Appendicitis Pathway v2.0: **Table of Contents**

Stop and **Review**

Inclusion Criteria

- Age > 3 months with confirmed appendicitis by the surgical team

Exclusion Criteria

- Age < 3 months and patients who do not have a confirmed appendicitis diagnosis by the surgical team

Appendicitis Care

Appendix

Last Updated: February 2023
Next Expected Review: February 2028

For questions concerning this pathway, contact:
Appendicitis@seattlechildrens.org

If you are a patient with questions contact your medical provider, Medical Disclaimer

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Appendicitis Pathway v2.0: **ED Suspected and Confirmed**

Stop and **Review**

Inclusion Criteria

- Age > 3 months with confirmed appendicitis by the surgical team

Exclusion Criteria

- Age < 3 months and patients who do not have a confirmed appendicitis diagnosis by the surgical team

ED Suspected Appendicitis Assessment

Workup

- CBC with differential + CRP
- Imaging
  - Ultrasound
  - Appendicitis imaging diagnostic criteria
  - If ultrasound is not diagnostic, consider repeat ultrasound versus MRI
  - If MRI is not available within 2 hours, consider CT

Appendicitis Diagnosis Confirmed:

1) Appendicitis diagnosis confirmed by surgical team

AND

2) Treatment plan includes either urgent appendectomy or non-operative management

No → **Off Pathway**

Yes

Communication of treatment plan + timing of surgery by Surgical Team to ED

!

If suspicion of Sepsis, see Sepsis Pathway

Confirmed Appendicitis

- NPO
- IV Fluids
- Pain Management
- Do NOT give antibiotics until approved by consulting surgeon
  - If child is at an outside hospital, have transferring hospital administer antibiotics prior to transfer
  - If going directly to OR from ED, do not give antibiotics in the ED
  - If going to the floor before the OR, give first dose of antibiotics in the ED
- Antibiotics (first dose)
  - Piperacillin/tazobactam
  - If severe piperacillin/tazobactam allergy, then ciprofloxacin + metronidazole

← Non-Operative Management

→ Operative Management

For questions concerning this pathway, contact:
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Appendicitis Pathway v2.0: **Operative Management**

Stop and **Review**

Inclusion Criteria

- Age > 3 months with confirmed appendicitis by the surgical team

Exclusion Criteria

- Age < 3 months and patients who do not have a confirmed appendicitis diagnosis by the surgical team

Care in the OR

- Broad-spectrum, prophylactic **IV antibiotics within one hour of the incision** to minimize the risk of Surgical Site Infection **(SSI pathway)**
  - If the patient has not received broad spectrum antibiotics within a hour prior to incision, then give cefoxitin in the operating room.
  - If **severe cefoxitin, cefuroxime or penicillin allergy**, then give **clindamycin + gentamicin**
  - If complicated appendicitis, then evaluate **IV access**
  - Appendectomy
  - Determination of complicated versus uncomplicated per surgeon discretion and operative findings

Complicated / Uncomplicated

Complicated Appendicitis Post Operative Care:

- Diet and NG tube per discretion of primary surgeon
- IV Fluids (1.25 to 1.5 X maintenance) initially
- Pain Management
- IV Antibiotics until **tolerating regular diet**
  - **Piperacillin/tazobactam**
  - If **severe piperacillin/tazobactam allergy,** then **ciprofloxacin + metronidazole**
- Daily creatinine while on **piperacillin/tazobactam** if receiving NSAIDs
- When tolerating a regular diet, change to PO antibiotics
  - Amoxicillin-clavulanate
  - If **severe penicillin/amoxicillin allergy**, then **ciprofloxacin + metronidazole**

Discharge Criteria

- Ambulating
- Afebrile (T<38.5C)
- Tolerating a regular diet
- Pain well managed on PO meds
- No sign of wound infection
- Tolerating PO antibiotics

IV + PO antibiotics = 7 days total

- PO amoxicillin-clavulanate
- If **severe penicillin/amoxicillin allergy**, then **ciprofloxacin + metronidazole**

Post Discharge Follow-up

- RN follow-up phone call 5-7 days post discharge
- Clinic appointment per surgeon/APP discretion

Uncomplicated Appendicitis Post Operative Care:

- Diet – Advance as tolerated
- IV Fluids (maintenance)
- Pain Management
- Labs – None
- Antibiotics – None
- For some patients **same day discharge may be possible**

Discharge Criteria

- Afebrile (T<38.5C)
- Tolerating PO
- No sign of wound infection
- Pain is controlled

Post Discharge Follow-up

- RN follow-up phone call 5-7 days post discharge

If patient has not met discharge criteria by POD #7 then continue antibiotics and reassess

7 Day Assessment. If not improving, consider:

- MRI (CT if MRI not available that day)
- CBC + differential
- CRP

Complicated Appendicitis Status Post Appendectomy- Prolonged Course

Appendicitis Pathway v2.0: **Complicated Appendicitis Status Post Appendectomy-Prolonged Course**

Stop and **Review**

Inclusion Criteria

- Age > 3 months with confirmed appendicitis by the surgical team requiring acute or delayed appendectomy

Exclusion Criteria

- Age < 3 months and patients who do not have a confirmed appendicitis diagnosis by the surgical team

If intra-abdominal or pelvic abscess, consider source control with IR drain

No source control

Source control

No source control

- IV + PO antibiotics for a total of 10 days
- Transition to PO antibiotics when tolerating a regular diet
  - Amoxicillin-clavulanate
  - If **severe penicillin/amoxicillin allergy**, then **ciprofloxacin + metronidazole**

Discharge Criteria

- Discharge when:
  - Ambulating
  - Pain well managed on PO meds
  - Afebrile (<38.5C)
  - Tolerating a regular diet
  - No sign of wound infection
  - Tolerating PO antibiotics
  - CBC with differential and CRP must be trending down from admission

Post Discharge Follow-up

APP follow-up on day 10 of antibiotics (day 8 or 9 if it falls on a weekend). If not clinically back to normal at clinic appointment, then get a CBC with differential + CRP

!

