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Cheng Y, Xiong X, Lu J, Wu S, Zhou R, Cheng N.
Early versus delayed appendicectomy for appendiceal phlegmon or abscess.
Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD011670.
DOI: [10.1002/14651858.CD011670.pub2](https://doi.org/10.1002/14651858.CD011670.pub2).

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[Intervention Review]

Early versus delayed appendicectomy for appendiceal phlegmon or abscess

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ABSTRACT

Background

Appendiceal phlegmon and abscess account for 2% to 10% of acute appendicitis. People with appendiceal phlegmon or abscess usually need an appendicectomy to relieve their symptoms and avoid complications. The timing of appendicectomy for appendiceal phlegmon or abscess is controversial.

Objectives

To assess the effects of early versus delayed appendicectomy for appendiceal phlegmon or abscess, in terms of overall morbidity and mortality.

Search methods

We searched the Cochrane Library (CENTRAL; 2016, Issue 7), MEDLINE Ovid (1950 to 23 August 2016), Embase Ovid (1974 to 23 August 2016), Science Citation Index Expanded (1900 to 23 August 2016), and the Chinese Biomedical Literature Database (CBM) (1978 to 23 August 2016). We also searched the World Health Organization (WHO) International Clinical Trials Registry Platform search portal (23 August 2016) and ClinicalTrials.gov (23 August 2016) for ongoing trials.

Selection criteria

We included all individual and cluster-randomised controlled trials, irrespective of language, publication status, or age of participants, comparing early versus delayed appendicectomy in people with appendiceal phlegmon or abscess.

Data collection and analysis

Two review authors independently identified the trials for inclusion, collected the data, and assessed the risk of bias. We performed meta-analyses using Review Manager 5. We calculated the risk ratio (RR) for dichotomous outcomes and the mean difference (MD) for continuous outcomes with 95% confidence intervals (CI).

Main results

We included two randomised controlled trials with a total of 80 participants in this review.

1. Early versus delayed open appendicectomy for appendiceal phlegmon

Forty participants (paediatric and adults) with appendiceal phlegmon were randomised either to early appendicectomy (appendicectomy as soon as appendiceal mass resolved within the same admission) ($n = 20$), or to delayed appendicectomy (initial conservative treatment followed by interval appendicectomy six weeks later) ($n = 20$). The trial was at high risk of bias. There was no mortality in either group. There is insufficient evidence to determine the effect of using either early or delayed open appendicectomy on overall morbidity (RR 13.00; 95% CI 0.78 to 216.39; very low-quality evidence), the proportion of participants who developed wound infection (RR 9.00; 95% CI 0.52 to 156.91; very low quality evidence) or faecal fistula (RR 3.00; 95% CI 0.13 to 69.52; very low quality evidence). The quality of evidence for increased length of hospital stay and time away from normal activities in the early appendicectomy group (MD 6.70 days; 95% CI 2.76 to 10.64, and MD 5.00 days; 95% CI 1.52 to 8.48, respectively) is very low quality evidence. The trial reported neither quality of life nor pain outcomes.

2. Early versus delayed laparoscopic appendicectomy for appendiceal abscess

Forty paediatric participants with appendiceal abscess were randomised either to early appendicectomy (emergent laparoscopic appendicectomy) ($n = 20$) or to delayed appendicectomy (initial conservative treatment followed by interval laparoscopic appendicectomy 10 weeks later) ($n = 20$). The trial was at high risk of bias. The trial did not report on overall morbidity or complications. There was no mortality in either group. We do not have sufficient evidence to determine the effects of using either early or delayed laparoscopic appendicectomy for outcomes relating to hospital stay between the groups (MD -0.20 days; 95% CI -3.54 to 3.14; very low quality of evidence). Health-related quality of life was measured with the Pediatric Quality of Life Scale-Version 4.0 questionnaire (a scale of 0 to 100 with higher values indicating a better quality of life). Health-related quality of life score measured at 12 weeks after appendicectomy was higher in the early appendicectomy group than in the delayed appendicectomy group (MD 12.40 points; 95% CI 9.78 to 15.02) but the quality of evidence was very low. This trial reported neither the pain nor the time away from normal activities.

Authors' conclusions

It is unclear whether early appendicectomy prevents complications compared to delayed appendicectomy for people with appendiceal phlegmon or abscess. The evidence indicating increased length of hospital stay and time away from normal activities in people with early open appendicectomy is of very low quality. The evidence for better health-related quality of life following early laparoscopic appendicectomy compared with delayed appendicectomy is based on very low quality evidence. For both comparisons addressed in this review, data are sparse, and we cannot rule out significant benefits or harms of early versus delayed appendicectomy.

Further trials on this topic are urgently needed and should specify a set of criteria for use of antibiotics, percutaneous drainage of the appendiceal abscess prior to surgery and resolution of the appendiceal phlegmon or abscess. Future trials should include outcomes such as time away from normal activities, quality of life and the length of hospital stay.

PLAIN LANGUAGE SUMMARY

Early or delayed surgical removal of appendix in people with symptomatic complicated appendicitis

Review question

What are the risks and benefits of early versus delayed removal of appendix in people with symptomatic complicated appendicitis?

Background

The human appendix is a tube at the connection of the small and the large intestines. Possible functions of the appendix may be to protect the body against infection and to maintain healthy levels bacteria in the gut when recovering from diarrhoea. Appendicitis covers a variety of clinical conditions resulting from inflammation of the appendix.

Complicated appendicitis is defined as appendiceal phlegmon (simple inflammatory mass without pus located in bottom right of the appendix) or appendiceal abscess (pocket of pus surrounding an acutely inflamed and/or ruptured appendix). People with this condition usually need surgical removal of the appendix to relieve their symptoms and avoid complications. The timing of surgical removal of the appendix is controversial. Immediate surgery is technically demanding. Some experts question the appropriateness of delayed appendectomy, as people are unlikely to experience a recurrence after a successful non-surgical treatment. However, the true diagnosis could be uncertain in some cases, and postponing the appendectomy may delay diagnosis of underlying disease.

Study characteristics

We searched for all relevant randomised controlled trials up to 23 August 2016. We identified two trials involving 80 participants. One compared early versus delayed open appendicectomy in 40 children and adults with appendiceal phlegmon. The other trial compared early versus delayed keyhole (laparoscopic) appendicectomy (where surgery is performed through a very small incision) in 40 children with appendiceal abscess. Studies took place in the USA and India. The age of the individuals in the trials varied between 1 year and 84 years, and 27.5% were females.

Key results

Both two studies were small and had a number of limitations so we cannot be certain about how the effects of the two surgical approaches compare. From one trial in children and adults comparing open with delayed appendicectomy, there was insufficient evidence to show the effect of using either approach on the overall complication rate or the proportion of participants who developed wound infection. Our certainty in a longer stay in hospital stay and time away from normal activities with open appendicectomy is very low. There were no deaths in the study. Quality of life, and pain were not reported in this trial.

The other trial in children with appendiceal abscess receiving either early or delayed keyhole appendicectomy did not report on overall complication rates. The trial did not provide enough evidence to show the effect of using either approach on the length of hospital stay among participants. We have very low certainty that children who had early keyhole appendicectomy had better quality of life compared with children who had delayed keyhole appendicectomy. The study did not report if there were any deaths, and did not provide information on pain, or time away from normal activities.

At present the benefits and harms of early versus delayed appendicectomy are not well understood because the current information is based upon very low quality evidence.

