DSA GUIDELINES



### OXFORD

# 2024 Clinical Practice Guideline Update by the Infectious Diseases Society of America on Complicated Intra-abdominal Infections: Diagnostic Imaging of Suspected Acute Appendicitis in Adults, Children, and Pregnant People

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This paper is part of a clinical practice guideline update on the risk assessment, diagnostic imaging, and microbiological evaluation of complicated intra-abdominal infections in adults, children, and pregnant people, developed by the Infectious Diseases Society of America (IDSA). In this paper, the panel provides recommendations for diagnostic imaging of suspected acute appendicitis. The panel's recommendations are based on evidence derived from systematic literature reviews and adhere to a standardized methodology for rating the certainty of evidence and strength of recommendation according to the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach.

Keywords. intra-abdominal infection; appendicitis; guideline; diagnostic imaging; radiology.

In adults with suspected acute appendicitis, should ultrasound (US), computed tomography (CT), or magnetic resonance imaging (MRI) be obtained as the initial imaging modality?

In adults with suspected appendicitis, if initial imaging is inconclusive, should US, CT, or MRI be obtained for subsequent imaging?

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**Recommendation:** In non-pregnant adults with suspected acute appendicitis, the panel suggests obtaining an abdominal CT as the initial imaging modality to diagnose acute appendicitis (*conditional recommendation, very low certainty of evidence*).

### **Remarks**:

- Intravenous (IV) contrast is usually appropriate whenever a CT is obtained in adults with suspected acute appendicitis; however, CT without IV contrast also has high diagnostic accuracy in detecting acute appendicitis and may be appropriate [1].
- Because of the accuracy of CT, immediate additional imaging studies beyond CT are usually not necessary. If a CT is negative but clinical suspicion for acute appendicitis persists, consider observation and supportive care, with or without antibiotics; if clinical suspicion is high, consider surgical intervention.
- Ultrasound, when definitively positive or definitively negative, and MRI are also reasonably accurate and may precede CT, depending on the patient and clinical circumstances.

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In children with suspected acute appendicitis, should US, CT, or MRI be obtained as the initial imaging modality?

In children with suspected appendicitis, if initial imaging is inconclusive, should US, CT, or MRI be obtained for subsequent imaging?

**Recommendation:** In children and adolescents with suspected acute appendicitis, the panel suggests obtaining an abdominal US as the initial imaging modality to diagnose acute appendicitis (*conditional recommendation, very low certainty of evidence*).

# Remarks:

• Ultrasound is generally readily available but is also operator-dependent and can yield equivocal results. MRI is not always readily available, and sedation may be required for young children. CT is generally readily available but involves radiation exposure and may require use of IV contrast or sedation.

**Recommendation:** In children and adolescents with suspected acute appendicitis, if initial US is equivocal/non-diagnostic and clinical suspicion persists, the panel suggests obtaining an abdominal MRI or CT as subsequent imaging to diagnose acute appendicitis rather than obtaining another US (*conditional recommendation, very low certainty of evidence*). *Remarks:* 

- Ultrasound is generally available but is also operatordependent and can yield equivocal results. MRI is not always readily available, and sedation may be required for young children. CT is generally readily available but involves radiation exposure and may require use of IV contrast or sedation.
- CT with IV contrast is usually appropriate when performed in children with suspected acute appendicitis after equivocal US; however, CT without IV contrast may be appropriate [2].
- Depending on the clinical situation, observation may be appropriate instead of subsequent imaging.
- If there is a strong clinical suspicion for appendicitis after equivocal imaging, exploratory laparoscopy or laparotomy may also be considered if subsequent imaging delays appropriate management.

In pregnant people with suspected acute appendicitis, should US or MRI be obtained as the initial imaging modality?

# In pregnant people with suspected appendicitis, if initial imaging is inconclusive, should US or MRI be obtained for subsequent imaging?

