National Institute for Health and Care Excellence

Final

Diverticular disease: diagnosis and management

[K] Evidence review for laparoscopic versus open sigmoid resection for acute diverticulitis

NICE guideline NG147

Intervention evidence review

November 2019

Final

This evidence review was developed by the National Guideline Centre

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1.1 Review question: What is the most appropriate method of resection in people with acute diverticulitis?

1.2 Introduction

Over the last decade there have been marked changes in the surgical management of patients with complications of acute complicated diverticular disease. Resections are now frequently undertaken laparoscopically with the use of laparoscopic lavage in the emergency setting. The thresholds for elective resection after recurrent episodes of acute diverticulitis have changed with a greater focus on tailored decision making with the patient. There have been alterations to the threshold for primary anastomosis especially in the emergency setting. This review of the evidence aimed to provide information for both clinicians and patient on what were the clinically and cost effective surgical approaches to the management of acute complicated diverticular disease.

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 acute diverticulitis
Intervention	Open resection
Comparison	Laparoscopic resection
Outcomes	Critical outcomes: Quality of life Mortality Morbidity Progression of disease Complications: • infections • abscesses • perforation • fistula • stricture Recurrence rates of acute diverticulitis Hospitalisation Need for further surgery Anastomotic leak rate Important outcomes: Symptom control/recurrence, for example pain relief, bowel habit
Study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, search for observational studies

1.4 Clinical evidence

1.4.1 Included studies

A search was conducted for randomised trials comparing the effectiveness of open surgery versus laparoscopic surgery for patients with acute diverticulitis

One systematic review (three RCTs)[1] was identified (see Table 2).

1.4.2 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Abraha 2017[1]	Gervaz 2010 Laparoscopic sigmoid colectomy N=59 Open sigmoid colectomy N=54 Raue 2011 Laparoscopic sigmoid colectomy N=75 Open sigmoid colectomy N=68 Sigma 2009 Laparoscopic sigmoid colectomy N=52 Open sigmoid colectomy N=52	Gervaz 2010 Participants between 18 and 85 years with diverticular disease defined as follows: "Diverticular disease of sigmoid colon documented by colonoscopy and 2 episodes of uncomplicated diverticulitis, 1 at least being documented with CT scan or 1 episode of complicated diverticulitis, with a pericolic abscess (Hinchey stage I) or pelvic abscess (Hinchey stage II) requiring percutaneous drainage." Raue 2011 Participants with a proven stage II/III disease (stage II: pericolic inflammation with or without local abscess; stage III: recurrent disease with stenosis, fistula, or bleeding) according to the classification of Stock and Hansen (Hansen 1999)	Quality of life Mortality Morbidity Major complications Recurrent diverticulitis	

Study	Intervention and comparison	Population	Outcomes	Comments
		Sigma 2009 Symptomatic diverticulitis of the sigmoid colon: previous 2 or more recurrent attacks of acute diverticulitis with (Hinchey I) or without pericolic abscess necessitating hospitalization with intravenous antibiotics and nil per os; previous recurrent attacks of acute diverticulitis with percutaneously drainable distant abscess necessitating CT-guided drainage (Hinchey IIa); presence of internal fistula between the sigmoid colon and a hollow organ with abscess (Hinchey IIb) or without; presence of symptomatic stricture of the sigmoid colon with no evidence of cancer; recurrent severe diverticular bleeding requiring blood transfusions verified at colonoscopy and/or arteriogram. Surgery was performed at least 3 months after the last attack of diverticulitis."		

See appendix D for full evidence tables.

1.4.3 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Laparoscopic versus open resection

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Open resection	Risk difference with laparoscopic resection (95% CI)
30-Day postoperative mortality	360 (3 studies)	⊕⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	OR 0.13 (0.01 to 1.21)[b]	Moderate	
				19 per 1000	20 fewer per 1000 (from 40 fewer to 10 more)[a]
Late overall mortality (more than 30 days post operation)	93 (1 study)	⊕⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	RR 2.04 (0.19 to 21.77)	Moderate	
				21 per 1000	22 more per 1000 (from 17 fewer to 436 more)
Surgical complications (follow-up 6 to 12 months)	360 (3 studies)	⊕⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	RR 0.84 (0.6 to 1.19)	Moderate	
				368 per 1000	59 fewer per 1000 (from 147 fewer to 70 more)
Early overall morbidity (30 postoperative days)	113 (1 study) 30 days	⊕⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	RR 1.46 (0.51 to 4.2)	Moderate	
				93 per 1000	43 more per 1000 (from 46 fewer to 298 more)
Late overall morbidity (after the first 30 postoperative days: within 6 months)	93 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	RR 0.6 (0.26 to 1.38)	Moderate	
				255 per 1000	102 fewer per 1000 (from 189 fewer to 97 more)
Major complications (follow up 6 to 12 months)	360 (3 studies)	⊕⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	RR 0.74 (0.43 to 1.25)	Moderate	
				118 per 1000	31 fewer per 1000 (from 67 fewer to 30 more)
Reoperation for anastomotic leak	349	⊕⊖⊖⊖	OR 0.74	Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Open resection	Risk difference with laparoscopic resection (95% CI)
(follow up 6 to 12 months)	(3 studies)	VERY LOW[c,d] due to risk of bias, imprecision	(0.27 to 2.02)[b]	59 per 1000	10 fewer per 1000 (from 60 fewer to 30 more)[a]
Other adverse outcomes - Anastomotic stricture (follow-up 6 months)	104 (1 study)	⨁⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	RR 1 (0.06 to 15.57)	Moderate	
				19 per 1000	0 fewer per 1000 (from 18 fewer to 277 more)
Other adverse outcomes - Small-bowel obstruction (follow-up 6 months)	104 (1 study)	⨁⊖⊖⊖ VERY LOW[c,d] due to risk of bias, imprecision	RR 0.25 (0.03 to 2.16)	Moderate	
				77 per 1000	58 fewer per 1000 (from 75 fewer to 89 more)

[a]Risk difference
[b]Peto odds ratio due to low event rate
[c]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[d]Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

See appendix F for full GRADE tables.