If not meeting discharge criteria by hospital day 10, then off pathway and consult with ID

Off Pathway

Source control

- IV + PO antibiotics for a total of 7 days from source control
- Transition to PO antibiotics when tolerating a regular diet
  - Amoxicillin-clavulanate
  - If **severe penicillin/amoxicillin allergy**, then **ciprofloxacin + metronidazole**

Discharge Criteria

- Discharge when:
  - Ambulating
  - Pain well managed on PO meds
  - Afebrile (<38.5C)
  - Tolerating a regular diet
  - No sign of wound infection
  - Tolerating PO antibiotics

Post Discharge Follow-up

- APP follow-up in 1 week
- If not clinically back to normal at clinic appointment, then get a CBC with differential + CRP

For questions concerning this pathway, contact:
Appendicitis@seattlechildrens.org

Appendicitis Pathway v2.0: **Non-Operative Management**

Stop and **Review**

Inclusion Criteria

- Age > 3 months with confirmed appendicitis by the surgical team requiring acute or delayed appendectomy

Exclusion Criteria

- Age < 3 months and patients who do not have a confirmed appendicitis diagnosis by the surgical team

Communication of treatment plan by Surgical Attending/Fellow to ED Attending/Fellow

- Discussion with family

Uncomplicated Non-Operative Appendicitis

Additional Exclusion Criteria

- >48 hours of symptoms
- Appendicolith, pregnant, peritonitis, concern for perforation, immunodeficiency, malignancy

Non-Operative Strategy

- NPO with IVF for a minimum of 12 hours and until improving. Advanced diet after 12 hours if clinically improved
- IV antibiotics until tolerating a regular diet
  - Piperacillin/tazobactam
  - If **severe piperacillin/tazobactam allergy**, then **ciprofloxacin + metronidazole**
- When tolerating a regular diet, change to PO antibiotics
  - Amoxicillin-clavulanate
  - If **severe piperacillin/amoxicillin allergy**, then **ciprofloxacin + metronidazole**
- IV + PO antibiotics for a total of 10 days
- Failure of non-operative management strategy:
  - Lack of improvement or worsening of symptoms over 24 hour

Phase Change
Operative Management

Discharge Criteria

- Tolerating a regular diet
- Tolerating initial dose of po antibiotics
- Resolution or near resolution of abdominal pain
- Discharge antibiotics:
  - Amoxicillin-clavulanate for a ten-day course
  - If **severe penicillin/amoxicillin allergy**, then **ciprofloxacin + metronidazole**

Post Discharge Follow-up
APP follow-up in 7 days

Complicated Non-Operative Appendicitis

Non-Operative Strategy

- IV antibiotics until tolerating a regular diet
- **IV piperacillin/tazobactam**
- If **severe piperacillin/tazobactam allergy**, then **ciprofloxacin + metronidazole**
- When tolerating a regular diet change to PO antibiotics
- Amoxicillin-clavulanate
- If **severe penicillin/amoxicillin allergy**, then **ciprofloxacin + metronidazole**
- IV + PO antibiotics for a total of 10 days

Discharge Criteria

- Ambulating
- Afebrile (T<38.5C)
- Tolerating Diet
- Pain well managed on PO meds
- No sign of wound infection
- Tolerating PO antibiotics

Post Discharge Follow-up
Surgeon follow-up in 2 weeks

If patient has not met discharge criteria by POD #7 then off pathway and discuss with ID

7 Day Assessment. If not improving, consider:

- MRI Scan (CT if MRI not available that day)
- CBC + differential
- CRP

For questions concerning this pathway, contact:
Appendicitis@seattlechildrens.org

Imaging Criteria

- Imaging Criteria for the diagnosis of Appendicitis
  - US with a maximal outer diameter of ≥ 7mm, OR wall thickness > 1.7mm
  - CT or MRI suggestive of acute appendicitis

Source

Goldin AB, Paritosh K,Thapa M, McBroom JA, Garrison MM, Parisi MT. Revised Ultrasound Criteria for Appendicitis in Children Improve Diagnostic Accuracy. Pediatr Radiol 41, 993-999 (2011).

Return to ED Suspected and Confirmed

IV Antibiotics: Care in the OR

- Children undergoing appendectomy require a dose of broad-spectrum prophylactic antibiotics within one hour of the incision to minimize the risk of **Surgical Site Infection** (SSI).

- If the patient has not received broad spectrum antibiotics for treatment of appendicitis (as outlined in previous pathway steps), or if these antibiotics have been given more than one hour from the time of incision, then antibiotics (either cefoxitin or gentamicin + clindamycin in patients with a severe allergy to cefoxitin, cefuroxime or penicillin), should be given in the operating room immediately prior to the incision.

- For SSI prophylaxis, the dose of cefoxitin in 40 mg/kg up to a maximum of 2 grams. The dose should be repeated every 2 hours during the operation.

Source

Solomkin JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Disease Society of America. Clinical Infectious Diseases 2010; 50:133-164

Return to Operative Management

If Severe Beta-lactam Allergy

- For patients with a **history of a severe* IgE-mediated beta-lactam allergy**, please consult the Beta-lactam Antibiotic Allergy reference in the SCH Formulary to assess likely cross-reactivity with the preferred therapies outlined in this pathway. Most beta-lactams are not cross-reactive and may safely be administered.
- Ceftriaxone is cross-reactive with cefepime, cefpodoxime, cefotaxime, and ceftizoxime. Patients with allergies to any of these related agents should use the alternative therapy of ciprofloxacin + metronidazole.
- *Definition of severe IgE-mediated beta-lactam allergy:
  - Exposure to a beta-lactam drug **and**
  - Reaction within 60 minutes consists of any of the following:
    - Angioedema
    - Bronchospasm
    - Hypotension
    - Anaphylaxis
- Or delayed type 4 hypersensitivity reaction like:
  - Stevens Johnson
  - Serum sickness
  - Toxic epidermal necrolysis
- Most patients who report a history of a penicillin allergy are no longer allergic to penicillin.
  - Patients with a history of a reaction to penicillin who have formal allergy testing will NOT have IgE-mediated penicillin allergy approximately 85-90% of the time.
  - If your patient had a reaction to a penicillin derivative but does not meet the criteria above for a severe* reaction, they may benefit from additional penicillin allergy screening. Please contact your team pharmacist, the Antimicrobial Stewardship Pharmacist, or email antimicrobialstewardship@seattlechildrens.org for more information.
- **The risk of a penicillin-allergic patient reacting to a cephalosporin is low.**
  - Approximately <1% of patients who are skin-test positive to penicillin will react to a cephalosporin.

Return to ED Suspected and Confirmed

Return to Operative Management

Complicated Appendicitis Status Post Appendectomy-Prolonged Course

Return to Non-Operative Management

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Communication of Treatment Plan

- The goal is for the patient to receive appropriate IV antibiotics as soon as possible after the surgery team confirms the diagnosis of appendicitis and makes a treatment plan, but to not receive too many antibiotics.
- To facilitate this goal the surgery attending/fellow will communicate the treatment plan directly to the ED attending/fellow as soon as possible.
- Once notified by the surgery team the ED team will order the ED Appendicitis Confirmed order set of the Appendicitis Pathway and expedite the administration of the appropriate antibiotics if the patient is being admitted prior to the OR. If the patient is going straight to the OR, antibiotics should not be given unless the patient is septic, as they will be administered in the OR.
- The surgery team should use the SUR appendicitis pre-procedure order set for patients going to the OR, and the SUR appendicitis admission order set for patients undergoing non-operative management.

Return to ED Suspected and Confirmed

Return to Non-Operative Management

Ciprofloxacin & Metronidazole

- Ciprofloxacin is the preferred alternative if a patient has a history of a severe allergy to the preferred beta-lactam therapy or one that shares a side-chain. Beta-lactams that do not share a side chain (e.g. penicillin and ceftriaxone do not share a side chain) may be safely administered without need for an alternative agent.
- The safety profile of ciprofloxacin in children makes it a reasonable second line drug.