Quality of the evidence

Both trials were at a high risk of bias. Overall, we judged the quality of the evidence to be very low. Thus, further well-designed trials are urgently needed.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Early versus delayed open appendicectomy for appendiceal phlegmon

Early versus delayed open appendicectomy for appendiceal phlegmon

Patient or population: paediatric and adult patients with appendiceal phlegmon

Setting: secondary and tertiary care

Intervention: early open appendicectomy

Comparison: delayed open appendicectomy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Delayed appendicectomy	Early appendicectomy				
Overall morbidity Median follow-up: 33,5 months	0 per 1000	300 per 1000	RR 13.00 (0.78 to 216.39)	40 (1 study)	⊕⊕⊕⊕ Very low a,b	—
Wound infection Median follow-up: 33,5 months	0 per 1000	200 per 1000	RR 9.00 (0.52 to 156.91)	40 (1 study)	⊕⊕⊕⊕ Very low a,b	—
Faecal fistula Median follow-up: 33,5 months	0 per 1000	50 per 1000	RR 3.00 (0.13 to 69.52)	40 (1 study)	⊕⊕⊕⊕ Very low a,b	—
Mortality Median follow-up: 33,5 months	See comment	See comment	Not estimable	40 (1 study)	⊕⊕⊕⊕ Low b	There was no mortality in either group.
Total length of hospital stay (days) Follow-up: 3 weeks	The mean total length of hospital stay in the delayed appendicectomy group was 14.7 days	The mean total length of hospital stay in the early appendicectomy group was 6.7 days higher (2.76 to 10.64 higher)	MD 6.70 (2.76 to 10.64)	40 (1 study)	⊕⊕⊕⊕ Very low a,b	—
Time away from normal activities (days) Median follow-up: 33,5 months	The mean time away from normal activities in the delayed appendicectomy group was 20 days	The mean time away from normal activities in the early appendicectomy group was 5 days higher	MD 5.00 (1.52 to 8.48)	40 (1 study)	⊕⊕⊕⊕ Very low a,b	—

(1.52 to 8.48 higher)

Quality of life Median follow-up: 33,5 months

Not reported

Pain (days) Follow-up: 3 weeks

Not reported

*The basis for the **assumed risk** was the control group proportion in the study. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR**: risk ratio; **MD**: mean difference.

GRADE Working Group grades of evidence

High quality: further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: we are very uncertain about the estimate.

^aDowngraded one level for serious risk of bias.

^bDowngraded two levels for very serious imprecision (small sample size).

Summary of findings 2. Early versus delayed laparoscopic appendicectomy for appendiceal abscess

Early versus delayed laparoscopic appendicectomy for appendiceal abscess

Patient or population: paediatric participants with appendiceal abscess

Setting: secondary and tertiary care

Intervention: early laparoscopic appendicectomy

Comparison: delayed laparoscopic appendicectomy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Delayed appendicectomy	Early appendicectomy				
Overall morbidity	Not reported					
Wound infection	Not reported					
Faecal fistula	Not reported					

Mortality Follow-up: 12 weeks	See comment	See comment	Not estimable	40 (1 study)	⊕⊕⊕⊕ Very low ^a	There was no mortality in either group.
Total length of hospital stay (days) Follow-up: 12 weeks	The mean total length of hospital stay in the delayed appendicectomy group was 6.7 days	The mean total length of hospital stay in the early appendicectomy group was 0.2 days lower (3.54 lower to 3.14 higher)	MD -0.20 (-3.54 to 3.14)	40 (1 study)	⊕⊕⊕⊕ Very low ^{a,b}	—
Time away from normal activities (days)	Not reported					
Quality of life (Pediatric Quality of Life Scale-Version 4.0, a scale of 0 to 100 with higher values indicating better quality of life) Follow-up: 12 weeks	The mean quality of life score in the delayed appendicectomy group was 84.37 points	The mean quality of life score in the early appendicectomy group was 12.40 points higher (9.78 to 15.02 higher)	MD 12.40 (9.78 to 15.02)	40 (1 study)	⊕⊕⊕⊕ Very low ^{a,b}	We considered the observed mean difference in quality of life score to be clinically significant.
Pain (days)	Not reported					

*The basis for the **assumed risk** was the control group proportion in the study. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference.

GRADE Working Group grades of evidence

High quality: further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: we are very uncertain about the estimate.

^aDowngraded two levels due to very serious imprecision (small sample size).

^bDowngraded one level for serious risk of bias.

BACKGROUND

Description of the condition

Appendicitis refers to inflammation of the appendix. Acute appendicitis is the most common cause of acute abdominal pain (Andersen 2005; Cheng 2015a; Rehman 2011; Wilms 2011). The overall incidence of acute appendicitis varies between 76 and 227 cases per 100,000 population per year in different countries (Addiss 1990; Andersson 1994; Andreu-Ballester 2009; Buckius 2012; Körner 1997; Lee 2010; Pieper 1982; Williams 1998). The overall lifetime risk for acute appendicitis is approximately 7% to 8% in the USA and 16% in South Korea (Addiss 1990; Lee 2010). It affects all age groups, with the highest incidence in the second decade of life (Addiss 1990; Anderson 2012; Wilms 2011).

Acute appendicitis can be broadly divided into two subgroups: simple appendicitis (e.g. early or uncomplicated appendicitis) and complicated appendicitis (e.g. gangrenous appendicitis and appendiceal phlegmon or abscess) (Andersen 2005; Cheng 2015a; Simillis 2010).

The most common type is simple appendicitis, which is the early stage of acute appendicitis (Andersen 2005; Cheng 2015a; Simillis 2010). In case of a missed or delayed diagnosis of simple appendicitis, the appendix may become gangrenous, potentially leading to perforation and localised or generalised peritonitis (inflammation of the peritoneum), resulting in complicated appendicitis (Andersen 2005; Cheng 2015a; Cheng 2015b; Deelder 2014; Simillis 2010).

Appendiceal phlegmon and appendiceal abscess present as a mass, resulting from both inflammation and walled-off perforation of the appendix (Ahmed 2005; Nitecki 1993). A walled-off appendiceal perforation differs from a simple inflammatory mass – consisting of the inflamed appendix, its adjacent viscera and the greater omentum (an appendiceal phlegmon) – in that it contains pus (an appendiceal abscess) (Ahmed 2005; Nitecki 1993). The proportion of appendiceal mass (phlegmon or abscess) in acute appendicitis ranges from 2% to 10% in different case series studies (Andersson 2007; Cueto 2006; Oliak 2000; Shipsey 1985; Willemsen 2002), with higher risk in children and the elderly whose diagnosis or therapy of acute appendicitis are delayed (Andersson 1994; Boomer 2010; Cirocchi 2008; Livingston 2007; Oliak 2000).

The prognosis for an appendiceal phlegmon or abscess is good (Markides 2010; Santacroce 2012). The overall mortality rate of appendiceal phlegmon or abscess is less than 1% (Cueto 2006; Markides 2010; Santacroce 2012). However, appendiceal phlegmon or abscess is associated with higher morbidity than simple appendicitis (Andersen 2005; Cheng 2015a; Cueto 2006; Simillis 2010). Common postoperative complications include wound infections, intra-abdominal abscesses, incisional hernias and bowel obstructions (Blakely 2011; Cueto 2006; Frazee 1996; Kang 2000; Kumar 2004; St Peter 2010; Yau 2007).

