# Discriminating complicated from uncomplicated appendicitis by ultrasound imaging, computed tomography or magnetic resonance imaging: systematic review and meta-analysis of diagnostic accuracy

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# Abstract

**Background:** Discriminating complicated from uncomplicated appendicitis is crucial. Patients with suspected complicated appendicitis are best treated by emergency surgery, whereas those with uncomplicated appendicitis may be treated with antibiotics alone. This study aimed to obtain summary estimates of the accuracy of ultrasound imaging, CT and MRI in discriminating complicated from uncomplicated appendicitis

**Methods:** A systematic literature review was conducted by an electronic search in PubMed, Embase and the Cochrane Library for studies describing the diagnostic accuracy of complicated *versus* uncomplicated appendicitis. Studies were included if the population comprised adults, and surgery or pathology was used as a reference standard. Risk of bias and applicability were assessed with QUADAS-2. Bivariable logitnormal random-effect models were used to estimate mean sensitivity and specificity.

**Results:** Two studies reporting on ultrasound imaging, 11 studies on CT, one on MRI, and one on ultrasonography with conditional CT were included. Summary estimates for sensitivity and specificity in detecting complicated appendicitis could be calculated only for CT, because of lack of data for the other imaging modalities. For CT, mean sensitivity was 78 (95 per cent c.i. 64 to 88) per cent, and mean specificity was 91 (85 to 99) per cent. At a median prevalence of 25 per cent, the positive predictive value of CT for complicated appendicitis would be 74 per cent and its negative predictive value 93 per cent.

**Conclusion:** Ultrasound imaging, CT and MRI have limitations in discriminating between complicated and uncomplicated appendicitis. Although CT has far from perfect sensitivity, its negative predictive value for complicated appendicitis is high.

# Introduction

Imaging is part of the standard workup for diagnosing appendicitis. Ultrasound imaging, CT and MRI are used most frequently. A diagnosis of acute appendicitis can be made adequately based on radiological findings<sup>1–6</sup>. The first choice of diagnostic modality differs. In Europe, ultrasonography is often used as the first approach to diagnose acute appendicitis, combined with CT if necessary in patients with inconclusive or negative results<sup>6–8</sup>; in Northern America, CT first is preferred over US<sup>9</sup>.

As well as confirming the diagnosis of appendicitis, imaging may also help in distinguishing between complicated and uncomplicated appendicitis. Nowadays, it is believed that uncomplicated and complicated appendicitis are different entities, and may require different treatment strategies. In patients with complicated appendicitis, early surgical treatment is necessary to avert a complicated postoperative course<sup>10</sup>. In uncomplicated appendicitis, semi-urgent surgery and antibiotic treatment may be an option, and even a wait-and-see policy is currently being investigated<sup>11,12</sup>.

Several studies<sup>13–15</sup> have evaluated non-operative treatment of uncomplicated appendicitis. Treatment with antibiotics may be just as safe and effective as surgical treatment, without the risk of surgical complications, similar to management strategies for other inflammatory bowel diseases, such as diverticulitis or colitis<sup>14–16</sup>. Although studies on antibiotic treatment have shown

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a low initial failure rate (below 10 per cent), 22 per cent of patients need an appendicectomy within 1 year of follow-up and up to 40 per cent within 5 years<sup>15,17</sup>. An essential factor in the success of non-operative treatment is the selection of patients with truly uncomplicated appendicitis.

Identifying uncomplicated appendicitis is improved by ruling out complicated appendicitis, which indirectly improves the selection of patients in need of urgent surgery. Thus, to employ different treatment strategies, a discriminatory test with high sensitivity and high negative predictive value (NPV) for ruling out complicated appendicitis is of the utmost importance. The two largest published RCTs<sup>18,19</sup> assessing the effectiveness of antibiotic treatment for uncomplicated appendicitis used CT alone to discriminate between uncomplicated and complicated appendicitis. They reported 18 per cent<sup>18</sup> and 1.5 per cent<sup>19</sup> complicated appendicitis in the surgery arm. Therefore, diagnosing complicated appendicitis by CT alone may not be good enough. Moreover, if ultrasound imaging or MRI is adequate in discriminating these entities, perforated appendicitis may be detected without the use of radiation or intravenous contrast agent. This systematic review was designed to obtain summary estimates of the accuracy of ultrasonography, CT and MRI in discriminating complicated from uncomplicated appendicitis.