Source

Solomkin JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Disease Society of America. Clinical Infectious Diseases 2010; 50:133-164 Adefurin A. Ciprofloxacin safety in pediatrics: a systematic review

Return to ED Suspected and Confirmed

Return to Operative Management

Complicated Appendicitis Status Post Appendectomy-Prolonged Course

Return to Non-Operative Management

Clindamycin & Gentamicin: Care in the OR

- To provide appropriate antibiotic prophylaxis in a timely manner for patients with a severe allergy to cefoxitin, cefuroxime, or penicillin, clindamycin and gentamicin will be used rather than ciprofloxacin and metronidazole since the latter combination has a prolonged administration time.
- If further antibiotic therapy is indicated postoperatively for patients with a severe allergy to ceftriaxone or drugs that share a side chain as outlined in the SCH Formulary Beta-Lactam Antibiotic Allergy Reference, then ciprofloxacin and metronidazole will be used.

Source

Bratzler DW, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health-Syst Pharm. 2013; 70:195-283.

Return to Operative Management

IV Access: Care in the OR

Recommendations

- If complicated appendicitis is found during the procedure, the anesthesia provider should ensure that there is a good peripheral IV in a “stable location” such as the hand or forearm prior to emergence from anesthesia.
- If the original PIV is working well and in a stable location, there is no need to move it.
- If a new IV is placed, the original PIV should be DC’ed prior to departure from the PACU.

Issues

- Patients with acute appendicitis often have small PIVs placed upon arrival in the ED.
- Small antecubital PIVs are uncomfortable for patients and have a tendency to infiltrate more quickly than PIVs placed in other locations.
- Since PICC lines are no longer routinely placed in patients with complicated appendicitis, it is optimal to have a comfortable PIV that will last for the duration of postoperative antibiotic treatment.

Return to Operative Management

Piperacillin-tazobactam

A multi-institutional prospective randomized control trial was performed in children with perforated appendicitis, comparing postoperative antibiotic regimens of piperacillin-tazobactam versus ceftriaxone and metronidazole. This study found that in children with perforated appendicitis, postoperative therapy with piperacillin-tazobactam was superior to ceftriaxone and metronidazole in preventing intra-abdominal abscess formation, and does not increase antibiotic-related complications or antibiotic exposure duration.

Source

Lee J, Garvey EM, Bundrant N, Hargis-Villanueva A, Kang P, Osuchukwu O, Dekonenko C, Svetanoff WJ, St Peter SD, Padilla B, Ostlie D. IMPPACT (Intravenous Monotherapy for Postoperative Perforated Appendicitis in Children Trial): Randomized Clinical Trial of Monotherapy Versus Multi-drug Antibiotic Therapy. Ann Surg. 2021 Sep 1;274(3):406-410. doi: 10.1097/SLA.0000000000005006. PMID: 34132703.

Return to ED Suspected and Confirmed **Return to Operative Management** **Return to Non-Operative Management**

Evidence Synthesis Statements: Diagnosis

Clinical Question #1: In pediatric patients with suspected acute appendicitis (AA) could the diagnosis be based only on clinical scores, digital rectal exam or procalcitonin levels?

In a systematic review of adults and children with suspected appendicitis, the Alvarado and Pediatric Appendicitis Score (PAS) were compared to a gold standard of surgical findings to detect acute appendicitis (n=7,967). The (+) PTP (true positives) is the probability that the person testing positive has the disease.

			Pretest Probability						
Adults (Alvarado)	**Points**	**LR**	**20%**	**33%**	**40%**	**50%**	**60%**	**66%**	**75%**
Low risk	< 4	0.03	0.7%	**1.5%**	2.0%	2.9%	4.3%	**5.5%**	8.3%
Low risk	< 5	0.02	0.5%	**1.0%**	1.3%	2.0%	2.9%	**3.7%**	5.7%
High risk	≥ 7	3.4	47%	**63%**	70%	78%	84%	**87%**	91%
High risk	≥ 9	6.7	63%	**77%**	82%	87%	91%	**93%**	95%
Children (Alvarado)	**Points**	**LR**	**20%**	**33%**	**40%**	**50%**	**60%**	**66%**	**75%**
Low risk	< 4	0.02	0.5%	**1.0%**	1.3%	2.0%	2.9%	**3.7%**	5.7%
Low risk	< 5	0.04	1.0%	**1.9%**	2.6%	3.8%	5.7%	**7.2%**	11%
High risk	≥ 7	4.2	51%	**67%**	74%	81%	86%	**89%**	93%
High risk	≥ 9	8.5	68%	**81%**	85%	90%	93%	**94%**	96%
Children (PAS)	**Points**	**LR**	**20%**	**33%**	**40%**	**50%**	**60%**	**66%**	**75%**
Low risk	< 4	0.13	3.1%	**6.0%**	8.0%	11.5%	16%	**20%**	28%
High risk	≥ 8	8.1	67%	**80%**	84%	89%	92%	**94%**	96%

Green indicates post test probability of appendicitis below 3% and red 85% or higher. Bold columns indicate typical pretest probability for children (33%) and adults (66%). LR, Likelihood ratio (adapted from Ebell 2014).

[Level of Evidence (LOE): +2 Low certainty (Ebell 2014)]

Return to ED Suspected and Confirmed

Continue to ESS 1, Pg 2

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Evidence Synthesis Statements: Diagnosis

Clinical Question #1: In pediatric patients with suspected acute appendicitis (AA) could the diagnosis be based only on clinical scores, digital rectal exam or procalcitonin levels?

Digital Rectal Exam

In a systematic review of 19 studies of patients with suspected appendicitis, digital rectal examination (DRE) was compared to a gold standard of histologically proven acute inflammation in the appendix to detect acute appendicitis (n=7,511). The pooled sensitivity and specificity were 0.49 (95% CI 0.42–0.56) and 0.61 (95% CI 0.53–0.67), respectively. The positive and negative likelihood ratios were 1.24 (95% CI 0.97–1.58) and 0.85 (95% CI 0.70–1.02), respectively.

For a disease prevalence of 33%, which is typically seen in children, the probability of having an appendicitis if the DRE is positive is between 32.3 and 43.8% with a midpoint of 37.9%. The probability of having an appendicitis if the DRE is negative is between 33.4 and 25.6% with a midpoint of 29.5%.

For a disease prevalence of 66%, which is typically seen in adults, the probability of having an appendicitis if the DRE is positive is between 65.3 and 75.4% with a midpoint of 70.6%. The probability of having an appendicitis if the DRE is negative is between 66.4 and 57.6% with a midpoint of 62.3%.

This outcome is downgraded for risk of bias, applicability, and inconsistency [Level of Evidence (LOE): +1 Very low certainty (Takada 2015)]

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Evidence Synthesis Statements: Diagnosis

Clinical Question #1: In pediatric patients with suspected acute appendicitis (AA) could the diagnosis be based only on clinical scores, digital rectal exam or procalcitonin levels?

