# National Institute for Health and Care Excellence

Draft for consultation

# Barrett's oesophagus

## 2.1b Evidence reviews for diagnostic accuracy of Endoscopic surveillance

*NICE guideline <number>*

*Evidence reviews underpinning recommendations 1.3.1 - 1.3.4 and research recommendations in the NICE guideline*

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*Draft for consultation*

*These evidence reviews were developed by Guideline Development Team NGC*

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# Contents

# 1 Diagnostic accuracy of endoscopic surveillance

## 1.1 Review question

What is the diagnostic accuracy of different endoscopic surveillance techniques including high resolution endoscopy and chromoendoscopy?

### 1.1.1 Introduction

Different techniques of endoscopic surveillance are currently used within clinical practice. It is not known how accurate those techniques are in comparison to what is held as the gold standard or reference for endoscopic surveillance (High resolution white light endoscopy).

### 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.

### 1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

**Table 1: PICO characteristics of review question**

| | |
|---|---|
| **Population** | Inclusion:<br>Adults, 18 years and over, with Barrett's Oesophagus (with or without dysplasia)<br><br>Exclusion:<br>Adults with Barrett's Oesophagus that does not fit within the definition |
| **Target condition** | Barrett's Oesophagus |
| **Index tests** | • Trans-nasal endoscopy<br>• Chromoendoscopy (e.g., narrow band imaging, blue laser imaging, confocal endomicroscopy, volumetric laser endomicroscopy, acetic acid)<br>• Endoscopic brushing (wide area transepithelial sampling wats3D)<br>• Artificial Intelligence (AI)<br>Strata:<br>Type of endoscopic surveillance (transnasal, chromoendoscopy, enodscopic brushing, AI) |
| **Reference standard** | High resolution white light endoscopy (with Seattle protocol biopsies) |
| **Outcome and statistical measures** | Detection of progression of dysplasia<br>• Sensitivity<br>• Specificity<br>• Data to calculate 2x2 tables to calculate sensitivity and specificity (number of true positives, true negatives, false positives and false negatives). |
| **Study design** | Observational studies: |

- Cross-sectional studies
- Prospective / Retrospective diagnostic studies
- Systematic Reviews of observational studies

Any study containing a diagnostic accuracy data or analysis

## 1.1.4 Diagnostic evidence

### 1.1.4.1 Included studies

15 diagnostic accuracy studies were included in the review; [1-9, 11-16] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below in Appendix C and references in 1.1.14 References .

The aim of the studies was to assess diagnostic test accuracy in identifying Barrett's oesophagus with dysplasia or cancer, low grade dysplasia, high grade intraepithelial dysplasia/ neoplasia/ cancer, T1a or T1b neoplasia.

12 studies provided information on the diagnostic accuracy of chromoendoscopy techniques, 1 study provided information on the diagnostic accuracy of endoscopic brushing (brush biopsy). 2 studies provided information on the diagnostic accuracy of artificial intelligence (AI): one study looking at convolutional neural networks and one looking at narrow-bang imaging + AI and white-light imaging +AI.

No evidence was identified for the diagnostic accuracy of trans-nasal endoscopy.

Meta-analysis was not conducted because where two or more studies examined the diagnostic accuracy of the same index test they looked at different target conditions (e.g. high grade dysplasia or low-grade dysplasia), or reported location based analysis while other studies reported per patient based analysis. Thus, results from these studies are presented individually on a per-study basis. Where studies provided insufficient information to extract 2x2 table data (true positives, true negatives, false positives, false negatives) this has been highlighted for each study in Table 3 and sensitivity and specificity measures were extracted as reported in the paper. Where confidence intervals were not available to assess imprecision in the effect measures, evidence quality was downgraded by 1 increment. Evidence was downgraded for indirectness where studies included a mixed population of people with and without known Barrett's oesophagus. Evidence was also downgraded for indirectness where there was a lack of clarity around the quality of endoscopy as a reference standard, or where histology was used as a reference standard with white-light endoscopy results provided separately to those of the index test.

The majority of studies were of cross-sectional design, 5 studies being prospective and 3 studies being retrospective. There were also 5 randomised cross-over studies and 2 prospective randomised controlled trials included in the review.

It was noted in the literature high-resolution white light endoscopy is also referred to as high-definition white-light endoscopy. It has been extracted as reported in the studies but the terms are used interchangeably within the evidence report with high-resolution white light endoscopy primarily used in the committee's discussion of the evidence.

See also the study selection flow chart in Appendix C, sensitivity and specificity forest plots in Appendix E, and study evidence tables in Appendix D.

### 1.1.4.2 Excluded studies

See the excluded studies list in Appendix G.

## 1.1.5 Summary of studies included in the diagnostic evidence

**Table 2: Summary of studies included in the evidence review**

| Study | Population | Target condition | Index test | Reference standard | Comments |
|---|---|---|---|---|---|
| ***Chromoendoscopy*** | | | | | |
| Bajbouj 2010 [2] | Participants aged 18 – 80 years; Barrett's length at least COM1 according to Prague classification; in the case of suspected intraepithelial neoplastic changes, lesion <1cm; acid-suppressive therapy at least at the standard dose for a minimum of 4 weeks (n=68)<br><br>Age, mean (SD): 60 ± 12 years<br><br>Germany | Barrett's Oesophagus: high grade intraepithelial neoplasia / carcinoma | Probe based confocal laser endomicroscopy | Standard endoscopy | Diagnostic data reported per biopsy and per patient<br><br>2x2 data not reported |
| Canto 2014[3] | Barrett's oesophagus patients undergoing routine surveillance or referred for confirmation of diagnosis and/or endoscopic therapy (n=192)<br><br>Median age (range): high-definition white-light endoscopy and random biopsy group: 62 (26 to 79); high-definition white-light endoscopy followed by laser endomicroscopy and targeted biopsy group: 62 (32 to 82) | Barrett's oesophagus confocal neoplasia | High-definition white light endoscopy alone with random biopsies (HDWLE+RB)<br><br>High-definition white light endoscopy + endoscope-based confocal laser endomicroscopy (CLE) with targeted | Blinded expert pathologic diagnosis | Multi-centre RCT<br><br>2x2 data not reported |

| Study | Population | Target condition | Index test | Reference standard | Comments |
|---|---|---|---|---|---|
| | USA | | biopsies (HDWLE+CLE+TB) | | |
| Curvers 2010 [4] | Patients with Barrett's oesophagus referred to 5 participating centres for work-up of endoscopically inconspicuous high-grade dysplasia/ early carcinoma (HGD/Ca) (n=87)<br><br>Age, mean (SD): 68 (9)<br><br>Netherlands & USA | Barrett's oesophagus with high grade dysplasia and early carcinoma | Endoscopic tri-modal imaging (incorporating high-resolution endoscopy, autofluorescence and narrow-band imaging) | Standard video endoscopy | Randomised cross-over multi-centre study<br><br>2x2 data calculated |
| Egger 2003[6] | Participants undergoing routine surveillance for non dysplastic, dysplastic or first time in surveillance for confirmed Barrett's Oesophagus without (n=18) or with (n=8) only low grade dysplasia<br><br>Age, mean (range): 64.8 years; range 29–78<br><br>Germany | Barrett's Oesophagus with intestinal metaplasia with columnar and goblet cells vs low or high grade dysplasia, cancer | Autofluorescence<br><br>Methylene blue staining | Standard endoscopy | Diagnostic data given per biopsy and per patient<br><br>2x2 data not reported<br><br>Indirectness: sensitivity and specificity were not reported separately for dysplasia or cancer but also include metaplasia findings. |
| Jayasekera 2012 [8] | Patients referred for endoscopic evaluation and treatment of dysplastic Barrett's oesophagus, which had been previously diagnosed by their referring physician (n=50) | Barrett's oesophagus with high grade dysplasia and intramucosal cancer. | Narrow-band imaging<br><br>Confocal laser endomicroscopy | Histology (Seattle protocol) | Study aim: to assess 3 consecutive imaging modalities with histological assessment (standard Seattle protocol biopsies) as the reference standard.<br><br>2x2 data calculated |

| Study | Population | Target condition | Index test | Reference standard | Comments |
|---|---|---|---|---|---|
| | Age, median (range): 66 (41-86) years<br><br>Australia | | High definition white light endoscopy | | Indirectness: Serious indirectness as results for white light endoscopy are given separately with biopsy as the reference standard |
| Longcroft-Wheaton [9] | People with biopsy-proven Barrett's oesophagus, no history or prior dysplasia or cancer, positive for intestinal metaplasia<br><br>Age, mean (SD): 66 (11.1)<br><br>UK | Barrett's oesophagus with neoplasia (high grade dysplasia, low grade dysplasia, cancer) | Acetic acid-targeted biopsies (Portsmouth protocol) | Seattle protocol-guided nontargeted biopsies. | Pilot multi-centre randomised cross-over trial<br><br>2x2 data calculated |
| Ormeci 2008 [11] | Patients older than 18 years with an indication for esophagogastroduodenoscopy were selected for this study (n=109)<br><br>Age, mean (SD): 62.32 (10.61 years); range, 33–82 years<br><br>Turkey | Barrett's Oesophagus with dysplasia or cancer | Chromoendoscopy with methylene blue | Standard endoscopy | Histopathologic diagnosis was accepted as the gold standard, and conventional endoscopic or chromoendoscopic diagnosis was compared with the histopathologic diagnosis.<br><br>Results from chromoendoscopy and standard/conventional endoscopy reported separately.<br><br>2x2 data not reported |
| Pascarenco 2016 [12] | Patients over 18 with endoscopic confirmation of Barrett's Oesophagus (n=84)<br><br>Age, mean (range): 57.4 (26-84) | Barrett's oesophagus with low grade dysplasia or indefinite for dysplasia | Narrow-band imaging | White light imaging | 2x2 data calculated |

| Study | Population | Target condition | Index test | Reference standard | Comments |
|---|---|---|---|---|---|
| | Romania | | | | |
| Ragunath 2003[13] | Patients with endoscopic and histological diagnosis of Barrett's oesophagus segments of 3cm or more in length, adults patients of any sex attending for endoscopy, including newly diagnosed patients as well as those undergoing surveillance endoscopy for Barrett's Oesophagus, and patients known to have dysplasia without mucosal abnormalities who were receiving follow up endoscopies (n=57)<br><br>Age: not reported<br><br>UK | Barrett's Oesophagus with dysplasia or carcinoma | Methylene blue | Standard endoscopy | 2x2 data not reported |
| Sharma 2011 [15] | Consecutive patients undergoing BE surveillance and/or referred for BE-associated neoplasia (HGD/oesophageal carcinoma) evaluation and treatment were prospectively enrolled in this trial at 5 hospitals (n=101)<br><br>Age, mean (range): 65.1 years (27–90 years)<br><br>France, Germany & USA | Barrett's Oesophagus: high grade dysplasia / oesophageal cancer | Narrow-band imaging<br><br>Probe-based confocal laser endomicroscopy | Histology | Diagnostic data reported per location<br><br>2x2 data calculated<br><br>Indirectness: the paper measures diagnostic accuracy of the visual findings from each HD-WLE, NBI, pCLE with reference to the full histological findings. i.e. reference standard was histology derived from biopsies from each procedure rather than |

| Study | Population | Target condition | Index test | Reference standard | Comments |
|---|---|---|---|---|---|
| | | | | | histology from biopsies from the HD-WLE |
| Sharma 2013[14] | Patients undergoing screening or surveillance for Barrett's oesophagus at three tertiary referral centres.<br><br>Age, mean (range): 61 (38-85) years<br><br>USA, Netherlands | Barrett's oesophagus with neoplasia (high grade dysplasia, oesophageal adenocarcinoma) | Narrow-band imaging | White-light endoscopy | Multi-centre randomised cross-over trial<br><br>2x2 data calculated |
| Vithayathil 2022 [16] | Non-dysplastic Barrett's oesophagus patients (n=134)<br><br>Age, median (range): 67.3 (38.0 to 89.0) years<br><br>UK | Dysplasia (dysplasia and high-grade dysplasia) | Autofluorescence imaging- guided probe-based confocal laser endomicroscopy and molecular biomarkers (3-biomarker panel) (AFI-guided pCLE)<br><br>High-resolution white-light endoscopy with Seattle protocol biopsies | Histology | Cross-over RCT<br><br>Biomarkers: p53 and cyclin A by immunohistochemistry; aneuploidy by image cytometry) |
| ***Endoscopic Brushing*** | | | | | |
| Anandasabapathy 2011 [1] | Subjects with a known prior history (recent or remote) of Barrett's oesophagus with dysplasia/neoplasia (indefinite for-dysplasia (IND), low-grade (LGD), high-grade dysplasia | Barrett's Oesophagus: Barrett's metaplasia (IM), indefinite for dysplasia (IND), dysplasia (LGD/ HGD/CA), and | Brush biopsy | Forceps biopsy (refers to Seattle protocol biopsy) | Study does not mention the type or methodology of endoscopic examination for biopsies and only notes the comparison of brush versus forceps. |

| Study | Population | Target condition | Index test | Reference standard | Comments |
|---|---|---|---|---|---|
| | (HGD) or intramucosal adenocarcinoma (IMCA) and no grossly evident lesion (n=181)<br><br>Age, mean (range): 65 (46 – 87)<br><br>USA | inadequate (no Barrett's oesophagus) | | | 2x2 data available |
| ***Artificial Intelligence*** | | | | | |
| Ebigbo 2020 [5] | Endoscopic, high resolution, white light images of T1a and T1b Barett's Cancer were collected retrospectively in three tertiary care centres in Germany (n=230 images)<br><br>Age not reported<br><br>Germany | Barrett's Oesophagus with T1a or T1b neoplasia | Convolutional neural networks | Histopathology (from white light imaging samples) | 2x2 data not reported |
| Hashimoto 2020 [7] | Images from participants with histologically proven dysplasia (high grade dysplasia and T1 adenocarcinoma) in Barrett's (n=100 patients; 1832 images)<br><br>Age: not reported<br><br>USA | Barrett's Oesophagus with high grade dysplasia | Narrow-band imaging + AI | White light imaging | Results for: narrow-band imaging +AI and white light imaging + AI, are provided separately with histology used as the reference standard<br><br>Diagnostic data given per image taken<br><br>2x2 data calculated |

1

See Appendix D for full evidence tables

### 1.1.6 Summary of the diagnostic evidence

Clinical decision thresholds were set as sensitivity/specificity =0.9 and 0.8 above which a test would be recommended and 0.6 and 0.5 below which a test is of no clinical use.

**Table 3: Clinical evidence summary: diagnostic test accuracy for chromoendoscopy**

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| Probe based confocal laser endomicroscopy to detect Barrett's Oesophagus: high grade intraepithelial neoplasia / carcinoma | | | | | | | |
| Probe based confocal laser endomicroscopy (reference standard: standard endoscopy) | 68 (1) | Very serious[1] | Not serious | Not serious | Serious [2] | Sensitivity=0.64 (0.31-0.89) | VERY LOW |
| | | Very serious[1] | Not serious | Not serious | Not serious | Specificity=0.95 (0.85-0.99) | LOW |
| Probe-based confocal laser endomicroscopy to detect Barrett's Oesophagus: high grade dysplasia / oesophageal cancer | | | | | | | |
| Probe-based confocal laser endomicroscopy (reference standard: histology) | 101 patients; results based on 874 locations (1) | Not serious | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.63 (0.53–0.71) | LOW |
| | | Not serious | Not serious | Serious[3] | Not serious | Specificity= 0.91 (0.89–0.93) | MODERATE |
| Confocal laser endomicroscopy to detect Barrett's oesophagus with high grade dysplasia and intramucosal cancer | | | | | | | |
| Confocal laser endomicroscopy (reference standard: biopsy) | 50; results based on 1117 | Very serious[1] | Not serious | Serious[3] | Not serious | Sensitivity= 0.76 (0.64-0.85) | VERY LOW |
| | | Very serious[1] | Not serious | Serious[3] | Serious[2] | Specificity= 0.80 (0.78-0.83) | VERY LOW |

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| | locations (1) | | | | | | |
| High-definition white light endoscopy to detect Barrett's oesophagus with high grade dysplasia and intramucosal cancer | | | | | | | |
| High-definition white light endoscopy (reference standard: biopsy) | 50; results based on 1190 locations (1) | Very serious[1] | Not serious | Serious[3] | Not serious | Sensitivity= 0.82 (0.73-0.90) | VERY LOW |
| | | Very serious[1] | Not serious | Serious[3] | Not serious | Specificity= 0.83 (0.81-0.85) | VERY LOW |
| High-definition white light endoscopy combined with confocal laser endomicroscopy with targeted biopsies to detect Barrett's oesophagus neoplasia | | | | | | | |
| HDWLE+CLE+TB (reference standard: blinded expert pathology) | 192 (1) | Not serious | Not serious | Serious[3] | Cannot be assessed[4] | Sensitivity= 0.95 | LOW |
| | | Not serious | Not serious | Serious[3] | Cannot be assessed[4] | Specificity= 0.92 | LOW |
| High-definition white light endoscopy with random biopsies to detect Barrett's oesophagus neoplasia | | | | | | | |
| HDWLE+RB (reference standard: blinded expert pathology) | 192 (1) | Not serious | Not serious | Serious[3] | Cannot be assessed[4] | Sensitivity: 0.40 | LOW |
| | | Not serious | Not serious | Serious[3] | Cannot be assessed[4] | Specificity= 0.98 | LOW |
| Autofluorescence-guided probe-based confocal laser endomicroscopy (with targeted biopsies) to detect Barrett's oesophagus with dysplasia | | | | | | | |
| Afi-guided pCLE (reference standard: histology) | 35 (1) | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.74 (0.57-0.88) | VERY LOW |
| | | Serious[1] | Not serious | Serious[3] | Cannot be assessed[4] | Specificity= 0.67 | VERY LOW |

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| Autofluorescence-guided probe-based confocal laser endomicroscopy (with targeted biopsies) to detect high-grade dysplasia | | | | | | | |
| Afi-guided pCLE (reference standard: histology) | 17 (1) | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.77 (0.50-0.93) | VERY LOW |
| | | Serious[1] | Not serious | Serious[3] | Cannot be assessed[4] | Specificity= 0.60 | VERY LOW |
| High resolution white light endoscopy to detect Barrett's oesophagus with dysplasia | | | | | | | |
| High-resolution white light endoscopy (reference standard: histology) | 35 (1) | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.80 (63.1-91.6) | VERY LOW |
| | | n/a | n/a | n/a | n/a | Specificity: not reported | n/a |
| High resolution white light endoscopy to detect high-grade dysplasia | | | | | | | |
| High-resolution white light endoscopy (reference standard: histology) | 17 (1) | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.77 (0.50-0.93) | VERY LOW |
| | | n/a | n/a | n/a | n/a | Specificity: not reported | n/a |
| Autofluorescence to detect Barrett's Oesophagus with intestinal metaplasia with columnar and goblet cells, low or high grade dysplasia, cancer | | | | | | | |
| Autofluorescence (reference standard: standard endoscopy) | 35 (1) | Serious[1] | Not serious | serious[3] | Cannot be assessed[4] | Sensitivity = 0.59 | VERY LOW |
| | | Serious[1] | Not serious | serious[3] | Cannot be assessed[4] | Specificity= 0.78 | VERY LOW |
| Methylene blue staining to detect Barrett's Oesophagus with intestinal metaplasia with columnar and goblet cells, low or high grade dysplasia, cancer | | | | | | | |

