National Institute for Health and Care Excellence

Final

Diverticular disease: diagnosis and management

[E] Evidence review for management of recurrent diverticular disease

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 clinically and cost effective management strategy for people with recurrent episodes of diverticular disease (including indications for elective surgery/surgical opinion)?

1.2 Introduction

This review evaluates the evidence for any treatment options for recurrent diverticular disease. These treatment options could be non-pharmacological treatments such as dietary advice or lifestyle changes or could include pharmacological treatment such as analgesia, aminosalicylates and antibiotics. The aim of these treatments would be to reduce the symptoms of diverticular disease and to also prevent future episodes of acute diverticulitis.

Patients with diverticular disease are generally given dietary advice to increase fibre intake maintain an adequate fluid intake and maybe avoid certain types of food. The aim of this question was to evaluate the evidence behind these common recommendations. There are currently no medicines routinely used to treat diverticular disease other than potentially recommending bulk forming laxatives if a high fibre diet is insufficient symptom control. Symptoms of diverticular disease often include abdominal pain and analgesia such as paracetamol may be recommended. Generally patients with diverticular disease are advised to avoid non-steroidal anti-inflammatories and opioid based pain killers. This question also aimed to determine if there is any evidence for any pharmacological treatments in the management of 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 aged 18 years and over with recurrent diverticular disease/in remission from a previous episode of diverticular disease at risk of recurrent diverticular disease.
Interventions	• Aminosalicylates • Antibiotics • Probiotics • Prebiotics • Elective surgery • Dietary modification • Smoking cessation • Weight loss • Exercise • Laxatives • Antispasmodics • Analgesics • Combinations of above treatments
Comparisons	Placebo

	No treatment Compared to each other

Outcomes	Critical outcomes:
	• Quality of life
	• Mortality
	• Morbidity
	• Progression of disease to acute diverticulitis (diagnosis)
	• Complications
	  ○ infections
	  ○ abscesses
	  ○ perforation
	  ○ fistula
	  ○ stricture
	
	Important outcomes:
	• Side effects of medications
	• Pain/symptom control
	• Hospitalisation
	• Recurrence of symptoms

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

No studies were included in the review. See the study selection flow chart in appendix C.

1.4.2 Excluded studies

See the excluded studies list in appendix H.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified.

1.5.2 Excluded studies

No relevant health economic studies were identified.

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 2: NHS drug costs

Drug	Assumed daily dose [BNF][a]	Cost per unit (£)	Cost per month (£)[b]	Source
Laxatives				
Isphagula husk 3.5g effervescent granules sachets	2 x 3.5g sachets [5-10g once daily]	£0.09	£5.52	NHS Drug Tariff
Methylcellulose 500mg	2 x 500mg tablets daily [3-6 x 500mg tablets twice daily]	£0.05	£2.89	NHS Drug Tariff
Sterculia 62% granules 7g sachets	2 x 7g sachets twice daily [1-2 sachets 1-2 times a day]	£0.11	£13.53	NHS Drug Tariff
Bisacodyl 5mg gastro-resistant tablets	2 x5mg tablets [5-10mg once daily increased if necessary up to 20mg once daily]	£0.21	£12.66	NHS Drug Tariff
Sodium picosulfate 5mg/5ml oral solution	2 x 5mg/ml solutions [5-10mg once daily]	£0.12	£7.20	NHS Drug Tariff
Senna 7.5mg tablets	2 x 7.5mg tablets [7.5-15mg daily (maximum dose 30 mg daily)]	£0.03	£1.67	NHS Drug Tariff
Lactulose 3.1g-3.7g/5ml oral solution	6 x 3.1g-3.7g/5ml oral solution [Initially 15ml twice daily, adjusted according to response]	£0.02	£4.13	NHS Drug Tariff
Macrogol 3350 oral powder 8.5g sachets	2 sachets [2 sachets once daily usually for up to 2 weeks]	£0.14	£3.89[c]	NHS Drug Tariff
Docusate sodium 100mg capsules (by mouth)	5 x 100mg capsules [Up to 500mg daily in divided doses, adjusted according to response]	£0.07	£10.60	NHS Drug Tariff
Glycerol (by rectum) 4g suppositories	1 x 4g suppository [4g, as required]	£0.10	£2.94	NHS Drug Tariff
Micralax (sodium citrate 90mg/ml) 5ml micro-enema	1 enema [1 enema per dose]	£0.41	£12.35	British National Formulary
Arachis oil 130ml enema	1 x 130ml enema [130ml, as required]	£47.50	£95[d]	NHS Drug Tariff
Antibiotics				
Rifaximin 200mg tablets	2 x 200mg tablets - 4 x 200mg tablets [200mg every 8 hours for 3 days]	£1.68	£33.67[e] - £67.33[e]	NHS Drug Tariff
Analgesia				
Paracetamol 500mg	2 x 500mg tablets	£0.02	£3.87	NHS Drug Tariff

