National Institute for Health and Care Excellence

Final

Diverticular disease: diagnosis and management

[C] Evidence review for diagnosis of diverticular disease

NICE guideline NG147

Diagnostic evidence review

November 2019

Final

This evidence review was developed by the National Guideline Centre

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

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Contents

1 Diverticular Disease

1.1 Review question: What is the diagnostic accuracy and cost effectiveness of tests to diagnose diverticular disease?

1.1.1 Introduction

At present, there exists a wide range of diagnostic tests available in the diagnosis of Diverticular Disease. This can give rise to significant regional variability in practice between clinical centres; as well as locally between different patient cohorts.

The choice of test used may depend on a variety of both clinical and non-clinical factors, including: symptoms at time of presentation, co-morbidity, clinical setting (primary or secondary care; routine or urgent indication), patient preference and tolerability, safety, cost, local clinical expertise, and availability.

Diverticular disease will often, for example, be diagnosed following the investigation of patient symptoms such as a change in bowel habit or rectal bleeding. In such instances, luminal endoscopy (colonoscopy or flexible sigmoidoscopy) is already established as the most sensitive test to exclude other important clinical conditions including colitis or colorectal cancer.

Equally, however, in patients who are frail and/or acutely unwell, especially if there is significant medical co-morbidity, non-invasive investigations such as CT may be preferred. This is particularly the case where the diagnostic test may need to allow for complications such as abscess formation or perforation to be excluded at the same time.

It is the aim of these guidelines to clarify the most accurate, cost effective and appropriate test to be used for a patient presenting with symptoms or signs suggestive of possible Diverticular Disease. It may be that in some clinical settings a number of different tests are appropriate, in which case the individual risks and benefits of each test should be explained to the patient.

1.1.2 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Adults aged 18 years and over with suspected diverticular disease
Target condition	Diverticular Disease
Index tests	• Sigmoidoscopy • CT • CT colonoscopy • MRI • Ultrasound • Barium enema • Colonoscopy
Reference standards	• Colonoscopy • Pathologically/surgically confirmed
Statistical measures	• Sensitivity • Specificity • Positive Predictive Value (PPV)

	• Negative Predictive Value (NPV) • Receiver Operating Characteristic (ROC) curve or area under curve
Study design	• Cohort studies • Cross-sectional studies

1.2 Clinical evidence

1.2.1 Included studies

No relevant diagnostic test accuracy studies of sigmoidoscopy, CT, CT colonoscopy, MRI, ultrasound, barium enema, or colonoscopy in people under investigation for diverticular disease were identified.

See also the study selection flow chart in appendix C.

1.2.2 Excluded studies

See the excluded studies list in appendix E.

1.2.3 Summary of clinical studies included in the evidence review

No included studies.

1.2.4 Quality assessment of clinical studies included in the evidence review

No included studies.

1.3 Economic evidence

1.3.1 Included studies

No relevant health economic studies were identified.

1.3.2 Excluded studies

No relevant health economic studies were identified.

1.3.3 Unit costs

The unit costs below were presented to the committee, to aid consideration of cost effectiveness.

Table 2: 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
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
RD40Z Ultrasound 20 minutes without contrast	£52
RD41Z Ultrasound 20 minutes with contrast	£76
Barium Enema (RD30Z Contrast Fluoroscopy Procedures with duration of less than 20 minutes)	£126

Source: NHS Reference Costs, 2016-2017

Table 3: 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
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
RD40Z Ultrasound, duration less than 20 minutes, without contrast	£51
RD41Z Ultrasound, duration less than 20 minutes, with contrast	£75
Barium Enema (RD30Z Contrast Fluoroscopy Procedures with duration of less than 20 minutes)	£118

Source: NHS Reference Costs, 2016-2017

1.4 Evidence statements

1.4.1 Clinical evidence statements

No relevant published evidence was identified.

1.4.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.5 The committee's discussion of the evidence

There was no clinical evidence included in this review.

