Supplementary Material for the 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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METHODS

Panel formation and conflicts of interest

The chair of the guideline panel was selected by the leadership of IDSA. Fifteen additional panelists comprised the full panel. The panel included clinicians with expertise in infectious diseases, pediatric infectious diseases, surgery, emergency medicine, microbiology, and pharmacology. Panelists were diverse in gender, geographic distribution, and years of clinical experience. Guideline methodologists oversaw all methodological aspects of the guideline development and identified and summarized the scientific evidence for each clinical question. IDSA staff oversaw all administrative and logistic issues related to the guideline panel.

All members of the expert panel complied with the IDSA policy on conflict of interest (COI), which requires disclosure of any financial, intellectual, or other interest that might be construed as constituting an actual, potential, or apparent conflict. Evaluation of such relationships as potential conflicts of interest was determined by a review process which included assessment by the Standards and Practice Guideline Committee (SPGC) Chair, the SPGC liaison to the Guideline panel and the Board of Directors liaison to the SPGC, and if necessary, the Conflicts of Interests Task Force of the Board. This assessment of disclosed relationships for possible COI was based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an independent observer might reasonably interpret an association as related to the topic or recommendation of consideration). The reader of these guidelines should be mindful of this when the list of disclosures is reviewed. See the Notes section at the end of this guideline for the disclosures reported to IDSA.

Practice recommendations

Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care by assisting practitioners and patients in making shared decisions about appropriate health care for specific clinical circumstances. These are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options [IOM 2011]. The “IDSA Handbook on Clinical Practice Guideline Development” provides more detailed information on the processes followed throughout the development of this guideline [IDSA CPG Handbook].

Review and approval process

Feedback was obtained from five external individual peer expert reviewers as well as the endorsing organizations. The IDSA Standards and Practice Guidelines Subcommittee (SPGS) and Board of Directors reviewed and approved the guideline prior to publication.

Process for updating

IDSA guidelines are regularly reviewed for currency. The need for updates to the guideline is determined by a scan of current literature and the likelihood that any new data would impact the recommendations. Any changes to the guideline will be submitted for review and approval to the appropriate Committees and Board of IDSA.

Clinical questions

Each clinical question was formatted according to the PICO style: Patient/Population (P), Intervention/Indicator (I), Comparator/Control (C), Outcome (O). For each PICO question, outcomes of interest were identified a priori and rated for their relative importance for decision-making.

Literature search

A medical librarian designed the literature searches and MeSH terms for Ovid Medline, Embase, and Cochrane Library. Searches were limited to studies published in English. The initial formal literature searches were performed in July to November 2018, and updated literature searches were conducted in March 2021 and October 2022. To supplement the electronic searches, reference lists of related articles and guidelines were reviewed for relevance.

MEDLINE

#1 exp Tomography, X-Ray Computed/

#2 exp Ultrasonography/

#3 (ultraso* or ultra-so* or echograph* or echo-graph* or echotomograph* or echoto-mograph* or sonograph* or sono-graph* or echocardiograph* or echo-cardiograph* or echoencephalograph* or echo-encephalograph* or endosonograph* or endo-sonograph*).tw,kf.

#4 ((tomodensitometr* or (ct or comput* or cat or electron)) adj3 (cine or scan* or xray* or x-ray* or tomograph*)).tw,kf.

#5 (HIDA or ((hepatobiliar* or hepato-biliar*) adj2 (scan* or imag*))).tw,kf.

#6 exp Magnetic Resonance Imaging/

#7 (MRI or MRIs or (magn* adj3 resonanc*) or ((magn* or MR or MRs) adj2 (imaging* or tomograph* or tomo-graph*))).tw,kf,jw.

#8 or/1-7

#9 Appendicitis/

#10 (appendicit* or ((appendix or appendectom* or appendic* or periappendic*) adj2 (complic* or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*))).tw,kf.

#11 or/9-10

#12 8 and 11

#13 Animals/ not (Animals/ and Humans/)

#14 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).ti,kf.

#15 12 not (13 or 14)

#16 limit 15 to english

#17 remove duplicates from 16

#18 limit 17 to yr="2021 -Current"

EMBASE

#1 exp x-ray computed tomography/

#2 exp echography/

#3 (ultraso* or ultra-so* or echograph* or echo-graph* or echotomograph* or echoto-mograph* or sonograph* or sono-graph* or echocardiograph* or echo-cardiograph* or

echoencephalograph* or echo-encephalograph* or endosonograph* or endo-sonograph*).tw,kw,kf.

#4 ((tomodensitometr* or (ct or comput* or cat or electron)) adj3 (cine or scan* or xray* or x-ray* or tomograph*)).tw,kw,kf.

#5 (HIDA or ((hepatobiliar* or hepato-biliar*) adj2 (scan* or imag*))).tw,kw,kf.

#6 exp nuclear magnetic resonance imaging/

#7 (MRI or MRIs or (magn* adj3 resonanc*) or ((magn* or MR or MRs) adj2 (imaging* or tomograph* or tomo-graph*))).tw,kf,jw,kf.

#8 or/1-7

#9 exp appendicitis/

#10 (appendicit* or ((appendix or appendectom* or appendic* or periappendic*) adj2 (complic* or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*))).tw,kw,kf.

#11 or/9-10

12 8 and 11

#13 (exp animal/ or exp juvenile animal/ or adult animal/ or animal cell/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not human/

#14 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).ti,kw,kf.

#15 12 not (13 or 14)

#16 limit 15 to english

#17 limit 16 to yr="2021 -Current"

#18 remove duplicates from 17

#19 limit 18 to (conference abstract or conference paper or "conference review")

#20 18 not 19

COCHRANE (WILEY)

#1 (ultraso* or ultra-so* or echograph* or echo-graph* or echotomograph* or echoto-mograph* or sonograph* or sono-graph* or echocardiograph* or echo-cardiograph* or echoencephalograph* or echo-encephalograph* or endosonograph* or endo-sonograph*):ti,ab,kw

#2 ((tomodensitometr* or (ct or comput* or cat or electron)) NEAR/3 (cine or scan* or xray* or x-ray* or tomograph*)):ti,ab,kw

#3 (HIDA or ((hepatobiliar* or hepato-biliar*) NEAR/2 (scan* or imag*))):ti,ab,kw

#4 (MRI or MRIs or (magn* NEAR/3 resonanc*) or ((magn* or MR or MRs) NEAR/2 (imaging* or tomograph* or tomo-graph*))):ti,ab,kw,so

#5 #1 OR #2 OR #3 OR #4

#6 (appendicit* or ((appendix or appendectom* or appendic* or periappendic*) NEAR/2 (complic* or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*))):ti,ab,kw

#7 #5 AND #6

Study selection

Titles and abstracts were screened in duplicate for all identified citations using Rayyan [Ouzzani 2016]. All potentially relevant citations were subjected to a full-text review, using predefined inclusion and exclusion criteria tailored to meet the specific population, intervention, and comparator of each clinical question. The steps of the literature selection process were supervised and reviewed by a guideline methodologist for the final selection of the relevant articles.

The following eligibility criteria were used:

Inclusion criteria:

- *Patient population*- Adults, children, or pregnant people with suspected acute appendicitis. For studies on subsequent imaging, patient population ideally had equivocal result on initial imaging.
- *Intervention (diagnostic imaging modalities)*- Ultrasound, graded compression US, CT (including contrast), MDCT, MRI, MRCP, or diffusion-weighted MRI
- *Comparator*- Clinical or surgical findings (e.g., histopathology), clinical course/resolution of symptoms
- *Outcomes*- Diagnostic accuracy (e.g., sensitivity, specificity)
- *Study design*- Randomized controlled trials (RCTs) with no date limit, observational studies published 2010-present, studies reporting diagnostic test accuracy data AND raw data to reconstruct contingency table, studies stratifying diagnostic accuracy of US by BMI/weight *in adults*, studies that differentiate complicated vs. uncomplicated appendicitis, articles published in English

Exclusion criteria:

- *Patient population*- Children and adults analyzed together, patients with abdominal pain not specific to suspected appendicitis
- *Intervention*- Unenhanced CT, Magnetic resonance elastography (MRE), ERCP, Acoustic radiation form impulse (ARFI), POCUS, surgeon-performed US, US as subsequent imaging study in adults (subsequent to radiology US, not POCUS), transvaginal-only US in non-pregnant people, evaluation of color doppler
- *Comparator*- Another imaging modality as a reference standard
- *Study design*- Observational studies published prior to 2010, studies stratifying diagnostic accuracy of US by BMI/weight *in children*, studies that combine imaging and clinical scores and then report diagnostic accuracy of both combined, studies comparing contrast vs. no contrast, studies comparing different weighting techniques of imaging modalities, studies reporting calculated diagnostic test accuracy measures but no raw data to construct contingency table, studies reporting diagnostic accuracy measures for distinguishing complicated vs. uncomplicated infection, abstracts and conference proceedings, letters to the editor, editorials, and review articles

Data extraction and analysis

A guideline methodologist in conjunction with panelists extracted the data for each pre-determined patient-important outcome. If a relevant publication was missing raw data for an outcome prioritized by the panel, an attempt was made to contact the author(s) for the missing data. Where applicable, data were pooled using random-effects model (fixed effects model for pooling of rates) using RevMan [RevMan].

Evidence to decision

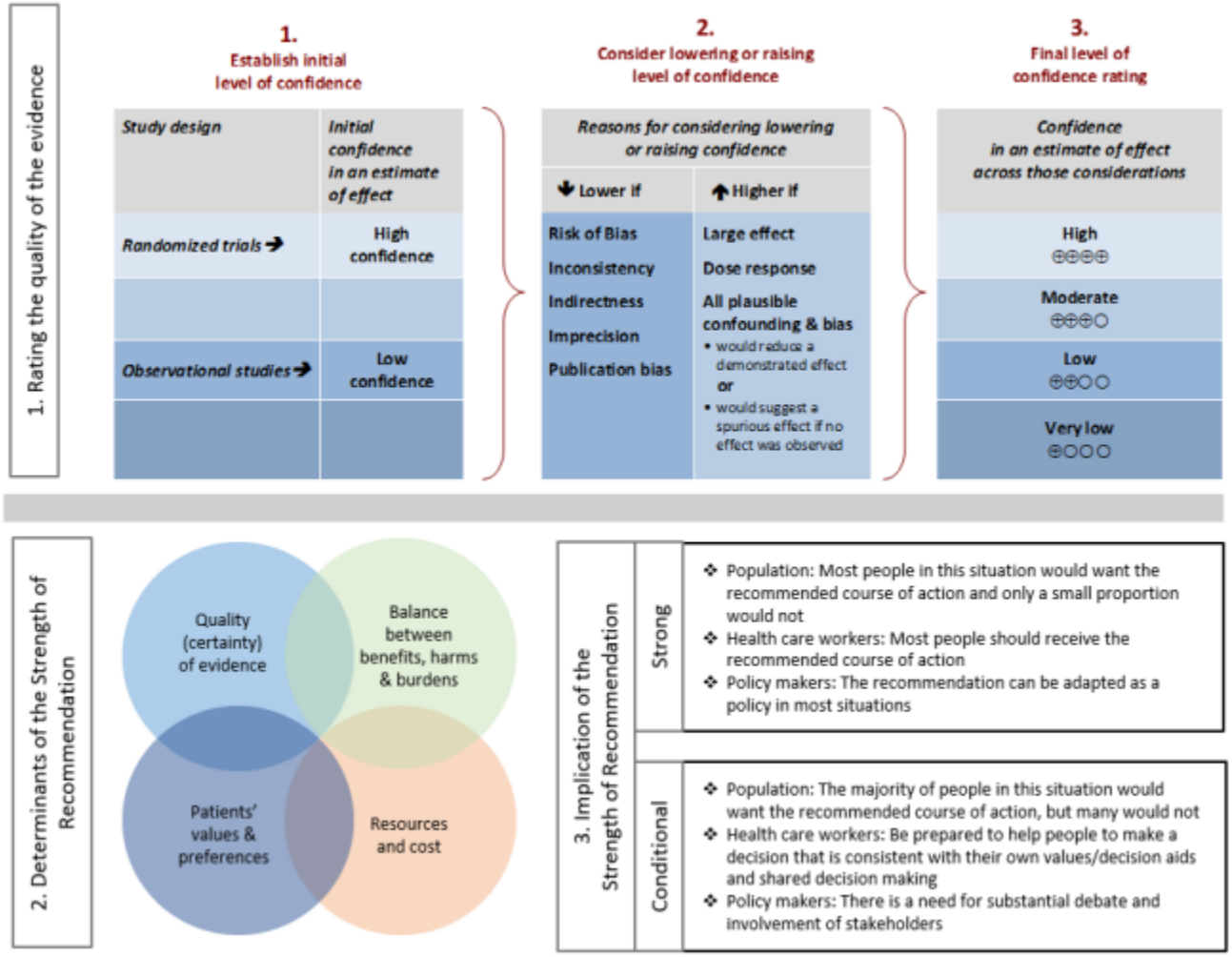
Guideline methodologists prepared the evidence summaries for each question and assessed the risk of bias and the certainty of evidence. Risk of bias was assessed by using the QUIPS tool for studies addressing risk/prognostic factors [Hayden 2013] and the QUADAS-2 tool for diagnostic test accuracy studies [Whiting 2011]. The certainty of evidence was determined first for each critical and important outcome and then for each recommendation using the GRADE approach for rating the confidence in the evidence [Guyatt 2008, GRADE Handbook]. Evidence profiles were developed using the GRADEpro Guideline Development Tool [Guyatt 2008] and reviewed by panel members responsible for each PICO.

The Evidence to Decision framework [GRADEpro] was used to translate the evidence summaries into practice recommendations. All recommendations were labeled as either “strong” or “conditional” according to the GRADE approach [IDSA CPG Handbook]. The words “we recommend” indicate strong recommendations and “we suggest” indicate conditional recommendations. Supplementary Figure 1 provides the suggested interpretation of strong and conditional recommendations for patients, clinicians, and healthcare policymakers. For recommendations where the comparator treatment or tests are not formally stated, the comparison of interest is implicitly referred to as “not using the intervention” (either not using a specific treatment or a diagnostic test).

All members of the panel participated in the preparation of the draft guideline and approved the recommendations.

TABLES AND FIGURES

Supplementary Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology (unrestricted use of figure granted by the U.S. GRADE Network)



ADULTS

In adults with suspected acute appendicitis, should US, CT, or 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?

Supplementary Table 1. Characteristics of included studies for acute appendicitis in adults

