National Institute of Health and Care Excellence

Final

Diverticular disease: diagnosis and management

[G] Evidence review for diagnostic tests for acute diverticulitis

NICE guideline NG147

Diagnostic evidence review

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Final

This evidence review was developed by the National Guideline Centre

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1.1.1 Introduction

For people presenting with suspected acute diverticulitis the majority can be managed in primary care. For this management strategy to be safe and effective there should be guidance on the investigations that need to be performed to support the diagnosis and assess the severity of the acute diverticulitis.

1.2 Review question: For people with suspected acute diverticulitis who are referred for urgent hospital assessment, which investigations are clinically and cost effective (for example full blood count, C-reactive protein (CRP), endoscopy, CT and MRI) in the diagnosis and assessment of acute diverticulitis during and after the acute episode?

1.2.1 Introduction

It is important to identify people with suspected acute diverticulitis early in order to identify who requires medical treatment such as antibiotics or to identify complications that may require surgical intervention. Complications include purulent peritonitis, uncontrolled sepsis, fistula and obstruction. The early use of diagnostic imaging tests may reduce unnecessary treatments or improve patient outcomes through early appropriate intervention. The purpose of this review is to identify the most clinically and cost effective strategies.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of diagnostic accuracy review question

Population	3.2 – Adults 18 years and over with suspected acute diverticulitis who are not referred for urgent hospital assessment, during and after the acute episode. 3.3 – Adults 18 years and over with suspected acute diverticulitis who are referred for urgent hospital assessment, during and after the acute episode.
Target condition	Acute diverticulitis
Index tests	• Full blood count • C-reactive protein (CRP) • Endoscopy

	• MRI • Ultrasound • CT colonoscopy • CT • Combination of above
Reference standard	• CT • Pathologically/surgically confirmed
Statistical measures	• Sensitivity • Specificity • Positive Predictive Value (PPV) • Negative Predictive Value (NPV) • Receiver Operating Characteristic (ROC) curve or area under curve • Relative risk (RR)
Study design	Cohort studies Cross-sectional studies

Table 2: PICO characteristics of diagnostic test and treat review question

Population	3.2 – Adults 18 years and over with suspected acute diverticulitis who <u>are not</u> referred for urgent hospital assessment, during and after the acute episode. 3.3 – Adults 18 years and over with suspected acute diverticulitis who <u>are</u> referred for urgent hospital assessment, during and after the acute episode.
Interventions	Index test considerations: • Full blood count • C-reactive protein (CRP) • Endoscopy • MRI • Ultrasound • CT colonoscopy • CT • Combination of above Treatment: • Any appropriate treatment for diverticulitis as long as it is the same in all arms of the study.
Comparisons	• Each other

Outcomes	<u>Critical outcomes</u>:
	• Progression of disease
	• Hospitalisation
	• Need for surgery
	• Complications (infections, abscesses, perforation)
	• Recurrence rates of acute diverticulitis (minimum 1year)
	• Quality of life
	
	<u>Important outcomes:</u>
	• Mortality
	• Symptom control (pain relief)
	• Side effects of
	  ○ Antibiotics: nausea and vomiting, diarrhoea, infections related to antibiotics
	  ○ Analgesics: nausea and vomiting, constipation

1.4 Clinical evidence

1.4.1 Included studies

A search was conducted for prospective and retrospective cohort studies assessing the diagnostic accuracy of tests to identify whether the condition is present (as indicated by the reference standard CT scan) in people under investigation for acute diverticulitis.

Five studies were included in the review on adults with suspected acute diverticulitis who are referred for urgent hospital assessment, during and after the acute episode (3.3)[5, 6, 36 59, 74]; these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

No studies were identified for the review on adults with suspected acute diverticulitis who are not referred for urgent hospital assessment, during and after the acute episode (3.2).

No diagnostic RCTs were identified for this review.

See also the study selection flow chart in appendix C and study evidence tables in appendix D.

1.4.2 Excluded studies

See the excluded studies list in appendix H.

1.4.3 Summary of clinical studies included in the evidence review

Table 3: Summary of studies included in the evidence review

Study	Population	Target condition	Index test	Reference standard	Comments
Ambrosetti 2000[5]	Patients presenting at emergency centre with a history and clinical findings suggestive of acute colonic diverticulitis underwent CT. (n=420)	Acute diverticulitis	CT scan	Surgically confirmed diagnosis	A subset of patients with a CT diagnosis had the diagnosis confirmed or rejected following surgery (n=136).
Andeweg 2011[6]	Adult patients who were hospitalized with acute abdominal pain and who did not require immediate surgery. (n=307)	Acute diverticulitis	C-reactive protein Leukocyte count	CT scan	Computed tomography was used as gold standard for diagnosis, in case of non-operative management. Pathology and operative reports were used as gold standard in case of operative management.
Jamal Talabani 2017[36]	All patients older than 18 years, who were admitted with acute abdominal pain with duration of less than 1 week. (n=833)	Acute diverticulitis	C-reactive protein Leukocyte count	CT scan	Acute diverticulitis was confirmed by CT scan in 83 of 95 patients. Five patients with recurrent acute diverticulitis had a recent CT verifying acute diverticulitis, and five had their diagnosis confirmed by an ambulant CT scan or colonoscopy after discharge. Discharge diagnosis based on clinical examination and laboratory tests occurred twice.

Study	Population	Target condition	Index test	Reference standard	Comments
Nielson 2014[59]	Patients admitted with CT proven left-sided colonic diverticulitis. (n=123)	Acute diverticulitis (uncomplicated and complicated)	Ultrasound	CT scan	Specificity, PPV and NPV could not be measured; only patients with CT confirmed diverticulitis were included in analysis.
Steffanson 1997[74]	All patients with acute abdominal disease referred to emergency hospital. (n=88)	Acute diverticulitis	CT Full blood test, elevated in one of: • WBC >9x10^9/l • ESR elevated • CRP ≥10mg/l	Laparoscopy	A subset of patients with a CT diagnosis confirmed or rejected following laparoscopy (n=30).

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 4: Clinical evidence summary: diagnostic test accuracy for index test computed tomography

Index Test	Reference standard	Number of studies	n	Quality	Sensitivity	Specificity	PPV	NPV
CT	Surgically confirmed diagnosis	1	136	MODERATE[a] due to risk of bias	98%	NA[b]	97%	NA
CT	Surgically confirmed diagnosis	1	30	MODERATE[a] due to risk of bias	65%	100%	100%	NA

(a) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.
(b) There was insufficient data to calculate specificity.

Table 5: Clinical evidence summary: diagnostic test accuracy for index test ultrasound

Index Test	Reference standard	Number of studies	n	Quality	Sensitivity	Specificity	PPV	NPV
US	CT	1	123	MODERATE[a] due to risk of bias	76%	NA	NA	NA
	CT		94 (uncomplicated)	MODERATE[a] due to risk of bias	83%	NA	NA	NA
	CT		29 (complicated)	MODERATE[a] due to risk of bias	23%	NA	NA	NA

(a) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.

Table 6: Clinical evidence summary: diagnostic test accuracy for index test full blood test

Index Test	Reference standard	Number of studies	n	Quality	Sensitivity	Specificity	PPV	NPV
Blood test	CT	1	30	MODERATE[a] due to risk of bias	95%	50%	79%	NA

(a) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.