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| Methylene blue staining (reference standard: standard endoscopy) | 35 (1) | Serious[1] | Not serious | Not serious | Cannot be assessed[4] | Sensitivity = 0.71 | LOW |
| | | Serious[1] | Not serious | Not serious | Cannot be assessed[4] | Specificity= 0.50 | LOW |
| Chromoendoscopy with methylene blue to detect Barrett's Oesophagus with dysplasia | | | | | | | |
| Chromoendoscopy with methylene blue | 109 (1) | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.68 (0.46-0.85) | VERY LOW |
| | | Serious[1] | Not serious | Serious[3] | Serious[2] | Specificity= 0.77(0.67-0.84) | VERY LOW |
| Chromoendoscopy with methylene blue to detect Barrett's Oesophagus with oesophageal cancer | | | | | | | |
| Conventional endoscopy | 109 (1) | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.95 (0.75-0.99) | VERY LOW |
| | | Serious[1] | Not serious | Serious[3] | Not serious | Specificity= 0.99 (0.94-0.98) | LOW |
| Chromoendoscopy with methylene blue | | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.95 (0.75-0.99) | VERY LOW |
| | | Serious[1] | Not serious | Serious[3] | Not serious | Specificity= 1.00 (0.94-0.98) | LOW |
| Methylene blue directed imaging and biopsy to detect Barrett's Oesophagus with dysplasia or carcinoma | | | | | | | |
| Methylane blue (reference standard: standard endoscopy) | 57 (1); per biopsy analysis | Serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.49 (0.38-0.61) | VERY LOW |
| | | Serious[1] | Not serious | Serious[3] | Serious[2] | Specificity= 0.85 (0.82-0.88) | VERY LOW |
| Narrow-band imaging to detect Barrett's Oesophagus: high grade dysplasia / oesophageal cancer | | | | | | | |
| Narrow-band imaging | 101 patients; | Not serious | Not serious | Serious[3] | Not serious | Sensitivity= 0.42 (0.33–0.51) | HIGH |

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| (reference standard: HD white light endoscopy) | results based on 874 locations (1) | Not serious | Not serious | Serious[3] | Not serious | Specificity= 0.89 (0.87–0.91) | HIGH |
| Narrow-band imaging to detect Barrett's Oesophagus: high grade dysplasia and intramucosal cancer | | | | | | | |
| Narrow-band imaging (reference standard: biopsy) | 50; results based on 1190 biopsies (1) | Very serious[1] | Not serious | Serious[3] | Serious[2] | Sensitivity= 0.89 (0.81 - 0.95) | VERY LOW |
| | | Very serious[1] | Not serious | Serious[3] | Serious[2] | Specificity= 0.81 (0.79 – 0.83) | VERY LOW |
| Narrow-band imaging to detect Barrett's Oesophagus: low grade dysplasia or indefinite for dysplasia | | | | | | | |
| Narrow-band imaging (reference standard: white light imaging) | 84 (1) | Not serious | Not serious | Not serious | Very serious[2] | Sensitivity= 1.00 (0.03 - 1.00) | MODERATE |
| | | Not serious | Not serious | Not serious | Serious[2] | Specificity=0.89 (0.80-0.95) | MODERATE |
| Endoscopic tri-modal imaging to detect Barrett's oesophagus with high grade dysplasia/ early carcinoma | | | | | | | |
| Endoscopic tri-modal imaging (reference standard: standard video endoscopy) | 87 (1) | Not serious | Not serious | Not serious | Not serious | Sensitivity= 0.78 (0.62-0.89) | HIGH |
| | | Not serious | Not serious | Not serious | Not serious | Specificity= 0.68 (0.53-0.81) | HIGH |
| Acetic acid-targeted biopsies (Portsmouth protocol) to detect Barrett's oesophagus with neoplasia (high-grade dysplasia, cancer) | | | | | | | |

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| Acetic acid-targeted biopsies (Portsmouth protocol) (reference standard: Seattle protocol-guided nontargeted biopsies) | 174 (1) | Not serious | Not serious | Not serious | Very serious[2] | Sensitivity= 1.00(0.16-1.00) | MODERATE |
| | | Not serious | Not serious | Not serious | Not serious | Specificity= 1.00 (0.98-1.00) | HIGH |

*1 Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the studies were rated at high risk of bias and downgraded by 2 increments if the studies were rated at very high risk of bias.*

*2 Imprecision was assessed based on inspection of the confidence intervals. For sensitivity, two clinical decision thresholds were determined at the value above which a test would be recommended (90%), and a second below which a test would be considered of no clinical use (60%). For specificity, two clinical decision thresholds were determined at the value above which a test would be recommended (80%), and a second below which a test would be considered of no clinical use (50%). The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate crossed one threshold and downgraded by 2 increments when the range covered two thresholds.*

*3 Evidence was downgraded by 1 increment if the study was rated as having serious indirectness and downgraded by 2 increments if the study was rated as having very serious indirectness.*

*4 Where the study does not report confidence intervals or the data to calculate 2x2 tables imprecision cannot be assessed. Where this is the case evidence quality was downgraded by 1 increment.*

**Table 4: Clinical evidence summary: diagnostic test accuracy for endoscopic brushing**

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| Brush biopsy to detect Barrett's Oesophagus: Barrett's metaplasia, indefinite for dysplasia, dysplasia and inadequate (no BE) | | | | | | | |

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| Brush biopsy (reference standard: forceps biopsy) | 151 (1) | Serious[1] | Not serious | Serious[2] | Not serious | Sensitivity= 0.81 (0.73-0.87) | LOW |
| | | Serious[1] | Not serious | Serious[2] | Serious [3] | Specificity=0.48 (0.30-0.67) | VERY LOW |

*1 Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the studies were rated at high risk of bias and downgraded by 2 increments if the studies were rated at very high risk of bias.*

*2 Evidence was downgraded by 1 increment if the majority of studies were rated as having serious indirectness.*

*3 Imprecision was assessed based on inspection of the confidence intervals. For sensitivity, two clinical decision thresholds were determined at the value above which a test would be recommended (90%), and a second below which a test would be considered of no clinical use (60%). For specificity, two clinical decision thresholds were determined at the value above which a test would be recommended (80%), and a second below which a test would be considered of no clinical use (50%). The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate crossed one threshold and downgraded by 2 increments when the range covered two thresholds.*

**Table 5: Clinical evidence summary: diagnostic test accuracy for artificial intelligence**

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| Convolutional neural networks to detect Barrett's Oesophagus with T1a or T1b neoplasia | | | | | | | |
| Convolutional neural networks (reference standard: histopathology (from white light imaging samples) | 116; 230 images (1) | Not Serious | Not serious | Serious[2] | Not serious | Sensitivity= 0.77 (0.75 – 0.78) | MODERATE |
| | | Not Serious | Not serious | Serious[2] | Not serious | Specificity= 0.64 (0.62 – 0.66) | MODERATE |
| Narrow-band imaging + AI to detect Barrett's Oesophagus with high grade dysplasia | | | | | | | |
| Narrow-band imaging +AI (reference | 100 patients;45 | Serious[1] | Not serious | Serious[2] | Serious[3] | Sensitivity= 0.92 (0.84-0.97) | VERY LOW |
| | | Serious[1] | Not serious | Serious[2] | Not serious | Specificity= 0.99 (0.96-1.00) | LOW |

| Index test | Number of patients (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect size (95%CI) | Quality |
|---|---|---|---|---|---|---|---|
| standard: histology) | 8 images (1) | | | | | | |
| White light imaging +AI to detect Barrett's Oesophagus with high grade dysplasia | | | | | | | |
| White light imaging +AI (reference standard: histology) | 100 patients; 458images (1) | Serious[1] | Not serious | Serious[2] | Not serious | Sensitivity= 0.99 (0.95-1.00) | LOW |
| | | Serious[1] | Not serious | Serious[2] | Serious[3] | Specificity= 0.89 (0.81-0.94) | VERY LOW |

*1 Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the studies were rated at high risk of bias and downgraded by 2 increments if the studies were rated at very high risk of bias.*

*2 Evidence was downgraded by 1 increment if the study was rated as having serious indirectness.*

*3 Imprecision was assessed based on inspection of the confidence intervals. For sensitivity, two clinical decision thresholds were determined at the value above which a test would be recommended (90%), and a second below which a test would be considered of no clinical use (60%). For specificity, two clinical decision thresholds were determined at the value above which a test would be recommended (80%), and a second below which a test would be considered of no clinical use (50%). The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate crossed one threshold and downgraded by 2 increments when the range covered two thresholds.*

## 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 F.

## 1.1.8 Summary of included economic evidence

There was no economic evidence found.

## 1.1.9 Economic model

This area was given medium priority for new cost-effectiveness analysis.

## 1.1.10 Unit costs

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

| 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 committee considered the diagnostic measures of sensitivity and specificity of the index tests for diagnosing dysplasia and early cancer. The sensitivity of tests was deemed the most important measure in this review because the committee agreed the most important outcome is to diagnose dysplasia which is associated with significant risk of progression to cancer. Thus, sensitivity was prioritised for decision making. Clinical decision thresholds were set by the committee as sensitivity/specificity =0.9 and 0.8 above which a test would be recommended and 0.6 and 0.5 below which a test is of no clinical use. The committee agreed that the default values of 0.9 and 0.8 that are widely used for decision making across clinical guidelines were also applicable to people with Barrett's oesophagus and that these were high enough to ensure almost all cases of dysplasia are detected and that the majority of non-cases are correctly identified as such.

### 1.1.12.2 The quality of the evidence

<u>Chromoendoscopy</u>

12 studies were included for the diagnostic accuracy of chromoendoscopy. 3 studies (1 RCT and 2 observational prospective studies) were for confocal laser endomicroscopy including outcomes of high-grade neoplasia/dysplasia and carcinoma, intramucosal or oesophageal cancer. One of these studies also examined the diagnostic accuracy of high-resolution white-light endoscopy (with biopsy as the reference standard) separately. One multi-centre RCT

looked at the diagnostic accuracy of high-resolution white light endoscopy combined with endoscope-based confocal laser endomicroscopy with targeted biopsies (HDWLE+CLE+TB) to detect neoplasia, reporting on the diagnostic accuracy high-resolution white light endoscopy alone with random biopsies (HDWLE+RB) separately.

Evidence on autofluorescence for detecting intestinal metaplasia with columnar and goblet cells, to detect low or high-grade dysplasia or cancer was available from 1 retrospective study. There was evidence from one RCT on the accuracy of autofluorescence imaging-guided probe-based confocal laser endomicroscopy and molecular biomarkers (3-biomarker panel) (AFI-guided pCLE) to detect dysplasia and high-grade dysplasia with the diagnostic accuracy of high-resolution white-light endoscopy given separately.

Evidence on methylene blue staining was available from 3 studies (1 retrospective, 1 prospective and 1 cross-over RCT), and related to the detection of dysplasia or carcinoma, oesophageal cancer or intestinal metaplasia with columnar and goblet cells.

Evidence on narrow-band imaging was available from 4 studies (2 prospective, 1 RCT, 1 cross-over RCT) and related to the detection of high-grade dysplasia and oesophageal cancer or intramucosal cancer, low grade dysplasia or indefinite for dysplasia findings.

There was evidence from one cross-over RCT on endoscopic tri-modal imaging (incorporating high-resolution endoscopy, autofluorescence and narrow-band imaging) for the detection of high-grade dysplasia and early carcinoma with standard video endoscopy used as the reference standard and one cross-over RCT on acetic acid-targeted biopsies for detecting low-or high-grade dysplasia or cancer.

Evidence for sensitivity and specificity for different chromoendoscopy techniques was mostly of low and very low quality. Moderate quality evidence was available for specificity of probe-based confocal laser endomicroscopy in one study, both sensitivity and specificity of narrow-band imaging in one study, and sensitivity of acetic acid-targeted biopsies from one study. High quality evidence from one study was available for both sensitivity and specificity of narrow-band imaging, endoscopic-trimodal imaging, and specificity of acetic acid-targeted biopsies. Evidence was mostly downgraded for indirectness (that was due to the reference standard being histology or biopsy, with results for the protocol reference standard: white-light imaging given separately, or the reference standard being ‘standard endoscopy’ the quality of which was not specified or due to the population including people with oesophagitis in one study and diagnostic accuracy in one study not being limited to detection of dysplasia but results also including metaplasia) and imprecision in the effect measures. Evidence was occasionally downgraded for risk of bias (that was due to lack of blinding in the interpretation of each test or lack of details over the interpretation of the index test and reference standard results). Overall, evidence for chromoendoscopy techniques was derived from studies including 35 to192 participants with results of 2 studies based on 874 to1190 locations, with standard endoscopy or biopsy from the white light imaging reported as the reference standard.

Endoscopic brushing

Clinical evidence for the diagnostic accuracy of endoscopic brushing to detect Barrett’s metaplasia, indefinite for dysplasia, dysplasia and inadequate (no Barrett’s oesophagus) findings was available from one prospective study. The evidence was of low quality for sensitivity and very low quality for specificity and was downgraded due to risk of bias and indirectness, with specificity also downgraded for imprecision in the effect measure. The study included 151 people with forceps biopsy used as the reference standard.

Artificial intelligence

Clinical evidence for the diagnostic accuracy of artificial intelligence (AI) was available from 2 retrospective studies. One study looked at the diagnostic accuracy of convolutional neural networks to detect T1a or T1b neoplasia and the other study looked at Narrow-band imaging + AI and white-light imaging +AI to detect high-grade dysplasia, both using histology as the reference standard. The quality of the evidence for sensitivity and specificity ranged from very low to low for narrow-band imaging and white-light imaging combined with AI but was moderate for convolutional neural networks. Evidence was downgraded mostly for indirectness *(due to AI combined with another technique for analysis of previously captured images, histology being the reference standard and results from white light endoscopy and narrow-band imaging given separately in one study and AI not being used immediately during endoscopy and the other study)* and occasionally for risk of bias and imprecision based on the width of the confidence intervals around the effect estimate. The two studies included 100 and 116 people with results of the former study corresponding to 458 images obtained from those people.

#### 1.1.12.3 Benefits and harms

Chromoendoscopy

The majority of the evidence for the diagnostic accuracy of different chromoendoscopy techniques suggested that both sensitivity and specificity did not meet the clinical threshold of 0.9 for sensitivity and 0.8 for specificity, that the committee had set above which a test would be recommended. Specificity evidence for probe-based confocal laser endomicroscopy did meet or exceeded the clinical threshold, but the committee noted that this was not the case for sensitivity which was prioritised for decision making. Sensitivity and Specificity of high-resolution white light endoscopy combined with confocal laser endomicroscopy with targeted biopsies to detect Barrett's oesophagus neoplasia exceeded clinical thresholds, but the committee noted this was supported by one study and the evidence was of low quality. The committee also noted the limited availability of this equipment within endoscopy services and the need for longer procedural time, compared to standard endoscopy. It was also noted that where sensitivity and specificity of narrow-band imaging exceeded the clinical thresholds set for decision making, results were based on only one true positive case and the measure was imprecise. This was also the case for acetic acid-targeted biopsies where diagnostic accuracy results were based on two true positive and 172 negative cases resulting in imprecise estimates.

Sensitivity and specificity of chromoendoscopy with methylene blue staining for detecting Barrett's oesophagus with oesophageal cancer in one study, also exceeded the clinical thresholds set by the committee. However, the committee noted evidence for sensitivity was of very low quality and was not supported by sensitivity or specificity evidence for methylene blue staining available from two other studies. The committee noted the diagnostic accuracy of methylene blue staining met clinical thresholds in relation to detecting oesophageal cancer whereas a lower sensitivity and specificity was shown in detecting dysplasia. The committee agreed this was in line with their clinical experience and emphasised that high and low-grade dysplasia are more difficult to detect compared to cancer, with dysplasia being flat which makes them easier to miss while cancer is often nodular. Hence image-enhanced techniques are required to detect lesions that may be missed by standard endoscopy.

Endoscopic brushing

Evidence for the diagnostic accuracy of endoscopic brushing showed sensitivity and specificity did not meet the clinical thresholds for decision making. The committee noted the evidence came from a single prospective study and was of low quality.

Artificial Intelligence

Evidence for the diagnostic accuracy of artificial intelligence (AI) showed high sensitivity and specificity for both narrow-band imaging combined with AI, and white-light imaging combined with AI, with both exceeding clinical thresholds of 0.9 and 0.8 respectively for detecting high grade dysplasia. The committee noted that sensitivity of white-light imaging when combined with AI was higher than that of the narrow-band imaging combined with AI (0.99 and 0.92 respectively) with the effect estimate for narrow-band imaging +AI being imprecise. The committee also noted that AI is currently not fully developed in the field of Barrett's oesophagus as the algorithms have not been fully developed and are not available for wider use.

Overall

Overall, the committee agreed the current evidence was limited both in terms of quality with the majority of the evidence graded very low to low, and in quantity with a limited number of small studies available for each surveillance technique, the characteristics of which did not allow for a meta-analysis of findings. They acknowledged that on the basis of the evidence available, it was not possible to make a recommendation for any of the newer technologies such as AI, pCLE (which is currently not used outside a research context) and volumetric laser endomicroscopy or endoscopic brushing (both used in the USA but the UK) and further research is needed. Therefore, the committee made a research recommendation to assess the utility of image enhanced endoscopy in surveillance of Barrett's oesophagus, including narrow band imaging, acetic acid and artificial intelligence.

No evidence was identified for trans-nasal endoscopy. The committee agreed, based on their clinical experience that trans-nasal endoscopy is unlikely to be better than standard endoscopy, given the lower quality of white light imaging and smaller size of biopsy forceps compared to conventional trans-oral endoscopy. They agreed not to make a recommendation for future research on trans-nasal endoscopy.

The committee decided to make a recommendation for surveillance of Barrett's oesophagus using white light endoscopy with Seattle protocol biopsies based on their clinical experience and in recognition that this reflects the current standard of care for endoscopic surveillance for Barrett's oesophagus. Seattle protocol biopsies entail 4 biopsies in different oesophageal quadrants taken every 2 centimetres within the Barrett's oesophagus. Random biopsies are advised as dysplasia is often invisible on white light endoscopy.

See also evidence review 2.1 endoscopic surveillance with white light endoscopy.

### 1.1.12.4 Cost effectiveness and resource use

There were no published economic evaluations found. In the absence of suitable clinical evidence, cost-effectiveness modelling was not feasible since a model will require good evidence of clinical effectiveness.

Standard white light endoscopy for surveillance of Barrett's oesophagus is commonly available in the NHS. The committee's decision to continue to recommend its use is unlikely to have an impact on resource use and ensures that patients continue to receive current standard of care. However, it should be noted that uptake of endoscopic surveillance in the NHS is currently sub-optimal and any changes in practice may result in subsequent changes in resource use.

The committee also made a research recommendation to assess the utility of image enhanced endoscopy for surveillance. If such techniques were to be recommended in future, it would be expected to cause a significant increase in resource use because of up-front staff training, an increase in costs associated with the new technologies and an increase in staff time for some procedures such as chromoendoscopy. However, the additional costs may be offset if there were evidence of increased diagnostic accuracy with the new technologies and a reduced need for biopsies.

### 1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.3.1 – 1.3.4 and the research recommendation on endoscopic surveillance techniques.

