National Institute for Health and Care Excellence

Draft for consultation

Barrett's oesophagus

2.3 Evidence review for frequency and duration of endoscopic surveillance techniques

NICE guideline <number>

Evidence reviews underpinning recommendations 1.3.3 to 1.3.4 and research recommendations in the NICE guideline

August 2022

Draft for consultation

These evidence reviews were developed by Guideline Development Team NGC

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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

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1 Frequency and duration of endoscopic Surveillance techniques

1.1 Review question

What is the optimal frequency and duration of endoscopic surveillance for adults with Barrett's oesophagus?

1.1.1 Introduction

Endoscopic surveillance for Barrett's oesophagus is a resource intensive area for Gastroenterology in the UK, and the frequency and duration is therefore of great importance as too much surveillance would result in patients undergoing unnecessary procedures, while too little surveillance would result in delays in cancer detection and reduced cancer prevention. Current UK practice is for endoscopy every 2 to 3 years for long segment Barrett's and 3-5 yearly for short segment Barrett's, with risk factors including smoking and family history determining precise intervals for individuals. Duration of surveillance is determined by whether the patient would continue to benefit, contingent on fitness to undergo and benefit from endoscopic procedures which would be necessary should a neoplastic lesion be discovered. These guidelines which are similar to European and US ones, are based largely on expert opinion in the absence of hard evidence.

1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Inclusion: Adults, 18 years and over, with non-dysplastic Barrett's oesophagus Exclusion: Adults with any level of dysplasia or indefinite dysplasia
Interventions	• Lower frequencies of: o High-resolution endoscopy o Chromoendoscopy • No surveillance
Comparison	Surveillance according to recommendations current ranges
Outcomes	• Health related quality of life • Progression to high grade dysplasia or cancer • Mortality • Adverse events / complications (bleeding, perforation, pain) • Adherence to surveillance (physician and patient) Time point: any time point available; no minimum follow-up
Study design	• 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 and results are based on a multi-variate analysis (adjusting for any confounder) • Cross sectional studies Published NMAs and IPDs will be considered for inclusion.

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 were identified comparing lower frequencies and duration of endoscopic surveillance or no surveillance with surveillance according to current guideline recommendations.

See also the study selection flow chart in Appendix C.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix E.

1.1.6 Summary of the effectiveness evidence

There was no clinical evidence found.

1.1.7 Economic evidence

1.1.7.1 Included studies

No health economic studies were included.

1.1.7.2 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.

1.1.8 Summary of included economic evidence

There was no economic evidence found.

1.1.9 Economic model

This area was given a high priority for new cost-effectiveness analysis. However, original economic modelling was not conducted due to a lack of clinical evidence.

1.1.10 Unit costs

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

Table 2: Unit costs

Resource	Unit costs	Source
diagnostic endoscopic upper gastrointestinal tract procedure with biopsy, (FE21Z)	£554	National Schedule of NHS Costs. 2019/20

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The outcomes considered for this review were health related quality of life, progression to high grade dysplasia or cancer, mortality, adverse events / complications, physician and patient adherence to surveillance. For purposes of decision making, all outcomes are considered equally important and were therefore rated as critical by the committee. No evidence was identified for any of the outcomes.

1.1.12.2 The quality of the evidence

No relevant clinical studies were identified comparing a different frequency and duration of endoscopic surveillance to the recommended ranges for surveillance given in current guidelines. Studies were commonly excluded because they were for a population not specified within the review protocol such as people with dysplasia, or they compared surveillance that did not match current guidelines as specified in the protocol to no surveillance.

1.1.12.3 Benefits and harms

The committee noted there was no evidence to recommend endoscopic surveillance that is of lower frequency compared to the current frequency recommended in guidelines or to support a definitive optimal frequency and duration. Based on their clinical experience and in line with the British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus, the committee agreed the frequency and duration of surveillance should be determined according to the individual patient's risk factors. The committee noted the frequency of endoscopic surveillance as recommended in the BSG guidelines would be appropriate as the risk of disease progression may vary between individuals. Currently the frequency of surveillance is 2-3 years for people with Barrett's oesophagus segment 3cm or longer, and 3-5 years for people with Barrett's oesophagus shorter than 3cm with intestinal metaplasia. The committee agreed the main risk factors included Barrett's segment size, age, gender, smoking status, and family history. In contrast to the BSG guideline, the European and US guidelines recommend a lower frequency of surveillance that is, 5 years for short segment and 3 years for long segment. The committee noted that surveillance according to the BSG guidelines is current practice across the UK and it would not be appropriate to recommend a lower frequency of surveillance given the lack of evidence to support such a change.

The committee considered the various factors that can influence the decision to recommend different frequencies of surveillance for each patient, which include age, co-morbidities, and the fitness of the patient for repeated invasive procedures.

The committee discussed age as a risk factor for disease progression which was hence considered a factor determining the appropriate duration of surveillance. The committee noted that the European guidelines advise against surveillance for people above the age of 75 whereas the BSG guidelines do not include an age cut-off but suggest ongoing surveillance based on an individual's clinical assessment. When discussing the duration of endoscopic surveillance, the committee agreed with the view of the BSG, arguing that an age-related threshold failed to recognise the heterogeneity of the population and the multitude of other factors that determine fitness for endoscopy. The committee agreed that surveillance should continue for as long as it was in the patient's interests, the benefits of surveillance outweigh any potential risks, and that this decision should be part of the ongoing patient/clinician discussion. They agreed that an important factor to consider would be the suitability of treatments involved in the entire endoscopic care pathway, which include endoscopy and intensive endoscopic treatment. Suitability should be based on a clinical assessment of the individual's general health that will determine the trade-off between the benefits and risks of undergoing the endoscopic pathway.