1.5.1 Interpreting the evidence

1.5.1.1 The diagnostic measures that matter most

Diagnostic accuracy for diverticular disease was the set of outcomes prioritised for this review. Sensitivity, specificity, positive predictive value, negative predictive value and receiver operating characteristic curve or area under curve were the measures considered by the committee for this review question. However there was no evidence identified for these measures.

1.5.1.2 The quality of the evidence

No clinical evidence included.

1.5.1.3 Benefits and harms

No clinical evidence included. The committee made a consensus recommendation to highlight that routine investigations can be made in the primary care setting. It was also important to highlight that some people will meet the referral criteria for suspected cancer and should be referred on the appropriate pathway.

1.5.2 Cost effectiveness and resource use

No evidence of clinical or cost effectiveness was found. The cost-effectiveness of diagnosis is not known. However, the recommendation does not represent a move away from current practice.

1.5.3 Other factors the committee took into account

The committee noted that current practice is to use imaging, blood tests and endoscopy. Therefore the committee drew on its knowledge and experience to make a recommendation about which investigations should be carried out to rule out other diseases in people with symptoms consistent with diverticular disease. Other diseases could include cancer and irritable bowel syndrome. The committee stated that in their experience patients suspected of having diverticular disease often are investigated to exclude other causes. Investigations may include blood tests to exclude anaemia and to ensure kidney function is normal prior to other investigations along with excluding acute inflammation. Patients will often have their bowel investigated by either endoscopy with a flexible sigmoidoscopy or colonoscopy or CT colonography. These tests will confirm the presence of diverticula or other pathologies.

The committee cross reference to the NICE guideline on 'Suspected cancer: recognition and referral' (NG12) and the NICE guideline on 'Faecal calprotectin diagnostic tests' (DG11).

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Appendices

Appendix A: Review protocols

Table 4: Review protocol: Diagnosis of diverticular disease

Field	Content
Review question	What is the diagnostic accuracy and cost effectiveness of tests to diagnose diverticular disease?
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 diverticular disease.
Eligibility criteria – population / disease / condition / issue / domain	Adults 18 years and over with suspected diverticular disease
Eligibility criteria – diagnostic tools	• Sigmoidoscopy • CT • CT colonoscopy • MRI • Ultrasound • Barium enema • Colonoscopy
Eligibility criteria – reference (gold) standard	Compared to each other • Colonoscopy • 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
Eligibility criteria – study design	Cohort studies Cross-sectional studies
Other inclusion exclusion criteria	Exclusions: Children and young people aged 17 years and younger
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 will be assessed using the adjusted QUIPS 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 C of the evidence report.
Data items – define all variables to be collected	For details, please see evidence tables in Appendix C (clinical evidence tables) or D (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. Results will not be pooled across differing gold standards i.e. colonoscopy and surgically confirmed diverticular disease.
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 the 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	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	The NGC is funded by NICE and hosted by the Royal College of

	Physicians.
Roles of sponsor	NICE funds the NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 5: 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).[13] **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 6: 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

Database	Dates searched	Search filter used
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 7: 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 8: 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 9: 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 10: 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 11: 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 12: 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.