### 1.1.14 References

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# Appendices

## Appendix A – Review protocols

**Review protocol for diagnostic accuracy of endoscopic surveillance**

| ID | Field | Content |
|---|---|---|
| 0. | PROSPERO registration number | CRD42021267466 |
| 1. | Review title | The diagnostic accuracy of different endoscopic surveillance techniques including high resolution endoscopy and chromoendoscopy |
| 2. | Review question | What is the diagnostic accuracy of different endoscopic surveillance techniques including high resolution endoscopy and chromoendoscopy? |
| 3. | Objective | To determine the accuracy of different endoscopic surveillance techniques in people with Barrett's oesophagus. |
| 4. | Searches | The following databases (from inception) will be searched:<br>Cochrane Central Register of Controlled Trials (CENTRAL)<br>Cochrane Database of Systematic Reviews (CDSR)<br>Embase<br>MEDLINE<br>Epistemonikos<br><br>Searches will be restricted by:<br>English language only<br>Human studies |

| | | |
|---|---|---|
| | | The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant.<br><br>The full search strategies f will be published in the final review.<br><br>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:<br>Adults, 18 years and over, with Barrett's Oesophagus (with or without dysplasia)<br>Exclusion:<br>Adults with Barrett's Oesophagus that does not fit within the definition<br>Strata:<br>Type of endoscopic surveillance (transnasal, chromoendoscopy, endscopic brushing, AI) |
| 7. | Test | • Trans-nasal endoscopy<br>• Chromoendoscopy (e.g. narrow band imaging, blue laser imaging, confocal endomicroscopy, volumetric laser endomicroscopy, acetic acid)<br>• Endoscopic brushing (wide area transepithelial sampling wats3D)<br>• Artificial Intelligence |
| 8. | Reference standard | • High resolution white light endoscopy (with Seattle protocol biopsies) |
| 9. | Types of study to be included | Observational studies:<br>• Cross-sectional studies |

| | | |
|---|---|---|
| | | • Prospective / Retrospective diagnostic studies<br>• Systematic Reviews of observational studies<br>• Any study containing a diagnostic accuracy data or analysis |
| 10. | Other exclusion criteria | Studies that do not report sensitivity and specificity, or insufficient data to derive these values.<br>Non-English language studies.<br>Before and after studies<br>Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available. |
| 11. | Context | Different techniques of endoscopic surveillance are currently used within clinical practice. It is not known how accurate those techniques are in comparison to what is held as the gold standard or reference for endoscopic surveillance (High resolution white light endoscopy) |
| 12. | Primary outcomes (critical outcomes) | All outcomes are considered equally important for decision making and therefore have all been rated as critical:<br>Detection of progression of dysplasia<br>• Sensitivity<br>• Specificity<br>• Data to calculate 2x2 tables to calculate sensitivity and specificity (number of true positives, true negatives, false positives and false negatives).<br>Time points: beyond 1 year of follow up (minimum) up to longest follow up period |

| | | |
|---|---|---|
| 13. | Data extraction (selection and coding) | All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated.<br><br>This review will make use of the priority screening functionality within the EPPI-reviewer software.<br><br>10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.<br><br>The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above.<br>A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).<br><br>10% of all evidence reviews are quality assured by a senior research fellow. This includes checking:<br>• papers were included /excluded appropriately<br>• a sample of the data extractions<br>• correct methods are used to synthesise data<br>• a sample of the risk of bias assessments<br>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. |
| 14. | Risk of bias (quality) assessment | Risk of bias quality assessment will be assessed using QUADAS-2 checklist |

| | | | |
|---|---|---|---|
| 15. | Strategy for data synthesis | Where possible data will be meta-analysed where appropriate (if at least 3 studies reporting data at the same diagnostic threshold) in WinBUGS.<br><br>Summary diagnostic outcomes will be reported from the meta-analyses with their 95% confidence intervals in adapted GRADE tables. Heterogeneity will be assessed by visual inspection of the sensitivity and specificity plots and summary area under the curve (AUC) plots. Particular attention will be placed on sensitivity, determined by the committee to be the primary outcome for decision making.<br><br>If meta-analysis is not possible, data will be presented as individual values in adapted GRADE profile tables and plots of un-pooled sensitivity and specificity from RevMan software. | |
| 16. | Analysis of sub-groups | Stratification:<br><br>Subgroups that will be investigated if heterogeneity is present: Histopathological diagnosis (Non-dysplastic Barrett's oesophagus, Barrett's oesophagus with indefinite dysplasia, Barrett's oesophagus with low-grade dysplasia, Barrett's oesophagus with high-grade dysplasia,Stage 1 oesophageal adenocarcinoma)<br>Quality of white light endoscopy<br>Enriched vs non-enriched population | |
| 17. | Type and method of review | ☐ | Intervention |
| | | ☒ | Diagnostic |
| | | ☐ | Prognostic |
| | | ☐ | Qualitative |
| | | ☐ | Epidemiologic |
| | | ☐ | Service Delivery |
| | | ☐ | Other (please specify) |

| | | | | |
|---|---|---|---|---|
| | | | | |
| 18. | Language | English | | |
| 19. | Country | England | | |
| 20. | Anticipated or actual start date | | | |
| 21. | Anticipated completion date | | | |
| 22. | 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 | ☐ | ☐ |
| 23. | Named contact | 5a. Named contact<br>National Guideline Centre<br><br>5b Named contact e-mail<br>[Guideline email]@nice.org.uk<br><br>5e Organisational affiliation of the review<br>National Institute for Health and Care Excellence (NICE) and National Guideline Centre | | |

| | | |
|---|---|---|
| 24. | Review team members | From the National Guideline Centre:<br>Amy Crisp<br>Gill Ritchie<br>Lina Gulhane<br>Muksitar Rahman<br>Stephen Deed<br>Vimal Bedia |
| 25. | Funding sources/sponsor | This systematic review is being completed by the National Guideline Centre which receives funding from NICE. |
| 26. | 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. |
| 27. | 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]. |
| 28. | Other registration details | |
| 29. | Reference/URL for published protocol | |

| | | | |
|---|---|---|---|
| 30. | Dissemination plans | NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:<br>• notifying registered stakeholders of publication<br>• publicising the guideline through NICE's newsletter and alerts<br>• 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. | |
| 31. | Keywords | Barrett's Oesophagus | |
| 32. | Details of existing review of same topic by same authors | | |
| 33. | Current review status | ☒ | Ongoing |
| | | ☐ | Completed but not published |
| | | ☐ | Completed and published |
| | | ☐ | Completed, published and being updated |
| | | ☐ | Discontinued |
| 34. | Additional information | | |
| 35. | Details of final publication | www.nice.org.uk | |

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2

## 1 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.<br>• 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).<br>• 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.)<br>• Unpublished reports will not be considered unless submitted as part of a call for evidence.<br>• 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.<br>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.<br>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). [10]<br><br>**Inclusion and exclusion criteria**<br>• 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.<br>• 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.<br>• 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.[10]

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 6: Database parameters, filters and limits applied**

| Database | Dates searched | Search filter used |
|---|---|---|
| Medline (OVID) | 1946 – 26 April 2022 | Randomised controlled trials<br>Systematic review studies<br>Observational studies<br>Diagnostic studies<br><br>Exclusions (animal studies, letters, comments, editorials, case studies/reports)<br><br>English language |
| Embase (OVID) | 1974 – 26 April 2022 | Randomised controlled trials<br>Systematic review studies<br>Observational studies<br>Diagnostic studies<br><br>Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts)<br><br>English language |
| The Cochrane Library (Wiley) | Cochrane Database of Systematic Reviews to Issue 4 of 12, April 2022<br><br>Cochrane Central Register of Controlled Trials to Issue 4 of 12, April 2022 | |
| Epistemonikos (The Epistemonikos Foundation) | Inception to 26 April 2022 | Systematic review<br><br>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. | exp "sensitivity and specificity"/ |
| 77. | (sensitivity or specificity).ti,ab. |
| 78. | ((pre test or pretest or post test) adj probability).ti,ab. |
| 79. | (predictive value* or PPV or NPV).ti,ab. |
| 80. | likelihood ratio*.ti,ab. |

| | |
|---|---|
| 81. | likelihood function/ |
| 82. | ((area under adj4 curve) or AUC).ti,ab. |
| 83. | (receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab. |
| 84. | gold standard.ab. |
| 85. | exp Diagnostic errors/ |
| 86. | (false positiv* or false negativ*).ti,ab. |
| 87. | Diagnosis, Differential/ |
| 88. | (diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness or precision or validat* or validity or differential or error*)).ti,ab. |
| 89. | or/76-88 |
| 90. | Epidemiologic studies/ |
| 91. | Observational study/ |
| 92. | exp Cohort studies/ |
| 93. | (cohort adj (study or studies or analys* or data)).ti,ab. |
| 94. | ((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab. |
| 95. | ((longitudinal or retrospective or prospective) and (study or studies or review or analys* or cohort* or data)).ti,ab. |
| 96. | Controlled Before-After Studies/ |
| 97. | Historically Controlled Study/ |
| 98. | Interrupted Time Series Analysis/ |
| 99. | (before adj2 after adj2 (study or studies or data)).ti,ab. |
| 100. | exp case control study/ |
| 101. | case control*.ti,ab. |
| 102. | Cross-sectional studies/ |
| 103. | (cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab. |
| 104. | or/90-103 |
| 105. | 56 and (64 or 75 or 89 or 104) |

**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. | exp "sensitivity and specificity"/ |
| 85. | (sensitivity or specificity).ti,ab. |
| 86. | ((pre test or pretest or post test) adj probability).ti,ab. |
| 87. | (predictive value* or PPV or NPV).ti,ab. |
| 88. | likelihood ratio*.ti,ab. |
| 89. | ((area under adj4 curve) or AUC).ti,ab. |
| 90. | (receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab. |
| 91. | diagnostic accuracy/ |
| 92. | diagnostic test accuracy study/ |
| 93. | gold standard.ab. |
| 94. | exp diagnostic error/ |
| 95. | (false positiv* or false negativ*).ti,ab. |
| 96. | differential diagnosis/ |
| 97. | (diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness or precision or validat* or validity or differential or error*)).ti,ab. |

| | |
|---|---|
| 98. | or/84-97 |
| 99. | Clinical study/ |
| 100. | Observational study/ |
| 101. | Family study/ |
| 102. | Longitudinal study/ |
| 103. | Retrospective study/ |
| 104. | Prospective study/ |
| 105. | Cohort analysis/ |
| 106. | Follow-up/ |
| 107. | cohort*.ti,ab. |
| 108. | 106 and 107 |
| 109. | (cohort adj (study or studies or analys* or data)).ti,ab. |
| 110. | ((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab. |
| 111. | ((longitudinal or retrospective or prospective) and (study or studies or review or analys* or cohort* or data)).ti,ab. |
| 112. | (before adj2 after adj2 (study or studies or data)).ti,ab. |
| 113. | exp case control study/ |
| 114. | case control*.ti,ab. |
| 115. | cross-sectional study/ |
| 116. | (cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab. |
| 117. | or/99-105,108-116 |
| 118. | 62 and (72 or 83 or 98 or 117) |

**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.1 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 7: Database parameters, filters and limits applied**

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

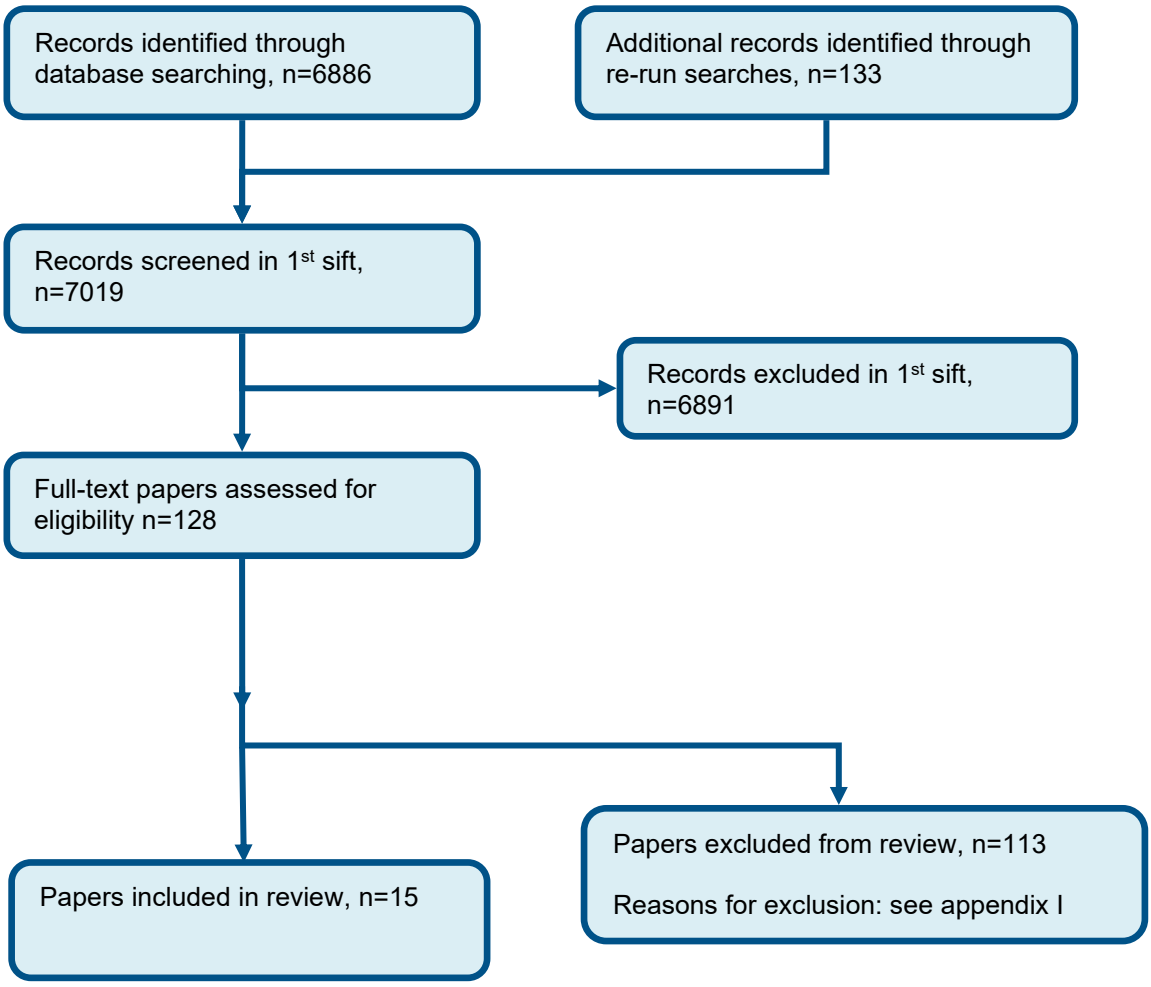
| | |
|---|---|
| #14. | #5 OR #13 |
| #15. | MeSH DESCRIPTOR Esophageal Neoplasms EXPLODE ALL TREES |
| #16. | #14 OR #15 |

**INAHTA search terms**

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

# Appendix C –Diagnostic evidence study selection

**Figure 1: Flow chart of clinical study selection for the review of diagnostic accuracy of different endoscopic surveillance techniques including**



# Appendix D –Diagnostic evidence

| | | |
|---|---|---|
| **Reference** | **Anandasabapathy 2011** [1] | |
| **Study type** | Prospective study | |
| **Study methodology** | Data source & Recruitment: subjects over the age of 18 scheduled for endoscopic surveillance for BE were recruited in four academic medical centers: The Mount Sinai Medical Center, The MD Anderson Cancer Center, The Hines-Illinois VA Medical Center, and Baylor College of Medicine-Houston VA Medical Center during the period 2004 – 2008. | |
| **Number of patients** | n = 151 | |
| **Patient characteristics** | Age, mean (range): 65 (46 – 87)<br><br>Gender (male to female ratio): 124 / 27<br><br>Ethnicity: White (n=126); African American (n=1); Hispanic (n=10); other (n=14)<br><br>Setting: The Mount Sinai Medical Center, New York<br><br>Country: USA<br><br>Inclusion criteria: Selectively enrolled subjects with a known prior history (recent or remote) of BE with dysplasia/neoplasia (indefinite for-dysplasia [IND], low-grade [LGD], high-grade dysplasia [HGD] or intramucosal adenocarcinoma [IMCA]) and no grossly evident lesion.<br><br>Exclusion criteria: Patients with a visible lesion requiring targeted biopsy prior to brushing were excluded. | |
| | Prior pathologic grade of Barrett's | |
| | IND | 14 |
| | LGD | 114 |
| | HGD | 21 |
| | IMCA | 2 |
| | Barrett's segment length (mean) | 4.6 (range 0–14 cm) |
| **Target condition(s)** | Barrett's Oesophagus: Barrett's metaplasia (IM), indefinite for dysplasia (IND), dysplasia (LGD/ HGD/CA), and inadequate (no BE) | |
| **Index test(s) and reference standard** | Index test: brush biopsy<br>Investigators were provided with a video demonstration and written instructions on how to perform the brush biopsy. The brush biopsies (mean of two per patient) were performed prior to the forceps biopsies (mean 12 per patient) in order to avoid obscuring the visual field | |

<table>
<tr><td>Reference</td><td colspan="4">Anandasabapathy 2011 [1]</td></tr>
<tr><td></td><td colspan="4">and artifact from excessive bleeding caused by the forceps. The brush, in its enclosed sheath, was passed through the working channel of the endoscope and placed against the surface of the mucosa. Sampling of any visualized columnar mucosa was performed by maintaining pressure against the mucosa and rotating the brush circumferentially along the epithelial surface. Pinkish-red tissue or pinpoint bleeding at the brush-biopsy site was evidence of proper technique. Up to 4 cm of the columnar-lined mucosa was sampled with a single brush. The cellular material collected on the brush was then transferred to a bar-coded glass slide and immersed in fixative. The procedure was then repeated using a second, new brush and the bristle portion of the brush clipped off into the vial of alcohol. After approximately 15 min, the dry slides were placed in a plastic slide container and together with the vial and bar-coded requisition form, sent in the preaddressed mailing container.<br><br><u>Reference standard: forceps biopsy</u><br><br>Following the two brush biopsies, standard four-quadrant forceps biopsies of the oesophagus were obtained at 1–2 cm intervals, based upon the prior pathologic grade.<br><br>Time between measurement of index test and reference standard: no time difference.</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td></td><td>Index test +</td><td>97</td><td>16</td><td>113</td></tr>
<tr><td></td><td>Index test −</td><td>23</td><td>15</td><td>38</td></tr>
<tr><td></td><td>Total</td><td>120</td><td>31</td><td>151</td></tr>
<tr><td>Statistical measures</td><td colspan="4"><u>Index text: brush biopsy</u><br>Sensitivity: 0.81 (0.73-0.87)<br>Specificity: 0.48 (0.30-0.67)</td></tr>
<tr><td>Source of funding</td><td colspan="4">Grant support for this study was provided by CDx Laboratories.<br>Sharmila Anandasabapathy, M.D. is supported in part by the National Institute of Health grant RO1CA140257. David Graham, M.D. is supported in part by the Office of Research and Development Medical Research Service Department of Veterans Affairs, by Public Health Service grant DK56338 which funds the Texas Medical Center Digestive Diseases Center, and grants DK067366 and CA116845.</td></tr>
<tr><td>Limitations</td><td colspan="4">Risk of bias: serious risk of bias<br>Indirectness: serious indirectness due to lack of clarity regarding quality of endoscopy for reference</td></tr>
<tr><td>Comments</td><td colspan="4">Not clear if high resolution white light endoscopy is clear reference standard</td></tr>
</table>

| | |
|---|---|
| **Reference** | **Bajbouj 2010** [2] |
| **Study type** | Prospective study |
| **Study methodology** | Data source & Recruitment: Patients known or suspected BE at three academic medical centers in Munich, Berlin and Dresden between May 2007 and July 2008 |
| **Number of patients** | n = 68 |
| **Patient characteristics** | Age, mean (SD): 60 ± 12 years<br><br>Gender (male to female ratio): 56/12<br><br>Ethnicity: not reported<br><br>Setting: Academic medical centres<br><br>Country: Germany<br><br>Inclusion criteria: 18 – 80 years; Barrett's length at least COM1 according to Prague classification; in the case of suspected intraepithelial neoplastic changes, lesion <1cm; acid-suppressive therapy at least at the standard dose for a minimum of 4 weeks.<br><br>Exclusion criteria: no informed consent; thrombocytopenia below 50x109/L; international normalised ration >1.5; partial thromboplastin time >50 seconds; coronary heart disease; existent valve plasty; potential pregnancy chronic renal failure; allergic diathesis; and chronic congestive pulmonary disease. |
| **Target condition(s)** | Barrett's Oesophagus: high grade intraepithelial neoplasia / carcinoma |
| **Index test(s) and reference standard** | Index test: probe based confocal laser endomicroscopy<br>The pCLE system used was the Cellvizio-GI system (Mauna Kea technologies, Paris, France), which comprises three parts; a laser scanning unit, an acquisition and image analysis software and an imaging probe. The pCLE miniproble (Gastroflex, Mauna Kea Technologies) has a 2.5mm outer diameter and can be passed through the working channel of any standard endoscopy, including diagnostic gastrocscopes. The probe was gently positioned on the mucosa. Following intravenous application of 5 – 10mL of the validated dose of 1% fluorescein, which was used as a contrast agent, pCLE video recordings with a duration of 30 seconds were then obtained immediately proximal to each spot mark. At least two of the five criteria below had to be detected to grade an area as suspicious for the presence of HGIN or carcinoma:<br>• Irregular epithelial lining<br>• Decreased epithelial width of epithelial layer<br>• Fusion of glands |