1.1.12.4 Cost effectiveness and resource use

In general, more frequent surveillance will be more costly but would potentially provide more health gain if more cancers are detected and treated early.

There were no published economic evaluations found. In the absence of suitable clinical evidence, cost-effectiveness modelling was not feasible.

The committee's decision to recommend offering:

- endoscopic surveillance every 2-3 years to people with long-segment Barrett's oesophagus and
- every 3-5 years to people with short-segment Barrett's oesophagus with intestinal metaplasia

Reflects current practice and is therefore unlikely to have a substantial impact on resource.

The committee also made a research recommendation to assess clinical and molecular biomarkers that can inform the optimal interval of and time for discharge from endoscopic surveillance. The cost associated with such biomarkers would lead to an increase in NHS resource use: the costs of the new technologies and associated staff time to conduct the tests. However, it would allow surveillance to be targeted on those patients that would most benefit, which could lead to more efficient use of resources. The impact of such technologies should be subject to cost effectiveness analysis.

1.1.12.5 Other factors the committee took into account

The committee emphasised they were aware of ongoing studies looking at clinical and molecular biomarkers for risk stratification of Barrett's oesophagus. They noted that evidence of biomarkers associated with a greater risk of progression of dysplasia or cancer could inform the appropriate frequency and duration of endoscopic surveillance and decided to make a recommendation for research in this area.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.3.3, 1.3.4 and the research recommendation on frequency and duration of endoscopic surveillance techniques.

1.1.14 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

Review protocol for frequency and duration of endoscopic Surveillance techniques

ID	Field	Content
0.	PROSPERO registration number	CRD42022306696
1.	Review title	The clinical and cost effectiveness of different frequencies and duration of endoscopic surveillance techniques (including high-resolution endoscopy and chromoendoscopy)
2.	Review question	What is the optimal frequency and duration of endoscopic surveillance for adults with Barrett's oesophagus?
3.	Objective	To assess the efficacy and cost effectiveness of different frequencies and duration of endoscopic surveillance techniques of people with Barrett's oesophagus
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 • Epistemokius 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
6.	Population	Inclusion: Adults, 18 years and over, with non-dysplastic Barrett's oesophagus Exclusion: Adults with any dysplasia or indefinite dysplasia

7.	Intervention	• Lower frequencies of:
		  ○ high-resolution endoscopy
		  ○ Chromoendoscopy
		• No surveillance

8.	Comparator	• Surveillance according to recommendations current ranges
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 and results are based on a multi-variate analysis (adjusting for any confounder) 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	Different endoscopic surveillance techniques are used for ongoing surveillance in people with Barrett's Oesophagus. This review aims to assess the clinical and cost effectiveness of the different techniques
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: • Health related quality of life • Progression to high grade dysplasia or cancer • Mortality • Adverse events / complications (bleeding, perforation, pain) • Adherence to surveillance (physician and patient)

		Time point: any time point available; no minimum follow-up
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	Where available, outcome data from new studies will be meta-analysed. 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	Subgrouping: If serious or very serious heterogeneity (I2>50%) is present, sub-grouping will occur according to the following strategies:

		Short vs. long segment of Barrett's Secondary vs. tertiary care centres			
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				
23.	Stage of review at time of this submission	Review stage		Started	Completed
		Preliminary searches		☐	☐
		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 Stephen Deed Vimal Bedia Muksitur Rahman Mark Perry Melina Vasileiou Maheen Qureshi		
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: [NICE guideline webpage].	
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	

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4 **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.

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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 3: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 26 April 2022	Randomised controlled trials Systematic review studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 26 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	
Epistemonikos (The Epistemonikos Foundation)	Inception to 26 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.	*Endoscopy, Gastrointestinal/
38.	Capsule Endoscopy/
39.	Esophagoscopy/
40.	Gastroscopy/
41.	(videoendoscop* or endomicroscop* or spectroscop* or endocytoscop* or oesophagoscop* or esophagoscop* or gastroscop*).ti,ab.
42.	(endoscop* adj3 (imag* or diagn* or identif* or surveillanc* or monitor* or observ* or detect*)).ti,ab.
43.	((capsule or transnasal or nasal) adj2 endoscop*).ti,ab.