Drug	Assumed daily dose [BNF][a]	Cost per unit (£)	Cost per month (£)[b]	Source
(by mouth)	every 6 hours [0.5-1g every 4-6 hours (maximum 4g per day)]			
Ibuprofen 400mg tablets	1 x 400mg tablet 4 times a day [Initially 300-400mg 3-4 times a day; increased if necessary to up to 600mg 4 times a day; maintenance 200-400mg 3 times a day, may be adequate]	£0.03	£3.25	NHS Drug Tariff
Dexibuprofen 400mg tablets	2 x 400mg tablets [600-900mg daily in up to 3 divided doses; increased if necessary up to 1.2g daily (maximum per dose 400mg)]	£0.16	£9.61	NHS Drug Tariff
Naproxen 250mg tablets	5 x 250mg tablets [Initially 500mg, then 250mg every 6-8 hours as required (maximum dose after the first day 1.25g daily)]	£0.03	£4.24	NHS Drug Tariff
Nefopam 30mg tablets	6 x 30mg tablets [Initially 60mg, 3 times a day, adjusted according to response; usual dose 30-90mg, 3 times a day]	£0.21	£38.90	NHS Drug Tariff
Antispasmodics				
Atropine sulfate 600 microgram tablets	2 x 600µg tablets [600-1200µg daily]	£1.89	£115.05	NHS Drug Tariff
Dicycloverine hydrochloride 20mg tablets	3 x 20mg tablets [10-25mg, 3 times a day]	£2.34	£213.81	NHS Drug Tariff
Propantheline bromide 15mg tablets	3 x 15mg tablets [15mg, 3 times a day (maximum 120mg per day)]	£0.19	£16.91	NHS Drug Tariff
Alverine citrate 60mg capsules	6 x 60mg capsules [60-120mg 1-3 times a day]	£0.05	£8.31	NHS Drug Tariff
Mebeverine hydrochloride 135mg tablets	3 x 135mg tablets [135mg-150mg 3 times a day]	£0.04	£4.01	NHS Drug Tariff
Peppermint oil 0.2ml gastro resistant	6 x 0.2ml capsules	£0.08	£15.31	NHS Drug Tariff

Drug	Assumed daily dose [BNF][a]	Cost per unit (£)	Cost per month (£)[b]	Source
capsules	[1-2 capsules 3 times a day for up to 2-3 months if necessary]			
Aminosalicylates				
Mesalazine (Octasa®) tablets 800mg gastro-resistant tablets	1 x 800mg tablet[d] -2 x 800mg tablets daily [2.4-4.8g daily]	£0.45	£4.49[e] - £27.31	NHS Drug Tariff
Probiotics and prebiotics				
VSL#3 Probiotic food supplement oral powder 4.4g sachets	1 x 4.4g sachet daily	£1.15	£34.86	BNF (NHS indicative price)

Sources: NHS Drug Tariff, February 2018; British National Formulary
(a) Dosages for adults, British National Formulary
(b) Depending on number of units taken
(c) Cost per 14 day course; not per month
(d) Cost per 2 days; not per month
(e) Cost when dose taken 10 days out of every month

Table 3: 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

No relevant published evidence was identified.

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

No evidence was identified for this review.

1.7.1.2 The quality of the evidence

No evidence was identified for this review.

1.7.1.3 Benefits and harms

The critical outcomes considered for this review were quality of life, mortality, morbidity, progression of disease to acute diverticulitis (diagnosis) and complications (infections, abscesses, perforation, fistula and stricture). Side effects of medication, pain/symptom control and hospitalisation were considered important outcomes. However, no evidence was identified for this review.

