National Institute for Health and Care Excellence

Final

Barrett's oesophagus and stage 1 oesophageal adenocarcinoma

[J] Evidence review for endoscopic and radiological follow-up after treatment

NICE guideline NG231

Evidence review underpinning recommendations 1.5.5 ,1.6.4 and 1.7.2 and research recommendations in the NICE guideline

February 2023

Final

National Institute for Health and Care Excellence

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Contents

1 Clinical and cost effectiveness of endoscopic and radiological follow-up after treatment

1.1 Review question

For people who have received endoscopic treatment for Barrett's oesophagus related stage 1 adenocarcinoma, what is the clinical and cost effectiveness of endoscopic follow-up with or without radiological follow-up?

1.1.1 Introduction

After the endoscopic treatment of Barrett's dysplasia or early stage 1 cancer it is a widely accepted clinical belief that follow up assessments are required to identify the development of metachronous neoplasia. Such recurrences are not uncommon and can be potentially treated, preventing progression to advanced cancer, and close endoscopic surveillance is current standard of care within the National Health Service. The frequency and duration of follow up should reflect the likelihood of recurrence and be based around detecting abnormalities before progression to advanced disease, whilst minimalizing the patient impact of invasive interventions, the risks associated with repeated procedures and the cost of such interventions. This evidence review evaluates the optimal frequency and duration of endoscopic follow-up for people who have received endoscopic treatment for dysplastic Barrett's oesophagus and stage 1 oesophageal adenocarcinoma.

1.1.2 Summary of the protocol

Table 1: PICO characteristics of review question

Population	Adults with endoscopic treatment, 18 years and over, with Barrett's oesophagus related stage 1 adenocarcinoma
Intervention	Endoscopy + Radiological follow up (CT, EUS, PET)
Comparison	Endoscopic follow up: standard endoscopy (any type)
Outcomes	• Mortality (all-cause mortality and disease specific mortality) • Health related quality of life (any validated scores) • Recurrence of cancer or dysplasia • Adverse events (infection, perforation, bleeding) Detection of incidental findings and subsequent investigations
Study design	RCT, Systematic Reviews of RCTs • If no RCT data is available, non-randomised studies will be considered if there is an active comparator component within the study • Systematic Reviews of RCTs Published NMAs and IPDs will be considered for inclusion.

For full details see the review protocol in Appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

No relevant clinical studies comparing endoscopy and radiologic follow up with Standard endoscopic follow up were identified.

See also the study selection flow chart in Appendix C.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix E.

1.1.5 Summary of the effectiveness evidence

There was no clinical evidence found.

1.1.6 Economic evidence

1.1.6.1 Included studies

No health economic studies were included.

1.1.6.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix D of included economic evidence

There was no economic evidence found.

1.1.7 Summary of included economic evidence

There was no economic evidence found.

1.1.8 Economic model

This area was not prioritised for new cost-effectiveness analysis.

1.1.9 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 2: Unit costs for radiological tests

Resource	Unit costs	Source
CT scan	£94	NHS Reference Costs 2019/20
MRI scan	£173	
Plain film imaging (including x-ray)	£56	
Ultrasound	£75	

The committee's discussion of this evidence is included in section 2.1.9.

2 Frequency and duration of endoscopic and radiological follow-up after treatment

2.1 Review question

For people who have received endoscopic treatment for Barrett's oesophagus or stage 1 adenocarcinoma, what is the optimal frequency and duration of endoscopic and radiological follow-up?

2.1.1 Summary of the protocol

Table 3: PICO characteristics of review question

Population	Adults, 18 years and over, with endoscopic treatment and dysplastic Barrett's oesophagus or stage 1 adenocarcinoma
Intervention	Less intensive endoscopic follow up (any differentiation from intensive follow up)
Comparison	Intensive endoscopic follow up (for example, as guideline recommendation - every 3 months for the first year, every 6 months in the second and then annually)
Outcomes	• Mortality (all cause and disease specific mortality) • Health related quality of life (any validated scores) • Patient preference • Recurrence of Barrett's Oesophagus • Recurrence Stage 1 adenocarcinoma • Adverse events (stricture, perforation, infection, bleeding) • Endoscopic reintervention • Non endoscopic intervention (oncological or surgical)
Study design	RCT, SR of RCTs • If no RCT data is available, non-randomised studies will be considered if there is an active comparator component within the study • Systematic Reviews of RCTs Published NMAs and IPDs will be considered for inclusion.

For full details see the review protocol in Appendix F.

2.1.2 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix F and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

2.1.3 Effectiveness evidence

2.1.3.1 Included studies

No relevant clinical studies comparing endoscopy and radiologic follow up with Standard endoscopic follow up were identified.

See also the study selection flow chart in Appendix H.

2.1.3.2 Excluded studies

See the excluded studies list in Appendix J.

2.1.4 Summary of the effectiveness evidence

There was no clinical evidence found.

2.1.5 Economic evidence

2.1.5.1 Included studies

No health economic studies were included.

2.1.5.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix I.

2.1.6 Summary of included economic evidence

There was no economic evidence found.

2.1.7 Economic model

This area was not prioritised for new cost-effectiveness analysis.

2.1.8 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 4: Unit costs for radiological tests

Resource	Unit costs	Source
CT scan	£94	NHS Reference Costs 2019/20
MRI scan	£173	
Plain film imaging (including x-ray)	£56	
Ultrasound	£75	

2.1.9 The committee's discussion and interpretation of the evidence

2.1.9.1 The outcomes that matter most

Clinical and cost effectiveness

The outcomes considered for this review were mortality (including all-cause mortality and disease specific mortality), health related quality of life, recurrence of cancer or dysplasia, adverse events (such as, infection, perforation, and bleeding), and detection of incidental findings and subsequent investigations. For purposes of decision making, all outcomes were considered equally important and were therefore rated as critical by the committee. No evidence was identified for any of the outcomes considered.

Optimal frequency and duration of endoscopic follow-up

The outcomes considered for this review were mortality (including all-cause mortality and disease specific mortality), health related quality of life, patient preference, recurrence of Barrett's oesophagus, recurrence of stage 1 Adenocarcinoma, adverse events (such as, stricture, perforation, infection, bleeding), endoscopic reintervention and non-endoscopic intervention (oncological or surgical). For purposes of decision making, all outcomes were considered equally important and were therefore rated as critical by the committee. No evidence was identified for any of the outcomes considered.

2.1.9.2 The quality of the evidence

No relevant studies comparing endoscopic and radiologic follow up with standard endoscopy in people with stage 1 adenocarcinoma were identified.

No relevant studies examining the optimal frequency and duration of endoscopic and radiologic follow up in people with stage 1 adenocarcinoma were identified.

2.1.9.3 Benefits and harms

Clinical and cost effectiveness

There was no evidence comparing endoscopic and radiological follow-up with standard endoscopy in people with stage 1 oesophageal adenocarcinoma, therefore the committee drew upon their clinical experience to make consensus recommendations. They emphasised that the likelihood of recurrence is high for people who have received endoscopic treatment for dysplastic Barrett's oesophagus and stage 1 oesophageal adenocarcinoma and agreed that endoscopic follow-up should be offered. The committee noted this was in line with current practice. The committee also agreed it would be usual practice to offer endoscopic follow-up to people with T1b oesophageal adenocarcinoma who have received radiotherapy as the risk of cancer progression is high. Optimal frequency and duration of endoscopic follow-up

The committee raised that in current practice, patients who receive endoscopic treatment for Barrett's oesophagus undergo an intensive surveillance protocol that consists of serial endoscopies with the aim to detect any recurrence. In line with current guidelines patients are usually followed-up every 3 months for the first year after treatment, every 6 months for the second year and annually thereafter.

The committee discussed that there is currently no evidence from comparative studies to suggest that a less intensive follow-up protocol would be more effective than what is currently done in practice.

The committee were aware of modelling studies using UK and USA data suggesting a less intensive follow-up protocol could be equally effective. The committee agreed this could be the case as the likelihood of missing significant disease at the start of the follow-up period after treatment is small and high frequency of surveillance may not be required.

The committee noted that the level of surveillance seen in current practice has been based on old and limited evidence and agreed its high frequency can be stressful for patients. However, the committee agreed that the current evidence base does not justify a change in current practice. The committee agreed based on their clinical experience that the frequency of follow-up should differ accordingly to the needs of each patient based on the likelihood of recurrence. The committee noted that because of the uncertainty on the optimum frequency and duration of follow up, this was a priority area for further research because it is important to identify people at higher risk of recurrence and provide guidance on the optimal frequency of follow-up. They agreed the focus should be on the utility of both clinical and molecular biomarkers to guide follow up appointments for people with dysplasia and stage 1 oesophageal adenocarcinoma who have had endoscopic treatment.

