Health Policy Advisory Committee on Technology

Technology Brief

Computed tomography to rule out suspected appendicitis in adults and reduce the negative appendectomy rate (NAR)

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ASERNIP/S

Australian Safety and Efficacy Register of New Interventional Procedures – Surgical

Royal Australasian College of Surgeons

HealthPACT

emerging health technology

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This brief was prepared by Deanne Forel from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

Summary of findings

The purpose of this Technology Brief was to examine the evidence base for the routine use of computed tomography (CT) in the diagnosis of suspected appendicitis in adults. Given the volume of literature available for diagnosing suspected appendicitis with CT, comparators were selected based on what was represented in the literature and included physical examination, imaging (ultrasound [US] and magnetic resonance imaging [MRI]) and diagnostic laparoscopy. Given the scope of a Technology Brief it was not possible to include all diagnostic techniques/protocols available to diagnose suspected appendicitis.

This Technology Brief assessed five studies; two systematic reviews with meta-analyses and three non-randomised comparative studies.

The results of the two systematic reviews confirm that CT, even when performed without contrast agents, yields high diagnostic accuracy, adequate for clinical decision making. In general, CT was found to lower negative appendectomy rate (NAR), and increase time to surgery. The effect of delaying surgery is inconsistent with one systematic review stating it did not negatively impact on the perforation rate and another study stating it did.

The comparative studies support the diagnostic performance of CT; however, accuracy appears to be equivalent to MRI and diagnostic laparoscopy. In the study comparing imaging with physical examination, CT or US was associated with significantly reduced NAR. Although the diagnostic performance of US among the included studies was generally poorer than CT, it is important to consider its value in regards to availability, cost and utility when imaging women of childbearing age.

Cost data from a randomised controlled trial found routine abdominal CT resulted in higher total treatment costs in patients with acute abdominal pain compared with patients who underwent selective imaging. These higher costs could not be attributed to a single factor in the CT group; they were the result of higher imaging costs, higher costs of other parallel diagnostic examinations and longer hospital stay.

Finally, all included studies noted the exposure to ionising radiation associated with CT. One systematic review found CT in adults to be justified if radiation exposure is considered in the clinical decision pathway. Two of the non-randomised comparative studies supported a shift away from routine CT to diagnose appendicitis via the routine use of MRI or laparoscopy. This was, in part, owing to a reduction in the risks associated with abdominal and pelvic radiation (particularly in children and women of childbearing age). It is important to note that Choosing Wisely Australia recommends that CT should not be used to diagnose appendicitis in children and young adults unless US has been carried out prior.

HealthPACT Advice

When patients present with uncertain symptoms of appendicitis, laparoscopy is often used to both diagnose and treat suspected appendicitis. As a result, negative appendectomy rates remain high, with many patients undergoing unnecessary surgery, which may result in poor patient outcomes from complications, and unnecessary health system costs of surgery and inpatient stays. Whilst ultrasound is the standard practice for appendicitis diagnosis, its diagnostic accuracy is operator dependent and scanning may fail to visualise the appendix sufficiently to enable an accurate diagnosis, especially in obese patients. When CT is used to diagnose appendicitis in adults, negative appendectomy rates are decreased; however routine CT is uncommon, is associated with ionising radiation exposure and is more expensive than US.

The decision to use CT to diagnose suspected appendicitis in adults will therefore be made at the individual hospital level. HealthPACT notes the Choosing Wisely Australia advice "Don't do computed tomography (CT) for the evaluation of suspected appendicitis in *children and young adults* until after ultrasound has been considered as an option". No further research on behalf of HealthPACT is warranted at this time.

Technology, Company and Licensing

Register ID	**WP233**
Technology name	**Computed tomography**
Patient indication	**Adults with acute abdomen and suspected appendicitis**

Description of the technology

Computed tomography (CT) is an imaging technique that uses x-rays to create cross-sectional images of the body. Unlike conventional x-rays which utilise a fixed x-ray tube, CT scanners use a motorised x-ray source that rotates around a gantry.[1] Each gantry rotation around the patient generates a thin two-dimensional image (or 'slice') of the body.[1] The thickness of the tissue represented by each 'slice' ranges from 1 to 10 mm depending on the CT machine used.[1] Successive 'slices' are 'stacked' to create a three-dimensional image.[1] These two- or three-dimensional images are used to visualise the internal structures of the patient's body and to identify abnormalities, such as those caused by disease or injury. In some cases, CT may be performed with the assistance of contrast agents to help to visualise soft tissue by increasing opacity to produce clearer images. Contrast agents, such as iodine or barium-based compounds, are typically administered orally, intravenously or rectally.

Sudden and severe abdominal pain, also known as acute abdomen, is a common complaint among patients presenting to an emergency department and may result from acute cholecystitis, acute appendicitis, acute pancreatitis and diverticulitis amongst other causes. It is important that cases that require urgent surgical intervention are identified and treated in a timely manner. Correct diagnosis based on clinical examination alone can be difficult, radiological examination, such as CT imaging, is often used to determine the appropriate course of management for acute abdomen.[2]

Company or developer

There are a range of companies that manufacturer and provide CT equipment in Australia. These include, but are not limited to: Toshiba Australia Pty Ltd.; Siemens Healthcare Pty Ltd.; GE Medical Systems Australia Pty Ltd.; and Philips Electronics Australia Ltd.