<table>
<tr><td>Reference</td><td colspan="5">Bajbouj 2010 [2]</td></tr>
<tr><td></td><td colspan="5">• Irregular vascular pattern<br>• Dark cells<br><br><u>Reference standard: Endoscopy</u><br>Endoscopy was performed after an overnight fasting period. All of the endoscopic procedures were performed by one of five endoscopists who had receiving training and gained experience with the pCLE system for at least 3 – 4 before the initiation of the study. Patients underwent careful endoscopic evaluation using state o the art high resolution white light videoendoscopy (GIF-Q160, GIF-H180, Olympus, Hamburg, Germany). Narrow band imaging was not routinely used because the time of the study initiation was not a standard tool.<br><br>A detailed inspection of the Barrett’s segment was undertaken, followed by marking the tentative biopsy sites with argon plasma coagulation (40X) including all four quadrant every 1 – 2 cm based on the recommended surveillance guidelines. All marked random and targeted areas were examined by cPLE and documented, and one biopsy was obtained for histologic evaluation.<br><br>Time between measurement of index test and reference standard: none</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td>2x2 calculated</td></tr>
<tr><td></td><td>Index test +</td><td>7</td><td>3</td><td>10</td><td></td></tr>
<tr><td></td><td>Index test −</td><td>4</td><td>54</td><td>58</td><td></td></tr>
<tr><td></td><td>Total</td><td>11</td><td>57</td><td>68</td><td></td></tr>
<tr><td>Statistical measures</td><td colspan="5"><u>Index text pCLE</u><br>Sensitivity: 0.64 (0.31 – 0.89) per patient based evaluation<br>Specificity: 0.95 (0.85 – 0.99) per patient based evaluation</td></tr>
<tr><td>Source of funding</td><td colspan="5">Not reported</td></tr>
<tr><td>Limitations</td><td colspan="5">Risk of bias: very high risk of bias<br>Indirectness: No indirectness</td></tr>
<tr><td>Comments</td><td colspan="5">The study did assessment of pCLE for diagnosing neoplastic Barrett’s Oesophagus twice “on site” & “blinded.” For the on site diagnosis, the respective endoscopists noted whether the pCLE video sequences acquired from the previously marked sports appeared normal or neoplastic. This was performed on the spot during the ongoing examination without later reviewing stored sequences. For the blinded diagnosis, all sequences were put into a random order and presented to a single examiner with the most extensive experience of pCLE video sequences. The results reported above only show those from the onsite diagnosis.</td></tr>
</table>

| | |
|---|---|
| **Reference** | **Canto 2014** [3] |
| **Study type** | Multicentre randomised controlled trial (prospective) |
| **Study methodology** | Data source: Adults with Barrett's oesophagus patients undergoing routine surveillance or referred for early neoplasia<br><br>Recruitment: Consecutive from February 2010 to December 2011 |
| **Number of patients** | n = 192 |
| **Patient characteristics** | Age, median (range):<br>High-definition white-light endoscopy and random biopsy (HDWLE-RB) group: 62 (26 to 79)<br>High-definition white-light endoscopy followed by confocal laser endomicroscopy and targeted biopsy (HDWLE+CLE-TB) group: 62 (32 to 82)<br><br>Gender (male to female ratio):<br>High-definition white-light endoscopy and random biopsy (HDWLE-RB) group: 73:25<br>High-definition white-light endoscopy followed by confocal laser endomicroscopy and targeted biopsy (HDWLE+CLE-TB) group: 70:24<br><br>Ethnicity: High-definition white-light endoscopy and random biopsy (HDWLE-RB) group: 98% white<br>High-definition white-light endoscopy followed by confocal laser endomicroscopy and targeted biopsy (HDWLE+CLE-TB) group: 89% white<br><br>Setting: Five academic medical centres<br><br>Country: USA<br><br>Inclusion criteria: Adult patients undergoing outpatient endoscopy for either routine surveillance of Barrett's oesophagus (surveillance group) or suspected or biopsy-proven unlocalized Barrett's oesophagus-associated high-grade dysplasia/ and or early intramucosal ECA (neoplasia group) referred for confirmation of diagnosis and/or endoscopic therapy<br><br>Exclusion criteria: patients with Barrett's oesophagus <1cm and >10 cm known ECA, advanced BE lesions 2cm or more in size, Paris classification of 0-1s (protruding sessile), 0-IIa (flat elevated), or 0-IIb (flat), any Paris 0-IIc (superficial shallow depressed or 0-III (excavated) lesions, oesophageal strictures or altered anatomy preventing passage of the endomicroscope, allergy to fluorescein or history of any severe anaphylactic reaction, and active gastrointestinal bleeding, coagulopathy, pregnancy and contraindications to endoscopy due to medical instability. |

| | | | | | |
|---|---|---|---|---|---|
| **Reference** | **Canto 2014** [3] | | | | |
| **Target condition(s)** | Barrett's oesophagus neoplasia | | | | |
| **Index test(s) and reference standard** | Index test: HDWLE+RB<br>After examination with HDWLE, endoscopic diagnoses were recorded in real-time based on the appearance of the BE. The management plan for lesions was made at the discretion of the endoscopist and recorded, including the option to take a biopsy, performing endoscopic mucosal resection (EMR), tattoo the lesion, or perform no intervention. Then biopsies from suspicious lesions were obtained or EMR performed. Four-quadrant mucosa biopsies were obtained every 2 cm from the entire length of the BE for surveillance patients, or every 1 cm in patients with BE and suspected neoplasia (RB protocol)<br><br>Comparison test: HDWLE+CLE+TB<br>Comparison test: HDWLE was performed as above. Immediately after eCLE imaging was performed with the endomicroscope on visible mucosal lesions as well as on four quadrants every 2 cm from the entire BE length and every 1 cm in patients referred for suspected neoplasia. The eCLE diagnoses using the Mainz confocal Barratts classification for all lesions and flat BE what documented for each imaging site in real time. Targeting biopsies (TB) were obtained or EMR performed only if there was eCLE evidence of neoplasia. In order to calculate performance characteristics for sCLE, 30% of eCLE imaging sites of flat BE mucosa were biopsied.<br><br>Reference standard: blinded expert pathological diagnosis<br>Pathology<br>Formalin-fixed mucosal biopsy specimens what processed routinely at each study site and were blindly interpreted by 2 expert gastrointestinal pathologists who graded the severity of neoplasia in each specimen. When there was a discordant reading a third pathologist was consulted and consensus reached.<br><br>Time between measurement of index test and reference standard: not reported | | | | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | 2x2 data not reported |
| | Index test + | | | | |
| | Index test − | | | | |
| | Total | | | | |

| | |
|---|---|
| **Reference** | **Canto 2014** [3] |
| **Statistical measures** | Index text: HDWLE-RB<br>Sensitivity: 40%<br>Specificity: 98%<br><br>Index text: HDWLE+CLE-TB<br>Sensitivity:95%<br>Specificity:92% |
| **Source of funding** | None stated |
| **Limitations** | Risk of bias: none<br>Indirectness: serious indirectness due to, histology being the reference standard and results from white light endoscopy with random biopsies and high-definition white light endoscopy combined with CLE given separately compared to histology. |
| **Comments** | |

| | |
|---|---|
| **Reference** | **Curves 2010** [4] |
| **Study type** | Multi-centre randomised cross-over study |
| **Study methodology** | Data source: 5 centres with a tertiary referral function for the detection and treatment of patients with early Barrett's oesophagus neoplasia<br><br>Recruitment: All patients with Barrett's oesophagus referred to the participating centres for work-up of endoscopically inconspicuous high-grade dysplasia/ early carcinoma (HGD/Ca) were eligible |
| **Number of patients** | n = 111; 87 analysed |
| **Patient characteristics** | Age, mean (SD): 68 (9)<br><br>Gender (male to female ratio): 92/19<br><br>Ethnicity:<br><br>Setting: Academic Medical Centre, Amsterdam, Netherlands; St Antonius Hospital, Niuwegein, Netherlands; Mayo Clinic, Jacksonville, Florida; Mayo Clinic, Rochester, Minnesota; Queens Medical Centre, Nottingham, United Kingdom<br><br>Country: Netherlands, USA, UK |

| | |
|---|---|
| **Reference** | **Curves 2010** [4] |
| | Inclusion criteria: age >18 years; prior diagnosis of Barrett's oesophagus, defined as the presence of columnar-lined epithelium with specialized intestinal metaplasia on histologic investigation; prior diagnosis of HGA/CA with no endoscopically visible abnormalities according to the referring physician; a minimum Barrett's length of C≥2, M≥2, or C.2, M≥4, according to the Prague C&M classification; and written informed consent.<br><br>Exclusion criteria: presence of active erosive esophagitis grade B or worse according to the Los Angeles classification of erosive esophagitis, description of an endoscopically visible suspicious lesion in the Barrett's segment in the referring centre; at first endoscopy: the presence of a type 0-1 or type 0-III lesion or a lesion that according to the discretion of the endoscopist did not allow a delay in intervention for a period of 6 weeks; presence of conditions that precluded safe histologic sampling of the oesophagus (e.g. oesophageal varices, coagulation disorders, anticogulant therapy). |
| **Target condition(s)** | Barrett's oesophagus with high grade dysplasia and early carcinoma |
| **Index test(s) and reference standard** | Index test: ETMI endoscopy system<br>The ETMI system consists of a high-resolution white-light endoscope with optical zoom (magnification 100X; XGIF-Q240/260FZ; Olympus Inc, Tokyo, Japan) equipped with an autofluorescence and narrow-band imaging mode. This endoscope has 2 separate monochromatic charge-couple devices; one for white-light imaging and NBI and one for AFI.<br>All 3 imaging modalities of the ETMI system provide real-time endoscopic images. The endoscopist can switch from one modality to another in 1-2 seconds by pushing control buttons on the handle of the endoscope.<br><br>Reference standard: standard video endoscopy (SVE)<br>SVE was performed (Olympus GIF-140, GIF-160). The oesophagus was inspected and the presence and length and length of the Barrett's segment and/or hiatal hernia were recorded according to the Prague C&M classification.<br><br>Histologic assessment: All biopsy specimens were routinely processed and evaluated in the participating centres. The histologic outcome was recorded according to the revised Vienna classification of gastrointestinal neoplasia in the following categories: nondysplastic BE, Indefinite for dysplasia (ID), low-grade dysplasia (LGD), HGD or Ca.<br><br>Time between measurement of index test and reference standard: 6-12 weeks; procedures were performed consecutively and each person acted as his/her own control. |
| **2×2 table** | |

| | Reference standard + | Reference standard − | Total | Calculated by taking reference standard and index test positives as those that had high grade dysplasia or early carcinoma (HGD/Ca) |
|---|---|---|---|---|
| Index test + | 31 | 15 | 46 | |
| Index test − | 9 | 32 | 41 | |
| Total | 40 | 47 | 87 | |

| | |
|---|---|
| **Reference** | **Curves 2010** [4] |
| **Statistical measures** | Index text: Endoscopic tri-modal imaging<br>Sensitivity: 0.78 (0.62-0.89)<br>Specificity: 0.68 (0.53-0.81) |
| **Source of funding** | Olympus Inc, Tokyo, Japan |
| **Limitations** | Risk of bias: none<br>Indirectness: none |
| **Comments** | |

| | |
|---|---|
| **Reference** | **Ebigbo 2020** [5] |
| **Study type** | Retrospective study |
| **Study methodology** | Data source & Recruitment: Universitatsklinikum Augsburg, Augsburg, Germany |
| **Number of patients** | n = 116 patients (230 images) |
| **Patient characteristics** | Age, mean (SD): not reported<br><br>Gender (male to female ratio): not reported<br><br>Ethnicity: not reported<br><br>Setting: three medical centres<br><br>Country: Germany<br><br>Inclusion criteria: Endoscopic, high resolution, white light images of T1a and T1b Barett's Cancer were collected retrospectively in three tertiary care centres in Germany.<br><br>For AI training and testing, a total of 230 white light images (Olympus GIF-HQ190; Olympus medical systems, Tokyo Japan)) from 116 patents were included. |

<table>
<tr><td>Reference</td><td colspan="5">Ebigbo 2020 [5]</td></tr>
<tr><td></td><td colspan="5">Exclusion criteria: Not reported</td></tr>
<tr><td>Target condition(s)</td><td colspan="5">Barrett’s Oesophagus with T1a or T1b neoplasia</td></tr>
<tr><td>Index test(s) and reference standard</td><td colspan="5"><u>Index test: Convolutional neural networks</u><br>The network architecture used was a 101-layer residual CNN. The convolutional model, pretrained on the non medical imageNet dataset, was mainly used as a feature extractor. Only the fully connected classifier at the end of the network was optimized with the Adam optimizer, a learn rate of 1e-4 with a polynomial leaning policy. For validation, which was as independent from the training as possible, a 5 fold cross validation was performed, but with different folds from those in the training phase.<br><br><u>Reference standard: Histopathology (from white light imaging samples)</u><br>Histopathology served as the reference standard for the characterisation of images. Based on the results of the histopathology, endoscopic images were divided into two categories: 1. Images with cancer infiltration limited to the mucosa (T1a) and 2. Images with cancer infiltration into the submucosa (T1b). Images of lesions with infiltration deeper than the submucosa (>T1b) were excluded from the study. The depth of mucosal or submucosal invasion was not further evaluated.<br><br>Time between measurement of index test and reference standard: Unclear</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td rowspan="4">2x2 data not reported</td></tr>
<tr><td></td><td>Index test +</td><td></td><td></td><td></td></tr>
<tr><td></td><td>Index test −</td><td></td><td></td><td></td></tr>
<tr><td></td><td>Total</td><td></td><td></td><td></td></tr>
<tr><td>Statistical measures</td><td colspan="5"><u>Index text CNN</u><br>Sensitivity: 0.77 (0.75 – 0.78)<br>Specificity: 0.64 (0.62 – 0.66)</td></tr>
<tr><td>Source of funding</td><td colspan="5">Bavarian Academic Forum (BayWISS)</td></tr>
<tr><td>Limitations</td><td colspan="5">Risk of bias: no serious risk of bias<br>Indirectness: serious indirectness as not using AI immediately during endoscopy</td></tr>
</table>

| | |
|---|---|
| **Reference** | **Ebigbo 2020** [5] |
| **Comments** | |

| | |
|---|---|
| **Reference** | **Egger 2003** [6] |
| **Study type** | Retrospective study |
| **Study methodology** | Data source & Recruitment: Department of Internal Medicine II, Technical University of Munich |
| **Number of patients** | n = 35; 345 biopsies |
| **Patient characteristics** | Age, mean (range): 64.8 years; range 29–78<br><br>Gender (male to female ratio):<br><br>Ethnicity: not reported<br><br>Setting: Barret's Surveillance, Technical University of Munich<br><br>Country: Germany<br><br>Inclusion criteria:<br>Routine surveillance of patients with known BO without (n=18) or with (n=8) only low grade dysplasia (LGD); Focused surveillance to help reach a treatment decision in patients with BO and high grade dysplasia (HGD) (n=1); Patients with a diagnosis of cancer, for treatment planning—for example, mucosectomy versus photodynamic therapy versus surgery (n=8); Patients with a new diagnosis of BO undergoing surveillance for the first time (n=18).<br><br>Exclusion criteria: not reported |
| **Target condition(s)** | Barrett's Oesophagus with intestinal metaplasia with columnar and goblet cells vs low or high grade dysplasia, cancer |
| **Index test(s) and reference standard** | Index test: Autofluorescence<br><br>The first examination conducted in all patients was tissue AF, with the Xillix/Olympus laser induced fluorescence endoscopy in the gastrointestinal tract (LIFE-GI) system, using a fibreglass endoscope. This technique is based on the principle that endogenous fluorophores (such as flavines, collagen, NADH, and porphyrins) are excited by monochromatic blue laser light at a wavelength of 437 nm. Depending on the characteristics of the tissue, light is reflected as green light (normal tissue) or dark red light (dysplastic areas), |

<table>
<tr><td>Reference</td><td colspan="5">Egger 2003 [6]</td></tr>
<tr><td></td><td colspan="5">corresponding to a higher loss of energy in the reflected light.20 These spectra are detected using a red-green camera on the fibreglass endoscope and are converted by a dedicated software program into a visible real time image. Each lesion positive on AF was carefully documented concerning distance (in cm) from the incisors and position at the circumference to locate it for later biopsy.<br><br><u>Index test: Methylene Blue Staining</u><br>After standard endoscopic examination, about two minutes after washing and spraying with 10% N-acetylcysteine to remove residual mucus, MB 0.5% was applied circumferentially over the entire length of the Barrett’s segment using a special spray catheter (Olympus PW-5L). After a further two minutes, rinsing with various volumes of water (100–200 ml) followed. Inhomogeneously stained areas or areas with weak staining were recorded as positive.<br><br><u>Reference standard: endoscopic examination</u><br>After the AF examination, a standard endoscopic examination was carried out using a high resolution standard video endoscope (Olympus GIF-140). Any macroscopically suspicious areas (ulcers, depressed and elevated lesions, irregular areas, areas of distinct colour change) were again documented carefully with regard to their longitudinal and circumferential location.<br><br>Note that histopathology from the endoscopic examination is given as the reference standard.<br><br>Finally, biopsies were taken only at the end of the endoscopic evaluations: firstly, from any areas regarded as suspicious using high resolution VE and, in addition, from areas positive on any of the two imaging tests (MB and AF), even if these areas were completely normal on VE; the precise location of AF and MB positive areas was documented previously. Secondly, in addition, 4QB at 12, 3, 6, and 9 o’clock were taken every 2 cm from the rest of BO which was normal on VE and negative on MB and AF; if a suspicious area (that is, positive on VE, AF, or MB) was located at one of the 4QB areas (that is, precisely at the same distance from the incisors and at either 12, 3 , 6, or 9 o’clock), no additional biopsy was taken from the same quadrant.<br><br>Time between measurement of index test and reference standard: consecutive examinations</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td rowspan="4">Final diagnoses:<br><br>Normal Barrett’s oesophagus without dysplasia: n=18; carcinoma: n=8; high grade dysplasia n=1, low grade dysplasia n=8.<br><br>Only true positive results given and 2x2 data cannot be calculated.</td></tr>
<tr><td>Index test +</td><td></td><td></td><td></td></tr>
<tr><td>Index test −</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td></td><td></td><td></td></tr>
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|---|---|
| **Reference** | **Egger 2003** [6] |
| **Statistical measures** | Index text AF<br>***Biopsy:***<br>Sensitivity – 21%<br>Specificity – 91%<br>***Per patient***<br>Sensitivity – 59%<br>Specificity – 78%<br><br>Index text MB<br>***Biopsy:***<br>Sensitivity – 37%<br>Specificity – 91%<br>***Per patient***<br>Sensitivity – 71%<br>Specificity – 50% |
| **Source of funding** | Not reported |
| **Limitations** | Risk of bias: serious risk of bias<br>Indirectness: Serious; sensitivity and specificity not given separately for dysplasia but include Barret's metaplasia |
| **Comments** | It was initially planned that the study would include 50 patients, with an interim analysis after 35 patients. These numbers were chosen as it was expected that a minimum of 10 biopsies had to be taken from each patient to ensure reliable statistical results (with this number of patients 350 biopsies were investigated). Due to the poor results it was therefore decided to discontinue the study after the interim analysis. |

