National Institute for Health and Care Excellence

Consultation

Diverticular disease

F. Evidence review: Referral criteria for acute diverticulitis

NICE guideline

Prognostic evidence review

June 2019

Draft for Consultation

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.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

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1 Referral criteria for acute diverticulitis

1.1 Review question: What are the referral criteria for urgent hospital assessment in people with acute diverticulitis?

1.2 Introduction

Acute diverticulitis is a common problem presenting in primary care. The major challenge for the health care professional in primary care is to ensure safe and effective treatment of their patients. The first step is to confirm the diagnosis of acute diverticulitis and its severity. Acute diverticulitis may be safely managed in the community. This guideline identifies those people whose illness is severe enough to require referral to secondary care.

1.3 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 acute diverticulitis
Prognostic variables under consideration	• Abdominal pain/tenderness • Change in bowel habit • Rectal bleeding • Co-morbidities (e.g. diabetes mellitus, end-stage chronic kidney disease, malignancy, cirrhosis, or is taking immunosuppressive drugs) • Dehydration/risk of dehydration • Intolerance to oral antibiotics • Suspected sepsis • Prior history of diverticular complications
Confounding factors	• Age • Gender
Outcomes	• Hospital admission • Discharge from A&E • Urgent outpatient appointment/ surgical triage
Study design	• RCT • Systematic review • Cohort studies • Cross-sectional studies

1.4 Clinical evidence

1.4.1 Included studies

No relevant clinical studies were identified for this evidence review.

1.4.2 Excluded studies

See the excluded studies list in appendix E.

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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 this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix D:

1.6 Evidence statements

1.6.1 Clinical evidence statements

No relevant clinical evidence was identified.

1.6.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.7 Recommendations

1.7.1 Symptoms and signs of acute diverticulitis

F1. Suspect acute diverticulitis if a person presents and constant abdominal pain, usually severe and localising in the left lower quadrant, with any of the following:

- fever **or**
- a change in bowel habit and significant rectal bleeding or passage of mucous per rectum **or**
- tenderness in the left lower quadrant, a palpable abdominal mass or distention on abdominal examination, with a previous history of diverticulosis or diverticulitis.

Be aware that in a minority of people and in people of Asian origin, pain and tenderness may be localised in the right lower quadrant.

1.8 Rationale and impact

1.8.1 Why the committee did make the recommendation

There was no relevant evidence on the symptoms and signs of acute diverticulitis, so recommendations were made using formal consensus methods. The committee thought that clearly defining the symptoms and signs of acute diverticulitis, along with its associated complications, would help clinicians and patients in clearly differentiating these distinct clinical conditions. Committee members thought that often diverticular disease, symptomatic diverticular disease and acute diverticulitis are used interchangeably, creating confusion about which condition the patient has and therefore what management is appropriate. The recommendation is focused on symptoms and signs that were specific to acute diverticulitis

and is consistent with current practice. It is aimed at primary care to support the identification of the condition.

1.8.2 Impact of the recommendation on practice

The recommendation reflects current practice.

1.9 The committee's discussion of the evidence

1.9.1 Interpreting the evidence

1.9.1.1 The outcomes that matter most

The committee decided that hospital admission, discharge from A&E and urgent outpatient appointment/ surgical triage were the most important outcomes for this review however there was no clinical evidence identified for these.

1.9.1.2 The quality of the evidence

There was no clinical evidence included in this evidence review.

1.9.1.3 Benefits and harms

There was no clinical evidence included in this evidence review.

1.9.2 Cost effectiveness and resource use

No evidence of clinical or cost effectiveness was found, so recommendations were made by a Delphi panel and minor edits made by the Committee. The cost-effectiveness of referral for suspected acute diverticulitis is not known. However, the panel prioritised only patients with certain symptoms for urgent referral and the recommendation does not represent a move away from current practice.

1.9.3 Other factors the committee took into account

The committee included statements in the Delphi survey on the common symptoms and signs of acute diverticulitis. They noted that acute diverticulitis occurs when a diverticulum becomes acutely inflamed. People with acute diverticulitis typically present with severe left sided pain and tenderness associated with fever, tachycardia, malaise, and altered bowel habit.