# **Methods**

The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD42020150771. PRISMA-DTA guidelines<sup>20</sup> for reporting systematic reviews of diagnostic test accuracy studies were used to prepare this manuscript.

# **Review** question

This review aimed to obtain summary estimates of the (comparative) accuracy of ultrasonography, CT and MRI in discriminating complicated from uncomplicated appendicitis. The secondary aim was to explore sources of heterogeneity of the accuracy of these modalities.

# Eligibility criteria

Diagnostic accuracy studies were eligible in which ultrasound imaging, CT, MRI, or a combination of these imaging modalities were used to discriminate between complicated and uncomplicated appendicitis. The definition of complicated appendicitis could differ among studies, but was used as defined in the original publications. In studies comparing 'perforated' and 'non-perforated appendicitis', perforated appendicitis was considered as complicated appendicitis and non-perforated appendicitis as uncomplicated appendicitis. Both histopathological and perioperative findings, or a combination, were valid as a reference standard.

An estimate of sensitivity and specificity for complicated appendicitis was mandatory for inclusion. Both retrospective and prospective studies were eligible. Studies had to mention the radiological diagnosis of complicated appendicitis, and either report or allow the construction of  $2\times2$  tables on accuracy. If the reported data were unclear, the authors were contacted by email. Only studies reporting only or predominantly on adults (at least 75 per cent; at least 15 years of age) were included, as diagnostic accuracy and workup are different in children<sup>21</sup>. If age was not mentioned, or the study did not report the incidence in adults, this was reported and marked as high risk of bias. The electronic search did not use any limitations, but in the full-text

selection only studies reported in English, German or Dutch were selected.

#### Information sources

An electronic search was performed in PubMed, Embase and the Cochrane Library. Reference lists of included full-text study reports were searched manually for missing relevant articles. Keywords assigned to the retrieved articles were used for the additional search. The final search date was 12 November 2019.

#### Literature search

The search strategy is described in Appendix S1.

#### Study selection

Two reviewers independently evaluated potentially eligible studies, assessed these for risk of bias, and extracted data. Disagreements were discussed. If no consensus was reached, a consensus meeting with a third reviewer was decisive.

#### Data extraction and critical appraisal

Data from the included studies were systematically, independently, and blindly extracted by two reviewers using a structured study record form. Disagreements were resolved in consensus meetings.

The following items were extracted: title, year of publication, journal of publication, name of first author, number of patients, study design, country, inclusion criteria, exclusion criteria, true positives, true negatives, false positives, false negatives, proportion of male patients, median (range) age, radiological features for complicated appendicitis, reference standard, definition of complicated appendicitis, imaging characteristics and protocols if reported, number of observers and observers' experience.

Risk of bias and concerns about applicability to the review questions were assessed with the QUality Assessment of Diagnostic Accuracy Studies tool, version 2 (QUADAS-2)<sup>22</sup>. Two reviewers independently assessed the included articles, and disagreements were resolved in consensus meetings including a third reviewer, if necessary. Studies that included patients retrospectively based on an appendicectomy registration code were marked as at high risk of bias in the patient selection domain, as this might have influenced radiologist judgement.

#### Statistical analysis

For all included studies, true positives, true negatives, false positives and false negatives for patients with complicated appendicitis were extracted. If data were available, the total number of patients was the number of patients with appendicitis according to the reference standard. Patients considered to have appendicitis by the radiologist, but without appendicitis in the reference group, were included for analyses, if the data were available.

When only sensitivity and specificity were mentioned, counts were combined with the prevalence of complicated appendicitis in the study and 2×2 tables for the diagnosis of complicated appendicitis were reconstructed. If possible, 3×3 tables were extracted, adding the diagnosis 'not appendicitis' in both reference and imaging groups. If two imaging observers were used, mean counts from contingency tables were used and rounded.

Study-specific estimates of sensitivity and specificity with 95 per cent c.i. are presented in forest plots. Bivariable logitnormal random-effect models were used to estimate mean sensitivity and specificity with 95 per cent confidence intervals. A hierarchical summary receiver operating characteristic (HSROC) curve was plotted. Projected post-test probabilities were calculated based on the median prevalence of complicated appendicitis in the eligible studies, and the summary estimates of sensitivity and specificity. As complicated appendicitis needs to be ruled out, a sensitivity of at least 90 per cent and a specificity of at least 50 per cent were deemed necessary. Data were analysed with Review Manager version 5.3 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) and R (The R Foundation for Statistical Computing, Vienna, Austria) using the mada package.