Cost effectiveness and resource use

In general, the addition of radiology or more frequent surveillances would be more costly but would potentially provide more health gains if more cancers were detected and treated early.

No economic evaluations were identified for this review question.

In absence of clinical and cost effectiveness evidence, the committee decided not to recommend radiological surveillance as an adjunct to endoscopic surveillance to patients who have received endoscopic treatment for Barrett's oesophagus and stage 1 adenocarcinoma. The committee decided to continue to offer endoscopic follow-up for these patients. This recommendation is unlikely to cause a resource impact as it is consistent with current practice in the management of Barrett's oesophagus.

The committee also made a research recommendation to assess the optimal frequency and duration of endoscopic follow up.

2.1.10 Recommendations supported by this evidence review

This evidence review supports recommendation 1.5.5 ,1.6.4 and 1.7.2 on treating people with dysplastic Barrett's oesophagus and stage 1 oesophageal adenocarcinoma. As there was no evidence comparing endoscopic and radiological follow-up with standard endoscopy in people with stage 1 oesophageal adenocarcinoma, the committee made a consensus recommendation in line with current practice. The evidence review also supports the research recommendation on the optimal frequency and duration of endoscopic follow up as there was no evidence comparing different frequencies and durations of follow-up.

2.1.11 References

1. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual [updated January 2022]. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

Appendices

Appendix A – Review protocols

A.1 Review protocol for clinical and cost effectiveness of endoscopic and radiological follow-up after treatment

ID	Field	Content
0.	PROSPERO registration number	CRD42021272041
1.	Review title	Clinical and cost effectiveness of endoscopic and radiological follow-up after treatment
2.	Review question	For people who have received endoscopic treatment for Barrett's oesophagus related stage 1 adenocarcinoma, what is the clinical and cost effectiveness of endoscopic follow-up with or without radiological follow up?
3.	Objective	To determine the clinical and cost effectiveness of different follow-up techniques, in people with stage 1 adenocarcinoma
4.	Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikus Searches will be restricted by:

		• English language studies • Human studies • Letters and comments are excluded Other searches: • Inclusion lists of systematic reviews will be checked by the reviewers The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Barrett's Oesophagus related stage 1 adenocarcinoma
6.	Population	Inclusion: Adults with endoscopic treatment, 18 years and over, with Barrett's Oesophagus related stage 1 adenocarcinoma Exclusion: Those without endoscopic treatment or who are beyond stage 1 adenocarcinoma
7.	Intervention	• Endoscopy + Radiological follow up

		○ CT ○ EUS ○ PET
8.	Comparator	• Endoscopic follow up ○ standard endoscopy (any type)
9.	Types of study to be included	• RCT • If no RCT data is available, non-randomised studies will be considered if there is an active comparator component within the study • Systematic Reviews of RCTs Published NMAs and IPDs will be considered for inclusion.
10.	Other exclusion criteria	Non-English language studies. Non comparative cohort studies Before and after studies Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	In adults who have had treatment for Barrett's oesophagus or stage 1 adenocarcinoma, it is important to follow up these patients to monitor them for the early possible recurrences of disease. This review aims to assess how clinically and cost effective follow up techniques are for those with Barrett's or stage 1 adenocarcinoma.
12.	Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical: All outcomes are considered equally important for decision making and therefore have all been rated as critical:

		• Mortality (all-cause mortality and disease specific mortality) • Health related quality of life (any validated scores) • Recurrence of cancer or dysplasia • Adverse events (infection, perforation, bleeding) • Detection of incidental findings and subsequent investigations
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. This review will make use of the priority screening functionality within the EPPI-reviewer software. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary. Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.

		For Intervention reviews the following checklist will be used according to study design being assessed: Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) Randomised Controlled Trial: Cochrane RoB (2.0) Nonrandomised study, including cohort studies: Cochrane ROBINS-I Case control study: CASP case control checklist
16.	Strategy for data synthesis	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. 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/ Where meta-analysis is not possible, data will be presented, and quality assessed individually per outcome.

		If sufficient data is available, WinBUGS will be used for network meta-analysis, if possible, given the data identified.	
17.	Analysis of sub-groups	Stratification: Stage 1 (T1a vs T1b) Subgroups that will be investigated if heterogeneity is present: : • Histopathological risk factors (lymph vascular invasion, grade of differentiation, incomplete resection or R1) • Radiological modality	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	
21.	Anticipated or actual start date		
22.	Anticipated completion date		

<table>
<tr><td rowspan="8">23.</td><td rowspan="8">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td>☐</td><td>☐</td></tr>
<tr><td>Piloting of the study selection process</td><td>☐</td><td>☐</td></tr>
<tr><td>Formal screening of search results against eligibility criteria</td><td>☐</td><td>☐</td></tr>
<tr><td>Data extraction</td><td>☐</td><td>☐</td></tr>
<tr><td>Risk of bias (quality) assessment</td><td>☐</td><td>☐</td></tr>
<tr><td>Data analysis</td><td>☐</td><td>☐</td></tr>
<tr><td>24.</td><td>Named contact</td><td colspan="3">5a. Named contact
National Guideline Centre

5b Named contact e-mail
@nice.org.uk

5e Organisational affiliation of the review
National Institute for Health and Care Excellence (NICE) and National Guideline Centre</td></tr>
<tr><td>25.</td><td>Review team members</td><td colspan="3">From the National Guideline Centre:
Norma O Flynn</td></tr>
</table>

		Gill Ritchie Amy Crisp Lina Gulhane Vimal Bedia Muksitur Rahman
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website.
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts

		• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Barrett's oesophagus	
33.	Details of existing review of same topic by same authors		
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information		
36.	Details of final publication	www.nice.org.uk	

A.2 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 for all years 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 2006, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2006 or later, that were included in the previous guidelines, will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. 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). [1] **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 2006 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2006 will be rated as 'Not applicable'. • Studies published before 2006 (including any such studies included in the previous guidelines) 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.[1]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 5: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 29 April 2022	Randomised controlled trials Systematic review studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 29 April 2022	Randomised controlled trials Systematic review studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
The Cochrane Library (Wiley)	Cochrane Database of Systematic Reviews to Issue 4 of 12, April 2022 Cochrane Central Register of Controlled Trials to Issue 4 of 12, April 2022	Exclusions (clinical trials, conference abstracts)
Epistemonikos (The Epistemonikos Foundation)	Inception to 29 April 2022	Systematic review Exclusions (Cochrane reviews)

Medline (Ovid) search terms

1.	exp Barrett esophagus/
2.	barrett*.ti,ab.
3.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.

4.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
5.	(intestin* adj2 metaplas*).ti,ab.
6.	or/1-5
7.	Precancerous conditions/
8.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
9.	7 or 8
10.	exp Esophagus/
11.	Esophageal Mucosa/
12.	(oesophag* or esophag* or intramucosal* or intra-mucosal*).ti,ab.
13.	or/10-12
14.	9 and 13
15.	exp Esophageal Neoplasms/
16.	6 or 14 or 15
17.	letter/
18.	editorial/
19.	news/
20.	exp historical article/
21.	Anecdotes as Topic/
22.	comment/
23.	case report/
24.	(letter or comment*).ti.
25.	or/17-24
26.	randomized controlled trial/ or random*.ti,ab.
27.	25 not 26
28.	animals/ not humans/
29.	exp Animals, Laboratory/
30.	exp Animal Experimentation/
31.	exp Models, Animal/
32.	exp Rodentia/
33.	(rat or rats or mouse or mice or rodent*).ti.
34.	or/27-33
35.	16 not 34
36.	limit 35 to English language
37.	(follow*-up* or followup* or surveillance or monitor* or check-up* or checkup*).ti,ab,kf.
38.	36 and 37
39.	Meta-Analysis/
40.	Meta-Analysis as Topic/
41.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
42.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
43.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
44.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.

