National Institute for Health and Care Excellence

Final

Diverticular disease: diagnosis and management

[I] Evidence review for indications for surgery

NICE guideline NG147

Prognostic evidence review

November 2019

Final

This evidence review was developed by the National Guideline Centre

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1.1 Review question: What are the indications for surgery in people with complicated acute diverticulitis and acute diverticulitis?

1.2 Introduction

Diverticulitis is one of the most common reasons for elective bowel resections after cancer. However, there seems to be significant differences between clinicians about how to treat acute diverticulitis. Treatment varies from 'watch and wait', medication and surgery. There are also great variances between clinicians about when to operate, it seems to differ on the number of recurrences, the severity of the condition and how the condition affects the patient's quality of life. Age and comorbidities are also taken into consideration.

This question is aimed to review the evidence and aid the clinician's decision when considering surgery on these patients.

1.3 PICO table

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Adults 18 years and over with complicated acute diverticulitis and acute diverticulitis

Prognostic variables under consideration	• Complications:
	  ○ Perforation
	  ○ Abscess
	  ○ Fistula
	  ○ Stricture
	  ○ Infection
	• Recurrent episode of acute diverticulitis

Confounding factors	• Age • Gender

Outcomes	Critical outcomes:
	• Mortality
	• morbidity
	• Recurrence rates of acute diverticulitis
	• Hospitalisation
	• Need for surgery
	• Progression of disease/ complications:
	  ○ Infections
	  ○ Abscesses
	  ○ Perforation
	  ○ Stricture
	  ○ Fistula

Study design	• Prospective and retrospective cohort studies • Randomised controlled trials (if appropriate)

- Systematic reviews of the above

1.4 Clinical evidence

1.4.1 Included studies

One study was included in the review;[49] this is summarised in Table 2 below. Evidence from this study is summarised in the clinical evidence summary below (Table 3).

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix F.

1.4.2 Excluded studies

See the excluded studies list in appendix I.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Population	Analysis	Prognostic variable	Confounders	Outcomes	Limitations
Pittet 2009[49]	Single cohort. Consecutive patients with CT diagnosis of diverticulitis. Patients were divided into two groups: those with an initial episode of diverticulitis and those with a recurrence. n=271	Prospective univariate analysis with matched (age and gender) comparison group.	Recurrent diverticulitis	Age Gender	• Mortality • Need for surgery • Presence of abscess	Risk of bias: high Univariate analysis

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Recurrent diverticulitis

Risk factor and outcome (population)	Number of studies	Effect (95% CI)	Imprecision	GRADE Quality
Mortality	1	Peto OR: 0.25 (95% CI 0.04 to 1.63)[a]	Serious[b]	LOW
Surgery	1	OR: 3.06 (95% CI 1.04 to 8.99) [a]	None	MODERATE
Presence of abscess	1	OR: 1.11 (95% CI 0.51 to 2.4) [a]	Serious[b]	LOW

Risk factor and outcome (population)	Number of studies	Effect (95% CI)	Imprecision	GRADE Quality

(a) Methods: univariate analysis, the two groups were similar regarding age and sex ratio.
(b) Imprecision was considered serious if the confidence intervals crossed the line of null effect.

See appendix F for full GRADE tables.

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 G

1.5.3 Unit costs

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

Table 4: NHS cost of non-elective sigmoid resection

Procedure (OPCS4)	Healthcare Resource Group (HRG) code and description	Unit Cost	Average Length of Stay	Source
Sigmoid colectomy and anastomosis	FF33 Distal Colon Procedures, 19 years and over, inclusive of non-elective short stay and non-elective long stay with excess bed days, weighted for complications and co morbidities for HRG codes: FF33A and FF33B; as recorded for Non-Elective Inpatients	£7,091	9.0 days	NHS Reference Costs 2016-2017
Sigmoid colectomy and ileostomy HFQ Or Sigmoid colectomy and exteriorisation of bowel NEC	FF31 Complex Large Intestine Procedures, 19 years and over, inclusive of non-elective short stay and non-elective long stay with excess bed days, weighted for complications and co morbidities for HRG codes: FF31A, FF31B, FF31C and FF31D; as recorded for Non-Elective Inpatients	£8,312	11.0 days	NHS Reference Costs 2016-2017