1.7.2 Cost effectiveness and resource use

No relevant economic evaluations were identified which addressed the cost effectiveness of management strategies for people with recurrent diverticular disease. In the absence of relevant economic evaluations and clinical evidence, the committee did not recommend any additional treatments for the prevention of recurrent diverticular disease.

1.7.3 Other factors the committee took into account

The committee defined recurrent diverticular disease as repeated episodes of symptomatic diverticular disease. The committee discussed that standard practice for people with recurrent diverticular disease would entail interventions such as dietary modifications and simple analgesics, for example paracetamol. They noted that antibiotics should be avoided routinely and if possible only considered in people with constitutional symptoms, for example fever and severe abdominal pain. The committee emphasised that surgery should be considered as a last resort as it carries the risk of recurrent symptoms and has significant mortality and morbidity risk.

It was agreed by the committee that further investigations may be required to rule out other conditions which give rise to similar symptoms. However, the committee were unable to make any consensus recommendations.

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Appendices

Appendix A: Review protocols

Table 4: Review protocol: Management of recurrent diverticular disease

Field	Content
Review question	What is the most clinically and cost-effective management strategy for recurrent diverticular disease?
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 find the most effective management strategy for recurrent diverticular disease
Eligibility criteria – population / disease / condition / issue / domain	Adults 18 years and over with recurrent diverticular disease/in remission from a previous episode of diverticular disease at risk of recurrent diverticular disease.
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	• aminosalicylates • antibiotics • probiotics • prebiotics • elective surgery • dietary modification • smoking cessation • weight loss • exercise • laxatives • antispasmodics • analgesics • combinations of above treatments
Eligibility criteria – comparator(s) / control or reference (gold) standard	• Placebo • No treatment • Comparing to each other

Outcomes and prioritisation	Critical outcomes:
	• Quality of life
	• Mortality
	• Morbidity
	• Progression of disease to acute diverticulitis (diagnosis)
	• Complications
	  ○ infections
	  ○ abscesses
	  ○ perforation
	  ○ fistula

	○ stricture Important outcomes: • Side effects of medications • Pain/symptom control • Hospitalisation • Recurrence of symptoms
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
Proposed sensitivity / subgroup analysis, or meta-regression	Subgroups: • <50 vs >50 years • people of Asian family origin as they are known to develop right-sided diverticula • Different types of surgical procedures: laparoscopic surgery and open surgery
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	Standard study checklists were used to critically appraise individual

assessing bias at outcome / study level	studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report (Chapter R) for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by James Dalrymple in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
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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 5: Health economic review protocol

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis,

	comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[19] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded

	before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'. • Studies published before 2002 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

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

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 6: Database date parameters and filters used

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

Table 7: Medline (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter/
4.	editorial/

5.	news/
6.	exp historical article/
7.	Anecdotes as Topic/
8.	comment/
9.	case report/
10.	(letter or comment*).ti.
11.	or/3-10
12.	randomized controlled trial/ or random*.ti,ab.
13.	11 not 12
14.	animals/ not humans/
15.	exp Animals, Laboratory/
16.	exp Animal Experimentation/
17.	exp Models, Animal/
18.	exp Rodentia/
19.	(rat or rats or mouse or mice).ti.
20.	or/13-19
21.	2 not 20
22.	randomized controlled trial.pt.
23.	controlled clinical trial.pt.
24.	randomi#ed.ti,ab.
25.	placebo.ab.
26.	randomly.ti,ab.
27.	Clinical Trials as topic.sh.
28.	trial.ti.
29.	or/22-28
30.	Meta-Analysis/
31.	exp Meta-Analysis as Topic/
32.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
33.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
34.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
35.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
36.	(search* adj4 literature).ab.
37.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
38.	cochrane.jw.
39.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
40.	or/50-59
41.	Epidemiologic studies/
42.	Observational study/
43.	exp Cohort studies/
44.	(cohort adj (study or studies or analys* or data)).ti,ab.
45.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
46.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
47.	Controlled Before-After Studies/

48.	Historically Controlled Study/
49.	Interrupted Time Series Analysis/
50.	(before adj2 after adj2 (study or studies or data)).ti,ab.
51.	or/30-39
52.	exp case control study/
53.	case control*.ti,ab.
54.	or/41-42
55.	40 or 43
56.	Cross-sectional studies/
57.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
58.	or/45-46
59.	40 or 47
60.	40 or 43 or 47
61.	21 and (29 or 40 or 60)