Outcomes not suitable for meta-analysis

Quality of life

Raue 2011 assessed global health status using the EORTC QLQ-C30 v3 questionnaire and found no significant differences between laparoscopic surgery and open surgery groups at 7, 30, and 90 days, and 12 months postoperatively (each $P > 0.05$)

Sigma Trial 2009 used the SF-36 questionnaire 6 weeks after surgery and found that participants who underwent laparoscopic surgery scored significantly better than those who underwent open surgery in terms of role limitations due to physical health (PRF) ($P = 0.039$) and role limitations due to emotional problems (ERF) ($P = 0.024$), social functioning (SF) ($P = 0.015$), and pain (PN) ($P = 0.032$)

Gervaz 2010 used the Gastrointestinal Quality of Life Index and reported that the median score was 115 in the open group vs 110 in the laparoscopic group (P = 0.17)

Recurrence diverticulitis rate

One trial - Gervaz 2010 - reported this outcome and provided no evidence of differences in the diverticulitis recurrence rate between laparoscopic (1.9%) and open surgery groups (3.8%) (P = 0.56). In a second trial, 2 participants (1 in each group) developed recurrent diverticulitis treated with antibiotics. This outcome therefore was not subjected to meta-analysis

1.5 Economic evidence

1.5.1 Included studies

Two health economic studies were identified with the relevant comparison and have been included in this review. [12, 13] These are summarised in the health economic evidence profile below (Table 4) and the health economic evidence tables in appendix H.

1.5.2 Excluded studies

One economic study relating to this review question was identified but was excluded due to methodological limitations. [7] This is listed in appendix I, with reasons for exclusion given.

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

1.5.3 Summary of studies included in the economic evidence review

Table 4: Health economic evidence profile: laparoscopic versus open sigmoid resection

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Klarenbeek 2011 [13] (The Netherlands)	Partially applicable[a]	Potentially serious limitations[c]	Within trial cost effectiveness analysis. one centre of the Sigma RCT (VU University Medical Centre). 6 month time horizon. Results were reported for 2 subgroups defined by availability of effectiveness evidence	**SF-36(g) Complete, 6 months:** £5,827[e] **Complication rate complete, 6 months:** £4,611[e]	**SF-36 complete, 6 months:** Incremental (2−1): 3.25 **Complication rate complete, 6 months:** Incremental (2−1): 31.90%	**SF-36 complete, 6 months:** £1,792 per SF-36 unit gained **Complication rate complete, 6 months:** £14,500 per complication averted	**SF-36, 6 months:** BCa95%CI: Dominant to £18,538 Excluding the costs incurred by one patient with severely complicated disease: £45 (95% CI: Dominant to £2,710) per SF36 unit gained **Complication rate, 6 months:** BCa95%CI: Dominant to £1,028 Excluding the costs incurred by one patient with severely complicated disease: Dominant (95% CI: dominant to £11,000) per complication averted.
Gervaz 2011 [12] (Switzerland)	Partially applicable[b]	Potentially serious limitations[d]	Within trial cost consequences analysis of an RCT. Overall costs were recorded as a secondary outcome, with median follow-up of 30 months.	Intervention 2 saves £391 [f]	**GIQLI[h]:** Incremental (2−1): 5 lower **Complication rate:** Incremental (2−1): 1.1% higher	N/a	N/a

Abbreviations: 95% CI: 95% confidence intervals; GIQLI=Gastrointestinal Quality of Life Index; ICER: incremental cost-effectiveness ratio; n/a: not applicable; QALY: quality-adjusted life years; RCT: randomised controlled trial

(a) The Netherlands, hospital perspective

(b) Switzerland, hospital perspective

(c) Only 57 of 104 included in the Sigma multicentre RCT were included in this analysis, as only those people treated in the VU University Medical Centre (n=57) were included. The people in the VU University subgroup had a 19.3% reduction in morbidity rate for laparoscopic resection, whereas the people in the wider trial had a 15.4% reduction in morbidity rate. This might mean that the ICER has been overestimated. Different total costs are presented for 'SF-36, 6 months' and 'complication rate, 6 months.' The number of people included in each analysis is not reported.

(d) There was a wide range for duration of follow up for costs and outcomes. No detailed breakdown of cost components incorporated. Unclear whether costs other than those incurred to the institution are included, such as GP appointments or the costs of people readmitted in other hospitals. Methods for obtaining costs and resource use data not reported. Sources for unit costs not reported. Cost year not reported, though study ran from 2005-2009. Two authors received funding from Covidien (formerly Tyco Healthcare). No discounting reported

(e) Converted using 2005 purchasing power parities[18]

(f) Converted using 2009 purchasing power parities[18]

(g) Scale=0-100 where 100 represents no disability.

(h) Scale=0-176; higher scores represent better quality of life.

1.6 Evidence statements

1.6.1 Clinical evidence statements

Evidence from the single included systematic review demonstrated a potential clinically important benefit of laparoscopic resection compared with open resection in terms of a number of mortality and morbidity-related outcomes, including 30-day postoperative mortality (3 studies, n=360, very low quality), surgical complications (6-12 month follow-up, 3 studies, n=360, very low quality), late overall morbidity (1 study, n=93, very low quality) and major complications (6-12 month follow-up, 3 studies, n=360, very low quality). Evidence for other similar outcomes suggested a benefit of open resection compared with laparoscopic resection in terms of mortality and morbidity, including late overall mortality (1 study, n=93, very low quality) and early overall morbidity (1 study, n=113, very low quality). However, substantial uncertainty was observed for all of the outcomes listed and therefore a benefit of either surgical approach could not be determined based on mortality and morbidity-related outcomes.