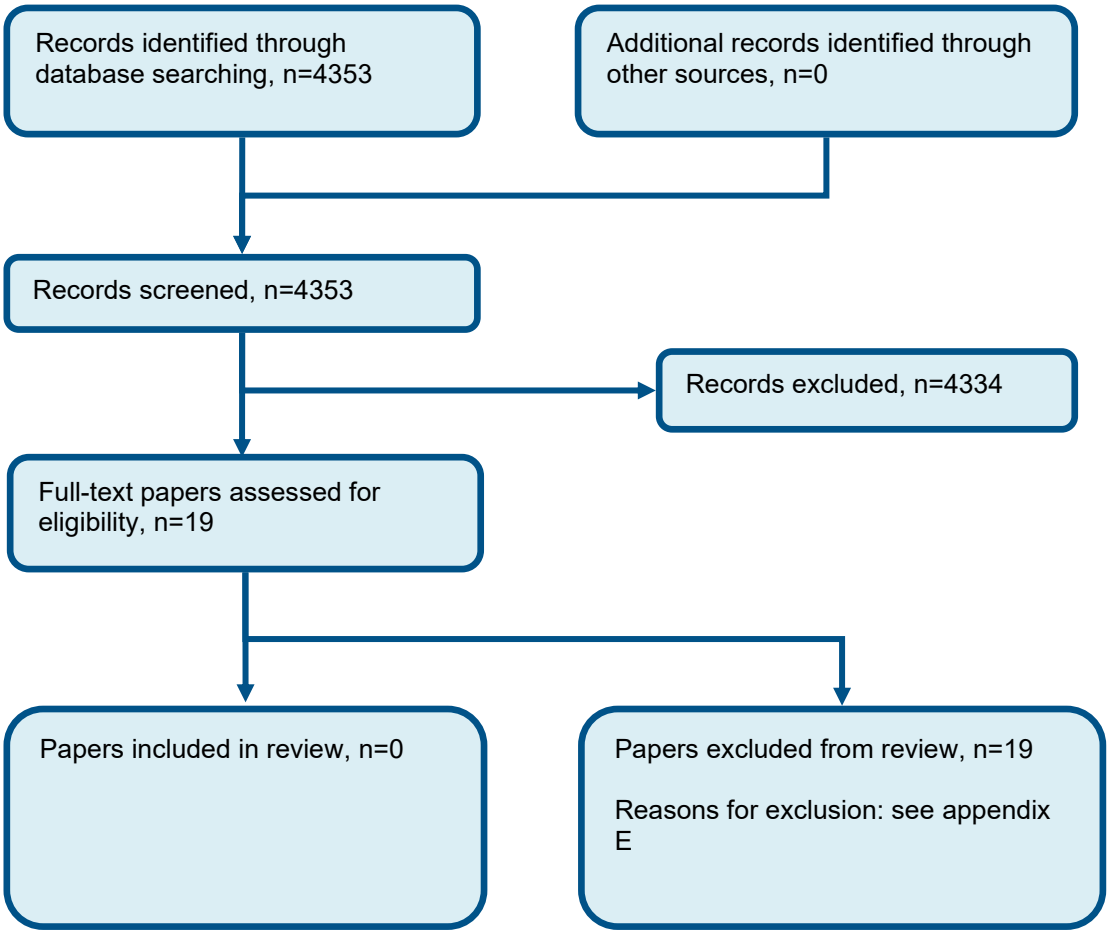
54.	(dynamic* adj2 (model* or system*)).ti,ab.
55.	(simulation adj3 (model* or discrete event* or agent)).ti,ab.
56.	(microsimulation* or "micro* simulation*").ti,ab.
57.	((flow or core) adj2 model*).ti,ab.
58.	(data adj2 envelopment*).ti,ab.
59.	system* model*.ti,ab.
60.	or/39-61
61.	quality adjusted 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 13: NHS EED and HTA (CRD) search terms