Table 7: Clinical evidence summary: diagnostic test accuracy for index test white blood cell count

Index Test	Reference standard	Number of studies	n	Quality	AUC (95% CI)
Leukocyte count	CT	1	307	MODERATE[a] due to risk of bias	0.61 (0.54-0.65)
Leukocyte count	CT	1	833	LOW[ab] due to risk of bias, indirectness	0.59 (0.53-0.65)

(a) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.
(b) Indirectness was assessed using the QUADAS-2 checklist items referring to applicability. The evidence was downgraded by 1 increment if the majority of studies were seriously indirect, and downgraded by 2 increments if the majority of studies are very seriously indirect.

Table 8: Clinical evidence summary: diagnostic test accuracy for index test C - reactive protein.

Index Test	Reference standard	Number of studies	n	Quality	AUC (95% CI)
C-Reactive Protein	CT	1	307	MODERATE[a] due to risk of bias	0.63 (0.57-0.69)
C-Reactive Protein	CT	1	833	LOW[ab] due to risk of bias, indirectness	0.83 (0.80-0.86)

(a) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.
(b) Indirectness was assessed using the QUADAS-2 checklist items referring to applicability. The evidence was downgraded by 1 increment if the majority of studies were seriously indirect, and downgraded by 2 increments if the majority of studies are very seriously indirect

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified.

1.5.2 Excluded studies

No health economic studies that were relevant to these questions were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix E.

1.5.3 Health economic modelling

An original **cost analysis** was conducted that compared for people with suspected severe or complicated diverticulitis:

- IV antibiotics (5 days) and no CT
- Initial IV antibiotics (2 days) and CT. Then, if uncomplicated, switch to oral antibiotics, monitor in-hospital for one day and then discharge with oral antibiotics
- Initial IV antibiotics (2 days) and CT. Then discharge with no antibiotics if uncomplicated.

Full details of the analysis can be found in a separate report (Appendix 1 of the guideline).The cost analysis employed a simple decision tree that differentiated patients according to their pathology and whether or not they were readmitted.

Model inputs were sourced as follows:

- Prevalence of complicated diverticulitis – a cohort of 3,222 patients admitted with diverticulitis.[9]
- Readmission rates – a trial of 528 patients with uncomplicated diverticulitis randomised to receive oral antibiotics or no antibiotics[24]
- Unit costs of hospitalisation and imaging – NHS reference costs[25]
- Unit cost of drugs – NHS electronic drug tariff[56] and British National Formulary[39]
- Other costs – Personal Social Services Research Unit[22], NHS supplies catalogue[57] and Committee members.

Table 9: Base case analysis results

	Mean cost					
Strategy	**CT**	**IV antibiotics**	**Oral antibiotics**	**Hospital stay**	**Re-hospitalisation**	**Total**
CT & no antibiotics	£106	£97	£0	£695	£684	£1,582
CT & oral antibiotics	£106	£97	£6	£949	£357	£1,514
IV antibiotics	£0	£208	£0	£1,456	£357	£2,021
CT&No vs IV	£106	-£111	£0	-£761	£327	-£439
CT&Oral vs IV	£106	-£111	£6	-£507	£0	-£507

CT and then oral antibiotics was the lowest cost strategy, followed by ‘CT and then no antibiotics’ - Table 9. This finding was robust to sensitivity analysis, with the cost savings compared with continued intravenous therapy ranging from £150 to £688 per patient. The

only scenario that 'CT and then no antibiotics' was lowest cost was when we used a lower cost of rehospitalisation. The only time that the IV antibiotics strategy was lowest cost was when we used a high estimate of the cost of readmission and made the extreme assumption that there would be no readmissions in the IV antibiotics arm.

1.5.4 Unit costs

The committee considered the direct access and outpatient unit costs of the investigations under consideration, noting that many of the investigations have high unit costs. The current national average direct access cost of a post-contrast CT scan is £106, while diagnostic colonoscopy as a day case currently costs £548 and as a gastroenterology outpatient costs £277. By contrast, the current unit costs of direct access pathology services are £3 for haematology (full blood count) and £1.13 for clinical biochemistry (C-reactive protein).

Table 10: UK costs of outpatient diagnostic tests

Currency Description	Unit Cost
RD21A Computerised Tomography Scan of One Area, with Post-Contrast Only, 19 years and over	£97
RD20A Computerised Tomography Scan of One Area, without Contrast, 19 years and over	£86
DAPS05 Full blood count (Directly-accessed pathology services: Haematology)	£3
DAPS04 C-reactive protein (Directly-accessed pathology services: Clinical Biochemistry)	£1.13
RD02A Magnetic Resonance Imaging Scan, One Area, Post-Contrast only, 19 years and over	£159
RD01A Magnetic Resonance Imaging Scan, One Area, No Contrast, 19 years and over	£139
FE32Z Diagnostic colonoscopy, 19 years and over, gastroenterology outpatient)	£277
FE32Z Diagnostic colonoscopy, 19 years and over, colorectal surgery outpatient)	£469
FE32Z Diagnostic colonoscopy, 19 years and over, upper gastrointestinal surgery outpatient)	£767
CT colonoscopy (RD28Z complex computerised tomography scan)	£148
FE35Z Diagnostic flexible sigmoidoscopy, 19 years and over, gastroenterology outpatient	£175
FE35Z Diagnostic flexible sigmoidoscopy, 19 years and over, colorectal surgery outpatient	£169
FE35Z Diagnostic flexible sigmoidoscopy, 19 years and over, upper gastrointestinal surgery outpatient	£222

Source: NHS Reference Costs, 2016-2017

Table 11: UK costs of direct access (GP referral) diagnostic tests

Currency Description	Unit Cost
RD21A Computerised Tomography Scan of One Area, with Post-Contrast Only, 19 years and over	£106
RD20A Computerised Tomography Scan of One Area, without Contrast, 19 years and over	£83
DAPS05 Full blood count (Directly-accessed pathology services: Haematology)	£3
DAPS04 C-reactive protein (Directly-accessed pathology services: Clinical Biochemistry)	£1.13
RD02A Magnetic Resonance Imaging Scan, One Area, Post-Contrast only, 19 years and over	£202
RD01A Magnetic Resonance Imaging Scan, One Area, No Contrast, 19 years and over	£135

Currency Description	Unit Cost
FE32Z Diagnostic colonoscopy, 19 years and over, non-elective short stay	£622
FE32Z Diagnostic colonoscopy, 19 years and over, day case	£548
CT colonoscopy (RD28Z complex computerised tomography scan)	£121
FE35Z Diagnostic flexible sigmoidoscopy, 19 years and over, non-elective short stay	£530
FE35Z Diagnostic flexible sigmoidoscopy, 19 years and over, day case	£415

Source: NHS Reference Costs, 2016-2017

1.6 Evidence statements

1.6.1 Clinical evidence statements

Review for people with suspected acute diverticulitis who are not referred for urgent hospital assessment : No published evidence was identified for this review.