**Recommendation:** In pregnant people with suspected acute appendicitis, the panel suggests obtaining an abdominal US as the initial imaging modality to diagnose acute appendicitis (*conditional recommendation, very low certainty of evidence*).

# Remarks:

• It would also be reasonable to initially obtain an MRI in pregnant people with suspected acute appendicitis if access to MRI is readily available. The conditional imaging strategy suggested (US, then MRI for equivocal results) would likely yield the same results as an MRI only.

**Recommendation:** In pregnant people with suspected acute appendicitis, if initial US is equivocal/non-diagnostic and clinical suspicion persists, the panel suggests obtaining an MRI as subsequent imaging to diagnose acute appendicitis (*conditional recommendation, very low certainty of evidence*). *Remarks:* 

 It would also be reasonable to initially obtain an MRI in pregnant people with suspected acute appendicitis if access to MRI is readily available. The conditional imaging strategy suggested (US, then MRI for equivocal results) would likely yield the same results as an MRI only.

### INTRODUCTION

This paper is part of a clinical practice guideline update on the risk assessment, diagnostic imaging, and microbiological evaluation of complicated intra-abdominal infections in adults, children, and pregnant people, developed by the Infectious Diseases Society of America [3–9]. Here, the guideline panel provides recommendations for diagnostic imaging of suspected acute appendicitis in adults, children, and pregnant people. Recommendations are stratified by initial imaging and then subsequent imaging if initial imaging is inconclusive. These recommendations replace previous statements in the last iteration of this guideline [10].

A complicated intra-abdominal infection extends beyond the hollow viscus of origin into the peritoneal space and is associated with either abscess formation or peritonitis; this term is not meant to describe the infection's severity or anatomy. An uncomplicated intra-abdominal infection involves intramural inflammation of the gastrointestinal tract and has a substantial probability of progressing to complicated infection if not adequately treated.

These recommendations are intended for use by healthcare professionals who care for patients with suspected intraabdominal infections.

### METHODS

The panel's recommendations are based on evidence derived from systematic literature reviews and adhere to a standardized methodology for rating the certainty of evidence and strength of recommendation according to the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach (Supplementary Figure 1) [11]. The recommendations have been endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Pediatric Infectious Diseases Society (PIDS).

Strong recommendations are made when the recommended course of action would apply to most people with few exceptions. Conditional recommendations are made when the suggested course of action would apply to the majority of people with many exceptions and shared decision making is important.

A comprehensive literature search (through October 2022) was conducted as part of a systematic review. Key eligibility criteria at both the topic and clinical question levels guided the search and selection of studies. For the clinical questions addressed here, the panel considered patients with suspected acute appendicitis, excluding studies that only enrolled patients with pathologically confirmed appendicitis. Studies that analyzed children and adults together were also excluded. Ultrasound, CT (including multidetector CT), MRI, and magnetic resonance cholangiopancreatography (MRCP) were reviewed as possible imaging modalities, but point-of-care US (POCUS), surgeon-performed US, transvaginal-only US, and unenhanced CT were excluded. Although POCUS is used frequently, only studies assessing US performed in a controlled manner and interpreted by a radiologist were included, primarily due to the variability in interpretation of POCUS. Observational studies published after 2010 and randomized controlled trials were screened for inclusion. Studies were excluded if the authors did not report the raw data necessary to calculate sensitivities and specificities and did not respond to email inquiries for data. Refer to the full list of eligibility criteria in the Supplementary Material.