Reason for assessment

Several studies have reported superior diagnostic performance of abdominal CT for suspected appendicitis, contributing to an increase in use. There is debate around the appropriateness of routine CT imaging in diagnosing appendicitis and its proposed benefits of reducing negative appendectomy rate (the rate of healthy appendixes surgically removed unnecessarily), treatment costs and hospital resource usage. There may be potential, in light of recent evidence and technology, to move towards selective imaging practices in identifying appendicitis.

Stage of development in Australia

- ☐ Yet to emerge
- ☐ Experimental
- ☐ Investigational
- ☐ Nearly established
- ☒ Established
- ☐ Established *but* changed indication or modification of technique
- ☐ Should be taken out of use

Licensing, reimbursement and other approval

CT technology is widely approved, available and used worldwide. Four Medicare Benefit Schedule (MBS) items for CT diagnosis of suspected appendicitis were identified .[3] These describe the use of CT to scan the upper abdomen and pelvis with or without the use of contrast agents, see Table 1 below.

Table 1 MBS items for CT diagnostic imaging services that may be used to diagnose appendicitis[3]

MBS item	Description	Fee	Benefit
56501	COMPUTED TOMOGRAPHY - scan of upper abdomen and pelvis without intravenous contrast medium, not for the purposes of virtual colonoscopy, not being a service to which item 56801 or 57001 applies (R) (K) (Anaes.)	$385.00	75% $288.75 85% $327.25
56541	COMPUTED TOMOGRAPHY - scan of upper abdomen and pelvis without intravenous contrast medium, not for the purposes of virtual colonoscopy, not being a service to which item 56841 or 57041 applies (R) (NK) (Anaes.)	$193.15	75% $144.90 85% $164.20
56507	COMPUTED TOMOGRAPHY - scan of upper abdomen and pelvis with intravenous contrast medium and with any scans of upper abdomen and pelvis prior to intravenous contrast injection, when undertaken, not for the purposes of virtual colonoscopy, not being a service to which item 56807 or 57007 applies (R) (K) (Anaes.)	$480.05	75% $360.05 85% $408.05
56547	COMPUTED TOMOGRAPHY - scan of upper abdomen and pelvis with intravenous contrast medium, and with any scans of upper abdomen and pelvis prior to intravenous contrast injection, when undertaken, not for the purposes of virtual colonoscopy, not being a service to which item 56847 or 57047 applies (R) (NK) (Anaes.)	$243.75	75% $182.85 85% $207.20

MBS: Medicare Benefits Schedule; R: 'requested'. A referral from a practitioner needed to claim benefit; K: service performed on newer diagnostic imaging equipment; NK: service performed on older diagnostic imaging equipment; Anaes.: can be claimed with an anaesthetic item.

Australian Therapeutic Goods Administration approval

- ☒ Yes
- ☐ No
- ☐ Not applicable

ARTG number (s) *There are many CT machines approved for use in Australia.

Technology type **Diagnostic**

Technology use **Diagnostic**

Patient Indication and Setting

Disease description and associated mortality and morbidity

The appendix is an 8 to 10 cm long, narrow, tube-shaped pouch structure, which protrudes from the caecum (colon) at the junction of the small and large intestines (Figure 1).[4] Although a part of the gastrointestinal tract, the appendix is considered a vestigial organ, in that it provides no vital function.[4] Acute appendicitis is one of the most common causes of acute abdominal pain among patients presenting to the emergency department.[5] Appendicitis is the inflammation of the inner lining of the appendix, brought about by a blockage or obstruction[6], typically resulting from a build-up of mucus, parasites or faecal matter within the appendix.[4]

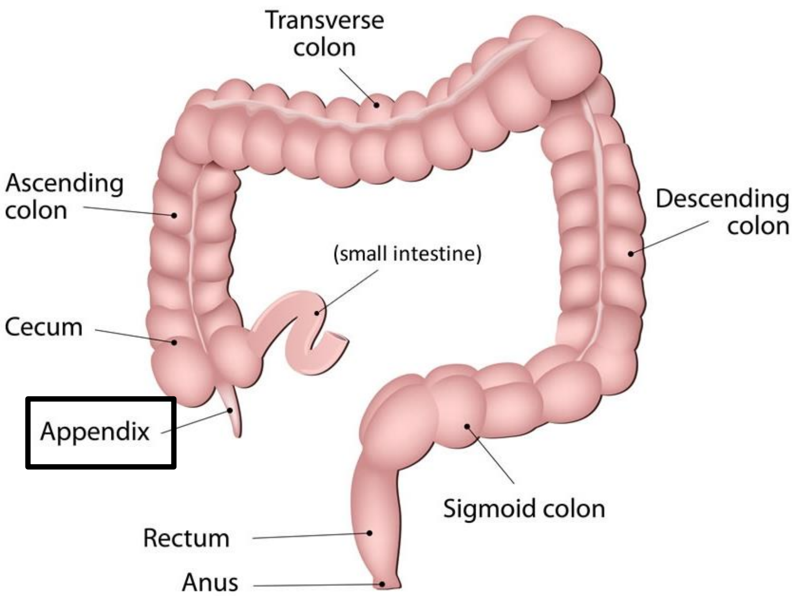

Figure 1 Location of the appendix[7]