Review For people with suspected acute diverticulitis who are not referred for urgent hospital assessment: Five studies that evaluated 4 diagnostic tests for identifying and assessing acute diverticulitis were included in the review. The quality of evidence ranged from Moderate to Low quality. Evidence was identified for the following diagnostic tests CT, ultrasound, full blood test and CRP, of which good sensitivity of 98% was identified for CT from 1 study (n=136), 95% for full blood from 1 study (n=30) and 83% for ultrasound within a subgroup with uncomplicated acute diverticulitis from 1 study(n=94). One study (n=833) demonstrated a good AUC value of 0.83 (0.80-0.86) for CRP. However, evidence obtained from one other included study reported a lower specificity value of 65% for CT (n=30) and the specificity of ultrasound in a subgroup with complicated acute diverticulitis was much lower (23% specificity) compared with the uncomplicated acute diverticulitis subgroup. Similarly, a lower AUC value of 0.63 (0.57-0.69) was reported by another study (n=307) assessing CRP. Additionally, two studies reported relatively low AUC values of 0.61 (0.54-0.65; n=307) and 0.59 (0.53-0.65; n=833) for leukocyte count as a diagnostic test.

1.6.2 Health economic evidence statements

- An original cost analysis found that 'CT then discharge with oral antibiotics if uncomplicated' was cost saving for people with suspected severe or complicated diverticulitis compared to both
  - 'No CT and intravenous antibiotics'; and
  - 'CT then discharge with no antibiotics if uncomplicated'

This was rated as partially applicable with minor limitations.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The diagnostic measures that matter most

Diagnostic accuracy for tests to diagnose acute diverticulitis was the outcome for this review. Sensitivity was considered important by the committee for this review question because a clinical decision rule should select all patients with suspected acute diverticulitis for conservative therapy and possible surgery. The consequences of missing a patient with

acute diverticulitis would have serious health implications, and could result in an increased length of hospital stay during acute episodes.

No evidence was identified for the diagnostic accuracy of endoscopy, MRI, ultrasound, or CT colonoscopy.

1.7.1.2 The quality of the evidence

The quality of evidence ranged from very low to low. This was mostly due to flow and timing bias, resulting in a high risk of bias rating.

Outcomes were downgraded if there was an inappropriate amount of time between the reference test and the index test, such as when a person received a CT diagnosis and then underwent surgery at a later date following secondary complications. Outcomes were also downgraded where they included an indirect population or reported an indirect outcome, including where the reference standard was not consistent across the study population.

1.7.1.3 Benefits and harms

The committee considered the trade-off between using a less costly clinical test such as full blood count and CRP test to inform the decision making and selection of patients for further investigation for acute diverticulitis (and therefore to minimize the impact of a false negative result) and also to reduce radiation risk of imaging patients who do not have any inflammation. Inflammatory markers, commonly the White Blood Cell (WBC) count and C-Reactive Protein (CRP) level, are frequently employed to assist in diagnosing diverticulitis and its complications.

The committee also considered the accuracy and utility of a CT scan to correctly diagnose acute diverticulitis. The committee acknowledged that the one study included in this review assessing the diagnostic accuracy of CT scan showed a high sensitivity and positive predictive value. It was noted that the population from this study were those who were more severely unwell and required surgery, meaning the diagnosis in this population would likely be more clear-cut than would be typical in people with acute diverticulitis.

The committee agreed that CT is recognised as the most effective tool at diagnosing acute diverticulitis, particularly given its capacity to be performed during or shortly after an acute episode. The committee highlighted that endoscopy and CT colonoscopy should not be performed until ~6-8 weeks after an acute episode to prevent risk of perforation of the inflamed tissue and that there was evidence that in the setting of a high quality CT scan this may not be required. CT evaluates the severity and extent of disease and indicates what further treatment is required. Importantly its rules out other causes of the symptoms.

The committee also considered the radiation risks associated with CT scans. Given the condition’s prevalence in older people, the committee felt the increased risk of cancer with radiation exposure was negligible. The committee did agree that pregnant women should not be exposed to the radiation from CT scans, and so should be offered alternative methods of diagnosis such as MRI or ultrasound.

1.7.2 Cost effectiveness and resource use

Diagnostic pathway by setting

The proportion of people requiring emergency surgery for acute diverticulitis is small and the majority of people are managed conservatively with or without antibiotics.

No clinical or economic evidence was identified for investigations in the primary care setting. The committee felt that current practice is to prescribe a course of oral antibiotics to those

who do not require urgent referral for hospital assessment or sometimes there may be a period of watchful waiting before an antibiotic is prescribed. Where no improvement is seen or the condition deteriorates, the person with suspected acute diverticulitis is reassessed and considered for referral to secondary care.

No health economic evidence was identified for investigations for acute diverticulitis in people who are urgently referred for hospital assessment. In the absence of economic evidence, the low to very low quality clinical evidence for CT, full blood count and C-reactive protein was interpreted alongside the unit costs of the interventions to enable the committee to make qualitative judgements of cost effectiveness.

Imaging

In Chapter H, the committee concluded switching from intravenous to less expensive oral antibiotics and early discharge is safe for people with uncomplicated diverticulitis.

An original cost analysis was conducted that compared for people with suspected severe or complicated diverticulitis

- IV antibiotics and no CT
- Initial IV antibiotics and CT. Then discharge with oral antibiotics if uncomplicated
- Initial IV antibiotics and CT. Then discharge with no antibiotics if uncomplicated

The lowest cost strategy was ‘CT and then discharge with oral antibiotics if uncomplicated’ due to the reduced hospital stay and other cost savings. Discharging with no antibiotics was more costly because of the increased rehospitalisation observed in the clinical review (albeit not statistically significant). These results were robust to sensitivity analysis.

Therefore the committee recommended that patients should receive a CT, as it is diagnostic and likely to be cost saving.

The committee noted that obtaining CT scans during the acute episode might also reduce the number of colonoscopies carried out downstream, which would mean even greater cost savings. The model did not include the cost of antimicrobial resistance but this too would favour the use of CT to step down or cease antibiotics use.

In current practice, the committee believe that about 60% of 15,000 emergency admissions for acute diverticulitis currently receive CT scans. Obtaining CT scans in this population is currently dependent on availability, time of day and severity of the condition. In recommending that CT scans be offered for suspected acute diverticulitis, the committee acknowledged that there might be a significant resource impact, as it anticipates an increase in the number of people requiring scans. However, the cost analysis suggests that this would be more than offset by cost savings from reduced nurse time and hospital bed days.

No clinical or economic evidence was identified for MRI or ultrasound. The committee noted that the use of MRI and ultrasound is current practice only in pregnancy or if contrast CT is contraindicated. Imaging and oral antibiotics was still cost saving when we assumed the cost of an MRI in the analysis instead of CT.

Blood tests

The committee believes that the measurement of electrolytes and a full blood count is current practice and that C-reactive protein is regularly carried out, but is not yet universal. In the hospital setting, the results of the tests can be available after around an hour. No evidence was identified which described the effectiveness and cost effectiveness of white blood cell count and C-reactive protein as risk stratification tools to determine whether CT scans should be carried out. However, the committee felt that the cost of these tests is small and normal results can mean that a CT scan is not needed and therefore it likely that these tests are cost effective.

1.7.3 Other factors the committee took into account

The committee noted that initial urea and electrolyte tests at admission should be carried out ahead of any anticipated CT to assess renal function and guide CT with relation to user needs. Subsequent non-contrast CT can be carried out if necessary.