For each population/modality combination, an existing meta-analysis was selected based on recency and rigor (according to AMSTAR-2 assessment) [12] as a starting point (Table 1). Eligibility criteria were applied, and any newer, relevant studies were added. References of newer meta-analyses found via the search update were reviewed and any new or missing studies were also added. Sensitivities, specificities, and corresponding 2×2 tables were plotted in RevMan based on the population and imaging study [21]. All included studies underwent critical appraisal according to the GRADE approach, and then an assessment of benefits and harms of care

#### Table 1. Selected Meta-analyses

			First Author, Year [Re	ference]		
	Initial US	Initial CT	Initial MRI	Subsequent US	Subsequent CT	Subsequent MRI
Children	Zhang, 2017 [13]	Zhang, 2017 [13]	D'Souza, 2021 [14]	Eng, 2018 [15]	Eng, 2018 [15]	D'Souza, 2021 [14]
Adults	Dahabreh, 2015 [16] + Arruzza, 2022 [17]	Rud, 2019 [18] + Arruzza, 2022 [17]	D'Souza, 2021 [14]	Eng, 2018 [15]	Eng, 2018 [15]	D'Souza, 2021 [14]
Pregnant people	Dahabreh, 2015 [16] + Li, 2022 [19] + Moghadam, 2022 [20]	Dahabreh, 2015 [16]	D'Souza, 2021 [14]	Eng, 2018 [15]	Eng, 2018 [15]	D'Souza, 2021 [14]

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; US, ultrasound.

options informed the recommendation(s) [11, 22]. Details of the systematic review and guideline development processes are available in the Supplementary Material.

### SUMMARY OF EVIDENCE

Almost all studies evaluated an imaging modality against some reference standard (eg, histopathology, surgical impression, and/or final diagnosis) instead of comparing the effectiveness of an imaging modality versus another.

Searches yielded 15 meta-analyses [13–16, 18, 23–31, 33] additional 3 were identified when updating the search in late 2022 [17, 19, 20]. A comprehensive search yielded 147 primary observational studies for the analyses on whether to use CT, US, or MRI to diagnose acute appendicitis in children, adults, and pregnant people (Supplementary Tables 1–3). Median (range) sensitivities and specificities are reported in Tables 2– 4 for initial and subsequent imaging (vs the reference standard) for adults, children, and pregnant people.

A large proportion of US results are classified as equivocal or indeterminate. In 9 studies evaluating initial US in adults, a median of 68% of patients (range, 8-84%) had equivocal or indeterminate results [34-41, 151]. In 16 studies evaluating initial US in children, a median of 36% of patients (range, 3-75%) had equivocal or indeterminate results [84-97, 99, 100]. In 2 studies evaluating initial US in pregnant people, a median of 95% of patients (range, 93-97%) had equivocal or indeterminate results [134, 135]. Because of this, 2 analyses were performed for each population receiving US: (1) an analysis of only the definitive results (definitively positive and definitively negative), and then (2) an analysis of all the results, including the equivocal and indeterminate results. For the latter, equivocal results were classified as negative on US (resulting in true negatives and false negatives, depending on the reference standard classification), or those that were probably positive (with secondary signs) or probably negative (without secondary signs) were classified as positive and negative, respectively. For the analyses, equivocal results included the following: indeterminate results, non-visualization of the appendix, "probably" positive or "probably" negative