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
US in adults						
Alnuaymah 2022	Saudi Arabia 2019-2021	Retrospective review	336 patients (148 had US, 245 had CT) Median age 25 years (range 14-80) 216 diagnosed with appendicitis; pre-test probability: 64%	Patients who underwent appendicectomy on account of presumed appendicitis and in whom histological examination of the appendix was done post-surgery	Histopathology	US and contrast-enhanced CT (either or both, order of imaging unclear)
Alshebromi 2019	Saudi Arabia 2015-2017	Retrospective	200 patients (63 underwent CT, 59 underwent US, 78 no imaging) Mean age 25.5 years (SD 9.6) 54/59 who underwent US diagnosed with appendicitis; pre-test probability: 92%	Patients admitted due to suspected appendicitis who had histopathological reports (/underwent surgery)	Histopathology	US (unclear if initial or subsequent)
Aras 2016	Turkey 2010-2015	Retrospective review	207 women (38 pregnant and 169 non-pregnant); 36/38 pregnant women had initial US Mean age of non-pregnant women 28.1 years 149/169 non-pregnant women diagnosed with appendicitis; pre-test probability: 88%	Women suspected of having appendicitis who underwent appendectomy	Histopathology	Initial US
Ashcroft 2021	UK 2019-2020	Retrospective	206 patients, 153 of whom underwent US or CT preoperatively (81 had US) Mean age for women 27.1 years, mean age for men 28.6 years 159 diagnosed with appendicitis; pre-test probability: 77%	Patients aged 16-45 years having an appendicectomy	Histopathology	Initial US or CT
Atwood 2021	USA 2016-2017	Retrospective	3,477 patients (2,392 with definitive US results and an additional 1,085 with indeterminate US results) Median age 28.0 years	Adults who received an US and underwent an appendectomy	Pathology	Initial US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			3,200 diagnosed with appendicitis; pre-test probability: 92%			
Crocker 2020	Canada 2013-2015	Retrospective	798 patients (562 had US alone or US, then CT) Mean age 32.7 years 127 diagnosed with appendicitis; pre-test probability: 23%	Patients who presented to the ED and underwent US, CT, or both for RLQ or abdominal pain and suspected appendicitis	Histopathology or 3 months of medical record follow-up if surgery wasn't performed	Initial US
Fatima 2021	Pakistan 2019-2020	Prospective	170 patients Age range 13-60 years 142 diagnosed with appendicitis; pre-test probability: 84%	Patients with a suspected clinical picture of appendicitis who underwent appendectomy	Histopathology	Initial US
Fedko 2014	USA 2010-2011	Retrospective	65 patients Median age 23 years 10 diagnosed with appendicitis; pre-test probability: 15%	Adult ED patients ≥18 years who underwent RLQ ultrasonography	Pathology or 90-day follow-up/clinical notes	Initial US
Ferrarese 2016	Italy 2010-2015	Retrospective	105 patients Mean age 35 years 97 diagnosed with appendicitis; pre-test probability: 92%	Patients who underwent appendectomies	Intraoperative findings	Initial US
Hussain 2014	Pakistan 2007-2008	Retrospective	60 patients Mean age 31.4 years (range 10-70) 34 diagnosed with appendicitis; pre-test probability: 57%	Patients with suspected acute appendicitis who underwent US	Histopathology or clinical follow-up	Initial US
Jakkula 2022	India 2019-2021	Prospective	100 patients Mean age not stated; range 18-85 years 89 diagnosed with appendicitis; pre-test probability: 89%	Adults >18 years admitted with acute abdomen, clinically diagnosed as acute appendicitis with pain duration up to 48 hours, who underwent surgery	Clinical findings and histopathology	Initial US
John 2011	India 2003-2005	Prospective	213 patients Mean age 27.4 years (range 15-64) 193 diagnosed with appendicitis; pre-test probability: 81%	Patients who had been clinically diagnosed with acute appendicitis and planned for appendectomy	Histopathology	Initial US
Kapoor 2010	India Years not stated	Prospective	40 patients Mean age 37 years (SD ±6.5) 25 diagnosed with appendicitis; pre-test probability: 63%	Patients who had a provisional clinical diagnosis of acute appendicitis	Surgical findings or clinical follow-up	Initial US
Karimi 2017	Iran 2015	Prospective	108 patients Mean age 23.91 years	Patients presenting to the ED with suspected appendicitis who underwent US by a radiologist	Pathology or 48-hour follow-up	Initial US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			37 diagnosed with appendicitis; pre-test probability: 34%			
Koc 2020	Turkey 2009-2019	Retrospective	431 patients (48 pregnant and 383 non-pregnant); 351 non-pregnant women had initial US Median age of non-pregnant females 28 years (range 18-45) 263 non-pregnant females diagnosed with appendicitis; pre-test probability: 75%	431 reproductive-aged (18-45 years) female patients who underwent appendectomy with a presumed diagnosis of acute appendicitis (48 pregnant, 383 non-pregnant)	Histopathology	Initial US
Kouame 2012	Cote d'Ivoire/West Africa 2005-2010	Retrospective	620 patients Mean age 29 years (range 15-45 years) 585 diagnosed with appendicitis; pre-test probability: 94%	Cases of appendectomy following prior ultrasound exam of the right iliac fossa	Surgery and anatomical pathology reports	Initial US
Leeuwenburgh 2013	Netherlands 2010	Prospective	230 (229 had US) Median age 36 years (IQR 25-50) 118 diagnosed with appendicitis; pre-test probability: 51%	Adult patients (18 years or older) who, prior to imaging, were clinically suspected of having acute appendicitis on the basis of medical history and physical and laboratory exam findings	Final diagnosis as determined by an expert panel, based on histopathology or clinical info, imaging findings, surgery, and at least 3 months of follow-up	Initial US
Leung 2017	Hong Kong 2011-2012	Retrospective	335 patients in Group A (90 underwent US ± CT, 67 underwent CT: 53 CT only, 14 CT and US) Median age of entire cohort (included patients with suspected appendicitis [Group A] and those with abdominal pain but unlikely appendicitis [Groups B and C]) 55 years 104/335 diagnosed with appendicitis; pre-test probability: 31%	Adults ≥18 years with strongly suspected appendicitis in the ED (study Group A)	Histopathology, surgeon diagnosis, or 1-month follow-up	Initial CT; Subsequent CT (presumably subsequent to US)
Luksaite-Lukste 2021	Lithuania 2016-2018	Prospective	1855 patients, 1851 of which underwent US Median age 34 years 490 diagnosed with appendicitis; pre-test probability: 26%	Adult (>18 years) ED patients with suspected acute appendicitis	Expert panel based on histopathology, imaging, surgical findings, clinical information, and at least 6 months of follow-up	Initial US
Poletti 2011	Switzerland 2008-2009	Prospective	183 patients Mean age 32 years 86 diagnosed with appendicitis; pre-test probability: 47%	Adults with suspicion of acute appendicitis and a BMI between 18.5 and 30	Surgery and follow-up	Initial US
Reich 2011	Israel 2005-2006	Retrospective	197 patients Mean age 30.2 years	Adults with an ED working diagnosis of appendicitis and ≥1 imaging study who went to the OR and had documented	Surgical pathology	Initial US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			177 diagnosed with appendicitis; pre-test probability: 90%	surgical pathology results; 197 in the US cohort in Israel		
Roberts 2021	Canada 2018-2019	Retrospective review	208 US reports (104 performed by radiology residents and 104 by departmental sonographers) Median age 24 years in the resident group and 27 years in the sonographer group 40 diagnosed with appendicitis (total from both groups); pre-test probability: 19%	Adult women <40 years imaged for clinically suspected appendicitis	Histopathology or absence of confirmed appendicitis in the EMR	Initial US
Sammalkorpi 2017	Finland 2014-2015	Prospective	1,545 patients, 489 of whom underwent CT and 497 US Mean age/age range not stated 177/497 patients undergoing US diagnosed with appendicitis; pre-test probability: 36%	Patients ≥16 years of age with suspected acute appendicitis; patients were evaluated with the Adult Appendicitis Score and based on their score, recommended for discharge, imaging, or surgery	Histological exam or 1-month follow-up	Initial US
Selassie 2021	Ethiopia Study period not stated	Prospective cohort	227 patients Mean age 27.6 years (range 18-70) 223 diagnosed with appendicitis; pre-test probability: 98%	Adults ≥18 years who had undergone appendectomy for a clinical diagnosis of appendicitis	Intraoperative findings (no histopathological analysis)	Initial US
Serinsoz 2021	Turkey 2018-2020	Retrospective	70 patients Mean age 31.8 years (range 11-71) 37 diagnosed with appendicitis; pre-test probability: 53%	Patients clinically diagnosed with acute appendicitis who underwent surgery	Surgical findings	All patients underwent US, unenhanced CT, and diffusion-weighted MRI
Sezer 2012	Turkey 2008-2010	Retrospective	91 patients Mean age 30.6 years (range 18-54) 77 diagnosed with appendicitis; pre-test probability: 85%	Adults with right lower abdomen pain who underwent appendicectomy; excluded 5 obese patients	Histopathology	Initial US
Singh 2022	India	Prospective cohort	80 adults Mean/Median age not stated 75 diagnosed with appendicitis; pre-test probability: 94%	Patients >18 years with clinically diagnosed acute appendicitis who were planned for (and underwent) surgery	Histopathology	Initial US
Sohail 2009	Pakistan 2005-2006	Prospective	100 adults Mean age 32.6 years (range 17-54) 94 diagnosed with appendicitis, pre-test probability: 94%	Adults with clinically suspected appendicitis referred during regular working hours and later operated on	Surgical findings	Subsequent US (2nd-line focused US on the point of maximal tenderness after conventional US; all patients underwent both)
Sukhani 2017	India 5-year period (years not stated)	Retrospective	200 women (50 pregnant and 150 non-pregnant) Mean age of non-pregnant women 29.1 years	Pregnant women aged 18-45 years who underwent appendectomy	Histopathology	Initial US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			132 pregnant women diagnosed with appendicitis; pre-test probability: 88%			
Tatli 2016	Turkey 2013-2014	Retrospective	148 patients Mean age 27.48 years (10-80 years) 123 diagnosed with appendicitis; pre-test probability: 83%	Patients with suspected acute appendicitis and studied preoperatively with US; all patients were operated on	Histopathology	Initial US
Tyler 2019	USA 2013-2015	Retrospective	174 patients 13-59 years 39 diagnosed with appendicitis; pre-test probability: 22%	Patients who underwent appendiceal US	Pathological diagnosis, if available (11/174); if not, CT (141/174) or MRI (19/174) results	Initial US
CT in adults						
Alnuaymah 2022	Saudi Arabia 2019-2021	Retrospective review	336 patients (148 had US, 245 had CT) Median age 25 years (range 14-80) 216 diagnosed with appendicitis; pre-test probability: 64%	Patients who underwent appendicectomy on account of presumed appendicitis and in whom histological examination of the appendix was done post-surgery	Histopathology	US and contrast-enhanced CT (either or both, order of imaging unclear)
Alshebromi 2019	Saudi Arabia 2015-2017	Retrospective	200 patients (63 underwent CT, 59 underwent US, 78 no imaging) Mean age 25.5 years (SD 9.6) 57/63 who underwent CT diagnosed with appendicitis; pre-test probability: 91%	Patients admitted due to suspected appendicitis who had histopathological reports (/underwent surgery)	Histopathology	CT (unclear if initial or subsequent; with IV contrast ± gastrografin)
Apisarnthanarak 2014	Thailand 2006-2009	Retrospective	158 patients Mean age 38.7 years (range 16-60) 73 diagnosed with appendicitis; pre-test probability: 46%	Hospitalized patients 16-60 years who underwent an abdominal CT scan for clinically suspected acute appendicitis	Surgical pathology and/or chart review	CT (unclear if initial imaging; various oral, rectal and IV contrast protocols)
Atema 2015	Netherlands 2005-2006	Prospective	422 patients Mean age 40 years (range 19-89) 251 diagnosed with appendicitis; pre-test probability; 60%	Adults with suspected appendicitis based on medical history, physical exam, and laboratory test results	Surgical findings, histopathology, and follow-up data	Initial and subsequent CT
Chu 2014	USA A 5-year period (years unclear)	Retrospective	1,865 CT studies (including 141 equivocal) Mean age 43 years (range 18-99) 393 diagnosed with appendicitis; pre-test probability: 23%	Patients ≥18 years who underwent CT scans for suspected appendicitis	Surgical and pathological diagnoses	Unclear if initial or subsequent CT
Coursey 2011	USA 1998-2007	Retrospective	473 adults Mean age of BMI cohorts ranged from 31.2-45.5 years 423 diagnosed with appendicitis; pre-test probability: 89%	Adults >18 years who underwent appendectomy and had a preoperative CT scan, broken into BMI categories	Pathology reports	Unclear if initial or subsequent CT

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
Crocker 2020	Canada 2013-2015	Retrospective	798 (294 US and CT, 228 CT alone = 522 total for CT) Mean age 32.7 years (for all study patients) 267 diagnosed with appendicitis; pre-test probability: 51%	Patients who presented to the ED and underwent US, CT, or both for RLQ or abdominal pain and suspected appendicitis	Histopathology or 3 months of medical record follow-up if surgery wasn't performed	Initial and subsequent CT
Donlon 2021	Ireland 2012-2018	Retrospective	1,153 patients Mean age males 24 years (SD 16.49), females 23 years (SD 15.6) 933 diagnosed with appendicitis; pre-test probability: 81%	Patients undergoing an appendicectomy	Pathology report	Initial CT
Dowhanik 2021	Canada 2018-2019	Retrospective	531 adults (181 reduced protocol, 350 standard protocol) Mean age in the reduced protocol 26 years (range 17-53), mean age in the standard protocol 55 years (range 19-93) 137 diagnosed with appendicitis; pre-test probability: 26%	Adults who underwent emergency CT for abdominal pain or suspected appendicitis	Histopathology or 3 months of medical record follow-up	Initial CT (contrast-enhanced)
Eurboonyanun 2021	Thailand 2016-2017	Retrospective	140 adults Mean age ~52 years (range 15-86) 57 diagnosed with appendicitis; pre-test probability: 41%	Adults who presented with RLQ pain, pelvic pain, or peritonitis and underwent an abdominal CT	Final diagnosis, including pathologic results or follow-up	Initial CT (contrast-enhanced)
Hekimoglu 2011	Turkey 2008-2010	Randomized	200 adults (100 in IV contrast group, 100 in IV + oral contrast group) IV contrast group: Mean age 42 years (range 20-66) IV and oral contrast group: Mean age 38 years (range 18-74) 58/200 diagnosed with appendicitis; pre-test probability: 29%	Adults ≥18 years who presented with clinical signs and symptoms suggestive of acute appendicitis	Histological examination and follow-up	Initial CT (with IV contrast ± oral contrast)
Jo 2010	Korea 2006-2007	Prospective	191 patients, 187 of whom had CT performed Mean age 37.3 years 109/187 diagnosed with appendicitis; pre-test probability: 58%	Patients ≥15 years presenting to the ED with pain in the right lower quadrant of the abdomen	Histological examination and follow-up	Initial CT
Jones 2015	USA 2009-2010	Retrospective	119 patients Mean age 28.5 years (range 19-69) 12 diagnosed with appendicitis; pre-test probability: 10%	Adults for whom the appendix was not seen on otherwise normal appendiceal sonography performed for suspected appendicitis, who subsequently underwent CT	Pathology and clinical follow-up	Subsequent CT
Karabulut 2014	Turkey 2005-2008	Prospective	104 patients Mean age 27 years (range 6-77)	Patients with suspected appendicitis	Histological examination, intraoperative findings and follow-up	Initial CT

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			40 diagnosed with appendicitis; pre-test probability: 39%			
Kepner 2012	USA MISSING Years	Randomized	227 (114 IV contrast and 113 IV + oral contrast) IV contrast: 22-40 years (mean 32) IV and oral contrast: 25-43 years (mean 32) 41/114 diagnosed with appendicitis; pre-test probability: 36%	Patients ≥18 years with clinically suspected appendicitis who were referred for CT by Emergency Department (ED) physicians	Intra-operative findings and follow-up	Initial CT
Kim 2011	Korea 2008-2009	Retrospective	257 patients (132 standard radiation dose) Mean age 27.6 years (range 15-40) 53/132 diagnosed with appendicitis; pre-test probability: 40%	Patients who underwent CT for suspected appendicitis	Surgical and pathologic findings, or chart review and 4-month telephone follow-up	Initial CT (with IV contrast, without enteral contrast)
Kim 2012	Korea 2009-2011	Randomized	873 patients: 433 low-dose CT and 440 standard dose-CT Low-dose: 22-36 years (mean 29) Standard-dose CT: 22-37 years (30 mean) 180/440 diagnosed with appendicitis; pre-test probability: 41%	Patients aged 15 to 44 years who were referred for CT examination by Emergency Department physicians due to clinically suspected appendicitis	Histological examination, intra-operative findings, and follow-up	Initial CT
Ko 2020	South Korea (20 hospitals) 2013-2016	Post-hoc analysis of a randomized trial (LOCAT trial)	2,773 patients (1,381 in the standard dose CT group) Median age 28 years 540/1381 diagnosed with appendicitis; pre-test probability: 39%	Patients aged 15-44 years referred for CT due to suspected appendicitis	Pathology or 3-month telephone follow-up	Initial CT
Kolb 2019	Unclear- either South Korea or Germany 2009-2010	Retrospective	51 patients Mean age 41.0 years 30 diagnosed with appendicitis; pre-test probability: 59%	Adults >18 years who underwent abdominal CT for clinically suspected appendicitis	Histopathology and surgery, or 3-month follow-up	CT (unclear if initial or subsequent)
Koo 2013	South Korea 2006-2011	Retrospective	52 patients Mean age 37.3 years (range 15-98) (24/52) 46%	Adolescent and adults (>15 years) who underwent sonography and CT to rule out acute appendicitis due to RLQ pain; patients whose appendices could not be visualized on sonography were excluded	Pathology and clinical follow-up	Subsequent CT
Latifi 2011	Sweden 2005-2006	Retrospective	246 CT exams Mean age not stated 69 diagnosed with appendicitis; pre-test probability: 28%	Adults ≥15 years who received CT exams for suspected appendicitis	Histopathology and 3-21-month follow-up	CT (unclear if initial or subsequent; all with IV contrast ± oral contrast ± rectal contrast)

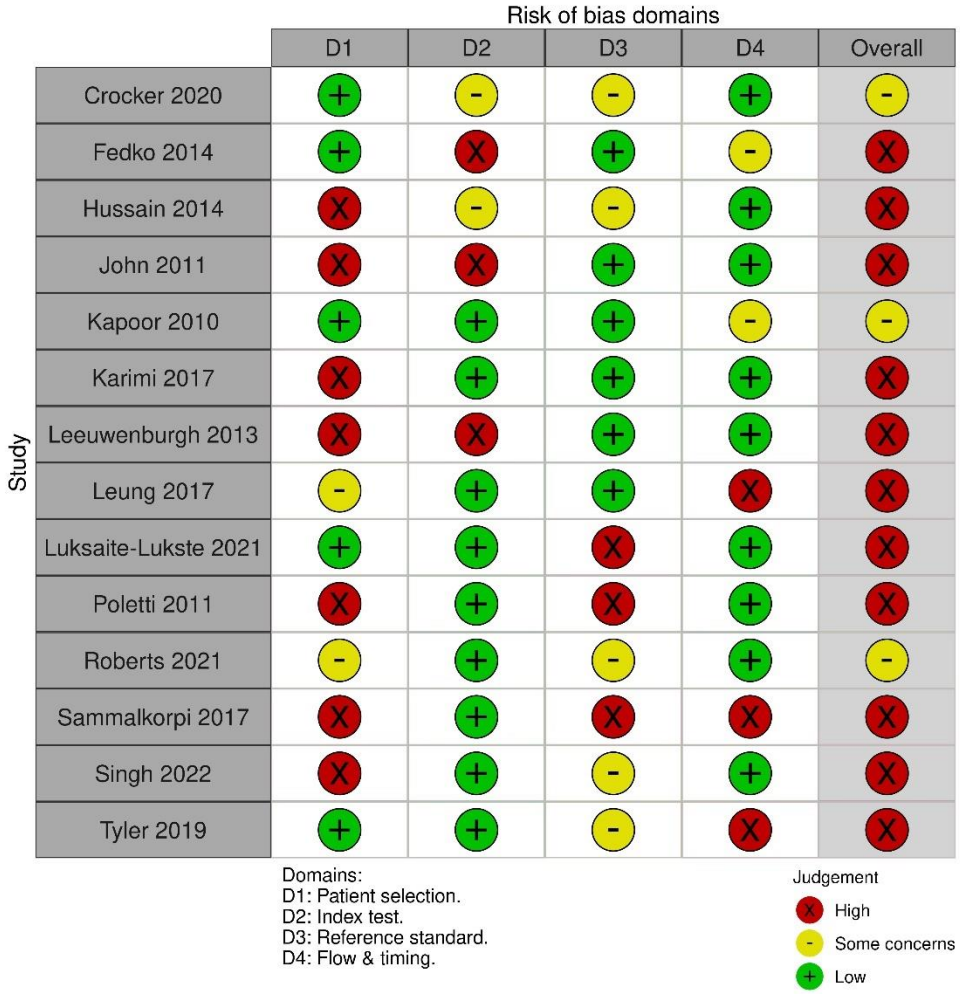
Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
Leung 2017	Hong Kong 2011-2012	Retrospective	335 patients in Group A (90 underwent US ± CT, 67 underwent CT: 53 CT only, 14 CT and US) Median age of entire cohort (included patients with suspected appendicitis [Group A] and those with abdominal pain but unlikely appendicitis [Groups B and C]) 55 years 104/335 diagnosed with appendicitis; pre-test probability: 31%	Adults ≥18 years with strongly suspected appendicitis in the ED (study Group A)	Histopathology, surgeon diagnosis, or 1-month follow-up	Initial CT; Subsequent CT (presumably subsequent to US)
Lietzen 2018	Finland (6 hospitals) 2009-2012	Retrospective review of prospectively obtained data	1,065 patients Mean age 36.2 years (range 17-65) 714 diagnosed with appendicitis; pre-test probability: 67%	Patients with clinical suspicion of acute appendicitis (clinical history, laboratory tests, and physical exam)	Surgical and histopathological findings or chart review	Initial CT
Liu 2015	China 2009-2012	Retrospective	297 patients Mean age 47.9 years (range 19-87) 187 diagnosed with appendicitis; pre-test probability: 63%	Adults who underwent MSCT prior to surgery for appendicitis	Pathology results and/or surgery	Initial CT
O'Malley 2016	Canada (2 EDs) 2011	Retrospective	99 patients Mean age 32 years (range 18-73) (26/99) 26%	Patients ≥18 years who presented with possible acute appendicitis	Pathology and chart review	Subsequent CT (following inconclusive US; with IV contrast)
Ozturk 2014	Turkey 2010-2011	Prospective	125 patients Mean age 33 years (range 5-85 years) 83 diagnosed with appendicitis; pre-test probability: 66%	Patients with suspected appendicitis	Histological exam and follow-up	Initial CT
Park 2016	Korea 2013	Prospective	107 patients Mean age 29.8 years (range 15-44) 42 diagnosed with appendicitis; pre-test probability: 39%	Patients aged 15-44 years with suspected appendicitis were referred for CT.	Histological exam and follow-up	Initial CT
Pickhardt 2011	USA 2000-2009	Retrospective	2,871 adults Mean age 38.8 years 675 diagnosed with appendicitis; pre-test probability: 24%	Adults ≥18 years referred from the ED or urgent care for MDCT for suspected acute appendicitis	Surgical pathology, intraoperative findings, and/or clinical follow-up	Initial CT (oral and IV contrast)
Poletti 2011	Switzerland 2008-2009	Retrospective	183 patients, 99 of whom had CT performed Mean age 32 years (range 16-86) 86 (of 183) diagnosed with appendicitis; pre-test probability: 47% (data not provided for only those patients undergoing CT)	Adults with suspected acute appendicitis and a BMI between 18.5 and 30	Surgery and clinical follow-up (6-8 weeks post-discharge)	Subsequent CT (low-dose CT and standard CT) after equivocal US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
Rait 2020	UK 2012–2018	Retrospective	1,344 patients, 227 of whom underwent CT abdomen and pelvis and 38 CTKUB Median age females 30 years, males 32 years 208 diagnosed with appendicitis; pre-test probability: 79%	Children (>5 years) and adults who underwent laparoscopic appendicectomy	Histology report	Initial CT
Repplinger 2018	USA 2012-2014	Prospective	198 patients Mean age 31.6 years (range 12–81) 64 diagnosed with appendicitis; pre-test probability: 32%	Patients over 12 years of age undergoing CT for suspected appendicitis	Histology or follow-up	Initial CT, MRI for research purposes
Sammalkorpi 2017	Finland 2014-2015	Prospective	1,545 patients, 489 of whom underwent CT and 497 US Mean age/age range not stated 257/489 patients undergoing CT diagnosed with appendicitis; pre-test probability: 53%	Patients ≥16 years of age with suspected acute appendicitis; patients were evaluated with the Adult Appendicitis Score and based on their score, recommended for discharge, imaging, or surgery	Histological exam or 1-month follow-up	Initial or subsequent CT (initial in patients >35 years, subsequent to US in patients ≤35 years; with IV contrast)
Scott 2015	England 2012-2013	Prospective	86 patients Median age 46 years (range 13-93) 34 diagnosed with appendicitis; pre-test probability: 40%	Patients admitted with suspected appendicitis who were referred for CT (clinician discretion)	Histological exam and follow-up	Initial CT
Sim 2013	Korea 2011	Prospective	869 patients, 738 ≥15 years Mean age 33 years (range 4-90) 320/738 diagnosed with appendicitis; pre-test probability: 43%	Patients who underwent CT examination for suspected appendicitis because of acute right lower abdominal pain	Histological exam and follow-up	Initial CT
Stabile Ianora 2010	Italy 2007-2008	Retrospective	43 patients, 33 with atypical appendicitis diagnosed after surgery (with histology) and an additional 10 with negative CT (controls) Mean age 47 years (range 20-75) 33 patients had appendicitis (pathologically confirmed); additional 10 selected as control group	Patients with suspected appendicitis (clinically and on US)	Pathology	Subsequent CT
Tan 2015	Singapore 2013-2014	Prospective	350 patients Median 33 years (range 15-82) 155 diagnosed with appendicitis; pre-test probability: 44%	Patients with suspected appendicitis who were referred for CT (attending surgeon discretion)	Histological exam and follow-up	Initial CT
Teo 2014	Australia 2012	Retrospective	64 adults Mean age of total population (which included children) 26.5 years (range 6-80)	Adults undergoing emergency appendectomies	Histology	CT ± US (order unclear)