Table 5: NHS cost of elective sigmoid resection

	Currency Description	Unit Cost	Average Length of Stay	Source
Sigmoid colectomy and anastomosis	FF33 Distal Colon Procedures, 19 years and over, inclusive of excess bed days, weighted for complications and co morbidities for HRG codes: FF33A and FF33B; as recorded for Elective Inpatients	£6,487	5.2 days	NHS Reference Costs 2016-2017
Sigmoid colectomy and ileostomy HFQ Or Sigmoid colectomy and exteriorisation of bowel NEC	FF31 Complex Large Intestine Procedures, 19 years and over, inclusive of excess bed days, weighted for complications and co morbidities for HRG codes: FF31A, FF31B, FF31C and FF31D; as recorded for Elective Inpatients	£8,140	7.6 days	NHS Reference Costs 2016-2017
Closure of ileostomy	FF22 Major Small Intestine Procedures, 19 years and over, inclusive of excess bed days, weighted for complications and co morbidities for HRG codes: FF22A, FF22B, FF22C and FF22C; as recorded for Elective Inpatients	£5,151	5.97 days	NHS Reference Costs 2016-2017

1.6 Evidence statements

1.6.1 Clinical evidence statements

One study reported on the association between recurrent episodes of diverticulitis and indications for surgery. The evidence suggested that recurrent diverticulitis was a possible indication for surgery when looking at the outcome need for surgery (n=271, moderate quality). However this was not consistent with the outcomes mortality and presence of an abscess on CT scan which suggested no association (low quality, n= 271).

1.6.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The outcomes that matter most

The guideline committee identified the following outcomes as critical outcomes for this review; mortality, morbidity, recurrence rates of acute diverticulitis, hospitalisation, need for surgery, progression of disease and complications including, infections, abscesses, perforation, stricture and fistula. Evidence from a single study was found for only three of the outcomes; mortality, need for surgery and presence of abscess.

1.7.1.2 The quality of the evidence

The quality of the evidence included was medium to low due to a high risk of bias from a single study with only a univariate analysis.

1.7.1.3 Benefits and harms

Only one study was identified comparing patients who had an initial episode of acute diverticulitis to those who had a recurrent episode. The committee were unable to make any evidence-based recommendations on this subject and therefore statements were included in the Delphi survey. The current guidance for surgery in patients with recurrent episodes of acute diverticulitis is to take a tailored approach to each individual patient as outlined by the ACPGBI guidance in 2008. No further clear indications for surgery in this patient group could be identified. A further group identified for surgery were those who had been treated for complications of acute diverticulitis conservatively but no evidence was found on subsequent surgical management of these patients with regard to indications for surgery.

The current evidence did not sufficiently address the harms and benefits associated with clear indications for surgery.

1.7.2 Cost effectiveness and resource use

No relevant economic evaluations were identified which address the indications for surgery in people with acute diverticulitis. The committee were presented with unit costs associated with surgery.

The clinical evidence was not sufficient for the committee to make a recommendation.

1.7.3 Other factors the committee took into account

The committee noted the main symptoms and signs associated with complicated acute diverticulitis. A person with a fistula may develop faecaluria (faeces in urine), pneumaturia (gas or air in urine) or pyuria (white blood cells or pus in urine). A stricture may lead to obstructive symptoms with complaints of nausea, vomiting and distension being present. Signs of sepsis including raised or lowered temperature or change in conscious level may also be present.

Statements were included in the Delphi survey on the symptoms and signs specific to complicated acute diverticulitis, namely abscess, perforation, fistula and intestinal obstruction. The committee also noted the importance of a statement on symptoms and signs of sepsis. The statement was modified after voting to be consistent with the NICE guideline on Sepsis (NG51).

All of the statements reached consensus in the first round.

Same day hospital assessment was recommended if any of the symptoms and signs of complicated acute diverticulitis are present.