Procalcitonin (PCT) Level

In a systematic review of 7 studies of patients with suspected appendicitis, procalcitonin level (0.1 ng/mL (1 study), 0.5 ng/mL (5 studies), 0.37 ng/mL (one study)) was compared to a gold standard of pathologic examination of the surgical specimen to detect acute appendicitis (n=872). The pooled sensitivity and specificity of PCT for the diagnosis of pediatric AA were 0.62 (95% CI: 0.57–0.66) and 0.86 (95% CI:0.82–0.89), respectively.

For a typical disease prevalence of 33% in children, the probability of having an appendicitis if the PCT level is > 0.1-0.5 ng/mL is between 46.9 and 88.6% with a midpoint of 72.4%; the probability of having an appendicitis if the PCT level is < 0.1-0.5 ng/mL is between 22.2 and 6.9% with a midpoint of 12.5%.

For a typical disease prevalence of 66% in adults, the probability of having an appendicitis if the PCT level is > 0.1-0.5 ng/mL is between 77.7 and 96.9% with a midpoint of 91.2%; the probability of having an appendicitis if the PCT level is < 0.1-0.5 ng/mL is between 53 and 22.6% with a midpoint of 36%.

This outcome is downgraded for imprecision and inconsistency. [Level of Evidence (LOE): +2 Low certainty (Cui 2019)]

The abovementioned finding are supported by a guideline which concluded that Procalcitonin (PCT) has little diagnostic value in diagnosing AA having lower diagnostic accuracy than CRP and WBC. [Level of Evidence (LOE): Guideline (Di Saverio 2020)]

Return to ED Suspected and Confirmed

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Evidence Synthesis Statements: Labs

Clinical Question #2: What is the role of serum biomarkers in evaluating pediatric patients presenting with clinical features highly suggestive of acute appendicitis?

CRP and WBC

CRP ≥ 10 mg/L and leukocytosis ≥ 16,000/mL are strong predictive factors for appendicitis in pediatric patient.

A retrospective study of 1197 patients reported a CRP > 40 mg/L in 58% of patients with complicated AA and 37% of patients with uncomplicated AA, and WBC > 15 × 109/L in 58% of patients with complicated AA and 43% of patients with uncomplicated AA.

Return to ED Suspected and Confirmed

Evidence Synthesis Statements: Imaging

Clinical Question #3: What is the optimum pathway (1st line and 2nd line) for imaging in pediatric patients with suspected acute appendicitis?

1st Line Imaging

In a systematic review of 29 studies of children with suspected appendicitis, ultrasound (US) computed tomography (CT) and magnetic resonance imaging (MRI) were compared to a gold standard of surgery and clinic follow up results to detect acute appendicitis (n=928). The pooled sensitivity and specificity of US, CT and MRI for the diagnosis of pediatric AA were 0.89 (95% CI: 0.87 to 1.0), 0.95 (95% CI:0.92 to 0.97) and 0.98 (95%CI: 0.96 to 0.99), respectively.

Ultrasound

For a disease prevalence of 33%, which is typically seen in children, the probability of having appendicitis if the US is positive is between 91.5 and 94.3% with a midpoint of 93.6%; the probability of having appendicitis if the US is negative is between 0 and 6.3% with a midpoint of 5.3%.

For a disease prevalence of 66%, which is typically seen in adults, the probability of having appendicitis if the US is positive is between 97.7 and 98.5% with a midpoint of 98.3%; the probability of having appendicitis if the US is negative is between 0 and 20.8% with a midpoint of 18%.

CT

For a disease prevalence of 33%, which is typically seen in children, the probability of having appendicitis if the CT (1st line) is positive is between 81.9 and 88.8% with a midpoint of 85.4%; the probability of having appendicitis if the CT (1st line) is negative is between 1.5 and 4.2% with a midpoint of 2.6%.

For a disease prevalence of 66%, which is typically seen in adults, the probability of having appendicitis if the CT is positive is between 94.7 and 96.9% with a midpoint of 95.8%; the probability of having appendicitis if the CT is negative is between 5.8 and 14.7% with a midpoint of 9.5%.

MRI

For a disease prevalence of 33%, which is typically seen in children, the probability of having appendicitis if the MRI is positive is between 92.2 and 96.1% with a midpoint of 94.1%; the probability of having appendicitis if the MRI is negative is between 0.5 and 2% with a midpoint of 1%.

For a disease prevalence of 66%, which is typically seen in adults, the probability of having appendicitis if the MRI is positive is between 97.9 and 99% with a midpoint of 98.4%. the probability of having appendicitis if the MRI is negative is between 1.9 and 7.5% with a midpoint of 3.8%.

This outcome is downgraded for inconsistency. [Level of Evidence (LOE): +3 Moderate certainty (Zhang 2017)]

Return to ED Suspected and Confirmed

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Evidence Synthesis Statements: Imaging

Clinical Question #3: What is the optimum pathway (1st line and 2nd line) for imaging in pediatric patients with suspected acute appendicitis?

2nd Line Imaging

In a systematic review of 20 studies of children with suspected appendicitis, ultrasound (US) (n=548), computed tomography (CT) (n=1498) and magnetic resonance imaging (MRI) (n=287) following initial US were compared to a gold standard of surgery or histopathologic examination alone or in combination with clinical follow-up or chart review. Pooled sensitivities and specificities of second-line US were 91.3% (95% confidence interval [CI]: 83.8% to 95.5%) and 95.2% (95% CI: 91.8% to 97.3%), respectively. For CT, the pooled sensitivities and specificities were 96.2% (95% CI: 93.2%, 97.8%) and 94.6% (95% CI: 92.8%, 95.9%). For MRI, the pooled sensitivities and specificities were 97.4% (95% CI: 85.8%, 100%) and 97.1% (95% CI: 92.1%, 99.0%).

US

For a disease prevalence of 33%, which is typically seen in children, the probability of having appendicitis if the follow-up US is positive is between 83.4 and 94.6% with a midpoint of 90.4%; the probability of having appendicitis if the US is negative is between 2.2 and 8% with a midpoint of 4.3%.

For a disease prevalence of 66%, which is typically seen in adults, the probability of having appendicitis if the follow-up US is positive is between 95.2 and 98.6% with a midpoint of 97.4%; the probability of having appendicitis if the US is negative is between 8.2 and 25.5% with a midpoint of 15.1%.

CT

For a disease prevalence of 33%, which is typically seen in children, the probability of having appendicitis if the follow-up CT is positive is between 86.4 and 92.2% with a midpoint of 89.8%; the probability of having appendicitis if the US is negative is between 8.2 and 25.5% with a midpoint of 15.1%.

For a disease prevalence of 66%, which is typically seen in adults, the probability of having appendicitis if the CT is positive is between 96.2 and 97.9% with a midpoint of 97.2%. For a disease prevalence of 66%, the probability of having appendicitis if the CT is negative is between 4.3 and 12.5% with a midpoint of 7.2%.