Description of the intervention

Appendectomy, or surgical removal of the appendix, is performed primarily as an emergency procedure to treat acute appendicitis (Andersen 2005; Andersen 2015). People with simple appendicitis usually need either an antibiotic treatment or an appendectomy to relieve their symptoms and avoid complications (Markides 2010; Salminen 2015; Santacroce 2012; Sauerland 2010; Vons 2011; Wilms

2011). Appendectomy is one of the most common emergency surgical procedures performed (Santacroce 2012); there are approximately 300,000 each year in the USA alone (Hall 2010). There are two types of appendectomy: open appendectomy (removal of the appendix by laparotomy) and laparoscopic appendectomy (removal of the appendix by keyhole surgery) (Cheng 2012; Cheng 2013; Markides 2010; Sauerland 2010).

Surgery for people with complicated appendicitis may be early or delayed (Andersson 2007; Markides 2010; Simillis 2010). While there is no universally accepted definition of early appendectomy (Andersson 2007; Simillis 2010), we considered that in people with appendiceal phlegmon or abscess, any appendectomy performed immediately or several days later within the same admission was early appendectomy. Delayed appendectomy (also known as interval appendectomy) is defined as initial conservative (non-surgical) treatment followed by appendectomy several weeks later within a later admission. The role of delayed appendectomy for people with appendiceal phlegmon or abscess is controversial: some authors have suggested that delayed appendectomy is not necessary unless the person presents with recurrent symptoms (Andersson 2007; Willemsen 2002), whereas others do not agree (Deelder 2014; Gillick 2001). Patients in the delayed appendectomy group usually need antibiotics to relieve their symptoms and sometimes require percutaneous drainage of appendiceal abscesses (Andersson 2007; Simillis 2010). Overall, studies report surgical morbidity ranging from 2% to 30% in different case series studies (Blakely 2011; Cueto 2006; Frazee 1996; Kang 2000; Kumar 2004; St Peter 2010; Yau 2007).

How the intervention might work

Common management of appendiceal phlegmon or abscess involves initial conservative treatment with antibiotics followed by delayed appendectomy (Andersson 2007; Kumar 2004; Simillis 2010). In theory, conservative treatment localises the inflammatory process and decreases the risk of surgical complications when compared with early appendectomy during the acute inflammatory phase (Andersson 2007; Kumar 2004; Simillis 2010). Delayed appendectomy can prevent the recurrence of appendicitis, which may occur if there is no appendectomy at all (Andersson 2007; Kumar 2004; Simillis 2010). However, delayed appendectomy involves waiting several weeks, during which time the appendicitis may worsen, develop complications or recur following the temporary success of the conservative treatment (Andersson 2007; Kumar 2004). Overall, the success rate of conservative treatment is approximately 90% (Andersson 2007), but when it fails, people may experience substantial morbidity (Andersson 2007; Simillis 2010). Moreover, the true diagnosis could be uncertain in some cases, and postponing surgery could delay diagnosis of underlying cancer or Crohn's disease.

With the growing experience of surgeons and the development of surgical instruments, authors have increasingly reported the safety and feasibility of early appendectomy in appendiceal phlegmon or abscess (Blakely 2011; Frazee 1996; Kang 2000; Markides 2010; St Peter 2010; Yau 2007). Early appendectomy can address appendiceal phlegmon or abscess in a single admission without the risk of recurrent appendicitis (Andersson 2007; Kumar 2004; Simillis 2010), and it may reduce the time away from normal activities for patients (Blakely 2011). However, there are concerns about the high morbidity associated with an early appendectomy (i.e. challenging closure, suture of the inflamed

appendix stump) (Andersson 2007; Simillis 2010), with the potential for unnecessary ileocaecal (ileum and cecum) resection or right-sided hemicolectomy (surgical removal of the right side of the colon) due to a technical problem or suspicion of malignancy (Andersson 2007; Simillis 2010).

Why it is important to do this review

Given the pros and cons for both early and delayed appendicectomy, the timing of appendicectomy for appendiceal phlegmon or abscess remains controversial (Ahmed 2005). Until now, there has been no Cochrane Review assessing the roles of early and delayed appendicectomy for appendiceal phlegmon or abscess.

OBJECTIVES

To assess the effects of early versus delayed appendicectomy for appendiceal phlegmon or abscess, in terms of overall morbidity and mortality.

METHODS

Criteria for considering studies for this review

Types of studies

We included all individual and cluster-randomised controlled trials (RCTs) comparing early versus delayed appendicectomy in people with appendiceal phlegmon or abscess. We excluded quasi-randomised trials (in which allocation is based on a pseudo-random sequence, e.g. odd/even hospital number or date of birth, alternation) and non-randomised studies because of the high risk of bias in such studies.

Types of participants

We included all people (both children and adults, irrespective of sex or ethnicity) who underwent appendicectomy (elective and emergent) for appendiceal phlegmon or abscess. Preoperative diagnosis of appendiceal phlegmon or abscess could be established using medical history, physical examination, and imaging results (e.g. ultrasonography, computer tomography). Use of antibiotics and percutaneous drainage of appendiceal abscess were allowed for participants in both groups.

Types of interventions

We included trials comparing early appendicectomy with delayed appendicectomy (irrespective of whether the surgical procedure was open or laparoscopic). We defined early appendicectomy as appendicectomy performed immediately or several days later within the same admission. Delayed appendicectomy was performed several weeks after initial diagnosis in a later admission.

Types of outcome measures

Primary outcomes

- Overall morbidity (overall complication rate defined by study authors and graded by the Clavien-Dindo complications classification system) (Clavien 2009)
 - * Wound infection (time point closest to 14 days)
 - * Abdominal abscess (time point closest to 14 days)
 - * Bowel obstruction (time point closest to 14 days)
 - * Incisional hernia (time point closest to 90 days)
 - * Faecal fistula (time point closest to 14 days)
- Mortality (death rate after operation, time point closest to 90 days)

Secondary outcomes

- Length of hospital stay
 - * Duration of first hospitalisation
 - * Total hospital stay
- Time away from normal activities
- Quality of life (time point closest to 90 days, any validated score)
- Pain (days with pain)

Search methods for identification of studies

We designed the search strategies with the help of the Cochrane Colorectal Cancer Group (CCCG) Information Specialist (Sys Johnsen). We conducted the searches irrespective of language, year or publication status.

Electronic searches

We searched the following electronic databases with no language or date of publication restrictions.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 7) in the Cochrane Library (Appendix 1).
- MEDLINE Ovid (1950 to 23 August 2016) (Appendix 2).
- Embase Ovid (1974 to 23 August 2016) (Appendix 3).
- Science Citation Index Expanded in the Web of Science (1900 to 23 August 2016) (Appendix 4).
- Chinese Biomedical Literature Database (CBM) (1978 to 23 August 2016) (Appendix 5).

Searching other resources

We searched the following databases to identify ongoing trials: the World Health Organization (WHO) International Clinical Trials Registry Platform search portal (apps.who.int/trialsearch), ClinicalTrials.gov (www.clinicaltrials.gov), Current Controlled Trials (www.controlled-trials.com), Chinese Clinical Trial Register (www.chictr.org), and the EU Clinical Trials Register (www.clinicaltrialsregister.eu). We searched the meeting abstracts via the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) (www.sages.org), the Society for Surgery of the Alimentary Tract (SSAT) (ssat.com), and Conference Proceedings Citation Index to explore further relevant clinical trials. We also searched the reference lists in included studies and any relevant systematic reviews identified.

Data collection and analysis

We conducted the systematic review according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011); we also guided our work according to the Cochrane Colorectal Cancer Group module.

Selection of studies

After completing the searches, we merged the search results using *Endnote X7* reference management software and removed duplicate records. Two review authors (LJ, WS) independently scanned the title and abstract of every record identified by the search for inclusion. We retrieved the full text for further assessment if the inclusion criteria were unclear from the abstract. We detected duplicate publications by identifying common authors, centres, details of the interventions, numbers of participants and baseline data (Higgins 2011). We excluded papers not meeting the inclusion criteria and listed the reasons for the exclusion. We included all eligible studies irrespective of whether they reported measured outcome data. The two review authors resolved any disagreements by discussion with a third review author (CY).