Appendicitis typically begins with a gradual onset of dull cramping or aching throughout the abdomen (uncomplicated appendicitis).[4] As the condition progresses (over 48 to 72 hours), and the appendix becomes more inflamed, this turns to localised constant and severe sharp pain in the right lower abdomen (acute appendicitis).[4] Other symptoms that accompany pain may include fever, nausea and vomiting, loss of appetite and constipation or diarrhoea.[4]

Acute appendicitis may become a clinical emergency if the infected appendix is left untreated and ruptures. A ruptured appendix can result in peritonitis, a serious condition that requires immediate medical attention. If not treated promptly, with intravenous antibiotics and in some cases surgical removal of infected tissue, peritonitis can become life-threatening.[8]

Number of patients

Acute abdominal pain comprises four to five per cent of all emergency department visits.[2] Appendicitis is most likely to occur in those persons aged 10 to 30 years, although it can strike at any age.[9] Appendicitis is slightly more common in men than in women and is more prevalent in Western countries.[10] This is thought to be due to the Western diet, which is often low in fibre.[10]

According to the Australian Institute of Health and Welfare's Australian hospital statistics for 2012-13, the most common principal diagnosis for 27,411 emergency admissions was acute appendicitis (24,308 and 3,103 in public and private hospitals, respectively).[11] The number of overnight acute separations for acute appendicitis during that same time period was 30,774 (26,126 and 4,648 in public and private hospitals, respectively).[11] The number of potentially preventable hospitalisations due to complications of appendicitis (generalised peritonitis) resulted in 8,692 separations across Australia in 2012-13.[11] More recent data, reports a total of 34,096 hospital separations for a principal diagnosis of acute appendicitis from 2013-14.[12]

According to New Zealand's Ministry of Health there were 4,990 and 106 publicly-funded and privately-funded hospital discharges for acute appendicitis in 2012-13, respectively.[13]

Speciality	**Radiology, imaging and nuclear medicine**
Technology setting	**General Hospital; Specialist Hospital**

Impact

Alternative and/or complementary technology

CT for the diagnosis of appendicitis is not new. It may be considered a complimentary technology used in conjunction with other diagnostic techniques, such as clinical examination, laboratory testing and other imaging modalities (such as US). In many cases; however, CT is solely used to identify appendicitis prior to surgery.

Current technology

The clinical presentation of appendicitis is inconsistent.[6] Currently, the diagnosis of appendicitis is established by a combination of physical findings from clinical examination, laboratory results and imaging tests.[5] Clinical examination of a patient with suspected appendicitis is likely to involve palpation of the abdomen to determine the presence of rebound tenderness, pain on percussion, rigidity and guarding.[6]

Laboratory testing is not specific for appendicitis but is useful to help confirm a diagnosis, particularly in patients presenting with atypical symptoms;[6] tests include:

- Complete blood counts

- C-reactive protein (CRP) levels
- Liver and pancreatic function tests
- Urinalysis
- Pregnancy test.[6]

Imaging techniques used to diagnose appendicitis, other than CT, are ultrasonography and magnetic resonance imaging (MRI).[6] Ultrasound (US) directs high-frequency sound waves at the internal structures of the body via a hand-held probe.[14] The same probe receives the reflected sounds, or echoes, to create an image.[14] Ultrasound is useful in diagnosing appendicitis because it is non-invasive, inexpensive and highly accessible. Several features indicative of appendicitis can be identified by US and include: an enlarged appendix, difficulty compressing bowel sections and reduced peristaltic motion of the intestine.[15] MRI uses magnetic fields to create images that are highly refined and may provide a level of detail which is not achievable with CT or US. Limitations associated with MRI include accessibility, cost and patient suitability.

In cases when diagnostic results are insufficient, patients progress from clinical assessment to diagnostic laparoscopy, or from imaging to laparoscopy.[16] where a surgeon can diagnose appendicitis from direct observation and move to surgical removal if required. The risks involved with laparoscopy include complications from general anaesthesia, inflammation of the abdominal wall and blood clot, as well as increased costs.[16]

Diffusion of technology in Australia

CT is widely used to diagnose appendicitis in Australia. Reasons for the increased use of CT may include its improved negative appendectomy rate (NAR) and that patients presenting to an emergency department with acute abdomen are generally first assessed by junior or less experienced clinicians who are more likely to opt for investigation (Personal communication, The Queen Elizabeth Hospital).

International utilisation

Country	Level of Use		
	Trials underway or completed	Limited use	Widely diffused
Australia			✓
Worldwide			✓

Cost infrastructure and economic consequences

As CT technology is an established and widespread technology, there would be no additional outlay costs for using CT to diagnose appendicitis.