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Appendices

Appendix A: Review protocols

Table 12: Review protocol: diagnosis of acute diverticulitis

Field	Content
Review question	What is the diagnostic accuracy and cost effectiveness of tests to diagnose acute diverticulitis?
Type of review question	Diagnostic review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
Objective of the review	To determine which test is the most accurate to diagnose acute diverticulitis.
Eligibility criteria – population / disease / condition / issue / domain	Adults 18 years and over with suspected acute diverticulitis who are not referred for urgent hospital assessment, during and after the acute episode.
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	• Full blood count • C-reactive protein (CRP) • Endoscopy • MRI • Ultrasound • CT colonoscopy • CT • • Combination of the above
Eligibility criteria – comparator(s) / control or reference (gold) standard	Gold/reference) standard: CT Pathologically/surgically confirmed
Outcomes and prioritisation	Statistical measure to detecting diverticular disease: • Sensitivity • Specificity • Positive Predictive Value (PPV) • Negative Predictive Value (NPV) • Receiver Operating Characteristic (ROC) curve or area under curve • Relative risk (RR)
Eligibility criteria – study design	Cohort studies Cross-sectional studies
Other inclusion exclusion criteria	Exclusions: • Children and young people aged 17 years and younger • Prevention
Proposed sensitivity / subgroup analysis, or meta-regression	Strata: Subgroups: • Age: <50 and >50 years • people of Asian family origin as they are known to develop right-

	sided diverticula
Selection process – duplicate screening / selection / analysis	Studies are sifted by title and abstract. Potentially significant publications obtained in full text are then assessed against the inclusion criteria specified in this protocol.
Data management (software)	• The methodological quality of each study outcome will be assessed using the adjusted QUADAS checklist. • Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5). • GRADEpro used to assess the quality of evidence for each outcome • Bibliographies, citations and study sifting managed using EndNote • Data extractions performed using EviBase, a platform designed and maintained by the National Guideline Centre (NGC)
Information sources – databases and dates	Medline, Embase, The Cochrane Library
Identify if an update	Not applicable
Author contacts	https://www.nice.org.uk/guidance/conditions-and-diseases/digestive-tract-conditions/diverticular-disease
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report (Chapter R) for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by James Dalrymple in line with section 3 of Developing NICE guidelines: the manual.

	Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 13: Review protocol: diagnosis of acute diverticulitis

Field	Content
Review question	What is the diagnostic accuracy and cost effectiveness of tests to diagnose acute diverticulitis?
Type of review question	Diagnostic review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
Objective of the review	To determine which test is the most accurate to diagnose acute diverticulitis.
Eligibility criteria – population / disease / condition / issue / domain	Adults 18 years and over with suspected acute diverticulitis who are referred for urgent hospital assessment, during and after the acute episode.
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	• Full blood count • C-reactive protein (CRP) • Endoscopy • MRI • Ultrasound • CT colonoscopy • CT • Combination of the above
Eligibility criteria – comparator(s) / control or reference (gold) standard	Gold/reference) standard: CT Pathologically/surgically confirmed
Outcomes and prioritisation	Statistical measure to detecting diverticular disease: • Sensitivity • Specificity • Positive Predictive Value (PPV) • Negative Predictive Value (NPV) • Receiver Operating Characteristic (ROC) curve or area under curve • Relative risk (RR)
Eligibility criteria – study design	Cohort studies Cross-sectional studies
Other inclusion	Exclusions:

exclusion criteria	• Children and young people aged 17 years and younger • Prevention
Proposed sensitivity / subgroup analysis, or meta-regression	Subgroups: • Age: <50 and >50 years • people of Asian family origin as they are known to develop right-sided diverticula
Selection process – duplicate screening / selection / analysis	Studies are sifted by title and abstract. Potentially significant publications obtained in full text are then assessed against the inclusion criteria specified in this protocol.
Data management (software)	• The methodological quality of each study outcome will be assessed using the adjusted QUADSAS checklist. • Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5). • GRADEpro used to assess the quality of evidence for each outcome • Bibliographies, citations and study sifting managed using EndNote • Data extractions performed using EviBase, a platform designed and maintained by the National Guideline Centre (NGC)
Information sources – databases and dates	Medline, Embase, The Cochrane Library
Identify if an update	Not applicable
Author contacts	https://www.nice.org.uk/guidance/conditions-and-diseases/digestive-tract-conditions/diverticular-disease
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report (Chapter R) for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.

Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by James Dalrymple in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 14: Health economic review protocol

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[54] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'.
- Studies published before 2002 will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well

described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 15: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 13 November 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 13 November 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2018 Issue 11 of 12 CENTRAL to 2018 Issue 11 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 of 4	None

Table 16: Medline (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter/
4.	editorial/
5.	news/
6.	exp historical article/
7.	Anecdotes as Topic/
8.	comment/
9.	case report/
10.	(letter or comment*).ti.
11.	or/3-10
12.	randomized controlled trial/ or random*.ti,ab.
13.	11 not 12
14.	animals/ not humans/
15.	exp Animals, Laboratory/
16.	exp Animal Experimentation/
17.	exp Models, Animal/
18.	exp Rodentia/
19.	(rat or rats or mouse or mice).ti.
20.	or/13-19
21.	2 not 20
22.	randomized controlled trial.pt.
23.	controlled clinical trial.pt.
24.	randomi#ed.ti,ab.
25.	placebo.ab.

26.	randomly.ti,ab.
27.	Clinical Trials as topic.sh.
28.	trial.ti.
29.	or/22-28
30.	Meta-Analysis/
31.	exp Meta-Analysis as Topic/
32.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
33.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
34.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
35.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
36.	(search* adj4 literature).ab.
37.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
38.	cochrane.jw.
39.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
40.	or/50-59
41.	Epidemiologic studies/
42.	Observational study/
43.	exp Cohort studies/
44.	(cohort adj (study or studies or analys* or data)).ti,ab.
45.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
46.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
47.	Controlled Before-After Studies/
48.	Historically Controlled Study/
49.	Interrupted Time Series Analysis/
50.	(before adj2 after adj2 (study or studies or data)).ti,ab.
51.	or/30-39
52.	exp case control study/
53.	case control*.ti,ab.
54.	or/41-42
55.	40 or 43
56.	Cross-sectional studies/
57.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
58.	or/45-46
59.	40 or 47
60.	40 or 43 or 47
61.	21 and (29 or 40 or 60)

Table 17: Embase (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter.pt. or letter/
4.	note.pt.
5.	editorial.pt.