Potentials sources of heterogeneity were explored, related to imaging characteristics, reader experience, use of intravenous contrast medium, slice thickness, and CT with a standard *versus* low radiation dose. Bivariable meta-regression was planned if sufficient studies were available.

# **Results**

The search identified 5285 studies, of which 147 potentially eligible studies were selected for full-text evaluation. After evaluation of eligibility, 13 studies<sup>23–35</sup> were included in the review (Fig. 1). Eleven studies<sup>23,25–33,35</sup> reported on CT, one study<sup>24</sup> on ultrasound imaging alone, and one study<sup>34</sup> described ultrasound imaging, ultrasonography with conditional CT (CT after negative or inconclusive ultrasound imaging) and MRI. Thus data on ultrasound imaging could be obtained from two studies, CT from 11 studies, and MRI from one study. The combination of ultrasonography with conditional CT was reported in one study<sup>34</sup>.

#### Study and patient characteristics

Study characteristics are shown in *Table* 1. Nine studies were retrospective, and two studies were prospective (1 study<sup>33</sup> reported on CT, and the other<sup>34</sup> on ultrasonography alone or with conditional CT, and MRI). In two studies<sup>23,25</sup>, it was unclear whether the study was performed prospectively or retrospectively. Three studies described the role of low- *versus* high-dose radiation CT, of which two<sup>29,31</sup> were performed retrospectively and one<sup>33</sup> prospectively. Ten studies<sup>23,24,26,28–33,35</sup> used perforated appendicitis (rather than complicated appendicitis) as the outcome. Only 3<sup>25,27,34</sup> of the 13 studies evaluated complicated appendicitis (rather than perforated appendicitis). One study<sup>23</sup> only used histopathology as the reference standard. One study<sup>34</sup> used an expert panel for final diagnosis.

In total, data on 1892 patients were reported, of which 620 had complicated appendicitis (*Table 2*). The median prevalence of complicated appendicitis was 25 per cent. For ultrasound imaging data were available on 218 patients, for CT 1667, for MRI 120, and the combination of US and CT 125. In four studies, the proportion of adults was unclear<sup>24–26,28</sup>. Two<sup>27,32</sup> of the studies included approximately 75 per cent adults (based on mean(s.d.) age) and were therefore included. The remaining seven studies<sup>23,29–31,33–35</sup> included only adult patients (above 15 years of age). For further details, see *Tables S1* and *S2*.

# **Risk of bias**

The risk of bias was high in 9 of 13 studies in the following domains: patient selection, index test and reference standard. Applicability concerns were considered high in 9 studies for the domains patient selection, index test and reference standard, and low in three studies. The QUADAS-2 characteristics and summary are depicted in Fig. 2 and Table 3.

#### Diagnostic accuracy Ultrasound imaging

One retrospective cohort<sup>24</sup>, based on patients with surgically and histopathology proven appendicitis, reported on the diagnostic accuracy of ultrasound imaging for complicated appendicitis, with a sensitivity of 86 per cent (19 of /22) and a specificity of 60 per cent (47 of 78). Based on a prevalence of 25 per cent, the positive predictive value (PPV) was calculated to be 42 per cent and the NPV as 93 per cent.

Another study<sup>34</sup>, of a prospective cohort, included all patients with clinically suspected appendicitis. If ultrasonography was inconclusive, conditional CT was performed. Outcomes for ultrasound imaging alone were not reported separately, but could be calculated from the data. For ultrasound imaging, the sensitivity was 32 per cent (10 of 31) and specificity was 93 per cent (81 of 87). Based on a prevalence of 25 per cent, PPV and NPV were 60 and 80 per cent respectively. Patients with a diagnosis other than appendicitis were excluded in these calculations.

Because of high heterogeneity, caused by differences in study design (retrospective *versus* prospective studies) and patient selection (proven *versus* suspected appendicitis), no meta-analysis was performed. For both studies<sup>24,34</sup>, it was not possible to construct a  $3 \times 3$  table that included the diagnosis 'no appendicitis'.