Table 2. Diagnostic Accuracy of Imaging in Adults

Imaging	Population	Studies Reporting on Sensitivity: No. of Studies; No. of Patients	Sensitivity, Median (Range)	Studies Reporting on Specificity: No. of Studies; No. of Patients	Specificity, Median (Range)
Initial US—definitive results only <sup>a</sup>	Adults with suspected appendicitis	7 observational studies [34–40]; 792 patients	0.99 (0.87–1.00) (Supplementary Figure 2)	7 observational studies [34–40]; 792 patients	0.95 (0.54–1.00) (Supplementary Figure 2)
Initial US—all results, including equivocal	Adults with suspected appendicitis	12 observational studies [34–36, 38– 46]; 2454 patients	0.68 (0.44–0.88) (Supplementary Figure 2)	12 observational studies [34–36, 38–46]; 2454 patients	0.96 (0.25–1.00) (Supplementary Figure 2)
Initial CT <sup>a</sup>	Adults with suspected appendicitis	28 observational studies [34, 36, 46–71]; 12 077 patients	0.97 (0.83-1.00) (Supplementary Figure 3)	27 observational studies [34, 36, 46–52, 54– 58, 60–72]; 12 047 patients	0.94 (0.64–1.00) (Supplementary Figure 3)
Initial MRI	Adults with suspected appendicitis	5 observational studies; [45, 73–76]; 527 patients	0.96 (0.85–0.97) (Supplementary Figure 4)	5 observational studies [45, 73–76]; 527 patients	0.97 (0.89–1.00) (Supplementary Figure 4)
Subsequent US—definitive results only	Adults with suspected appendicitis	1 observational study [77]; 190 patients	0.98 (Supplementary Figure 5)	0.98 (Supplementary Figure 5) 1 observational study [77]; 190 patients	0.97 (Supplementary Figure 5)
Subsequent US—all results, including equivocal	Adults with suspected appendicitis	2 observational studies [77, 78]; 364 patients	0.84 (0.77–0.90) (Supplementary Figure 5)	2 Observational studies [77, 78]; 364 patients	0.91 (0.83–0.98) (Supplementary Figure 5)
Subsequent CT	Adults with suspected appendicitis	9 observational studies [34, 36, 38, 48, 79–83]; 1329 patients	0.97 (0.80-1.00) (Supplementary Figure 6)	9 observational studies [34, 36, 38, 48, 79–83]; 1329 patients	0.97 (0.84–1.00) (Supplementary Figure 6)
Subsequent MRI	Adults with suspected appendicitis	No studies found	:	No studies found	:
Abbreviations: CT, computed tomogra	phy; ED, emergency departmer	Abbreviations: CT, computed tomography; ED, emergency department; MRI, magnetic resonance imaging; US, ultrasound	nd.		

<sup>a</sup>One additional study [32] performed a head-to-head comparison of US and CT in adults presenting to the ED with abdominal pain. For the 284 diagnosed with appendicitis, US (definitive results only) and CT yielded sensitivities of 76% and 94%, respectively, and specificities of 95% and 95%, respectively.

# Table 3. Diagnostic Accuracy of Imaging in Children

Imaging	Population	No. of Studies; No. of Patients	Sensitivity, Median (Range)	No. of Studies; No. of Patients	Specificity, Median (Range)
Initial US— definitive results only	Children with suspected appendicitis	15 observational studies [72, 84–98]; 11 825 patients	0.99 (0.84–1.00) (Supplementary Figure 7)	15 observational studies [72, 84–98]; 11 825 patients	0.96 (0.71-0.98) (Supplementary Figure 7)
Initial US—all results, including Children with suspected equivocal appendicitis	Children with suspected appendicitis	22 observational studies [84–97, 99–106]; 16 252 patients	0.82 (0.56–1.00) (Supplementary Figure 7)	22 observational studies [84–97, 99–106]; 16 252 patients	0.94 (0.17–0.99) (Supplementary Figure 7)
Initial CT	Children with suspected appendicitis	3 observational studies [106–108]; 393 patients	0.96 (0.91–0.98) (Supplementary Figure 8)	3 observational studies [106–108]; 393 patients	0.96 (0.87–1.00) (Supplementary Figure 8)
Initial MRI	Children with suspected appendicitis	11 observational studies [72, 88, 100, 109– 117]; 2799 patients	0.98 (0.92–1.00) (Supplementary Figure 9)	11 observational studies [72, 88, 100, 109– 117]; 2799 patients	0.97 (0.89–1.00) (Supplementary Figure 9)
Subsequent US— definitive results only	Children with suspected appendicitis	2 observational studies [84, 118]; 39 patients	1.00 (1.00–1.00) (Supplementary Figure 10)	2 observational studies [4, 89]; 39 patients	0.96 (0.91–1.00) (Supplementary Figure 10)
Subsequent US—all results, including equivocal	Children with suspected appendicitis	3 observational studies [84, 118, 119]; 148 patients	0.83 (0.71–0.98) (Supplementary Figure 10)	3 observational studies [84, 118, 119]; 148 patients	0.96 (0.96–1.00) (Supplementary Figure 10)
Subsequent CT	Children with suspected appendicitis	6 observational studies [97, 119–123]; 908 patients	0.98 (0.86–1.00) (Supplementary Figure 11)	6 observational studies [97, 119–123]; 908 patients	0.98 (0.94–1.00) (Supplementary Figure 11)
Subsequent MRI	Children with suspected appendicitis	Children with suspected 14 observational studies [98, 100, 120, appendicitis 121, 124–133]; 1971 patients	0.95 (0.84–1.00) (Supplementary Figure 12)	14 observational studies [98, 100, 120, 121, 124-133]; 1971 patients	0.97 (0.88–1.00) (Supplementary Figure 12)