6.	case report/ or case study/
7.	(letter or comment*).ti.
8.	or/3-7
9.	randomized controlled trial/ or random*.ti,ab.
10.	8 not 9
11.	animal/ not human/
12.	nonhuman/
13.	exp Animal Experiment/
14.	exp Experimental Animal/
15.	animal model/
16.	exp Rodent/
17.	(rat or rats or mouse or mice).ti.
18.	or/10-17
19.	2 not 18
20.	random*.ti,ab.
21.	factorial*.ti,ab.
22.	(crossover* or cross over*).ti,ab.
23.	((doubl* or singl*) adj blind*).ti,ab.
24.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
25.	crossover procedure/
26.	single blind procedure/
27.	randomized controlled trial/
28.	double blind procedure/
29.	or/20-28
30.	systematic review/
31.	meta-analysis/
32.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
33.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
34.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
35.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
36.	(search* adj4 literature).ab.
37.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
38.	cochrane.jw.
39.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
40.	or/30-39
41.	Clinical study/
42.	Observational study/
43.	family study/
44.	longitudinal study/
45.	retrospective study/
46.	prospective study/
47.	cohort analysis/
48.	follow-up/

49.	cohort*.ti,ab.
50.	48 and 49
51.	(cohort adj (study or studies or analys* or data)).ti,ab.
52.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
53.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
54.	(before adj2 after adj2 (study or studies or data)).ti,ab.
55.	or/41-47,50-54
56.	exp case control study/
57.	case control*.ti,ab.
58.	or/56-57
59.	55 or 58
60.	cross-sectional study/
61.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
62.	or/60-61
63.	55 or 62
64.	55 or 58 or 62
65.	19 and (29 or 40 or 64)

Table 18: Cochrane Library (Wiley) search terms

#1.	diverticul*.mp.

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to Diverticular Disease population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 19: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1946 – 13 November 2018	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Embase	1974 – 13 November 2018	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 13 November 2018 NHSEED - Inception to March 2015	None

Table 20: Medline (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter/
4.	editorial/
5.	news/
6.	exp historical article/
7.	Anecdotes as Topic/
8.	comment/
9.	case report/
10.	(letter or comment*).ti.
11.	or/3-10
12.	randomized controlled trial/ or random*.ti,ab.
13.	11 not 12
14.	animals/ not humans/
15.	exp Animals, Laboratory/
16.	exp Animal Experimentation/
17.	exp Models, Animal/
18.	exp Rodentia/
19.	(rat or rats or mouse or mice).ti.
20.	or/13-19
21.	2 not 20
22.	Economics/
23.	Value of life/
24.	exp "Costs and Cost Analysis"/
25.	exp Economics, Hospital/
26.	exp Economics, Medical/
27.	Economics, Nursing/
28.	Economics, Pharmaceutical/
29.	exp "Fees and Charges"/
30.	exp Budgets/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/22-37
39.	exp models, economic/
40.	*Models, Theoretical/
41.	markov chains/
42.	monte carlo method/

43.	exp Decision Theory/
44.	(markov* or monte carlo).ti,ab.
45.	econom* model*.ti,ab.
46.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
47.	Models, Organizational/
48.	*models, statistical/
49.	*logistic models/
50.	models, nursing/
51.	((organi?ation* or operation* or service* or concept*) adj3 (model* or map* or program* or simulation* or system* or analys*)).ti,ab.
52.	(econom* adj2 (theor* or system* or map* or evaluat*)).ti,ab.
53.	(SSM or SODA).ti,ab.
54.	(strateg* adj3 (option* or choice*) adj3 (analys* or decision*)).ti,ab.
55.	soft systems method*.ti,ab.
56.	(Meta-heuristic* or Metaheuristic*).ti,ab.
57.	(dynamic* adj2 (model* or system*)).ti,ab.
58.	(simulation adj3 (model* or discrete event* or agent)).ti,ab.
59.	(microsimulation* or "micro* simulation*").ti,ab.
60.	((flow or core) adj2 model*).ti,ab.
61.	(data adj2 envelopment*).ti,ab.
62.	system* model*.ti,ab.
63.	or/41-64
64.	quality-adjusted life years/
65.	sickness impact profile/
66.	(quality adj2 (wellbeing or well being)).ti,ab.
67.	sickness impact profile.ti,ab.
68.	disability adjusted life.ti,ab.
69.	(qal* or qtime* or qwb* or daly*).ti,ab.
70.	(euroqol* or eq5d* or eq 5*).ti,ab.
71.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
72.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
73.	(hui or hui1 or hui2 or hui3).ti,ab.
74.	(health* year* equivalent* or hye or hyes).ti,ab.
75.	discrete choice*.ti,ab.
76.	rosser.ti,ab.
77.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
78.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
79.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
80.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
81.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
82.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
83.	or/22-40
84.	21 and (38 or 63 or 83)

Table 21: Embase (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter.pt. or letter/
4.	note.pt.
5.	editorial.pt.
6.	case report/ or case study/
7.	(letter or comment*).ti.
8.	or/3-7
9.	randomized controlled trial/ or random*.ti,ab.
10.	8 not 9
11.	animal/ not human/
12.	nonhuman/
13.	exp Animal Experiment/
14.	exp Experimental Animal/
15.	animal model/
16.	exp Rodent/
17.	(rat or rats or mouse or mice).ti.
18.	or/10-17
19.	2 not 18
20.	Economics/
21.	Value of life/
22.	exp "Costs and Cost Analysis"/
23.	exp Economics, Hospital/
24.	exp Economics, Medical/
25.	Economics, Nursing/
26.	Economics, Pharmaceutical/
27.	exp "Fees and Charges"/
28.	exp Budgets/
29.	budget*.ti,ab.
30.	cost*.ti.
31.	(economic* or pharmaco?economic*).ti.
32.	(price* or pricing*).ti,ab.
33.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
34.	(financ* or fee or fees).ti,ab.
35.	(value adj2 (money or monetary)).ti,ab.
36.	or/20-35
37.	statistical model/
38.	*theoretical model/
39.	nonbiological model/

40.	stochastic model/
41.	decision theory/
42.	decision tree/
43.	exp nursing theory/
44.	monte carlo method/
45.	(markov* or monte carlo).ti,ab.
46.	econom* model*.ti,ab.
47.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
48.	((organi?ation* or operation* or service* or concept*) adj3 (model* or map* or program* or simulation* or system* or analys*)).ti,ab.
49.	(econom* adj2 (theor* or system* or map* or evaluat*)).ti,ab.
50.	(SSM or SODA).ti,ab.
51.	(strateg* adj3 (option* or choice*) adj3 (analys* or decision*)).ti,ab.
52.	soft systems method*.ti,ab.
53.	(Meta-heuristic* or Metaheuristic*).ti,ab.
54.	(dynamic* adj2 (model* or system*)).ti,ab.
55.	(simulation adj3 (model* or discrete event* or agent)).ti,ab.
56.	(microsimulation* or "micro* simulation*").ti,ab.
57.	((flow or core) adj2 model*).ti,ab.
58.	(data adj2 envelopment*).ti,ab.
59.	system* model*.ti,ab.
60.	or/39-61
61.	quality adjusted life year/
62.	"quality of life index"/
63.	short form 12/ or short form 20/ or short form 36/ or short form 8/
64.	sickness impact profile/
65.	(quality adj2 (wellbeing or well being)).ti,ab.
66.	sickness impact profile.ti,ab.
67.	disability adjusted life.ti,ab.
68.	(qal* or qtime* or qwb* or daly*).ti,ab.
69.	(euroqol* or eq5d* or eq 5*).ti,ab.
70.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
71.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
72.	(hui or hui1 or hui2 or hui3).ti,ab.
73.	(health* year* equivalent* or hye or hyes).ti,ab.
74.	discrete choice*.ti,ab.
75.	rosser.ti,ab.
76.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
77.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
78.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
79.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.