44.	exp Optical Imaging/
45.	exp Acetic Acid/
46.	Molecular Imaging/
47.	(molecular adj3 (imag* or endoscop*)).ti,ab.
48.	((magnif* or high resolution or high definition) adj3 endoscop*).ti,ab.
49.	(chromatograph* or chromoendoscop* or chromoscop* or volumetric laser* or acetic acid or methylene blue or indigo carmine or narrow band or white light or blue laser or blue light or flexible spectral imaging colo?r enhancement or autofluorescen* or fluorescen* or optical coherence tomography or trimodal or tri modal or optical enhancement).ti,ab.
50.	exp Artificial Intelligence/
51.	(artificial intelligence or (computer adj (assisted or aided)) or ((deep or machine) adj learning) or neural network*).ti,ab.
52.	(wide area transepithelial sampling or WATS3D or WATS 3D).ti,ab.
53.	((endoscop* or oesophagoscop* or esophagoscop*) adj2 brush*).ti,ab.
54.	(HRE or WLE or NBI or BLI or FICE or AFI or OCT or ETMI or OE or AI or CAD).ti,ab.
55.	or/37-54
56.	36 and 55
57.	randomized controlled trial.pt.
58.	controlled clinical trial.pt.
59.	randomi#ed.ab.
60.	placebo.ab.
61.	randomly.ab.
62.	clinical trials as topic.sh.
63.	trial.ti.
64.	or/57-63
65.	Meta-Analysis/
66.	Meta-Analysis as Topic/
67.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
68.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
69.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
70.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
71.	(search* adj4 literature).ab.
72.	(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.
73.	cochrane.jw.
74.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
75.	or/65-74
76.	56 and (64 or 75)

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.	*gastrointestinal endoscopy/
37.	gastroscopy/
38.	*endoscopy/
39.	endocytoscopy/
40.	high resolution endoscopy/
41.	magnifying endoscopy/
42.	narrow band imaging/
43.	videoendoscopy/
44.	white light endoscopy/
45.	capsule endoscopy/
46.	esophagoscopy/
47.	exp fluorescence imaging/
48.	exp acetic acid/
49.	molecular imaging/

50.	chromoendoscopy/
51.	exp artificial intelligence/
52.	(videoendoscop* or endomicroscop* or spectroscop* or endocytoscop* or oesophagoscop* or esophagoscop* or gastroscop* or chromatograph* or chromoendoscop* or chromoscop* or volumetric laser or acetic acid or methylene blue or indigo carmine or narrow band or white light or blue laser or blue light or flexible spectral imaging colo?r enhancement or autofluorescen* or fluorescen* or optical coherence tomography or trimodal or tri modal or optical enhancement).ti,ab.
53.	(endoscop* adj3 (imag* or diagn* or identif* or surveillanc* or monitor* or observ* or detect*)).ti,ab.
54.	((capsule or transnasal or nasal) adj2 endoscop*).ti,ab.
55.	(molecular adj3 (imag* or endoscop*)).ti,ab.
56.	((magnif* or high resolution or high definition) adj3 endoscop*).ti,ab.
57.	(artificial intelligence or (computer adj (assisted or aided)) or ((deep or machine) adj learning) or neural network*).ti,ab.
58.	(wide area transepithelial sampling or WATS3D or WATS 3D).ti,ab.
59.	((endoscop* or oesophagoscop* or esophagoscop*) adj2 brush*).ti,ab.
60.	(HRE or WLE or NBI or BLI or FICE or AFI or OCT or ETMI or OE or AI or CAD).ti,ab.
61.	or/36-60
62.	35 and 61
63.	random*.ti,ab.
64.	factorial*.ti,ab.
65.	(crossover* or cross over*).ti,ab.
66.	((doubl* or singl*) adj blind*).ti,ab.
67.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
68.	crossover procedure/
69.	single blind procedure/
70.	randomized controlled trial/
71.	double blind procedure/
72.	or/63-71
73.	Systematic Review/
74.	Meta-Analysis/
75.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
76.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
77.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
78.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
79.	(search* adj4 literature).ab.
80.	(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.
81.	cochrane.jw.
82.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
83.	or/73-82
84.	62 and (72 or 83)

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.	MeSH descriptor: [Endoscopy, Gastrointestinal] this term only
#18.	MeSH descriptor: [Capsule Endoscopy] this term only
#19.	MeSH descriptor: [Esophagoscopy] this term only
#20.	MeSH descriptor: [Gastroscopy] this term only
#21.	(videoendoscop* or endomicroscop* or spectroscop* or endocytoscop* or oesophagoscop* or esophagoscop* or gastroscop*):ti,ab
#22.	(endoscop* near/3 (imag* or diagn* or identif* or surveillanc* or monitor* or observ* or detect*)):ti,ab
#23.	((capsule or transnasal or nasal) near/2 endoscop*):ti,ab
#24.	MeSH descriptor: [Optical Imaging] explode all trees
#25.	MeSH descriptor: [Acetic Acid] explode all trees
#26.	MeSH descriptor: [Molecular Imaging] this term only
#27.	(molecular near/3 (imag* or endoscop*)):ti,ab
#28.	((magnif* or high resolution or high definition) near/3 endoscop*):ti,ab
#29.	(chromatograph* or chromoendoscop* or chromoscop* or volumetric laser or acetic acid or methylene blue or indigo carmine or narrow band or white light or blue laser or blue light or flexible spectral imaging colo?r enhancement or autofluorescen* or fluorescen* or optical coherence tomography or trimodal or tri modal or optical enhancement):ti,ab
#30.	MeSH descriptor: [Artificial Intelligence] explode all trees
#31.	(artificial intelligence or (computer next (assisted or aided)) or ((deep or machine) next learning) or neural network*):ti,ab
#32.	(wide area transepithelial sampling or WATS3D or WATS 3D):ti,ab
#33.	((endoscop* or oesophagoscop* or esophagoscop*) near/2 brush*):ti,ab
#34.	(HRE or WLE or NBI or BLI or FICE or AFI or OCT or ETMI or OE or AI or CAD):ti,ab
#35.	(or #17-#34)
#36.	#16 and #35