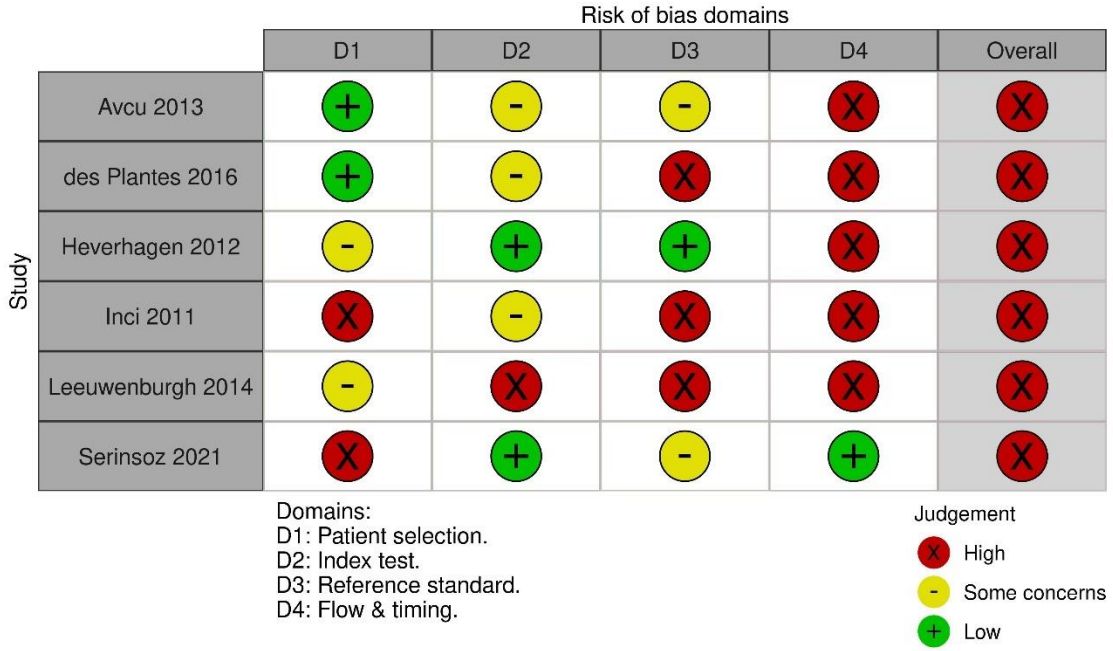
Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			56 diagnosed with appendicitis; pre-test probability: 88%			
Uzunosmanoglu 2017	Turkey 2012-2013	Prospective	60 patients Mean 30.3 years (range 19-61) 46 diagnosed with appendicitis; pre-test probability: 77%	Patients between 18 and 65 years of age with suspected appendicitis who presented during the day	Histological examination	Initial CT
Wagner 2020	Ireland 2015-2018	Retrospective	204 patients, 32 of whom underwent preoperative CT Mean age of CT cohort 33.1 years 26/32 diagnosed with appendicitis; pre-test probability: 81%	Patients <40 years with a provisional diagnosis of acute appendicitis who had an Alvarado score between 3 and 6	Histology results, intraoperative notes, and history of readmission	CT (unclear if initial or subsequent imaging study; study states that 98% of the females enrolled also had US to exclude gynecological issues; unclear if contrast-enhanced or not)
Wang 2012	Taiwan 2010	Prospective	59 patients 18 years and older 26 diagnosed with appendicitis; pre-test probability: 44%	Adults presenting to the ED with RLQ pain, lower abdominal tenderness, and an Alvarado score of 4 to 7	Histological examination and follow-up	Initial CT
Wongwaisayawan 2021	Thailand 2016-2017	Retrospective	421 patients Mean age 39.5 years 163 diagnosed with appendicitis; pre-test probability: 39%	Adults 15-99 years with clinically suspected appendicitis who had an appendiceal CT scan	Pathology or telephone follow-up	Subsequent CT (after initial US)
MRI in adults						
Avcu 2013	Turkey 2009-2010	Prospective	55 patients Mean: 35.6 years 40 diagnosed with appendicitis; pre-tests probability: 73%	Consecutive patients with suspected appendicitis	Histology or follow-up	Initial MRI
Chabanova 2011	Denmark Unclear	Prospective	48 patients Mean age 37.1 years (range 18-70) 30 patients diagnosed with appendicitis; pre-test probability: 63%	Adults with clinically diagnosed appendicitis scheduled for appendectomy	Histology or operative findings	MRI obtained for research purposes in patients scheduled for appendectomy
Ziedses des Plantes 2016	Netherlands Unclear	Prospective	112 patients Mean age 22 years 29 diagnosed with appendicitis; pre-test probability: 26%	Female patients with suspected appendicitis	Histology or follow-up	Initial MRI
Heverhagen 2012	Germany 2008	Prospective	52 patients Mean age 44.7 years (range 18-88) 13 patients diagnosed with appendicitis; pre-test probability: 25%	Patients presenting to the ED with suspected appendicitis	Histology or follow-up	Initial MRI
Inci 2011	Turkey Unclear	Prospective	85 patients Mean age 26.5 years (range 14-72)	Adults with clinically suspected acute appendicitis	Histology or follow-up	Initial MRI

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			57 diagnosed with appendicitis; pre-test probability: 86%			
Leeuwenburgh 2014	Netherlands 2010	Prospective	223 patients Median age 35 years 117 diagnosed with appendicitis; pre-test probability: 53%	Adults with suspected appendicitis	Histology or follow-up	Initial MRI
Serinsoz 2021	Turkey 2018-2020	Retrospective	70 patients Mean age 31.8 years (range 11-71) 37 diagnosed with appendicitis; pre-test probability: 53%	Patients clinically diagnosed with acute appendicitis who underwent surgery	Surgical findings	All patients underwent US, unenhanced CT, and diffusion-weighted MRI

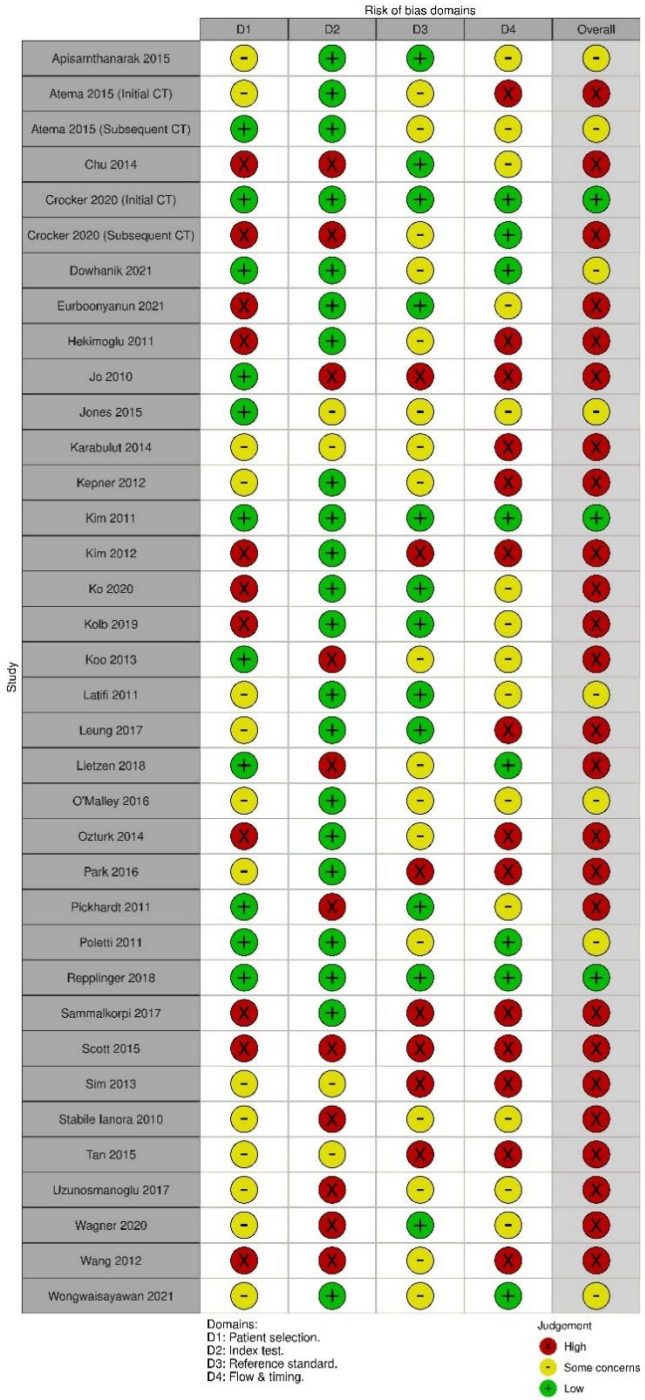
Supplementary Table 4a. Risk of bias for included studies on US in adults



Supplementary Table 4b. Risk of bias for included studies on MRI in adults



Supplementary Table 4c. Risk of bias for included studies on CT in adults



Supplementary Table 7. GRADE Evidence Profile: Should US (definitive results only) be used to diagnose acute appendicitis in adults?

US vs. reference standard; definitive results only (Crocker 2020, Fedko 2014, Leung 2017, Luksaite-Lukste 2021, Poletti 2011, Roberts 2021, Tyler 2019)	
Sensitivity	0.87 to 1.00
Specificity	0.54 to 1.00

Prevalence	26% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of26%	
True positives (patients with acute appendicitis)	7 studies (Crocker 2020, Fedko 2014, Leung 2017, Luksaite-Lukste 2021, Poletti 2011, Roberts 2021, Tyler 2019) 792 patients	cross-sectional (cohort type accuracy study)	very serious [a]	Serious [b]	not serious	not serious	none	226 to 260	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 34	
True negatives (patients without acute appendicitis)	7 studies (Crocker 2020, Fedko 2014, Leung 2017, Luksaite-Lukste 2021, Poletti 2011, Roberts 2021, Tyler 2019) 792 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	serious [c]	none	400 to 740	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 340	

Explanations

a. Per QUADAS-2 assessment
b. Indirect comparisons
c. Wide CIs

Supplementary Table 8. GRADE Evidence Profile: Should US (all results, including equivocal/indeterminate) be used to diagnose acute appendicitis in adults?

US vs. reference standard; all results, including equivocal/indeterminate (Crocker 2020, Fedko 2014, Hussain 2014, John 2011, Kapoor 2010, Karimi 2017, Leeuwenburgh 2013, Leung 2017, Poletti 2011, Roberts 2021, Sammalkorpi 2017, Singh 2022, Tyler 2019)	
Sensitivity	0.44 to 0.88
Specificity	0.25 to 1.00

Prevalence	44% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of44%	
True positives (patients with acute appendicitis)	13 studies (Crocker 2020, Fedko 2014, Hussain 2014, John 2011, Kapoor 2010, Karimi 2017, Leeuwenburgh 2013, Leung 2017, Poletti 2011, Roberts 2021, Sammalkorpi 2017, Singh 2022, Tyler 2019) 2534 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	serious [c]	serious [d]	none	194 to 387	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								53 to 246	
True negatives (patients without acute appendicitis)	13 studies (Crocker 2020, Fedko 2014, Hussain 2014, John 2011, Kapoor 2010, Karimi 2017, Leeuwenburgh 2013, Leung 2017, Poletti 2011, Roberts 2021, Sammalkorpi 2017, Singh 2022, Tyler 2019) 2534 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	serious [c]	serious [d]	none	140 to 560	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 420	

Explanations

a. Per QUADAS-2 assessment
b. Indirect comparisons
c. CIs not overlapping
d. Wide CIs

Supplementary Table 9. GRADE Evidence Profile: Should CT be used to diagnose acute appendicitis in adults?

CT vs. reference standard (Apisarnthanarak 2015, Atema 2015, Chu 2013, Crocker 2020, Dowhanik 2021, Eurboonyanun 2021, Hekimoglu 2011, Jo 2010, Karabulut 2014, Kepner 2012, Kim 2011, Kim 2012, Ko 2020, Kolb 2019, Latifi 2011, Leung 2017, Lietzen 2018, Ozturk 2014, Park 2016, Pickhardt 2011, Repplinger 2018, Sammalkorpi 2017, Scott 2015, Sim 2013, Tan 2015, Uzunosmanoglu 2017, Wagner 2020, Wang 2012)	
Sensitivity	0.83 to 1.00
Specificity	0.64 to 1.00

Prevalence	45% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of45%	
True positives (patients with acute appendicitis)	28 studies (Apisarnthanarak 2015, Atema 2015, Chu 2013, Crocker 2020, Dowhanik 2021, Eurboonyanun 2021, Hekimoglu 2011, Jo 2010, Karabulut 2014, Kepner 2012, Kim 2011, Kim 2012, Ko 2020, Kolb 2019, Latifi 2011, Leung 2017, Lietzen 2018, Ozturk 2014, Park 2016, Pickhardt 2011, Repplinger 2018, Sammalkorpi 2017, Scott 2015, Sim 2013, Tan 2015, Uzunosmanoglu 2017, Wagner 2020, Wang 2012) 12077 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	374 to 450	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 76	
True negatives (patients without acute appendicitis)	27 studies (Apisarnthanarak 2015, Atema 2015, Chu 2013, Crocker 2020, Dowhanik 2021, Eurboonyanun 2021, Hekimoglu 2011, Jo 2010, Karabulut 2014, Kepner 2012, Kim 2011, Kim 2012, Ko 2020, Latifi 2011, Leung 2017, Lietzen 2018, Ozturk 2014, Park 2016, Pickhardt 2011, Repplinger 2018, Sammalkorpi 2017, Scott 2015, Sim 2013, Tan 2015, Uzunosmanoglu 2017, Wagner 2020, Wang 2012) 12047 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	serious [c]	serious [d]	none	352 to 550	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 198	

Explanations

a. Per QUADAS-2 assessment
b. Indirect comparisons
c. CIs not overlapping
d. Wide CIs

Supplementary Table 10. GRADE Evidence Profile: Should MRI be used to diagnose acute appendicitis in adults?

MRI vs. reference standard (Avcu 2013, Ziedses des Plantes 2016, Heverhagen 2012, Inci 2011, Leeuwenburgh 2014, Serinsoz 2021)	
Sensitivity	0.85 to 1.00
Specificity	0.89 to 1.00

Prevalence	53% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of53%	
True positives (patients with acute appendicitis)	6 studies (Avcu 2013, Ziedses des Plantes 2016, Heverhagen 2012, Inci 2011, Leeuwenburgh 2014, Serinsoz 2021)	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	451 to 530	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)	597 patients							0 to 79	
True negatives (patients without acute appendicitis)	6 studies (Avcu 2013, Ziedses des Plantes 2016, Heverhagen 2012, Inci 2011, Leeuwenburgh 2014, Serinsoz 2021)	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	418 to 470	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)	597 patients							0 to 52	

Explanations

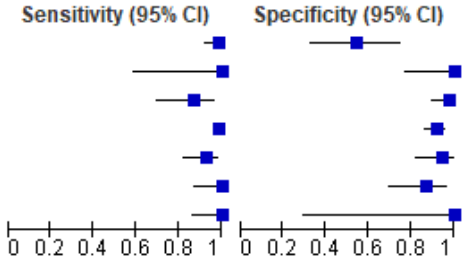
a. Per QUADAS-2 assessment

b. Indirect comparisons

Supplementary Figure 2. Initial US for adults with suspected appendicitis

a) definitive US results only

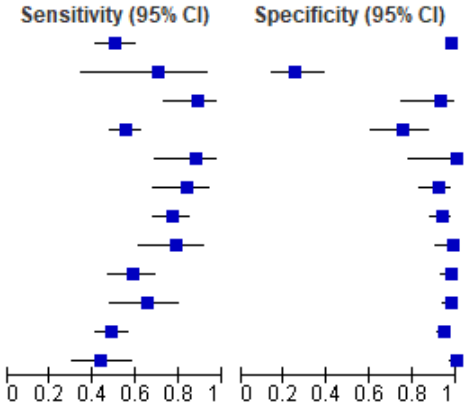
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Crocker 2020	64	11	1	13	0.98 [0.92, 1.00]	0.54 [0.33, 0.74]
Fedko 2014	7	0	0	14	1.00 [0.59, 1.00]	1.00 [0.77, 1.00]
Leung 2017	26	1	4	52	0.87 [0.69, 0.96]	0.98 [0.90, 1.00]
Luksaite-Lukste 2021	266	13	3	141	0.99 [0.97, 1.00]	0.92 [0.86, 0.95]
Poletti 2011	50	2	4	36	0.93 [0.82, 0.98]	0.95 [0.82, 0.99]
Roberts 2021	26	4	0	26	1.00 [0.87, 1.00]	0.87 [0.69, 0.96]
Tyler 2019	25	0	0	3	1.00 [0.86, 1.00]	1.00 [0.29, 1.00]