Table 8: Embase (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter.pt. or letter/
4.	note.pt.
5.	editorial.pt.
6.	case report/ or case study/
7.	(letter or comment*).ti.
8.	or/3-7
9.	randomized controlled trial/ or random*.ti,ab.
10.	8 not 9
11.	animal/ not human/
12.	nonhuman/
13.	exp Animal Experiment/
14.	exp Experimental Animal/
15.	animal model/
16.	exp Rodent/
17.	(rat or rats or mouse or mice).ti.
18.	or/10-17
19.	2 not 18
20.	random*.ti,ab.
21.	factorial*.ti,ab.
22.	(crossover* or cross over*).ti,ab.
23.	((doubl* or singl*) adj blind*).ti,ab.
24.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
25.	crossover procedure/
26.	single blind procedure/
27.	randomized controlled trial/
28.	double blind procedure/
29.	or/20-28
30.	systematic review/

31.	meta-analysis/
32.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
33.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
34.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
35.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
36.	(search* adj4 literature).ab.
37.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
38.	cochrane.jw.
39.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
40.	or/30-39
41.	Clinical study/
42.	Observational study/
43.	family study/
44.	longitudinal study/
45.	retrospective study/
46.	prospective study/
47.	cohort analysis/
48.	follow-up/
49.	cohort*.ti,ab.
50.	48 and 49
51.	(cohort adj (study or studies or analys* or data)).ti,ab.
52.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
53.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
54.	(before adj2 after adj2 (study or studies or data)).ti,ab.
55.	or/41-47,50-54
56.	exp case control study/
57.	case control*.ti,ab.
58.	or/56-57
59.	55 or 58
60.	cross-sectional study/
61.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
62.	or/60-61
63.	55 or 62
64.	55 or 58 or 62
65.	19 and (29 or 40 or 64)

Table 9: Cochrane Library (Wiley) search terms

#1.	diverticul*.mp.

B.2 Health Economics literature search strategy

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

Table 10: Database date parameters and filters used

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

Table 11: Medline (Ovid) search terms

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

22.	Economics/
23.	Value of life/
24.	exp "Costs and Cost Analysis"/
25.	exp Economics, Hospital/
26.	exp Economics, Medical/
27.	Economics, Nursing/
28.	Economics, Pharmaceutical/
29.	exp "Fees and Charges"/
30.	exp Budgets/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/22-37
39.	exp models, economic/
40.	*Models, Theoretical/
41.	markov chains/
42.	monte carlo method/
43.	exp Decision Theory/
44.	(markov* or monte carlo).ti,ab.
45.	econom* model*.ti,ab.
46.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
47.	Models, Organizational/
48.	*models, statistical/
49.	*logistic models/
50.	models, nursing/
51.	((organi?ation* or operation* or service* or concept*) adj3 (model* or map* or program* or simulation* or system* or analys*)).ti,ab.
52.	(econom* adj2 (theor* or system* or map* or evaluat*)).ti,ab.
53.	(SSM or SODA).ti,ab.
54.	(strateg* adj3 (option* or choice*) adj3 (analys* or decision*)).ti,ab.
55.	soft systems method*.ti,ab.
56.	(Meta-heuristic* or Metaheuristic*).ti,ab.
57.	(dynamic* adj2 (model* or system*)).ti,ab.
58.	(simulation adj3 (model* or discrete event* or agent)).ti,ab.
59.	(microsimulation* or "micro* simulation*").ti,ab.
60.	((flow or core) adj2 model*).ti,ab.
61.	(data adj2 envelopment*).ti,ab.
62.	system* model*.ti,ab.
63.	or/41-64
64.	quality-adjusted life years/
65.	sickness impact profile/

66.	(quality adj2 (wellbeing or well being)).ti,ab.
67.	sickness impact profile.ti,ab.
68.	disability adjusted life.ti,ab.
69.	(qal* or qtime* or qwb* or daly*).ti,ab.
70.	(euroqol* or eq5d* or eq 5*).ti,ab.
71.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
72.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
73.	(hui or hui1 or hui2 or hui3).ti,ab.
74.	(health* year* equivalent* or hye or hyes).ti,ab.
75.	discrete choice*.ti,ab.
76.	rosser.ti,ab.
77.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
78.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
79.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
80.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
81.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
82.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
83.	or/22-40
84.	21 and (38 or 63 or 83)