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:("endoscop* imag*" OR "endoscop* diagn*" OR "endoscop* identif*" OR "endoscop* surveillanc*" OR "endoscop* monitor*" OR "endoscop* observ*" OR "endoscop* detect*" OR "capsule endoscop*" OR "transnasal endoscop*" OR "nasal endoscop*" OR "magnif* endoscop*" OR "high resolution endoscop*" OR "high definition endoscop*" OR videoendoscop* OR endomicroscop* OR spectroscop* OR endocytoscop* OR oesophagoscop* OR esophagoscop* OR gastroscop* OR chromatograph* OR chromoendoscop* OR chromoscop* OR "volumetric laser" OR "acetic acid" OR "methylene blue" OR "indigo carmine" OR "narrow band" OR "white light" OR "blue laser" OR "blue light" OR "flexible spectral imaging" OR autofluorescen* OR fluorescen* OR "optical coherence tomography" OR trimodal OR "tri modal" OR "optical enhancement" OR "artificial intelligence" OR "computer assisted" "computer aided" OR "deep learning" OR "machine learning" OR "neural network" OR "wide area transepithelial sampling" OR WATS3D OR "WATS 3D") OR abstract:("endoscop* imag*" OR "endoscop* diagn*" OR "endoscop* identif*" OR "endoscop* surveillanc*" OR "endoscop* monitor*" OR "endoscop* observ*" OR "endoscop* detect*" OR "capsule endoscop*" OR "transnasal endoscop*" OR "nasal endoscop*" OR "magnif* endoscop*" OR "high resolution endoscop*" OR "high definition endoscop*" OR videoendoscop* OR endomicroscop* OR spectroscop* OR endocytoscop* OR oesophagoscop* OR esophagoscop* OR gastroscop* OR chromatograph* OR chromoendoscop* OR chromoscop* OR "volumetric laser" OR "acetic acid" OR "methylene blue" OR "indigo carmine" OR "narrow band" OR "white light" OR "blue laser" OR "blue light" OR "flexible spectral imaging" OR autofluorescen* OR fluorescen* OR "optical coherence tomography" OR trimodal OR "tri modal" OR "optical enhancement" OR "artificial intelligence" OR "computer assisted" "computer aided" OR "deep learning" OR "machine learning" OR "neural network" OR "wide area transepithelial sampling" OR WATS3D OR "WATS 3D")

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 4: 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 Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
	Quality of Life 1946 – 29 April 2022	

Database	Dates searched	Search filters and limits applied
Embase (OVID)	Health Economics 1 January 2014 – 29 April 2022	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
	Quality of Life 1974 – 29 April 2022	
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

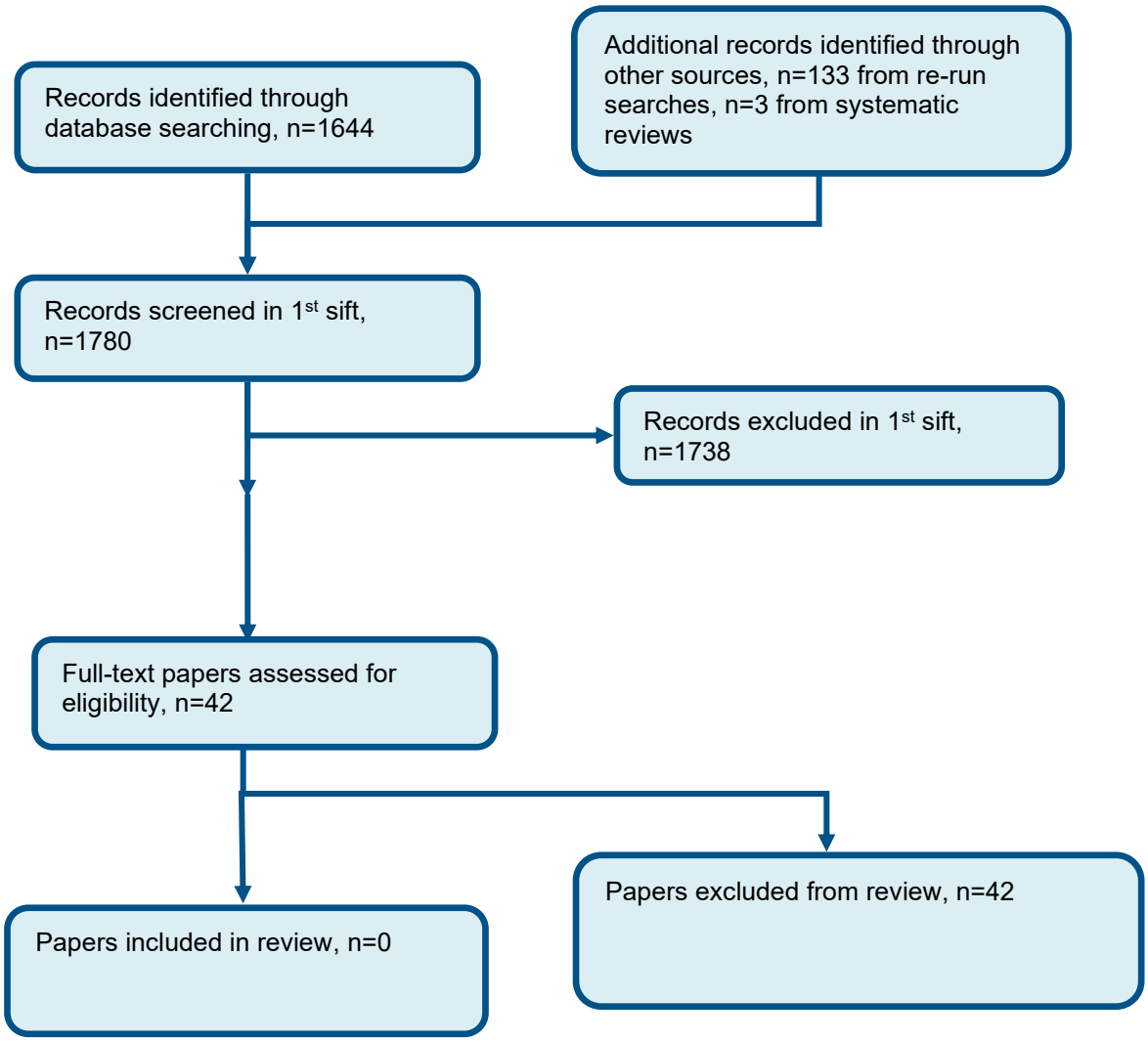
#1.	MeSH DESCRIPTOR Barrett Esophagus EXPLODE ALL TREES
#2.	(barrett*)
#3.	(speciali*) AND (epithel* or oesophag* or esophag* or mucos*)
#4.	(column*) AND (epithel* or oesophag* or esophag* or mucos* or lined or lining or metaplas*)
#5.	#1 OR #2 OR #3 OR #4
#6.	MeSH DESCRIPTOR Precancerous Conditions 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