Evidence was also available indicating a slight benefit of laparoscopic resection over open resection in terms of reoperation for anastomotic leak at 6-12 months follow-up (3 studies, n=349, very low quality) and small bowel obstruction at 6 months follow-up (1 study, n=104, very low quality). However, again there was substantial uncertainty and imprecision in these results meaning the committee considered the evidence not to be strong enough to recommend laparoscopic resection over open resection. There was also evidence to suggest no clinical difference between laparoscopic resection and open resection in terms of anastomotic stricture at 6 months follow-up (1 study, n=104, very low quality).

1.6.2 Health economic evidence statements

Two economic evaluations found similar total costs for both laparoscopic and open surgery. One found a lower rate of complications in the laparoscopic arm.

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 critical outcomes outlined for this review were; quality of life, mortality, morbidity, progression of disease, complications (infections, abscesses, perforation, fistula and stricture), recurrence rates of acute diverticulitis, hospitalisation, need for further surgery and anastomotic leak rate. The important outcomes were symptom control/recurrence for example pain relief and bowel habit.

The quantitative evidence included in this review was for the outcomes mortality, morbidity, complications and need for further surgery. Evidence for quality of life and recurrence of acute diverticulitis was included narratively as it could not be analysed qualitatively. No evidence was found for progression of disease, hospitalisation, anastomotic leak rate or symptom control/recurrence.

1.7.1.2 The quality of the evidence

All the outcomes included in this evidence review were of very low quality assessed using GRADE. This was due to the high risk of bias and imprecision present.

1.7.1.3 Benefits and harms

Although there was some evidence of benefit favouring laparoscopic resection over open resection for mortality and morbidity, these outcomes had wide confidence intervals and thus imprecision which caused uncertainty in these results. Furthermore, the committee noted there was no clinical difference between the two procedures for the remaining outcomes, therefore they were unable to make a recommendation favouring either laparoscopic or open resection. The committee noted that laparoscopic resection has been associated with shorter recovery times and a quicker return to activities of daily living in cancer resections but there was no evidence available to support this in diverticular disease. The committee agreed that the decision to perform either surgery should be left to the surgeons based on their experience. It was noted that a laparoscopic approach has become the approach of choice for colorectal surgeons within the NHS.

1.7.2 Cost effectiveness and resource use

Laparoscopic surgery is typically harder to perform and involves more costly equipment/consumables and more theatre time than open surgery. However, laparoscopic surgery is expected to have a quicker recovery time and shorter hospital stay.

There were two cost effectiveness studies included in the review, each based on a within randomised trial analysis.

Both studies were relatively small (n=113 and n=57) and had wide confidence for both costs and effects.

One study in a Swiss setting found near equivalence of outcomes at 30 months. Mean cost was marginally lower in the laparoscopic arm.

The other study, set in the Netherlands, found adverse events to be lower in the laparoscopic arm but costs were around £5,000 higher. However, this difference was down to a single high-cost patient. When that patient was removed then the open surgery arm was more costly. Even before the patient was removed, length of hospital stay was lower on average by 0.9 days per patient in the laparoscopic arm.

The committee noted that the cost of laparoscopic surgery may have decreased since the studies were conducted due to decreased theatre time and cheaper consumables.

The committee concluded that the studies were inconclusive with regard to which surgical approach is more costly and which was most cost effective and therefore they recommended that the approach taken should reflect the experience of the surgeon.

1.7.3 Other factors the committee took into account

The committee acknowledged that there were potential benefits to the laparoscopic approach such as reduced pain, reduced length of stay and quicker return to function that had been reported in other areas of colorectal surgery so a laparoscopic approach has become the approach of choice for colorectal surgeons within the NHS. Patients might require resection for example if they have a diverticular fistula or stricture which is symptomatic and causing obstructive symptoms. There was no clear evidence on the role of subsequent resection following a conservatively treated perforation or abscess.

Elective surgery for acute diverticulitis is an option if symptoms continue, for example in people with fistula or stricture. The committee noted that patients were more likely to opt for laparoscopic resection over open resection. Thus, the committee expressed the importance for surgeons to disclose their conversion rate of laparoscopic to open resection, along with the national conversion rate, to allow the patient to give informed consent. This information should be provided in conjunction with the risks and benefits of each type of resection.

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Appendices

Appendix A: Review protocols

Table 5: Review protocol: Laparoscopic versus open resection

Field	Content
Review question	What is the most appropriate method of resection in people with acute diverticulitis?
Type of review question	intervention 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 most appropriate method of resection in people with acute complicated 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)	• Open resection • Laparoscopic resection
Eligibility criteria – comparator(s) / control or reference (gold) standard	Compared to each other

Outcomes and prioritisation	Critical outcomes:
	• Quality of life
	• Mortality
	• Morbidity
	• Progression of disease
	• Complications:
	  ○ infections
	  ○ abscesses
	  ○ perforation
	  ○ fistula
	  ○ stricture
	• Recurrence rates of acute diverticulitis
	• Hospitalisation
	• Need for further surgery
	• Anastomotic leak rate
	
	Important outcomes:
	Symptom control/recurrence, for example pain relief, bowel habit

Eligibility criteria – study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, search for observational studies
Other inclusion exclusion criteria	Exclusions: • Children and young people aged 17 years and younger

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

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

Table 6: 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).[16] **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 7: 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
Embase (OVID)	1974 – 13 November 2018	Exclusions Randomised controlled trials Systematic review 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 8: 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.	21 and (29 or 40)

Table 9: 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.	19 and (29 or 40)

Table 10: 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 11: 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 12: 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 13: 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.