Table 12: Embase (Ovid) search terms

1.	diverticul*.mp.
2.	limit 1 to English language
3.	letter.pt. or letter/
4.	note.pt.
5.	editorial.pt.
6.	case report/ or case study/
7.	(letter or comment*).ti.
8.	or/3-7
9.	randomized controlled trial/ or random*.ti,ab.
10.	8 not 9
11.	animal/ not human/
12.	nonhuman/
13.	exp Animal Experiment/
14.	exp Experimental Animal/
15.	animal model/
16.	exp Rodent/
17.	(rat or rats or mouse or mice).ti.
18.	or/10-17
19.	2 not 18
20.	Economics/
21.	Value of life/
22.	exp "Costs and Cost Analysis"/

23.	exp Economics, Hospital/
24.	exp Economics, Medical/
25.	Economics, Nursing/
26.	Economics, Pharmaceutical/
27.	exp "Fees and Charges"/
28.	exp Budgets/
29.	budget*.ti,ab.
30.	cost*.ti.
31.	(economic* or pharmaco?economic*).ti.
32.	(price* or pricing*).ti,ab.
33.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
34.	(financ* or fee or fees).ti,ab.
35.	(value adj2 (money or monetary)).ti,ab.
36.	or/20-35
37.	statistical model/
38.	*theoretical model/
39.	nonbiological model/
40.	stochastic model/
41.	decision theory/
42.	decision tree/
43.	exp nursing theory/
44.	monte carlo method/
45.	(markov* or monte carlo).ti,ab.
46.	econom* model*.ti,ab.
47.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
48.	((organi?ation* or operation* or service* or concept*) adj3 (model* or map* or program* or simulation* or system* or analys*)).ti,ab.
49.	(econom* adj2 (theor* or system* or map* or evaluat*)).ti,ab.
50.	(SSM or SODA).ti,ab.
51.	(strateg* adj3 (option* or choice*) adj3 (analys* or decision*)).ti,ab.
52.	soft systems method*.ti,ab.
53.	(Meta-heuristic* or Metaheuristic*).ti,ab.
54.	(dynamic* adj2 (model* or system*)).ti,ab.
55.	(simulation adj3 (model* or discrete event* or agent)).ti,ab.
56.	(microsimulation* or "micro* simulation*").ti,ab.
57.	((flow or core) adj2 model*).ti,ab.
58.	(data adj2 envelopment*).ti,ab.
59.	system* model*.ti,ab.
60.	or/39-61
61.	quality adjusted life year/