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| **Reference** | **Hashimoto 2020** [7] |
| **Study type** | Retrospective study |
| **Study methodology** | Data source & Recruitment: University of California Irvine Histology Database (Jan 2016 – Nov 2018) |
| **Number of patients** | n = 100 patients (458 images) |
| **Patient characteristics** | Age, mean (SD): Not reported<br><br>Gender (male to female ratio): Not reported |

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| **Reference** | **Hashimoto 2020** [7] | | | | |
| | Ethnicity: Not reported<br><br>Setting: University of California, medical centre<br><br>Country: USA<br><br>Inclusion criteria: Histologically proven dysplasia (high grade dysplasia and T1 adenocarcinoma) in Barrett's (n=70) and 916 control images (n=30) with proven Barrett's Oesophagus without dysplasia<br><br>Exclusion criteria: Low grade dysplasia | | | | |
| **Target condition(s)** | Barrett's Oesophagus with high grade dysplasia | | | | |
| **Index test(s) and reference standard** | Index test<br>Narrow-band imaging + AI<br><br>Reference standard<br>White light imaging (Olympus 190 series upper endoscope – 190 HQ and 190 H; Olympus, Centre valley, USA) + AI<br><br>A retrospective review of all endoscopic images of patients with early oesophageal neoplasia in BE proven by histology were found from an electronic database. Images were captured via white light imaging, narrow-band imaging and standard focus or near focus. 916 images from 70 patients were retrospectively collected of histologically proven dysplasia (HGD or T1 adenocarcinoma) and 916 control images from 30 patients were collected of proven dysplasia. A CNN was set up to assess the endoscopic detection of early oesophageal neoplasia for Barrett's using a deep learning process.<br><br>Convolutional neural network:<br>The CNN was developed and designed for two primary functions: feature extraction and classification. The base module is responsible for the automated feature extraction and borrowed from the Inception-ResNet-V2 algorithm developed by Google A. The head module of the algorithm is designed for transforming extracted features from base layers into a graded scale that allows for pathologic classification. The first step was for CNN binary classification assessing the presence of any neoplastic lesion and or area on the image. If the binary classification classified the image as containing neoplasia, the second step was object detection (localization of the lesion).<br><br>Time between measurement of index test and reference standard: not reported | | | | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | 2x2 calculated from data reported in the study |
| | Index test + | 73 | 1 | 74 | |

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|---|---|---|---|---|---|
| **Reference** | **Hashimoto 2020** [7] | | | | |
| | Index test − | 6 | 125 | 131 | Test: AI diagnosis by narrow-band imaging |
| | Total | 79 | 126 | 205 | |
| **2x2 table** | | Reference standard + | Reference standard − | Total | 2x2 calculated from data reported in the study<br><br>Test: AI diagnosis by white light imaging |
| | Index test + | 144 | 12 | 156 | |
| | Index test − | 2 | 95 | 97 | |
| | Total | 146 | 107 | 253 | |
| **Statistical measures** | Index test: AI diagnosis by narrow-band imaging<br>***Per image***<br>Sensitivity –0.92 (0.84-0.97)<br>Specificity – 0.99 (0.96, 1.00)<br><br>Reference test: AI diagnosis by white light imaging<br>***Per image***<br>Sensitivity – 0.99 (0.95-1.00)<br>Specificity – 0.89 (0.81-0.94) | | | | |
| **Source of funding** | Not reported | | | | |
| **Limitations** | Risk of bias: serious risk of bias<br>Indirectness: serious indirectness due to AI combined with another technique for analysis of previously captured images, histology being the reference standard and results from white light endoscopy and narrow-band imaging given separately | | | | |
| **Comments** | | | | | |

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| **Reference** | **Longcroft-Wheaton** [9] |
| **Study type** | Pilot multi-centre randomised cross-over trial |
| **Study methodology** | Data source: six UK centres representing the diversity of institutions involved in Barrett's surveillance (ranging from small district hospitals to university hospitals)<br><br>Recruitment: Participants with Barrett's oesophagus meeting the inclusion criteria |
| **Number of patients** | n = 174 (analysed in paired analysis) |
| **Patient characteristics** | Age, mean (SD): 66 (11.1) |

<table>
<tr><td>Reference</td><td colspan="5">Longcroft-Wheaton [9]</td></tr>
<tr><td></td><td colspan="5">Gender (male to female ratio): 126/48<br><br>Ethnicity: not specified<br><br>Setting: six UK Barrett’s surveillance centres ranging from small district hospitals to university hospitals<br><br>Country: UK<br><br>Inclusion criteria: at least C0M2 (i.e. Barrett’s mucosa length of at least 2 cm) biopsy-proven Barrett’s oesophagus, no history or prior dysplasia or cancer, positive for intestinal metaplasia if the Barrett’s classification was less than C0M3</td></tr>
<tr><td>Target condition(s)</td><td colspan="5">Neoplasia (high grade dysplasia, low grade dysplasia, cancer)</td></tr>
<tr><td>Index test(s) and reference standard</td><td colspan="5">Index test: Acetic acid-assisted gastroscopy (targeted biopsies)<br>The Barrett’s segment was inspected using standard white-light endoscopy and visible abnormalities were noted. Acetic acid 2.5% was sprayed onto the Barrett’s mucosa under direct visual guidance using a spray catheter. The endoscopist only biopsies areas that appeared abnormal, as identified using the PREDICT classification system. If no visible lesions were seen, no biopsies were required under the Portsmouth protocol.<br><br>Reference standard: Standard gastroscopy following the Seattle protocol (nontargeted mapping biopsies)<br>Standard gastroscopy followed the Seattle protocol of quadrantic biopsies every 2cm, in addition to biopsies of visible abnormalities.<br><br>Time between measurement of index test and reference standard: 6-8 weeks</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td rowspan="4">Calculated using gold standard and index test positives those with high grade-dysplasia or carcinoma</td></tr>
<tr><td></td><td>Index test +</td><td>2</td><td>0</td><td>2</td></tr>
<tr><td></td><td>Index test −</td><td>0</td><td>172</td><td>172</td></tr>
<tr><td></td><td>Total</td><td>2</td><td>172</td><td>174</td></tr>
<tr><td>Statistical measures</td><td colspan="5">Index text: Acetic acid-assisted gastroscopy (targeted biopsies- Portsmouth protocol)<br>Sensitivity: 1.00(0.16-1.00)<br>Specificity: 1.00 (0.98-1.00)</td></tr>
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|---|---|
| **Reference** | **Longcroft-Wheaton [9]** |
| **Source of funding** | NIHR Research for Patient Benefit Grant |
| **Limitations** | Risk of bias: none<br>Indirectness: none |
| **Comments** | |

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|---|---|
| **Reference** | **Ormeci 2008 [11]** |
| **Study type** | Prospective study |
| **Study methodology** | Data source & Recruitment: Ankara University,School of Medicine, Turkey |
| **Number of patients** | n = 109 |
| **Patient characteristics** | Age, mean (range): 62.32 ± 10.61 years; range, 33–82 years<br><br>Gender (male to female ratio): 66/43<br><br>Ethnicity: not reported<br><br>Setting: Department of gastroenterology, Ankara University,<br><br>Country: Turkey<br><br>Inclusion criteria: Patients older than 18 years with an indication for esophagogastroduodenoscopy were selected for this study. Between January 2003 and September 2005, 109 patients (43 women and 66 men) who had undergone conventional endoscopy and chromoendoscopy were enrolled in this study.<br><br>Exclusion criteria: Not reported |
| **Target condition(s)** | Barrett's Oesophagus (Intestinal metaplasia, dysplasia, cancer) |
| **Index test(s) and reference standard** | Index test: Chromoendoscopy with methylene blue<br>During chromoendoscopy, a 10% solution of N-acetyl cystein (10 ml) was sprayed on the oesophagus using the Olympus washing catheter (PW-5L; Olympus America, Inc., Melville, NY, USA) to remove superficial mucus. Then 1 min after N-acetyl cystein application, a |

<table>
<tr><td>Reference</td><td colspan="5">Ormeci 2008 [11]</td></tr>
<tr><td></td><td colspan="5">0.5% solution of methylene blue (10 ml) was sprayed on the oesophagus. After a 2-min interval, 300 ml of tap water was routinely sprayed from the washing catheter onto the oesophageal mucosa to wash off excess dye. Lower oesophagus sphincter function also was recorded.<br><br><u>Reference standard: Standard endoscopy</u><br>All the patients were sedated during endoscopic examination. During conventional endoscopy, patients who had normal-appearing mucosa (n = 7), esophagitis (n = 61), Barrett’s oesophagus (n = 50: 7 long- and 43 short-segment Barrett’s epithelium), or oesophageal tumour (n = 18, advanced cancer) underwent chromoendoscopy. When the columnar epithelium was longer than 3 cm, it was accepted as long-segment Barrett’s epithelium. Otherwise, it was designated as a short-segment condition.<br><br>All biopsies were taken with the same jumbo biopsy forceps. Histopathologic diagnosis was accepted as the gold standard, and conventional endoscopic or chromoendoscopic diagnosis was compared with the histopathologic diagnosis.<br><br>Time between measurement of index test and reference standard: consecutively completed</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td colspan="2">2x2 data not available.</td></tr>
<tr><td></td><td>Index test +</td><td></td><td></td><td></td><td colspan="2" rowspan="3"></td></tr>
<tr><td></td><td>Index test −</td><td></td><td></td><td></td></tr>
<tr><td></td><td>Total</td><td></td><td></td><td></td></tr>
<tr><td>Statistical measures</td><td colspan="5"><u>Index text Chromoendscopy</u></td></tr>
<tr><td></td><td colspan="2"></td><td>Dysplasia</td><td colspan="2">Oesophageal cancer</td></tr>
<tr><td></td><td>Sensitivity</td><td>Conventional endoscopy</td><td>NR</td><td colspan="2">0.95 (0.75–0.99)</td></tr>
<tr><td></td><td></td><td>Chromoendoscopy</td><td>0.68 (0.46–0.85)</td><td colspan="2">0.95 (0.75–0.99)</td></tr>
<tr><td></td><td>Specificity</td><td>Conventional endoscopy</td><td>NR</td><td colspan="2">0.99 (0.94–0.98)</td></tr>
<tr><td></td><td></td><td>Chromoendoscopy</td><td>0.77 (0.67–0.84)</td><td colspan="2">1.00 (0.95–1.00)</td></tr>
<tr><td>Source of funding</td><td colspan="5">Sandoz Corporation</td></tr>
<tr><td>Limitations</td><td colspan="5">Risk of bias: serious risk of bias<br>Indirectness: Serious Indirectness due to inclusion of population with Oesophagitis and not known Barrett’s oesophagus.</td></tr>
<tr><td>Comments</td><td colspan="5"></td></tr>
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|---|---|
| **Reference** | **Pascarenco 2016** [12] |
| **Study type** | Retrospective study |
| **Study methodology** | Data source & Recruitment: Department of Gastroenterology, University of Medicine and Pharmacy, Romania |
| **Number of patients** | n = 84 |
| **Patient characteristics** | Age, mean (range): 57.4 (26-84)<br><br>Gender (male to female ratio): 58/26<br><br>Ethnicity: not reported<br><br>Setting: Gastroenterology Clinic of Mures Clinical Country Hospital<br><br>Country: Romania<br><br>Inclusion criteria: over 18; endoscopic aspect of Barrett's Oesophagus and the patient's consent<br>Exclusion criteria: contraindications to Oesophageal biopsy (Oesophageal varices; coagulation disorders, anticoagulation treatment) and the endoscopic aspect of a oesophageal tumour. |
| **Target condition(s)** | Barrett's oesophagus with low grade dysplasia or indefinite for dysplasia |
| **Index test(s) and reference standard** | Index test Narrow-band imaging (NBI)<br>The NBI examinations were performed using Olympus EvisExera III CV-190 endoscopic equipment and comprised the use of the NBI mode activated during the whole examination, a with a thorough examination of oesophageal mucosa for visualizing any eventual surface anomalies of mucosa or vascular abnormalities. The images of the obtained patterns were recorded and then targeted biopsies of each NBI different pattern were taken.<br><br>Reference standard: white light standard imaging (WLSE)<br>Each patient had a white light standard endoscopy done with biopsies taken from the columnar mucosa. Examinations were performed by three experienced endoscopists using Olympus EvisExera II CLE-165 endoscopic equipment. During the endoscopy, the columnar mucosa was inspected thoroughly for detecting any visible mucosa modifications. BE length was recorded according to the Prague classification, followed by 4 quadrant biopsies taken every 1 – 2 cm of circumferential Barrett' segment according to the Seattle protocol, or taking biopsies from the cranial extensions of columnar mucosa under the form of islands of non circumferential BE.<br><br>Time between measurement of index test and reference standard: The white light endoscopic examination procedure was followed after a period of between 4 – 6 weeks by a NBI endoscopic examination, but the endoscopists were not informed of histological results. |

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| **Reference** | **Pascarenco 2016** [12] | | | | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | 2x2 data calculated using WLSE the gold standard and NBI as the index test. The threshold for positivity was indefinite for dysplasia or low-grade dysplasia. Non-dysplastic and intestinal metaplasia negative were taken as negative for dysplasia. |
| | Index test + | 1 | 9 | 10 | |
| | Index test − | 0 | 74 | 74 | |
| | Total | 1 | 83 | 84 | |
| **Statistical measures** | Index text NBI<br>Sensitivity= 1.00 (0.03-1.00)<br>Specificity= 0.89 (0.80-0.95) | | | | |
| **Source of funding** | Not reported | | | | |
| **Limitations** | Risk of bias: no serious risk of bias<br>Indirectness: No indirectness | | | | |
| **Comments** | | | | | |

| | |
|---|---|
| **Reference** | **Ragunath 2003** [13] |
| **Study type** | Prospective randomized cross over trial |
| **Study methodology** | Data source & Recruitment: Department of gastroenterology, University Hospital, Aintree, UK |
| **Number of patients** | n = 57; 618 biopsies |
| **Patient characteristics** | Age, mean (SD): Not reported<br><br>Gender (male to female ratio): 44/13<br><br>Ethnicity: Not reported<br><br>Setting: Department of gastroenterology, University Hospital Aintree<br><br>Country: UK |

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| **Reference** | **Ragunath 2003** [13] | | | | |
| | Inclusion criteria: endoscopic and histological diagnosis of Barrett's oesophagus segments of 3cm or more in length, adults patients of any sex attending for endoscopy, including newly diagnosed patients as well as those undergoing surveillance endoscopy for Barrett's Oesophagus, and patients known to have dysplasia without mucosal abnormalities who were receiving follow up endoscopies.<br><br>Exclusion criteria: those with macroscopic evidence of erosive or ulcerative esophagitis; those with nodules or mucosal irregularities suspicious of dysplasia or cancer; and those with obvious cancerous growth detected on endoscopy. | | | | |
| **Target condition(s)** | Barrett's Oesophagus with dysplasia or carcinoma | | | | |
| **Index test(s) and reference standard** | The patients were assigned by computer generated randomization to undergo either random biopsy follow by methylene blue directed biopsy 4 – 6 weeks later; or to Methylene directed biopsy followed by random biopsy 4 – 6 weeks later.<br><br><u>Index test Methylene blue directed imaging and biopsies</u><br>A special spray catheter producing a fine mist was used to spray reagnets onto the columnar lined oesophagus (Olympus washing catheter PW-5l; KeyMed, Southend-on-Sea, UK). The reagents were sprayed onto the columnar lined oesophagus in the following order: within a 1 minute interval between each step: 1) 10%n=acetylcysteine 2) 0.5% methylene blue until excess methylene blue was washed out. Endoscopic photographs were taken before and after methylene blue staining. Biopsy specimens were taken depending on the type of staining pattern.<br><br><u>Reference standard: Standard endoscopy</u><br>Endoscopy was carried out using the Olympus or Fujinon video endoscopes (Olympus Keymed, Southend-on-Sea, UK; Fujinon Optics, Japan). Standard endoscopy biopsy forceps with an 8mm cup were used to obtain the biopsy specimens, from the four quadrants at 2cm intervals, starting at the proximal margin of the gastric folds and proceeding to the proximally squamocolumnar junction.<br><br>Time between measurement of index test and reference standard: 4 - 6 weeks | | | | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | 2x2 data not reported |
| | Index test + | | | | |
| | Index test − | | | | |
| | Total | | | | |

| Reference | **Ragunath 2003** [13] |
|---|---|
| **Statistical measures** | Index text Methylene Blue (biopsy results)<br>Sensitivity – 49% (38 – 61%)<br>Specificity – 85% (82 – 88%) |
| **Source of funding** | Cook UK and Wyeth Pharmaceuticals UK funded this research project. The study was presented at the annual meeting of the British Society of Gastroenterology in March 2002 |
| **Limitations** | Risk of bias: serious risk of bias<br>Indirectness: Serious; unclear if the "standard endoscopy" technique is HD white light imaging |
| **Comments** | |

| Reference | **Sharma 2011** [15] |
|---|---|
| **Study type** | Prospective randomised controlled trial |
| **Study methodology** | Data source & Recruitment: Multiple medical centres in USA, France and Germany |
| **Number of patients** | n = 101; 874 locations analysed |
| **Patient characteristics** | Age, mean (range): 65.1 years (27–90 years)<br><br>Gender (male to female ratio):<br><br>Ethnicity: not reported<br><br>Setting: Multiple medical centres for BE surveillance<br><br>Country: France, Germany & USA<br><br>Inclusion criteria: Consecutive patients undergoing BE surveillance and/or referred for BE-associated neoplasia (HGD/EC) evaluation and treatment were prospectively enrolled in this trial at 5 hospitals<br><br>Exclusion criteria: Patients with erosive esophagitis, inability to obtain biopsy samples because of anticoagulation, varices, known allergy to sodium fluorescein, pregnancy, presence of an oesophageal mass or nodule greater than 10 mm, and renal insufficiency were excluded from the trial. |

| Reference | Sharma 2011 [15] |
|---|---|
| | |
| **Target condition(s)** | Barrett's Oesophagus: high grade dysplasia / oesophageal cancer |
| **Index test(s) and reference standard** | a randomization was performed between the HD-WLE and NBI endoscopic procedures to evaluate the individual diagnostic performances and contribution of each imaging modality. A tandem design was adopted in which each location/patient acted as its/his or her own control. All patients underwent examination of their BE segment by 3 imaging modalities: HD-WLE, NBI, and pCLE (procedures 1, 2, and 3). The order of procedures 1 and 2 was randomized before pCLE imaging and tissue sampling. Every attempt was made to blind the endoscopist to each patient's history and previous endoscopic findings. Patients were randomized in a 1:1 ratio in blocks of 2 stratified by study site and procedure indication (BE surveillance or BE treatment). The electronic data capture system was used to collect data starting with patient screening and eligibility check and to randomize patients.<br><br>Reference standard (Procedure 1): HD-WLE<br>All patients underwent standard HD-WLE examination using an Olympus 180 HD endoscope (Olympus Inc, Center Valley, Pa) in white-light mode (using a 4-mm clear cap distal attachment without magnification). The BE length was measured from the gastroesophageal junction to the proximally displaced squamocolumnar junction and recorded using the Prague C & M criteria.If visible lesions were identified (suspicious for neoplasia), they were graded using the Paris classification system and their distance and clock position (eg, 38 cm, 8 o'clock) were recorded. Biopsy samples were not obtained until after all procedures (1, 2, and 3) were complete.<br><br>The paper measures diagnostic accuracy of the visual findings from each HD-WLE, NBI, pCLE with reference to the full histological findings. i.e. reference standard was histology derived from biopsies from each procedure rather than histology from biopsies from the HD-WLE<br><br>Index test (Procedure 2): narrow-band imaging NBI<br>Each patient also underwent NBI endoscopy examination using the same Olympus 180 HD endoscope in the NBI mode (using a 4-mm clear cap distal attachment without magnification). In addition to the recording of all visible lesions by NBI (as described for procedure 1), any abnormal mucosal and/or vascular patterns seen with NBI were also identified as suspicious locations.<br><br>Index test (Procedure 3): Probe-based confocal laser endomicroscopy pCLE<br>pCLE examination was performed using a confocal miniprobe (GastroFlex UHD, Cellvizio; Mauna Kea Technologies, Paris, France), which has a field of view of 240 µm, a lateral resolution of 1 µm, and an imaging depth of 60 µm below the tissue surface. The immediate vicinity of each location was "marked" using spot coagulation with argon plasma coagulation (ERBE, Tübingen, Germany). Suspicious (targeted) locations were marked first, followed by nontargeted (NBI and HD-WLE) normal random sites. After injection of sodium fluorescein (2.5 mL, 10%), the pCLE miniprobe was passed through the endoscope accessory channel and placed in gentle contact with the BE surface. pCLE imaging was performed at all suspicious (observed by either WLE or NBI) and random locations (ie, 4 quadrants every 2 cm per the Seattle surveillance protocol). The investigator made a presumptive diagnosis of dysplastic (HGD/EC) or nondysplastic at each site examined by pCLE before biopsy samples were obtained. |