Total n: 7 studies, 792 patients
Median (range) sensitivity: 0.99 (0.87-1.00); Median (range) specificity: 0.95 (0.54-1.00)

b) all US results, including equivocal/indeterminate*

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Crocker 2020	64	11	63	424	0.50 [0.41, 0.59]	0.97 [0.96, 0.99]
Fedko 2014	7	41	3	14	0.70 [0.35, 0.93]	0.25 [0.15, 0.39]
Hussain 2014	30	2	4	24	0.88 [0.73, 0.97]	0.92 [0.75, 0.99]
John 2011	106	11	87	34	0.55 [0.48, 0.62]	0.76 [0.60, 0.87]
Kapoor 2010	22	0	3	15	0.88 [0.69, 0.97]	1.00 [0.78, 1.00]
Karimi 2017	31	6	6	65	0.84 [0.68, 0.94]	0.92 [0.83, 0.97]
Leeuwenburgh 2013	90	7	27	105	0.77 [0.68, 0.84]	0.94 [0.88, 0.97]
Leung 2017	26	1	7	56	0.79 [0.61, 0.91]	0.98 [0.91, 1.00]
Poletti 2011	50	2	36	95	0.58 [0.47, 0.69]	0.98 [0.93, 1.00]
Roberts 2021	26	4	14	164	0.65 [0.48, 0.79]	0.98 [0.94, 0.99]
Sammalkorpi 2017	86	18	91	302	0.49 [0.41, 0.56]	0.94 [0.91, 0.97]
Tyler 2019	25	0	32	117	0.44 [0.31, 0.58]	1.00 [0.97, 1.00]

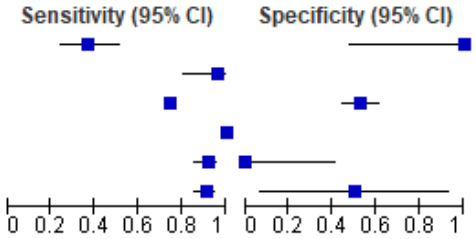


Total n: 12 studies, 2,454 patients
Median (range) sensitivity: 0.68 (0.44-0.88); Median (range) specificity: 0.96 (0.25-1.00)

Supplementary Figure 16. Initial US for adults with suspected appendicitis *undergoing surgery*

a) definitive US results only

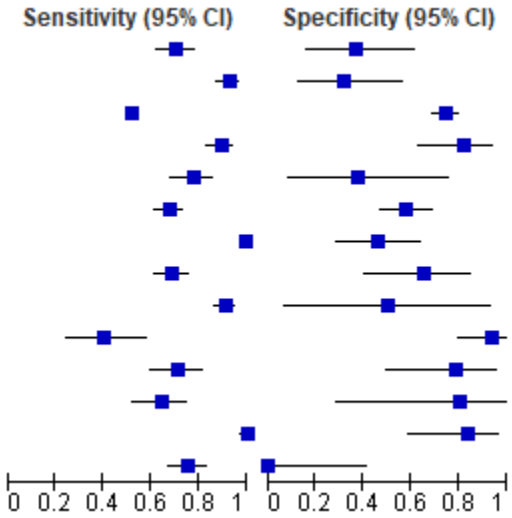
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alshebromi 2019	20	0	34	5	0.37 [0.24, 0.51]	1.00 [0.48, 1.00]
Ashcroft 2021	25	0	1	0	0.96 [0.80, 1.00]	Not estimable
Atwood 2021	1664	71	577	80	0.74 [0.72, 0.76]	0.53 [0.45, 0.61]
Kouame 2011	448	0	0	0	1.00 [0.99, 1.00]	Not estimable
Reich 2011	121	7	11	0	0.92 [0.86, 0.96]	0.00 [0.00, 0.41]
Selassie 2021	156	2	16	2	0.91 [0.85, 0.95]	0.50 [0.07, 0.93]



Total n: 6 studies, 3,240 patients
Median (range) sensitivity: 0.92 (0.37-1.00); Median (range) specificity: 0.50 (0.00-1.00)

b) all US results, including equivocal/indeterminate*

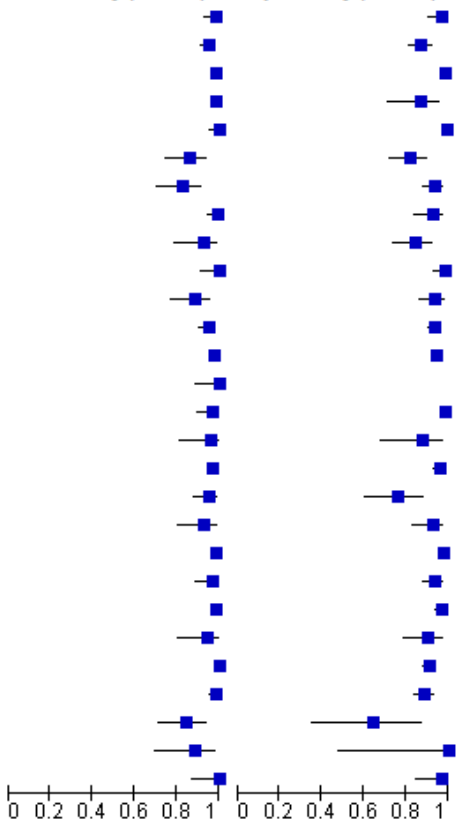
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alnuaymah 2022	91	12	38	7	0.71 [0.62, 0.78]	0.37 [0.16, 0.62]
Aras 2016	132	13	10	6	0.93 [0.87, 0.97]	0.32 [0.13, 0.57]
Atwood 2021	1664	71	1536	206	0.52 [0.50, 0.54]	0.74 [0.69, 0.79]
Fatima 2021	127	5	15	23	0.89 [0.83, 0.94]	0.82 [0.63, 0.94]
Ferrarese 2016	75	5	22	3	0.77 [0.68, 0.85]	0.38 [0.09, 0.76]
Koc 2020	177	37	86	51	0.67 [0.61, 0.73]	0.58 [0.47, 0.68]
Kouame 2011	581	19	4	16	0.99 [0.98, 1.00]	0.46 [0.29, 0.63]
Reich 2011	121	7	56	13	0.68 [0.61, 0.75]	0.65 [0.41, 0.85]
Selassie 2021	164	2	16	2	0.91 [0.86, 0.95]	0.50 [0.07, 0.93]
Serinsoz 2021	15	2	22	31	0.41 [0.25, 0.58]	0.94 [0.80, 0.99]
Sezer 2012	55	3	22	11	0.71 [0.60, 0.81]	0.79 [0.49, 0.95]
Singh 2022	48	1	27	4	0.64 [0.52, 0.75]	0.80 [0.28, 0.99]
Sukhani 2017	132	3	0	15	1.00 [0.97, 1.00]	0.83 [0.59, 0.96]
Tatli 2016	93	7	30	0	0.76 [0.67, 0.83]	0.00 [0.00, 0.41]



Total n: 14 studies, 5,934 patients
Median (range) sensitivity: 0.74 (0.41-1.00); Median (range) specificity: 0.62 (0.00-0.94)

Supplementary Figure 3. Initial CT for adults with suspected appendicitis

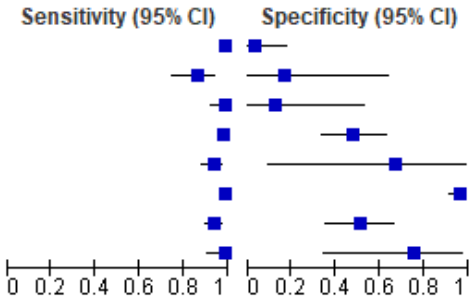
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Apisarnthanarak 2015	72	3	1	82	0.99 [0.93, 1.00]	0.96 [0.90, 0.99]
Atema 2015	238	22	13	149	0.95 [0.91, 0.97]	0.87 [0.81, 0.92]
Chu 2014	388	18	5	1313	0.99 [0.97, 1.00]	0.99 [0.98, 0.99]
Crocker 2020	187	5	2	32	0.99 [0.96, 1.00]	0.86 [0.71, 0.95]
Dowhanik 2021	78	1	0	263	1.00 [0.95, 1.00]	1.00 [0.98, 1.00]
Eurboonyanun 2021	49	15	8	68	0.86 [0.74, 0.94]	0.82 [0.72, 0.90]
Hekimoglu 2011	48	9	10	133	0.83 [0.71, 0.91]	0.94 [0.88, 0.97]
Jo 2010	108	6	1	72	0.99 [0.95, 1.00]	0.92 [0.84, 0.97]
Karabulut 2014	36	10	3	55	0.92 [0.79, 0.98]	0.85 [0.74, 0.92]
Kepner 2012	41	1	0	72	1.00 [0.91, 1.00]	0.99 [0.93, 1.00]
Kim 2011	47	5	6	74	0.89 [0.77, 0.96]	0.94 [0.86, 0.98]
Kim 2012	171	16	9	244	0.95 [0.91, 0.98]	0.94 [0.90, 0.96]
Ko 2020	529	49	11	792	0.98 [0.96, 0.99]	0.94 [0.92, 0.96]
Kolb 2019	30	0	0	0	1.00 [0.88, 1.00]	Not estimable
Latifi 2011	67	2	2	175	0.97 [0.90, 1.00]	0.99 [0.96, 1.00]
Leung 2017	27	3	1	21	0.96 [0.82, 1.00]	0.88 [0.68, 0.97]
Lietzen 2018	700	14	24	327	0.97 [0.95, 0.98]	0.96 [0.93, 0.98]
Ozturk 2014	79	10	4	32	0.95 [0.88, 0.99]	0.76 [0.61, 0.88]
Park 2016	39	5	3	60	0.93 [0.81, 0.99]	0.92 [0.83, 0.97]
Pickhardt 2011	665	43	10	2153	0.99 [0.97, 0.99]	0.98 [0.97, 0.99]
Repplinger 2018	62	9	2	125	0.97 [0.89, 1.00]	0.93 [0.88, 0.97]
Sammalkorpi 2017	253	7	4	225	0.98 [0.96, 1.00]	0.97 [0.94, 0.99]
Scott 2015	32	5	2	47	0.94 [0.80, 0.99]	0.90 [0.79, 0.97]
Sim 2013	320	37	0	381	1.00 [0.99, 1.00]	0.91 [0.88, 0.94]
Tan 2015	153	22	2	173	0.99 [0.95, 1.00]	0.89 [0.83, 0.93]
Uzunosmanoglu 2017	39	5	7	9	0.85 [0.71, 0.94]	0.64 [0.35, 0.87]
Wagner 2020	23	0	3	5	0.88 [0.70, 0.98]	1.00 [0.48, 1.00]
Wang 2012	26	1	0	32	1.00 [0.87, 1.00]	0.97 [0.84, 1.00]



Total n: 28 studies, 12,077 patients
Median (range) sensitivity: 0.97 (0.83-1.00); Median (range) specificity: 0.94 (0.64-1.00)

Supplementary Figure 17. Initial CT for adults with suspected appendicitis *undergoing surgery*

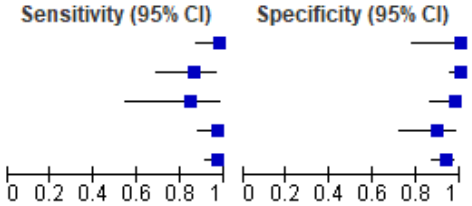
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alnuaymah 2022	213	28	3	1	0.99 [0.96, 1.00]	0.03 [0.00, 0.18]
Alshebromi 2019	49	5	8	1	0.86 [0.74, 0.94]	0.17 [0.00, 0.64]
Ashcroft 2021	67	7	1	1	0.99 [0.92, 1.00]	0.13 [0.00, 0.53]
Coursey 2011	413	26	10	24	0.98 [0.96, 0.99]	0.48 [0.34, 0.63]
Donlon 2021	140	1	10	2	0.93 [0.88, 0.97]	0.67 [0.09, 0.99]
Liu 2015	185	4	2	106	0.99 [0.96, 1.00]	0.96 [0.91, 0.99]
Rait 2020	184	22	12	23	0.94 [0.90, 0.97]	0.51 [0.36, 0.66]
Teo 2014	55	2	1	6	0.98 [0.90, 1.00]	0.75 [0.35, 0.97]



Total n: 8 studies, 1,612 patients
Median (range) sensitivity: 0.98 (0.86-0.99); Median (range) specificity: 0.50 (0.03-0.96)

Supplementary Figure 4. Initial MRI for adults with suspected appendicitis

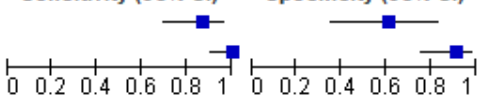
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Avcu 2013	39	0	1	15	0.97 [0.87, 1.00]	1.00 [0.78, 1.00]
des Plantes 2016	25	0	4	83	0.86 [0.68, 0.96]	1.00 [0.96, 1.00]
Heverhagen 2012	11	1	2	38	0.85 [0.55, 0.98]	0.97 [0.87, 1.00]
Inci 2011	55	3	2	25	0.96 [0.88, 1.00]	0.89 [0.72, 0.98]
Leeuwenburgh 2014	113	7	4	99	0.97 [0.91, 0.99]	0.93 [0.87, 0.97]



Total n: 5 studies, 527 patients
Median (range) sensitivity: 0.96 (0.85-0.97); Median (range) specificity: 0.97 (0.89-1.00)

Supplementary Figure 18. Initial MRI for adults with suspected appendicitis *undergoing surgery*

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chabanova 2011	26	7	4	11	0.87 [0.69, 0.96]	0.61 [0.36, 0.83]
Serinsoz 2021	37	3	0	30	1.00 [0.91, 1.00]	0.91 [0.76, 0.98]



Total n: 2 studies, 118 patients
Median (range) sensitivity: 0.94 (0.87-1.00); Median (range) specificity: 0.76 (0.61-0.91)

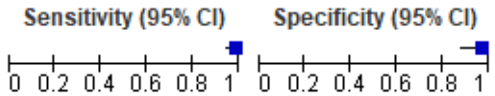
Summary: When assessing only definitive US results, US exhibits acceptable sensitivity and specificity. When including equivocal results, the sensitivity of US is lowered. Both CT and MRI yield acceptable sensitivities and specificities, in general.

Subsequent Imaging in Adults

Supplementary Figure 5. Subsequent US for adults with suspected appendicitis

a) definitive US results only

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gungor 2017	130	2	2	56	0.98 [0.95, 1.00]	0.97 [0.88, 1.00]



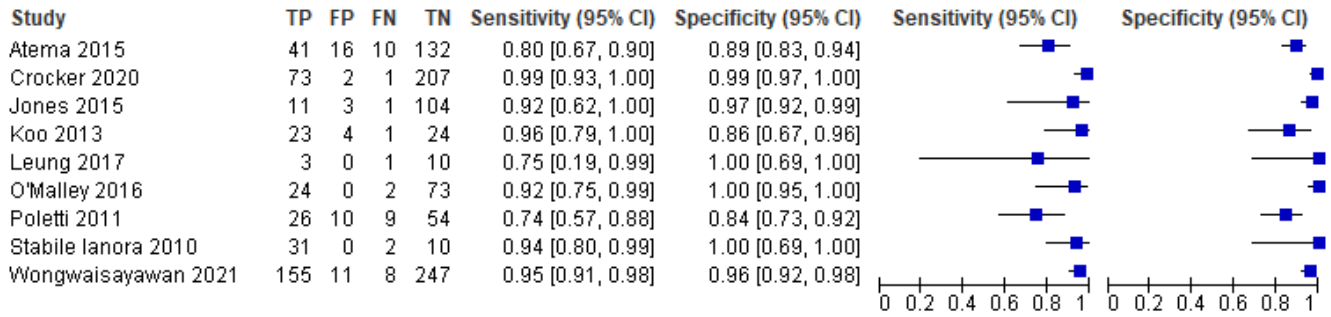
Total n: 1 study, 190 patients

b) all US results, including equivocal/indeterminate*

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gungor 2017	130	2	39	93	0.77 [0.70, 0.83]	0.98 [0.93, 1.00]
Sohail 2019	85	1	9	5	0.90 [0.83, 0.96]	0.83 [0.36, 1.00]

Total n: 2 studies, 364 patients
Median (range) sensitivity: 0.84 (0.77-0.90); Median (range) specificity: 0.91 (0.83-0.98)

Supplementary Figure 6. Subsequent CT for adults with suspected appendicitis



Total n: 9 studies, 1,329 patients
Median (range) sensitivity: 0.97 (0.80-1.00); Median (range) specificity: 0.97 (0.84-1.00)

Summary: There was only one study on subsequent US in adults and no studies on subsequent MRI. Both CT yields acceptable sensitivities and specificities, in general.

CHILDREN

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?

Supplementary Table 2. Characteristics of included studies for acute appendicitis in children

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
US in children						
Ahmad 2020	Canada Not stated	Retrospective	206 children Mean age 7 years, 5 months 73 diagnosed with appendicitis, pre-test probability: 35%	Children presenting to the ED with acute abdominal pain who underwent US for suspected appendicitis	Intraoperative confirmation or histology (unclear), or resolution with antibiotics/drainage, or final clinical outcome	Initial US, then repeat US if inconclusive, then CT it both inconclusive
Ashjaei 2022	Iran Not stated	Prospective	108 children Mean age 8.02 years 82 diagnosed with appendicitis; pre-test probability: 76%	Children 1-15 years presenting to the ED with suspected acute appendicitis	Surgical and clinical findings	Initial US
Austin-Page 2020	USA 2009-2014	Retrospective	1,058 children Mean age 10.4 years 383 diagnosed with appendicitis, pre-test probability: 36%	Patient encounters for children 1-18 years who underwent US as the initial imaging modality for appendicitis	CT reports, pathology reports, operative notes, and the final diagnosis	Initial US
Aydin 2018	Turkey 2014-2016	Prospective	288 children, 212 of whom underwent US Mean age 11.1 years 119 diagnosed with appendicitis, pre-test probability: 56%	Children 4-17 years with suspected appendicitis and PAS score of 5-7 (medium-risk group)	Histopathology or clinical follow-up (via hospital records or phone call)	Initial US
Binkovitz 2015	USA 2010-2014	Retrospective	790 children Mean age 10.4 years (range 0-17) 146 diagnosed with appendicitis, pre-test probability: 18%	Patients <18 years with abdominal US for suspected appendicitis	Histopathology or clinical outcome	Initial US
Cundy 2016	Australia 2009-2014	Retrospective	3,799 children Mean age 11.5 years 1,049 diagnosed with appendicitis, pre-test-probability: 28%	Patients investigated with ultrasound for suspected appendicitis	Operative findings and histopathology or clinical follow-up	Initial US
Dibble 2018	USA 2011-2012	Retrospective	1,982 children Mean age 11.2 years (range 1.2-18) 407 diagnosed with appendicitis, pre-test probability: 21%	Patients ≤18 years who underwent diagnostic imaging for suspected appendicitis	Surgical notes, pathology reports, and clinical information	Initial US
Gungor 2017	Turkey 2014-2015	Prospective	264 patients Mean age 30 years	Patients >18 years who presented to the ED with abdominal pain and underwent	Surgery, pathologic evaluation of appendectomy specimens, or clinical follow-up	Subsequent radiology-performed US (after initial POCUS)