#1.	diverticul*

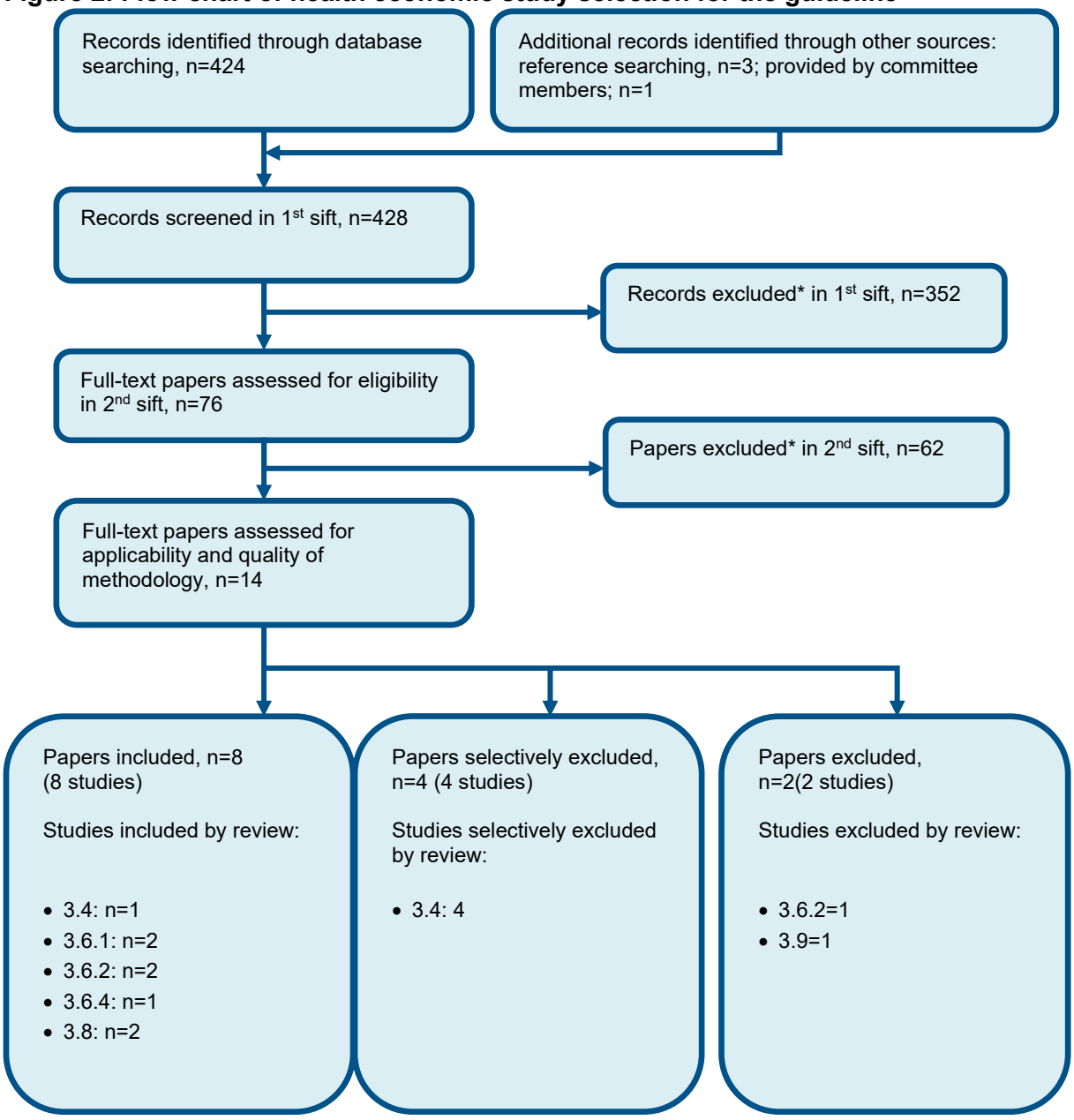
Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of diagnosis of diverticular disease



Appendix D: 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 E: Excluded studies

E.1 Excluded clinical studies

Table 14: Studies excluded from the clinical review

Reference	Reason for exclusion
Al-Shehri 1999[1]	Excluded due to incorrect review population
Bayasgalan 2017[2]	Citation only
Daker 2012[3]	Citation only
Hjern 2007[4]	Excluded due to incorrect analysis
Ince 2014[5]	Excluded due to incorrect target condition
Kato 2016[6]	Citation only
Kinoshita 2017[7]	Citation only
Kohler 1999[8]	Excluded due to incorrect study outcomes
Limsrivilai 2017[9]	Excluded due to incorrect target condition
Mansoori 2016[10]	Excluded due to incorrect study outcomes
Morosi 1991[11]	Excluded due to incorrect target condition
Narciso 2009[12]	Excluded due to incorrect study design
Nielsen 2014[14]	Excluded due to incorrect target condition
Niikura 2013[15]	Excluded due to incorrect reference standard
Sanford 2006[16]	Excluded due to incorrect target condition
Schreyer 2004[17]	Excluded due to incorrect target condition
Steenvoorde 2004[18]	Excluded due to incorrect study outcomes
Stefansson 1997[19]	Excluded due to incorrect target condition
Vally 2017[20]	Excluded due to incorrect study outcomes