# СТ

Eleven studies evaluated the diagnostic accuracy of CT for detecting complicated appendicitis: eight retrospective studies<sup>26–32,35</sup>, one prospective study<sup>33</sup>, and two studies<sup>23,25</sup> with unclear design. Reported estimates ranged from 28 to 95 per cent for sensitivity and 71 to 100 per cent for specificity. The forest plot is depicted in Fig. 3. The summary estimates were 78 (95 per cent c.i. 64 to 88) per cent for sensitivity, with a specificity of 91 (85 to 99) per cent. See Fig. 4 for the HSROC curve. At a median prevalence of complicated appendicitis of 25 per cent, the PPV of CT would be 74 per cent and the NPV 93 per cent.

The only prospective study<sup>33</sup> on the diagnostic accuracy of CT for complicated appendicitis reported a sensitivity of 55 per cent and a specificity of 88 per cent. For the eight retrospective studies<sup>26–32,35</sup>, the summary estimate of sensitivity was 81 (95 per cent c.i. 62 to 91) per cent with a specificity of 93 (84 to 97) per cent. The two studies<sup>23,25</sup> with unclear design were not analysed separately

Three studies<sup>29,31,33</sup> compared accuracy for low *versus* standard radiation dose CT. The estimates for sensitivity and specificity were not significantly different (P = 0.286). For regular-dose CT, the sensitivity was 68 (95 per cent c.i. 45 to 85) per cent at a specificity of 88 (80 to 93) per cent; for low-dose CT, these estimates were 58 (32 to 80) and 75 (40 to 94) per cent respectively. There were insufficient data to test for differences related to radiologist experience, intravenous contrast or slice thickness (*Table* S3). It was not possible to construct a 3×3 table that included the diagnosis of no appendicitis for any of these studies.

#### MRI

One study<sup>34</sup> reported on the diagnostic accuracy of MRI in detecting complicated appendicitis: sensitivity was 57 (95 per cent c.i. 37 to 75) per cent and specificity was 86 (77 to 92) per cent. At a prevalence of 25 per cent, this would indicate a PPV of 58 per cent and NPV of 86 per cent. The  $3\times3$  table, including the diagnosis of no appendicitis, is shown in Table S4.

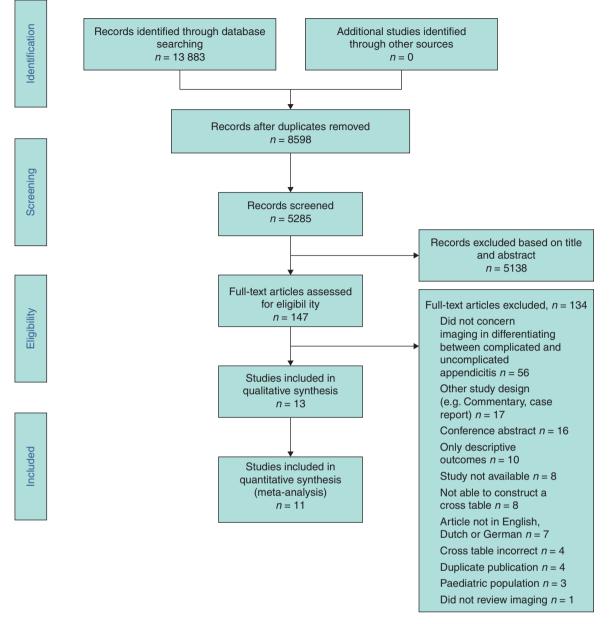


Fig. 1 PRISMA diagram for the review

#### Ultrasonography with conditional CT

One study<sup>34</sup> reported accuracy estimates for ultrasound imaging followed by CT in patients with an inconclusive or negative ultrasound scan. The sensitivity was 48 (95 per cent c.i. 30 to 67) per cent at a specificity of 93 (85 to 97) per cent. At a prevalence of 25 per cent, a PPV of 70 per cent and NPV of 84 per cent was calculated. The 3×3 table, including the diagnosis of no appendicitis, is seen in *Table* S4.

# Discussion

Based on currently available evidence, ultrasonography, CT, MRI alone, or a combination ultrasound imaging and CT (conditional CT) have limitations in discriminating between complicated and uncomplicated appendicitis. Imaging cannot reliably rule out a complicated presentation of acute appendicitis in need of urgent surgery, as a sensitivity of 90 per cent does not appear to be reached and there is high heterogeneity between studies. With respect to ruling in complicated appendicitis, CT seems to reach a specificity above 90 per cent but still is not perfect, and ruling in is considered less important. In the absence of comparative studies, no head-to-head comparisons could be made between imaging techniques or strategies. In a meta-regression comparing low-dose with normal-dose radiation CT, no significant difference that caused the heterogeneity in CT studies was found. Diagnostic accuracy was worse in prospective studies, which is important as these are the closest to daily clinical practice.