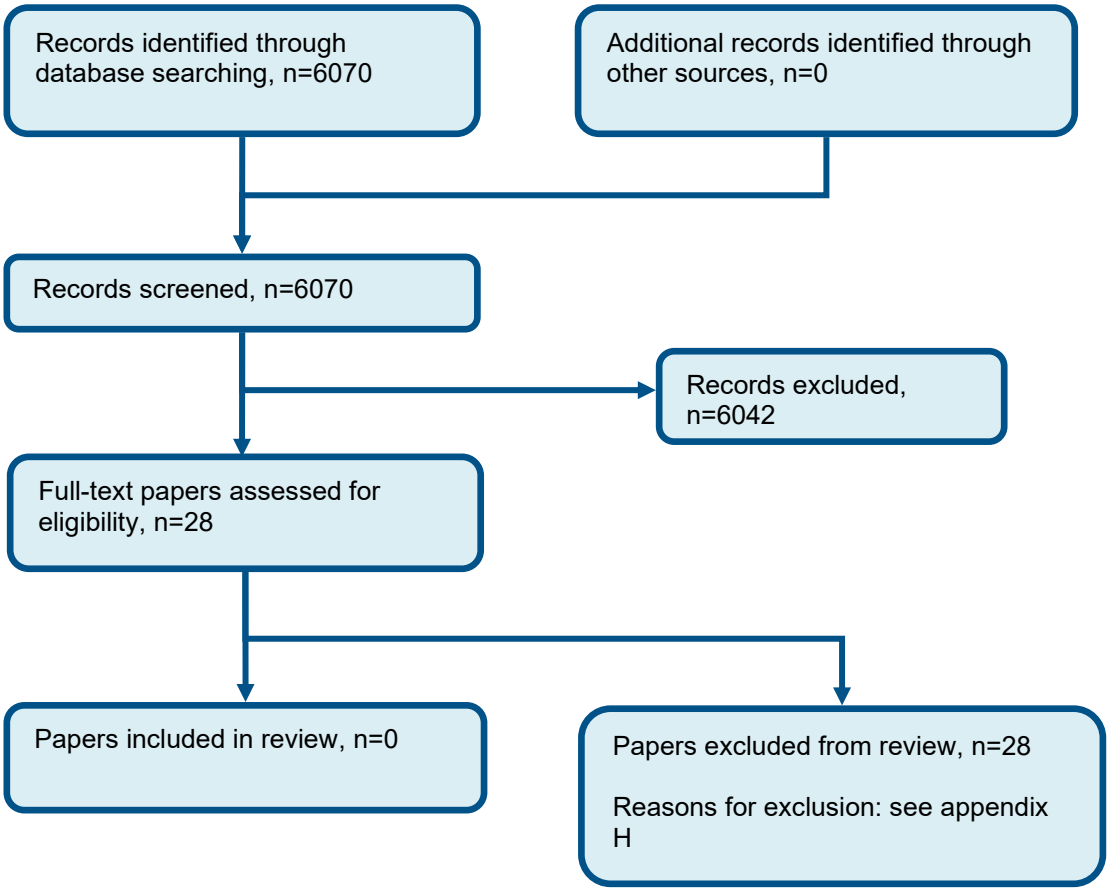
62.	"quality of life index"/
63.	short form 12/ or short form 20/ or short form 36/ or short form 8/
64.	sickness impact profile/
65.	(quality adj2 (wellbeing or well being)).ti,ab.
66.	sickness impact profile.ti,ab.
67.	disability adjusted life.ti,ab.
68.	(qal* or qtime* or qwb* or daly*).ti,ab.
69.	(euroqol* or eq5d* or eq 5*).ti,ab.
70.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
71.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
72.	(hui or hui1 or hui2 or hui3).ti,ab.
73.	(health* year* equivalent* or hye or hyes).ti,ab.
74.	discrete choice*.ti,ab.
75.	rosser.ti,ab.
76.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
77.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
78.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
79.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
80.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
81.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
82.	or/20-40
83.	19 and (36 or 60 or 82)

Table 13: NHS EED and HTA (CRD) search terms

#1.	diverticul*

Appendix C: Clinical evidence selection

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



Appendix D: Clinical evidence tables

No evidence was identified.