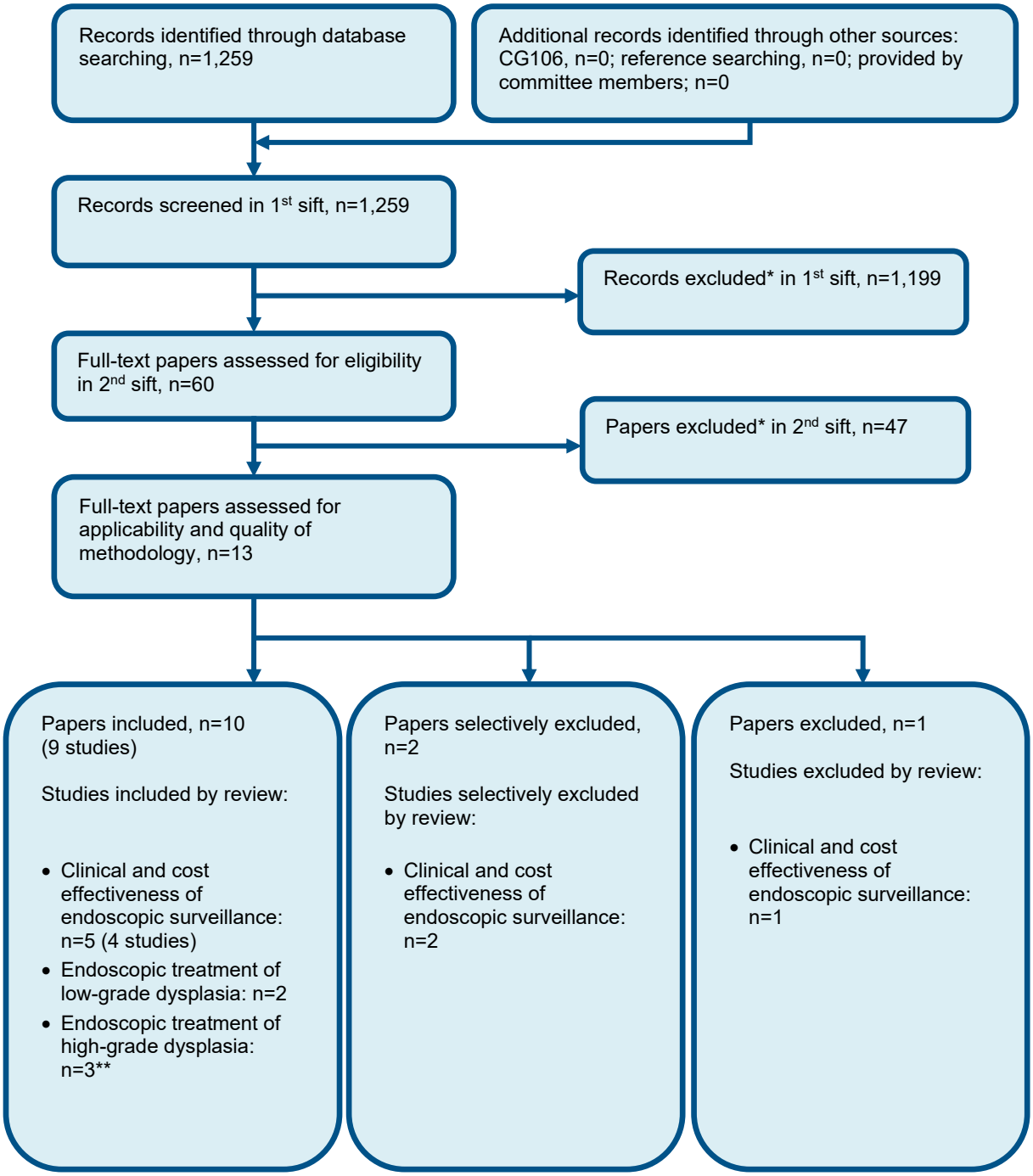
1.	("Barrett Esophagus"[mh]) OR (Barrett*) OR (Esophageal Neoplasms)[mh]