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			169 diagnosed with appendicitis; pre-test probability: 64%	diagnostic evaluation for acute appendicitis		
Harel 2022	USA 2016-2017	Retrospective	543 children Age not described 75 diagnosed with appendicitis, pre-test probability: 14%	Children 0-18 years presenting to a pediatric ED with clinical suspicion for appendicitis who underwent US	Chart review, including discharge diagnosis, and return visits	Initial US
Imler 2017	USA 2014	RCT	82 patients (45 had US first, 37 had rapid MRI first) Mean age US cohort 12.3 years, mean age rapid MRI cohort 13.5 years Overall cohort: 0-5 years: n = 7, 6-10 years: n = 26, 11-30 years: n = 49 20 diagnosed with appendicitis; pre-test probability: 24%	Patients 2-30 years presenting to the ED with suspected appendicitis	EMR data (including return visits) and telephone follow-up at least 7 days after ED visit	Initial US or rapid MRI depending on the day of the week (unit of randomization)
Kearl 2016	USA 2010-2013	Retrospective	521 children Mean age 14.5 years 144 diagnosed with appendicitis, pre-test probability: 28%	Pediatric ED patients 3-21 years who underwent US for the evaluation of appendicitis and had follow-up available	Final diagnosis	Initial US
Kelly 2019	Ireland 2011-2016	Retrospective	189 children Mean age 11 years (range 2-16) 102 diagnosed with appendicitis, pre-test probability: 54%	Patients ≤16 years who had a preoperative ultrasound and proceeded to appendicectomy	Histopathology	Initial US
Limchareon 2014	Thailand 2009-2012	Retrospective	428 children Mean age 9 years (range 1-16) 49 diagnosed with appendicitis, pre-test probability: 11%	Children who underwent US for suspected appendicitis	Surgical pathology or treatments for other abdominal conditions (clinical follow-up)	Initial US
Lofvenberg 2016	Sweden 2012-2015	Retrospective	438 children Mean 8.5 years 125 diagnosed with appendicitis, pre-test probability: 29%	Patients <15 years who underwent abdominal US for suspected appendicitis	Histopathology or intraoperative notes, or clinical follow-up	Initial US
Mangona 2017	USA 2013-2014	Retrospective	2,935 patients Ages not described 628 diagnosed with appendicitis, pre-test probability: 21%	Patients <19 years who underwent a limited RLQ US examination for suspected appendicitis	Operative diagnosis (not pathology) or clinical follow-up	Initial US
Mirza 2018	Pakistan	Retrospective	1116 children	Patients 2-16 years with acute abdominal pain suspicious for	Histopathology or CT confirmation	Initial US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
	2003-2016		Mean age 9.4 years (range 2-16) 337 diagnosed with appendicitis, pre-test probability: 30%	acute appendicitis who underwent RLQ US		
Nandan 2022	India 2013-2017	Prospective	205 children Mean age 9.3 years (range 3-12) 159 diagnosed with appendicitis, pre-test probability: 78%	Children 3-12 years with suspected appendicitis (right iliac fossa pain, periumbilical pain) and duration of pain <5 days	Histopathology	Initial US
Pedram 2019	Iran 2017	Retrospective	230 children Mean age 11.4 years (range 5-15) 150 diagnosed with appendicitis, pre-test probability: 65%	Children 5-15 years with a clinical diagnosis of acute appendicitis	Pathology	Initial US
Salim 2022	Indonesia 2018-2019	Prospective	21 patients Mean age 6.76 years (range 1-15) 10 diagnosed with appendicitis, pre-test probability: 48%	Pediatric surgery patients who visited the ED with symptoms of appendicitis	"Data available after surgery"	Initial US
Salman 2022	USA 2020	Retrospective	1,693 patients (1,682 had US performed; 397 were equivocal) Mean age of entire cohort not stated; range 9 months-17.9 years 838 diagnosed with appendicitis; pre-test probability: 50%	Children <18 years old imaged for suspected appendicitis who also had a SARS-CoV-2 test	Pathology or a lack of follow-up operative or pathological report in the EMR	Initial US
Sayed 2017	Egypt 2015-2016	Retrospective	38 children Mean age 11 years 18 diagnosed with appendicitis, pre-test probability: 48%	Children 4-18 years who were admitted with clinically suspected acute appendicitis and had US as the first imaging modality	Final diagnosis as determined via operative, histopathological analysis or follow-up (1 week)	Initial US; other patients in the total study population (n = 140) received CT as the initial imaging study
Scammell 2011	UK 2004-2006	Retrospective	311 children Ages not described 84 diagnosed with appendicitis, pre-test probability: 27%	Infants and children up to 16 years who received an abdominal US for abdominal pain and equivocal cases of appendicitis (i.e., didn't proceed directly to surgery)	Pathology	Initial US
Schuh 2011	Canada 2007-2008	Prospective	39 patients who underwent a second US Ages not described for smaller cohort who underwent a second US 12 diagnosed with appendicitis, pre-test probability: 31%	Children 4-17 years who underwent US for suspected appendicitis ordered by the ED physician	Histopathology or clinical follow-up at 1 month	Repeat US or subsequent CT or both with uncertain diagnosis of appendicitis after an initial screening US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
Schuh 2015	Canada 2012-2013	Prospective	294 children, 40 of whom went on to interval US Mean age 10.4 years 17 diagnosed with appendicitis, pre-test probability: 43%	Children 4-17 years with abdominal pain and RLQ tenderness (initial PAS ≥2) who required imaging for suspected appendicitis	Histopathology or clinical follow-up at 1 month	Repeat US and surgical consultation with persistent clinical concern after initial equivocal US
Tantisook 2021	USA 2010-2014	Retrospective	1,059 children Median age 11.3 years 382 diagnosed with appendicitis, pre-test probability: 36%	Patients >2 years and <18 years who presented to the ED with suspected appendicitis and had an US performed	Pathology after post-operative diagnosis of appendicitis or follow-up (14 days)	Initial US
Thieme 2014	Netherlands 2009	Prospective	104 children Age range 4-18 years 58 diagnosed with appendicitis, pre-test probability: 56%	Children 4-18 years with clinically suspected acute appendicitis	Expert panel review (including labs, US and MRI findings, histopathology, etc.), including 3 months' follow-up	Initial US
Toprak 2014	Turkey 2011	Retrospective	122 children Mean age 11 years (range 2-15) 58 diagnosed with appendicitis, pre-test probability: 48%	Pediatric patients with suspected appendicitis who underwent US and had available follow-up (3 months)	Surgical/Pathology reports and clinical follow-up (3 months)	Initial US
van Atta 2015	USA 2009-2012	Retrospective	512 children Ages not described 167 diagnosed with appendicitis, pre-test probability: 33%	Children presenting with RLQ abdominal pain but an H&P equivocal for appendicitis (those with compelling clinical evidence of appendicitis went straight to surgery)	Concordant surgical and pathology reports or clinical follow-up (record review within 2 weeks of the initial encounter)	Initial US
CT in children						
Akhtar 2011	Pakistan 2007-2008	Retrospective	71 children Mean age 11.8 years (range 4-15) 23 diagnosed with appendicitis; pre-test probability: 32%	Children with acute abdomen and clinical findings suggestive of equivocal acute appendicitis	Histopathology or follow-up	Initial CT (focused CT)
Didier 2015	USA 2008-2010 (group A)	Retrospective	192 scans in 192 children Mean age 9.3 years 51/192 diagnosed with appendicitis; pre-test probability: 27%	Patients <18 years who underwent non-angiographic contrast-enhanced abdominopelvic CT	Surgical pathology and/or ≥2 months clinical follow-up	Initial CT
Dillman 2016	USA 2012-2014	Retrospective	161 children, 58 of whom had CT Mean age 11.5 years (range 3-18) 11 diagnosed with appendicitis, pre-test probability: 19%	Pediatric patients ≤18 years with suspected appendicitis who underwent CT or MRI after an equivocal US	Surgical reports, pathology, and 30-day follow-up medical records	Subsequent CT after equivocal US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
James 2022	USA 2012-2014	Retrospective	499 patients (125 had CT, 117 had MRI) Mean age 11.2 years 60 diagnosed with appendicitis; pre-test probability: 12%	Patients 5-18 years who presented to a pediatric ED with suspected appendicitis and ≤5 days of symptoms; all patients had initial US	Pathology, operative findings, abdominal abscess treated non-operatively, or discharge without representation within 2 weeks	Subsequent CT or MRI (clinician discretion) following US
Krishnamoorthi 2011	USA 2003-2008	Retrospective	631 children (333 US only, 298 CT following equivocal US) Mean age 10.4 years (range 2 months to 18 years) 63/298 diagnosed with appendicitis; pre-test probability: 21%	Children in a pediatric ED suspected of having appendicitis who followed a staged pathway (CT following equivocal US only)	Pathology or chart review	Subsequent CT (with IV contrast; some also had oral contrast), following equivocal US
Sayed 2017	Egypt 2015-2016	Retrospective	140 children; CT initial imaging in 102 patients Mean age 11 years 45 (of 140) diagnosed with appendicitis; pre-test probability: 32%	Children 4-18 years admitted with clinically suspected appendicitis	Histopathology or follow-up (1 week)	Initial CT (low-dose CT)
Schuh 2011	Canada 2007-2008	Prospective	263 children, 30 of whom underwent subsequent CT Range 4-17 years 7 of 30 diagnosed with appendicitis; pre-test probability: 23%	Children 4-17 years of age undergoing US for suspected appendicitis	Pathology and clinical follow-up	Subsequent CT after equivocal US
Srinivasan 2015	USA 2006-2008	Retrospective	218 children, 211 of whom had CT after US Mean age 11.3 years (range 1-20 years) 42 of 211 diagnosed with appendicitis; pre-test probability: 20%	Children with suspected appendicitis	Pathology and chart review	Subsequent CT after US (all patients had both)
van Atta 2015	USA 2009-2012	Prospective	512 children, 187 of whom underwent CT Range 1-18 years 31 of 187 diagnosed with appendicitis; pre-test probability: 17%	Children who presented with RLQ abdominal pain but with a history and physical exam equivocal for appendicitis	Pathology and chart review	Subsequent CT after equivocal US
MRI in children						
Aspelund 2014	USA 2008-2012 (Group A 2008-2010, Group B 2010-2012)	Retrospective	662 children (224 had CT initially in Group A; 142 children had MRI following equivocal US in Group B) Group B mean age 12.3 years	Children <18 years who presented to the ED with suspected appendicitis	Histology or follow-up	Subsequent MRI following equivocal US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			61/142 diagnosed with appendicitis; pre-test probability: 43%			
Bayraktutan 2014	Turkey Unclear	Prospective	45 children Mean age 7 years (range 0-14) 36 diagnosed with appendicitis; pre-test probability: 80%	Children with a clinical diagnosis of acute appendicitis, with suspected appendicitis, or with an appendix not visualized on US	Histology or follow-up (minimum 2 weeks)	Initial and subsequent MRI (31 patients had MRI subsequent to US)
Corkum 2018	USA 2015-2016	Retrospective	135 children Mean age 11.2 years 17/125 diagnosed with appendicitis; pre-test probability: 14%	Children aged 5-18 who presented to the ER with suspected appendicitis and underwent US and MRI	Histology or follow-up	Subsequent MRI following equivocal US
Covelli 2019	USA 2012-2016	Retrospective	528 children Mean age 9.9 years (range 1-17) 55 diagnosed with appendicitis, pre-test probability: 10%	Pediatric patients who underwent dedicated MRI for clinically suspected appendicitis after having undergone US evaluation that yielded equivocal findings and whose exams were interpreted by non-pediatric-trained radiologists	Operative or pathology report	Subsequent MRI following equivocal US
Davis 2022	USA 2017-2019	Retrospective	209 children, 102 of whom had 2nd-line MRI (75 of which weren't equivocal) Median age 10 years (range 2-18 years) 18/75 diagnosed with appendicitis; pre-test probability: 24%	Pediatric patients who had a POCUS ordered in the ED for evaluation of pediatric appendicitis	Pathology, clinical follow-up, or consensus of the team for equivocal pathology	Subsequent MRI after POCUS
Dibble 2018	USA 2011-2012	Retrospective	1982 patients, 77 of whom had a 2nd-line MRI Mean age 11.2 years (range 1-18 years) 407 diagnosed with appendicitis, pre-test probability: 20%	Pediatric patients who underwent US and then MR for equivocal US	Pathology or clinical follow-up (within 4 weeks of initial presentation and imaging)	Subsequent MRI following equivocal US
Didier 2017	USA 2013-2015	Some patients enrolled prospectively, some retrospectively	97 children (98 scans) Mean age 11.0 years (range 4.2-17.9) 33 diagnosed with appendicitis; pre-test probability: 34%	Patients aged 4 to 18 with suspected appendicitis and an Alvarado score ≥4	Histology or follow-up	Initial rapid MRI (without contrast)
Dillman 2016	USA 2012-2014	Retrospective	161 children, 103 of whom had MRI Mean age 11.5 years (range 3-18) 18 diagnosed with appendicitis, pre-test probability: 17%	Pediatric patients ≤18 years with suspected appendicitis who underwent CT or MRI after an equivocal US	Surgical reports, pathology, and 30-day follow-up medical records	Subsequent MRI after equivocal US

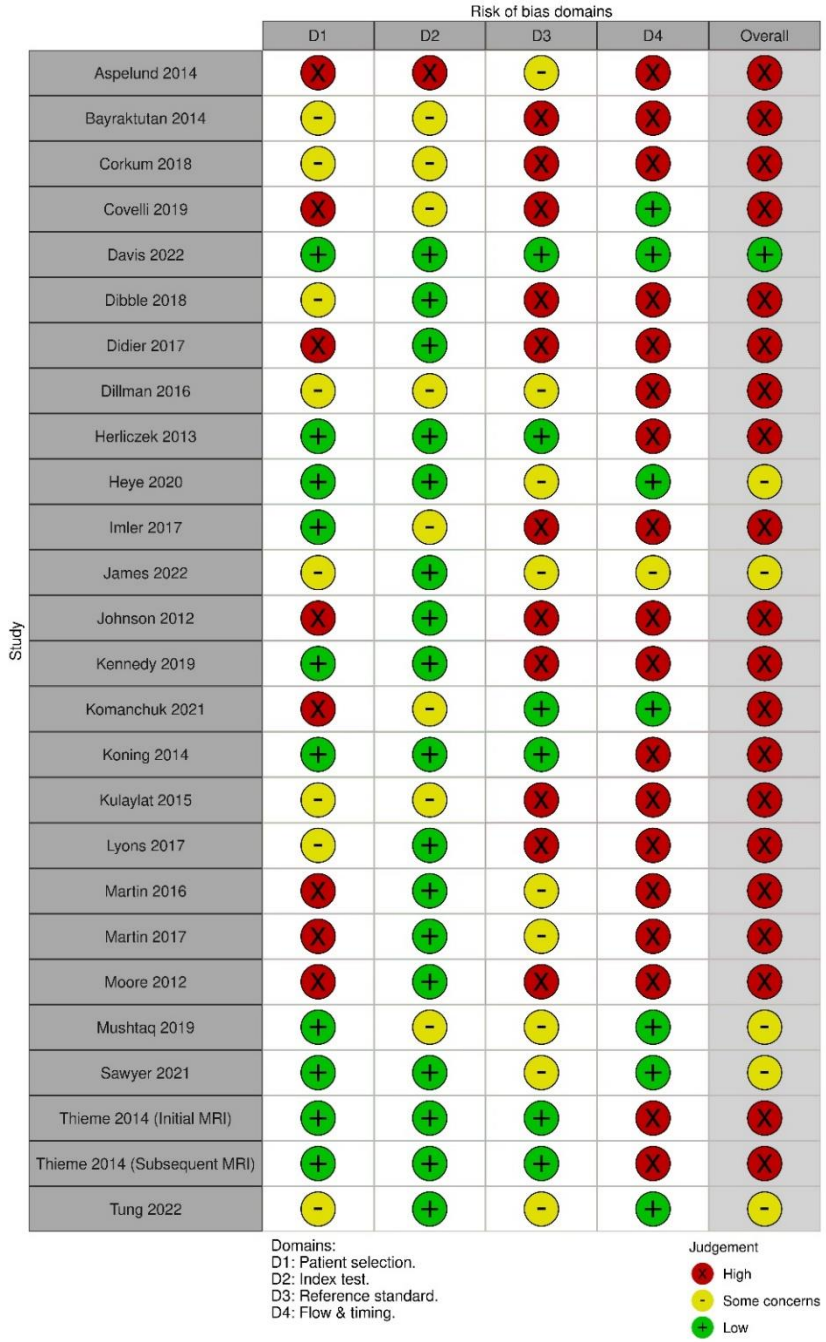
Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
Herliczek 2013	USA 2009-2012	Retrospective	60 children Mean age 13.4 years (range 7-17) 10 diagnosed with appendicitis, pre-test probability: 17%	Pediatric patients who had MRI	Pathology and chart review	Subsequent MRI
Heye 2020	USA 2014-2018	Retrospective	350 children Median age 12 years (range 3-18) 61 diagnosed with appendicitis, pre-test probability: 17%	Pediatric patients with MRI done as the second-line imaging study after equivocal first-line imaging	Pathology or clinical follow-up (within 30 days)	Subsequent MRI after equivocal initial imaging
Imler 2017	USA 2014	RCT	82 patients (45 had US first, 37 had rapid MRI first) Mean age US cohort 12.3 years, mean age rapid MRI cohort 13.5 years Overall cohort: 0-5 years: n = 7, 6-10 years: n = 26, 11-30 years: n = 49 20 diagnosed with appendicitis; pre-test probability: 24%	Patients 2-30 years presenting to the ED with suspected appendicitis	EMR data (including return visits) and telephone follow-up at least 7 days after ED visit	Initial US or rapid MRI depending on the day of the week (unit of randomization)
James 2022	USA 2012-2014	Retrospective	499 patients (125 had CT, 117 had MRI) Mean age 11.2 years 60 diagnosed with appendicitis; pre-test probability: 12%	Patients 5-18 years who presented to a pediatric ED with suspected appendicitis and ≤5 days of symptoms; all patients had initial US	Pathology, operative findings, abdominal abscess treated non-operatively, or discharge without representation within 2 weeks	Subsequent CT or MRI (clinician discretion) following US
Johnson 2012	USA Unclear (a 23-month period)	Prospective	42 children Mean age 11.5 years (range 4-17) 12 diagnosed with appendicitis; pre-test probability: 29%	Pediatric patients aged 4 to 17 years with suspected appendicitis	Histology or follow-up	Initial ultrafast MRI
Kennedy 2019	USA 2014-2017	Retrospective	612 children Mean age 11.7 years 130 diagnosed with appendicitis; pre-test probability: 21%	Patients ≤18 years with suspected appendicitis	Histology or follow-up	Initial MRI (some had a preceding US)
Komanchuk 2021	Canada 2013-2014	Prospective	101 children Mean age 11.9 years 37 diagnosed with appendicitis, pre-test probability: 37%	Children 5-17 years presenting to the ED with suspected appendicitis (defined as having a clinically indicated US of the appendix or a surgical consult for appendicitis)	Pathology or clinical follow-up (7 days)	Subsequent MRI
Koning 2014	USA 2012-2013	Retrospective	364 patients Mean age 11.3 years	Pediatric patients with suspected appendicitis	Histology or follow-up	Initial MRI (contrast-enhanced MRI)