MRI

For a disease prevalence of 33%, which is typically seen in children, the probability of having appendicitis if the follow-up MRI is positive is between 84.3 and 98% with a midpoint of 94.3%; the probability of having appendicitis if the MRI is negative is between 0 and 7.1% with a midpoint of 1.3%.

For a disease prevalence of 66%, which is typically seen in adults, the probability of having appendicitis if the follow-up MRI is positive is between 95.5 and 99.5% with a midpoint of 98.5%. For a disease prevalence of 66%, the probability of having appendicitis if the MRI is negative is between 0 and 23% with a midpoint of 4.9%.

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Evidence Synthesis Statements: Imaging

Clinical Question #3: What is the optimum pathway (1st line and 2nd line) for imaging in pediatric patients with suspected acute appendicitis?

The findings for US and MRI are downgraded for risk of bias and inconsistency [Level of Evidence (LOE): +2 Low certainty (Eng 2018)]. The findings for CT are downgraded for inconsistency [Level of Evidence (LOE): +3 Moderate certainty (Eng 2018)].

Return to ED Suspected and Confirmed

Return to ESS 3, Pg 1

Evidence Synthesis Statements: Non-Operative Management

Clinical Question #4: Is non-operative management with or without antibiotics a safe and effective treatment option for pediatric patients with uncomplicated acute appendicitis?

Efficacy and Failure Rates
Definitions of Failure in systematic review by Huang 2017 (1 RCT, 5 cohort studies): Antibiotic therapy group: non-resolution of symptoms or need for surgery in the first 48 hours or recurrence in the first month; Appendectomy group: (-) appendectomy or need for re-operation).

All Children
In a meta-analysis of children with appendicitis, antibiotic therapy may increase failure rate over 1 month compared to appendectomy. RR 8.92 (2.67, 29.79), NNTH 31 (10 to 143). At one year follow up, 26.8% of patients required appendectomy. [LOE: +2 Low Certainty (Huang 2017)]

The antibiotic first strategy appears effective in 97% of children with a recurrence rate of 14%. [LOE: Guideline (Di Saverio 2020)]

A systematic review of 13 studies showed an initial success rate of 58-100% with recurrence rate of 0.1-31.8% (4 retrospective, 4 prospective studies, 4 non-randomized, 1 RCT). [LOE: Guideline (De Saverio 2020)]

A meta analysis showed reduced treatment efficacy (RR 0.71-0.84) and increased risk of readmission for NOM (RR 2.07-23.6). [LOE: Guideline (De Saverio 2020)]

Children with Appendolith
In a meta-analysis of children with an appendolith, antibiotic therapy may result in a large increase in failure over 1 month compared to appendectomy. RR 10.43 (1.46, 74.26). There were no failures in cohort with appendolith receiving appendectomy This outcome is downgraded for imprecision. [LOE: +1 Very Low Certainty (Huang 2017)]

A prospective trial showed that failure rate of NOM with the presence of appendicolith was high (60%) and this was validated by several systematic reviews showing failure rates of 47-60%. [LOE: Guideline (De Saverio 2020)]

Children without Appendolith
In a meta-analysis of children without an appendolith, antibiotic therapy may increase failure over 1 month compared to appendectomy. RR 7.87 (1.8, 34.33), NNTH 33 (8 to 274). [LOE: +2 Low Certainty (Huang 2017)]

Continue to ESS 4, Pg 2

Evidence Synthesis Statements: Non-Operative Management

Clinical Question #4: Is non-operative management with or without antibiotics a safe and effective treatment option for pediatric patients with uncomplicated acute appendicitis?

Cost
In a meta-analysis of children with appendicitis, antibiotic therapy may reduce cost (total appendicitis associated costs) over 1 year compared to appendectomy. MD -1.31 (US $1000) (-1.69, -0.92). [LOE: +2 Low Certainty (Huang 2017)]

Furthermore, antibiotic therapy may reduce initial cost (cost during first hospitalization) over 1 month compared to appendectomy. MD -0.7 (US $1000) (-0.89, -0.51). [LOE: +2 Low Certainty (Huang 2017)]

Complications
In a meta-analysis of children with appendicitis, antibiotic therapy may result in little to no difference in complications (perforations, abscess, gangrene, and/or postoperative complications over 1 month compared to appendectomy. RR 0.65 (0.18, 2.37). This outcome is downgraded for imprecision. [LOE: +1 Very Low Certainty (Huang 2017)]

A prospective patient choice study showed that after 1 year children managed with NOM had fewer disability days and lower appendectomy related health care cost. [LOE: Guideline (De Saverio 2020)]

A systematic review of five studies (RCT/cohort) showed that complication rates ranged from 0-13% for NOM and 0-17% for appendectomy. [LOE: Guideline (Di Saverio 2020)]

Length of Stay
In a meta-analysis of children with appendicitis, antibiotic therapy may reduce length of stay compared to appendectomy. MD 14.32 hours (7.49, 21.150. [LOE: +2 Low Certainty (Huang 2017)]

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Evidence Synthesis Statements: Surgery Timing

Clinical Question #5: Does in-hospital delay increase the rate of complications or perforation for pediatric patients with uncomplicated acute appendicitis?

Guideline Recommendation
A guideline recommended against delaying appendectomy for pediatric patients with uncomplicated acute appendicitis needing surgery beyond 24 h from the admission. Early appendectomy within 8 h should be performed in case of complicated appendicitis.

Rationale
In multivariate logistic regression analysis increased time to surgery was not associated with perforation, wound infection, abscess, reoperation, readmission.

Data from NSQIP- Pediatrics demonstrated that 16h delay from ER arrival or 12h delay from hospital admission was not associated with increased risk of SSI.

Retrospective analysis of data from 484 pediatric patients showed that those who underwent appendectomy at 6, 8, and 12h after hospital admission had no difference in SBO, SSI, or perforation.

The pediatric surgical associations outcomes and evidence based practice committee stated that appendectomy performed within first 24hrs of presentation is not associated with perforation or adverse outcomes based on a systematic review.

In complicated appendicitis a population based study showed higher rates of complications in the late treatment group at 1yr.

[LOE: Guideline (Di Saverio 2020)]

Return to ED Suspected and Confirmed

Evidence Synthesis Statements: OR Timing for Complicated Appendicitis with Phlegmon or Abscess

Clinical Question #6: Is early appendectomy an appropriate treatment compared with delayed appendectomy for patients with perforated acute appendicitis with phlegmon or abscess?

Guideline Recommendation
A guideline recommended that a laparoscopic approach is recommended as treatment of choice where expertise is available and that there should be a low threshold for conversion to open procedure.