45.	(search* adj4 literature).ab.
46.	(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.
47.	cochrane.jw.
48.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
49.	or/39-48
50.	randomized controlled trial.pt.
51.	controlled clinical trial.pt.
52.	randomi#ed.ab.
53.	placebo.ab.
54.	randomly.ab.
55.	clinical trials as topic.sh.
56.	trial.ti.
57.	or/50-56
58.	38 and (49 or 57)

Embase (Ovid) search terms

1.	exp Barrett esophagus/
2.	barrett*.ti,ab.
3.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.
4.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
5.	(intestin* adj2 metaplas*).ti,ab.
6.	or/1-5
7.	Precancer/
8.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
9.	7 or 8
10.	exp Esophagus/
11.	Esophagus Mucosa/
12.	(oesophag* or esophag*).ti,ab.
13.	or/10-12
14.	9 and 13
15.	exp Esophagus Tumor/
16.	6 or 14 or 15
17.	letter.pt. or letter/
18.	note.pt.
19.	editorial.pt.
20.	case report/ or case study/
21.	(letter or comment*).ti.
22.	(conference abstract or conference paper).pt.
23.	or/17-22
24.	randomized controlled trial/ or random*.ti,ab.
25.	23 not 24
26.	animal/ not human/
27.	nonhuman/

28.	exp Animal Experiment/
29.	exp Experimental Animal/
30.	animal model/
31.	exp Rodent/
32.	(rat or rats or mouse or mice or rodent*).ti.
33.	or/25-32
34.	16 not 33
35.	limit 34 to English language
36.	(follow*-up* or followup* or surveillance or monitor* or check-up* or checkup*).ti,ab,kf.
37.	35 and 36
38.	random*.ti,ab.
39.	factorial*.ti,ab.
40.	(crossover* or cross over*).ti,ab.
41.	((doubl* or singl*) adj blind*).ti,ab.
42.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
43.	crossover procedure/
44.	single blind procedure/
45.	randomized controlled trial/
46.	double blind procedure/
47.	or/38-46
48.	Systematic Review/
49.	Meta-Analysis/
50.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
51.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
52.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
53.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
54.	(search* adj4 literature).ab.
55.	(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.
56.	cochrane.jw.
57.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
58.	or/48-57
59.	37 and (47 or 58)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Barrett Esophagus] explode all trees
#2.	barrett*:ti,ab
#3.	speciali* near/3 (epithel* or oesophag* or esophag* or mucos*):ti,ab
#4.	column* near/3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*):ti,ab
#5.	(intestin* near/2 metaplas*):ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Precancerous Conditions] explode all trees
#8.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or

	carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*):ti,ab
#9.	#7 or #8
#10.	MeSH descriptor: [Esophagus] explode all trees
#11.	MeSH descriptor: [Esophageal Mucosa] explode all trees
#12.	(oesophag* or esophag* or intramucosal* or intra-mucosal*):ti,ab
#13.	(or #10-#12)
#14.	#9 and #13
#15.	MeSH descriptor: [Esophageal Neoplasms] explode all trees
#16.	#6 or #14 or #15
#17.	(follow* up* or followup* or surveillance or monitor* or check up* or checkup*):ti,ab,kw
#18.	#16 and #17
#19.	conference:pt or (clinicaltrials or trialsearch):so
#20.	#18 not #19

Epistemonikos search terms

1.	(title:(Barrett* OR "oesophageal adenocarcinoma*" OR "esophageal adenocarcinoma*" OR "oesophageal cancer*" OR "esophageal cancer*" OR "oesophageal carcinoma*" OR "esophageal carcinoma*" OR "oesophageal metaplas*" OR "esophageal dysplas*" OR "column* epithel*" OR "intestin* metaplas*" OR "intestin* dysplas*") OR abstract:(Barrett* OR "oesophageal adenocarcinoma*" OR "esophageal adenocarcinoma*" OR "oesophageal cancer*" OR "esophageal cancer*" OR "oesophageal carcinoma*" OR "esophageal carcinoma*" OR "oesophageal metaplas*" OR "esophageal dysplas*" OR "column* epithel*" OR "intestin* metaplas*" OR "intestin* dysplas*")) AND (title:("follow* up*" OR followup* OR surveillance OR monitor* OR (check up*) OR checkup*) OR abstract:("follow* up*" OR followup* OR surveillance OR monitor* OR (check up*) OR checkup*))

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting searches using terms for a broad Barrett's Oesophagus population. The following databases were searched: NHS Economic Evaluation Database (NHS EED - this ceased to be updated after 31st March 2015), Health Technology Assessment database (HTA - this ceased to be updated from 31st March 2018) and The International Network of Agencies for Health Technology Assessment (INAHTA). Searches for recent evidence were run on Medline and Embase from 2014 onwards for health economics, and all years for quality-of-life studies.

Table 6: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 29 April 2022	Health economics studies Quality of life studies
	Quality of Life 1946 – 29 April 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	Health Economics 1 January 2014 – 29 April 2022	Health economics studies Quality of life studies

Database	Dates searched	Search filters and limits applied
	Quality of Life 1974 – 29 April 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception - 29 April 2022	English language

Medline (Ovid) search terms

1.	exp Barrett esophagus/
2.	barrett*.ti,ab.
3.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.
4.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
5.	or/1-4
6.	Precancerous conditions/
7.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
8.	6 or 7
9.	exp Esophagus/
10.	Esophageal Mucosa/
11.	(oesophag* or esophag* or intramucosal* or intra-mucosal*).ti,ab.
12.	or/9-11
13.	8 and 12
14.	exp Esophageal Neoplasms/
15.	5 or 13 or 14
16.	letter/
17.	editorial/
18.	news/
19.	exp historical article/
20.	Anecdotes as Topic/
21.	comment/

22.	case report/
23.	(letter or comment*).ti.
24.	or/16-23
25.	randomized controlled trial/ or random*.ti,ab.
26.	24 not 25
27.	animals/ not humans/
28.	exp Animals, Laboratory/
29.	exp Animal Experimentation/
30.	exp Models, Animal/
31.	exp Rodentia/
32.	(rat or rats or mouse or mice or rodent*).ti.
33.	or/26-32
34.	15 not 33
35.	limit 34 to English language
36.	economics/
37.	value of life/
38.	exp "costs and cost analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, medical/
41.	Economics, nursing/
42.	economics, pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	quality-adjusted life years/
54.	sickness impact profile/
55.	(quality adj2 (wellbeing or well being)).ti,ab.
56.	sickness impact profile.ti,ab.
57.	disability adjusted life.ti,ab.
58.	(qal* or qtime* or qwb* or daly*).ti,ab.
59.	(euroqol* or eq5d* or eq 5*).ti,ab.
60.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
61.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
62.	(hui or hui1 or hui2 or hui3).ti,ab.

63.	(health* year* equivalent* or hye or hyes).ti,ab.
64.	discrete choice*.ti,ab.
65.	rosser.ti,ab.
66.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
67.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
68.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
69.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
70.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
71.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
72.	or/53-71
73.	35 and (52 or 72)

Embase (Ovid) search terms

1.	exp Barrett esophagus/
2.	barrett*.ti,ab.
3.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.
4.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
5.	or/1-4
6.	Precancer/
7.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
8.	6 or 7
9.	exp Esophagus/
10.	Esophagus Mucosa/
11.	(oesophag* or esophag*).ti,ab.
12.	or/9-11
13.	8 and 12
14.	exp Esophagus Tumor/
15.	5 or 13 or 14
16.	letter.pt. or letter/
17.	note.pt.
18.	editorial.pt.
19.	case report/ or case study/
20.	(letter or comment*).ti.
21.	(conference abstract or conference paper).pt.
22.	or/16-21
23.	randomized controlled trial/ or random*.ti,ab.
24.	22 not 23
25.	animal/ not human/
26.	nonhuman/
27.	exp Animal Experiment/
28.	exp Experimental Animal/

29.	animal model/
30.	exp Rodent/
31.	(rat or rats or mouse or mice or rodent*).ti.
32.	or/24-31
33.	15 not 32
34.	limit 33 to English language
35.	health economics/
36.	exp economic evaluation/
37.	exp health care cost/
38.	exp fee/
39.	budget/
40.	funding/
41.	budget*.ti,ab.
42.	cost*.ti.
43.	(economic* or pharmaco?economic*).ti.
44.	(price* or pricing*).ti,ab.
45.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
46.	(financ* or fee or fees).ti,ab.
47.	(value adj2 (money or monetary)).ti,ab.
48.	or/35-47
49.	quality-adjusted life years/
50.	"quality of life index"/
51.	short form 12/ or short form 20/ or short form 36/ or short form 8/
52.	sickness impact profile/
53.	(quality adj2 (wellbeing or well being)).ti,ab.
54.	sickness impact profile.ti,ab.
55.	disability adjusted life.ti,ab.
56.	(qal* or qtime* or qwb* or daly*).ti,ab.
57.	(euroqol* or eq5d* or eq 5*).ti,ab.
58.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
59.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
60.	(hui or hui1 or hui2 or hui3).ti,ab.
61.	(health* year* equivalent* or hye or hyes).ti,ab.
62.	discrete choice*.ti,ab.
63.	rosser.ti,ab.
64.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
65.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
66.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
67.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
68.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
69.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
70.	or/49-69
71.	34 and (48 or 70)