The statement on constant abdominal pain reached consensus in the first round. However, the phrase 'starting in the hypogastrium' was removed from the statement referring to constant abdominal pain. Respondents indicated this is an outdate word and the committee supported its removal. Right-sided symptoms in people or Asian origin also formed part of these statements,

The statements on bloating and the passage of mucus rectally were removed from the survey. Respondents either indicated that this was a non-specific symptom or was more likely to indicate irritable bowel disorder or inflammatory disease. The committee revised the statements to make fever optional. Some people may be systemically well. These people may later develop a fever in which case a review is important if symptoms change. Some people may also have a flare up of diverticular disease rather than acute diverticulitis.

References

1. Alvarez JA, Baldonedo RF, Bear IG, Otero J, Pire G, Alvarez P et al. Presentation, management and outcome of acute sigmoid diverticulitis requiring hospitalization. Digestive Surgery. 2007; 24(6):471-6

2. Alvarez JA, Baldonedo RF, Bear IG, Otero J, Pire G, Alvarez P et al. Outcome and prognostic factors of morbidity and mortality in perforated sigmoid diverticulitis. International Surgery. 2009; 94(3):240-8

3. Ambrosetti P. Indications to elective surgery in diverticular disease. Techniques in Coloproctology. 2010; 14(1):87-88

4. Ambrosetti P, Morel P. Acute left colonic diverticulitis: Indications for operation and predictive parameters of early and late medical treatment failure: A prospective non-randomized study of 423 patients. Digestive Surgery. 1996; 13(4-5):349-352

5. Ambrosetti P, Robert JH, Witzig JA, Rohner A. Acute left colonic diverticulitis: Management controversies. A prospective non-randomized study of 226 patients. Digestive Surgery. 1993; 10(4):176-181

6. Arora G, Mannalithara A, Mithal A, Triadafilopoulos G, Singh G. Concurrent conditions in patients with chronic constipation: A population-based study. PloS One. 2012; 7(10):e42910

7. Bolkenstein HE, van de Wall BJM, Consten ECJ, Broeders I, Draaisma WA. Risk factors for complicated diverticulitis: systematic review and meta-analysis. International Journal of Colorectal Disease. 2017; 32:1375-83

8. Broderick-Villa G, Burchette RJ, Collins JC, Abbas MA, Haigh PI. Hospitalization for acute diverticulitis does not mandate routine elective colectomy. Archives of Surgery. 2005; 140(6):576-83

9. Chabok A, Andreasson K, Nikberg M. Low risk of complications in patients with first-time acute uncomplicated diverticulitis. International Journal of Colorectal Disease. 2017; 32:1699-702

10. Hall JF, Roberts PL, Ricciardi R, Read T, Scheirey C, Wald C et al. Long-term follow-up after an initial episode of diverticulitis: What are the predictors of recurrence? Diseases of the Colon and Rectum. 2011; 54(3):283-8

11. Jamal Talabani A, Lydersen S, Ness-Jensen E, Endreseth BH, Edna TH. Risk factors of admission for acute colonic diverticulitis in a population-based cohort study: The North Trondelag Health Study, Norway. World Journal of Gastroenterology. 2016; 22(48):10663-10672

12. Jarbrink-Sehgal ME, Andreasson A, Talley NJ, Agreus L, Song JY, Schmidt PT. Symptomatic diverticulosis is characterized by loose stools. Clinical Gastroenterology and Hepatology. 2016; 14(12):1763-1770

13. Jaung R, Kularatna M, Robertson JP, Vather R, Rowbotham D, MacCormick AD et al. Uncomplicated acute diverticulitis: Identifying risk factors for severe outcomes. World Journal of Surgery. 2017; 41(9):2258-65

14. Juvonen P, Lehtimäki T, Eskelinen M, Ilves I, Vanninen R, Miettinen P et al. The need for surgery in acute abdominal pain: a randomized study of abdominal computed tomography. In Vivo. 2014; 28(3):305-309

15. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

Appendices

Appendix A: Review protocols

Table 2: Review protocol: Referral criteria for acute diverticulitis

Field	Content
Review question	What are the referral criteria for urgent hospital assessment in people with acute diverticulitis?
Type of review question	Prognostic 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 the referral criteria for urgent hospital assessment.
Eligibility criteria – population / disease / condition / issue / domain	Adults 18 years and over with suspected acute diverticulitis
Eligibility criteria – prognostic factor(s)	• Abdominal pain/tenderness • Change in bowel habit • Rectal bleeding • Co-morbidities (e.g. diabetes mellitus, end-stage chronic kidney disease, malignancy, cirrhosis, or is taking immunosuppressive drugs) • Dehydration/risk of dehydration • Intolerance to oral antibiotics • Suspected sepsis • Prior history of diverticular complications
Eligibility criteria – confounders	• Age • Gender
Outcomes and prioritisation	• Hospital admission • Discharge from A&E • Urgent outpatient appointment/ surgical triage
Eligibility criteria – study design	RCT Systematic review 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	• Subgroups: People of Asian family origin as they are known to develop right-sided diverticula
Selection process –	Studies are sifted by title and abstract. Potentially significant

duplicate screening / selection / analysis	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 D 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.
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