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			132 diagnosed with appendicitis; pre-test probability: 36%			
Kulaylat 2015	USA 2011-2013	Retrospective	510 patients Mean age 11.3 years 126 diagnosed with appendicitis; pre-test probability: 25%	Pediatric patients (<18 years) with suspected appendicitis	Histology or follow-up	Initial MRI (non-contrast MRI, no sedation)
Lyons 2017	USA 2013-2015	Retrospective	112 MRI scans (89 with IV contrast, 23 without) Mean age 12.7 years 23/89 diagnosed with appendicitis; pre-test probability: 26%	Patients ≤21 years who had undergone an MRI for suspected appendicitis following nondiagnostic US	Pathology and nonsurgical clinical outcome	Subsequent MRI (some with and some without contrast) following nondiagnostic US
Martin 2017	USA 2015	Retrospective	30 patients who underwent MR following equivocal US Mean age 12.2 years 10/30 diagnosed with appendicitis; pre-test probability: 33%	Children 5-18 years with suspected appendicitis land equivocal US who underwent MR or CT as secondary imaging in a pediatric ED	Pathology or no return visit within 7 days	Subsequent MRI (without contrast)
Moore 2012	USA 2009-2011	Retrospective	208 patients Mean age 11.2 years 41 diagnosed with appendicitis; pre-test probability: 20%	Pediatric patients (3 to 17 years) with suspected appendicitis	histology or follow-up	Initial MRI (non-contrast MRI, no sedation)
Mushtaq 2019	USA 2013-2016	Retrospective	402 patients Median age 13 years 97 diagnosed with appendicitis; pre-test probability: 24%	Patients ≤18 years presenting with acute abdominal pain who underwent MRI as the initial imaging study	Surgical pathology and follow-up	Initial MRI (sedation permitted)
Sawyer 2021	USA 2013-2016	Retrospective	377 MRI exams Median age 13 years (range 9-15) 91 diagnosed with appendicitis; pre-test probability: 24%	Patients 21 years or younger who presented with acute abdominal pain and underwent an unenhanced MRI	EMR, including histopathology or follow-up clinical evaluations	Initial MRI
Thieme 2014	The Netherlands 2009	Prospective	55 children Age range 4-18 years 14 diagnosed with appendicitis, pre-test probability: 25%	Children with suspected appendicitis	Pathology and clinical follow-up	Initial and subsequent MRI
Tung 2022	USA 2014-2017	Retrospective	204 patients Median age 13 years, 11 months (range 4-18)	ED patients ≥4 and <20 years old with acute abdominal or pelvic pain who had MRI for suspected appendicitis;	Surgical pathology or symptom resolution after antibiotics, or	Subsequent unenhanced MRI following initial US

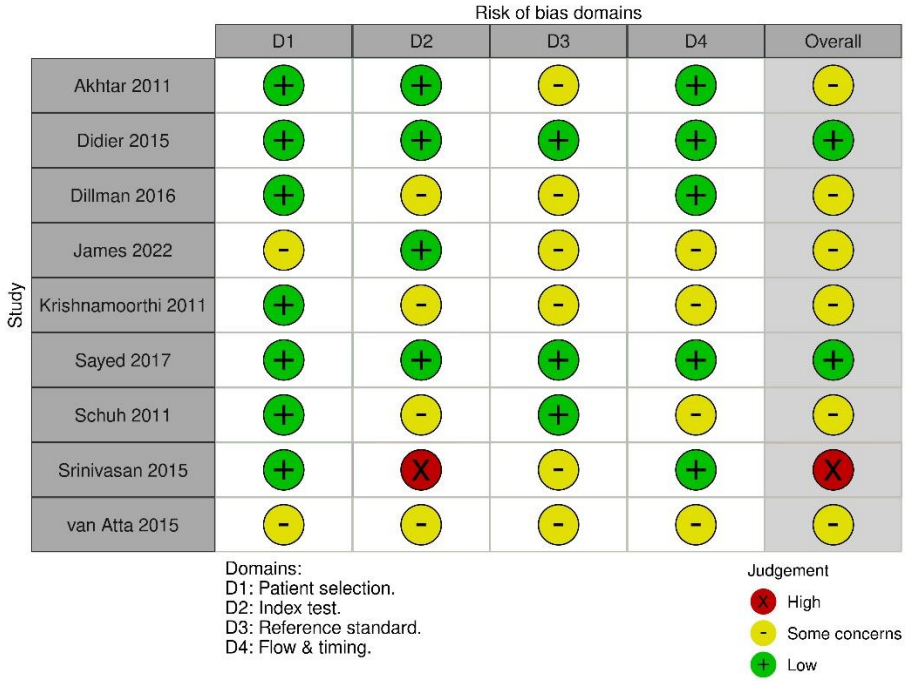
Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			102 diagnosed with appendicitis; pre-test probability: 50%	patients were excluded if IV contrast was used or the appendix wasn't visualized by MRI		

Supplementary Table 5a. Risk of bias for included studies on US in children

Supplementary Table 5b. Risk of bias for included studies on MRI in children



Supplementary Table 5c. Risk of bias for included studies on CT in children



Supplementary Table 11. GRADE Evidence Profile: Should US (definitive results only) be used to diagnose acute appendicitis in children?

US vs. reference standard; definitive results only (Ahmad 2020, Austin-Page 2020, Binkovitz 2015, Cundy 2016, Dibble 2018, Imler 2017, Kearl 2016, Limchareon 2014, Lofvenberg 2016, Mangona 2017, Salman 2022, Scammell 2011, Tantisook 2021, Toprak 2014, van Atta 2015)	
Sensitivity	0.84 to 1.00
Specificity	0.71 to 0.98

Prevalence	30% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of30%	
True positives (patients with acute appendicitis)	15 studies (Ahmad 2020, Austin-Page 2020, Binkovitz 2015, Cundy 2016, Dibble 2018, Imler 2017, Kearl 2016, Limchareon 2014, Lofvenberg 2016, Mangona 2017, Salman 2022, Scammell 2011, Tantisook 2021, Toprak 2014, van Atta 2015) 11825 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	252 to 300	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 48	
True negatives (patients without acute appendicitis)	15 studies (Ahmad 2020, Austin-Page 2020, Binkovitz 2015, Cundy 2016, Dibble 2018, Imler 2017, Kearl 2016, Limchareon 2014, Lofvenberg 2016, Mangona 2017, Salman 2022, Scammell 2011, Tantisook 2021, Toprak 2014, van Atta 2015) 11825 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	497 to 686	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								14 to 203	

Explanations

a. Per QUADAS-2 assessment

b. Indirect comparisons

Supplementary Table 12. GRADE Evidence Profile: Should US (all results, including equivocal/indeterminate) be used to diagnose acute appendicitis in children?

US vs. reference standard; all results, including equivocal/indeterminate (Ahmad 2020, Ashjaei 2022, Austin-Page 2020, Aydin 2018, Binkovitz 2015, Cundy 2016, Harel 2022, Imler 2017, Kearl 2016, Limchareon 2014, Lofvenberg 2016, Mangona 2017, Mirza 2018, Nandan 2022, Salim 2022, Salman 2022, Sayed 2017, Scammell 2011, Tantisook 2021, Thieme 2014, Toprak 2014, van Atta 2015)	
Sensitivity	0.56 to 1.00
Specificity	0.17 to 0.99

Prevalence	38% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of38%	
True positives (patients with acute appendicitis)	22 studies (Ahmad 2020, Ashjaei 2022, Austin-Page 2020, Aydin 2018, Binkovitz 2015, Cundy 2016, Harel 2022, Imler 2017, Kearl 2016, Limchareon 2014, Lofvenberg 2016, Mangona 2017, Mirza 2018, Nandan 2022, Salim 2022, Salman 2022, Sayed 2017, Scammell 2011, Tantisook 2021, Thieme 2014, Toprak 2014, van Atta 2015) 16252 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [c]	not serious	serious [b]	none	213 to 380	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 167	
True negatives (patients without acute appendicitis)	22 studies (Ahmad 2020, Ashjaei 2022, Austin-Page 2020, Aydin 2018, Binkovitz 2015, Cundy 2016, Harel 2022, Imler 2017, Kearl 2016, Limchareon 2014, Lofvenberg 2016, Mangona 2017, Mirza 2018, Nandan 2022, Salim 2022, Salman 2022, Sayed 2017, Scammell 2011, Tantisook 2021, Thieme 2014, Toprak 2014, van Atta 2015) 16252 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [c]	not serious	serious [b]	none	105 to 614	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								6 to 515	

Explanations

a. Per QUADAS-2 assessment
b. Wide CIs
c. Indirect comparisons

Supplementary Table 13. GRADE Evidence Profile: Should CT be used to diagnose acute appendicitis in children?

CT vs. reference standard (Akhtar 2011, Didier 2015, Sayed 2017)	
Sensitivity	0.91 to 0.98
Specificity	0.87 to 1.00

Prevalence	30% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of30%	
True positives (patients with acute appendicitis)	3 studies (Akhtar 2011, Didier 2015, Sayed 2017) 393 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious [b]	not serious	not serious	none	273 to 294	⊕⊕◯◯ LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								6 to 27	
True negatives (patients without acute appendicitis)	3 studies (Akhtar 2011, Didier 2015, Sayed 2017) 393 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious [b]	not serious	not serious	none	609 to 700	⊕⊕◯◯ LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 91	

Explanations

a. Per QUADAS-2 assessment

b. Indirect comparisons

Supplementary Table 14. GRADE Evidence Profile: Should MRI be used to diagnose acute appendicitis in children?

MRI vs. reference standard (Bayraktutan 2014, Didier 2017, Imler 2017, Johnson 2012, Kennedy 2019, Koning 2014, Kulaylat 2015, Moore 2012, Mushtaq 2019, Sawyer 2021, Thieme 2014)	
Sensitivity	0.92 to 1.00
Specificity	0.89 to 1.00

Prevalence	31% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of31%	
True positives (patients with acute appendicitis)	11 studies (Bayraktutan 2014, Didier 2017, Imler 2017, Johnson 2012, Kennedy 2019, Koning 2014, Kulaylat 2015, Moore 2012, Mushtaq 2019, Sawyer 2021, Thieme 2014) 2799 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	285 to 310	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 25	
True negatives (patients without acute appendicitis)	11 studies (Bayraktutan 2014, Didier 2017, Imler 2017, Johnson 2012, Kennedy 2019, Koning 2014, Kulaylat 2015, Moore 2012, Mushtaq 2019, Sawyer 2021, Thieme 2014) 2799 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	614 to 690	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 76	

Explanations

a. Per QUADAS-2 assessment

b. Indirect comparisons

Supplementary Table 15. GRADE Evidence Profile: Should CT be used to diagnose acute appendicitis in children with equivocal/non-diagnostic initial imaging?

CT vs. reference standard (Dillman 2016, James 2022, Krishnamoorthi 2011, Schuh 2011, Srinivasan 2015, van Atta 2015)	
Sensitivity	0.86 to 1.00
Specificity	0.94 to 1.00

Prevalence	19% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of19%	
True positives (patients with acute appendicitis)	6 studies (Dillman 2016, James 2022, Krishnamoorthi 2011, Schuh 2011, Srinivasan 2015, van Atta 2015) 908 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious [b]	not serious	not serious	none	163 to 190	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 27	
True negatives (patients without acute appendicitis)	6 studies (Dillman 2016, James 2022, Krishnamoorthi 2011, Schuh 2011, Srinivasan 2015, van Atta 2015) 908 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious [b]	not serious	not serious	none	761 to 810	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 49	

Explanations

a. Per QUADAS-2 assessment

b. Indirect comparisons

Supplementary Table 16. GRADE Evidence Profile: Should MRI be used to diagnose acute appendicitis in children with equivocal/non-diagnostic initial imaging?

MRI vs. reference standard (Aspelund 2014, Corkum 2018, Covelli 2019, Davis 2022, Dibble 2018, Dillman 2016, Herliczek 2013, Heye 2020, James 2022, Komanchuk 2021, Lyons 2017, Martin 2017, Thieme 2014, Tung 2022)	
Sensitivity	0.84 to 1.00
Specificity	0.88 to 1.00

Prevalence	25% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of25%	
True positives (patients with acute appendicitis)	14 studies (Aspelund 2014, Corkum 2018, Covelli 2019, Davis 2022, Dibble 2018, Dillman 2016, Herliczek 2013, Heye 2020, James 2022, Komanchuk 2021, Lyons 2017, Martin 2017, Thieme 2014, Tung 2022) 1971 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	210 to 250	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 40	
True negatives (patients without acute appendicitis)	14 studies (Aspelund 2014, Corkum 2018, Covelli 2019, Davis 2022, Dibble 2018, Dillman 2016, Herliczek 2013, Heye 2020, James 2022, Komanchuk 2021, Lyons 2017, Martin 2017, Thieme 2014, Tung 2022) 1971 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	660 to 750	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 90	

Explanations

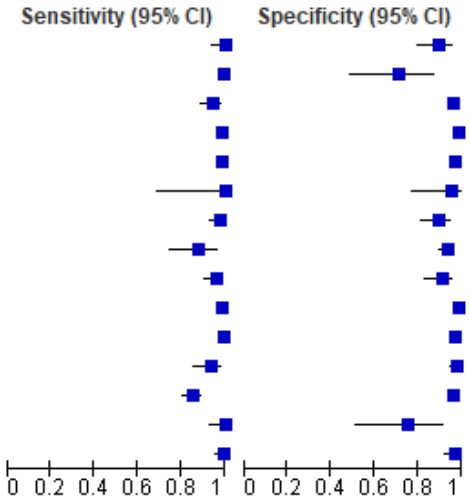
a. Per QUADAS-2 assessment

b. Indirect comparisons

Supplementary Figure 7. Initial US for children with suspected appendicitis

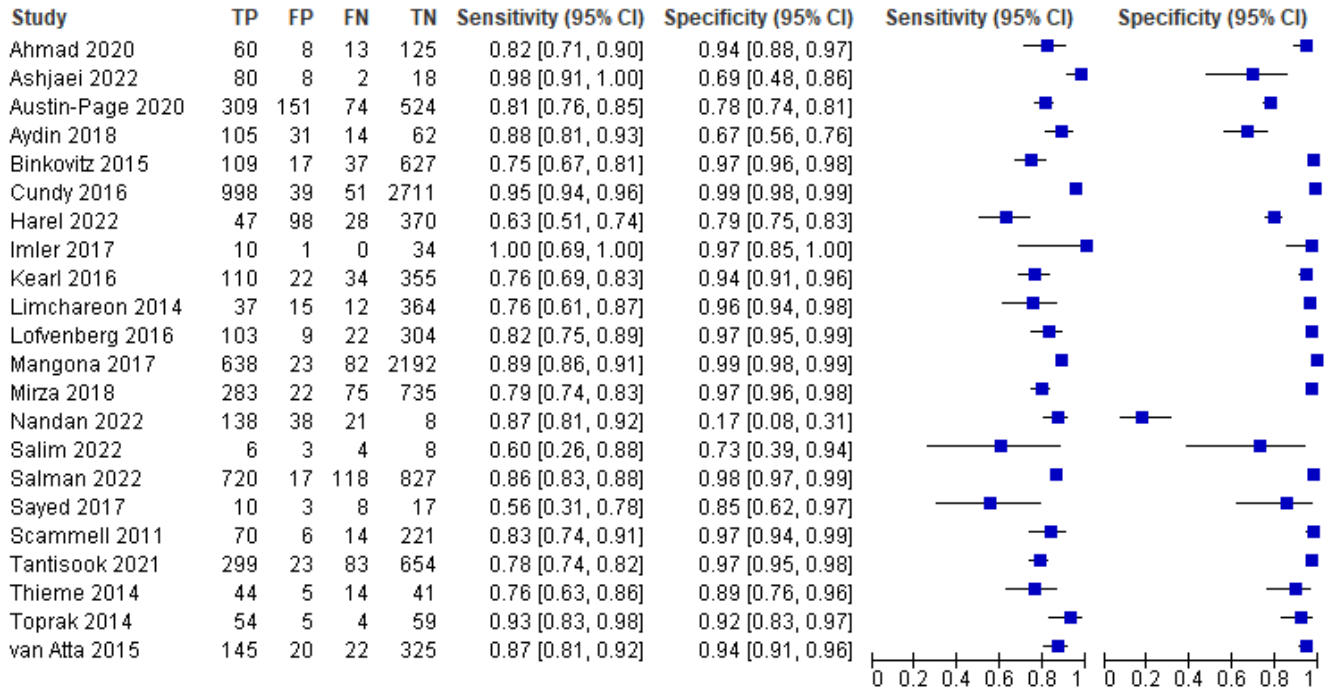
a) definitive US results only

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmad 2020	60	8	0	66	1.00 [0.94, 1.00]	0.89 [0.80, 0.95]
Austin-Page 2020	242	7	1	17	1.00 [0.98, 1.00]	0.71 [0.49, 0.87]
Binkovitz 2015	109	17	6	440	0.95 [0.89, 0.98]	0.96 [0.94, 0.98]
Cundy 2016	998	39	12	2311	0.99 [0.98, 0.99]	0.98 [0.98, 0.99]
Dibble 2018	386	44	5	1470	0.99 [0.97, 1.00]	0.97 [0.96, 0.98]
Imler 2017	10	1	0	21	1.00 [0.69, 1.00]	0.95 [0.77, 1.00]
Kearl 2016	103	11	2	89	0.98 [0.93, 1.00]	0.89 [0.81, 0.94]
Limchareon 2014	37	15	5	213	0.88 [0.74, 0.96]	0.93 [0.89, 0.96]
Lofvenberg 2016	103	9	4	89	0.96 [0.91, 0.99]	0.91 [0.83, 0.96]
Mangona 2017	638	23	11	1380	0.98 [0.97, 0.99]	0.98 [0.98, 0.99]
Salman 2022	720	17	5	543	0.99 [0.98, 1.00]	0.97 [0.95, 0.98]
Scammell 2011	70	6	5	221	0.93 [0.85, 0.98]	0.97 [0.94, 0.99]
Tantisook 2021	299	23	53	558	0.85 [0.81, 0.89]	0.96 [0.94, 0.97]
Toprak 2014	52	5	0	15	1.00 [0.93, 1.00]	0.75 [0.51, 0.91]
van Atta 2015	127	3	1	100	0.99 [0.96, 1.00]	0.97 [0.92, 0.99]



Total n: 15 studies (including 1 RCT- Imler 2017), 11,825 patients
Median (range) sensitivity: 0.99 (0.84-1.00); Median (range) specificity: 0.96 (0.71-0.98)

b) US results, including equivocal/indeterminate*

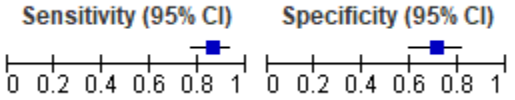


Total n: 22 studies, 16,252 patients
Median (range) sensitivity: 0.82 (0.56-1.00); Median (range) specificity: 0.94 (0.17-0.99)

Supplementary Figure 19. Initial US for children with suspected appendicitis *undergoing surgery*

a. definitive US results only

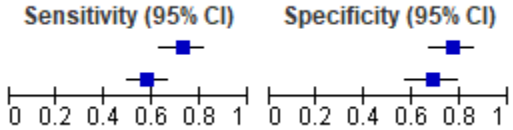
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kelly 2019	74	20	12	50	0.86 [0.77, 0.93]	0.71 [0.59, 0.82]



Total n: 1 study, 156 patients

b. including equivocal/indeterminate*

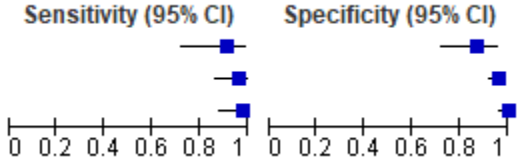
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kelly 2019	74	20	28	67	0.73 [0.63, 0.81]	0.77 [0.67, 0.85]
Pedram 2019	87	25	63	55	0.58 [0.50, 0.66]	0.69 [0.57, 0.79]



Total n: 2 studies, 419 patients
Median (range) sensitivity: 0.66 (0.58-0.73); Median (range) specificity: 0.73 (0.69-0.77)