NHS EED and HTA (CRD) search terms

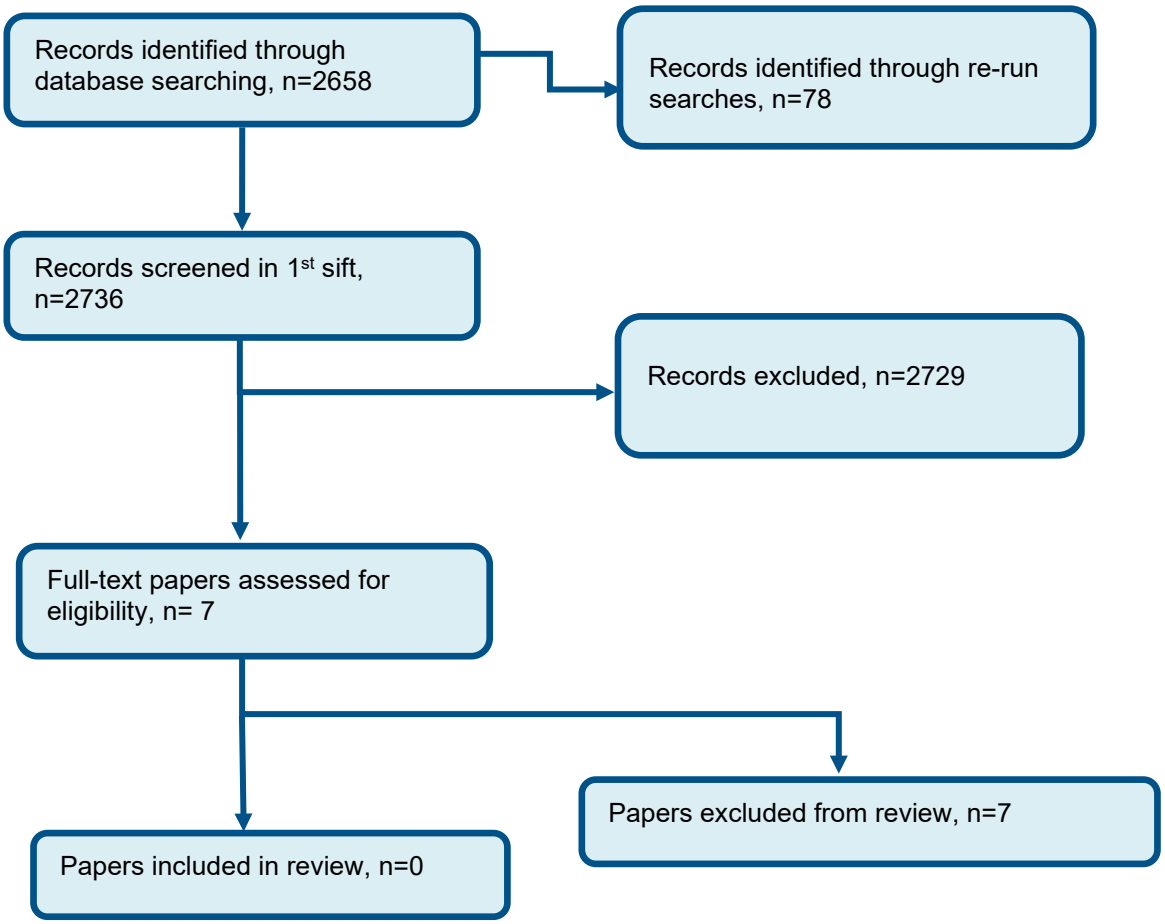
#1.	MeSH DESCRIPTOR Barrett Esophagus EXPLODE ALL TREES
#2.	(barrett*)
#3.	(speciali*) AND (epithel* or oesophag* or esophag* or mucos*)
#4.	(column*) AND (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)
#5.	#1 OR #2 OR #3 OR #4
#6.	MeSH DESCRIPTOR Precancerous Conditions EXPLODE ALL TREES
#7.	((dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma*or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*))
#8.	#6 OR #7
#9.	MeSH DESCRIPTOR Esophagus EXPLODE ALL TREES
#10.	MeSH DESCRIPTOR Esophageal Mucosa EXPLODE ALL TREES
#11.	(oesophag* or esophag* or intramucosal* or intra-mucosal*)
#12.	#9 OR #10 OR #11
#13.	#8 AND #12
#14.	#5 OR #13
#15.	MeSH DESCRIPTOR Esophageal Neoplasms EXPLODE ALL TREES
#16.	#14 OR #15

INAHTA search terms

1.	("Barrett Esophagus"[mh]) OR (Barrett*) OR (Esophageal Neoplasms)[mh]

Appendix C – Effectiveness evidence study selection

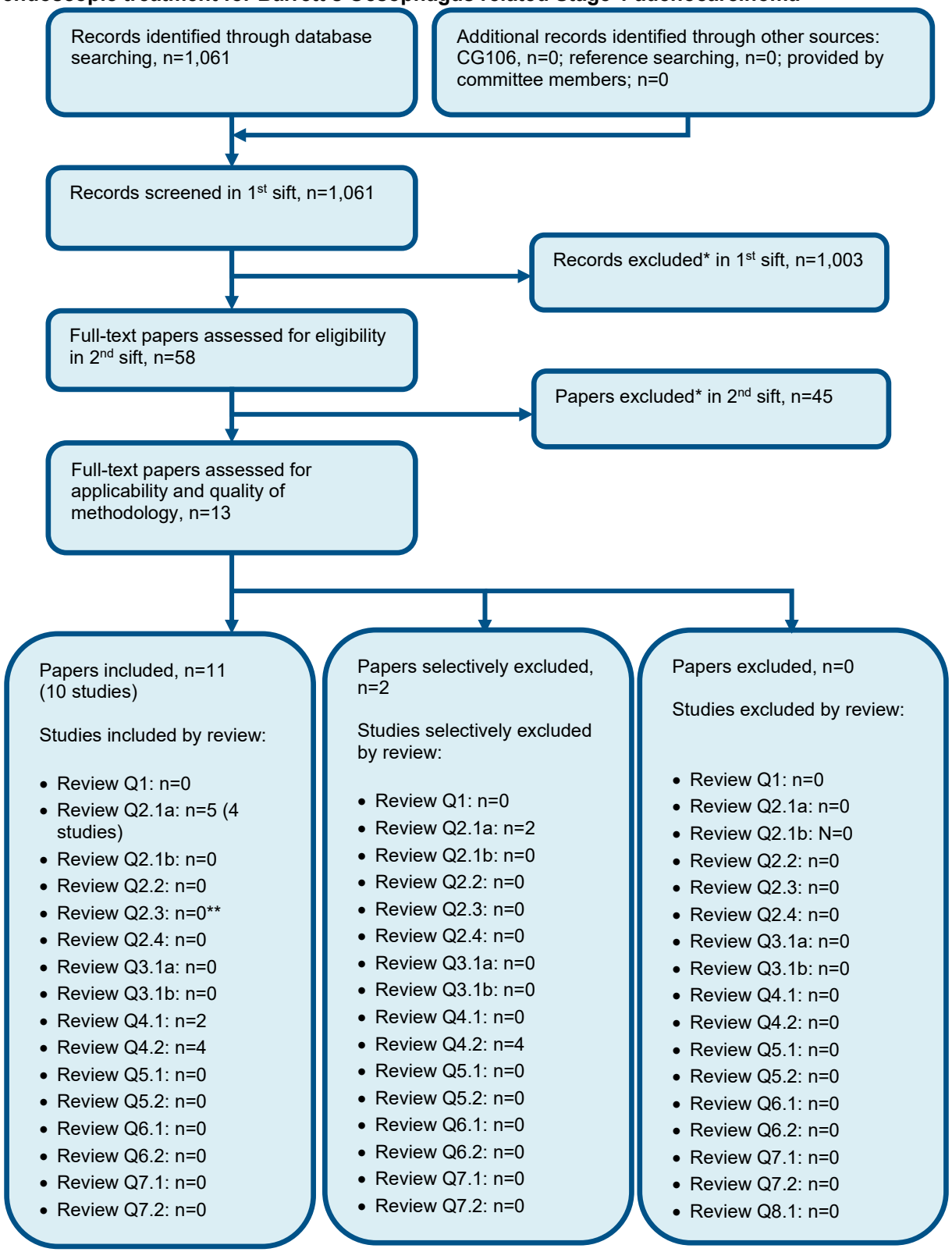
Figure 1: Flow chart of clinical study selection for the review of clinical and cost effectiveness of endoscopic and radiological follow up in people who have received endoscopic treatment for Barrett's Oesophagus related Stage 1 adenocarcinoma



Appendix D – Economic evidence study selection

Figure 2:Flow chart of health economic study selection for the review of clinical and cost effectiveness of endoscopic and radiological follow up in people who have received

endoscopic treatment for Barrett's Oesophagus related Stage 1 adenocarcinoma



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

** Two articles identified were applicable to Q2.1a and Q2.3, for the purposes of this diagram they have been included under Q2.1a only.