A recent meta-analysis<sup>37</sup> described 10 CT features to discriminate between complicated and uncomplicated appendicitis, nine of which showed high individual specificity but low sensitivity. Periappendicular fat infiltration had a sensitivity of 94 per cent, but a specificity of 40 per cent<sup>37</sup>. Another study<sup>38</sup> built a regression model based on radiological features. Although the authors of that study did not report results for diagnostic accuracy, only

#### Table 1 Study characteristics

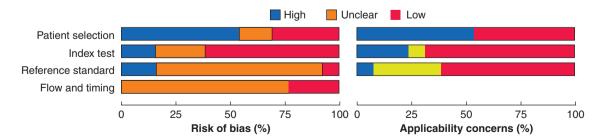
Reference	Year	Country	Study design	Modality	Reference standard	Definition target condition
Borushok et al. <sup>24</sup>	1990	USA	R	US	S+PA	Perforated
Choi et al. <sup>25</sup> 1998		USA	U	СТ	S+PA	Necrotizing and perforated ap- pendicitis
Foley et al. <sup>26</sup>	2005	USA	R	CT	S+PA	Perforated
Miki et al. <sup>27</sup>	2005	Japan	R	СТ	S+PA	Gangreneous and perforated ap- pendicitis
Tsuboi et al. <sup>28</sup>	2008	Japan	R	CT	S+PA	Perforated
Seo et al. <sup>29</sup>	2009	South Korea	R	CT H/L	S+PA	Perforated
Suthikeeree et al. <sup>30</sup>	2010	Thailand	R	CT	S+PA	Perforated
Kim et al. <sup>31</sup>	2011	South Korea	R	CT H/L	S+PA	Perforated
Suh et al. <sup>32</sup>	2011	South Korea	R	CT	S+PA	Perforated
Kim et al. <sup>33</sup>	2012	South Korea	Р	CT H/L	S+PA	Perforated
Leeuwenburgh et al. <sup>34</sup>	2014	Netherlands	Р	US, US+CT, MRI	S+PA	Perforated appen- dicitis or pus in abdomen
Liu et al. <sup>35</sup>	2015	China	R	CT	S+PA	Perforated
Ali et al. <sup>23</sup>	2018	Pakistan	U	CT	PA	Perforated

R, retrospective; US, ultrasonography; S, surgery; PA, histopathology; U, uncertain; H/L, high and low radiation dose; P, prospective.

# Table 2 Patient characteristics

Reference	No. with appendicitis	No. with complicated ap- pendicitis	Age (years) <sup>*</sup>	% aged $\geq$ 15 years
Ali et al. <sup>23</sup>	236	42 (17.8)	40 (15–n.r.)	100
Borushok et al. <sup>24</sup>	100	22 (22.0)	29 (1–71)	n.r.
Choi et al. <sup>25</sup>	105	69 (65.7)	n.r.	n.r.
Foley et al. <sup>26</sup>	86	21 (24)	34 (8–87)	n.r.
Kim et al. <sup>31</sup>	52	7 (13)	28 (15-40)	100
Kim et al. <sup>33</sup>	180	42 (23.3)	30 (22–37)	100
Leeuwenburgh et al. <sup>34</sup> (US)	125	31 (26.3)	35 (24–49)†	100
Leeuwenburgh et al. <sup>34</sup> (US+CT)	125	31 (24.8)	35 (24–49)†	100
Leeuwenburgh et al. <sup>34</sup> (MRI)	120	30 (25.0)	35 (24–49)†	100
Liù et al. <sup>35</sup>	187	41 (21.9)	48 (19-87)	100
Miki et al. <sup>27</sup>	64	28 (44)	32 (4–78)	~75
Seo et al. <sup>29</sup>	79	24 (30)	39 (15–8Ó)	100
Suh et al. <sup>32</sup>	528	226 (42.8)	29 28 (15 20)	~75
Suthikeeree et al. <sup>30</sup>	48	27 (56)	56 (15–96)	100
Tsuboi et al. <sup>28</sup>	102	40 (39.2)	37 (4-82)	n.r.