Supplementary Figure 8. Initial CT for children with suspected appendicitis

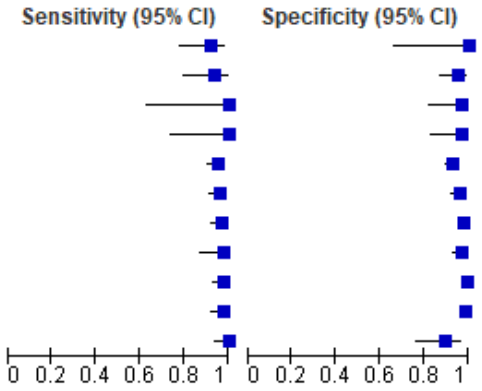
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Akhtar 2011	21	5	2	33	0.91 [0.72, 0.99]	0.87 [0.72, 0.96]
Didier 2015	49	5	2	136	0.96 [0.87, 1.00]	0.96 [0.92, 0.99]
Sayed 2017	44	0	1	95	0.98 [0.88, 1.00]	1.00 [0.96, 1.00]



Total n: 3 studies, 393 patients
Median (range) sensitivity: 0.96 (0.91-0.98); Median (range) specificity: 0.96 (0.87-1.00)

Supplementary Figure 9. Initial MRI for children with suspected appendicitis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bayraktutan 2014	33	0	3	9	0.92 [0.78, 0.98]	1.00 [0.66, 1.00]
Didier 2017	31	3	2	62	0.94 [0.80, 0.99]	0.95 [0.87, 0.99]
Imler 2017	8	1	0	28	1.00 [0.63, 1.00]	0.97 [0.82, 1.00]
Johnson 2012	12	1	0	29	1.00 [0.74, 1.00]	0.97 [0.83, 1.00]
Kennedy 2019	124	36	6	446	0.95 [0.90, 0.98]	0.93 [0.90, 0.95]
Koning 2014	127	10	5	222	0.96 [0.91, 0.99]	0.96 [0.92, 0.98]
Kulaylat 2015	122	10	4	374	0.97 [0.92, 0.99]	0.97 [0.95, 0.99]
Moore 2012	40	5	1	162	0.98 [0.87, 1.00]	0.97 [0.93, 0.99]
Mushtaq 2019	95	3	2	302	0.98 [0.93, 1.00]	0.99 [0.97, 1.00]
Sawyer 2021	89	3	2	283	0.98 [0.92, 1.00]	0.99 [0.97, 1.00]
Thieme 2014	58	5	0	41	1.00 [0.94, 1.00]	0.89 [0.76, 0.96]



Total n: 11 studies (including 1 RCT- Imler 2017), 2,799 patients
Median (range) sensitivity: 0.98 (0.92-1.00); Median (range) specificity: 0.97 (0.89-1.00)

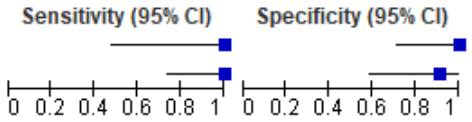
Summary: When assessing only definitive US results, US exhibits acceptable sensitivity and specificity. When including equivocal results, the sensitivity of US is lowered. Both CT and MRI yield acceptable sensitivities and specificities, in general.

Subsequent Imaging in Children

Supplementary Figure 10. Subsequent US for children with suspected appendicitis

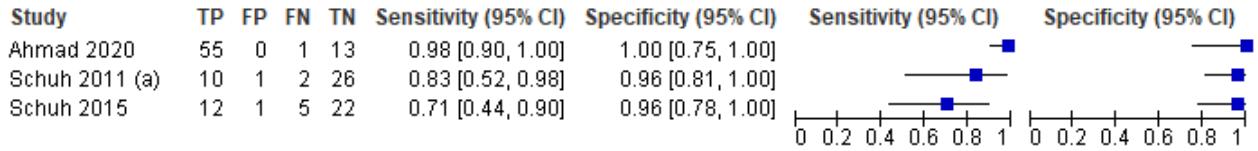
a) definitive US results only

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ahmad 2020	5	0	0	11	1.00 [0.48, 1.00]	1.00 [0.72, 1.00]
Schuh 2015	12	1	0	10	1.00 [0.74, 1.00]	0.91 [0.59, 1.00]



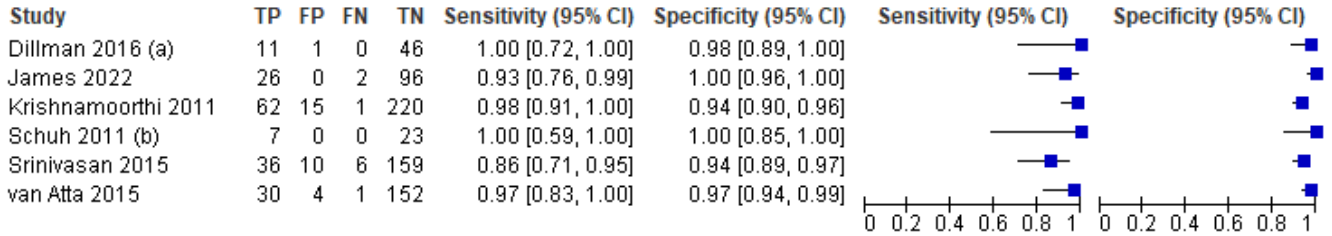
Total n: 2 studies, 39 patients
Median (range) sensitivity: 1.00 (1.00-1.00); Median (range) specificity: 0.96 (0.91-1.00)

b) all US results, including equivocal/indeterminate*



Total n: 3 studies, 148 patients
Median (range) sensitivity: 0.83 (0.71-0.98); Median (range) specificity: 0.96 (0.96-1.00)

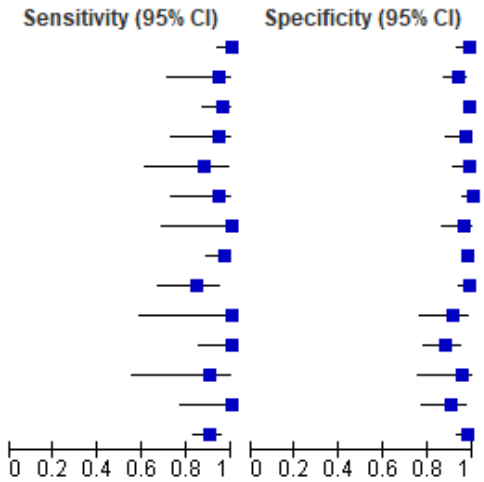
Supplementary Figure 11. Subsequent CT for children with suspected appendicitis



Total n: 6 studies, 908 patients
Median (range) sensitivity: 0.98 (0.86-1.00); Median (range) specificity: 0.98 (0.94-1.00)

Supplementary Figure 12. Subsequent MRI for children with suspected appendicitis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aspelund 2014	61	1	0	80	1.00 [0.94, 1.00]	0.99 [0.93, 1.00]
Corkum 2018	16	7	1	101	0.94 [0.71, 1.00]	0.94 [0.87, 0.97]
Covelli 2019	53	5	2	468	0.96 [0.87, 1.00]	0.99 [0.98, 1.00]
Davis 2022	17	2	1	55	0.94 [0.73, 1.00]	0.96 [0.88, 1.00]
Dibble 2018	14	1	2	60	0.88 [0.62, 0.98]	0.98 [0.91, 1.00]
Dillman 2016 (b)	17	0	1	85	0.94 [0.73, 1.00]	1.00 [0.96, 1.00]
Herliczek 2013	10	2	0	48	1.00 [0.69, 1.00]	0.96 [0.86, 1.00]
Heye 2020	59	6	2	254	0.97 [0.89, 1.00]	0.98 [0.95, 0.99]
James 2022	27	1	5	84	0.84 [0.67, 0.95]	0.99 [0.94, 1.00]
Komanchuk 2021	7	3	0	31	1.00 [0.59, 1.00]	0.91 [0.76, 0.98]
Lyons 2017	23	8	0	58	1.00 [0.85, 1.00]	0.88 [0.78, 0.95]
Martin 2016	9	1	1	19	0.90 [0.55, 1.00]	0.95 [0.75, 1.00]
Thieme 2014	14	4	0	37	1.00 [0.77, 1.00]	0.90 [0.77, 0.97]
Tung 2022	94	2	10	102	0.90 [0.83, 0.95]	0.98 [0.93, 1.00]



Total n: 14 studies, 1,971 patients
Median (range) sensitivity: 0.95 (0.84-1.00); Median (range) specificity: 0.97 (0.88-1.00)

Summary: When assessing only definitive US results, US exhibits acceptable sensitivity and specificity. When including equivocal results, the sensitivity of US is lowered. Both CT and MRI yield acceptable sensitivities and specificities, in general.

PREGNANT PEOPLE

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?

Supplementary Table 3. Characteristics of included studies for acute appendicitis in pregnant people

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
US in pregnant people						
Ahmed 2022	USA 2012-2017	Retrospective review	364 pregnant patients with clinical suspicion of acute appendicitis (363 underwent US first, and 144 underwent subsequent MRI) Mean age 26 years (range 15-45); gestational age range 3-38 weeks 19 diagnosed with appendicitis; pre-test probability: 5%	Pregnant patients over 15 years old with abdominal pain and suspected acute appendicitis who underwent US and/or MRI	Pathology	Initial US
Aras 2016	Turkey 2010-2015	Retrospective review	207 women (38 pregnant and 169 non-pregnant) Mean age of pregnant women 27 years 32 pregnant women diagnosed with appendicitis; pre-test probability: 84%	Women suspected of having appendicitis who underwent appendectomy	Histopathology	Initial US
Baruch 2019	2005-2017	Retrospective	180 women (90 pregnant and 90 non-pregnant; 86/90 pregnant women had US performed) Mean age 31.3 years 59 pregnant women diagnosed with appendicitis; pre-test probability: 66%	Pregnant women aged 18-45 years who underwent appendectomy and matched controls of nonpregnant women	Surgical pathology	Initial US
Kapan 2013	Turkey 2009-2011	Retrospective	20 patients operated on for appendicitis Mean age 26 years (range 19-35); mean GA 17.6 weeks (range 4-33 weeks)	Pregnant patients operated on for appendicitis	Surgery and pathology	Initial US

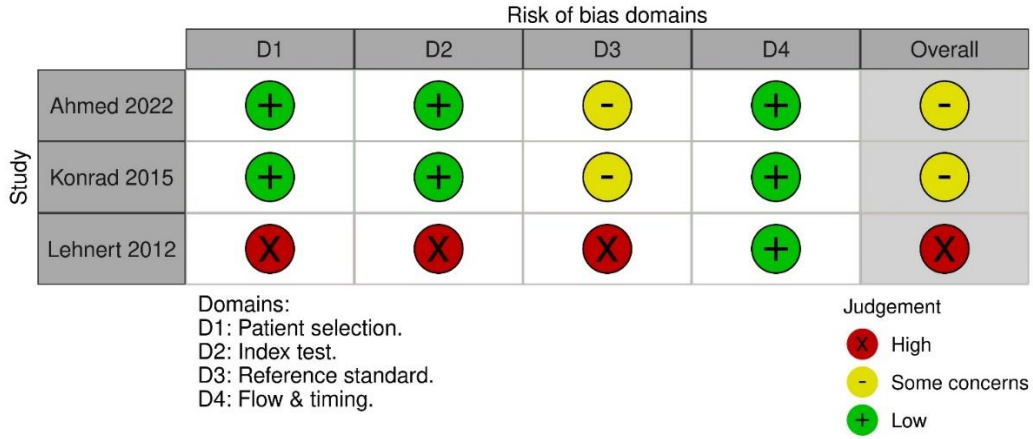
Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			17 diagnosed with appendicitis; pre-test probability: 85%			
Kazemini 2017	Iran 2014-2016	Prospective	52 pregnant women with highly suspected appendicitis Mean age 27.1 years; mean GA 13 weeks 40 diagnosed with appendicitis; pre-test probability: 77%	Pregnant women admitted to the ED who were highly suspected of acute appendicitis and underwent appendectomy; all 3 trimesters	Intraoperative confirmation (which was said to be compatible with histological findings)	Initial US
Koc 2020	Turkey 2009-2019	Retrospective	431 patients (48 pregnant and 383 non-pregnant); 41 pregnant women had initial US Median age of pregnant females 27.5 years (range 19-45) 38 pregnant females diagnosed with appendicitis; pre-test probability: 79%	431 reproductive-aged (18-45 years) female patients who underwent appendectomy with a presumed diagnosis of acute appendicitis (48 pregnant, 383 non-pregnant)	Histopathology	Initial US
Konrad 2015	USA 2009-2011	Retrospective	140 pregnant patients, 117 of whom underwent US Patient age not stated; average GA 19 weeks for all patients 11 diagnosed with appendicitis; pre-test probability: 9%	Pregnant patients who underwent US and/or MRI for clinically suspected appendicitis; range 4-37 weeks pregnant	Surgical pathology or EMR (for patients who did not undergo surgery)	Initial US
Lehnert 2012	USA 2001-2011	Retrospective	99 pregnant patients Mean age 28 years, mean GA 28 weeks (range 14-38) 7 diagnosed with appendicitis; pre-test probability: 7%	Pregnant patients >16 years who presented during the second (at least 14 weeks gestation) or third trimester for RLQ US to evaluate the appendix who were initially evaluated with US	Surgical and clinical outcomes (successful nonoperative management)	Initial US
Mejri 2022	Tunisia 2005-2019	Retrospective	36 patients Mean age 27 years 36 diagnosed with appendicitis; pre-test probability: 100%	Patients who underwent surgery for acute appendicitis during pregnancy	Pathology reports	Initial US
Sukhani 2017	India 5-year period (years not stated)	Retrospective	200 women (50 pregnant and 150 non-pregnant) Mean age of pregnant women 28.3 years 32 pregnant women diagnosed with appendicitis; pre-test probability: 64%	Pregnant women aged 18-45 years who underwent appendectomy	Histopathology	Initial US
Unal 2011	Turkey 2007-2010	Prospective	20 pregnant patients with acute abdomen requiring surgery	Pregnant patients with acute abdomen requiring surgical exploration; appendicitis was	Surgical findings, pathology reports, response to clinical management and follow-up	Initial US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			Mean age 32 years; mean GA 15 weeks (range 6-33) 6 diagnosed with appendicitis; pre-test probability: 30%	the most common reason (30%)		
CT in pregnant people						
N/A						
MRI in pregnant people						
Aguilera 2018	USA 2014-2016	Retrospective	52 patients Median age 25 years (range 17-40); median gestational age 14 weeks (range 5-30) 11 diagnosed with appendicitis; pre-test probability: 21%	Pregnant women with suspected appendicitis	Histology or follow-up	MRI (unclear if initial or subsequent; no contrast)
Ahmed 2022	USA 2012-2017	Retrospective review	364 pregnant patients with clinical suspicion of acute appendicitis (363 underwent US first, and 144 underwent subsequent MRI) Mean age 26 years (range 15-45); gestational age range 3-38 weeks 19 diagnosed with appendicitis; pre-test probability: 5%	Pregnant patients over 15 years old with abdominal pain and suspected acute appendicitis who underwent US and/or MRI	Pathology	Subsequent MRI after US
Amitai 2016	Israel 2007-2013	Retrospective	49 pregnant women Age range 19-42 years; mean GA 25 weeks 5 diagnosed with appendicitis, pre-test probability: 10%	Pregnant women who had MRI for suspected appendicitis	Surgical confirmation	Subsequent MRI after US (most patients had both)
Burke 2015	USA 2009-2014	Retrospective	709 patients Mean age 27.8 years (16-46 years); mean GA 17 weeks 61 diagnosed with appendicitis; pre-test probability: 9%	Pregnant women ≥16 years with suspected appendicitis	Histology or follow-up	Initial MRI for most (>75% of patients; remaining had MRI after US)
Burns 2017	USA 2006-2012	Retrospective	63 patients (total of 71 MRI scans) Mean age 31 years (range 19-41); mean GA 22 weeks 13 diagnosed with appendicitis; pre-test probability: 21%	Pregnant women with suspected appendicitis	Histology or follow-up	MRI (non-contrast MRI); 83% had US prior to MRI
Donlon 2019	Ireland 2013-2018	Retrospective	29 patients	Pregnant patients with suspected appendicitis	Histopathology	MRI (contrast-enhanced MRI); 59% had initial US, followed by MRI

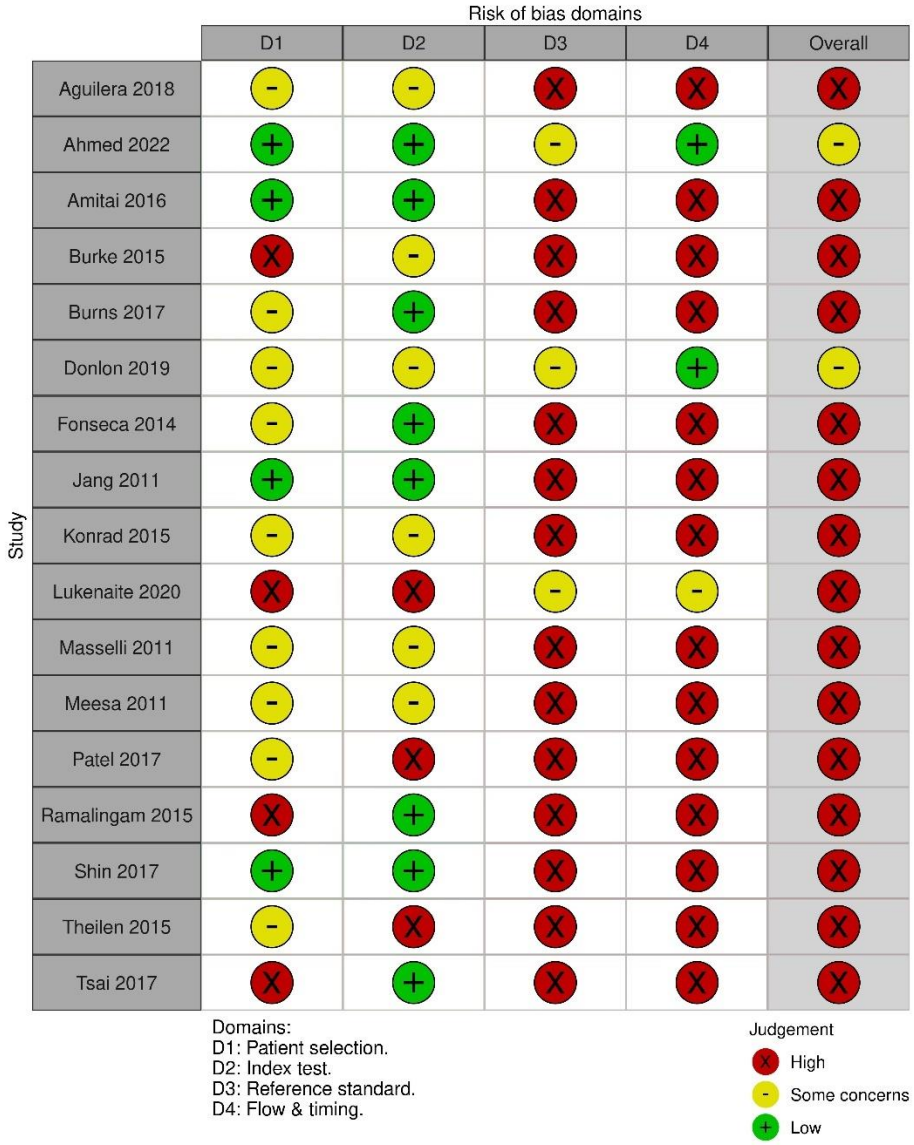
Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			Median age 29 years (range 23-35); majority of patients in 2nd trimester 3 diagnosed with appendicitis; pre-test probability: 10%			
Fonseca 2014	USA 11-year period (years not mentioned)	Retrospective	79 patients, 31 of whom underwent MR Mean/Median age/age range not stated 11/31 diagnosed with appendicitis, pre-test probability: 35%	Pregnant patients with abdominal pain and suspected appendicitis	Pathology and chart review	Subsequent MRI following non-diagnostic US
Jang 2011	Korea 2008-2010	Retrospective	18 patients Mean age 31.7 years (range 23-37); mean gestational age 21.2 weeks (range 9-38) 5 diagnosed with appendicitis; pre-test probability: 28%	Pregnant women with suspected appendicitis	Histology or follow-up	MRI (unclear if initial or subsequent; no contrast)
Konrad 2015	USA 2009-2011	Retrospective	140 pregnant patients; 114 MRI exams performed Mean GA 19 weeks 16 diagnosed with appendicitis, pre-test probability: 11%	Pregnant patients with suspected appendicitis	Surgical pathology or chart review	MRI (some after US and some as initial imaging study)
Lukenaite 2020	Lithuania 2012-2019	Prospective	38 pregnant women Mean age 30.4 years; mean gestational age 23.6 weeks 6 diagnosed with appendicitis, pre-test probability: 16%	Pregnant women with suspected acute appendicitis who underwent MRI after inconclusive US	Pathology	Subsequent MRI following inconclusive US
Masselli 2011	Italy 2006-2010	Prospective	40 patients Mean age 30.6 years (range 20-35) 5 diagnosed with appendicitis, pre-test probability: 13%	Pregnant patients who underwent MRI after indeterminate US (transabdominal and transvaginal US; MRI obtained at clinician discretion)	Pathology and clinical follow-up	Subsequent MRI after indeterminate US
Meesa 2011	USA 2008-2010	Retrospective	22 patients Mean age 28 years (range 17-39) 8 diagnosed with appendicitis; pre-test probability: 36%	Pregnant women with suspected appendicitis who underwent MRI of the abdomen	Clinical outcome	MRI (unclear if initial or subsequent; without contrast)
Patel 2017	Canada 2008-2015	Retrospective	42 pregnant women	Pregnant women with suspected appendicitis	Histology or follow-up	Subsequent MRI (non-contrast MRI) after US