Data extraction and management

To extract study characteristics and outcome data, we used a standard data collection form that we had piloted on at least one study in the review. Two review authors (XX, ZR) extracted the following study characteristics from included studies.

- Methods: study design, total duration study and run-in, number of study centres and location, study setting, withdrawals, date of study.
- Participants: total number of participants, mean age, age range, sex, severity of condition, diagnostic criteria, inclusion criteria, exclusion criteria.
- Interventions: intervention, comparison.
- Outcomes: primary and secondary outcomes specified and collected, time points reported.
- Notes: funding for trial, notable conflicts of interest of trial authors.

Two review authors (XX, ZR) independently extracted outcome data from included studies. We resolved disagreements by consensus or by involving a third person (CY). One review author (CN) copied across the data from the data collection form into the Review Manager 5 (RevMan 5) file (RevMan 2014). We double checked that the data were entered correctly by comparing the study reports with the presentation of the data in the systematic review. A second review author (CY) spot-checked study characteristics for accuracy against the trial report.

Assessment of risk of bias in included studies

Two review authors (LJ, WS) independently assessed risk of bias in the included trials based on the following domains: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; and differences in baseline characteristics (Appendix 6). Following evaluation of the above domains, we assigned a 'low risk of bias' judgement to included trials with a low risk of bias in all of the assessed domains. If we judged the risk of bias to be unclear or high, we

listed the trial under the group of trials as 'high risk of bias' trials. We resolved any difference in opinion by discussion. In cases of unsettled disagreements, a third review author (CY) adjudicated. We presented the results of the risk of bias assessment in two figures (a 'Risk of bias' graph figure and a 'Risk of bias' summary figure), which we generated using *RevMan 2014*.

Measures of treatment effect

We performed the meta-analysis using RevMan 5 software (RevMan 2014). For dichotomous outcomes, we calculated risk ratio (RR) with 95% confidence interval (CI) (Deeks 2011). In case of rare events (e.g. mortality), we planned to calculate the Peto odds ratio (OR) (Deeks 2011). For continuous outcomes, we calculated the mean difference (MD) with 95% confidence interval (Deeks 2011). For continuous outcomes with different measurement scales in different randomised controlled trials, we planned to calculate the standardised mean differences (SMD) with 95% CIs (Deeks 2011).

Unit of analysis issues

The unit of analysis was the individual participant. We did not find any cluster-randomised trial for this review. In case of a cluster-randomised trial, we intended to analyse the data adjusted for clustering using the generic inverse-variance method in RevMan 5 (Higgins 2011).

Dealing with missing data

We contacted the original investigators to request further information in case of missing data. However, there was no reply. Thus, we used only the available data in the analyses.

Assessment of heterogeneity

We planned to describe the heterogeneity in the data using the χ^2 test (Deeks 2011). We considered a P value less than 0.10 to indicate statistically significant heterogeneity (Deeks 2011). We also planned to use the I^2 statistic to measure the quantity of heterogeneity. In case of statistical heterogeneity, clinical heterogeneity (variability in the participants, interventions and outcomes studied) or both, we planned to perform the meta-analysis but interpret the result cautiously and to investigate potential sources of heterogeneity.

Assessment of reporting biases

We planned to use funnel plots to assess reporting biases, using visual asymmetry to determine the presence of reporting biases (Sterne 2011). We also planned to perform linear regression to determine funnel plot asymmetry (Egger 1997). We did not create funnel plots to assess reporting biases, as the number of trials included was fewer than 10 (Sterne 2011).

Data synthesis

We planned to perform the meta-analysis using *RevMan 2014*. We would have employed the random-effects model for the analysis. We considered a P value less than 0.05 to be statistically significant.

However, we did not perform any meta-analysis because we included only a single trial for each outlined outcome.

Subgroup analysis and investigation of heterogeneity

We would have performed the following subgroup analyses if we had found enough trials.

- Laparoscopic versus open appendicectomy.
- Adults versus children.
- One type of appendix stump closure versus another.

Sensitivity analysis

We would have performed the following sensitivity analyses if we had found enough trials.

- Excluding trials with a high or unclear risk of bias.
- Consecutively excluding every study from the meta-analysis to explore the impact of individual studies on the overall effect.
- Changing between worst/best-case scenario analysis and best/worst-case scenario analysis for the binary outcomes in case of missing data.

Summary of findings table

We evaluated the quality of evidence using the GRADE approach for each outcome, including any subgroup analysis or sensitivity analysis ([Schünemann 2009](#)). We presented the quality of evidence in 'Summary of findings' tables for the following comparisons: early versus delayed open appendicectomy for appendiceal phlegmon and early versus delayed laparoscopic appendicectomy for appendiceal abscess. We downgraded the quality of evidence by one (serious concern) or two (very serious concerns) levels for the following reasons: risk of bias, inconsistency (unexplained heterogeneity, inconsistency of results), indirectness

(indirect population, intervention, control, outcomes), imprecision (wide confidence intervals) and publication bias. We justified, documented and incorporated our judgements about the quality of the evidence (high, moderate, low or very low) into the reporting of results for each outcome.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Results of the search

We identified a total of 4696 records through the electronic searches: 691 in the Cochrane Library, 2390 in MEDLINE Ovid, 979 in Embase Ovid, 56 in Science Citation Index Expanded in the Web of Science and 579 in the Chinese Biomedical Literature Database (CBM). We identified one record through scanning reference lists of the identified randomised controlled trials ([Handa 1997](#)). We excluded 552 duplicates and 4134 clearly irrelevant records through screening titles and abstracts. We retrieved the remaining 10 records for further assessment. We excluded eight studies for the reasons listed in the [Characteristics of excluded studies](#) table. In total, two randomised controlled trials fulfilled the inclusion criteria. We searched trial registers for ongoing trials, but did not identify any additional studies to be considered for future updates of this review. The study flow diagram is shown in [Figure 1](#).

Figure 1. Study flow diagram.

Included studies

Both of the included trials contributed data to the analyses. We provide details of the trials in the [Characteristics of included studies](#) table. One trial compared early open appendicectomy with delayed open appendicectomy for paediatric and adult participants with appendiceal phlegmon (Kumar 2004), while the other trial compared early laparoscopic appendicectomy with delayed laparoscopic appendicectomy for paediatric participants with appendiceal abscess (St Peter 2010). Overall, the two trials included 80 participants. Participants' age ranged from 1 year to 84 years. The mean proportion of females was 5% in Kumar

2004 and 47.5% in St Peter 2010. There was no difference in the characteristics of participants in the intervention group or control in either of the trials. Overall, 40 (50%) participants had appendiceal phlegmon (Kumar 2004), and the other 40 (50%) had appendiceal abscess (St Peter 2010). The duration of short term follow-up in the two trials was 3 weeks and 12 weeks, respectively.

For Kumar 2004, short-term outcome measures included operative time, operative difficulty, postoperative complications, length of hospital stay, and duration of time away from work. Long-term outcome measures were: number of hospital visits made, presence of severe incisional pain, scar appearance, and patients with

recurrent appendicitis, during a follow-up period of 24-52 (median 33.5) months.

Excluded studies

We excluded one randomised controlled trial because it focused on perforated appendicitis without appendiceal abscess (Blakely 2011). None of the other excluded studies were randomised

controlled trials (Aranda-Narváez 2010; Bahram 2011; Erdoğan 2005; Goh 2005; Handa 1997; Senapathi 2002; Weber 2003).