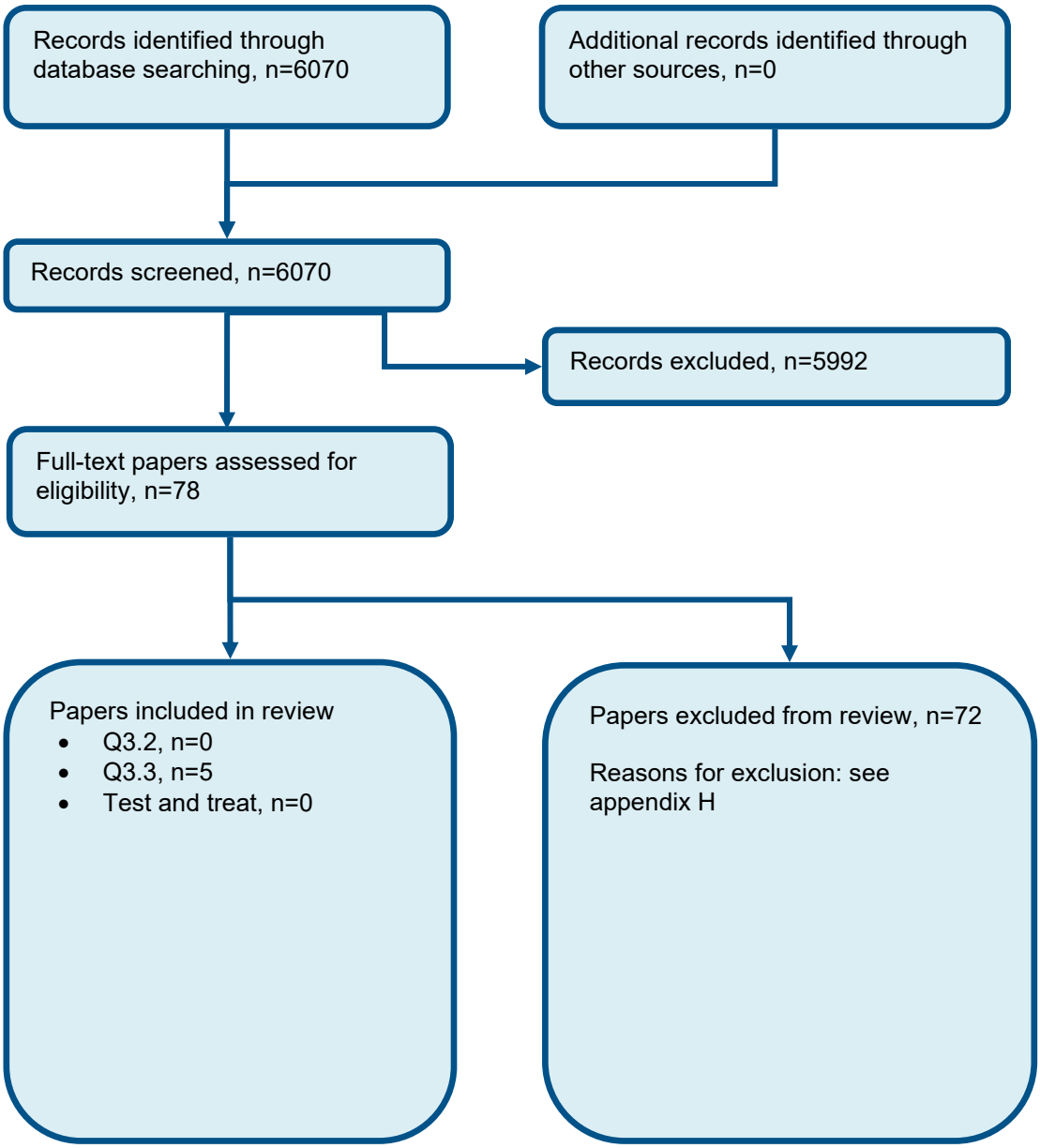
80.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
81.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
82.	or/20-40
83.	19 and (36 or 60 or 82)

Table 22: NHS EED and HTA (CRD) search terms

#1.	diverticul*

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection f or the review of diagnosis of acute diverticulitis



Appendix D: Clinical evidence tables

Table 23: Clinical evidence tables

Reference	Ambrosetti 2000[5]
Study type	Cohort
Study methodology	Data source/recruitment: all patients presenting for the first time at the authors emergency centre with a history and clinical findings suggestive of acute colonic diverticulitis underwent CT and a water soluble contrast enema. A subset of patients with a CT diagnosis indicating acute colonic diverticulitis had the diagnosis confirmed or rejected following surgery.
Number of patients	n = 420 (136 had CT diagnosis and later underwent surgery)
Patient characteristics	Median age (range): 63 years (24-94) Gender (male to female ratio): 201/219 Country: Switzerland Inclusion criteria: patients presenting with a history and clinical findings suggestive of acute colonic diverticulitis Exclusion criteria: not reported
Target condition(s)	Diverticulitis
Index test(s) and reference standard	Index test CT scan Reference standard Surgically confirmed diagnosis Time between measurement of index test and reference standard: NA – 38/134 patients were operated on during first hospital stay, 94 operated later on for secondary complications.

Reference	**Ambrosetti 2000[5]**
Statistical measures	Index text Outcome / Positive / Negative Test – Positive: True positives 130; False positives 4; PPV 97% Test – Negative: False Negative 2; True negative NA; NPV NA Sensitivity: 98%; Specificity: NA 2 patients with a negative CT diagnosis were operated on following complications, showing a false negative diagnosis.
Source of funding	No funding received
Limitations	Risk of bias: High – flow and timing Indirectness: none
Comments	Specificity could not be measured; only patients undergoing surgery could confirm index test diagnosis.

Reference	**Andeweg 2011[6]**
Study type	Cohort
Study methodology	Data source: medical records and CT scan results of adult patients who were hospitalized with acute abdominal pain and who did not require immediate surgery. Recruitment: selection based on the abdominal CT request forms.
Number of patients	n = 307
Patient characteristics	Age (n) <40 years: 57 41-70 years: 175 >71 years: 55

Reference	Andeweg 2011[6]
	Gender (male to female ratio):110/177 Country: The Netherlands Inclusion criteria: suspected ALCD based on the CT request forms and the crosscheck with the medical records Exclusion criteria: incomplete medical records
Target condition(s)	Diverticulitis
Index test(s) and reference standard	Index test C-reactive protein Thresholds of: ≤10 mg/L 11-49 mg/L ≤50mg/L White blood cell count Thresholds of: <10 ($\times 10^9$/L) 10-12 ($\times 10^9$/L) 13-15 ($\times 10^9$/L) >15 ($\times 10^9$/L) Reference standard CT scan Time between measurement of index test and reference standard: NA – index test at admission, final diagnosis (reference standard) confirmed at discharge

Reference	**Andeweg 2011[6]**
Statistical measures	Index text AUC (95% CI) C-reactive protein: 0.63 (0.57-0.69) Leukocyte count: 0.61 (0.54-0.65)
Source of funding	No funding received
Limitations	Risk of bias: High – flow and timing Indirectness: None
Comments	Computed tomography was used as gold standard for diagnosis, in case of non-operative management. Pathology and operative reports were used as gold standard in case of operative management.