Values in parentheses are percentages unless indicated otherwise; \*values are mean (range), except <sup>†</sup> median (i.q.r.). n.r., not reported.



#### Fig. 2 Risk of bias and applicability concerns

Review authors' judgements about each domain presented as percentages across the included studies.

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Table 3 Summary o	nt risk of higs an	d annlicability conce	erns, teniem anth	nors' illidgements	s about each don	nain for each study
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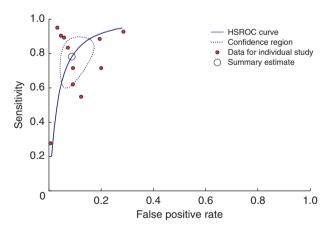
Reference		Risk	of bias	Applicability concerns			
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Ali et al. <sup>23</sup>	?	?	_	?	+	?	_
Borushok et al. <sup>24</sup>	-	_	+	+	_	_	+
Choi et al. <sup>25</sup>	-	?	?	?	_	+	+
Foley et al. <sup>26</sup>	-	+	?	?	_	+	+
Kim et al. <sup>31</sup>	+	_	?	?	+	_	+
Kim et al. <sup>33</sup>	+	+	?	?	+	+	+
Leeuwenburgh et al. <sup>34</sup>	+	+	?	?	+	+	+
Liu et al. <sup>35</sup>	?	+	?	?	+	+	?
Miki et al. <sup>27</sup>	_	+	?	?	_	+	?
Seo et al. <sup>29</sup>	+	+	?	+	+	+	+
Suh et al. <sup>32</sup>	_	?	?	?	_	_	?
Suthikeeree et al. <sup>30</sup>	_	+	_	?	_	+	?
Tsuboi et al. <sup>28</sup>	_	+	?	+	_	+	+

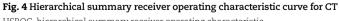
?, Unclear; +, high; -, low.

Reference	ТР	FP	FN	TN	Sensitivity	Specificity	Sensitivity	Specificity
Choi <i>et al.</i> <sup>25</sup>	61	7	8	29	0.88 (0.78, 0.95)	0.81 (0.64, 0.92)		
Miki <i>et al.</i> 27	25	2	3	34	0.89 (0.72, 0.98)	0.94 (0.81, 0.99)		
Foley et al. <sup>26</sup>	13	6	8	59	0.62 (0.38, 0.82)	0.91 (0.81, 0.97)		
Tsuboi <i>et al.</i> <sup>28</sup>	38	2	2	60	0.95 (0.83, 0.99)	0.97 (0.89, 1.00)		
Seo et al.29	20	4	4	51	0.83 (0.63, 0.95)	0.93 (0.82, 0.98)		
Sulhikeeree et al.30	25	6	2	15	0.93 (0.76, 0.99)	0.71 (0.48, 0.89)		
Suh <i>et al</i> . <sup>31</sup>	63	1	163	301	0.28 (0.22, 0.34)	1.00 (0.98, 1.00)	+	
Kim <i>et al.</i> <sup>31</sup>	5	9	2	36	0.71 (0.29, 0.96)	0.80 (0.65, 0.90)		
Kim <i>et al.</i> <sup>33</sup>	23	17	19	121	0.55 (0.39, 0.70)	0.88 (0.81, 0.93)		
Liu <i>et al.</i> <sup>35</sup>	37	7	4	139	0.90 (0.77, 0.97)	0.95 (0.90, 0.98)		-
Ali <i>et al.</i> <sup>23</sup>	30	18	12	176	0.71 (0.55, 0.84)	0.91 (0.86, 0.94)		
						0	0.2 0.4 0.6 0.8 1 0	0.2 0.4 0.6 0.8 1

#### Fig. 3 Forest plots of sensitivity and specificity for the diagnostic accuracy of CT in detecting complicated appendicitis

Bivariable logitnormal random-effect models were used for meta-analysis. Mean sensitivity and specificity values are shown with 95 per cent confidence intervals. TP, true positives; FP, false positives; FN, false negatives; TN, true negatives.





HSROC, hierarchical summary receiver operating characteristic.