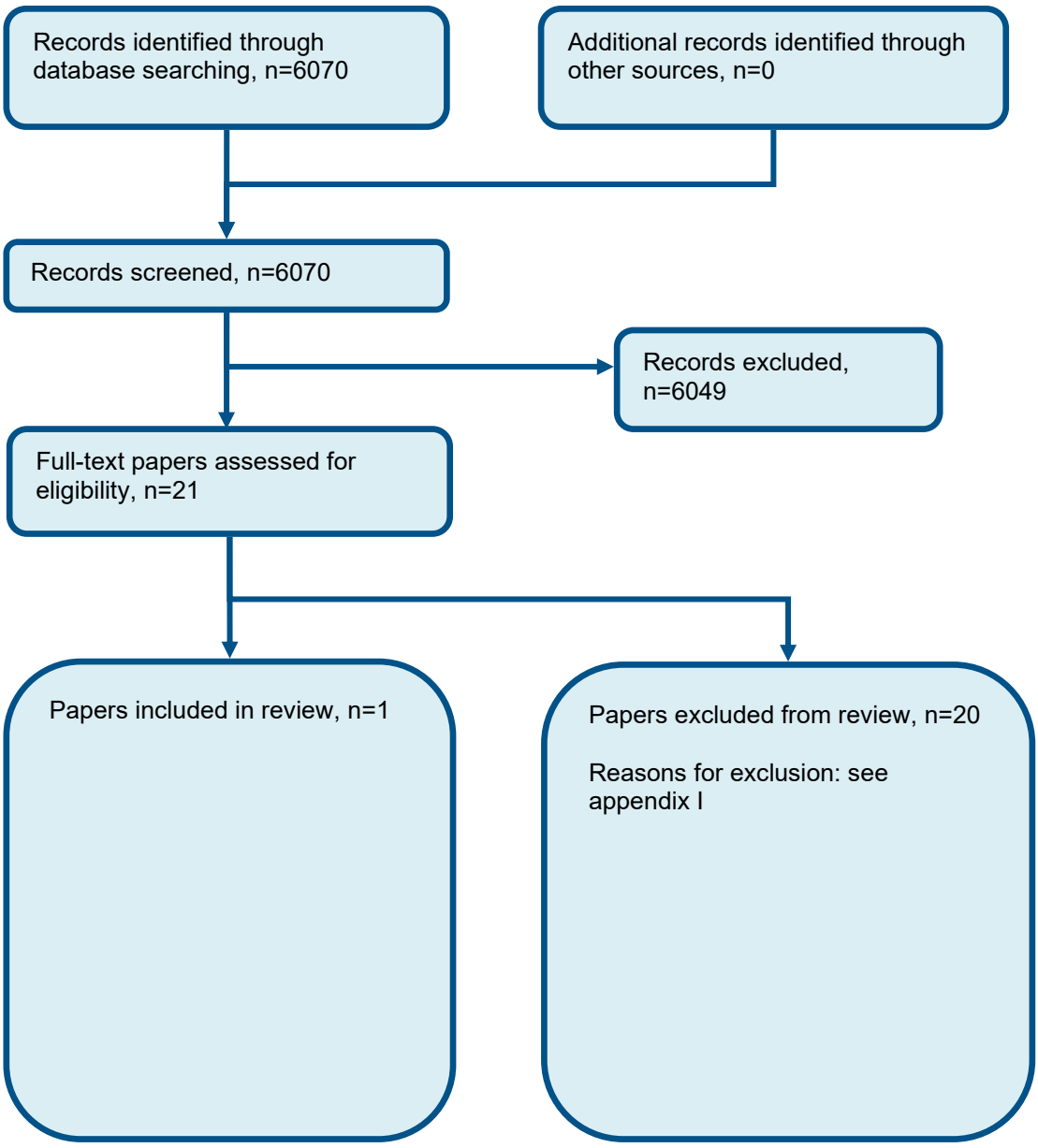
80.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
81.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
82.	or/20-40
83.	19 and (36 or 60 or 82)

Table 14: 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 laparoscopic versus open resection



Appendix D: Clinical evidence tables

Table 15: Clinical evidence tables

Study	Abraha 2017[1]
Study type	Systematic Review
Number of studies (number of participants)	3 (n=392)
Countries and setting	Conducted in Germany, Netherlands, Switzerland
Line of therapy	Mixed line
Duration of study	Intervention + follow up: Up to 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Age, gender and ethnicity	Age - Median (range): 62 to 66. Gender (M:F): SR- not defined. Ethnicity: SR - not stated
Further population details	1. Age: Systematic review: mixed 2. Ethnicity: Systematic review: mixed
Indirectness of population	No indirectness
Interventions	(n=197) Intervention 1: Open resection. Open sigmoid colectomy. Duration Surgery. Concurrent medication/care: Not stated. Indirectness: No indirectness (n=195) Intervention 2: Laparoscopic resection - Laparoscopic resection. Laparoscopic sigmoid colectomy. Duration Surgery. Concurrent medication/care: Not stated. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OPEN RESECTION versus LAPARAROSCOPIC RESECTION

Protocol outcome 1: Quality of life at Define
- Actual outcome: Quality of life at Unclear; Raue 2011