The Medicare reimbursement rate of an abdominal and pelvic CT scan ranges from $193 to $385 (without contrast agents) and $243 to $480 (with contrast agents), depending on the

CT equipment age.[3] In comparison, the Medicare reimbursement rate of an US is significantly lower at $18 to $111 for an abdominal US and $17 to $98 for a pelvic US (depending on the age of the technology used).[3]

Ethical, cultural, access or religious considerations

Concerns with exposure to ionising radiation and consequent increased lifetime cancer risks exist regarding the use of CT to diagnose appendicitis, especially in children. In Australia, US is the preferred initial consideration for imaging examination in children and young adults with suspected appendicitis.[17] If the results of the US exam are equivocal, it may be followed by CT.[17]

It is important that patients, and caregivers, are made aware of the risks associated with CT radiation so they can make an informed decision about CT imaging risks.

Evidence and Policy

Safety and effectiveness

There is a wealth of published literature available regarding the use of CT to diagnose suspected appendicitis. To identify and include the highest quality and most recent literature, as well as provide a thorough representation of current practice, several inclusion criteria were applied to the search results, detailed in Table 2 below.

Table 2 Study selection criteria

Search limits	Inclusion criteria	Exclusion criteria
• Publication date: last 5 years • Publication type: comparative studies, reviews and clinical trials (where possible)	• Evidence ≥ level III diagnostic evidence • Studies using CT to diagnose suspected appendicitis compared with a another method of diagnosing suspected appendicitis • Studies reporting the outcomes of interests: negative appendectomy rate; sensitivity; specificity • Eligible comparators include: clinical examination, ultrasound, magnetic resonance imaging and diagnostic laparoscopy	• Evidence < level III • Studies comparing different modalities of CT (i.e. low-dose CT versus standard-dose CT) • Studies looking at the effects of patient characteristics (e.g. BMI) on CT diagnostic accuracy • Studies reporting the effectiveness of their own 'diagnostic protocols' (i.e. negative appendectomy rate before and after introducing a particular protocol or care pathway)

CT: computed tomography; BMI: body mass index.

After applying these inclusion criteria, five studies were considered eligible for inclusion in this Technology Brief, including two systematic literature reviews with meta-analyses[5, 20] and three non-randomised comparative studies.[19, 21, 22] The level III diagnostic evidence compared CT with one or more of the eligible comparators so that each alternative diagnostic method was compared with CT at least once. An overview of the included studies is provided in Table 3.

Table 3 Overview of included studies

Study details	Inclusion criteria	Exclusion criteria	Number of studies/ patients	Outcomes
Xiong et al (2015)[5] China Systematic review with meta-analysis (level II diagnostic evidence) CT	Prospective studies evaluating the diagnostic accuracy of non-contrast CT in detecting acute appendicitis. Studies reporting operative or histological findings after surgery and providing a minimum 2 weeks follow-up.	Retrospective studies, review articles, case reports or editorials and studies that could not provide data for extraction.	7 studies 845 patients	Sensitivity; specificity; positive likelihood ratio; negative likelihood ratio; diagnostic odds ratio.
Krajewski et al (2011)[20] Canada Systematic review with meta-analysis (level II diagnostic evidence) CT versus clinical examination	Studies including adult patients with acute right lower quadrant pain; studies comparing patients undergoing CT with clinical examination alone and providing at least one of the following outcomes of interest: negative appendectomy rate (determined by a formal pathology report), perforation rate (determined by a formal pathology report) or time from presentation in emergency room to operating theatre.	Studies on mostly paediatric patients (< 18 years of age); case-control studies, case reports and case series.	28 studies 9,330 patients	Negative appendectomy rate; perforation rate; time from presentation in emergency room to operating theatre; subgroup sex analysis.
Bachar et al (2013)[19] Israel Retrospective non-randomised comparative study (level III-2 diagnostic evidence) CT versus US versus diagnostic laparoscopy	Patients who underwent laparoscopic appendectomy for acute appendicitis at a single centre between January 2000 and December 2009	NR	887 patients (total) 171 (CT) 83 (US)	Negative appendectomy rate; sensitivity; specificity; positive predictive value; negative predictive value; postoperative complications
Leeuwenburgh et al (2013)[21] The Netherlands Prospective non-randomised comparative study (level III-2 diagnostic evidence) CT versus MRI	Patients ≥ 18 years with clinically suspected acute appendicitis based on medical history and physical and laboratory examination findings.	Patients with a contraindication for MRI and critically ill patients who needed intensive vital organ function monitoring as well as pregnant women.	230 patients (total) 115 (CT) 229 (US) 223 (MRI)	Final diagnosis; sensitivity; specificity; missed appendicitis; false-positive (negative appendectomy); positive likelihood ratio; negative likelihood ratio.
Park et al (2013)[22] Korea Retrospective non-randomised comparative study (level III-2 diagnostic evidence) CT versus US or clinical examination	Patients who presented to the emergency department or outpatient clinical between January 2004 and December 2008 with acute abdominal pain and who underwent diagnostic examination to rule out acute appendicitis.	NR	3,045 patients (total) 965 (CT) 1,777 (US) 303 (physical exam)	True positive; false negative; true negative; false positive; negative appendectomy rate.