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Appendices

Appendix A: Review protocols

Table 6: Review protocol: Indications for surgery for acute diverticulitis

Field	Content
Review question	What are the indications for surgery in people with complicated acute diverticulitis and 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 criteria which indicate that surgery is appropriate in people with acute diverticulitis.
Eligibility criteria – population / disease / condition / issue / domain	Adults 18 years and over with complicated acute diverticulitis and acute diverticulitis

Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	• Complications:
	  ○ Perforation
	  ○ Abscess
	  ○ Fistula
	  ○ Stricture
	  ○ Infection
	• Recurrent episode of acute diverticulitis

Eligibility criteria – confounders	• Age • Gender

Outcomes and prioritisation	Critical outcomes:
	• Mortality
	• morbidity
	• Recurrence rates of acute diverticulitis
	• Hospitalisation
	• Need for surgery
	• Progression of disease/ complications:
	  ○ Infections
	  ○ Abscesses
	  ○ Perforation
	  ○ Stricture
	  ○ Fistula

Eligibility criteria – study design	RCT Systematic review Cohort studies Note: in the absence of evidence, cross-sectional studies and case series will be considered.

Other inclusion exclusion criteria	Exclusions: • Children and young people aged 17 years and younger • Prevention
Proposed sensitivity / subgroup analysis, or meta-regression	Strata: Subgroups: • 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)	• 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 –	For details, please see section 6.2 of Developing NICE guidelines: the manual.

publication bias, selective reporting bias	
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	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 7: 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).[43] **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)

Table 8: 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 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.	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 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.	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 11: 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 12: 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	None

Database	Dates searched	Search filter used
	2015	

Table 13: 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 14: 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.

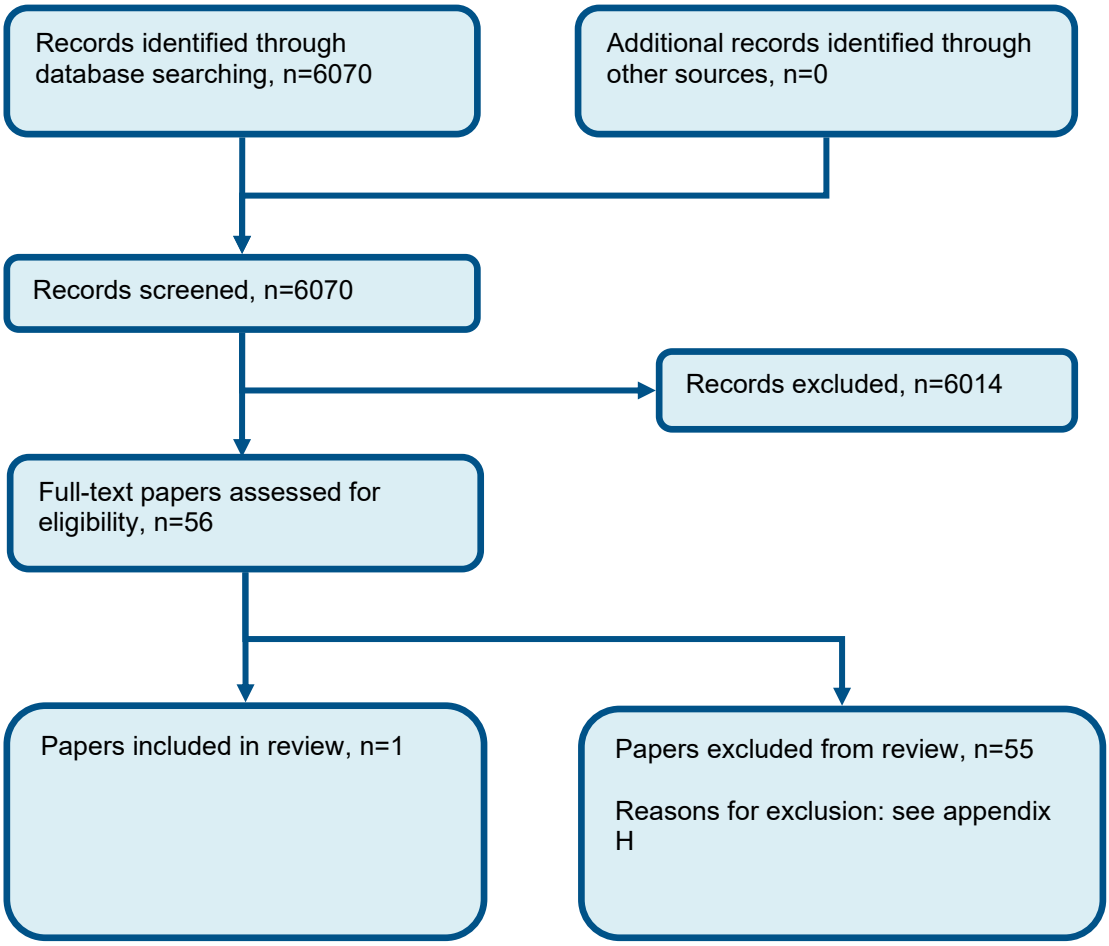
77.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
78.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
79.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
80.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
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 15: 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 indications for surgery.