Risk of bias in included studies

The risk of bias of the included studies is shown in Figure 2 and Figure 3. None of the trials were at low risk of bias across all domains.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Differences in baseline characteristics
Kumar 2004	?	?	-	?	+	-	+
St Peter 2010	?	?	-	?	+	+	+

Allocation

Both trials were at unclear risk for random sequence generation and allocation concealment.

Blinding

Both trials were at high risk of bias for blinding of participants and personnel because it was impossible to blind the participants or healthcare providers (Kumar 2004; St Peter 2010). It was unclear whether trials blinded outcome assessors.

Incomplete outcome data

There was a low risk of bias for incomplete outcome data in both trials because there were no missing data (Kumar 2004; St Peter 2010).

Selective reporting

The trial protocol was available for one trial (St Peter 2010), which reported all pre-specified outcomes. Thus, we considered the trial to be free from selective reporting bias. The trial protocol was not available for the other trial (Kumar 2004), and as some outcomes of

interest for this review (mortality, quality of life and pain) were not reported, we considered the trial to be high risk of bias for selective reporting.

Other potential sources of bias

With regard to differences in baseline characteristics, we did not observe any baseline imbalances, therefore we considered both trials to be at low risk in this domain (Kumar 2004; St Peter 2010).

Effects of interventions

See: [Summary of findings for the main comparison Early versus delayed open appendicectomy for appendiceal phlegmon](#); [Summary of findings 2 Early versus delayed laparoscopic appendicectomy for appendiceal abscess](#)

Early versus delayed open appendicectomy for appendiceal phlegmon

One trial (N = 40) compared early open appendicectomy with delayed open appendicectomy in paediatric and adult participants with appendiceal phlegmon (Kumar 2004). Twenty participants were randomised to the early appendicectomy

group (appendicectomy as soon as appendiceal mass resolved within the same admission) and 20 participants to the delayed appendicectomy group (initial conservative treatment followed by interval appendicectomy six weeks later). None of the participants crossed from the delayed appendicectomy group to the early appendicectomy group or underwent percutaneous drainage of the appendiceal phlegmon. There was no clinical or statistical heterogeneity, as the analysis included only one trial. We summarise the results in [Summary of findings for the main comparison](#).

[Kumar 2004](#) evaluated the following outcomes.

Overall morbidity

The overall complication rate was 30% in the early appendicectomy group and 0% in the delayed appendicectomy group. There was no evidence of difference in the rate of overall morbidity between the groups (risk ratio (RR) 13.00; 95% confidence interval (CI) 0.78 to 216.39; $P = 0.07$; [Analysis 1.1](#)).

The overall wound infection rate was 20.0% in the early appendicectomy group and 0% in the delayed appendicectomy group. There was no evidence of difference between the groups (RR 9.00; 95% CI 0.52 to 156.91; $P = 0.13$; [Analysis 1.2](#)).

The proportion of participants experiencing faecal fistula was 5.0% in the early appendicectomy group and 0% in the delayed appendicectomy group. There was no evidence of difference between the groups (RR 3.00; 95% CI 0.13 to 69.52; P value = 0.49; [Analysis 1.3](#)).

The trial did not report the rates of abdominal abscess, bowel obstruction or incisional hernia.

We downgraded the quality of evidence to very low due to risk of bias (lack of blinding, unclear random sequence generation and allocation concealment) and very serious imprecision.

Mortality

There was no mortality in either group. We downgraded the quality of evidence to low due to very serious imprecision.

Length of hospital stay

The mean length of hospital stay was 21.4 days in the early appendicectomy group and 14.7 days in the delayed appendicectomy group. Total hospital stay for participants in the delayed appendicectomy group included a combination of the first and second admissions. The total hospital stay was longer in the early appendicectomy group than in the delayed appendicectomy group (mean difference (MD) 6.70 days; 95% CI 2.76 to 10.64; $P < 0.001$; [Analysis 1.4](#)).

We downgraded the quality of the evidence to very low due to risk of bias (lack of blinding, unclear random sequence generation and allocation concealment) and very serious imprecision.

Time away from normal activities

The mean time away from normal activities was 25.0 days in the early appendicectomy group and 20.0 days in the delayed appendicectomy group. The time away from normal activities was longer in the early appendicectomy group than in the delayed

appendicectomy group (MD 5.00 days; 95% CI 1.52 to 8.48; $P = 0.005$; [Analysis 1.5](#)).

We downgraded the quality of the evidence to very low due to risk of bias (lack of blinding, unclear random sequence generation and allocation concealment) and very serious imprecision.

[Kumar 2004](#) did not report on quality of life or pain.

Early versus delayed laparoscopic appendicectomy for appendiceal abscess

One trial ($N = 40$) compared early laparoscopic appendicectomy with delayed laparoscopic appendicectomy in paediatric participants with appendiceal abscess ([St Peter 2010](#)). Twenty participants were randomised to the early appendicectomy group (emergent laparoscopic appendicectomy), and 20 participants to the delayed appendicectomy group (initial conservative treatment followed by interval appendicectomy 10 weeks later). Four participants crossed from the delayed appendicectomy group to the early appendicectomy group. Eleven participants in the delayed appendicectomy group underwent percutaneous drainage of the appendiceal abscess. There was no clinical or statistical heterogeneity, as the analysis included only one trial. We summarise the results in [Summary of findings 2](#).

Overall morbidity

[St Peter 2010](#) did not report this outcome.

Mortality

There was no mortality in either group. We downgraded the quality of the evidence to low due to very serious imprecision.

Length of hospital stay

The mean length of hospital stay was 6.7 days in the early appendicectomy group versus 6.5 days in the delayed appendicectomy group. Total hospital stay for participants in the delayed appendicectomy group included a combination of the first and second admissions. There was no evidence of difference in the total hospital stay between the groups (MD -0.20 days; 95% CI -3.54 to 3.14; $P = 0.91$; [Analysis 2.1](#)).

We downgraded the quality of the evidence to very low due to risk of bias (lack of blinding, unclear random sequence generation and allocation concealment) and very serious imprecision.

Time away from normal activities

[St Peter 2010](#) did not report this outcome.

Quality of life

[St Peter 2010](#) used the Pediatric Quality of Life Scale-Version 4.0 to assess quality of life, a scale of 0 to 100 with higher values indicating better quality of life. The mean quality of life score at 12 weeks after appendicectomy was 96.77 points in the early appendicectomy group and 84.37 points in the delayed appendicectomy group. The quality of life score at 12 weeks after appendicectomy was higher in the early appendicectomy group than in the delayed appendicectomy group (MD 12.40 points; 95% CI 9.78 to 15.02; P value < 0.001 ; [Analysis 2.2](#)). We downgraded the quality of the evidence to very low due to risk of bias (lack of blinding, unclear

random sequence generation and allocation concealment) and very serious imprecision.

Pain

[St Peter 2010](#) did not report this outcome.

Subgroup analysis

We did not perform any planned subgroup analysis because too few trials were included in this review.

Sensitivity analysis

We did not perform any planned sensitivity analysis because we included only two trials in this review, and both were at high risk of bias but had no missing data.

Reporting biases

We did not create funnel plots to assess reporting biases because the number of trials included was fewer than 10. We identified a study protocol for one trial ([St Peter 2010](#)). The trial was free of reporting bias because it reported all of the pre-specified outcomes. The trial protocol was not available for the [Kumar 2004](#) trial, but it reported both primary and secondary outcomes of this review. Thus we considered both included trials to be free of reporting bias.