CT: computed tomography; NR: not reported; US: ultrasound; MRI: magnetic resonance imaging; US: ultrasound.

Xiong et al (2015)[5]

This systematic review aimed to determine the diagnostic accuracy of non-contrast CT in detecting acute appendicitis through a meta-analysis of the literature. Searches of PubMed, EMBASE and *The Cochrane Library* were undertaken, as well as hand-searching of relevant studies' reference lists. No language restrictions were applied. Prospective studies where operative or histological findings post-surgery were reported were eligible for inclusion. Data extraction was undertaken by two independent reviewers and cross-checked for discrepancies. Included studies were appraised using the Quality Assessment of Diagnostic Accuracy Studies tool.[23]

Pooled sensitivity, specificity, positive/negative likelihood ratios and diagnostic odds ratios (OR) of non-contrast CT detection of acute appendicitis were obtained using a random-effects model. A summary receiver-operating characteristic curve was constructed and the area under the curve was calculated, providing the overall diagnostic accuracy of non-contrast CT.

Seven studies were eligible for inclusion in the meta-analysis. These studies were published from 1998 to 2010 and reported on 845 patients in total. The authors concluded the overall quality of their included studies was moderate (study design was not reported).

Safety: No safety outcomes were reported.

Effectiveness: Data from the forest plot of sensitivity and specificity for non-contrast CT in detecting acute appendicitis are summarised below in Table 4. Non-contrast CT used for the detection of acute appendicitis has a high sensitivity and specificity but importantly a good positive likelihood ratio [a] (>10) rules in disease.

Table 4 Xiong et al meta-analysis findings[5]

	Finding	I^2 values	*p* value
Mean sensitivity	90%, range (76- 97%), 95% CI [86, 92]	84%	<0.05
Mean specificity	94%, range (75-90%), 95% CI [92, 97]	75%	<0.05
Positive likelihood ratio	12.90, 95% CI [4.80, 34.67]	74%	<0.05
Negative likelihood ratio	0.09, 95% CI [0.04, 0.20]	86%	<0.05
Diagnostic odds ratio	162.76, 95% CI [31.05, 853.26]	83%	<0.05

CI: confidence interval.

The summary receiver-operating characteristic curve was symmetrical and the area under the curve was 0.97 (95% confidence interval [CI] 0.95 to 0.99), suggesting high diagnostic accuracy of non-contrast CT when detecting acute appendicitis. The I^2 values indicated

a Positive likelihood ratio = probability of an individual without the condition having a positive test; Negative likelihood ratio = probability of an individual without the condition having a negative test significant heterogeneity among the included studies; however, the funnel plot showed no statistically significant asymmetry suggesting no major publication bias in this meta-analysis.

Krajewski et al (2011)[20]

This systematic review examined if CT reduced NAR, time to operating room and perforation rate, when compared with clinical examination alone to diagnose acute appendicitis. Searches of MEDLINE, EMBASE and *The Cochrane Library* were performed. Two independent reviewers identified the studies eligible for inclusion and extracted data using extraction forms created *a priori*. Discrepancies were resolved through discussion. Manual searching of reference lists was undertaken and enquiries with corresponding authors for additional data where made when necessary. The authors used pooled estimates of the OR using a random-effects model for their meta-analyses as there was notable heterogeneity among the included studies.

Twenty-eight studies met the inclusion criteria, two randomised controlled trials and 26 cohort studies, reporting outcomes from 9,330 patients. In the studies that reported the type of contrast used, 1,156 patients (38%) received combination intravenous/oral contrast, 827 patients (27%) underwent non-contrast CT, 527 patients (17%) received rectal contrast, 134 patients (4%) received intravenous contrast alone, 32 patients (1%) received oral contrast alone, and 368 patients (12%) received a combination of the above contrast modalities.

Safety*:* No safety outcomes were reported.

Effectiveness**:** The median sensitivity and specificity across all 28 included studies was 95 per cent (range 84% to 99%) and 97 per cent (range 85% and 100%), respectively. The authors made a distinction between the 11 included studies which compared outcomes before the use of CT became widespread (pre-CT era) with outcomes after the use of CT become widespread and the remaining 17 studies which compared CT with clinical evaluation. These distinctions are relevant in the way the following outcomes are reported.

Negative appendectomy rate

A meta-analysis of 10 studies found that NAR was significantly reduced after the adoption of routine CT to diagnose suspected acute appendicitis (pooled OR= 0.52, 95% CI [0.36, 0.76]). Similarly, NAR was significantly reduced in patients who underwent CT versus clinical examination (meta-analysis of 20 studies; pooled OR= 0.57, 95% CI [0.45, 0.72]).

Time to operating room: Ten studies reported the time from emergency department to operating room. The mean waiting time was 800 minutes in the CT group and 468 minutes in the clinical examination group. Five studies described a statistically significant increase in this time in patients who underwent CT compared with those who did not (data reported qualitatively).