Study	Abraha 2017[1]
assessed global health status using the EORTC QLQ-C30 v3 questionnaire and found no significant differences between laparoscopic surgery and open surgery groups at 7, 30, and 90 days, and 12 months postoperatively (each P > 0.05) Sigma Trial 2009 used the SF-36 questionnaire 6 weeks after surgery and found that participants who underwent laparoscopic surgery scored significantly better than those who underwent open surgery in terms of role limitations due to physical health (PRF) (P = 0.039) and role limitations due to emotional problems (ERF) (P = 0.024), social functioning (SF) (P = 0.015), and pain (PN) (P = 0.032) Gervaz 2010 used the Gastrointestinal Quality of Life Index and reported that the median score was 115 in the open group vs 110 in the laparoscopic group (P = 0.17) ; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcome 2: Mortality at Define - Actual outcome: Post-operative mortality at 30 day; RR; 0.24 (95%CI 0.03 to 2.07); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Late overall mortality at > 30 days post-operation; RR; 2.04 (95%CI 0.19 to 21.77); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcome 3: Morbidity at Define - Actual outcome: Early overall morbidity at 30 days post-operation; RR; 1.46 (95%CI 0.51 to 4.2);	

Study	Abraha 2017[1]
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Late overall morbidity at > 30 days post-operation but within 6 months; RR; 0.6 (95%CI 0.26 to 1.38); Risk of bias: All domain - ; Indirectness of outcome: No indirectness Protocol outcome 4: Complications (infections) at Define - Actual outcome: Surgical complications at 6-12 months; RR; 0.84 (95%CI 0.6 to 1.19); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Major complications at 6-12 months; RR; 0.74 (95%CI 0.27 to 2.02); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Complications (stricture) at Define - Actual outcome: Anastomotic stricture at 6 months; RR; 1.00 (95%CI 0.06 to 15.57); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Small bowel obstruction at 6 months; RR; 0.25 (95%CI 0.03 to 2.16); Risk of bias: All domain - ; Indirectness of outcome: No indirectness Protocol outcome 6: Anastomotic leak rate at Define - Actual outcome: Reoperation for anastomotic leak at 6-12 months; RR; 0.75 (95%CI 0.29 to 1.95); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Progression of disease at Define; Complications (abscesses) at Define; Complications (perforation) at Define; Complications (fistula) at Define; Recurrence rates of acute diverticulitis at Define; Hospitalisation at Define; Need for further surgery at Define; Symptom control/recurrence (e.g. pain relief, bowel habit) at Define