DISCUSSION

Summary of main results

This review includes two randomised controlled trials involving 80 paediatric and adult participants undergoing open or laparoscopic appendicectomy for appendiceal phlegmon or abscess. Both trials were at a high risk of bias ([Kumar 2004](#); [St Peter 2010](#)). We found no evidence of differences in overall morbidity or mortality between the early appendicectomy group and the delayed appendicectomy group. One very low-quality trial showed that early open appendicectomy increased total hospital stay and time away from normal activities for paediatric and adult participants with appendiceal phlegmon ([Kumar 2004](#)). However, the other very low-quality trial suggested that early laparoscopic appendicectomy was better than delayed laparoscopic appendicectomy in terms of health-related quality of life for paediatric participants with appendiceal abscess ([St Peter 2010](#)).

There are several possible reasons for the differences in findings between the two studies. First, the types of participants of interest between the two studies were different. One trial included both paediatric and adult participants with appendiceal phlegmon ([Kumar 2004](#)), while the other trial only included paediatric participants with appendiceal abscess ([St Peter 2010](#)). Additionally, the types of interventions between the two studies were different. Participants in one trial underwent early open appendicectomy as soon as the appendiceal mass resolved ([Kumar 2004](#)), while participants in the other trial underwent early (emergent) laparoscopic appendicectomy ([St Peter 2010](#)). Laparoscopic appendicectomy appears to be superior to open appendicectomy for suspected appendicitis ([Sauerland 2010](#)). Moreover, most participants with appendiceal abscess underwent percutaneous drainage of the abscess (when possible) and delayed appendicectomy in one trial, while participants with appendiceal phlegmon in the other trial did not need percutaneous drainage of

the phlegmon. Thus, we did not pool the two studies because of the obvious clinical heterogeneity between them.

There was no mortality in either trial. Although overall morbidity was higher in the early appendicectomy group (30%) than in the delayed appendicectomy group (0%) for participants with appendiceal phlegmon, the difference was not statistically significant. Appendicectomy is one of the most common operations performed in the world, yet there were only 80 participants contributing data to this review, so it lacked the statistical power to detect any clinically meaningful difference between early and delayed appendicectomy for preventing complications, even if such a difference were present. In addition, where we detected differences, our confidence was low, as the small numbers mean results could be spurious, and moreover underpowered analyses can exacerbate the impact of bias. Thus, it is unclear whether early appendicectomy prevents complications compared to delayed appendicectomy for people with appendiceal phlegmon or abscess; the data are sparse, and we cannot rule out significant benefits or harms for either intervention.

Overall completeness and applicability of evidence

The need for an appendicectomy after successful conservative management of complicated appendicitis remains controversial ([Simillis 2010](#)). Because of the risk of recurrent appendicitis and missed finding of malignancy, appendicectomy is a common treatment for complicated appendicitis (appendiceal phlegmon or abscess). Both trials included participants undergoing emergent or elective appendicectomy for appendiceal phlegmon or abscess. Most participants with appendiceal abscesses in one trial underwent percutaneous drainage of the abscess before delayed appendicectomy. Thus, the results of this review are applicable to participants who are about to undergo emergent or elective appendicectomy for appendiceal phlegmon or abscess. In addition, participants who are about to undergo delayed appendicectomy require percutaneous drainage of appendiceal abscesses (when possible).

Quality of the evidence

Overall, we considered the quality of the evidence to be very low ([Summary of findings for the main comparison](#); [Summary of findings 2](#)). The main reason for downgrading was wide confidence intervals for the effect estimates. We also downgraded further for risk of bias. Neither of the trials was at a low risk of bias across all domains; one major source of risk was lack of blinding, which might introduce detection bias and performance bias. Although it was impossible to blind the participants or healthcare providers, blinding of outcome assessors could be achieved with appropriate study design. Likewise, there was an unclear risk of selection bias in both trials, as authors did not report details on random sequence generation or allocation concealment. We could not assess statistical heterogeneity because there was only one trial in each comparison.

Potential biases in the review process

There were several potential biases of note in the review process. First, only two trials with 80 participants were identified, reflecting a lack of data on this topic to date. Second, we were unable to assess the impact of publication bias by visual inspection of the funnel plot.

Agreements and disagreements with other studies or reviews

Another systematic review compared early appendicectomy and conservative treatment (antibiotic treatment without delayed appendicectomy) for appendiceal phlegmon or abscess ([Simillis 2010](#)), concluding that conservative treatment was better than early appendicectomy in terms of complication and reoperation rate. However, the data did not justify a general recommendation because of significant heterogeneity between included studies. The present review is the first systematic review comparing early versus delayed appendicectomy for appendiceal phlegmon or abscess that includes only randomised controlled trials. Our findings, that early open appendicectomy increases hospital stay and time away from normal activities compared to appendicectomy in people with appendiceal phlegmon, and that early laparoscopic appendicectomy improves health-related quality of life for participants with appendiceal abscess, is consistent with the findings of [Simillis 2010](#).

AUTHORS' CONCLUSIONS

Implications for practice

It is unclear whether early appendicectomy prevents complications compared to delayed appendicectomy for people with appendiceal phlegmon or abscess. The evidence indicating increased length of hospital stay and time away from normal activities in people with early open appendicectomy is of very low quality. The evidence for better health-related quality of life following early laparoscopic

appendicectomy compared with delayed appendicectomy is based on very low quality evidence. For both comparisons addressed in this review, data are sparse, and we cannot rule out significant benefits or harms of early versus delayed appendicectomy.

Implications for research

High quality trials are urgently required. Investigators should employ adequate methods of randomisation, allocation concealment and blinding of outcome assessors to reduce the risk of bias. Future trials should specify a set of criteria for antibiotics use, percutaneous drainage of the appendiceal abscess, and resolution of the appendiceal mass. Authors should define all of the patient-important outcomes (e.g. time away from normal activities, quality of life) more accurately and report them in accordance with validated criteria. The choice of surgical procedure for removal of phlegmon or abscess appendicitis (e.g. open versus laparoscopic) is of interest but outside the scope of this review, and is the topic of another Cochrane Review ([Sauerland 2010](#)).

ACKNOWLEDGEMENTS

We would like to thank the Cochrane Colorectal Cancer Group (CCCG), including Henning Keinke Andersen and Sara Hallum, both assisting in the development of the review, and Sys Johnsen and Marija Barbateskovic, who developed the search strategies. Furthermore, Dr Jianping Gong for careful revision of the final review. We also want to thank the involved editors, peer reviewers, sign off editor and the CEU screening editor for valuable input and comments to this review. And finally, the Copy Edit Support for careful revision of the final manuscript.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Kumar 2004

Methods

Randomised controlled trial

Kumar 2004 (Continued)