Appendix D: Clinical evidence tables

Table 16: Clinical evidence tables

Reference	Pittet 2009[49]
Study type and analysis	Cohort; prospective analysis with matched (age and gender) comparison group.
Number of participants and characteristics	All consecutive patients with a diagnosis of diverticulitis on their CT report at admission and those with a final diagnosis of diverticulitis on their discharge summary. Patients were divided into two groups: those with an initial episode of diverticulitis and those with a recurrence. Recurrence was defined as a new episode of diverticulitis provided a previous CT scan confirmed the first episode. First episode (n) = 202 Recurrent episode (n) = 69 Mean age (SD) First: 61 (±14) years Recurrent: 62 (±13) years Gender (male) First: 48% Recurrent: 45%
Prognostic variable	Recurrent diverticulitis
Confounders/ Stratification strategy	The two groups were similar regarding age and sex ratio.
Outcomes and effect sizes	Mortality Peto OR: 0.25 (95% CI 0.04 to 1.63) Surgery OR: 3.06 (95% CI 1.04 to 8.99)

Reference	Pittet 2009[49]
	Presence of abscess OR: 1.11 (95% CI 0.51 to 2.4)
Comments	Risk of bias: high – statistical analysis.

Appendix E: Forest plots

E.1 Recurrent diverticulitis

Figure 2: Mortality

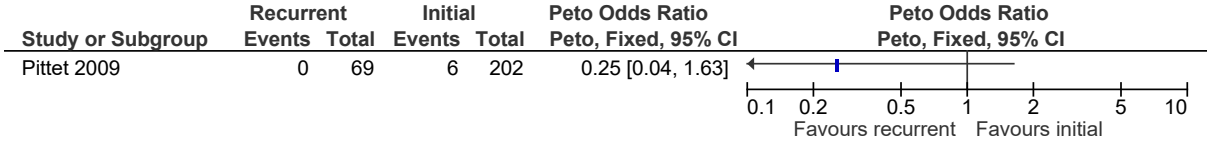


Figure 3: Need for surgery

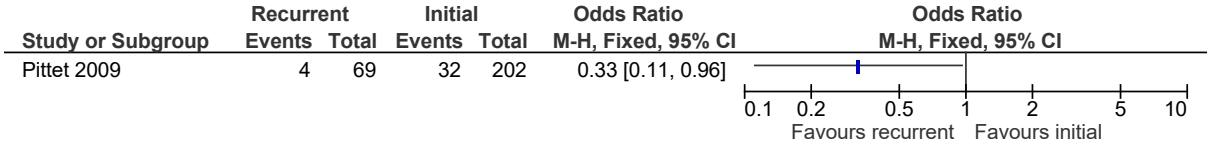
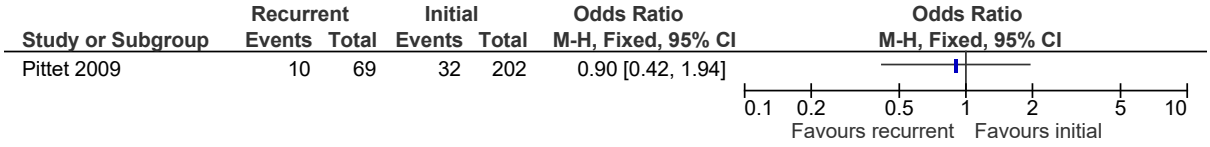