Appendix E: Forest plots

E.1 Laparoscopic versus open surgery

Figure 2: 30 day postoperative mortality

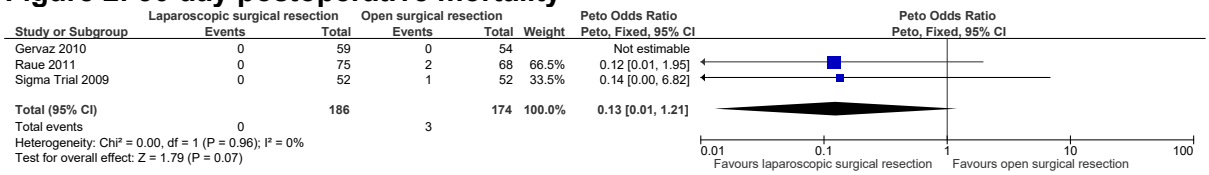


Figure 3: Late overall mortality

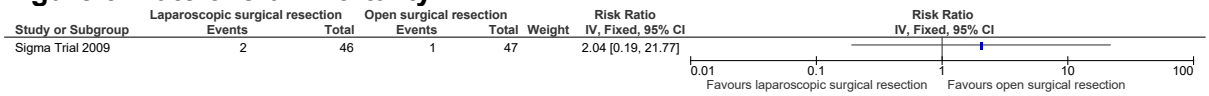


Figure 4: Surgical complications

Figure 5: Early overall morbidity

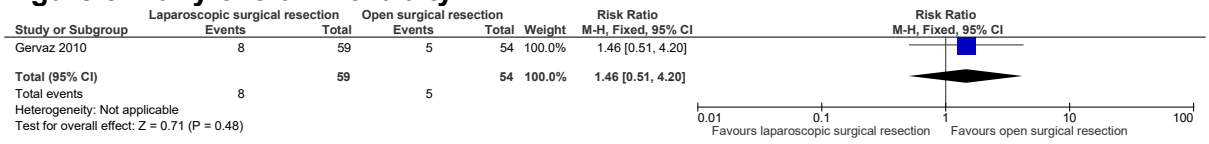


Figure 6: Late overall morbidity

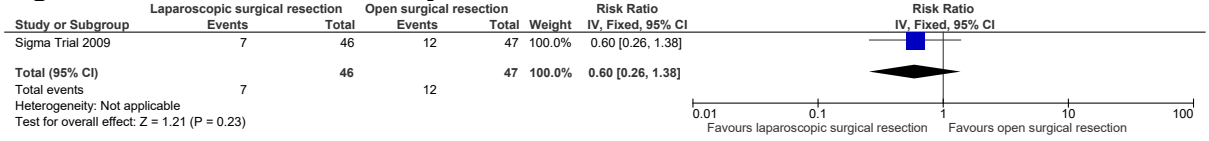


Figure 7: Major complications

Figure 8: Reoperation for anastomotic leak

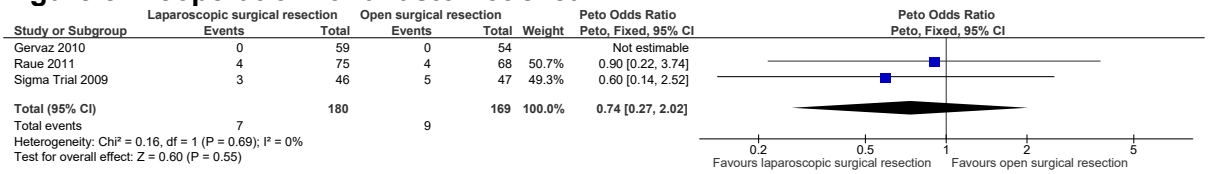
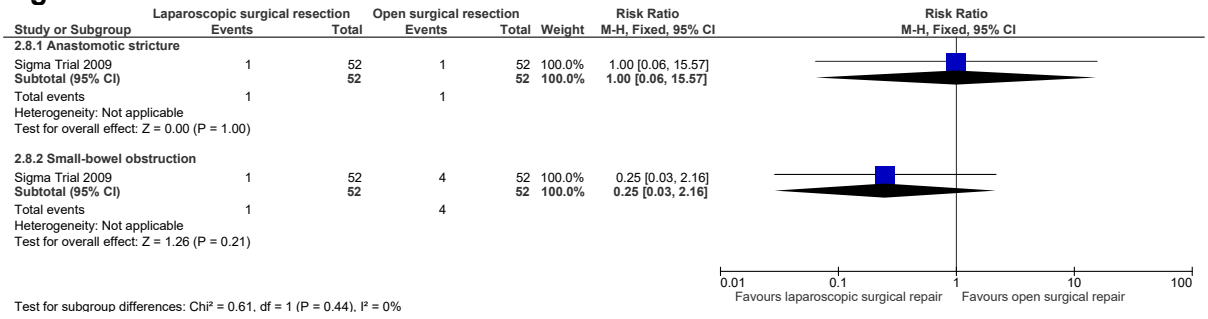


Figure 9: Other adverse outcomes



Appendix F: GRADE tables

Table 16: Clinical evidence profile: Laparoscopic versus open surgery

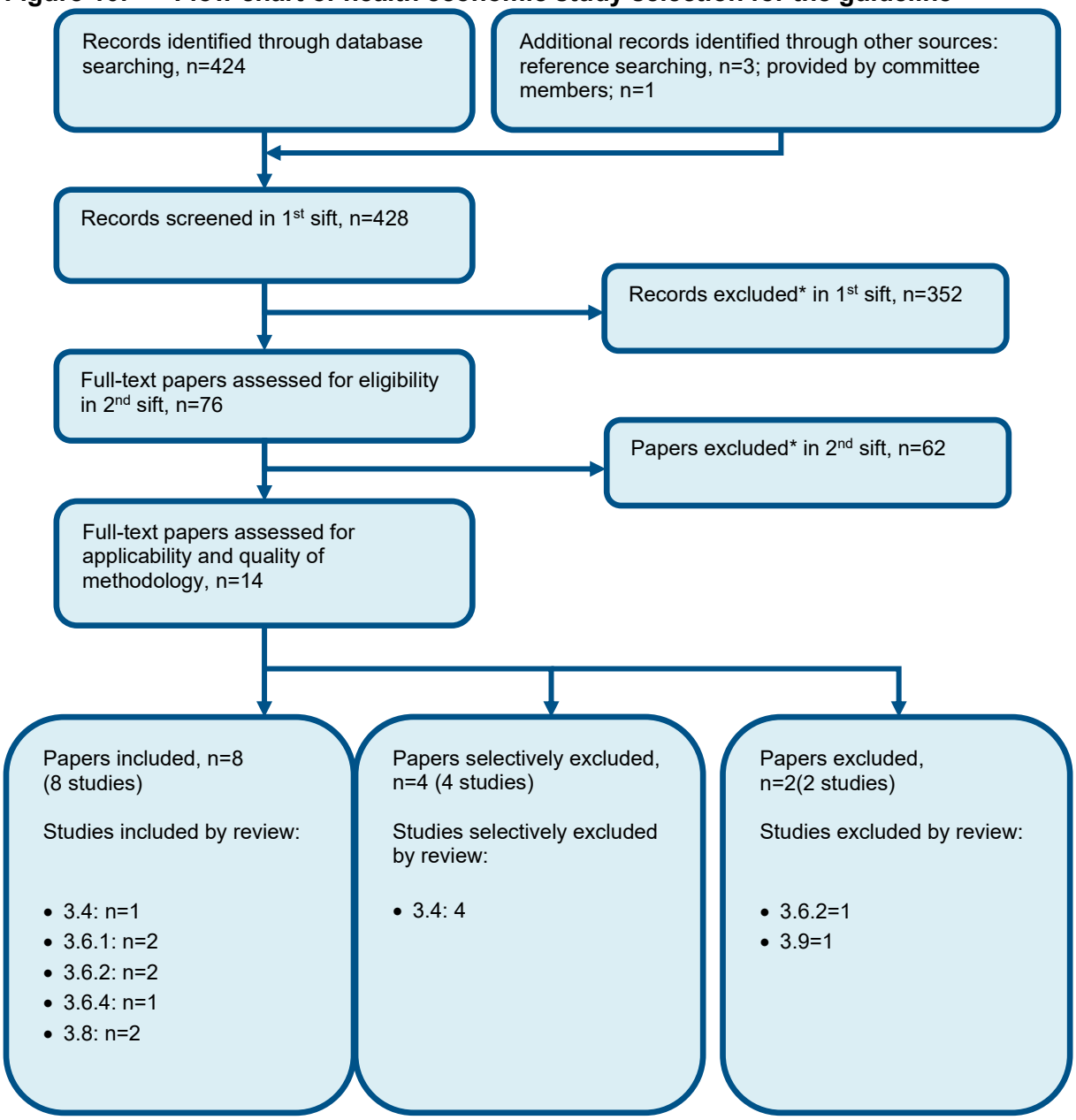
Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Secondary outcomes	Control	Relative (95% CI)	Absolute		
30-Day postoperative mortality												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/186 (0%)	1.9%	OR 0.13 (0.01 to 1.21)[3]	20 fewer per 1000 (from 40 fewer to 10 more)[4]	⊕OOO VERY LOW	CRITICAL
Late overall mortality (more than 30 days post-operation)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/46 (4.3%)	2.1%	RR 2.04 (0.19 to 21.77)	22 more per 1000 (from 17 fewer to 436 more)	⊕OOO VERY LOW	CRITICAL
Surgical complications (follow up 6 to 12 months)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	43/186 (23.1%)	36.8%	RR 0.84 (0.6 to 1.19)	59 fewer per 1000 (from 147 fewer to 70 more)	⊕OOO VERY LOW	CRITICAL
Early overall morbidity (follow-up mean 30 days)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/59 (13.6%)	9.3%	RR 1.46 (0.51 to 4.2)	43 more per 1000 (from 46 fewer to 298 more)	⊕OOO VERY LOW	CRITICAL
Late overall morbidity (follow-up mean 6 months)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/46 (15.2%)	25.5%	RR 0.6 (0.26 to 1.38)	102 fewer per 1000 (from 189 fewer to 97 more)	⊕OOO VERY LOW	CRITICAL