Table 5 NAR reported by Krajewski et al[20]

	Pre-CT era	CT-era	*p* value	CT	Clinical examination	*p* value
N	4,485	1,629		2,491	3,125	
NAR	21.5%	10%	<0.001	8.6%	16.7%	<0.001
Heterogeneity	Significant p<0.001, I^2=70.0%			Non-significant p=0.09, I^2=31.6%		

CT: computed tomography; NAR: negative appendectomy rate.

Perforation rate: Seven studies compared perforation rate before and after the adoption of CT use to diagnose suspected acute appendicitis and eight studies compared perforation rate in patients who underwent CT versus clinical examination alone (Table 6). For the first group of studies, pooled OR was 0.97 (95% CI 0.80-1.18) and for the second group, pooled OR was 1.33 (95% CI 0.91-1.94), indicating no significant difference in perforation rate.

Table 6 Perforation rate reported by Krajewski et al[20]

	Pre-CT era	CT-era	*p* value	CT	Clinical examination	*p* value
N	1,502	1,293		802	855	
Perforation rate	20.0%	19.6%	0.74	23.4%	16.7%	0.15
Heterogeneity	Non-significant p=0.56, I^2=0%			Non-significant p=0.07, I^2=47.0%		

CT: computed tomography.

Bachar et al (2013)[19]

This non-randomised comparative study evaluated the benefits, clinical outcomes and diagnostic accuracy of CT, US and laparoscopy in acute appendicitis. Medical records of patients who underwent laparoscopic appendectomy between January 2000 and December 2009 were reviewed. All patients were assessed initially by an on-call surgical team. Those with obvious clinical diagnosis for appendicitis (local tenderness, guarding, fever and leucocytosis) and those with a high suspicion for appendicitis (local tenderness and guarding only) were considered for urgent laparoscopy ('laparoscopy overall' group, N = 887). Laparoscopic appendectomy was performed in patients whose laparoscopy revealed acute appendicitis ('laparoscopic appendectomy' group, N = 754). Where acute appendicitis was not found, laparoscopy was considered as diagnostic only ('diagnostic laparoscopy' group, N = 133). Other patients with suspected appendicitis underwent diagnostic imaging; US was considered for non-obese patients (N = 83) and CT was indicated for all other patients and those with inconclusive US findings (N = 171).

Diagnosis of acute appendicitis was based on pathological findings of the appendix. Complicated appendicitis was defined by a gangrenous or perforated appendix, as well as presence of an intra-abdominal abscess. Patients with histologically normal appendixes or whose intraoperative findings were that of other pathologies were 'negative' for appendicitis.

Safety: Surgical outcomes, including complications, were recorded for all of the patients who underwent laparoscopy (laparoscopic appendectomy group, and, diagnostic laparoscopy group) and those who underwent CT or US (Table 7).

Table 7 Complications reported by Bachar et al

N (%)	All patients	Laparoscopic appendectomy	Diagnostic laparoscopy	CT	US	*p* value
Complicated appendicitis	94 (10.9)	94 (12.9)	0	29 (17.0)	9 (10.8)	<0.001
Postoperative complications	76 (7.8)	69 (9.2)	7 (5.3%)	20 (11.7)	8 (9.6)	<0.001
Infectious complications	44 (5.0)	41 (5.5)	3 (2.3)	9 (5.3)	6 (7.3)	0.453
Additional surgery	33 (3.7)	28 (3.7)	5 (3.8)	9 (5.3)	6 (5.0)	0.835

CT: computed tomography; US: ultrasound.

The incidence of complicated appendicitis was significantly lower in patients who underwent laparoscopy, compared with those patients who had preoperative CT. Operative time, antibiotic duration and length of hospitalisation were also significantly shorter in patients who underwent laparoscopy compared with CT.

Effectiveness: Overall, younger patients underwent laparoscopy more frequently than CT or US and diagnostic laparoscopy was used more in women than in men. Patients referred for laparoscopy had a shorter time to surgery than those who underwent CT or US. Laparoscopy was 'negative' for appendicitis in 15 per cent (133/887) of patients. Of these, 63 per cent (84/133) had gynaecological pathologies, 20 per cent (26/133) had non-gynaecological pathologies (including mesenteric torsion, diverticulitis, mesenteric lymphadenitis, etc.) and 17 per cent (23/133) had no diagnosis. In the diagnostic laparoscopy group, 45 patients underwent preoperative imaging; their findings are presented in Table 8.

Table 8 Imaging findings prior to laparoscopy

Finding	US group (N = 20)	CT group (N = 25)
Normal pathology	11 (55%)	9 (69%)
Suspected acute appendicitis	4 (20%)	6 (24%)
Suspected non-appendiceal pathology	5 (25%)	9 (36%)
Suspected parasitic infection	NA	1 (4%)

US: ultrasound; CT: computed tomography

The sensitivity and specificity (in complicated appendicitis and in women) of CT was lower than that of laparoscopic appendectomy (Table 9). The sensitivity of CT and US was lower in younger patients (<60 years) compared with laparoscopy. The negative predictive value for patients who underwent laparoscopic appendectomy was higher in all subgroups, except uncomplicated appendicitis.