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| **Reference** | **Sharma 2011** [15] | | | | |
| | Time between measurement of index test and reference standard: consecutive imagine | | | | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | 2x2 data calculated for NBI (per location analysis) |
| | Index test + | 50 | 80 | 130 | |
| | Index test − | 70 | 674 | 744 | |
| | Total | 120 | 754 | 874 | |
| 2x2 table | Index test + | 75 | 68 | 143 | 2x2 data calculated for pCLE (per location analysis) |
| | Index test − | 45 | 686 | 731 | |
| | Total | 120 | 754 | 874 | |
| **Statistical measures** | Index text NBI<br>***Per location analysis***<br>Sensitivity 0.42 (0.33–0.51)<br>Specificity 0.89 (0.87–0.91)<br><br>Index text pCLE<br>***Per location analysis***<br>Sensitivity 0.63 (0.53–0.71)<br>Specificity 0.91 (0.89–0.93) | | | | |
| **Source of funding** | The study was funded by Mauna Kea Technologies. The following authors disclosed financial relationships relevant to this publication: Dr. Wallace: unrestricted educational grant, Mauna Kea Technologies, Dr. Meining, coinventor on a patent for another product, study Mauna Kea Technologies. | | | | |
| **Limitations** | Risk of bias: no serious risk of bias<br>Indirectness: Serious indirectness as the reference standard was not histology from the standard endoscopy | | | | |
| **Comments** | | | | | |

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|---|---|
| **Reference** | **Sharma 2013** [14] |
| **Study type** | Multi-centre randomised cross-over trial |
| **Study methodology** | Data source: Patients referred for Barrett's oesophagus screening/surveillance at three tertiary referral centres<br><br>Recruitment: prospective |

| | | | | | |
|---|---|---|---|---|---|
| **Reference** | **Sharma 2013** [14] | | | | |
| **Number of patients** | n = 123 | | | | |
| **Patient characteristics** | Age, mean (range): 61 (38-85) years<br><br>Gender (male to female ratio): 115/8<br><br>Ethnicity: 97% Caucasian<br><br>Setting: 3 tertiary referral centres<br><br>Country: USA<br><br>Inclusion criteria: patients over 18 undergoing screening or surveillance for Barrett's oesophagus<br><br>Exclusion criteria: Patients with erosive oesophagitis, grossly visible nodules or lesions (.5mm) within the BO segment suggestive of invasive OAC and those with contraindications to oesophageal biopsies such as anticoagulation or varices were excluded. Patients with BO length <1cm were also excluded as previous studies have documented poor interobserver agreement in diagnosing BO of this length. | | | | |
| **Target condition(s)** | Barrett's oesophagus: high grade dysplasia, oesophageal adenocarcinoma | | | | |
| **Index test(s) and reference standard** | Index test: Narrow-band imaging<br>Endoscopies were performed using a high-definition endoscope with NBI capability (Olympus GIF-H180, Centre Valley, Pennsylvania, USA; available at all centres) and all biopsy forceps (radial jaw 3; Boston Scientific,Massachusetts, USA)<br><br>Reference standard: Standard white-light endoscopy<br>Patients were evaluated using high-definition white light endoscopy according to the Seattle protocol.<br><br>Time between measurement of index test and reference standard: 3-8 weeks | | | | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | Calculated considering reference standard and index test positives those that had high grade dysplasia or oesophageal adenocarcinoma. |
| | Index test + | 7 | 5 | 12 | |
| | Index test − | 2 | 109 | 111 | |
| | Total | 9 | 114 | 123 | |

| | |
|---|---|
| **Reference** | **Sharma 2013** [14] |
| **Statistical measures** | Index text: NBI<br>Sensitivity= 0.78 (0.40-0.97)<br>Specificity= 0.96 (0.90-0.99) |
| **Source of funding** | ASGE research award; grant from Olympus America |
| **Limitations** | Risk of bias: None<br>Indirectness: No indirectness |
| **Comments** | |

| | |
|---|---|
| **Reference** | **Jayasekara 2012**[8] |
| **Study type** | Prospective cross-sectional study |
| **Study methodology** | Data source: St Vincent's Hospital, Melbourne<br><br>Recruitment: Consecutive patients referred for endoscopic evaluation and treatment of dysplastic Barrett's oesophagus, |
| **Number of patients** | n = 50; 1190 biopsies |
| **Patient characteristics** | Age, median (range): 66 (41-86) years<br><br>Gender (male to female ratio): 42/8<br><br>Ethnicity: Not specified<br><br>Setting: Tertiary referral setting, St Vincent's hospital, Melbourne<br><br>Country: Australia<br><br>Inclusion criteria: Patients referred to St Vincent's Hospital, Melbourne for endoscopic evaluation and treatment of dysplastic Barrett's oesophagus, which had been previously diagnosed by their referring physician, over the age of 18 years. Patients were referred for consideration of combination endoscopic therapy.<br><br>Exclusion criteria: not specified |

| | | | | | |
|---|---|---|---|---|---|
| **Reference** | **Jayasekara 2012[8]** | | | | |
| | Referral pathology: intramucosal cancer (n=8), high grade dysplasia (n=18), low grade dysplasia (n=23), intestinal metaplasia (n=1) | | | | |
| **Target condition** | Barrett's oesophagus with high grade dysplasia and intramucosal cancer. | | | | |
| **Index tests and reference standard** | Index test: High-definition white light endoscopy (HD-WLE)<br>The initial HD-WLE components of the mapping protocol were performed by an Olympus H180 endoscope.<br><br>Index test: Narrow-band imaging (NBI)<br>The initial NBI components of the mapping protocol were performed by an Olympus H180 (PCF-Q180AL/I; Olympus, Tokyo, Japan) which had the NBI feature incorporated into the endoscope and was activated by the touch of a button mounted on the controls of the endoscope.<br><br>Index test: Confocal laser endomicroscopy (CLE)<br>CLE was performed using the Pentax confocal endomicroscope (EC3870k system; Pentax, Tokyo, Japan) with the ISC-1000 confocal endomicroscopy processor, developed by Optiscan (notting hill, Victoria, Australia), which has the confocal lense incorporated within the framework of the endoscope.To obtain images at depths below the surface, an exogenous fluorescent contrast agent was required; a 5ml dose of 10% fluorescein sodium was injected intravenously prior to commencement of CLE. The contrast agent usually lasted 30 minutes.<br><br>The mapping procedures were performed by two expert endoscopists utilising three imaging modalities in a sequential manner. The first two assessments (HD-WLE and NBI) were performed by the same endoscopist. The second endoscopist performing CLE was aware of the location of any abnormal mucosal areas identified by either HD-WLE or NBI.<br><br>Reference standard: Biopsy (Seattle protocol)<br>Biopsies were performed using the Olympus endoscope. Each biopsy was placed in a separate specimen pot and labelled with the location according to depth in cm and o'clock position with the endoscope in a neutral position. The histological assessment by an expert gastrointestinal pathologist was used as the gold standard to determine the accuracy of endoscopic predictions by each imaging modality.<br><br>Time between measurement of index test and reference standard: Endoscopic assessments were performed sequentially in a nonblinded manner | | | | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | Index test: High-definition white light endoscopy |
| | Index test + | 75 | 184 | 259 | |
| | Index test − | 16 | 915 | 931 | |
| | Total | 91 | 1099 | 1190 biopsies | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | Index test: Narrow-band imaging |

| | | | | | |
|---|---|---|---|---|---|
| **Reference** | **Jayasekara 2012[8]** | | | | |
| | Index test + | 81 | 208 | 289 | |
| | Index test − | 10 | 891 | 901 | |
| | Total | 91 | 1099 | 1190 biopsies | |
| **2×2 table** | | Reference standard + | Reference standard − | Total | Index test: Confocal-laser endo-microscopy |
| | Index test + | 50 | 208 | 258 | |
| | Index test − | 16 | 843 | 859 | |
| | Total | 66 | 1051 | 1117 biopsies | |
| **Statistical measures** | Index text: High-definition white light endoscopy<br>Sensitivity: 0.82 (0.73 – 0.90)<br>Specificity: 0.83 (0.81- 0.85)<br><br>Index text: Narrow-band imaging<br>Sensitivity: 0.89 (0.81-0.95)<br>Specificity: 0.81 (0.79-0.83)<br><br>Index test: Confocal-laser endo-microscopy<br>Sensitivity: 0.76 (0.64-0.85)<br>Specificity: 0.80 (0.78-0.83) | | | | |
| **Source of funding** | Not specified | | | | |
| **Limitations** | Risk of bias: Very serious risk of bias due to lack of blinding in the interpretation of each test (the first two being performed by the same endoscopist and the endoscopist performing the third index test having access to results from the previous tests)<br>Indirectness: Serious indirectness as results for white light endoscopy are given separately with biopsy as the reference standard. | | | | |
| **Comments** | | | | | |

| | |
|---|---|
| **Reference** | **Vithayathil 2022[16]** |
| **Study type** | Two tertiary centres randomised crossover study (prospective) |
| **Study methodology** | Data source: Adult Barrett's oesophagus patients with no dysplastic lesions<br><br>Recruitment: Consecutive |

| | |
|---|---|
| **Reference** | **Vithayathil 2022[16]** |
| **Number of patients** | n = 134 |
| **Patient characteristics** | Age, median (range): 67.3 (38.0 to 89.0) years<br><br>Gender (male to female ratio): 104:30<br><br>Ethnicity: not stated<br><br>Setting: Two tertiary medical centres<br><br>Country: UK<br><br>Inclusion criteria: patients aged 18 years and older diagnosed with Barrett's oesophagus greater than C2 and/ or M3 on pretrial endoscopy (as per the Prague Classification) referred for surveillance of non-dysplastic Barrett's oesophagus or assessment of flat dysplasia. The reason for inclusions of BE segments at least C2 or M3 was 2-fold: image-enhanced assisted detection is expected to be more advantageous for long-segment BE, and AFI has a high false-positive rate at the oesophagogastric junction<br><br>Exclusion criteria: previous evidence of BE-related neoplasia visible on endoscopy, previous histologic evidence of oesophageal adenocarcinoma, esophagitis (Los Angeles grade ≥ B), previous oesophagectomy, fluorescein allergy, severe/uncontrolled asthma, coagulopathy or anticoagulant/antiplatelet therapy for high-risk conditions, active/severe cardiopulmonary disease, or decompensated liver disease |
| **Target condition(s)** | Barrett's oesophagus neoplasia |
| **Index test(s) and reference standard** | Index test: high-resolution white-light endoscopy (HRWLE) with Seattle protocol biopsies<br>HRWLE only was allowed for inspection using FQ260Z, HQ290, or H290Z endoscopes (Olympus, Tokyo, Japan). Subtle lesions were allowed if not clearly in keeping with BE-related neoplasia, and therefore received targeted biopsies. Random biopsy specimens then were taken every 2 cm of the length of BE.<br><br>Index test: endoscopy with autofluorescence imaging (AFI)-directed probe-based confocal laser endomicroscopy (pCLE) and targeted biopsies for molecular biomarkers<br>FQ260Z endoscopes were used. The initial inspection was performed with HRWLE only. The endoscopist then switched to AFI mode and areas of purple–red colour within a green background (AFIþ) were identified. At the discretion of the endoscopists, AFIþ lesions were marked with argon-plasma coagulation (VIO 200; ERBE, Tuebingen, Germany) or snare tip to delineate the area for interest. AFIþ areas, together with subtle HRWLE lesions if present, then were studied with pCLE after intravenous fluorescein (10% solution, 2.5 ml) and then |

<table>
<tr><td>Reference</td><td colspan="5">Vithayathil 2022[16]</td></tr>
<tr><td></td><td colspan="5">received 2 targeted biopsies stored in formalin. At least 2 pCLE videos per endoscopic location were recorded. A maximum of 4 AFIþ areas per patient were allowed for pCLE analysis. In patients with no AFIþ areas, 1 random location was used for pCLE analysis and targeted biopsies for every 5 cm of BE maximum length. The endoscopist made a live pCLE diagnosis and then reviewed pCLE videos offline to make the final pCLE diagnosis.<br><br>Patients crossed over to the other arm after 6 to 12 weeks<br><br><u>Reference standard: histology</u><br>Tissue biopsy specimens from both arms were formalin-fixed and paraffin-embedded for histopathologic assessment. Biopsy specimens were reviewed by a gastrointestinal (GI) pathologist with extensive expertise in BE in accordance with the Vienna classification. All dysplastic cases, including indefinite for dysplasia were reviewed by a second expert GI pathologist from the other institution, with consensus diagnosis achieved for discordant cases. For the purpose of the analysis, indefinite for dysplasia was grouped with NDBE. In the standard arm, p53 immunohistochemistry was performed at the discretion of the pathologist, as per the standard of care.<br><br>Molecular Biomarker Assays<br>A 3-biomarker panel including cyclin A, p53, and aneuploidy was selected based on previously published data. Cyclin A and p53 expression were assessed with immunohistochemistry and aneuploidy with image cytometry. A full panel of biomarkers was available in 96.3% of cases. In line with committee discussions, data for the added diagnostic value of the biomarker panel were not extracted for this review as it did not meet the protocol for the index test.<br><br>Time between measurement of index test and reference standard: not reported; 6-12 week interval between index tests</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td>2x2 data not reported</td></tr>
<tr><td></td><td>Index test +</td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td>Index test −</td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td>Total</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Statistical measures</td><td colspan="5">Dysplasia (n = 35)<br><br><u>HRWLE with Seattle protocol biopsies</u><br>Sensitivity:  80.0% (95% CI 63.1 to 91.6)<br>Specificity: not reported<br><br><u>AFI-guided pCLE</u><br>Sensitivity: 74.3% (95% CI 56.7 to 87.5)<br>Specificity: 66.7%</td></tr>
</table>

| Reference | Vithayathil 2022[16] |
|---|---|
| | **High-grade dysplasia (n = 17)**<br><br>HRWLE with Seattle protocol biopsies<br>Sensitivity: 76.5% (95% CI 50.1 to 93.2)<br>Specificity: not reported<br><br>AFI-guided pCLE<br>Sensitivity: 76.5% (95% CI 50.1 to 93.2)<br>Specificity: 60.7% |
| **Source of funding** | Cancer Research UK, Cambridge Cancer Research Fund charity (Cambridge, UK), Experimental Cancer Medicine Centre and National Institute of Health Research (NIHR), United Kingdom Cambridge Biomedical Research Centre, United Kingdom (BRC-1215-20014), Medical Research Council, United Kingdom (RG84369). |
| **Limitations** | Risk of bias: serious due to flow and timing<br>Indirectness: serious due to the results of the high resolution white-light endoscopy given separately with histology being the reference standard. |
| **Comments** | |

# Appendix E – Sensitivity and specificity forest plots

## E.1 Chromoendoscopy

**Figure 2: Sensitivity and specificity of confocal laser endomicroscopy (reference standard: biopsy) for Barrett's Oesophagus with high grade dysplasia and intramucosal cancer (per location analysis)**

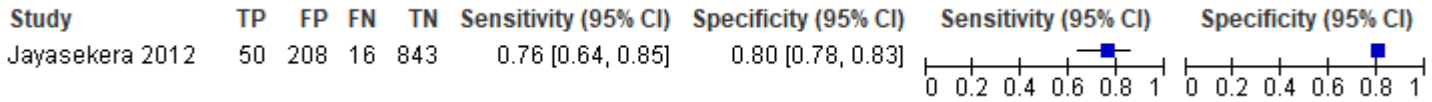



**Figure 3: Sensitivity and specificity of probe-based confocal laser endomicroscopy (reference standard: standard endoscopy) for Barrett's Oesophagus with high grade intraepithelial neoplasia / carcinoma (per patient analysis)**

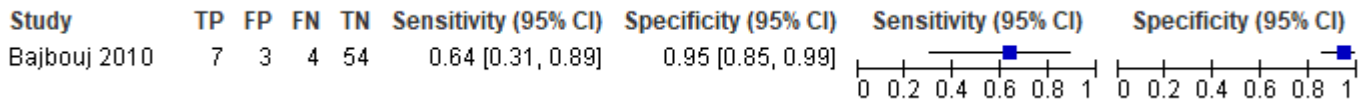



**Figure 4: Sensitivity and specificity of probe-based confocal laser endomicroscopy (reference standard: histology) for Barrett's Oesophagus with high grade dysplasia / oesophageal cancer (per patient analysis)**

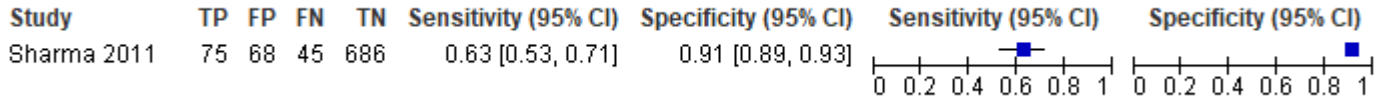


**Figure 5: Sensitivity and specificity of high-definition white light endoscopy (reference standard: biopsy) for Barrett's Oesophagus with high grade dysplasia and intramucosal cancer**

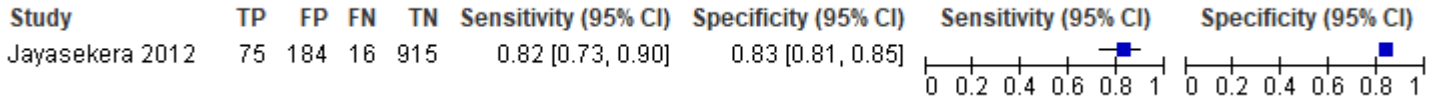



**Figure 6: Sensitivity and specificity of narrow-band imaging (reference standard: biopsy) for Barrett's Oesophagus with high grade dysplasia and intramucosal cancer (per location analysis)**

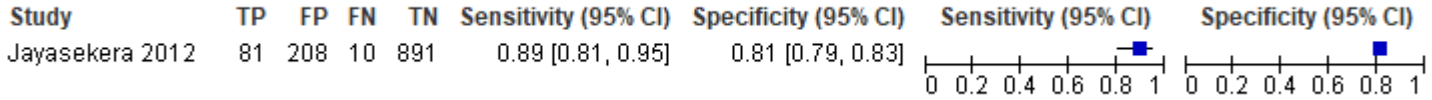



**Figure 7: Sensitivity and specificity of narrow-band imaging (reference standard: white light endoscopy) for Barrett's Oesophagus with low grade dysplasia or indefinite for dysplasia (per patient analysis)**