Appendix E – Excluded studies

Clinical studies

Study	Reason for exclusion
Bratlie, S. O., Johnsson, E., Jonsson, C. et al. (2015) Multiple-Band Imaging Provides Better Value Than White-light Endoscopy in Detection of Dysplasia in Patients With Barrett's Esophagus. Clinical Gastroenterology & Hepatology 13(6): 1068-74.e2	- Study does not contain an intervention relevant to this review protocol Comparing standard white light endoscopy (SDWLE) with High-definition magnifying endoscopy with multiple-band imaging (HDMEMBI)
Curvers, W. L., Alvarez Herrero, L., Wallace, M. B. et al. (2010) Endoscopic tri-modal imaging is more effective than standard endoscopy in identifying early-stage neoplasia in Barrett's esophagus. Gastroenterology 139(4): 1106-1114	- Study does not contain an intervention relevant to this review protocol Comparing Endoscopic trimodal imaging (ETMI) with standard video endoscopy (SVE)
DeMeester, S. R. (2001) Surveillance endoscopy and follow-up for Barrett's esophagus. Problems in General Surgery 18(2): 94-98	Study design not relevant to this review protocol. Review article
Dunbar, K. B., Okolo, P., 3rd, Montgomery, E. et al. (2009) Confocal laser endomicroscopy in Barrett's esophagus and endoscopically inapparent Barrett's neoplasia: a prospective, randomized, double-blind, controlled, crossover trial. Gastrointestinal Endoscopy 70(4): 645-54	- Study does not contain an intervention relevant to this review protocol Comparing CLE with optical biopsy and targeted mucosal biopsy (CLE-TB) with standard endoscopy with a 4-quadrant random biopsy (SE-RB)
Hajelssedig, O. E., Zorron Cheng Tao Pu, L., Thompson, J. Y. et al. (2021) Diagnostic Accuracy of Narrow Band Imaging Endoscopy with targeted biopsies compared to Standard Endoscopy with Random Biopsies in Patients with Barrett's Esophagus: A Systematic Review and Meta-analysis. Journal of Gastroenterology and Hepatology	- Study does not contain an intervention relevant to this review protocol Comparing Diagnostic accuracy of narrow-band imaging endoscopy with targeted biopsies compared with standard endoscopy with random biopsies
Sami, S. S., Subramanian, V., Butt, W. M. et al. (2015) High definition versus standard definition white light endoscopy for detecting dysplasia in patients with Barrett's esophagus. Diseases of the Esophagus 28(8): 742-749	- Study design not relevant to this review protocol; incorrect population: non-dysplastic Barrett’s oesophagus
Sloof, G. W. (2006) Response monitoring of neoadjuvant therapy using CT, EUS, and FDG-PET. Best Practice & Research in Clinical Gastroenterology 20(5): 941-57	- Study design not relevant to this review protocol Review article

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2006 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.

Appendix F – Review protocols

F.1 Review protocol for frequency and duration of endoscopic and radiological follow-up after treatment

ID	Field	Content
0.	PROSPERO registration number	CRD42021272043
1.	Review title	Frequency and duration of endoscopic and radiological follow-up after treatment
2.	Review question	For people who have received endoscopic treatment for Barrett's oesophagus or stage 1 adenocarcinoma, what is the optimal frequency and duration of endoscopic and radiological follow-up?
3.	Objective	To determine the clinical and cost effectiveness of different frequency and duration follow up techniques, in people with Barrett's oesophagus or stage 1 adenocarcinoma
4.	Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Epistemonikus Searches will be restricted by: • English language studies • Human studies • Letters and comments are excluded

		Other searches: • Inclusion lists of systematic reviews will be checked by the reviewers The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Barrett's Oesophagus with dysplasia Stage 1 adenocarcinoma
6.	Population	Inclusion: Adults, 18 years and over, with endoscopic treatment and dysplastic Barrett's Oesophagus or stage 1 adenocarcinoma Exclusion: people without endoscopic intervention, non-dysplastic Barrett's Oesophagus, and those beyond stage 1 adenocarcinoma
7.	Intervention	• Less intensive endoscopic follow up (any differentiation from intensive follow up)
8.	Comparator	• Intensive endoscopic follow up (for example, as guideline recommendation - every 3 months for the first year, every 6 months in the second and then annually)
9.	Types of study to be included	• RCT

		• SR of RCTs • If no RCT data is available, non-randomised studies will be considered if there is an active comparator within the study Published NMAs and IPDs will be considered for inclusion.
10.	Other exclusion criteria	Non-English language studies. Non comparative cohort studies Before and after studies Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.		In adults who have had treatment for Barrett's oesophagus or stage 1 adenocarcinoma, it is important to follow up these patients to monitor them for the early possible recurrences of disease. However, it is not known how often follow up needs to be completed, and for how long. This review aims to assess how clinically and cost effective different frequencies and durations of follow up techniques are for those with Barrett's or stage 1 adenocarcinoma.
12.	Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical: • Mortality (all cause and disease specific mortality) • Health related quality of life (any validated scores) • Patient preference • Recurrence of Barrett's Oesophagus • Recurrence Stage 1 adenocarcinoma • Adverse events (stricture, perforation, infection, bleeding) • Endoscopic reintervention • Non endoscopic intervention (oncological or surgical)

14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. This review will make use of the priority screening functionality within the EPPI-reviewer software. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary. Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For Intervention reviews the following checklist will be used according to study design being assessed: Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) Randomised Controlled Trial: Cochrane RoB (2.0)

		Nonrandomised study, including cohort studies: Cochrane ROBINS-I Case control study: CASP case control checklist
16.	Strategy for data synthesis	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. 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/ Where meta-analysis is not possible, data will be presented, and quality assessed individually per outcome. If sufficient data is available, WinBUGS will be used for network meta-analysis, if possible, given the data identified.
17.	Analysis of sub-groups	Stratification:

<table>
<tr><td></td><td></td><td colspan="3">• Barrett's Oesophagus (low grade dysplasia
• high grade dysplasia or Stage 1 adenocarcinoma (T1a)
• Stage 1 adenocarcinoma (T1b)

Subgroups that will be investigated if heterogeneity is present:
None</td></tr>
<tr><td rowspan="8">18.</td><td rowspan="8">Type and method of review</td><td>☒</td><td colspan="2">Intervention</td></tr>
<tr><td>☐</td><td colspan="2">Diagnostic</td></tr>
<tr><td>☐</td><td colspan="2">Prognostic</td></tr>
<tr><td>☐</td><td colspan="2">Qualitative</td></tr>
<tr><td>☐</td><td colspan="2">Epidemiologic</td></tr>
<tr><td>☐</td><td colspan="2">Service Delivery</td></tr>
<tr><td>☐</td><td colspan="2">Other (please specify)</td></tr>
<tr><td></td></tr>
<tr><td>19.</td><td>Language</td><td colspan="3">English</td></tr>
<tr><td>20.</td><td>Country</td><td colspan="3">England</td></tr>
<tr><td>21.</td><td>Anticipated or actual start date</td><td colspan="3"></td></tr>
<tr><td>22.</td><td>Anticipated completion date</td><td colspan="3"></td></tr>
<tr><td rowspan="2">23.</td><td rowspan="2">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td>☐</td><td>☐</td></tr>
</table>

		Piloting of the study selection process	☐	☐
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail @nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Centre		
25.	Review team members	From the National Guideline Centre: Norma O Flynn Gill Ritchie Amy Crisp Lina Gulhane		

		Vimal Bedia Muksitur Rahman
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website.
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

32.	Keywords	Barrett's Oesophagus	
33.	Details of existing review of same topic by same authors		
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information		
36.	Details of final publication	www.nice.org.uk	

F.2 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 for all years 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 2006, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2006 or later, that were included in the previous guidelines, will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. 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).[1] **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 2006 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2006 will be rated as 'Not applicable'. • Studies published before 2006 (including any such studies included in the previous guidelines) 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 G – Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[1]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

G.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 as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 7: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 29 April 2022	Randomised controlled trials Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 29 April 2022	Randomised controlled trials Systematic review studies Observational studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
The Cochrane Library (Wiley)	Cochrane Database of Systematic Reviews to Issue 4 of 12, April 2022 Cochrane Central Register of Controlled Trials to Issue 4 of 12, April 2022	Exclusions (clinical trials, conference abstracts)
Epistemonikos (The Epistemonikos Foundation)	Inception to 29 April 2022	Systematic review Exclusions (Cochrane reviews)

Medline (Ovid) search terms

59.	exp Barrett esophagus/
60.	barrett*.ti,ab.
61.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.