Reference	**Jamal Talabani 2017[36]**
Study type	Cohort
Study methodology	Data source: Department of Surgery at Levanger Hospital inpatients Recruitment: all patients older than 18 years, who were admitted to the Department of Surgery at Levanger Hospital with acute abdominal pain with a duration of less than 1 week, were invited to participate in the study.
Number of patients	n = 833
Patient characteristics	Age (n) <65 years: 537 <65 years: 296 Gender (male to female ratio): 356/477 Country: Norway Inclusion criteria: all patients older than 18 years, who were admitted to the Department of Surgery at Levanger Hospital with acute

Reference	**Jamal Talabani 2017[36]**
	abdominal pain with a duration of less than 1 week, were invited to participate in the study. Exclusion criteria: not reported
Target condition(s)	Diverticulitis
Index test(s) and reference standard	Index test C-reactive protein Leukocyte count Thresholds not reported Reference standard CT scan Time between measurement of index test and reference standard: NA – index test at admission, final diagnosis (reference standard) confirmed at discharge or by ambulant scan after discharge.
Statistical measures	Index text AUC (95% CI) C-reactive protein: 0.83 (0.80-0.86) Leukocyte count: 0.59 (0.53-0.65)
Source of funding	Not reported
Limitations	Risk of bias: High – flow and timing Indirectness: Proportion of cohort did not receive CT as reference standard
Comments	Acute diverticulitis was confirmed by CT scan in 83 of 95 patients. Five patients with recurrent acute diverticulitis had a recent CT verifying acute diverticulitis, and five had their diagnosis confirmed by an ambulant CT scan or colonoscopy after discharge. Discharge diagnosis based on clinical examination and laboratory tests occurred twice.

Reference	**Nielson 2014[59]**
Study type	Cohort
Study methodology	Data source/recruitment: medical records of all patients admitted with proven left-sided colonic diverticulitis via emergency department. Patients who received both CT and ultrasound were included in analysis.
Number of patients	n = 123 (CT confirming diverticulitis)
Patient characteristics	Mean age (range): 57.2 years (30-92) Gender (male to female ratio): 41/82 Country: Netherlands Inclusion criteria: patients admitted with CT proven left-sided colonic diverticulitis Exclusion criteria: not reported
Target condition(s)	Diverticulitis (uncomplicated and complicated) Uncomplicated can include thickening of bowel wall, inflamed diverticula, or stranding of diverticula fat; complicated by abscess formation, stenosis, fistula, free fluid, or intramural free air.
Index test(s) and reference standard	Index test Ultrasound Reference standard Computed Tomography Time between measurement of index test and reference standard: tests conducted during the same admission.
Statistical measures	Index text Uncomplicated diverticulitis

		Outcome		
		Positive	Negative	
Test	Positive	True positives 78	False positives NA	PPV NA
	Negative	False Negative	True negative	NPV

Reference	**Nielson 2014[59]**

		16	NA	NA
		Sensitivity: 83%	Specificity: NA	

False negative: No diverticulitis (13), US inconclusive (3)

Complicated diverticulitis

		Outcome		
		Positive	Negative	
Test	Positive	True positives 6	False positives NA	PPV NA
	Negative	False Negative 23	True negative NA	NPV NA
		Sensitivity: 23%	Specificity: NA	

False negative: Uncomplicated on US (10), No diverticulitis (8), US inconclusive (5)

Diverticulitis

		Outcome		
		Positive	Negative	
Test	Positive	True positives 94	False positives NA	PPV NA
	Negative	False Negative 29	True negative NA	NPV NA
		Sensitivity: 76%	Specificity: NA	

Source of funding	No funding received
Limitations	Risk of bias: High – flow and timing Indirectness: none
Comments	Specificity, PPV and NPV could not be measured; only patients with CT confirmed diverticulitis were included in analysis.

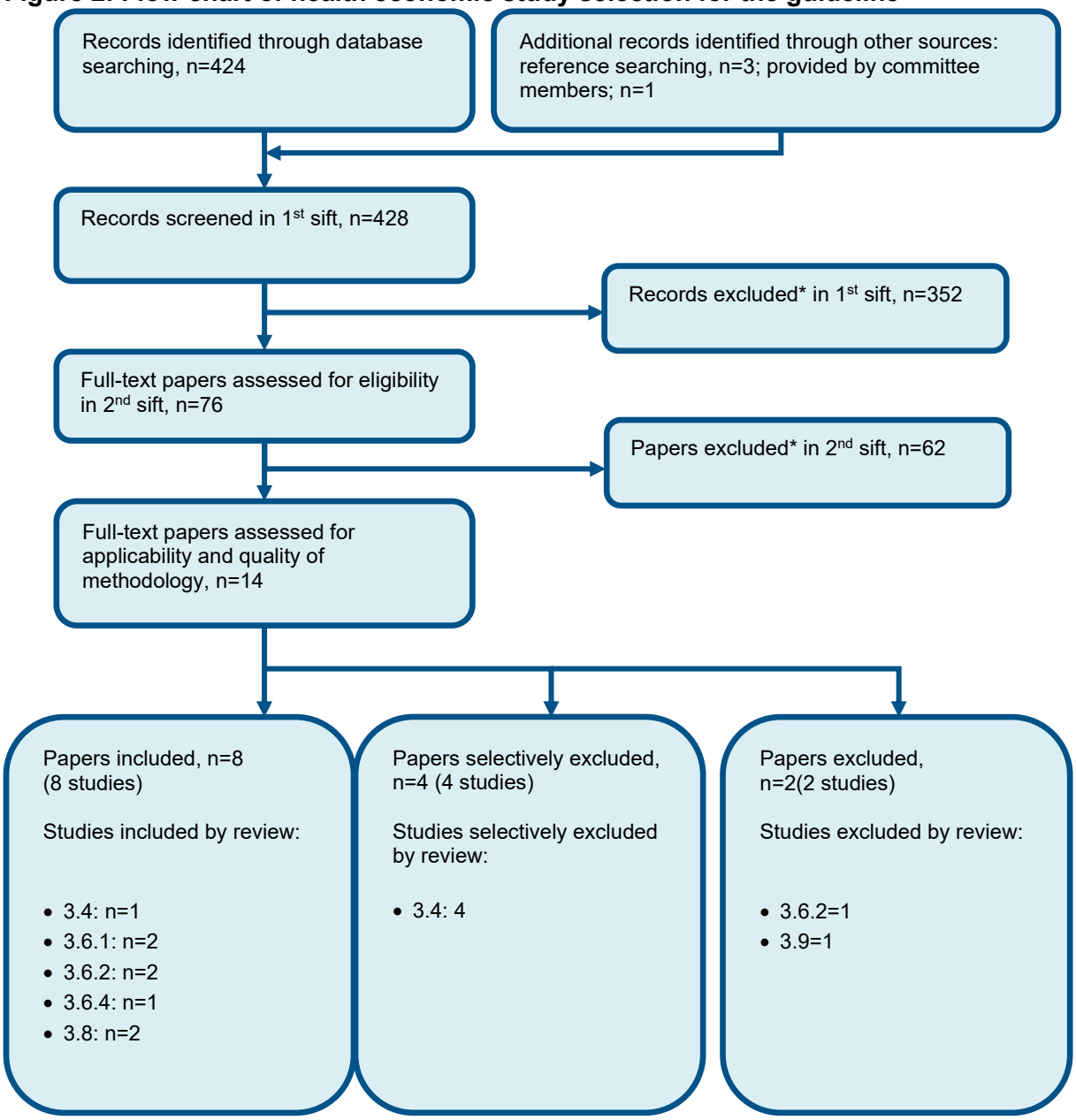
Reference	**Steffanson 1997[74]**
Study type	Cohort
Study methodology	Data source/recruitment: all patients with acute abdominal disease referred to emergency hospital. A subset of patients with a CT diagnosis confirmed or rejected following laparoscopy.
Number of patients	n = 88 (30 had CT diagnosis and later underwent laparoscopy)
Patient characteristics	Median age (SD): 62 years (14) Gender (male to female ratio): 24/64 Country: Iceland Inclusion criteria: patients presenting with acute lower abdominal pain with suspicion of diverticulitis Exclusion criteria: patients subjected to acute surgery
Target condition(s)	Diverticulitis
Index test(s) and reference standard	Index test CT scan White blood cell count, C-reactive protein, and erythrocyte sedimentation rate Reference standard Surgically (laparoscopy) confirmed diagnosis Time between measurement of index test and reference standard: Not reported.
Statistical measures	
Source of funding	Funding not reported
Limitations	Risk of bias: High – flow and timing