Appendix C – Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of: frequency and duration of endoscopic surveillance techniques



Appendix D – 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 E – Excluded studies

Clinical studies

Table 5: Studies excluded from the clinical review

Study	Exclusion reason
Ackroyd, R., Tam, W., Schoeman, M. et al. (2004) Prospective randomized controlled trial of argon plasma coagulation ablation vs. endoscopic surveillance of patients with Barrett's esophagus after antireflux surgery. Gastrointestinal endoscopy 59(1): 1-7	- Study does not contain an intervention relevant to this review protocol
Ajumobi A, Bahjri K, Jackson C et al. (2010) Surveillance in Barrett's esophagus: an audit of practice. Digestive diseases and sciences 55(6): 1615-1621	- Population not relevant to this review protocol
Aldulaimi, D. M., Cox, M., Nwokolo, C. U. et al. (2005) Barrett's surveillance is worthwhile and detects curable cancers. A prospective cohort study addressing cancer incidence, treatment outcome and survival. European journal of gastroenterology & hepatology 17(9): 943-50	- Comparator in study does not match that specified in this review protocol
Barbiere, J. M. and Lyratzopoulos, G. (2009) Cost-effectiveness of endoscopic screening followed by surveillance for Barrett's esophagus: a review. Gastroenterology 137(6): 1869-76	- Systematic review used as source of primary studies
Barr, H.; Stone, N.; Rembacken, B. (2005) Endoscopic therapy for Barrett's oesophagus. Gut 54(6): 875-84	- Review article but not a systematic review
Bulamu, N. B., Chen, G., Bright, T. et al. (2019) Preferences for Surveillance of Barrett's Oesophagus: a Discrete Choice Experiment. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract 23(7): 1309-1317	- Non-randomised study with no comparison group
Chandan, S., Mashiana, H. S., Dhaliwal, A. J. et al. (2020) CLINICAL APPLICABILITY OF WIDE AREA TRANSEPITHELIAL SAMPLING (WATS-3D) IN SCREENING & SURVEILLANCE OF BARRETT'S ESOPHAGUS - A SYSTEMATIC REVIEW & SENSITIVITY META-ANALYSIS. Gastrointest. Endosc. 91(6): AB395-AB396	- Conference abstract

Study	Exclusion reason
Codipilly, D. C., Chandar, A. K., Singh, S. et al. (2018) The Effect of Endoscopic Surveillance in Patients With Barrett's Esophagus: A Systematic Review and Meta-analysis. Gastroenterology 154(8): 2068-2086.e5	- Systematic review used as source of primary studies - Comparator in study does not match that specified in this review protocol
Cooper, G. S., Yuan, Z., Chak, A. et al. (2002) Association of prediagnosis endoscopy with stage and survival in adenocarcinoma of the esophagus and gastric cardia. Cancer 95(1): 32-8	- Comparator in study does not match that specified in this review protocol
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	- Population not relevant to this review protocol
Craanen, M. E., Blok, P., Meijer, G. A. et al. (2002) Surveillance in Barrett's oesophagus: a critical reappraisal. Scandinavian Journal of Gastroenterology - Supplement: 4-8	- Review article but not a systematic review
DeMeester, S. R. (2001) Surveillance endoscopy and follow-up for Barrett's esophagus. Problems in General Surgery 18(2): 94-98	- Review article but not a systematic review
Ding, Y. E., Li, Y., He, X. K. et al. (2018) Impact of Barrett's esophagus surveillance on the prognosis of esophageal adenocarcinoma: A meta-analysis. Journal of digestive diseases 19(12): 737-744	- Systematic review used as source of primary studies
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	- Population not relevant to this review protocol
Falk, G. W.; Ours, T. M.; Richter, J. E. (2000) Practice patterns for surveillance of Barrett's esophagus in the united states. Gastrointestinal endoscopy 52(2): 197-203	- Study design not relevant to this review protocol
Fountoulakis A, Zafirellis KD, Dolan K et al. (2004) Effect of surveillance of Barrett's oesophagus on the clinical outcome of	- Comparator in study does not match that specified in this review protocol