Author, year of publication	Location, years of data collection	Study design	Number of patients pertinent for analysis, age, pre-test probability	Population included	Reference standard	Flow and timing
			Mean age 25.5 years (range 17-39); mean GA 18.6 weeks 5 diagnosed with appendicitis; pre-test probability: 12%			
Ramalingam 2015	USA 2007-2012	Retrospective	127 patients Age range 16-41 years 8 diagnosed with appendicitis, pre-test probability: 8%	Patients with suspected appendicitis who underwent MRI after inconclusive US	Pathology and chart review	Subsequent MRI after inconclusive MRI
Shin 2017	Korea 2008-2015	Retrospective	125 patients Mean age 30.6 years; mean gestational age 20.4 weeks 22 diagnosed with appendicitis; pre-test probability: 18%	Pregnant women with suspected appendicitis	Surgical findings or 2-week follow-up	MRI (unclear if initial or subsequent)
Theilen 2015	USA 2007-2012	Retrospective	171 patients Median age 24-26 years 12 diagnosed with appendicitis; pre-test probability: 7%	Pregnant women with suspected appendicitis	Histology or follow-up	MRI (non-contrast MRI); 27% had US before MRI
Tsai 2017	USA 2003-2015	Retrospective	233 patients Mean age 28.4 years; mean GA 15.1 weeks 13 diagnosed with appendicitis; pre-test probability: 6%	Pregnant women with suspected appendicitis who underwent MRI	Surgical pathology or follow-up	MRI (unclear on timing of study)

Supplementary Table 6a. Risk of bias for included studies on US in pregnancy



Supplementary Table 6b. Risk of bias for included studies on MRI in pregnancy



Supplementary Table 17. GRADE Evidence Profile: Should US (definitive results only) be used to diagnose acute appendicitis in pregnant people?

US vs. reference standard; definitive results only (Konrad 2015, Lehnert 2012)	
Sensitivity	1.00 to 1.00
Specificity	0.83 to 1.00

Prevalence	8% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of8%	
True positives (patients with acute appendicitis)	2 studies (Konrad 2015, Lehnert 2012) 11 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	extremely serious [c]	none	0 to 80	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 80	
True negatives (patients without acute appendicitis)	2 studies (Konrad 2015, Lehnert 2012) 11 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	extremely serious [c]	none	764 to 920	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 156	

Explanations

a. Per QUADAS-2 assessment

b. Indirect comparisons

c. Wide CIs

Supplementary Table 18. GRADE Evidence Profile: Should US (all results, including equivocal/indeterminate) be used to diagnose acute appendicitis in pregnant people?

US vs. reference standard; all results, including equivocal/indeterminate (Ahmed 2022, Konrad 2015, Lehnert 2012)	
Sensitivity	0.18 to 0.29
Specificity	0.99 to 1.00

Prevalence	7% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of7%	
True positives (patients with acute appendicitis)	3 studies (Ahmed 2022, Konrad 2015, Lehnert 2012) 579 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	extremely serious [c]	none	13 to 20	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								50 to 57	
True negatives (patients without acute appendicitis)	3 studies (Ahmed 2022, Konrad 2015, Lehnert 2012) 579 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	921 to 930	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 9	

Explanations

a. Per QUADAS-2 assessment

b. Indirect comparisons

c. Wide CIs

Supplementary Table 19. GRADE Evidence Profile: Should MRI be used to diagnose acute appendicitis in pregnant people?

MRI vs. reference standard (Aguilera 2018, Amitai 2016, Burke 2015, Burns 2017, Donlon 2019, Jang 2011, Meesa 2011, Patel 2017, Shin 2017, Theilen 2015, Tsai 2017)	
Sensitivity	0.18 to 1.00
Specificity	0.54 to 1.00

Prevalence	16% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability	
True positives (patients with acute appendicitis)	11 studies (Aguilera 2018, Amitai 2016, Burke 2015, Burns 2017, Donlon 2019, Jang 2011, Meesa 2011, Patel 2017, Shin 2017, Theilen 2015, Tsai 2017) 1512 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	serious [c]	very serious [d]	none	29 to 160	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 131	
True negatives (patients without acute appendicitis)	11 studies (Aguilera 2018, Amitai 2016, Burke 2015, Burns 2017, Donlon 2019, Jang 2011, Meesa 2011, Patel 2017, Shin 2017, Theilen 2015, Tsai 2017) 1512 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	serious [c]	not serious	none	454 to 840	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 386	

Explanations

a. Per QUADAS-2 assessment
b. Indirect comparisons
c. CIs not overlapping
d. Wide CIs

Supplementary Table 20. GRADE Evidence Profile: Should MRI be used to diagnose acute appendicitis in pregnant people with equivocal/non-diagnostic initial imaging?

MRI vs. reference standard (Ahmed 2022, Amitai 2016, Fonseca 2014, Konrad 2015, Lukenaite 2020, Masselli 2011, Ramalingam 2015)	
Sensitivity	1.00 to 1.00
Specificity	0.94 to 1.00

Prevalence	14% (average from included studies)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of14%	
True positives (patients with acute appendicitis)	7 studies (Ahmed 2022, Amitai 2016, Fonseca 2014, Konrad 2015, Lukenaite 2020, Masselli 2011, Ramalingam 2015) 479 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	serious [c]	none	0 to 140	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having acute appendicitis)								0 to 140	
True negatives (patients without acute appendicitis)	7 studies (Ahmed 2022, Amitai 2016, Fonseca 2014, Konrad 2015, Lukenaite 2020, Masselli 2011, Ramalingam 2015) 479 patients	cross-sectional (cohort type accuracy study)	very serious [a]	serious [b]	not serious	not serious	none	808 to 860	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having acute appendicitis)								0 to 52	

Explanations

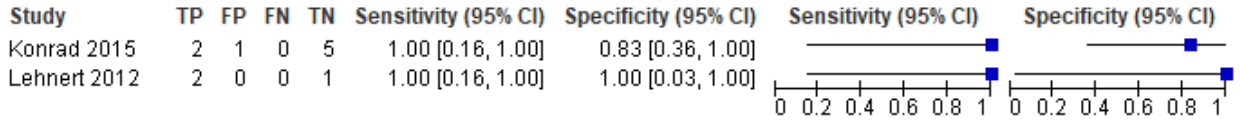
a. Per QUADAS-2 assessment

b. Indirect comparisons

c. Wide CIs

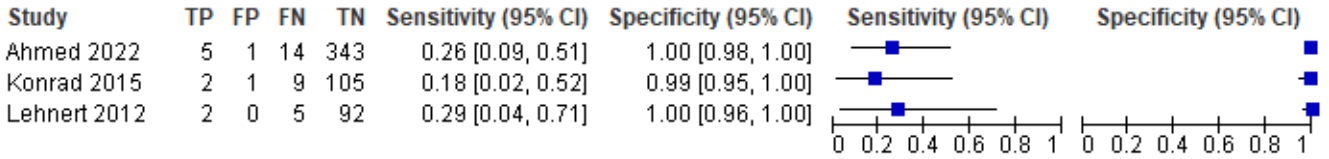
Supplementary Figure 13. Initial US for pregnant people with suspected appendicitis

a) definitive US results only



Total n: 2 studies, 11 patients
Median (range) sensitivity: 1.00 (1.00-1.00); Median (range) specificity: 0.92 (0.83-1.00)

b) all US results, including equivocal/indeterminate*

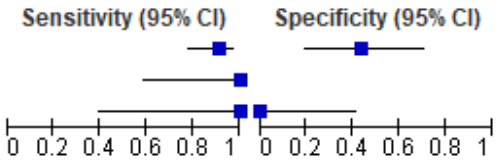


Total n: 3 studies, 579 patients
Median (range) sensitivity: 0.26 (0.18-0.29); Median (range) specificity: 1.00 (0.99-1.00)

Supplementary Figure 20. Initial US for pregnant people with suspected appendicitis *undergoing surgery*

a) definitive US results only

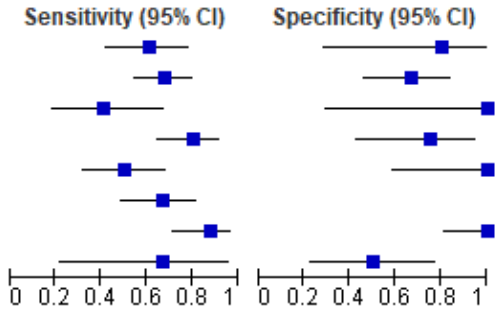
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Baruch 2019	40	9	4	7	0.91 [0.78, 0.97]	0.44 [0.20, 0.70]
Kapan 2013	7	0	0	0	1.00 [0.59, 1.00]	Not estimable
Unal 2011	4	7	0	0	1.00 [0.40, 1.00]	0.00 [0.00, 0.41]



Total n: 3 studies, 78 patients
Median (range) sensitivity: 1.00 (0.91-1.00); Median (range) specificity: 0.22 (0.00-0.44)

b) US results, including equivocal/indeterminate*

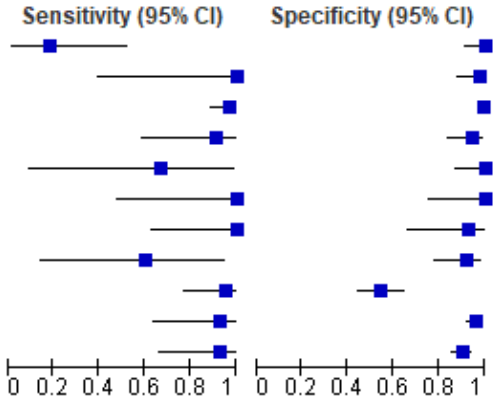
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aras 2016	19	1	12	4	0.61 [0.42, 0.78]	0.80 [0.28, 0.99]
Baruch 2019	40	9	19	18	0.68 [0.54, 0.79]	0.67 [0.46, 0.83]
Kapan 2013	7	0	10	3	0.41 [0.18, 0.67]	1.00 [0.29, 1.00]
Kazemini 2017	32	3	8	9	0.80 [0.64, 0.91]	0.75 [0.43, 0.95]
Koc 2020	17	0	17	7	0.50 [0.32, 0.68]	1.00 [0.59, 1.00]
Mejri 2022	24	0	12	0	0.67 [0.49, 0.81]	Not estimable
Sukhani 2017	28	0	4	18	0.88 [0.71, 0.96]	1.00 [0.81, 1.00]
Unal 2011	4	7	2	7	0.67 [0.22, 0.96]	0.50 [0.23, 0.77]



Total n: 8 studies, 341 patients
Median (range) sensitivity: 0.67 (0.41-0.88); Median (range) specificity: 0.80 (0.50-1.00)

Supplementary Figure 14. Initial MRI for pregnant people with suspected appendicitis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Aguilera 2018	2	0	9	41	0.18 [0.02, 0.52]	1.00 [0.91, 1.00]
Amitai 2016	4	1	0	44	1.00 [0.40, 1.00]	0.98 [0.88, 1.00]
Burke 2015	61	5	2	641	0.97 [0.89, 1.00]	0.99 [0.98, 1.00]
Burns 2017	10	3	1	48	0.91 [0.59, 1.00]	0.94 [0.84, 0.99]
Donlon 2019	2	0	1	26	0.67 [0.09, 0.99]	1.00 [0.87, 1.00]
Jang 2011	5	0	0	13	1.00 [0.48, 1.00]	1.00 [0.75, 1.00]
Meesa 2011	8	1	0	13	1.00 [0.63, 1.00]	0.93 [0.66, 1.00]
Patel 2017	3	3	2	34	0.60 [0.15, 0.95]	0.92 [0.78, 0.98]
Shin 2017	21	47	1	56	0.95 [0.77, 1.00]	0.54 [0.44, 0.64]
Theilen 2015	12	6	1	152	0.92 [0.64, 1.00]	0.96 [0.92, 0.99]
Tsai 2017	13	21	1	198	0.93 [0.66, 1.00]	0.90 [0.86, 0.94]

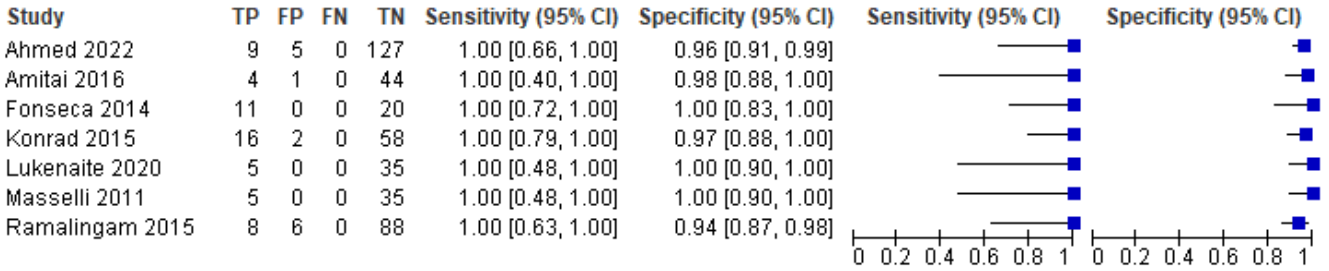


Total n: 11 studies, 1,512 patients
Median (range) sensitivity: 0.93 (0.18-1.00); Median (range) specificity: 0.96 (0.54-1.00)

Summary: When assessing only definitive US results, US exhibits acceptable sensitivity and specificity. When including equivocal results, the sensitivity of US is lowered greatly in this population. Both CT and MRI yield acceptable sensitivities and specificities, in general. Many of the studies, particularly for US and MRI, are limited by small sample sizes.

Subsequent Imaging in Pregnant People

Supplementary Figure 15. Subsequent MRI for pregnant people with suspected appendicitis



Total n: 7 studies, 479 patients
Median (range) sensitivity: 1.00 (1.00-1.00); Median (range) specificity: 0.98 (0.94-1.00)

Summary: There were no studies addressing subsequent US or CT in pregnant people. Subsequent MRI yields acceptable sensitivities and specificities, in general.

Supplementary Table 21. Results of additional analyses for patients *undergoing surgery*

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	**Adults** with suspected appendicitis ***undergoing surgery***	6 (Alshebromi 2019, Ashcroft 2021, Atwood 2021, Kouame 2012, Reich 2011, Selassie 2021)	3,240	0.92 (0.37-1.00)	4 (Alshebromi 2019, Atwood 2021, Reich 2011, Selassie 2021)	2,766	0.50 (0.00-1.00)
Initial US- all results, including equivocal	**Adults** with suspected appendicitis ***undergoing surgery***	14 (Alnuaymah 2022, Aras 2016, Atwood 2021, Fatima 2021, Ferrarese 2016, Koc 2020, Kouame 2012, Reich 2011, Selassie 2021, Serinsoz 2021, Sezer 2012,	5,934	0.74 (0.41-1.00)	14 (Alnuaymah 2022, Aras 2016, Atwood 2021, Fatima 2021, Ferrarese 2016, Koc 2020, Kouame 2012, Reich 2011, Selassie 2021, Serinsoz 2021, Sezer 2012,	5,934	0.62 (0.00-0.94)

		Singh 2022, Sukhani 2017, Tatli 2016)			Singh 2022, Sukhani 2017, Tatli 2016)		
Initial CT	**Adults** with suspected appendicitis ***undergoing surgery***	8 (Alnuaymah 2022, Alshebromi 2019, Ashcroft 2021, Coursey 2011, Donlon 2021, Liu 2015, Rait 2020, Teo 2014)	1,612	0.98 (0.86-0.99)	8 (Alnuaymah 2022, Alshebromi 2019, Ashcroft 2021, Coursey 2011, Donlon 2021, Liu 2015, Rait 2020, Teo 2014)	1,612	0.50 (0.03-0.96)
Initial MRI	**Adults** with suspected appendicitis ***undergoing surgery***	2 (Chabanova 2011, Serinsoz 2021)	118	0.94 (0.87-1.00)	2 (Chabanova 2011, Serinsoz 2021)	118	0.76 (0.61-0.91)
Initial US- definitive results only	**Children** with suspected appendicitis ***undergoing surgery***	1 (Kelly 2019)	156	0.86	1 (Kelly 2019)	156	0.71
Initial US- all results, including equivocal	**Children** with suspected appendicitis ***undergoing surgery***	2 (Kelly 2019, Pedram 2019)	419	0.66 (0.58-0.73)	2 (Kelly 2019, Pedram 2019)	419	0.73 (0.69-0.77)
Initial US- definitive results only	**Pregnant people** with suspected appendicitis ***undergoing surgery***	3 (Baruch 2019, Kapan 2013, Unal 2011)	78	1.00 (0.91-1.00)	2 (Baruch 2019, Unal 2011)	71	0.22 (0.00-0.44)
Initial US- all results, including equivocal	**Pregnant people** with suspected appendicitis ***undergoing surgery***	8 (Aras 2016, Baruch 2019, Kapan 2013, Kazemini 2017, Koc 2020, Mejri 2022, Sukhani 2017, Unal 2011)	341	0.67 (0.41-0.88)	7 (Aras 2016, Baruch 2019, Kapan 2013, Kazemini 2017, Koc 2020, Sukhani 2017, Unal 2011)	305	0.80 (0.50-1.00)

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