62.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
63.	(intestin* adj2 metaplas*).ti,ab.
64.	or/1-5
65.	Precancerous conditions/
66.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
67.	7 or 8
68.	exp Esophagus/
69.	Esophageal Mucosa/
70.	(oesophag* or esophag* or intramucosal* or intra-mucosal*).ti,ab.
71.	or/10-12
72.	9 and 13
73.	exp Esophageal Neoplasms/
74.	6 or 14 or 15
75.	letter/
76.	editorial/
77.	news/
78.	exp historical article/
79.	Anecdotes as Topic/
80.	comment/
81.	case report/
82.	(letter or comment*).ti.
83.	or/17-24
84.	randomized controlled trial/ or random*.ti,ab.
85.	25 not 26
86.	animals/ not humans/
87.	exp Animals, Laboratory/
88.	exp Animal Experimentation/
89.	exp Models, Animal/
90.	exp Rodentia/
91.	(rat or rats or mouse or mice or rodent*).ti.
92.	or/27-33
93.	16 not 34
94.	limit 35 to English language
95.	(follow*-up* or followup* or surveillance or monitor* or check-up* or checkup*).ti,ab,kf.
96.	36 and 37
97.	Meta-Analysis/
98.	Meta-Analysis as Topic/
99.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
100.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
101.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
102.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
103.	(search* adj4 literature).ab.

104.	(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.
105.	cochrane.jw.
106.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
107.	or/39-48
108.	randomized controlled trial.pt.
109.	controlled clinical trial.pt.
110.	randomi#ed.ab.
111.	placebo.ab.
112.	randomly.ab.
113.	clinical trials as topic.sh.
114.	trial.ti.
115.	or/50-56
116.	Epidemiologic studies/
117.	Observational study/
118.	exp Cohort studies/
119.	(cohort adj (study or studies or analys* or data)).ti,ab.
120.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
121.	((longitudinal or retrospective or prospective) and (study or studies or review or analys* or cohort* or data)).ti,ab.
122.	Controlled Before-After Studies/
123.	Historically Controlled Study/
124.	Interrupted Time Series Analysis/
125.	(before adj2 after adj2 (study or studies or data)).ti,ab.
126.	exp case control study/
127.	case control*.ti,ab.
128.	Cross-sectional studies/
129.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
130.	or/58-71
131.	38 and (49 or 57 or 72)

Embase (Ovid) search terms

60.	exp Barrett esophagus/
61.	barrett*.ti,ab.
62.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.
63.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
64.	(intestin* adj2 metaplas*).ti,ab.
65.	or/1-5
66.	Precancer/
67.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
68.	7 or 8
69.	exp Esophagus/
70.	Esophagus Mucosa/
71.	(oesophag* or esophag*).ti,ab.

72.	or/10-12
73.	9 and 13
74.	exp Esophagus Tumor/
75.	6 or 14 or 15
76.	letter.pt. or letter/
77.	note.pt.
78.	editorial.pt.
79.	case report/ or case study/
80.	(letter or comment*).ti.
81.	(conference abstract or conference paper).pt.
82.	or/17-22
83.	randomized controlled trial/ or random*.ti,ab.
84.	23 not 24
85.	animal/ not human/
86.	nonhuman/
87.	exp Animal Experiment/
88.	exp Experimental Animal/
89.	animal model/
90.	exp Rodent/
91.	(rat or rats or mouse or mice or rodent*).ti.
92.	or/25-32
93.	16 not 33
94.	limit 34 to English language
95.	(follow*-up* or followup* or surveillance or monitor* or check-up* or checkup*).ti,ab,kf.
96.	35 and 36
97.	random*.ti,ab.
98.	factorial*.ti,ab.
99.	(crossover* or cross over*).ti,ab.
100.	((doubl* or singl*) adj blind*).ti,ab.
101.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
102.	crossover procedure/
103.	single blind procedure/
104.	randomized controlled trial/
105.	double blind procedure/
106.	or/38-46
107.	Systematic Review/
108.	Meta-Analysis/
109.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
110.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
111.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
112.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
113.	(search* adj4 literature).ab.
114.	(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.
115.	cochrane.jw.
116.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

117.	or/48-57
118.	Clinical study/
119.	Observational study/
120.	Family study/
121.	Longitudinal study/
122.	Retrospective study/
123.	Prospective study/
124.	Cohort analysis/
125.	Follow-up/
126.	cohort*.ti,ab.
127.	66 and 67
128.	(cohort adj (study or studies or analys* or data)).ti,ab.
129.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
130.	((longitudinal or retrospective or prospective) and (study or studies or review or analys* or cohort* or data)).ti,ab.
131.	(before adj2 after adj2 (study or studies or data)).ti,ab.
132.	exp case control study/
133.	case control*.ti,ab.
134.	cross-sectional study/
135.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
136.	or/59-65,68-76
137.	37 and (47 or 58 or 77)

Cochrane Library (Wiley) search terms

#21.	MeSH descriptor: [Barrett Esophagus] explode all trees
#22.	barrett*:ti,ab
#23.	speciali* near/3 (epithel* or oesophag* or esophag* or mucos*):ti,ab
#24.	column* near/3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*):ti,ab
#25.	(intestin* near/2 metaplas*):ti,ab
#26.	(or #1-#5)
#27.	MeSH descriptor: [Precancerous Conditions] explode all trees
#28.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*):ti,ab
#29.	#7 or #8
#30.	MeSH descriptor: [Esophagus] explode all trees
#31.	MeSH descriptor: [Esophageal Mucosa] explode all trees
#32.	(oesophag* or esophag* or intramucosal* or intra-mucosal*):ti,ab
#33.	(or #10-#12)
#34.	#9 and #13
#35.	MeSH descriptor: [Esophageal Neoplasms] explode all trees
#36.	#6 or #14 or #15
#37.	(follow* up* or followup* or surveillance or monitor* or check up* or checkup*):ti,ab,kw
#38.	#16 and #17
#39.	conference:pt or (clinicaltrials or trialsearch):so
#40.	#18 not #19

Epistemonikos search terms

2.	(title:(Barrett* OR "oesophageal adenocarcinoma*" OR "esophageal adenocarcinoma*" OR "oesophageal cancer*" OR "esophageal cancer*" OR "oesophageal carcinoma*" OR "esophageal carcinoma*" OR "oesophageal metaplas*" OR "esophageal dysplas*" OR "column* epithel*" OR "intestin* metaplas*" OR "intestin* dysplas*") OR abstract:(Barrett* OR "oesophageal adenocarcinoma*" OR "esophageal adenocarcinoma*" OR "oesophageal cancer*" OR "esophageal cancer*" OR "oesophageal carcinoma*" OR "esophageal carcinoma*" OR "oesophageal metaplas*" OR "esophageal dysplas*" OR "column* epithel*" OR "intestin* metaplas*" OR "intestin* dysplas*")) AND (title:("follow* up*" OR followup* OR surveillance OR monitor* OR (check up*) OR checkup*) OR abstract:("follow* up*" OR followup* OR surveillance OR monitor* OR (check up*) OR checkup*))

G.2 Health Economics literature search strategy

Health economic evidence was identified by conducting searches using terms for a broad Barrett's Oesophagus population. The following databases were searched: NHS Economic Evaluation Database (NHS EED - this ceased to be updated after 31st March 2015), Health Technology Assessment database (HTA - this ceased to be updated from 31st March 2018) and The International Network of Agencies for Health Technology Assessment (INAHTA). Searches for recent evidence were run on Medline and Embase from 2014 onwards for health economics, and all years for quality-of-life studies.

Table 8: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 29 April 2022	Health economics studies Quality of life studies
	Quality of Life 1946 – 29 April 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	Health Economics 1 January 2014 – 29 April 2022	Health economics studies Quality of life studies
	Quality of Life 1974 – 29 April 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception - 29 April 2022	English language

Medline (Ovid) search terms

1.	exp Barrett esophagus/
2.	barrett*.ti,ab.
3.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.
4.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
5.	or/1-4
6.	Precancerous conditions/
7.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
8.	6 or 7
9.	exp Esophagus/
10.	Esophageal Mucosa/
11.	(oesophag* or esophag* or intramucosal* or intra-mucosal*).ti,ab.
12.	or/9-11
13.	8 and 12
14.	exp Esophageal Neoplasms/
15.	5 or 13 or 14
16.	letter/
17.	editorial/
18.	news/
19.	exp historical article/
20.	Anecdotes as Topic/
21.	comment/
22.	case report/
23.	(letter or comment*).ti.
24.	or/16-23
25.	randomized controlled trial/ or random*.ti,ab.
26.	24 not 25
27.	animals/ not humans/
28.	exp Animals, Laboratory/
29.	exp Animal Experimentation/
30.	exp Models, Animal/
31.	exp Rodentia/
32.	(rat or rats or mouse or mice or rodent*).ti.
33.	or/26-32
34.	15 not 33
35.	limit 34 to English language
36.	economics/
37.	value of life/
38.	exp "costs and cost analysis"/
39.	exp Economics, Hospital/