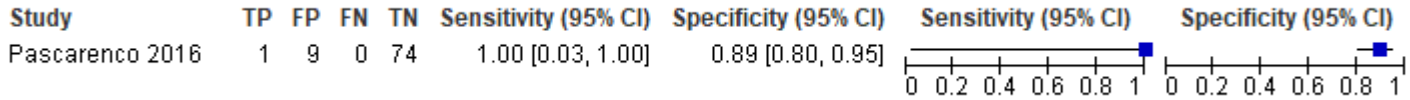



**Figure 8: Sensitivity and specificity of narrow-band imaging (reference standard: histology) for Barrett's Oesophagus with high grade dysplasia/oesophageal cancer (per location analysis)**

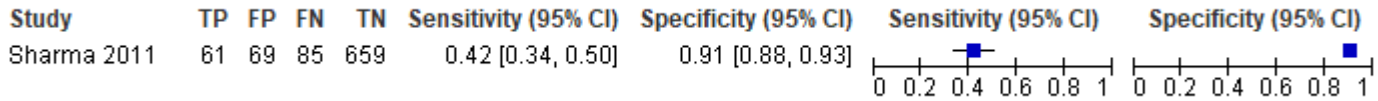



**Figure 9: Sensitivity and specificity of narrow-band imaging (reference standard: white-light endoscopy) for Barrett's Oesophagus with neoplasia (high grade dysplasia, oesophageal adenocarcinoma) (per patient analysis)**

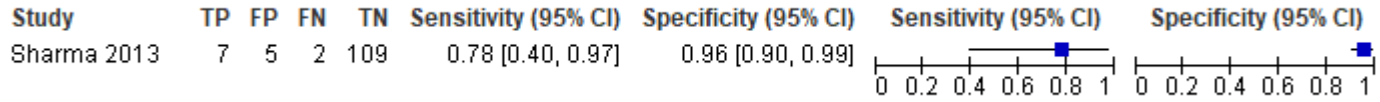



**Figure 10: Sensitivity and specificity of endoscopic tri-modal imaging (reference standard: standard video endoscopy) for Barrett's Oesophagus with high grade dysplasia/early carcinoma**

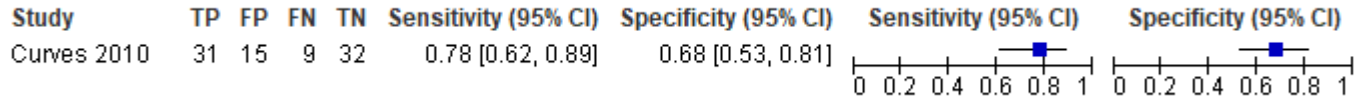
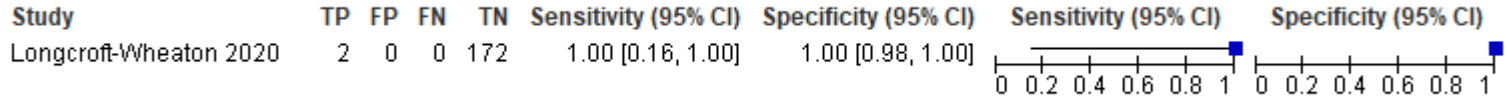
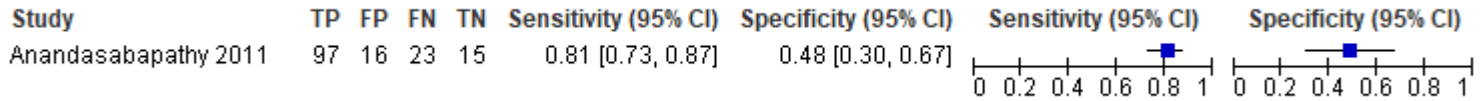



**Figure 11: Sensitivity and specificity of acetic acid-targeted biopsies (Portsmouth protocol) (reference standard: Seattle protocol-guided nontargeted biopsies) for neoplasia**




## E.3 Endoscopic brushing

**Figure 12:Sensitivity and specificity of brush biopsy (reference standard: forceps biopsy) for Barrett's metaplasia, indefinite for dysplasia, dysplasia and inadequate (no BE)**



## E.4 Artificial intelligence

**Figure 13: Sensitivity and specificity of narrow-band imaging + AI (reference standard: histology) for Barrett's Oesophagus with high grade dysplasia**

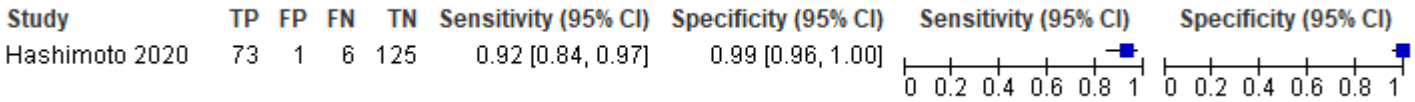
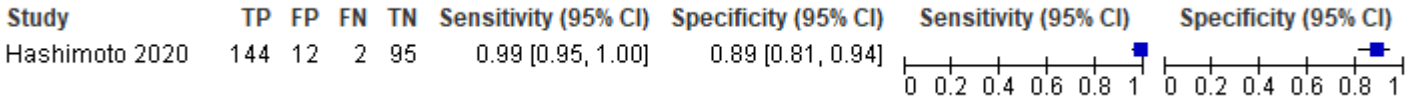
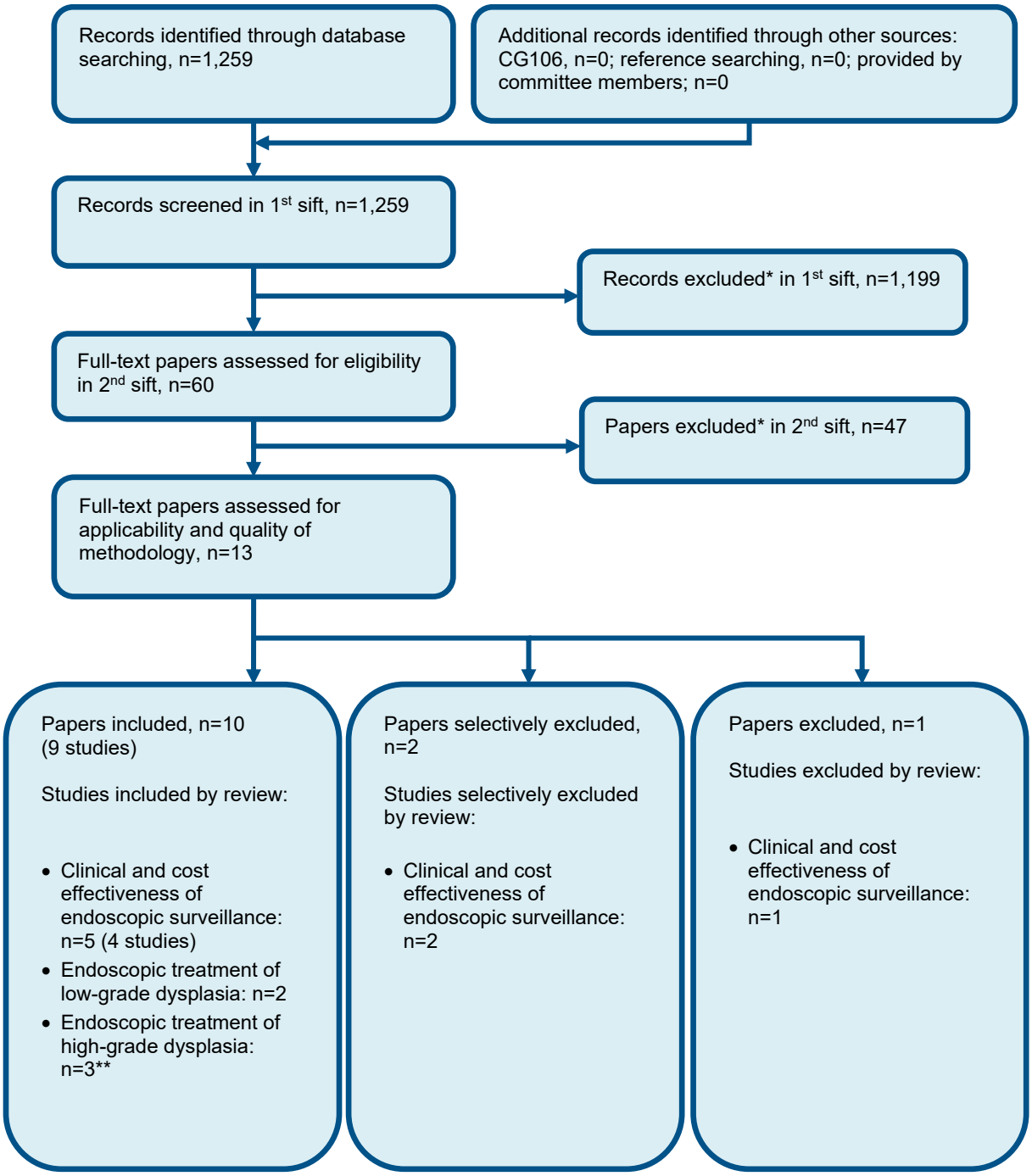



**Figure 14: Sensitivity and specificity of white-light imaging + AI (reference standard: histology) for Barrett's Oesophagus with high grade dysplasia**



# Appendix F – 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 G – Excluded studies

### Clinical studies

**Table 8: Studies excluded from the clinical review**

| Study | Exclusion reason |
|---|---|
| Admad, N. Z. and Ahmed, A. (2010) A meta-analysis of randomized controlled trials comparing methylene blue-directed biopsies with random biopsies in the surveillance of Barrett's esophagus. Esophagus 7(4): 207-213 | - Study design not relevant to this review protocol |
| Aedo, M. R., Zavala-Gonzalez, M. A., Meixueiro-Daza, A. et al. (2014) Accuracy of transnasal endoscopy with a disposable esophagoscope compared to conventional endoscopy. World Journal of Gastrointestinal Endoscopy 6(4): 128-36 | - Population not relevant to this review protocol |
| Alves, J. R., Graffunder, F. P., Rech, J. V. T. et al. (2020) Diagnosis, Treatment and Follow-up of Barrett's Esophagus: A Systematic Review. Arquivos de Gastroenterologia 57(3): 289-295 | - Data not reported in an extractable format or a format that can be analysed |
| Anagnostopoulos, G. K., Yao, K., Kaye, P. et al. (2007) Novel endoscopic observation in Barrett's oesophagus using high resolution magnification endoscopy and narrow band imaging. Alimentary Pharmacology & Therapeutics 26(3): 501-7 | - Study does not contain an intervention relevant to this review protocol<br>*non comparative use of NBI in addition to standard endoscopy to calculate its diagnostic accuracy. Amsterdam protocol for biopsies.* |
| Ang, T. L., Pittayanon, R., Lau, J. Y. et al. (2015) A multicenter randomized comparison between high-definition white light endoscopy and narrow band imaging for detection of gastric lesions. European Journal of Gastroenterology & Hepatology 27(12): 1473-1478 | - Population not relevant to this review protocol<br>*participants not with Barrett's Oesophagus, but for general investigation* |
| Areia, M., Amaro, P., Dinis-Ribeiro, M. et al. (2008) External validation of a classification for methylene blue magnification chromoendoscopy in premalignant gastric lesions. Gastrointestinal Endoscopy 67(7): 1011-8 | - Population not relevant to this review protocol<br>*magnification chromoendoscopy for gastric atrophy and dysplasia* |
| Arribas, J., Antonelli, G., Frazzoni, L. et al. (2020) Standalone performance of artificial intelligence for upper GI neoplasia: a meta-analysis. Gut 70: 1458-1468 | - Systematic review used as source of primary studies |

| Study | Exclusion reason |
|---|---|
| Bang, C. S.; Lee, J. J.; Baik, G. H. (2021) Computer-aided diagnosis of esophageal cancer and neoplasms in endoscopic images: a systematic review and meta-analysis of diagnostic test accuracy. Gastrointestinal Endoscopy 93(5): 1006-1015.e13 | - Systematic review used as source of primary studies |
| Bhardwaj, A., Hollenbeak, C. S., Pooran, N. et al. (2009) A meta-analysis of the diagnostic accuracy of esophageal capsule endoscopy for Barrett's esophagus in patients with gastroesophageal reflux disease. American Journal of Gastroenterology 104(6): 1533-9 | - Systematic review used as source of primary studies |
| Bhatti, K. M., Khanzada, Z. S., Kuzman, M. et al. (2021) Diagnostic Performance of Artificial Intelligence-Based Models for the Detection of Early Esophageal Cancers in Barret's Esophagus: A Meta-Analysis of Patient-Based Studies. Cureus 13(6): e15447 | - Systematic review used as source of primary studies |
| Borovicka, J., Fischer, J., Neuweiler, J. et al. (2006) Autofluorescence endoscopy in surveillance of Barrett's esophagus: a multicenter randomized trial on diagnostic efficacy. Endoscopy 38(9): 867-872 | - Study design not relevant to this review protocol<br><br>*Crossover RCT with some diagnostic data, however incomplete and unclear of analysis* |
| 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'sEsophagus. Clinical Gastroenterology and Hepatology 13(6): 1068-1074.e2 | - Data not reported in an extractable format or a format that can be analysed<br><br>*relevant comparison, data incomplete with only sensitivity narratively reported. Data in table also incomplete* |
| Camus, M., Coriat, R., Leblanc, S. et al. (2012) Helpfulness of the combination of acetic acid and FICE in the detection of Barrett's epithelium and Barrett's associated neoplasias. World Journal of Gastroenterology 18(16): 1921-5 | - Data not reported in an extractable format or a format that can be analysed<br><br>*Data reported narratively, table with analysis does not correlate and cannot calculate diagnostic accuracy from this data* |
| Canto, M. I., Setrakian, S., Willis, J. et al. (2000) Methylene blue-directed biopsies improve detection of intestinal metaplasia and dysplasia in Barrett's esophagus. Gastrointestinal Endoscopy 51(5): 560-8 | - Study design not relevant to this review protocol<br><br>*cost and correlation of biopsies with standard endoscopy versus endoscopy + staining to diagnosis. Cannot use data for diagnostic accuracy analysis.* |
| Chai, T. H., Jin, X. F., Li, S. H. et al. (2014) A tandem trial of HD-NBI versus HD-WL to | - Population not relevant to this review protocol |

| Study | Exclusion reason |
|---|---|
| compare neoplasia miss rates in esophageal squamous cell carcinoma. Hepato-Gastroenterology 61(129): 120-124 | *Squamous cell carcinoma and no relevant outcomes* |
| 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 |
| Chedgy, F., Fogg, C., Kandiah, K. et al. (2018) Acetic acid-guided biopsies in Barrett's surveillance for neoplasia detection versus non-targeted biopsies (Seattle protocol): A feasibility study for a randomized tandem endoscopy trial. The ABBA study. Endoscopy International Open 6(1): E43-E50 | - Study design not relevant to this review protocol<br>*study protocol only* |
| Chen, B. L., Xing, X. B., Wang, J. H. et al. (2014) Improved biopsy accuracy in Barrett's esophagus with a transparent cap. World Journal of Gastroenterology 20(16): 4718-4722 | - Study does not contain an intervention relevant to this review protocol<br>*the addition of a cap compared to no cap for endoscopy.* |
| Chen, H., Liu, Y., Lu, Y. et al. (2018) Ability of blue laser imaging with magnifying endoscopy for the diagnosis of gastric intestinal metaplasia. Lasers in Medical Science 33(8): 1757-1762 | - Population not relevant to this review protocol<br>*participants under investigation for gastric cancer not oesophageal cancer* |
| Chen, H., Wu, X., Liu, Y. et al. (2019) Blue laser imaging with acetic acid enhancement improved the detection rate of gastric intestinal metaplasia. Lasers in Medical Science 34(3): 555-559 | - Population not relevant to this review protocol<br>*participants under investigation for gastric / intestinal metaplasia* |
| Chen, Q., Cheng, H. H., Deng, S. et al. (2018) Diagnosis of Superficial Gastric Lesions Together with Six Gastric Lymphoma Cases via Probe-Based Confocal Laser Endomicroscopy: A Retrospective Observational Study. Gastroenterology research & practice 2018: 5073182 | - Population not relevant to this review protocol<br>*Participants under investigation for or with gastric lesions* |
| Chen, J., Yang, J., Chang, T. S. et al. (2022) Detection of Barrett's Neoplasia with Near-infrared Fluorescent Heterodimeric Peptide. Endoscopy 17: 17 | - Comparator in study does not match that specified in this review protocol<br>unclear if white light imaging was used as a reference standard for comparison |

| Study | Exclusion reason |
|---|---|
| Chung, C. S., Liao, L. J., Lo, W. C. et al. (2013) Risk factors for second primary neoplasia of esophagus in newly diagnosed head and neck cancer patients: a case-control study. BMC Gastroenterology 13: 154 | - Population not relevant to this review protocol<br><br>*Squamous cell carcinoma in the head and neck (comparing narrow band magnified imaging with white light imaging)* |
| Codipilly, D. C., Krishna Chandar, A., Wang, K. K. et al. (2022) Wide-area transepithelial sampling for dysplasia detection in Barrett's esophagus: a systematic review and meta-analysis. Gastrointestinal Endoscopy 95(1): 51-59.e7 | - Systematic review used as source of primary studies |
| 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 | - Data not reported in an extractable format or a format that can be analysed<br><br>*only partial results reported with false positive* |
| Curvers, W. L., Bohmer, C. J., Mallant-Hent, R. C. et al. (2008) Mucosal morphology in Barrett's esophagus: interobserver agreement and role of narrow band imaging. Endoscopy 40(10): 799-805 | - Study design not relevant to this review protocol<br><br>*assessing inter observer agreement for proposed morphological classification, comparing white light imaging with narrow band imaging.* |
| Curvers, W., Baak, L., Kiesslich, R. et al. (2008) Chromoendoscopy and narrow-band imaging compared with high-resolution magnification endoscopy in Barrett's esophagus. Gastroenterology 134(3): 670-9 | - Study design not relevant to this review protocol<br><br>*no relevant outcomes - comparing the interobserver agreement between different modalities only. No diagnostic accuracy data.* |
| Dave, U.; Shousha, S.; Westaby, D. (2001) Methylene blue staining: is it really useful in Barrett's esophagus?. Gastrointestinal Endoscopy 53(3): 333-335 | - Data not reported in an extractable format or a format that can be analysed<br><br>*not clear comparison to reference standard* |
| de Groof, A. J., Struyvenberg, M. R., Fockens, K. N. et al. (2020) Deep learning algorithm detection of Barrett's neoplasia with high accuracy during live endoscopic procedures: a pilot study (with video). Gastrointestinal Endoscopy 91(6): 1242-1250 | - Study design not relevant to this review protocol<br><br>*white light imaging + blue light imaging tested against a computer aided design software* |
| de Groof, A. J., Swager, A. F., Pouw, R. E. et al. (2019) Blue-light imaging has an additional value to white-light endoscopy in visualization of early Barrett's neoplasia: an international | - Study design not relevant to this review protocol |