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maging	Population	No. of Studies; No. of Patients	Sensitivity, Median (Range)	No. of Studies; No. of Patients	Specificity, Median (Range)
nitial US— definitive results Pregnant people with only suspected appendic	Pregnant people with suspected appendicitis	2 observational studies [134, 135]; 11 patients	1.00 (1.00–1.00) (Supplementary Figure 13)	2 observational studies [134, 135]; 11 patients	0.92 (0.83–1.00) (Supplementary Figure 13)
Initial US—all results, P including equivocal	Pregnant people with suspected appendicitis	3 observational studies [134–136]; 579 patients	0.26 (0.18–0.29) (Supplementary Figure 13)	3 observational studies [134–136]; 579 patients	1.00 (0.99–1.00) (Supplementary Figure 13)
Initial MRI	Pregnant people with suspected appendicitis	11 observational studies [72, 137–146]; 1512 patients	0.93 (0.18–1.00) (Supplementary Figure 14)	11 observational studies [72, 137–146]; 1512 patients	0.96 (0.54–1.00) (Supplementary Figure 14)
Subsequent US	Pregnant people with suspected appendicitis	No studies found	÷	No studies found	÷
Subsequent MRI	Pregnant people with suspected appendicitis	7 observational studies [134, 136, 137, 147–150]; 479 patients	1.00 (1.00–1.00) (Supplementary Figure 15)	7 observational studies [134, 136, 137, 147–150]; 479 patients	0.98 (0.94–1.00) (Supplementary Figure 15)

determinations, and results based only on secondary signs (eg, periappendiceal fat thickening, increased echogenicity or hyperemia, right lower quadrant inflammation, intraperitoneal collection, or complex free fluid). Patients with an alternative diagnosis found on US (eg, cancer) were considered negative for appendicitis on US. Although results from MRI and CT can also be equivocal/indeterminate, the panel believed that this was less likely to happen than with US, and thus less of a concern.

The evidence for all imaging recommendations was of very low certainty due to study risk of bias concerns (according to the QUADAS-2 assessment; Supplementary Tables 4–6) [152, 153], along with indirectness of comparisons (eg, lack of head-to-head studies comparing various imaging modalities) (Supplementary Tables 7–20). Inconsistent results and imprecision of results were also concerns for many of the imaging modalities studied. Additional analyses were performed that were considered informative but not essential to formulating the recommendation (Supplementary Table 21, Supplementary Figures 16–20).

# **RATIONALE FOR RECOMMENDATIONS**

# Imaging in Adults

Abdominal CT is suggested as the initial imaging modality for adults with suspected acute appendicitis. Although US seems highly accurate when yielding definitive results, abdominal CT can be used to identify other potential causes of abdominal pain (eg, colon cancer) that are more likely to be seen in adults. Because of this, the panel suggests CT as the initial imaging modality for adults. Because of the accuracy of CT in diagnosing acute appendicitis, additional imaging studies beyond CT should not be necessary. Ultrasound, when definitively positive or definitively negative, and MRI are also reasonably accurate and may precede CT, depending on the patient and clinical circumstances.