40.	exp Economics, medical/
41.	Economics, nursing/
42.	economics, pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	quality-adjusted life years/
54.	sickness impact profile/
55.	(quality adj2 (wellbeing or well being)).ti,ab.
56.	sickness impact profile.ti,ab.
57.	disability adjusted life.ti,ab.
58.	(qal* or qtime* or qwb* or daly*).ti,ab.
59.	(euroqol* or eq5d* or eq 5*).ti,ab.
60.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
61.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
62.	(hui or hui1 or hui2 or hui3).ti,ab.
63.	(health* year* equivalent* or hye or hyes).ti,ab.
64.	discrete choice*.ti,ab.
65.	rosser.ti,ab.
66.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
67.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
68.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
69.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
70.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
71.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
72.	or/53-71
73.	35 and (52 or 72)

Embase (Ovid) search terms

1.	exp Barrett esophagus/
2.	barrett*.ti,ab.
3.	(speciali* adj3 (epithel* or oesophag* or esophag* or mucos*)).ti,ab.
4.	(column* adj3 (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)).ti,ab.
5.	or/1-4
6.	Precancer/

7.	(dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma* or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*).ti,ab.
8.	6 or 7
9.	exp Esophagus/
10.	Esophagus Mucosa/
11.	(oesophag* or esophag*).ti,ab.
12.	or/9-11
13.	8 and 12
14.	exp Esophagus Tumor/
15.	5 or 13 or 14
16.	letter.pt. or letter/
17.	note.pt.
18.	editorial.pt.
19.	case report/ or case study/
20.	(letter or comment*).ti.
21.	(conference abstract or conference paper).pt.
22.	or/16-21
23.	randomized controlled trial/ or random*.ti,ab.
24.	22 not 23
25.	animal/ not human/
26.	nonhuman/
27.	exp Animal Experiment/
28.	exp Experimental Animal/
29.	animal model/
30.	exp Rodent/
31.	(rat or rats or mouse or mice or rodent*).ti.
32.	or/24-31
33.	15 not 32
34.	limit 33 to English language
35.	health economics/
36.	exp economic evaluation/
37.	exp health care cost/
38.	exp fee/
39.	budget/
40.	funding/
41.	budget*.ti,ab.
42.	cost*.ti.
43.	(economic* or pharmaco?economic*).ti.
44.	(price* or pricing*).ti,ab.
45.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
46.	(financ* or fee or fees).ti,ab.
47.	(value adj2 (money or monetary)).ti,ab.
48.	or/35-47
49.	quality-adjusted life years/
50.	"quality of life index"/
51.	short form 12/ or short form 20/ or short form 36/ or short form 8/

52.	sickness impact profile/
53.	(quality adj2 (wellbeing or well being)).ti,ab.
54.	sickness impact profile.ti,ab.
55.	disability adjusted life.ti,ab.
56.	(qal* or qtime* or qwb* or daly*).ti,ab.
57.	(euroqol* or eq5d* or eq 5*).ti,ab.
58.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
59.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
60.	(hui or hui1 or hui2 or hui3).ti,ab.
61.	(health* year* equivalent* or hye or hyes).ti,ab.
62.	discrete choice*.ti,ab.
63.	rosser.ti,ab.
64.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
65.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
66.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
67.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
68.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
69.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
70.	or/49-69
71.	34 and (48 or 70)

NHS EED and HTA (CRD) search terms

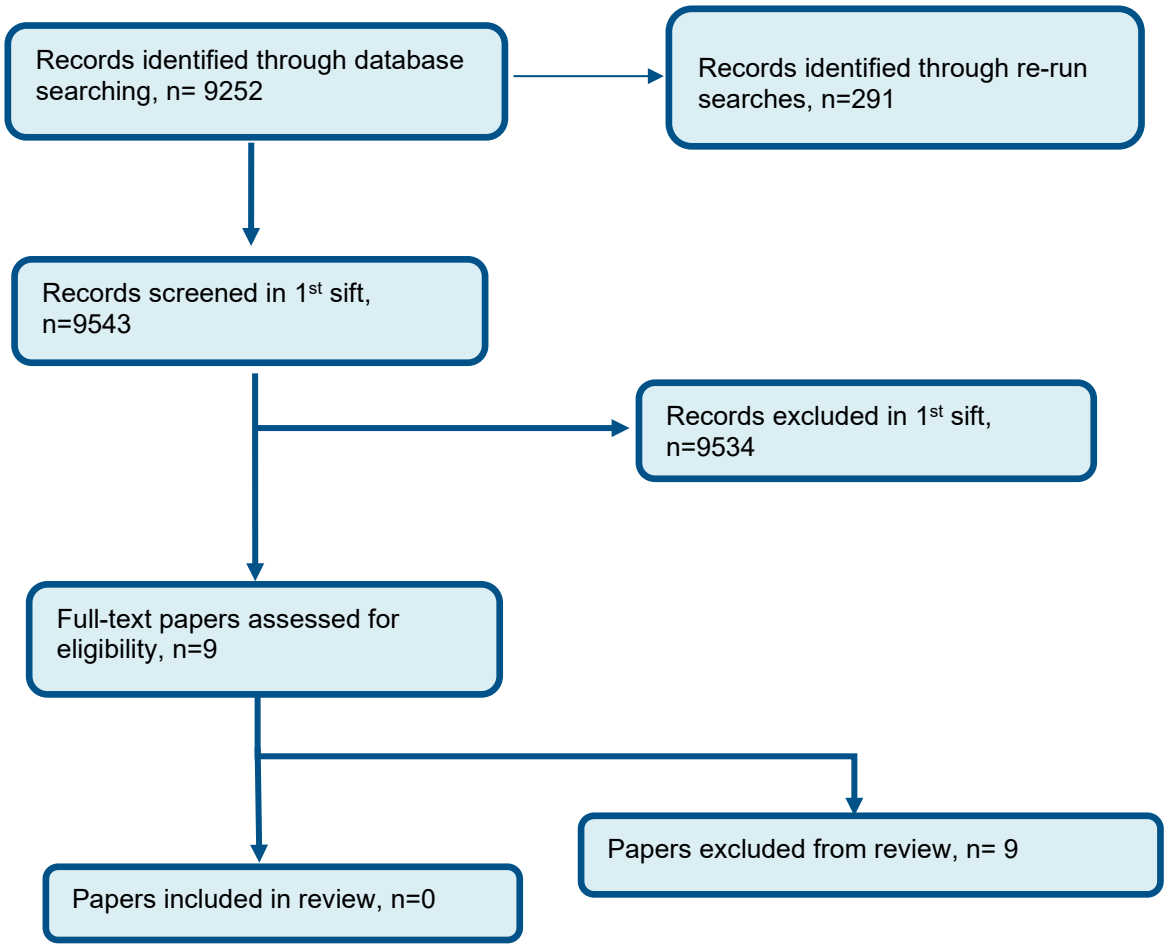
#1.	MeSH DESCRIPTOR Barrett Esophagus EXPLODE ALL TREES
#2.	(barrett*)
#3.	(speciali*) AND (epithel* or oesophag* or esophag* or mucos*)
#4.	(column*) AND (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)
#5.	#1 OR #2 OR #3 OR #4
#6.	MeSH DESCRIPTOR Precancerous Conditions EXPLODE ALL TREES
#7.	((dysplasia* or precancer* or pre-cancer* or premalign* or pre-malign* or preneoplast* or pre-neoplastic* or preneoplasia* or pre-neoplasia* or neoplasm* or cancer* or carcinoma* or adenocarcinom* or adenoma*or tumour* or tumor* or malignan* or metaplas* or metast* or nodul* or node* or lump* or lymphoma*))
#8.	#6 OR #7
#9.	MeSH DESCRIPTOR Esophagus EXPLODE ALL TREES
#10.	MeSH DESCRIPTOR Esophageal Mucosa EXPLODE ALL TREES
#11.	(oesophag* or esophag* or intramucosal* or intra-mucosal*)
#12.	#9 OR #10 OR #11
#13.	#8 AND #12
#14.	#5 OR #13
#15.	MeSH DESCRIPTOR Esophageal Neoplasms EXPLODE ALL TREES
#16.	#14 OR #15