Table 9 Diagnostic accuracy of laparoscopy and imaging [19]

	CT	US
Overall		
Sensitivity	94%	74%
Specificity	69%	39%
PPV	96%	82%
NPV	58%	28%
Uncomplicated appendicitis		
Sensitivity	90%	66%
Specificity	73%	64%
PPV	90%	71%
NPV	74%	59%
Complicated appendicitis		
Sensitivity	97%	78%
Specificity	13%	37%
PPV	25%	23%
NPV	92%	88%
Sex (male / female)		
Sensitivity	94% / 87%	55% / 69%
Specificity	77% / 72%	100% / 63%
PPV	95% / 86%	100% / 66%
NPV	71% / 74%	17% / 66%
Age (> 60 years / < 60 years)		
Sensitivity	98% / 87%	100% / 64%
Specificity	67% / 74%	50% / 63%
PPV	95% / 88%	80% / 67%
NPV	80% / 73%	100% / 60%

CT: computed tomography; US: ultrasound; PPV: positive predictive value; NPV: negative predictive value.

Leewenburgh et al (2013)[21]

This prospective, multicentre, non-randomised comparative study compared the diagnostic performance of MRI and CT in adult patients with suspected acute appendicitis. Consecutive adults presenting with suspected appendicitis underwent US and CT (when US did not confirm appendicitis). Additional MRI was performed within two hours by an individual blinded to previous imaging results with results presented in four groups:

- Ultrasound, where US results were used only
- 'Conditional CT', where US results were used (when appendicitis was detected) or CT results were used (when the initial US was negative or inconclusive for appendicitis)
- 'Conditional MRI', where US results were used (when appendicitis was detected) or MRI results were used (when the initial US was negative or inconclusive for appendicitis)
- 'Immediate MRI', where MRI results were used only.

A total of 230 patients were included: 229 ultrasounds, 115 CT scans and 223 MRI examinations. Seven patients were unable to undergo MRI due to claustrophobia or unexpected technical failures.

Safety: The authors reported no adverse events occurred during imaging.

Effectiveness: Diagnosis, as determined by an expert panel, identified: 118 patients had acute appendicitis; 87 of these were considered simple appendicitis and 31 had perforated appendicitis. The diagnostic accuracy of the imaging strategies is presented in Table 10.

The specificity and sensitivity of MRI (conditional and immediate) was comparable to that of US and conditional CT. The specificity of conditional MRI was lower than that of immediate MRI (88% versus 93%; p=0.01) but comparable to CT.

Subgroup analyses found no statistically significant differences in the specificity and sensitivity of the various imaging techniques employed; however, the conditional imaging strategies generated more false positives in women than in men. Conditional CT resulted in 17 per cent versus no false positives (p=0.03) and conditional MRI resulted in 19 per cent versus 1 per cent false positives (p=0.04) in women compared with men.

Table 10 Diagnostic performance[21]

	US only	Conditional CT	Conditional MRI	Immediate MRI
All patients (N = 230)	N = 229	N = 230	N = 230	N = 223
Sensitivity	77%	97%	98%	97%
Specificity	94%	91%	88%	93%
Missed appendicitis	23%	3%	2%	3%
False positive	7%	8%	10%	6%
Positive likelihood ratio	12	11	8	15
Negative likelihood ratio	0.25	0.03	0.02	0.04
Men (N = 92)	N = 92	N = 92	N = 92	N = 91
Sensitivity	79%	96%	97%	97%
Specificity	100%	100%	96%	96%
Missed appendicitis	21%	4%	3%	3%
False positive	0%	0%	1%	2%
Positive likelihood ratio			23	23
Negative likelihood ratio	0.21	0.04	0.03	0.03
Women (N = 138)	N = 137	N = 138	N = 138	N = 132
Sensitivity	73%	100%	100%	96%
Specificity	92%	89%	86%	93%
Missed appendicitis	27%	0%	0%	4%
False positive	16%	17%	19%	11%
Positive likelihood ratio	9	9	7	13
Negative likelihood ratio	0.29	0.00	0.00	0.04

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

Park et al (2013)[22]

This non-randomised comparative study retrospectively analysed the medical records of 3,045 patients with acute abdominal pain who underwent diagnostic examination. The diagnostic method used was determined by a senior resident or staff surgeon based on physical examination, surgeon preference and the general condition of the patient. Patients received US (N = 1,777), CT (N = 965) or physical examination only (N = 303). Patients in the CT group were significantly older compared with the US (p<0.01) and physical examination (p<0.01) groups, respectively. Only patients with complete results (i.e. positive or negative imaging result) were included in the final analysis.

Safety: No safety outcomes were reported.

***Effectiveness**:* Imaging results were considered positive, negative or inconclusive for acute appendicitis; the initial and confirmed diagnostic results are reported in Table 11 . The inconclusive result rate was significantly higher in the US group (13.9%) compared with the CT group (3.6%; *p*<0.01).