Rationale
Several meta-analyses as well as a Cochrane review (2017) have addressed this clinical question. However, much of the data included in these analyses are of poor quality (retrospective and observational in nature). Observational studies summarized in a meta-analysis in 2010, suggested that conservative treatment was associated with less overall complications. More recent meta-analyses from 2019 have the overall same conclusions that conservative treatment was associated with lower rate of complications, recurrent abscess, wound infections, unplanned procedures, and readmissions. However, the data evaluated in each of these more recent meta-analyses continues to be largely observational.

A sub-analysis of the three RCTs included showed no significant difference in recurrent abscess but did show shorter hospital length of stay for patients receiving early laparoscopic appendectomy vs conservative management. The high quality RCT included in the Cochrane review found that early laparoscopic appendectomy was associated with fewer readmissions, fewer additional interventions, and lower likelihood of bowel resection when compared to conservative management. Additional RCTs showed that early operative management was associated with a longer operative time but no difference in rate of abscess recurrence or length of stay and that early appendectomy was associated with reduced time away from normal activities and overall reduced adverse event rate.

[LOE: Guideline (Di Saverio 2020)]

Evidence Synthesis Statements: Interval Appendectomy

Clinical Question #7: Is interval appendectomy always indicated for patients with acute appendicitis following successful non-operative management of complicated appendicitis?

Guideline Recommendation

A guideline recommended that routine interval appendectomy is not recommended after successful NOM and that interval appendectomy is recommended for those with recurrent symptoms.

Rationale

Two meta-analyses from 2016 and 2011 addressed this clinical question. However, much of the data included in these analyses are of poor quality, consisting of retrospective case series and retrospective cohort studies. The analysis from 2016 included 26 case series (21 reporting morbidity among patients treated with non-operative management and 5 reporting on patient treated with interval appendectomy), totaling 1943 patients. They concluded that each approach had similar rates of morbidity, but that interval appendectomy was associated with additional operative costs. They estimated a number needed to treat with interval appendectomy of eight patients to prevent one episode of recurrence. The analysis from 2011 included 3 retrospective case series of patients undergoing non-operative management, totaling 127 patients, and 23 studies evaluating patients undergoing interval appendectomy, totaling 1247 patients. Of these 23 studies, 22 were retrospective case series. No studies reported a direct comparison between operative and non-operative management. They concluded that up to 80% of children may not need interval appendectomy after successful non-operative treatment of acute appendicitis. They also report a complication rate of 3.4% following interval appendectomy.

A recent RCT from 2017 randomized 106 children to interval appendectomy vs active observation. Of these, 12% of children in the active observation group experienced recurrent acute appendicitis during the study period. 6% of children in the interval appendectomy group experienced severe complications. They concluded that active observation was associated with shorter hospital length of stay, shorter return to normal activity, and lower cost.

[LOE: Guideline (Di Saverio 2020)]

Return to Non-Operative Management

Evidence Synthesis Statements: Perioperative Antibiotics

Clinical Question #8: Is perioperative antibiotic therapy recommended for patients with acute appendicitis?

Guideline Recommendations

1. Children undergoing appendectomy should receive a single dose of broad spectrum antibiotics preoperatively from 0 to 60 minutes before the surgical incision.

Rationale

Preoperative Antibiotics: In regard to preoperative antibiotics, there is high quality evidence to support the use of a single dose of broad spectrum antibiotics 0 to 60 minutes prior to the surgical skin incision. Across many RCTs this has been associated with decreased risk of surgical site infection and intra-abdominal abscesses.

[LOE: Guideline (Di Saverio 2020)]

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Evidence Synthesis Statements: Perioperative Antibiotics

Clinical Question #8: Is perioperative antibiotic therapy recommended for patients with acute appendicitis?

Guideline Recommendations

1. Children undergoing appendectomy for uncomplicated appendicitis should not receive post-operative antibiotics.

2. Broad spectrum postoperative antibiotics should be administered to children with complicated appendicitis. Recommend early transition to oral antibiotics and a total duration of no greater than 7 days.

Rationale

Post-Operative Ant biotics: There is less robust evidence in support of recommendations regarding use of post-operative antibiotics. Di Saverio recommends that children should not receive post-operative antibiotics after appendectomy performed for uncomplicated appendicitis. For complicated appendicitis, this guideline recommends initiation of antibiotics effective against enteric gram-negatives and anaerobes as soon as the diagnosis is established. They recommend a single broad-spectrum or double agent therapy over triple agent therapy. A recent RCT of 82 pediatric patients randomized to either oral and IV post-operative antibiotics for treatment of perforated appendicitis found no difference in length of stay, postoperative abscess rate, or readmission; charges were higher for the IV group. The guidelines recommend transition to oral antibiotics after 48 hours and a total antibiotic duration of no greater than 7 days.

[LOE: Guideline (Di Saverio 2020)]

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Evidence Synthesis Statements: Imaging Studies vs Lab Test

Clinical Question #9: Can imaging studies or lab tests differentiate uncomplicated from complicated appendicitis?

Procalcitonin (PCT) Level

In a systematic review of 4 studies of children with suspected appendicitis, the procalcitonin level (0.18 ng/mL (one study), 0.5 ng/mL (two studies), 0.74 ng/mL (one study)) was compared to a gold standard of pathologic examination of the surgical specimen to detect complicated acute appendicitis (n=372). The pooled sensitivity and specificity was 0.89 (95% CI: 0.84–0.93; I2 = 76.1%) and 0.90 (95% CI: 0.86–0.94; I2 = 75.3%), respectively. The combined (+) LR was 7.68 (95% CI: 3.66–16.14); the combined (-) LR of 0.12 (95% CI: 0.05–0.27).

For a disease prevalence of 33% which is typically in children, the probability of having a complicated appendicitis if the PCT level is >0.18-0.74 ng/mL is between 64.3 and 88.8% with a midpoint of 79.1%.The probability of having an complicated appendicitis if the PCT level is <0.18-0.74 ng/mL is between 11.7 and 2.4% with a midpoint of 5.6%.

For a typical disease prevalence of 66% which is typically seen in adults, the probability of having a complicated appendicitis if the PCT level is >0.18-0.74 ng/mL is between 87.7 and 96.9% with a midpoint of 93.7%. The probability of having an complicated appendicitis if the PCT level is <0.18-0.74 ng/mL is between 34.4 and 8.8% with a midpoint of 18.9%.

This outcome is downgraded for imprecision and inconsistency. [(LOE): +2 Low certainty (Cui 2019)]

Computed Tomographic (CT) Findings

In a systematic review of 23 studies of adults and children with suspected appendicitis, CT findings were compared to a gold standard of either pathologic results only vs. pathologic results in combination with the surgical record to detect complicated appendicitis (perforation and/or gangrene) (n=4,383). The CT features with the highest (+) LRs were: abscess 40.4 (95% CI: 17.6 to 92.7), extraluminal air 28.8 (95% CI: 9.9 to 83.6) and appendiceal wall enhancement defect 15.5 (95% CI: 6.1 to 39.4). The CT features with the lowest (-) LRs were: appendiceal wall enhancement defect 0.4 (95% CI: 0.3-0.7) and periappendiceal fat stranding 0.1 (95% CI: 0.1-0.3).