INAHTA search terms

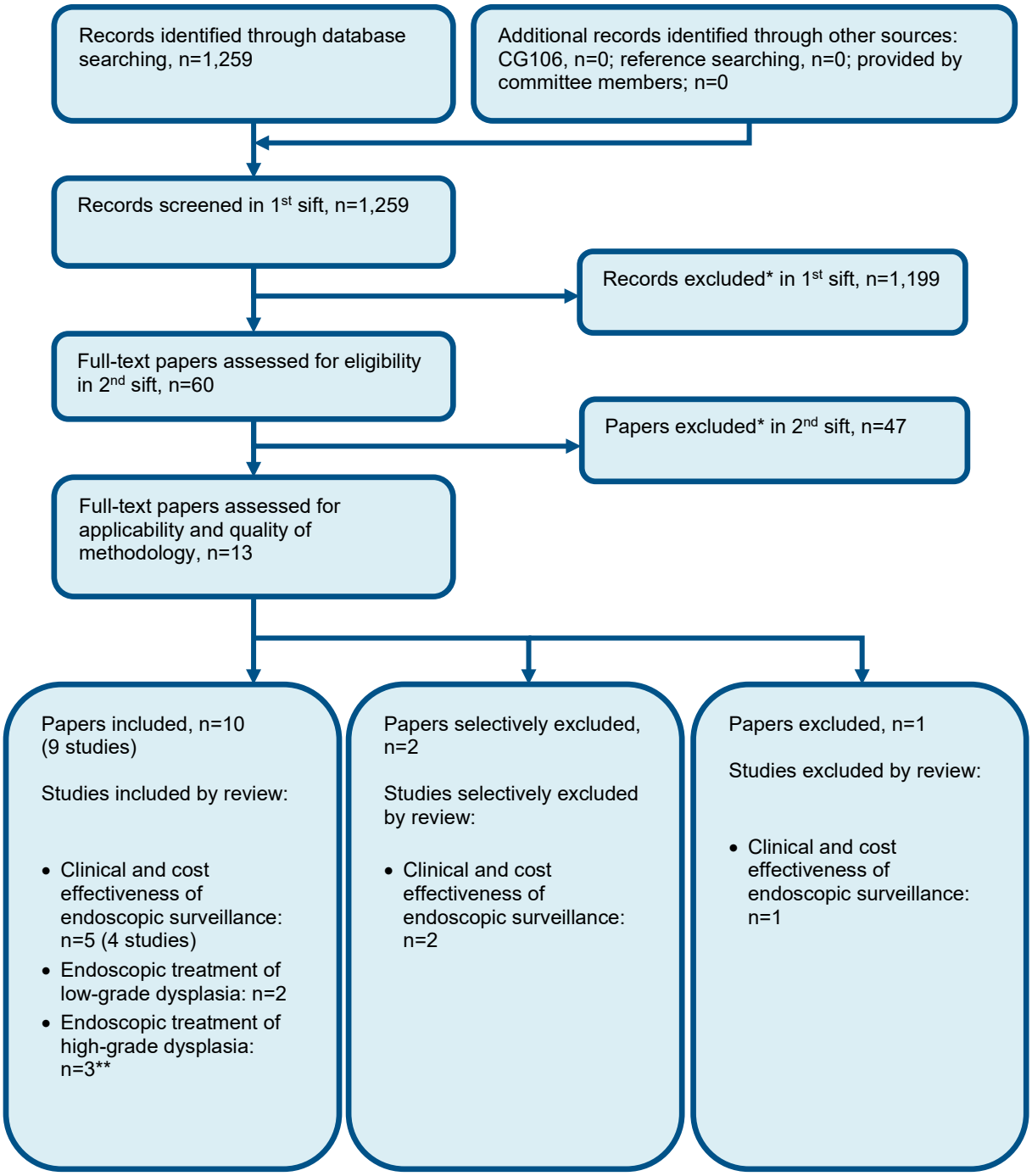
1.	("Barrett Esophagus"[mh]) OR (Barrett*) OR (Esophageal Neoplasms)[mh]

Appendix H – Effectiveness evidence study selection

Figure 3: Flow chart of clinical study selection for the review of frequency and duration of endoscopic and radiological follow-up after intervention



Appendix I – Economic evidence study selection



* Non-relevant population, intervention, comparison, design or setting; non-English language
** One article identified was applicable to endoscopic treatment of low-grade dysplasia and endoscopic treatment for high-grade dysplasia, for the purposes of this diagram they have been included under endoscopic treatment of low-grade dysplasia only.

Appendix J – Excluded studies

Study	Reason for exclusion
Ajumobi, A., Bahjri, K., Jackson, C. et al. (2010) Surveillance in Barrett's esophagus: an audit of practice. Digestive Diseases & Sciences 55(6): 1615-21	- Study does not contain an intervention relevant to this review protocol Observational study assessing rate of follow-up of surveillance endoscopy and pathologic changes
Basu, K. K.; Pick, B.; de Caestecker, J. S. (2004) Audit of a Barrett's epithelium surveillance database. European Journal of Gastroenterology & Hepatology 16(2): 171-5	- Study does not contain outcomes relevant to this review protocol Assessing incidence of dysplasia and cancer
Bright, T., Schloithe, A., Bull, J. A. et al. (2009) Outcome of endoscopy surveillance for Barrett's oesophagus. ANZ Journal of Surgery 79(11): 812-6	- Study does not contain outcomes relevant to this review protocol Assessing impact of surveillance programme
Corley, D. A., Mehtani, K., Quesenberry, C. et al. (2013) Impact of endoscopic surveillance on mortality from Barrett's esophagus-associated esophageal adenocarcinomas. Gastroenterology 145(2): 312-9.e1	- Intervention in study does not match that specified in this review protocol Evaluated whether endoscopic surveillance of Barrett's oesophagus is associated with a lower risk of death from oesophageal/gastroesophageal junction adenocarcinoma
DeMeester, S. R. (2001) Surveillance endoscopy and follow-up for Barrett's esophagus. Problems in General Surgery 18(2): 94-98	- Study design not relevant to this review protocol Review article
El-Serag, H. B., Duan, Z., Hinojosa-Lindsey, M. et al. (2012) Practice patterns of surveillance endoscopy in a Veterans Affairs database of 29,504 patients with Barrett's esophagus. Gastrointestinal Endoscopy 76(4): 743-55	- Population not relevant to this review protocol Patients with endoscopic treatment not meeting inclusion criteria
El-Serag, H. B., Naik, A. D., Duan, Z. et al. (2016) Surveillance endoscopy is associated with improved outcomes of oesophageal adenocarcinoma detected in patients with Barrett's oesophagus. Gut 65(8): 1252-60	- Study does not contain an intervention relevant to this review protocol Observational study assessing the effectiveness of surveillance endoscopy

Study	Reason for exclusion
Fitzgerald, R. C., Saeed, I. T., Khoo, D. et al. (2001) Rigorous surveillance protocol increases detection of curable cancers associated with Barrett's esophagus. Digestive Diseases & Sciences 46(9): 1892-8	- Study does not contain an intervention relevant to this review protocol Not comparing frequency and duration of endoscopic follow-up
Hurschler, D., Borovicka, J., Neuweiler, J. et al. (2003) Increased detection rates of Barrett's oesophagus without rise in incidence of oesophageal adenocarcinoma. Swiss Medical Weekly 133(3738): 507-14	- Study does not contain an intervention relevant to this review protocol Not comparing frequency and duration of endoscopic follow up

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2006 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.

Appendix K – Research recommendations

Optimal frequency and duration of endoscopic follow-up

What is the optimal frequency and duration of endoscopic follow up for patients who have received endoscopic treatment for Barrett's oesophagus with dysplasia and stage 1 adenocarcinoma?

Why this is important
People that have received endoscopic treatment for Barrett's oesophagus with dysplasia or stage 1 oesophageal adenocarcinoma and have achieved endoscopic and histological remission are at risk of recurrence of Barrett's oesophagus and neoplasia. Previous research has showed that this risk can be as high as 30% at 5 years. It is therefore important to identify people at higher risk of recurrence and provide guidance on the optimal frequency of follow-up. This has important resource implications as intensive follow-up may not be cost effective and would increase the overall costs of the endoscopic treatment, while less intensive follow-up might not detect recurrence early enough to allow repeat endoscopic treatment. There are no comparative data on different follow-up strategies and further research can help future recommendations on the optimal frequency of follow-up.

Rationale for research recommendation

Importance to 'patients' or the population	If patients at high risk of recurrence could be identified and receive close monitoring this would allow early detection of recurrence and prompt treatment. On the other hand, if low-risk patients could be monitored less intensively compared to current practice this might translate to a lower psychological burden and reduced risk from invasive procedures for these people.
Relevance to NICE guidance	A recommendation was made to follow up people that received treatment for Barrett's oesophagus with dysplasia or stage 1 oesophageal adenocarcinoma, but it was not possible to give specific guidance on the intervals for follow up. Further research might produce more specific recommendations on the frequency of follow-up needed.
Relevance to the NHS	Reducing the burden of follow-up endoscopy post treatment would reduce overall costs to the NHS and shift resources to higher risk people.
National priorities	N/A
Current evidence base	There exist long term data on all people that received endoscopic treatment, however, there are no comparative data on different follow up intervals and no data on molecular biomarkers to inform follow-up strategies.
Equality considerations	None.

K.1.1 Modified PICO table

Intervention	People receive an individualised follow-up plan based on clinical and molecular biomarkers of risk

Comparator	Usual care based on standard recommended follow-up intervals
Outcome	Quality of life, rate of recurrence or progression, type of treatment required, stage of cancer, grade of dysplasia, complications
Study design	Randomised controlled trial
Timeframe	5 years with possibility to collect longer term data
Additional information	None