Table 11 Confirmed appendicitis and initial diagnostic test result in initial 3,045 patients seen[22]

			Confirmed appendicitis	
			Positive	Negative
US (N = 1,777)	Positive	1,101	1,063	38
	Negative	429	10	419
	Inconclusive*	247		
CT (N = 965)	Positive	473	452	21
	Negative	457	17	440
	Inconclusive*	35		
Physical examination (N = 303)	Positive	218	192	86
	Negative	85	2	83

*These patients were excluded. CT: computed tomography; US: ultrasound.

The diagnostic performance of the imaging and non-imaging modalities used to detect acute appendicitis is reported in Table 12. Specificity and positive predictive value for CT was significantly higher when compared to US or physical examination (*p*<0.01). The NAR was significantly lower in the CT group when compared to the US and physical examination groups, respectively (*p* < 0.01).

Table 12 Diagnostic performance of ultrasound, CT and physical examination[22]

	US	CT	Physical examination
Sensitivity	99.1%	96.4%	99.0%
Specificity	91.7%	95.4%	76.1%
PPV	96.5%	95.6%	88.1%
NPV	97.7%	96.3%	97.6%
Negative appendectomy rate	5.2%	4.3%	12.2%

US: ultrasound; CT: computed tomography; PPV: positive predictive value; NPV: negative predictive value.

Economic evaluation

A European randomised controlled trial (RCT) investigating the impact of routine contrast-enhanced CT on treatment costs and the use of hospital resources in patients with acute abdomen was identified.[2] This study randomly assigned 300 patients with acute abdominal pain of unknown cause lasting more than two hours but less than 7-days into one of two groups: a CT group (N = 150) and a selective imaging practice (SIP) group (N = 150). Patients in the CT group underwent contrast-enhanced abdominopelvic CT imaging within 24 hours of admission to the emergency department. Patients in the SIP group underwent imaging according to a surgeon's decision based on clinical assessment.

The final cost analysis included 254 patients (143 in the CT group and 111 in the SIP group). Patients lost to follow-up did not receive the allocated intervention (CT N = 3; SIP N = 7), did not meet inclusion criteria (CT N = 2; SIP N = 4), withdrew consent (CT N = 1; SIP N = 3) or had missing data (CT N = 4; SIP N = 32). There were no significant differences in the treatment groups with regards to age, sex, diagnoses or surgical operation rate. There was a tendency for a lower proportion of non-specific abdominal pain diagnoses in the CT group at discharge, by final diagnosis this difference had reached statistical significance (p=0.043).

The mean total treatment cost per patient who went on to have surgery in the CT group was $5,985[b] (range $2,645-$34,752) compared to $4,114 (range $2,296-$10,051) in the SIP group (p=0.063). There was one case of negative appendectomy in each treatment group. Overall, routine abdominal CT resulted in 57 per cent higher total treatment costs in patients with acute abdominal pain compared with patients who underwent selective imaging

Ongoing research

Searches of clinicaltrials.gov identified four ongoing studies. All of the studies which reported the use of CT to diagnose appendicitis are included. Details of these studies are outlined in Table 13.

Table 13 Ongoing trials

Trial ID Country	Study design	N	Intervention/aim	Primary outcomes	Trial status Estimated completion date
NCT01925014 Korea	RCT	3000	Low-dose versus standard-dose CT to diagnose appendicitis in adolescence and young adults	Negative appendectomy rate	Recruiting April 2016
NCT02742402 Finland	RCT	200	Observation versus CT imaging in early equivocal appendicitis	Appendicitis requiring surgery	Recruiting April 2019

b EUD = 1.53 AUD, currency conversion performed on 8 May 2016, source XE Currency Converter

Trial ID Country	Study design	N	Intervention/aim	Primary outcomes	Trial status Estimated completion date
NCT02533869 Finland	Case series	40	Low-dose CT to diagnose acute uncomplicated appendicitis	Specificity and sensitivity of low-dose CT based on operative and histopathological findings	Recruiting December 2015
NCT02556983 Korea	Case series	30	Determine the lowest CT dose possible to achieve diagnosis of appendicitis	5-grade Likert score for the likelihood of appendicitis	Recruiting September 2017

CT: computed tomography; RCT: randomised controlled trial.

Other issues

The included studies reported their concern with CT-related exposure to ionising radiation. Krajewski et al found CT in adults to be justified if the poorly-defined risks with radiation exposure are considered. Leeuwenburgh et al and Bachar et al suggested MRI or laparoscopy, respectively, may be used in place of CT for reasons including the reduction in radiation exposure.

It is also important to consider the utility of laparoscopy in identifying and treating other causes of acute abdomen. There are some cases, for example in women with right iliac fossa pain, where there is a low threshold for intervention. In these cases surgery is likely to occur despite imaging findings.

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies	5
Total number of Level I studies	2
Total number of Level III studies	3

Search criteria to be used (MeSH terms)

Search terms: computed tomography scan; computed tomography; appendicitis; appendectomy; negative appendectomy rare; negative appendectomy.

Publication date: last 5 years.

Publication type: comparative study/review/clinical trial (where possible).

Date searched

29/03/2016

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