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Evidence Synthesis Statements: Imaging Studies vs Lab Test

Clinical Question #9: Can imaging studies or lab tests differentiate uncomplicated from complicated appendicitis?

Abscess

For a disease prevalence of 33% which is typically seen in children, the probability of having a complicated appendicitis when there is a CT finding of abscess is between 89.7 and 97.9% with a midpoint of 95.2%; the probability of having a complicated appendicitis without a CT finding of abscess is between 25.6 and 19.8% with a midpoint of 22.8%. This outcome is downgraded for inconsistency. [(LOE): +3 Moderate certainty (Cui 2019)]

Extraluminal Air

For a disease prevalence of 33% which is typically seen in children, the probability of having a complicated appendicitis when there is a CT finding of extraluminal air is between 83 and 97.6% with a midpoint of 93.4%; the probability of having a complicated appendicitis without a CT finding of extraluminal air is between 28.3 and 22.8% with a midpoint of 25.6%. This outcome is downgraded for risk of bias. [(LOE): +3 Moderate certainty (Cui 2019)]

Appendiceal Wall Enhancement

For a disease prevalence of 33% which is typically seen in children, the probability of having a complicated appendicitis when there is a CT finding of an appendiceal wall enhancement defect is between 75 and 95.1% with a midpoint of 88.4%, the probability of having a complicated appendicitis without a CT finding of appendiceal wall enhancement defect is between 25.6 and 12.9% with a midpoint of 16.5% This outcome is downgraded for imprecision and inconsistency. [(LOE): +2 Low certainty (Cui 2019)]

Periappendiceal Fat Stranding

For a disease prevalence of 33% which is typically seen in children, the probability of having a complicated appendicitis when there is a CT finding of periappendiceal fat stranding is between 37.1 and 50.8% with a midpoint of 44.1%.the probability of having a complicated appendicitis without a CT finding of periappendiceal fat stranding is between 12.9 and 4.7% with a midpoint of 4.7%.This outcome is downgraded for risk of bias. [(LOE): +3 Moderate certainty (Cui 2019)]

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Evidence Synthesis Statements: Discharge Timing

Clinical Question #10: Is outpatient laparoscopic appendectomy safe and feasible for patients with uncomplicated acute appendicitis?

Guideline Recommendations
A guideline recommended the adoption of outpatient laparoscopic appendectomy (LA) for uncomplicated appendicitis, provided that an ambulatory pathway with well-defined ERAS protocols and patient information/consent are locally established.

Rationale
In a study of 484 patients undergoing LA for uncomplicated appendicitis 85% were able to be managed as an outpatient with only 7 being readmitted.

A RCT showed that ERAS implementation showed significantly decreased length of stay allowing for outpatient management with similar morbidity and readmission rates to standard care.

[LOE: Guideline (Di Saverio 2020)]

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Summary of Version Changes

- **Version 1.0 (7/9/2013):** Go live.
- **Version 1.1 (7/8/2014):** Additional information slide attached to beta lactam allergy description.
- **Version 1.2 (3/13/2015):** Added page 2 of Executive Summary.
- **Version 2.0 (2/28/2023):** 5 year Periodic Review. Medication dosages reviewed and approved by Pharmacy and Therapeutics Committee on 10/18/2022.

Approval & Citation

Approved by the CSW Appendicitis Pathway team for February 28, 2023, go-live

CSW Appendicitis Pathway Team:

Department of General Surgery, Owner	Sarah Greenberg, MD
General Surgery, Team Member	Michelle Botchey, NP
Antimicrobial Stewardship, Pharmacist	Adam Brothers, PharmD
Emergency Department, CNS	Sara Fenstermacher, ARNP-CS
General Surgery, Team Member	Casey, Golden, NP
Division of Infectious Disease, Team Member	Tori Konold, MD
Surgical Unit, CNS	Kristine Lorenzo, MSN, ARNP-CS, ACCNS-P
Division of Infectious Disease, Team member	Scott Weissman, MD

Clinical Effectiveness Team:

Consultant	Coral Ringer, MN, RN, CPN
Project Manager	Pauline O'Hare, MBA, RN
Project Manager	Asa Herrman
Data Analyst	Noah Espinoza
EHR Informatician	Carlos Villavicencio, MD
EHR Analyst	Gaurav Gupta
Librarian	Sue Groshong
Literature Reviewer	Darren Migita, MD
Literature Reviewer	Paul Morales, MD
Literature Reviewer	Eileen Reichert, RN
Literature Reviewer	Matthew Test, MD
Program Coordinator	Ann Yi, MPA

Clinical Effectiveness Leadership:

Medical Director	Darren Migita, MD
Operations Director	Jaleh Shafii, MS, RN, CPHQ

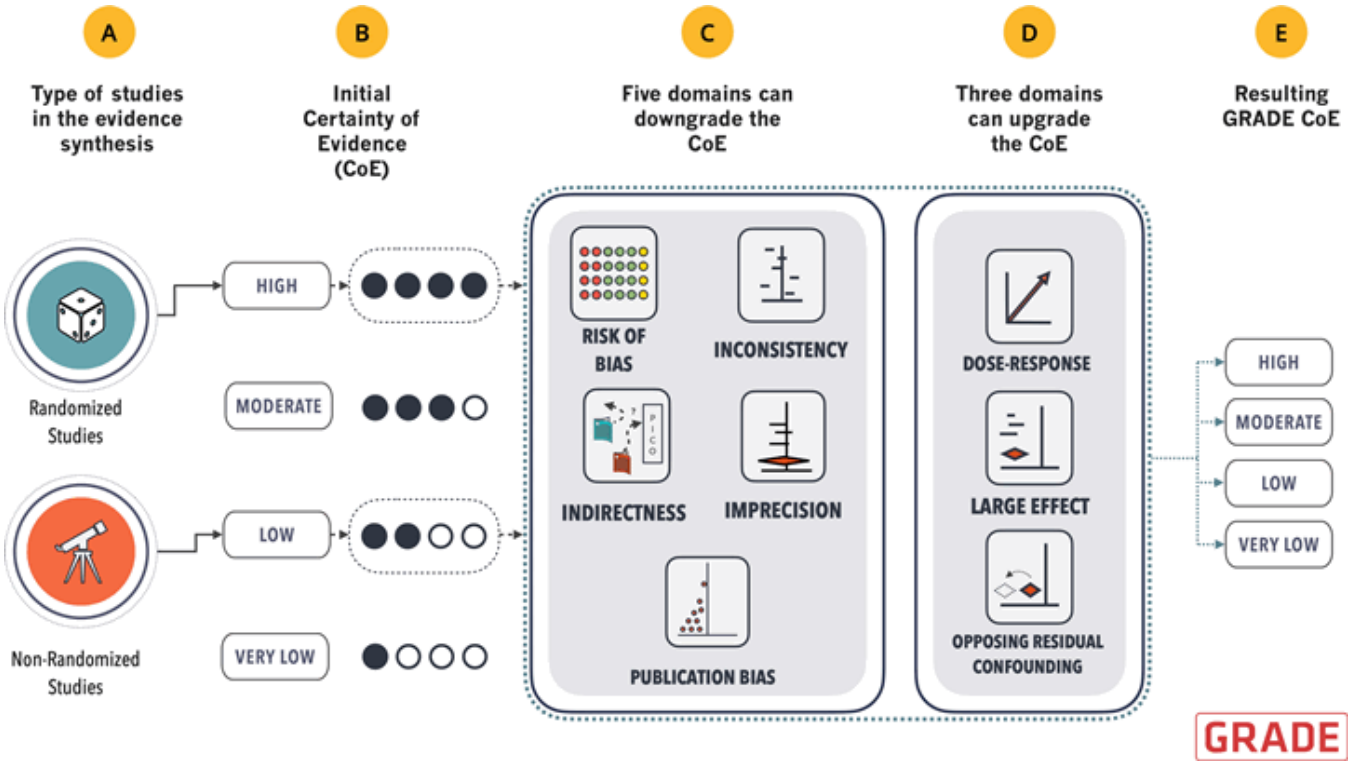
Retrieval Website: https://www.seattlechildrens.org/pdf/appendicitis-pathway.pdf