Study	Exclusion reason
oesophageal cancer. The British journal of surgery 91(8): 997-1003	
Garside, R., Pitt, M., Somerville, M. et al. (2006) Surveillance of Barrett's oesophagus: exploring the uncertainty through systematic review, expert workshop and economic modelling. Health Technology Assessment (Winchester, England) 10(8): 1-142, iii	- Systematic review used as source of primary studies
Gerson, L. B. and Triadafilopoulos, G. (2002) Screening for esophageal adenocarcinoma: an evidence-based approach. American Journal of Medicine 113(6): 499-505	- Systematic review does not contain factors of interest
Grover, M., Strickland, C., Kesler, E. et al. (2006) How should patients with Barrett's esophagus be monitored?. Journal of Family Practice 55(3): 243-7	- Review article but not a systematic review
Hirst, N. G., Gordon, L. G., Whiteman, D. C. et al. (2011) Is endoscopic surveillance for non-dysplastic Barrett's esophagus cost-effective? Review of economic evaluations. Journal of Gastroenterology & Hepatology 26(2): 247-54	- Systematic review used as source of primary studies
Kastelein, F., van Olphen, S. H., Steyerberg, E. W. et al. (2016) Impact of surveillance for Barrett's oesophagus on tumour stage and survival of patients with neoplastic progression. Gut 65(4): 548-54	- Comparison group population does not match protocol: people with OAC from the general population; population is not a single cohort with Barrett’s oesophagus
Macdonald, C. E.; Wicks, A. C.; Playford, R. J. (2000) Final results from 10 year cohort of patients undergoing surveillance for Barrett's oesophagus: observational study. BMJ 321(7271): 1252-5	- Population does not meet guideline agreed definition of Barrett's oesophagus
Ofman, J. J., Lewin, K., Ramers, C. et al. (2000) The economic impact of the diagnosis of dysplasia in Barrett's esophagus. American journal of gastroenterology 95(10): 2946-2952	- No relevant outcomes reported
Old, O., Moayyedi, P., Love, S. et al. (2015) Barrett's Oesophagus Surveillance versus endoscopy at need Study (BOSS): protocol and analysis plan for a multicentre randomized controlled trial. Journal of medical screening 22(3): 158-164	- Protocol and analysis plan; no extractable results

Study	Exclusion reason
Provenzale, D., Kemp, J. A., Arora, S. et al. (1994) A guide for surveillance of patients with Barrett's esophagus. American journal of gastroenterology 89(5): 670-80	- Study design not relevant to this review protocol
Qiao, Y., Hyder, A., Bae, S. J. et al. (2015) Surveillance in Patients With Barrett's Esophagus for Early Detection of Esophageal Adenocarcinoma: A Systematic Review and Meta-Analysis. Clinical and Translational Gastroenterology 6: e131	- Systematic review used as source of primary studies
Quera, R.; O'Sullivan, K.; Quigley, E. M. M. (2006) Surveillance in barrett's oesophagus: Will a strategy focused on a high-risk group reduce mortality from oesophageal adenocarcinoma?. Endoscopy 38(2): 162-169	- Population not relevant to this review protocol
Roberts, K. J., Harper, E., Alderson, D. et al. (2010) Long-term survival and cost analysis of an annual Barrett's surveillance programme. Eur J Gastroenterol Hepatol 22(4): 399-403	- Comparator in study does not match that specified in this review protocol
Royston, C., Caygill, C., Charlett, A. et al. (2016) The evolution and outcome of surveillance of Barrett's oesophagus over four decades in a UK District General Hospital. Eur J Gastroenterol Hepatol 28(12): 1365-1373	- Comparator in study does not match that specified in this review protocol
Rubenstein JH, Sonnenberg A, Davis J et al. (2008) Effect of a prior endoscopy on outcomes of esophageal adenocarcinoma among United States veterans. Gastrointestinal endoscopy 68(5): 849-855	- Population not relevant to this review protocol
Rubenstein, J. H. and Inadomi, J. M. (2021) Cost-Effectiveness of Screening, Surveillance, and Endoscopic Eradication Therapies for Managing the Burden of Esophageal Adenocarcinoma. Gastrointestinal endoscopy clinics of North America 31(1): 77-90	- Systematic review used as source of primary studies
Shaheen, N. J.; Provenzale, D.; Sandler, R. S. (2002) Upper endoscopy as a screening and surveillance tool in esophageal adenocarcinoma: a review of the evidence. American journal of gastroenterology 97(6): 1319-27	- Review article but not a systematic review