Participants	<p>Country: India</p> <p>Study dates: from 1998 to 2001</p> <p>Number randomised: 60</p> <p>Postrandomisation dropout: 0 (0%)</p> <p>Children: not mentioned</p> <p>Adults: not mentioned</p> <p>Females: 3 (5%)</p> <p>Appendiceal phlegmon: 60 (100%)</p> <p>Appendiceal abscess: 0 (0%)</p> <p>Inclusion criteria:</p> <p>Participants with appendiceal mass determined on medical history, physical examination, and imaging results (e.g. ultrasonography, plain abdominal X-ray)</p> <p>Exclusion criteria:</p> <ol style="list-style-type: none"> 1. Free air in the peritoneal cavity (on plain films) 2. Pus collection in the right iliac fossa or pelvis 3. Colonic malignancy or ileocaecal tuberculosis
Interventions	<p>Participants with appendiceal mass (N = 60) were randomly assigned to 3 groups</p> <p>Group 1: early open appendicectomy (n = 20)</p> <p>Further details: open appendicectomy as soon as appendiceal mass resolved within the same admission</p> <p>Group 2: delayed open appendicectomy (n = 20)</p> <p>Further details: initial conservative treatment followed by interval open appendicectomy 6 weeks later</p> <p>Group 3: conservative treatment without appendicectomy (n = 20). Group excluded from review</p>
Outcomes	<p>Short-term outcome measures (< 3 weeks): Operative time, operative difficulty, postoperative complications, length of hospital stay, and duration of time away from work.</p> <p>Long-term outcome measures (median 33,5 weeks): number of hospital visits made, presence of severe incisional pain, scar appearance, and patients with recurrent appendicitis.</p>
Notes	<p>Funding source: no information provided</p> <p>Declarations of interest: no information provided</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: no information provided
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: it is not possible to blind the participants and healthcare providers unless sham surgery was provided, which may be unethical
Blinding of outcome assessment (detection bias)	Unclear risk	Comment: no information provided

Kumar 2004 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts
Selective reporting (reporting bias)	High risk	Comment: the trial protocol was not available. Some outcomes of interest in the review were not reported so that the trial was considered to be high risk of bias for selective reporting.
Differences in baseline characteristics	Low risk	Comment: there was no baseline imbalance in important characteristics.

St Peter 2010

Methods	Randomised controlled trial
Participants	Country: USA Study dates: from 2006 to 2009 Number randomised: 40 Postrandomisation dropout: 0 (0%) Children: 40 (100%) Adults: 0 (0%) Girls: 19 (47.5%) Appendiceal phlegmon: 0 (0%) Appendiceal abscess: 40 (100%) Inclusion criteria: 1. 7-18 years old 2. Well-defined abdominal abscess determined on computer tomography imaging Exclusion criteria: 1. People with a postoperative abscess 2. People with a comorbid condition
Interventions	Participants with appendiceal abscess (N = 40) were randomly assigned to 2 groups Group 1: early laparoscopic appendicectomy (n = 20) Further details: emergent (immediate) laparoscopic appendicectomy Group 2: delayed laparoscopic appendicectomy (n = 20) Further details: initial conservative treatment and percutaneous drainage of the abscess (when possible), followed by interval laparoscopic appendicectomy approximately 10 weeks later
Outcomes	Mortality, total hospital stay, total hospital costs, and quality of life (Pediatric Quality of Life Scale-Version 4.0)
Notes	Funding source: no information provided Declarations of interest: no information provided

Risk of bias
Early versus delayed appendicectomy for appendiceal phlegmon or abscess (Review)

St Peter 2010 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: no information provided
Allocation concealment (selection bias)	Unclear risk	Quote: "[t]he randomisation sequence was accessed to identify the next allotment" Comment: no information provided about the method of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: it is not possible to blind the participants and healthcare providers unless sham surgery was provided, which may be unethical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there were no postrandomisation dropouts
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is available. All of the study's pre-specified outcomes were reported
Differences in baseline characteristics	Low risk	Comment: no baseline imbalance in important characteristics

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Aranda-Narváez 2010	A non-randomised study
Bahram 2011	A non-randomised study
Blakely 2011	Randomised controlled trial about perforated appendicitis without appendiceal abscess
Erdoğan 2005	A non-randomised study
Goh 2005	A non-randomised study
Handa 1997	A non-randomised study
Senapathi 2002	A non-randomised study
Weber 2003	A non-randomised study

DATA AND ANALYSES

Comparison 1. Early appendicectomy versus delayed appendicectomy for appendiceal phlegmon

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Overall morbidity	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2 Wound infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3 Faecal fistula	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4 Total length of hospital stay (days)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5 Time away from normal activities (days)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1 Early appendicectomy versus delayed appendicectomy for appendiceal phlegmon, Outcome 1 Overall morbidity.

Analysis 1.2. Comparison 1 Early appendicectomy versus delayed appendicectomy for appendiceal phlegmon, Outcome 2 Wound infection.

Analysis 1.3. Comparison 1 Early appendicectomy versus delayed appendicectomy for appendiceal phlegmon, Outcome 3 Faecal fistula.

Analysis 1.4. Comparison 1 Early appendicectomy versus delayed appendicectomy for appendiceal phlegmon, Outcome 4 Total length of hospital stay (days).

Study or subgroup	Early appendicectomy		Delayed appendicectomy		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Kumar 2004	20	21.4 (8.5)	20	14.7 (2.9)		0%	6.7[2.76,10.64]
					Favors 'early'		Favors 'delayed'

Analysis 1.5. Comparison 1 Early appendicectomy versus delayed appendicectomy for appendiceal phlegmon, Outcome 5 Time away from normal activities (days).

Study or subgroup	Early appendicectomy		Delayed appendicectomy		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Kumar 2004	20	25 (7.4)	20	20 (2.9)		0%	5[1.52,8.48]
					Favors 'early'		Favors 'delayed'

Comparison 2. Early appendicectomy versus delayed appendicectomy for appendiceal abscess

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total length of hospital stay (days)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2 Quality of life (score on a scale from 0-100)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Analysis 2.1. Comparison 2 Early appendicectomy versus delayed appendicectomy for appendiceal abscess, Outcome 1 Total length of hospital stay (days).

Study or subgroup	Early appendicectomy		Delayed appendicectomy		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
St Peter 2010	20	6.5 (3.8)	20	6.7 (6.6)		0%	-0.2[-3.54,3.14]
					Favors 'early'		Favors 'delayed'

Analysis 2.2. Comparison 2 Early appendicectomy versus delayed appendicectomy for appendiceal abscess, Outcome 2 Quality of life (score on a scale from 0-100).

Study or subgroup	Early appendicectomy		Delayed appendicectomy		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
St Peter 2010	20	96.8 (4.4)	20	84.4 (4.1)		0%	12.4[9.78,15.02]
					Favors 'delayed'		Favors 'early'

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Appendectomy] explode all trees
#2 MeSH descriptor: [Appendicitis] explode all trees
#3 appendectom* or appendic*:ti,ab,kw
#4 (#1 or #2 or #3)
#5 MeSH descriptor: [Gangrene] explode all trees
#6 MeSH descriptor: [Intestinal Perforation] explode all trees
#7 MeSH descriptor: [Rupture, Spontaneous] explode all trees
#8 MeSH descriptor: [Abdominal Abscess] explode all trees
#9 MeSH descriptor: [Peritonitis] explode all trees
#10 (complicat* or gangren* or perforat* or ruptur* or phlegmon* or abscess* or periton*):ti,ab,kw
#11 (#5 or #6 or #7 or #8 or #9 or #10)
#12 (#4 and #11)

Appendix 2. MEDLINE search strategy

1. exp Appendectomy/
2. exp Appendicitis/
3. (appendectom* or appendic*).mp.
4. 1 or 2 or 3
5. exp Gangrene/
6. exp Intestinal Perforation/
7. exp Rupture, Spontaneous/
8. exp Abdominal Abscess/
9. exp Peritonitis/
10. (complicat* or gangren* or perforat* or ruptur* or phlegmon* or abscess* or periton*).mp.
11. 5 or 6 or 7 or 8 or 9 or 10
12. 4 and 11
13. randomized controlled trial.pt.
14. controlled clinical trial.pt.
15. random*.ab.
16. placebo.ab.
17. drug therapy.fs..
18. trial.ab.
19. groups.ab.
20. 13 or 14 or 15 or 16 or 17 or 18 or 19
21. exp animals/ not humans.sh.
22. 20 not 21
23. 12 and 22

Appendix 3. Embase search strategy

1. exp appendectomy/
2. exp acute appendicitis/
3. exp appendicitis/
4. (appendectom* or appendic*).mp.
5. 1 or 2 or 3 or 4
6. exp gangrene/
7. exp intestinal perforation/ or exp phlegmon/
8. exp rupture/ or exp abdominal organ rupture/
9. exp abscess/ or exp abdominal abscess/
10. exp peritonitis/ or exp bacterial peritonitis/
11. (complicat* or gangren* or perforat* or ruptur* or phlegmon* or abscess* or periton*).mp.
12. 6 or 7 or 8 or 9 or 10 or 11
13. 5 and 12
14. CROSSOVER PROCEDURE.sh.
15. DOUBLE-BLIND PROCEDURE.sh.
16. SINGLE-BLIND PROCEDURE.sh.

