients treated initially with antibiotics can avoid surgery, at least in the short term. However, recurrence rates approaching 39% over five years remain an important limitation.

Current evidence suggests that treatment decisions should be individualized using imaging findings, clinical status, patient preference, and recurrence risk. Shared decision-making has become central to modern management of uncomplicated appendicitis.

Future advances in predictive biomarkers, imaging techniques, and personalized medicine may further refine the role of conservative management in appendicitis care [1-10].

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