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2 **Table 3: 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).[15] **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 without Prognostic/risk factor terms using the following approach:

- Population AND Study filter(s)

1 **Table 4: 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

2 **Table 5: 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)

1 **Table 6: 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 and 64)

Table 7: 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 8: 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 9: 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)

1 **Table 10: 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.

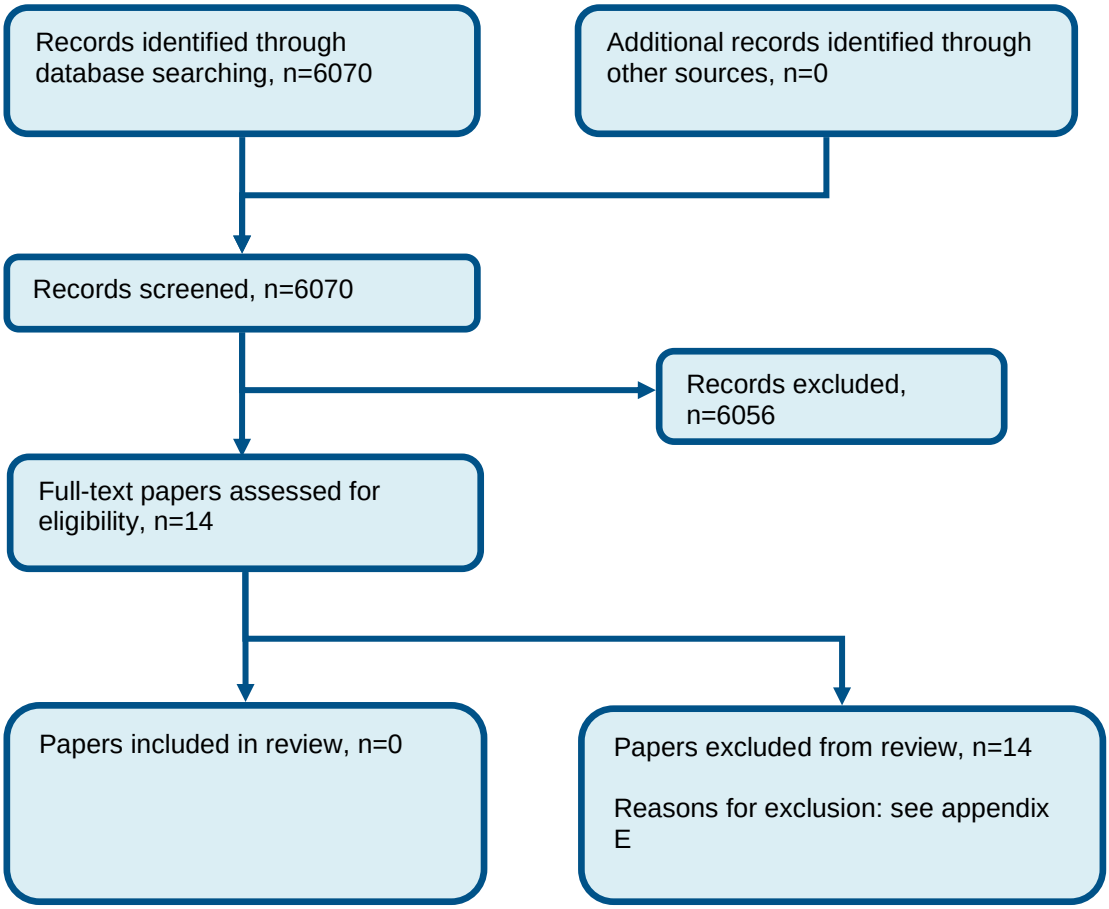
80.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
81.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
82.	or/20-40
83.	19 and (36 or 60 or 82)