17. (crossover* or cross over*).ti,ab.
18. placebo*.ti,ab.
19. (doubl* adj blind*).ti,ab.
20. allocat*.ti,ab.
21. trial.ti.
22. RANDOMIZED CONTROLLED TRIAL.sh.
23. random*.ti,ab.
24. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25. (exp animal/ or exp invertebrate/ or animal.hw. or nonhuman/) not (exp human/ or human cell/or (human or humans or man or men or wom?n).ti.)
26. (animal* or nonhuman*).ti,ab. 27. 25 or 26 28. 24 not 27
29. 13 and 28

Appendix 4. Science Citation Index Expanded search strategy

- #1 Topic=(appendectom* OR appendic*)
#2 Topic=(complicat* or gangren* or perforat* or ruptur* or phlegmon* or abscess* or periton*)
#3 Topic=(random* OR control* OR RCT* OR placebo OR trial* OR group*)
#4 (#3 AND #2 AND #1)

Appendix 5. Chinese Biomedical Literature Database search strategy

1. 主题词:随机对照试验/全部树/全部副主题词
2. 主题词:临床对照试验/全部树/全部副主题词
3. 主题词:临床试验/全部树/全部副主题词
4. 主题词:病例对照研究/全部树/全部副主题词
5. 主题词:随机分配/全部树/全部副主题词
6. 主题词:对比研究/全部树/全部副主题词
7. 主题词:前瞻性研究/全部树/全部副主题词
8. 主题词:安慰剂/全部树/全部副主题词
9. 全部字段:随机
- 10.全部字段:单盲
- 11.全部字段:双盲
- 12.全部字段:盲法
- 13.(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)
- 14.主题词:阑尾切除术/全部树/全部副主题词
- 15.主题词:阑尾炎/全部树/全部副主题词
- 16.全部字段:阑尾
- 17.(#14 OR #15 OR #16)
- 18.主题词:坏疽/全部树/全部副主题词
- 19.主题词:肠穿孔/全部树/全部副主题词
- 20.主题词:穿孔, 自发性/全部树/全部副主题词
- 21.主题词:腹腔脓肿/全部树/全部副主题词
- 22.主题词:腹膜炎全部树/全部副主题词
- 23.全部字段:复杂
- 24.全部字段:坏疽
- 25.全部字段:穿孔
- 26.全部字段:蜂窝组织炎
- 27.全部字段:脓肿
- 28.全部字段:腹膜炎
- 29.(#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28)
- 30.(#13 AND #17 AND #29)

Appendix 6. Criteria for judging risk of bias within each domain

Sequence generation

- Low risk of bias: the method used was either adequate (e.g. computer-generated random numbers, table of random numbers) or unlikely to introduce confounding.
- Unclear risk of bias: there was insufficient information to assess whether the method used was likely to introduce confounding.
- High risk of bias (the method used was improper and likely to introduce confounding, e.g. quasi-randomised studies). We excluded such studies.

Allocation concealment

- Low risk of bias: the method used was unlikely to induce bias on the final observed effect (e.g. central allocation).
- Unclear risk of bias: there was insufficient information to assess whether the method used was likely to induce bias on the estimate of effect.
- High risk of bias: the method used was likely to induce bias on the final observed effect (e.g. open random allocation schedule).

Blinding of participants and personnel

- Low risk of bias: blinding was performed adequately, or the outcome measurement was not likely to be influenced by lack of blinding.
- Unclear risk of bias: there was insufficient information to assess whether the type of blinding used was likely to induce bias on the estimate of effect.
- High risk of bias: no blinding or incomplete blinding, and the outcome or outcome measurement was likely to be influenced by lack of blinding.

Blinding of outcome assessors

- Low risk of bias: blinding was performed adequately, or the outcome measurement was not likely to be influenced by lack of blinding.
- Unclear risk of bias: there was insufficient information to assess whether the type of blinding used was likely to induce bias on the estimate of effect.
- High risk of bias: no blinding or incomplete blinding, and the outcome or the outcome measurement was likely to be influenced by lack of blinding.

Incomplete outcome data

- Low risk of bias: the underlying reasons for missing data were unlikely to make treatment effects depart from plausible values, or proper methods were employed to handle missing data.
- Unclear risk of bias: there was insufficient information to assess whether the missing data mechanism in combination with the method used to handle missing data was likely to induce bias on the estimate of effect.
- High risk of bias: the crude estimate of effect was clearly biased due to the underlying reasons for missing data, and the methods used to handle missing data were unsatisfactory (e.g. complete case estimate).

Selective outcome reporting

- Low risk of bias: the trial protocol was available and all of the trial's pre-specified outcomes that were of interest to this review were reported; if the trial protocol was not available, all the primary outcomes in this review were reported.
- Unclear risk of bias: there was insufficient information to assess whether the magnitude and direction of the observed effect was related to selective outcome reporting.
- High risk of bias: not all of the trial's pre-specified primary outcomes were reported.

Differences in baseline characteristics

- Low risk of bias: there was no baseline imbalance in important characteristics.
- Unclear risk of bias: the baseline characteristics were not reported.
- High risk of bias: there was a baseline imbalance due to chance or due to imbalanced exclusion after randomisation.

WHAT'S NEW

Date	Event	Description
2 June 2017	Amended	Contact author changed to Dr Yao Cheng

CONTRIBUTIONS OF AUTHORS

Cheng Y and Xiong X: drafted the protocol and drafted the final review.

Lu J: selected which trials to include and assessed the risk of bias of the trials.

Wu S: selected which trials to include and assessed the risk of bias of the trials.

Xiong X: extracted data from the trials.

Zhou R: extracted data from the trials.

Cheng N: revised the protocol, entered data into RevMan, and carried out the analysis.

Cheng Y and Xiong X: contributed equally to developing the review.

DECLARATIONS OF INTEREST

Cheng Y: none known.

Xiong X: none known.

Lu J: none known.

Wu S: none known.

Zhou R: none known.

Cheng N: none known.

SOURCES OF SUPPORT

Internal sources

- The Second Affiliated Hospital, Chongqing Medical University, China.
- West China Hospital, Sichuan University, China.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made clarifications to the types of participants according to the reviewer's suggestion. Hospital costs are neither comparable nor reliable among included studies due to inflation and inter-country economic differences. Thus, we did not include hospital costs as an outcome in the review stage.

We applied the GRADE approach for evaluating the quality of evidence for each outcome, which we had not stated in the protocol.

INDEX TERMS

Medical Subject Headings (MeSH)

*Time-to-Treatment; Abscess [complications] [mortality] [*surgery]; Appendectomy [*methods] [mortality]; Appendicitis [complications] [mortality] [*surgery]; Cellulitis [complications] [mortality] [*surgery]; Conservative Treatment; Emergencies; Length of Stay; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Adult; Child; Humans