Figure 4: Presence of abscess of CT scan



Appendix F: GRADE tables

Table 17: Clinical evidence profile: Recurrent diverticulitis

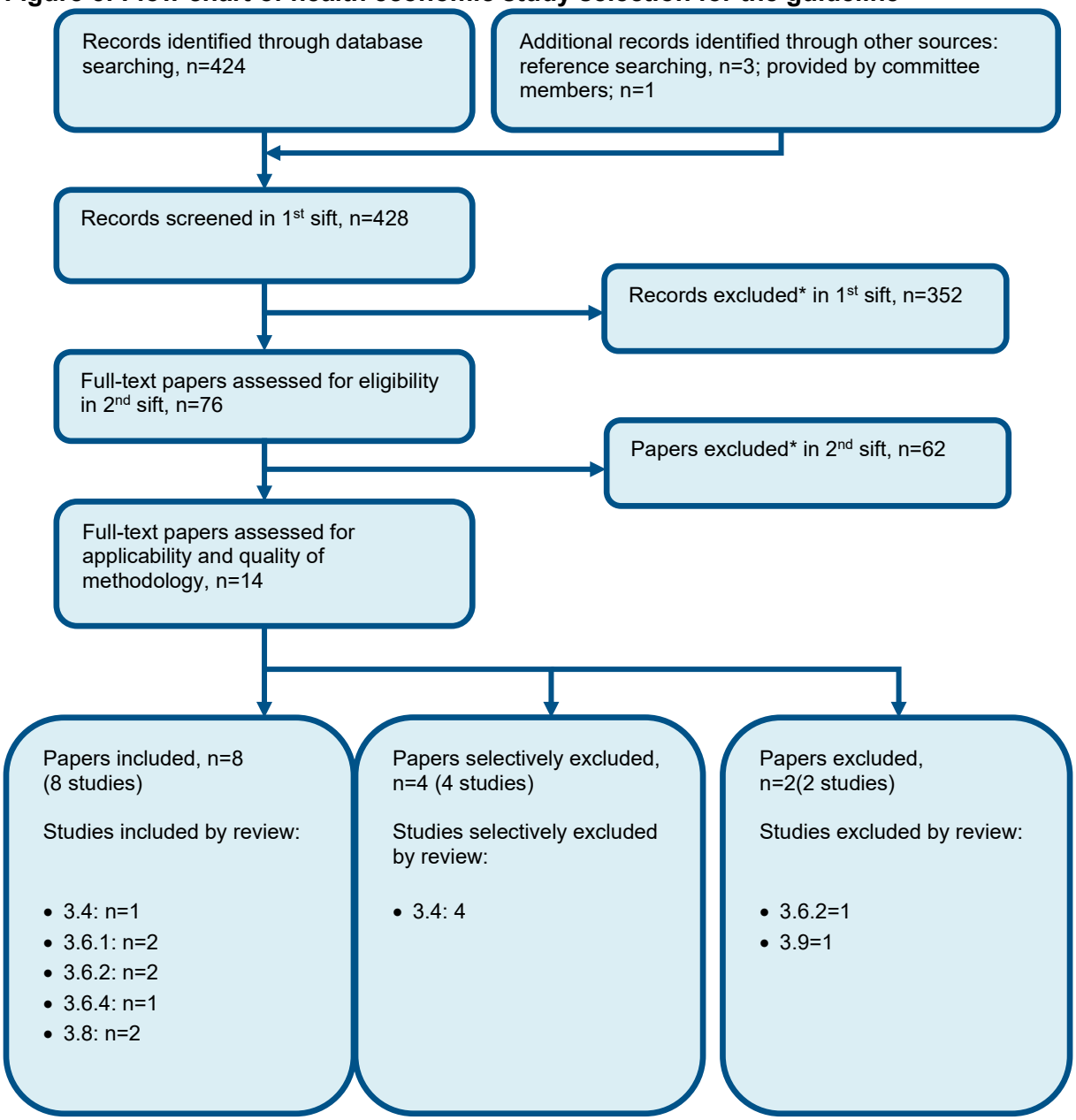
Quality assessment							Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (including publication bias where possible)	Pooled effect (95% CI)	
Mortality								
1	Cohort study	serious[1]	none	no serious indirectness	serious[2]	Univariate analysis. Groups were similar regarding confounding factors.	Peto OR: 0.25 (95% CI 0.04 to 1.63)	LOW
Need for surgery								
1	Cohort study	serious[1]	none	no serious indirectness	none	Univariate analysis. Groups were similar regarding confounding factors.	OR: 3.06 (95% CI 1.04 to 8.99)	MODERATE
Presence of abscess								
1	Cohort study	serious[1]	none	no serious indirectness	serious[2]	Univariate analysis. Groups were similar regarding confounding factors.	OR: 1.11 (95% CI 0.51 to 2.4)	LOW