Appendix E: Forest plots

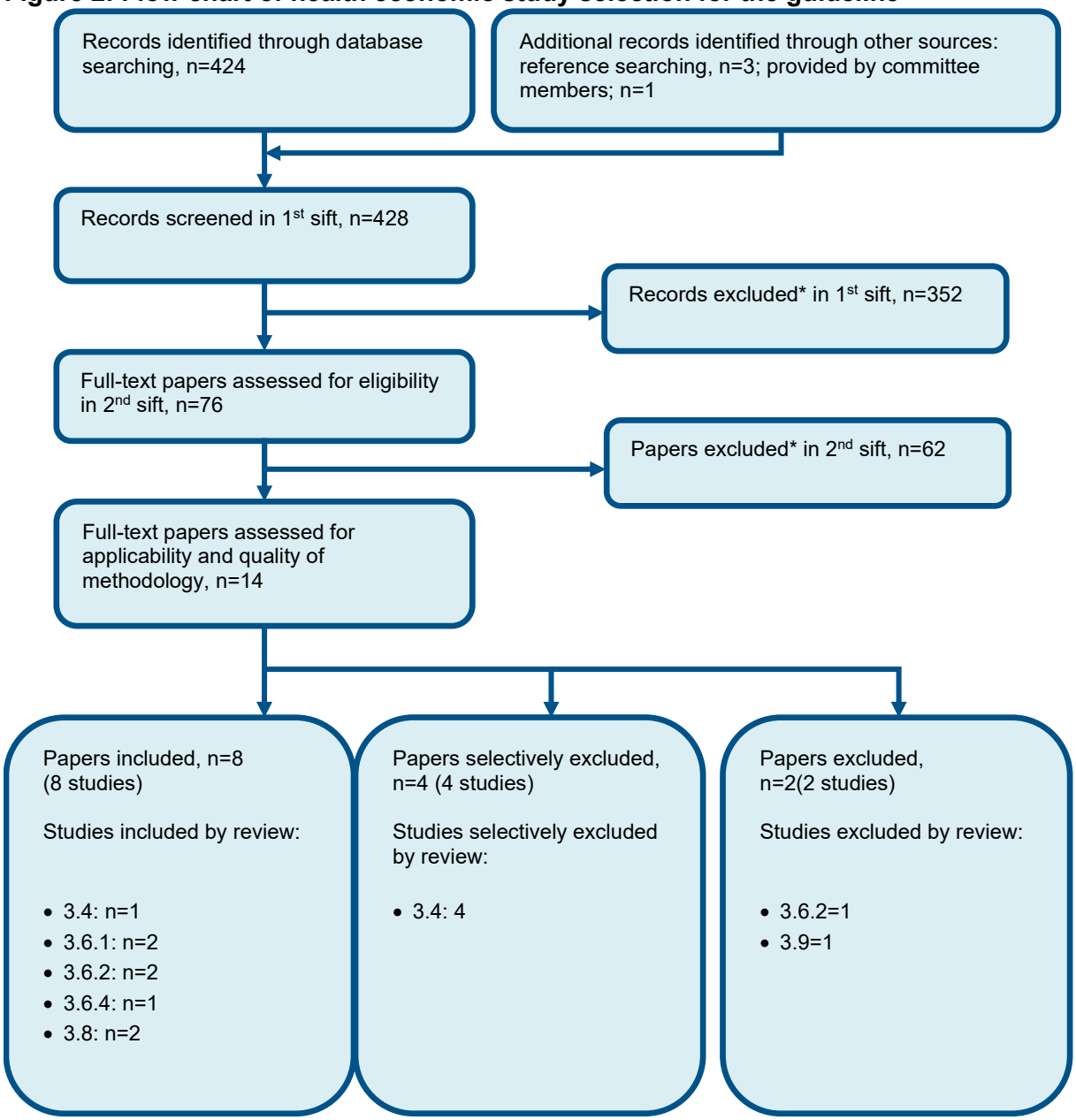
No evidence was identified.

Appendix F: GRADE tables

No evidence was identified.

Appendix G: Health economic evidence selection

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



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

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

3.6.1 Timing of surgery (Evidence review J)

3.6.2 Laparoscopic versus open resection (Evidence review K)

3.6.4 Primary versus secondary anastomosis (Evidence review M)

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

3.9 Management of recurrent diverticulitis (Evidence review P)

Appendix H: Excluded studies

H.1 Excluded clinical studies

Table 14: Studies excluded from the clinical review

Study	Exclusion reason
Andeweg 2016[1]	Not review population
Annibale 2011[2]	Not review population
Brandimarte 2004[3]	Not review population. Incorrect study design. Inappropriate comparison. Incorrect interventions
Brodribb 1977[4]	Not review population
Buchs 2013[5]	Not review population
Cirocchi 2015[6]	Not review population
Colecchia 2007[7]	Not review population
Comparato 2007[8]	Not review population
Fric 2003[9]	Crossover study
Gatta 2012[10]	Not review population
Hodgson 1977[11]	Not review population
Khan 2018[12]	Systematic review: methods are not adequate/unclear
Kruis 2013[13]	Not review population
Kvasnovsky 2017[14]	Not review population
Lahner 2012[16]	Not review population
Lahner 2016[15]	Not review population
Latella 2003[17]	Not review population
Mario 2005[18]	Not review population
Papi 1992[20]	Not review population
Papi 1995[21]	Not review population
Smits 1990[22]	Not review population
Tursi 2006[25]	Not review population
Tursi 2007[26]	Inappropriate comparison. Incorrect interventions
Tursi 2008[27]	Not review population
Tursi 2013[24]	Not review population
Tursi 2013[28]	Not review population
Tursi 2013[23]	Abstract only
Unlü 2010[29]	Not review population