Please cite as:
Seattle Children's Hospital, Greenberg, S., Botchey, M., Brothers, A., Fenstermacher, S., Golden, C., Herrman, A., Konold, T., Lorenzo, K., O'Hare, P., Reichert, E., Ringer, C., Villavicencio, C., Weissman, S., Migita, D., 2023 February Appendicitis Pathway. Available from: https://www.seattlechildrens.org/pdf/appendicitis-pathway.pdf

Evidence Ratings

This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children's. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94, Hultcrantz M et al. J Clin Epidemiol. 2017;87:4-13, Klugar et al. J Clin Epidmiol. 2021 Nov 11;S0895-4356(21)00361-9.):



Source: Carlos Cuello

Certainty of Evidence

✪✪✪✪ High certainty: The authors have a lot of confidence that the true effect is similar to the estimated effect
✪✪✪○ Moderate certainty: The authors believe that the true effect is probably close to the estimated effect
✪✪○○ Low certainty: The true effect might be markedly different from the estimated effect
✪○○○ Very low certainty: The true effect is probably markedly different from the estimated effect
Guideline: Recommendation is from a published guideline that used methodology deemed acceptable by the team
Expert Opinion: Based on available evidence that does not meet GRADE criteria (for example, case-control studies)

Deductions labeled 1=risk bias, 2=indirectness, 3=imprecision, 4=inconsistency, 5=publication bias

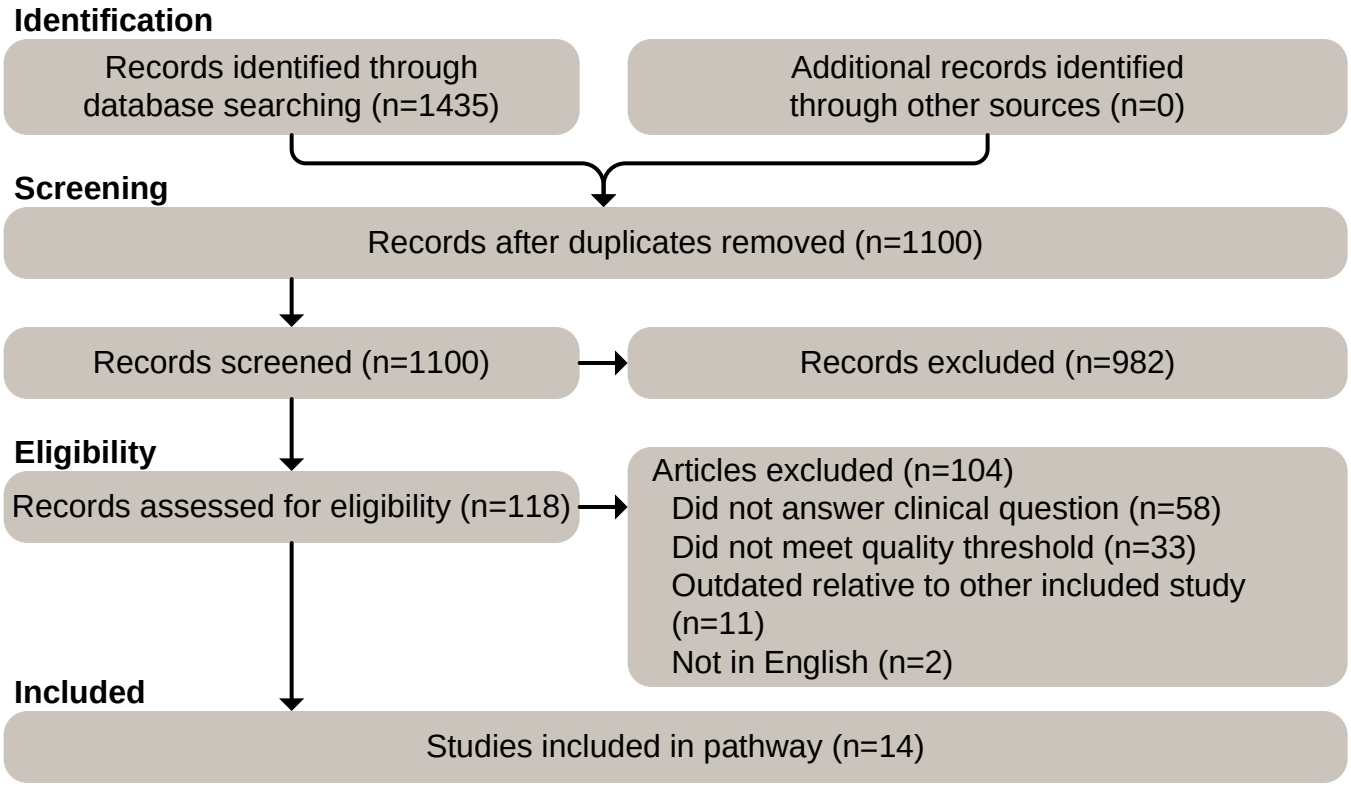
Bibliography

Literature Search Methods

Screening and data extraction were completed using DistillerSR (Evidence Partners, Ottawa, Canada). Two reviewers independently screened abstracts and included guidelines and systematic reviews that addressed optimal diagnosis, treatment, and prognosis of patients who meet pathway inclusion/exclusion criteria. One reviewer screened full text and extracted data and a second reviewer quality checked the results. Differences were resolved by consensus.

Literature Search Results

For this update, we revised the search strategies in line with current Library practices. A literature search was conducted in April 2021 to target synthesized literature on appendix, appendicitis and appendectomy for 2014 to current and limited to humans and English. The search was executed in Ovid Medline, Embase, Cochrane Database of Systematic Reviews (CDSR) and Turning Research into Practice (TRIP) databases.



Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535

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Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

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