12 of 21 patients with a gangrenous appendicitis were identified as such, leading to a sensitivity of 57 per cent. However, in clinical practice, radiological features are not interpreted separately. The radiologist's decision will be based on a combination of specific features, together with the severity of the feature. Ultrasound imaging has limitations as a single technique in detecting acute appendicitis (sensitivity 69–83 per cent and specificity 81–93 per cent)<sup>16,19</sup>. Thus it is intrinsically limited in distinguishing between complicated and uncomplicated appendicitis. This was also shown in the one prospective study<sup>34</sup>, which reported a sensitivity of 32 per cent and specificity of 93 per cent for ultrasonography. CT and MRI were better at detecting acute appendicitis. CT had a sensitivity for acute appendicitis of 91–94 per cent and specificity of 90–94 per cent<sup>3,21</sup>, whereas MRI had a sensitivity of 96 per cent and specificity of 96 per cent<sup>39</sup>. The 3×3 tables, including the diagnosis of no appendicitis, were performed in only one study<sup>34</sup>, which evaluated conditional CT (CT after ultrasound imaging if necessary) and MRI. The 3×3 tables, including the diagnosis of no appendicitis, were performed in only one study<sup>34</sup>, describing both ultrasonography with CT if necessary and MRI. Merely reporting the discriminatory capacity of imaging, in which the radiologist is confident of the final diagnosis of appendicitis, might lead to bias. Incorrect classification of appendicitis type may be associated with the wrong treatment choice. In addition, patients without acute appendicitis, but falsely diagnosed as having simple appendicitis, are overtreated.

Studies not included in this review have reported data on the performance of the Alvarado and Appendicitis Inflammatory Response (AIR) scores, with respect to discrimination between complicated and uncomplicated appendicitis<sup>35,40–42</sup>. The authors concluded there might be an association between score level and complexity of appendicitis, but no data on diagnostic accuracy measures were presented. Other authors<sup>43,44</sup> created a prediction model for complicated appendicitis using clinical features, but also failed to report diagnostic accuracy statistics. Two further studies<sup>45,46</sup> reported on a combination of clinical and radiological features. Atema and colleagues<sup>45</sup> developed two scoring systems, combining clinical and radiological features: one with ultrasonographic and one with CT features. The ultrasonographic system reached a sensitivity of 96.6 per cent and a specificity of 45.7 per cent; for CT, sensitivity and specificity were 90.2 and 70.3 per cent respectively<sup>45</sup>. Avanesov and co-workers<sup>46</sup> developed a scoring system with CT features; the sensitivity was 82 per cent and the specificity 93 per cent. However, these scoring models have not yet been validated externally. Current studies on surgery versus antibiotics in uncomplicated appendicitis have shown that, on average, 18 per cent of patients considered before surgery to have uncomplicated appendicitis were found to have complicated appendicitis at operation<sup>14</sup>. Most studies used imaging to rule out complicated appendicitis, but misclassified about one in six patients. The only study<sup>19</sup> with a low proportion of false negatives for patients with complicated appendicitis in the surgery arm used CT alone, and was probably biased by the preselection of patients eligible for non-operative treatment.

Limitations of the studies included in this review involve the predominantly retrospective designs, which may have resulted in an overestimation of accuracy. Another limitation is the variation in the diagnostic accuracy of the radiologists reading the examinations. For two studies<sup>26,29</sup> in the meta-analysis, the outcomes of two readers were reported; both reported differences in diagnostic accuracy. Kim *et al.*<sup>47</sup>. reported on the performance of CT in differentiating between complicated and uncomplicated appendicitis. Their study was not included in the present review, as they used CT scans from an RCT that already had been included<sup>3</sup>. However, in that more recent report<sup>47</sup>, the sensitivity of the radiologists' assessment for complicated appendicitis ranged from 31 to 81 per cent, and the specificity ranged from 60 to 93 per cent, indicating that the performance of radiologists in detecting complicated appendicitis is likely to vary.

The debate regarding the best strategy to discriminate complicated from uncomplicated appendicitis will probably continue. Scoring systems seem to perform better in ruling out complicated appendicitis, but there are no adequately validated scoring systems yet. Most studies reporting on the effect of non-operative treatment for uncomplicated appendicitis have included patients based on CT alone. Although CT has a far from perfect, and highly varying, sensitivity, its NPV for complicated appendicitis is high. Ultrasound imaging, CT and MRI all have limitations in discriminating between complicated and uncomplicated appendicitis.

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# Supplementary material

Supplementary material is available at BJS Open online.

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