### Imaging in Children

The panel suggests US as the preferred initial imaging modality in children with suspected acute appendicitis. If an initial US is equivocal/indeterminate, the panel suggests either MRI or CT for subsequent imaging. Both CT and MRI demonstrated very high sensitivities and specificities. Ultrasound had comparable results when considering only definitively positive and definitively negative imaging interpretations. When adding in the equivocal/indeterminate results, the sensitivity of US decreased from 99% to 82%. Because US is readily available, inexpensive, and highly accurate when yielding a definitive result, the panel suggests obtaining an US first in children with suspected appendicitis. MRI may not be as readily available and may necessitate sedation in young children. CT is associated with radiation exposure, which is of particular concern in children. However, US often yields equivocal/indeterminate

Table 4. Diagnostic Accuracy of Imaging in Pregnant People

results, in which case the panel suggests either MRI or CT as subsequent imaging in children with suspected appendicitis. Allergies or contraindications to IV contrast may preclude the use of CT.

### **Imaging in Pregnant People**

Abdominal US is suggested as the initial imaging modality for pregnant people with suspected acute appendicitis. If the initial US is equivocal, the panel suggests obtaining an MRI as subsequent imaging to diagnose acute appendicitis. While limited by an extremely small sample size (n = 11), combined data suggest that initial US results are accurate when definitive results are reported. For most pregnant people reporting pain congruent with suspected acute appendicitis, practitioners would likely perform an initial US as part of the assessment because of the ease of access to US. MRI following an initial US is also highly accurate and is suggested for subsequent imaging beyond US. It would also be reasonable for a practitioner to proceed directly to an MRI as the initial imaging modality, if available and feasible.

### IMPLEMENTATION CONSIDERATIONS

Intravenous contrast is usually appropriate whenever a CT scan is obtained in adults with suspected acute appendicitis; however, CT without IV contrast also has high diagnostic accuracy in detecting acute appendicitis and may be appropriate [1]. Similarly, CT with IV contrast is usually appropriate when performed in children with suspected acute appendicitis after equivocal US; however, CT without IV contrast may be appropriate [2]. Reduced-dose CT has demonstrated similar diagnostic performance to that of standard-dose CT in both children and adults; therefore, reduced-dose CT is a reasonable option to consider where available [33].

### **RESEARCH NEEDS**

While a few studies comparing multiple diagnostic imaging strategies in the same study sample were identified, more "head-to-head" studies would be useful, especially considering the plethora of studies comparing various imaging modalities with a reference standard.

### Supplementary Data

Supplementary Material is available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

### Notes

Author contributions. Dr. Robert Bonomo is chair of the panel. Drs. Pranita Tamma and Robert Bonomo served as clinical leads for the questions addressed in this manuscript. Remaining panelists assisted with the conception and design of the analysis, interpretation of data, drafting and revising the recommendations and manuscript, and final approval of the recommendations and manuscript to be published. Jennifer Loveless, lead methodologist, and Katelyn Donnelly, methodologist, were responsible for project management, designing and performing the data analyses, and leading the panel according to the GRADE process.

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Additional information. More detailed information on the analysis and development of recommendations is available in the Supplementary Material.

**Potential conflicts of interest.** Evaluation of relationships as potential conflicts of interest (COIs) is determined by a review process. The assessment of disclosed relationships for possible COIs is based on the relative weight of the financial relationship (ie, monetary amount) and the relevance of the relationship (ie, the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or

recommendation of consideration). A. W. C. receives honoraria from UpToDate, Inc, and serves on an Agency for Healthcare Research and Quality technical expert panel for diagnosis of acute right lower quadrant abdominal pain (suspected acute appendicitis). J. R. B. serves as past president of the European Society of Clinical Microbiology and Infectious Diseases. M. S. E. receives royalties from UpToDate, Inc, as co-section editor of Pediatric Infectious Diseases. M. K. H. serves on the Society for Healthcare Epidemiology of America (SHEA) Board of Directors. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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