[1] *Methods: univariate analysis, the two groups were similar regarding age and sex ratio.*

[2] *95% CI around the median crosses null line.*

Appendix G: Health economic evidence selection

Figure 5: 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 H: Excluded studies

H.1 Excluded clinical studies

Table 18: Studies excluded from the clinical review

Reference	Reason for exclusion
Abbas 2007[1]	Excluded due to incorrect comparison
Alvarez 2009[2]	Excluded due to incorrect comparison/analysis
Ambrosetti 1996[3]	Excluded due to incorrect analysis
Ambrosetti 1994[4]	Excluded due to incorrect comparison/analysis
Ames 2009[5]	Excluded due to incorrect comparison/analysis
Amin 1984[6]	Excluded due to incorrect comparison/analysis
Andeweg 2016[7]	Excluded due to incorrect Intervention
Anonymous 2002[8]	Excluded due to incorrect study design
Aydinli 2017[9]	Excluded due to incorrect comparison/analysis
Bauer 2009[10]	Excluded due to incorrect study design
Bielecki 2002[11]	Excluded due to incorrect comparison/analysis
Biondo 2012[12]	Excluded due to incorrect comparison
Bohm 2015[13]	Excluded due to incorrect study design
Bolkenstein 2017[14]	Excluded due to incorrect comparison/analysis
Broderick-Villa 2005[15]	Excluded due to incorrect comparison
Carpenter 1972[16]	Excluded due to incorrect study design
Ceresoli 2017[17]	Excluded due to incorrect study design
Chapman 2005[18]	Excluded due to no relevant outcome
Chapman 2006[19]	Excluded due to incorrect comparison/analysis
Chiu 2001[20]	Excluded due to incorrect Intervention
Damle 2014[21]	Excluded due to inappropriate review population
Deenichin 2008[22]	Excluded due to incorrect comparison/analysis
Elliott 1997[23]	Excluded due to incorrect analysis
Gala 2014[24]	Excluded due to incorrect study design
Garfinkle 2016[25]	Excluded due to incorrect comparison/analysis
Gregersen 2016[26]	Excluded due to incorrect comparison/analysis
Haglund 1979[27]	Excluded due to incorrect Intervention
Himal 1977[28]	Excluded due to incorrect comparison/analysis
Howe 1979[29]	Excluded due to incorrect comparison/analysis
Hussain 2008[30]	Excluded due to incorrect comparison/analysis
Isbister 1997[31]	Excluded due to incorrect comparison/analysis
Jalouta 2017[32]	Excluded due to incorrect comparison/analysis
Jamal Talabani 2016[33]	Excluded due to no relevant outcome
Janes 2009[34]	Excluded due to incorrect study design
Kaewlai 2007[35]	Excluded due to incorrect comparison/analysis
Kakodkar 2005[36]	Excluded due to incorrect comparison
Kiani 2015[37]	Excluded due to inappropriate review population
Kronborg 1993[38]	Excluded due to incorrect comparison
Ladwa 2012[39]	Excluded due to abstract only
Lahat 2013[40]	Excluded due to incorrect analysis
Lanas 2011[41]	Excluded due to incorrect not review population
Medina 1991[42]	Excluded due to incorrect comparison

Reference	Reason for exclusion
Nelson 2008[44]	Excluded due to incorrect analysis
Niebling 2013[45]	Excluded due to incorrect comparison/analysis
Nishikawa 2013[46]	Excluded due to incorrect comparison/analysis
Nord 1995[47]	Excluded due to abstract only
O'Leary 2013[48]	Excluded due to incorrect comparison/analysis
Rahbour 2013[50]	Excluded due to incorrect comparison/analysis
Shah 2011[51]	Excluded due to incorrect comparison/analysis
Solkar 2005[52]	Excluded due to incorrect comparison/analysis
Soreide 2016[53]	Excluded due to incorrect study design
Thorson 2012[54]	Excluded due to systematic review with irrelevant PICO
Vasilevsky 1998[55]	Excluded due to incorrect comparison/analysis
Vinas-Salas 2001[56]	Excluded due to incorrect comparison/analysis
Wood 1977[57]	Excluded due to incorrect comparison/analysis