Index test	Sensitivity	95% CI	Specificity	95% CI	PPV	95% CI
CT	65%	44-82%	100%	79-100%	100%	74-100%
WBC, ESR & CRP	95%	78-98%	50%	22-78%	79%	61-91%

Reference	**Steffanson 1997[74]**
	Indirectness: none
Comments	Negative predictive value could not be measured; only patients undergoing laparoscopy could confirm index test diagnosis.

Appendix E: Health economic evidence selection

Figure 2: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

3.4 Non-surgical treatment of acute diverticulitis (Evidence review H)

3.6.1 Timing of surgery (Evidence review J)

3.6.2 Laparoscopic versus open resection (Evidence review K)

3.6.4 Primary versus secondary anastomosis (Evidence review M)

3.8 Laparoscopic lavage versus resection for perforated diverticulitis (Evidence review O)

3.9 Management of recurrent diverticulitis (Evidence review P)

Appendix F:Excluded studies

F.1 Excluded clinical studies

Table 24: Studies excluded from the clinical review

Reference	Reason for exclusion
Abedi 2004[1]	Excluded due to inappropriate study design
Ahn 2002[2]	Excluded due to inappropriate comparison
Alshamari 2016[3]	Excluded due to inappropriate study population
Ambrosetti 1997[4]	Excluded due to updated study already being included
Andeweg 2014[8]	Excluded due to inappropriate reference standard
Andeweg 2013[7]	Excluded due to inappropriate outcomes
Biondo 2012[10]	Excluded due to inappropriate outcomes
Braden 2010[11]	Excluded due to inappropriate outcomes
Brown 2002[12]	Excluded due to inappropriate comparison; analysis
Brown 2016[13]	Excluded due to inappropriate study population; incorrect interventions
Buckley 2004[14]	Excluded due to inappropriate study design
Bugiantella 2015[15]	Excluded due to inappropriate outcomes
Camera 2017[16]	Excluded due to inappropriate study population
Caputo 2015[17]	Excluded due to inappropriate comparison
Chabok 2013[18]	Excluded due to inappropriate comparison; outcome
Choi 2013[19]	Excluded due to inappropriate comparison
Cobben 2003[20]	Excluded due to inappropriate study population
Coogan 1997[21]	Excluded due to inappropriate study design
Daniels 2015[23]	Excluded due to inappropriate study population
Dombal 1972[26]	Excluded due to inappropriate diagnostic tests
Domjan 1998[27]	Excluded due to inappropriate outcomes
Eisenberg 2017[28]	Excluded due to inappropriate diagnostic tests
Etzioni 2010[29]	Excluded due to inappropriate comparison
Floch 2006[30]	Excluded due to inappropriate study design
Gallo 2016[31]	Excluded due to inappropriate reference standard
Gans 2015[32]	Excluded due to inappropriate diagnostic tests
Gong 2015[33]	Excluded due to inappropriate study population
Halligan 2002[34]	Excluded due to inappropriate study design
Ince 2014[35]	Excluded due to inappropriate outcomes
Jang 2014[37]	Excluded due to inappropriate study population
Jensen 2000[38]	Excluded due to inappropriate intervention
Jung 2010[40]	Excluded due to inappropriate comparison
Juvonen 2014[41]	Excluded due to inappropriate study population
Kaser 2010[42]	Excluded due to inappropriate outcome
Kawatkar 2015[43]	Excluded due to inappropriate intervention
Kechagias 2014[44]	Excluded due to inappropriate outcome
Kessner 2017[45]	Excluded due to inappropriate comparison
Lameris 2008[46]	Excluded due to inappropriate reference standard

Reference	Reason for exclusion
Lameris 2008[47]	Excluded due to inappropriate reference standard
Laurell 2007[48]	Excluded due to inappropriate comparison
Liljegren 2007[49]	Excluded due to inappropriate diagnostic tests
Lindsay 1988[50]	Excluded due to inappropriate study population
Longstreth 2016[51]	Excluded due to inappropriate comparison
Macconaill 2014[52]	Excluded due to inappropriate study design
Millet 2017[53]	Excluded due to inappropriate diagnostic tests
Ng 2002[55]	Excluded due to inappropriate diagnostic tests
Nicholas 1972[58]	Excluded due to inappropriate comparison
Oistamo 2013[60]	Excluded due to inappropriate outcomes
Padidar 1994[61]	Excluded due to inappropriate study design; comparison; population
Porten 2008[62]	Excluded due to inappropriate study population; outcome
Pradel 1997[63]	Excluded due to inappropriate reference standard
Rampton 2001[64]	Excluded due to inappropriate study design
Sala 2007[65]	Excluded due to inappropriate study design
Sanford 2006[66]	Excluded due to inappropriate comparison
Schnyder 1979[67]	Excluded due to inappropriate outcomes
Schreyer 2004[68]	Excluded due to inappropriate outcome
Shen 2002[69]	Excluded due to inappropriate outcome
Shrier 1991[70]	Excluded due to inappropriate outcome
Sirany 2017[71]	Excluded due to inappropriate intervention; comparison
Snyder 2004[72]	Excluded due to inappropriate study design, no relevant outcomes
Spinzi 2001[73]	Excluded due to inappropriate outcomes
Stromberg 2007[75]	Excluded due to inappropriate comparison
Thorisson 2016[76]	Excluded due to inappropriate diagnostic tests
Toorenvliet 2010[77]	Excluded due to inappropriate comparison
Tursi 2016[78]	Excluded due to inappropriate comparison
Turvill 2016[79]	Excluded due to inappropriate study population; intervention
van de Wall 2013[80]	Excluded due to inappropriate outcome
Wolff 2008[82]	Excluded due to inappropriate outcome
Won 2016[83]	Excluded due to inappropriate comparison
Wong 2012[84]	Excluded due to inappropriate comparison
Yardimci 2017[85]	Excluded due to inappropriate study design; comparison
Zia 2008[86]	Excluded due to inappropriate study population
Zielke 1997[87]	Excluded due to inappropriate comparison