Major complications (follow up 6 to 12 months												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	20/186 (10.8%)	11.8%	RR 0.74 (0.43 to 1.25)	31 fewer per 1000 (from 67 fewer to 30 more)	⊕OOO VERY LOW	CRITICAL
Reoperation for anastomotic leak (follow up 6 months)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/180 (3.9%)	5.9%	OR 0.74 (0.27 to 2.02)[3]	10 fewer per 1000 (from 60 fewer to 30 more)[4]	⊕OOO VERY LOW	CRITICAL
Other adverse outcomes - Anastomotic stricture (follow up six months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/52 (1.9%)	1.9%	RR 1 (0.06 to 15.57)	0 fewer per 1000 (from 18 fewer to 277 more)	⊕OOO VERY LOW	CRITICAL
Other adverse outcomes - Small-bowel obstruction												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/52 (1.9%)	7.7%	RR 0.25 (0.03 to 2.16)	58 fewer per 1000 (from 75 fewer to 89 more)	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Peto odds ratio due to low event rate
[4] Risk difference

Appendix G: Health economic evidence selection

Figure 10: 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: Health economic evidence tables

Table 17: Health economic evidence tables

Study	Klarenbeek 2011 [13]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA (health outcome:SF-36, complication rate) **Study design:** **Approach to analysis:** Data were obtained from a software database that prospectively records resource use for those treated in one centre of the Sigma RCT (VU University Medical Centre). A further software programme was used to apply unit costs per intervention unit per patient. Differences in total costs were then compared with differences in VAS pain score, SF-36 values and complication rates. **Perspective:** The Netherlands, hospital **Follow-up:** 6 months	**Population:** Symptomatic diverticulitis defined as: recurrent Hinchey I, IIa, IIb, symptomatic stricture, severe rectal bleeding **Patient characteristics:** Start age: NR Male: NR **Intervention 1:** Open sigmoid resection **Intervention 2:** Laparoscopic sigmoid resection	**SF-36, 6 months. Total costs (mean per patient) n=22/22:** Intervention 1: £9,074 Intervention 2: £14,900 Incremental (2−1): £5,827 (95% CI: NR; p=NR) **Complication rate, 6 months. Total costs (mean per patient) n=27/30:** Intervention 1: £8,958 Intervention 2: £13,659 Incremental (2−1): £4,611 (95% CI: Dominant to £14,037; p=NR) **Currency & cost year:** 2005 euros (presented here as 2005 UK pounds[(b)]) **Cost components incorporated:** Hospital stay. Operating time: room use per hour, disposable materials, sterilisation costs, fees. Imaging: CT, ultrasound, X-ray, barium enema. Diagnostics: colonoscopy, EKG, laboratory tests. Blood products. Consultant appointments.	**SF-36(d), 6 months n=22/22:** Intervention 1: 56.98 Intervention 2: 60.23 Incremental (2−1): 3.25 (95% CI: NR; p=0.588) **Complication rate, 6 months n=22/22:** Intervention 1: 46.70% Intervention 2: 14.80% Incremental (2−1): 31.90% decrease in complication rate (95% CI: NR; p=0.010)	**ICER (Intervention 2 versus Intervention 1) (SF-36) n=22/22:** £1,792 per SF-36 unit gained (pa) BCa95%CI: Dominant to £18,538 Probability Intervention 2 cost effective: NR/NR **ICER (Intervention 2 versus Intervention 1) (complication rate) n=22/22:** £14,500 per complication averted (pa) BCa95%CI: Dominant to £102,800 Probability Intervention 2 cost effective: NR/NR **Analysis of uncertainty:** 95% confidence intervals around cost differences were estimated using a nonparametric bootstrap with 2000 replications. Uncertainty around cost-effectiveness ratios was estimated using the bias-corrected and accelerated bootstrapping method (5000 replications). A sensitivity analysis was carried out which excluded the costs incurred by one patient with severely complicated disease. The total cost difference between intervention 1 and 2 fell to $9 when this person was

Treatment effect duration: 6 months **Discounting:** Costs: n/a; Outcomes: n/a		Physiotherapy, dietician and stoma care services. Emergency and outpatient attendances. Other infrequently used resource items not shown, but included in total costs.		excluded. The ICER fell to £45 (95% CI: Dominant to £2,710) per SF36 unit gained and dominant (95% CI: dominant to £110) per percentage decrease in complication rate.
Data sources				
Health outcomes: Subgroup of patients treated in the VU University Medical Centre as part of the Sigma multicentre RCT. [14] **Quality-of-life weights:** SF-36 **Cost sources:** Resource use aggregated from TOREN software programme® which allows prospective recording of actual resource use per patient. TRAG PI software programme® used to translate resource use into costs, applying direct costs from TOREN registry per intervention unit per patient.				
Comments				
Source of funding: NR **Limitations:** Only 57 of 104 included in the Sigma multicentre RCT were included in this analysis, as only those people treated in the VU University Medical Centre (n=57) were included. This was due to lack of transparency and uniformity in cost registration across different sites. The people in the VU University subgroup had a 19.3% reduction in morbidity rate for laparoscopic resection, whereas the people in the wider trial had a 15.4% reduction in morbidity rate. This might mean that the ICER has been overestimated. Different total costs are presented for 'SF-36, 6 months' and 'complication rate, 6 months.' The number of people included in each analysis is not reported. **Other:**				
Overall applicability: Partially applicable(c)		**Overall quality:** Potentially serious limitations(d)		