Table 11: NHS EED and HTA (CRD) search terms

#1.	diverticul*

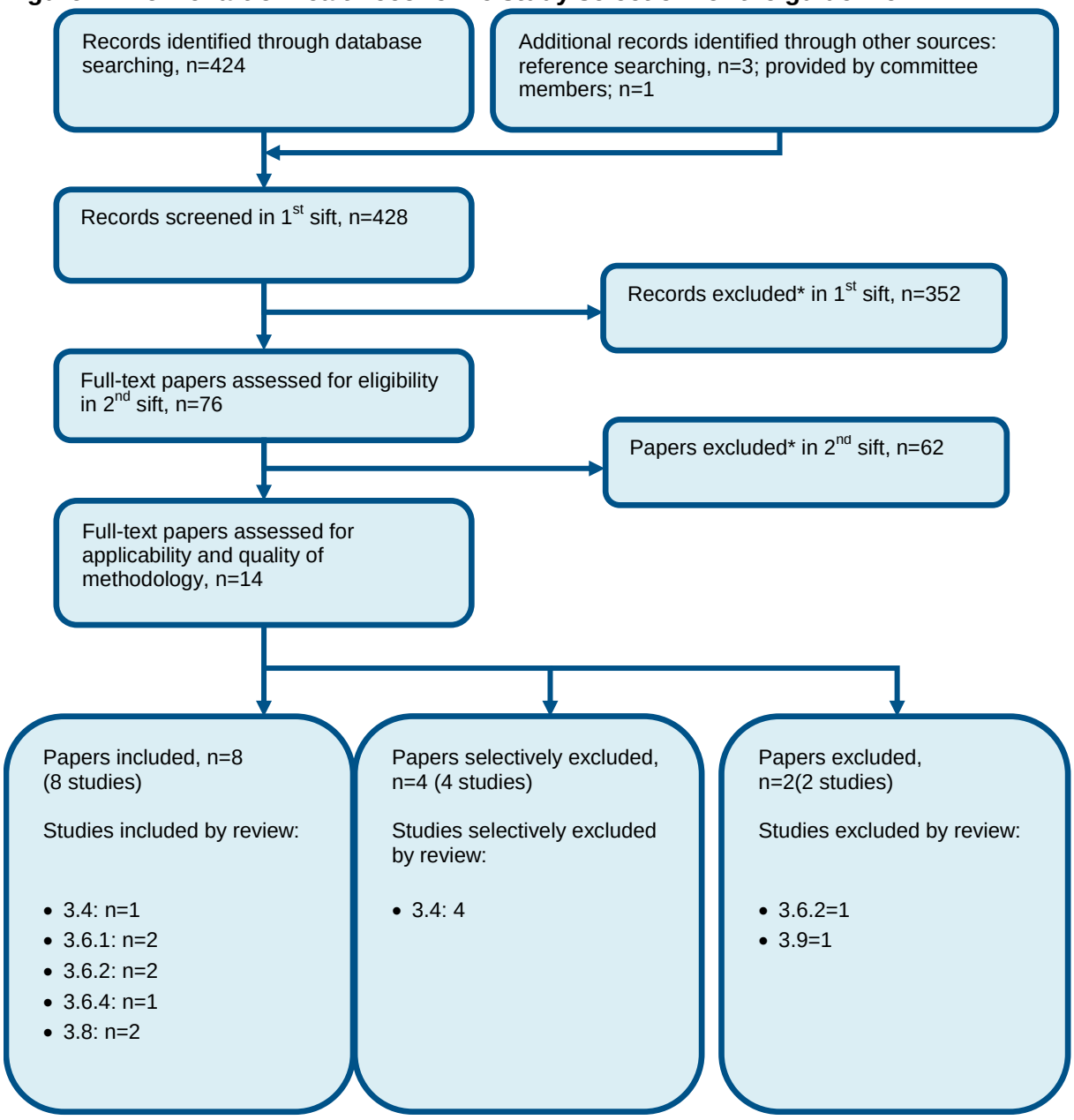
Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of referral criteria for acute diverticulitis



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 12: Studies excluded from the clinical review

Reference	Reason for exclusion
Alvarez 2007[1]	No relevant outcomes
Alvarez 2009[2]	Incorrect population
Ambrosetti 1993[5]	No relevant outcomes
Ambrosetti 1996[4]	No relevant outcomes
Ambrosetti 2010[3]	Conference abstract
Arora 2012[6]	Incorrect population
Bolkenstein 2017[7]	Incorrect population
Broderick-Villa 2005[8]	No relevant outcomes
Chabok 2017[9]	No relevant outcomes
Hall 2011[10]	No relevant outcomes
Jamal Talabani 2016[11]	No relevant outcomes
Jarbrink-Sehgal 2016[12]	Incorrect population
Jaung 2017[13]	No relevant outcomes
Juvonen 2014[14]	No relevant outcomes