Study	Exclusion reason
Shen, E. F., Gladstone, S., Milne, G. et al. (2003) Endoscopic surveillance practice for Barrett's oesophagus in Scotland and early experience in implementing local guidelines. Scottish Medical Journal 48(2): 43-45	- No relevant outcomes reported
Singh, R.; Ragunath, K.; Jankowski, J. (2007) Barrett's Esophagus: Diagnosis, Screening, Surveillance, and Controversies. Gut & Liver 1(2): 93-100	- Review article but not a systematic review
Theron, B. T., Padmanabhan, H., Aladin, H. et al. (2016) The risk of oesophageal adenocarcinoma in a prospectively recruited Barrett's oesophagus cohort. United european gastroenterology journal 4(6): 754-761	-Study does not contain an intervention relevant to this review protocol
van Sandick, J. W., van Lanschot, J. J., Kuiken, B. W. et al. (1998) Impact of endoscopic biopsy surveillance of Barrett's oesophagus on pathological stage and clinical outcome of Barrett's carcinoma. Gut 43(2): 216-22	- Population not relevant to this review protocol
Verbeek, R. E., Leenders, M., Ten Kate, F. J. et al. (2014) Surveillance of Barrett's esophagus and mortality from esophageal adenocarcinoma: a population-based cohort study. Am J Gastroenterol 109(8): 1215-22	- Population not relevant to this review protocol
Vissapragada, R., Bulamu, N. B., Brumfitt, C. et al. (2021) Improving cost-effectiveness of endoscopic surveillance for Barrett's esophagus by reducing low-value care: a review of economic evaluations. Surgical endoscopy 26: 26	- Systematic review used as source of primary studies
Vogt, J. S., Larsen, A. C., Sommer, T. et al. (2018) Quality of endoscopic surveillance of Barrett's esophagus. Scandinavian journal of gastroenterology 53(3): 256-259	- Population not relevant to this review protocol *includes dysplastic Barrett's*
Wani, S. and Sharma, P. (2006) The rationale for screening and surveillance of Barrett's metaplasia. Best Practice & Research in Clinical Gastroenterology 20(5): 829-42	- Review article but not a systematic review
Wong, T.; Tian, J.; Nagar, A. B. (2010) Barrett's surveillance identifies patients with early esophageal adenocarcinoma. American Journal of Medicine 123(5): 462-7	- Comparator in study does not match that specified in this review protocol

Study	Exclusion reason
Yang, Y., Chen, H. N., Wang, R. et al. (2015) Cost-Effectiveness Analysis on Endoscopic Surveillance Among Western Patients With Barrett's Esophagus for Esophageal Adenocarcinoma Screening. Medicine 94(39): e1105	- Systematic review used as source of primary studies

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 – Research recommendation

Frequency and duration of endoscopic surveillance

What is the usefulness of clinical and molecular biomarkers to inform the optimal frequency and duration of endoscopic surveillance for adults with Barrett's oesophagus?

Why this is important

Barrett's surveillance is currently performed at 2–5-year intervals in patients who are deemed to potentially benefit from surveillance. This interval is based on consensus opinion rather than evidence, although it is to some extent tailored according to known clinical determinants of progression. The length of Barrett's oesophagus appears to be the strongest risk factor for progression (<3cm, lower risk vs 3cm or longer, higher risk), but other clinical risk factors for oesophageal cancer have been described, including male gender, increasing age, positive family history and smoking status. If further factors associated with a greater risk of progression of non-dysplastic Barrett's are identified and a stronger association between already identified factors and risk of progression is established through research, this would allow more precise individual tailoring of follow-up intervals, reducing frequency in those at low risk and intensifying it in those at high risk.

Rationale for research recommendation

Importance to 'patients' or the population	If biomarkers for progression are identified, patients with Barrett's oesophagus could be better risk stratified such that those at low risk would need to undergo fewer endoscopic procedures, and those at higher risk would have an enhanced opportunity for earlier detection of neoplastic progression, with clear benefits in terms of cancer prevention and reduction of associated morbidity and mortality.
Relevance to NICE guidance	Research in this area will inform guidance on the optimal frequency and duration of endoscopic surveillance based on molecular biomarkers that are shown to be associated with a greater risk of progressions rather than this being based on consensus opinion. Identifying an association between clinical risk factors and progression to dysplasia or cancer will enable clinicians to develop a personalised risk of progression to inform the optimal surveillance interval for each patient.
Relevance to the NHS	Barrett's surveillance consumes a large amount of NHS gastroenterology resources. While routinely using biomarkers may increase resource requirements for pathology departments, it would have the benefit of identifying the high proportion of Barrett's oesophagus patients who are at lower risk of progression, thereby reducing surveillance intervals and reducing both endoscopy and pathology requirements in the long run. Patients who are at higher risk would potentially have

	their neoplasia detected at an earlier stage when it would be easier and perhaps cheaper to treat or receive ablation treatment prior to neoplastic progression.
National priorities	None
Current evidence base	The current evidence base for the interval of surveillance, is very weak. There are no relevant studies comparing current guidance with alternative strategies (surveillance of lower frequency or no surveillance). There are several retrospective studies looking at risk of progression to dysplasia and cancer with different biomarkers. Most of the evidence relates to p53 immunohistochemistry. A recent American study included a prospective validation cohort. However, some concerns exist regarding the quality of pathology reporting in community/private laboratories in USA, which is evident from the very high proportion of Indefinite and low-grade dysplasia at index endoscopy, relative to non-dysplastic Barrett's oesophagus. There is therefore currently insufficient evidence to recommend a change in practice
Equality considerations	The recommendation is unlikely to impact on equality issues.

Modified PICO table

Population	Patients with non-dysplastic Barrett's oesophagus and indefinite dysplasia
Intervention	Application of biomarkers to biopsies of Barrett's oesophagus. Biomarkers most likely to be considered are those which have been highlighted in the existing evidence base from retrospective studies, including p53 immunohistochemistry, p53 mutation, digital image cytometry, possibly AI algorithms (no current evidence but rapidly growing field).
Comparator	Biomarker status, positive or negative
Outcome	Time to development of dysplasia or cancer in those positive and negative for each biomarker,
Study design	Prospective, but possibility of using biopsies and data collected from previously performed large scale UK prospective study (Aspect). This would facilitate more rapid introduction of technology, if proven useful and cost-effective
Timeframe	Long term, 10years plus
Additional information	None