Abbreviations: CT: computed tomography imaging; BCa95%CI: 95% confidence intervals calculated using the bias-corrected and accelerated bootstrapping method; *CEA: cost-effectiveness analysis; 95% CI: 95% confidence interval; ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported; pa: probabilistic analysis; RCT: randomised controlled trial; SF-36: Short-form 36 questionnaire*

(a) Converted using 2005 purchasing power parities[18]
(b) Directly applicable / Partially applicable / Not applicable
(c) Minor limitations / Potentially serious limitations / Very serious limitations
(d) Scale=0-100 where 100 represents no disability.

Study	Gervaz 2011 [12]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CCA (health outcomes: GIQLI, complication rate) **Study design:** Within-trial analysis of a randomised controlled trial **Approach to analysis:** Overall costs were recorded as a secondary outcome of the RCT. Analysis was by intention- to-treat, with converted patients included as part of the laparoscopic group. **Perspective:** Switzerland, hospital **Follow-up. Median (range)**: 30 months (9-63 months) **Discounting:** Costs: NR; Outcomes: NR	**Population:** Patients with complicated diverticular disease who are candidates for elective sigmoidectomy **Patient characteristics:** n: 113 (Intervention 1: 54; Intervention 2: 59) Median age: Intervention 1: 63 (range 38-84).; Intervention 2: 59 (range 29-82) Male/female ratio: Intervention 1: 21/20; Intervention 2: 24/30 **Intervention 1:** Open sigmoid resection **Intervention 2:** Laparoscopic sigmoid resection	**Total costs (median per patient):** Intervention 1: £6,056 (range £2,945 to £19,218) Intervention 2:£5,665 (range £2,526 to £71,479) Incremental (2−1): Saves £391 (95% CI: NR; p=0.47) **Currency & cost year:** 2005- 2009 Swiss Francs (presented here as 2009 UK pounds[(b)]) **Cost components incorporated:** Costs related to readmissions and reoperations.	**GIQLI scores(d):** Intervention 1: 115 (range 57-144) Intervention 2: 110 (range 61-134) Incremental (2−1): 5 lower (95% CI: NR; p=0.17) **Complication rate:** Intervention 1: 13.7% Intervention 2: 14.8% Incremental (2−1): 1.1% higher (95% CI: NR; p=0.87)	**ICER (Intervention 2 versus Intervention 1):** n/a **Analysis of uncertainty:** n/a
Data sources				
Health outcomes: From a single centre randomised controlled trial in the Department of Surgery, University Hospital, Geneva. [12] Clinical examinations were conducted by a surgeon. Wounds were assessed to detect incisional hernia and CT imaging was performed where there was doubt. For small bowel obstruction, subsequent admissions to the hospital were reviewed to determine their cause. **Quality-of-life weights:** GIQLI **Cost sources:** A single centre randomised controlled trial at University Hospital, Geneva. [12] Sources of unit costs not reported.				
Comments				
Source of funding: Sponsored by University Hospital, Geneva **Limitations:** There was a wide range for duration of follow up for costs and outcomes. No detailed breakdown of cost components incorporated. Unclear whether costs other than those incurred to the institution are included, such as GP appointments or the costs of people readmitted in other hospitals. Methods for obtaining costs and resource use data not reported. Sources for unit costs not reported. Cost year not reported, though study ran from 2005-2009. Two authors received funding from Covidien (formerly Tyco Healthcare). No discounting reported. **Other:**				
Overall applicability: Partially applicable[(c)] **Overall quality:** Potentially serious limitations[(d)]				

Abbreviations: CCA: cost–consequences analysis; 95% CI: 95% confidence interval; GIQLI: Gastrointestinal Quality of Life Index: ICER: incremental cost-effectiveness ratio; n/a: not applicable; NR: not reported
(a) Converted using 2009 purchasing power parities[18]
(b) Directly applicable / Partially applicable / Not applicable
(c) Minor limitations / Potentially serious limitations / Very serious limitations
(d) Scale=0-176; higher scores represent better quality of life

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 18: Excluded clinical studies

Study	Exclusion reason
Alves 2005[2]	Non-randomised study
Badic 2017[3]	Non-randomised study
Bartels 2010[4]	SR checked for references
Bissolati 2015[5]	Non-randomised study
Cirocchi 2011[6]	Non-randomised study
Dwivedi 2002[8]	Abstract
Eijsbouts 1997[9]	Non-randomised study
Gaertner 2013[10]	SR checked for references
Gervaz 2010[11]	Included in SR
Gervaz 2011[12]	Included in SR
Larach 2004[15]	Review
Noel 2007[17]	Non-randomised study
Purkayastha 2006[19]	Abstract
Raue 2011[21]	Included in SR
Raue 2011[20]	Included in SR
Schwenk 2005[22]	Non-randomised study
Siddiqui 2010[24]	SR checked for references
Siddiqui 2010[23]	SR checked for references
Vennix 2016[25]	SR checked for references
Wu 2017[26]	SR checked for references

I.2 Excluded health economic studies

Table 19: Studies excluded from the health economic review

Reference	Reason for exclusion
De'Angelis 2013 [7]	This study was assessed as partially applicable but with very serious limitations, since the costs were limited to the initial index admission.