| Study | Exclusion reason |
|---|---|
| multicenter cohort study. Gastrointestinal Endoscopy 89(4): 749-758 | *assessing correlation of specialists views and agreement on endoscopy results* |
| de Groof, J., van der Sommen, F., van der Putten, J. et al. (2019) The Argos project: The development of a computer-aided detection system to improve detection of Barrett's neoplasia on white light endoscopy. United European Gastroenterology Journal 7(4): 538-547 | - Study design not relevant to this review protocol<br>*using previous endoscopy images to develop a computer aided software to detect Barrett's oesophagus; the population from which images were obtained was not defined.* |
| Diao, W., Huang, X., Shen, L. et al. (2018) Diagnostic ability of blue laser imaging combined with magnifying endoscopy for early esophageal cancer. Digestive & Liver Disease 50(10): 1035-1040 | - Population not relevant to this review protocol<br>*general population under investigation - not specific to Barrett's oesophagus patients* |
| Dobashi, A., Goda, K., Furuhashi, H. et al. (2019) Diagnostic efficacy of dual-focus endoscopy with narrow-band imaging using simplified dyad criteria for superficial esophageal squamous cell carcinoma. Journal of Gastroenterology 54(6): 501-510 | - Population not relevant to this review protocol<br>*investigating participants with or for squamous cell oesophageal carcinoma* |
| Dutta, A. K., Sajith, K. G., Pulimood, A. B. et al. (2013) Narrow band imaging versus white light gastroscopy in detecting potentially premalignant gastric lesions: a randomized prospective crossover study. Indian Journal of Gastroenterology 32(1): 37-42 | - Population not relevant to this review protocol<br>*gastric examination via gastroscopy for gastric cancers* |
| Ebi, M., Shimura, T., Yamada, T. et al. (2015) Multicenter, prospective trial of white-light imaging alone versus white-light imaging followed by magnifying endoscopy with narrow-band imaging for the real-time imaging and diagnosis of invasion depth in superficial esophageal squamous cell carcinoma. Gastrointestinal Endoscopy 81(6): 1355-1361.e2 | - Population not relevant to this review protocol<br>*squamous cell carcinoma only* |
| Elsheaita, A., El-Bially, M. A., Shamseya, M. M. et al. (2020) Seattle protocol vs narrow band imaging guided biopsy in screening of Barrett's esophagus in gastroesophageal reflux disease patients. Medicine (United States) 99 (8) | - Population not relevant to this review protocol<br>*patients with known Barrett's Oesophagus were excluded* |
| Everson, M. A., Lovat, L. B., Graham, D. G. et al. (2019) Virtual chromoendoscopy by using optical enhancement improves the detection of | - Study design not relevant to this review protocol |

| Study | Exclusion reason |
|---|---|
| Barrett's esophagus-associated neoplasia. Gastrointestinal Endoscopy 89(2): 247-256.e4 | *diagnostic accuracy of different endoscopists in detecting dysplasia from images obstained from HD imaging or iScan images + interobserver agreement.* |
| Ezoe, Y., Muto, M., Uedo, N. et al. (2011) Magnifying narrowband imaging is more accurate than conventional white-light imaging in diagnosis of gastric mucosal cancer. Gastroenterology 141(6): 2017-2025.e3 | - Population not relevant to this review protocol<br>*gastric mucosal cancer* |
| Gai, W., Jin, X. F., Du, R. et al. (2018) Efficacy of narrow-band imaging in detecting early esophageal cancer and risk factors for its occurrence. Indian Journal of Gastroenterology 37(2): 79-85 | - Population not relevant to this review protocol<br>*population mainly made up of squamous cell carcinoma of the head and neck* |
| Gangarosa, L. M.; Halter, S.; Mertz, H. (2000) Methylene blue staining and endoscopic ultrasound evaluation of Barrett's esophagus with low-grade dysplasia. Digestive Diseases & Sciences 45(2): 225-9 | - Study design not relevant to this review protocol<br>*no comparator* |
| Ghatwary, N.; Zolgharni, M.; Ye, X. (2019) Early esophageal adenocarcinoma detection using deep learning methods. International Journal of Computer Assisted Radiology & Surgery 14(4): 611-621 | - Study design not relevant to this review protocol<br>*deep learning neural networks tested to see if they can detect esophageal cancer from HD-white light imaging done previously (not at the same time)* |
| Giacchino, M., Bansal, A., Kim, R. E. et al. (2013) Clinical utility and interobserver agreement of autofluorescence imaging and magnification narrow-band imaging for the evaluation of Barrett's esophagus: a prospective tandem study. Gastrointestinal Endoscopy 77(5): 711-8 | - Study design not relevant to this review protocol<br>*Unclear if HD white light imaging is being used as a reference standard, as all biopsies were taken from AFI or NBI (from those seen as reactive)* |
| Gilani, N., Stipho, S., Shaukat, M. S. et al. (2007) The yield and safety of string capsule endoscopy in patients with dysphagia. Gastrointestinal Endoscopy 66(6): 1091-5 | - Population not relevant to this review protocol<br>*Patients with oesophageal symptoms - not Barrett's Oesophagus* |
| Goda, K., Takeuchi, M., Ishihara, R. et al. (2021) Diagnostic utility of a novel magnifying endoscopic classification system for superficial Barrett's esophagus-related neoplasms: a nationwide multicenter study. Esophagus 30: 30 | - Study design not relevant to this review protocol<br>*validation and test phase of criteria to diagnose HD-narrow band images for superficial non dysplastic Barrett's* |

| Study | Exclusion reason |
|---|---|
| Gralnek, I. M., Adler, S. N., Yassin, K. et al. (2008) Detecting esophageal disease with second-generation capsule endoscopy: initial evaluation of the PillCam ESO 2. Endoscopy 40(4): 275-279 | - Incorrect target condition: not dysplasia |
| Guo, J., Li, C. Q., Li, M. et al. (2015) Diagnostic value of probe-based confocal laser endomicroscopy and high-definition virtual chromoendoscopy in early esophageal squamous neoplasia. Gastrointestinal Endoscopy 81(6): 1346-54 | - Population not relevant to this review protocol<br>*Squamous cell carcinoma* |
| Hamamoto, Y., Endo, T., Nosho, K. et al. (2004) Usefulness of narrow-band imaging endoscopy for diagnosis of Barretts's esophagus. Journal of Gastroenterology 39(1): 14-20 | - Data not reported in an extractable format or a format that can be analysed<br>*diagnostic accuracy data not reported* |
| Haringsma, J. (2002) Barrett's oesophagus: New diagnostic and therapeutic techniques. Scandinavian Journal of Gastroenterology, Supplement 37(236): 9-14 | - Review article but not a systematic review |
| Heresbach, D., Leray, E., d'Halluin, P. N. et al. (2010) Diagnostic accuracy of esophageal capsule endoscopy versus conventional upper digestive endoscopy for suspected esophageal squamous cell carcinoma. Endoscopy 42(2): 93-7 | - Population not relevant to this review protocol<br>*investigating squamous cell carcinoma* |
| 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 | - Study design not relevant to this review protocol<br>*cost effectiveness analysis* |
| Hoffman, A., Kiesslich, R., Bender, A. et al. (2006) Acetic acid-guided biopsies after magnifying endoscopy compared with random biopsies in the detection of Barrett's esophagus: a prospective randomized trial with crossover design. Gastrointestinal Endoscopy 64(1): 1-8 | - Study design not relevant to this review protocol<br>*Diagnostic analysis unclear. Reports sensitivity stratified by Guelrud Classification* |
| Horie, Y., Yoshio, T., Aoyama, K. et al. (2019) Diagnostic outcomes of esophageal cancer by artificial intelligence using convolutional neural networks. Gastrointestinal Endoscopy 89(1): 25-32 | - Population not relevant to this review protocol<br>*mixed population of squamous and adenocarcinoma, results not stratified* |

| Study | Exclusion reason |
|---|---|
| Horwhat, J. D., Maydonovitch, C. L., Ramos, F. et al. (2008) A randomized comparison of methylene blue-directed biopsy versus conventional four-quadrant biopsy for the detection of intestinal metaplasia and dysplasia in patients with long-segment Barrett's esophagus. American Journal of Gastroenterology 103(3): 546-554 | - Data not reported in an extractable format or a format that can be analysed<br>*only reports sensitivities and no raw data for analysis* |
| Ikenoyama, Y., Yoshio, T., Tokura, J. et al. (2021) Artificial intelligence diagnostic system predicts multiple Lugol-voiding lesions in the esophagus and patients at high risk for esophageal squamous cell carcinoma. Endoscopy 04: 04 | - Population not relevant to this review protocol<br>*Squamous cell carcinoma* |
| Imaeda, H., Hosoe, N., Kashiwagi, K. et al. (2014) Surveillance using trimodal imaging endoscopy after endoscopic submucosal dissection for superficial gastric neoplasia. World Journal of Gastroenterology 20(43): 16311-7 | - Population not relevant to this review protocol<br>*investigating imaging techniques for gastric cancer* |
| Ishimura, N., Amano, Y., Uno, G. et al. (2012) Endoscopic characteristics of short-segment Barrett's esophagus, focusing on squamous islands and mucosal folds. Journal of Gastroenterology & Hepatology 27suppl3: 82-7 | - Population not relevant to this review protocol<br>*Squamous cell carcinoma* |
| Iwagami, H., Ishihara, R., Aoyama, K. et al. (2021) Artificial intelligence for the detection of esophageal and esophagogastric junctional adenocarcinoma. Journal of Gastroenterology & Hepatology 36(1): 131-136 | - Study design not relevant to this review protocol<br>*AI software diagnostic accuracy compared with white light imaging OR narrow band imaging* |
| Johanson, J. F.; Frakes, J.; Eisen, D. (2011) Computer-assisted analysis of abrasive transepithelial brush biopsies increases the effectiveness of esophageal screening: a multicenter prospective clinical trial by the endocdx collaborative group. Digestive Diseases and Sciences 56(3): 767-772 | - Study does not contain an intervention relevant to this review protocol<br>*forceps biopsy vs brush biopsies (not clear if using WLI as comparison). Also, mixed population with non BE participants for general investigation.* |
| Kara, M. A., Peters, F. P., Ten Kate, F. J. W. et al. (2005) Endoscopic video autofluorescence imaging may improve the detection of early neoplasia in patients with Barrett's esophagus. Gastrointestinal Endoscopy 61(6): 679-685 | - Data not reported in an extractable format or a format that can be analysed<br>*only some analysis of diagnostic data provided narratively - not enough for calculation* |
| Katada, C., Tanabe, S., Wada, T. et al. (2019) Retrospective Assessment of the Diagnostic | - Population not relevant to this review protocol |

| Study | Exclusion reason |
|---|---|
| Accuracy of the Depth of Invasion by Narrow Band Imaging Magnifying Endoscopy in Patients with Superficial Esophageal Squamous Cell Carcinoma. Journal of Gastrointestinal Cancer 50(2): 292-297 | *Squamous cell carcinoma* |
| Kaul, V., Gross, S., Corbett, F. S. et al. (2020) Clinical utility of wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS3D) in identifying Barrett's esophagus and associated neoplasia. Diseases of the Esophagus 33 (12) | - Study does not contain an intervention relevant to this review protocol<br>*no comparison to white light imaging* |
| Kodashima, S., Fujishiro, M., Ono, S. et al. (2014) Evaluation of a new image-enhanced endoscopic technology using band-limited light for detection of esophageal squamous cell carcinoma. Digestive Endoscopy 26(2): 164-71 | - Population not relevant to this review protocol<br>*Squamous cell carcinoma* |
| Kouklakis, G. S., Kountouras, J., Dokas, S. M. et al. (2003) Methylene blue chromoendoscopy for the detection of Barrett's esophagus in a Greek cohort. Endoscopy 35(5): 383-7 | - Data not reported in an extractable format or a format that can be analysed<br>*no diagnostic accuracy data* |
| Kuraoka, K., Hoshino, E., Tsuchida, T. et al. (2009) Early esophageal cancer can be detected by screening endoscopy assisted with narrow-band imaging (NBI). Hepato-Gastroenterology 56(89): 63-6 | - Population not relevant to this review protocol<br>*participants under investigation for high risk of oesophageal cancer (not Barrett's Oesophagus surveillance)* |
| Lee, C. T., Chang, C. Y., Lee, Y. C. et al. (2010) Narrow-band imaging with magnifying endoscopy for the screening of esophageal cancer in patients with primary head and neck cancers. Endoscopy 42(8): 613-9 | - Population not relevant to this review protocol<br>*majority of participants not Barrett's Oesophagus (2 out of 68)* |
| Leggett, C. L., Gorospe, E. C., Chan, D. K. et al. (2016) Comparative diagnostic performance of volumetric laser endomicroscopy and confocal laser endomicroscopy in the detection of dysplasia associated with Barrett's esophagus. Gastrointestinal Endoscopy 83(5): 880-888.e2 | - Study does not contain an intervention relevant to this review protocol<br>*probe based confocal laser endomicroscopy compared with volumetric laser endomicrosocopy (not compared to white light imaging)* |
| Li, B., Cai, S. L., Tan, W. M. et al. (2021) Comparative study on artificial intelligence systems for detecting early esophageal squamous cell carcinoma between narrow-band and white-light imaging. World Journal of Gastroenterology 27(3): 281-293 | - Population not relevant to this review protocol<br>*Squamous cell carcinoma* |

| Study | Exclusion reason |
|---|---|
| Li, H. Y., Dai, J., Xue, H. B. et al. (2012) Application of magnifying endoscopy with narrow-band imaging in diagnosing gastric lesions: a prospective study. Gastrointestinal Endoscopy 76(6): 1124-32 | - Population not relevant to this review protocol<br>*investigating for gastric cancer* |
| Lin, O. S., Schembre, D. B., Mergener, K. et al. (2007) Blinded comparison of esophageal capsule endoscopy versus conventional endoscopy for a diagnosis of Barrett's esophagus in patients with chronic gastroesophageal reflux. Gastrointestinal Endoscopy 65(4): 577-583 | - Incorrect target condition: not dysplasia |
| Liu, G., Hua, J., Wu, Z. et al. (2020) Automatic classification of esophageal lesions in endoscopic images using a convolutional neural network. Annals of Translational Medicine 8(7): 486 | - Study does not contain an intervention relevant to this review protocol<br>*building a computer based neural network to appropriately diagnose lesions via AI. Reference images a mixed population of White light imaging, narrow band imaging and Autofluorescence.* |
| Lui, T. K. L.; Tsui, V. W. M.; Leung, W. K. (2020) Accuracy of artificial intelligence-assisted detection of upper GI lesions: a systematic review and meta-analysis. Gastrointestinal Endoscopy 92(4): 821-830.e9 | - Systematic review used as source of primary studies |
| Mayinger, B., Oezturk, Y., Stolte, M. et al. (2006) Evaluation of sensitivity and inter- and intra-observer variability in the detection of intestinal metaplasia and dysplasia in Barrett's esophagus with enhanced magnification endoscopy. Scandinavian Journal of Gastroenterology 41(3): 349-356 | - Data not reported in an extractable format or a format that can be analysed<br>*diagnostic data reported according to experience and inter observer agreement between blinding* |
| Ngamruengphong, S.; Sharma, V. K.; Das, A. (2009) Diagnostic yield of methylene blue chromoendoscopy for detecting specialized intestinal metaplasia and dysplasia in Barrett's esophagus: a meta-analysis. Gastrointestinal Endoscopy 69(6): 1021-8 | - Systematic review used as source of primary studies |
| Ohmori, M., Ishihara, R., Aoyama, K. et al. (2020) Endoscopic detection and differentiation of esophageal lesions using a deep neural network. Gastrointestinal Endoscopy 91(2): 301-309.e1 | - Study not reported in English |

| Study | Exclusion reason |
|---|---|
| Qumseya, B. J., Wang, H., Badie, N. et al. (2013) Advanced imaging technologies increase detection of dysplasia and neoplasia in patients with Barrett's esophagus: a meta-analysis and systematic review. Clinical Gastroenterology & Hepatology 11(12): 1562-70.e1 | - Systematic review used as source of primary studies |
| Rogart, J. N.; Aslanian, H. R.; Siddiqui, U. D. (2011) Narrow band imaging to detect residual or recurrent neoplastic tissue during surveillance endoscopy. Digestive Diseases and Sciences 56(2): 472-478 | - Population not relevant to this review protocol<br><br>*gastric or colorectal cancer* |
| Ross-Innes, C. S., Debiram-Beecham, I., O'Donovan, M. et al. (2015) Evaluation of a minimally invasive cell sampling device coupled with assessment of trefoil factor 3 expression for diagnosing Barrett's esophagus: a multi-center case-control study. PLoS Medicine / Public Library of Science 12(1): e1001780 | - Comparator in study does not match that specified in this review protocol<br><br>*non endoscopic cell collection device compared to endoscopic* |
| 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 does not contain an intervention relevant to this review protocol<br><br>*high resolution white light endoscopy compared to standard endoscopy white light endoscopy* |
| Saxena, P. and Canto, M. I. (2013) Red flag imaging techniques in Barrett's esophagus. Gastrointestinal Endoscopy Clinics of North America 23(3): 535-47 | - Review article but not a systematic review |
| Shah, T., Lippman, R., Kohli, D. et al. (2018) Accuracy of probe-based confocal laser endomicroscopy (pCLE) compared to random biopsies during endoscopic surveillance of Barrett's esophagus. Endoscopy International Open 6(4): E414-E420 | - Study design not relevant to this review protocol<br><br>*white light imaging and narrow band imaging compared to probe based confocal laser endomicroscopy* |
| Shariff, M. K., Bird-Lieberman, E. L., O'Donovan, M. et al. (2012) Randomized crossover study comparing efficacy of transnasal endoscopy with that of standard endoscopy to detect Barrett's esophagus. Gastrointestinal Endoscopy 75(5): 954-961 | - Incorrect target condition: not dysplasia |
| Sharma, P., Wani, S., Rastogi, A. et al. (2008) The diagnostic accuracy of esophageal capsule endoscopy in patients with gastroesophageal reflux disease and Barrett's esophagus: a | - Incorrect target condition: not dysplasia |

| Study | Exclusion reason |
|---|---|
| blinded, prospective study. American Journal of Gastroenterology 103(3): 525-32 | |
| Singh, R., Jayanna, M., Wong, J. et al. (2015) Narrow-band imaging and white-light endoscopy with optical magnification in the diagnosis of dysplasia in Barrett's esophagus: results of the Asia-Pacific Barrett's Consortium. Endoscopy International Open 3(1): E14-8 | - Study design not relevant to this review protocol<br><br>*comparison of interobserver agreement and diagnostic accuracy of different endoscopists to identify the histology* |
| Singh, R., Karageorgiou, H., Owen, V. et al. (2009) Comparison of high-resolution magnification narrow-band imaging and white-light endoscopy in the prediction of histology in Barrett's oesophagus. Scandinavian Journal of Gastroenterology 44(1): 85-92 | - Study design not relevant to this review protocol<br><br>*prediction of morphology by multiple endoscopists to differentiate between WLI and NBI* |
| Smith, M. S., Ikonomi, E., Bhuta, R. et al. (2019) Wide-area transepithelial sampling with computer-assisted 3-dimensional analysis (WATS) markedly improves detection of esophageal dysplasia and Barrett's esophagus: Analysis from a prospective multicenter community-based study. Diseases of the Esophagus 32(3) | - Data not reported in an extractable format or a format that can be analysed<br><br>*detection rates of yield with WATS3D and forceps biopsy* |
| Song, J., Zhang, J., Wang, J. et al. (2015) Meta-analysis of the effects of endoscopy with narrow band imaging in detecting dysplasia in Barrett's esophagus. Diseases of the Esophagus 28(6): 560-6 | - Systematic review used as source of primary studies |
| Struyvenberg, M. R., de Groof, A. J., van der Putten, J. et al. (2021) A computer-assisted algorithm for narrow-band imaging-based tissue characterization in Barrett's esophagus. Gastrointestinal Endoscopy 93(1): 89-98 | - Study design not relevant to this review protocol<br><br>*computer aided diagnosis using previous images from white light imaging and narrow band imaging* |
| Su, Z., Wang, L., Wei, S. et al. (2019) Clinical diagnostic value of digestive endoscopic narrow-band imaging in early esophageal cancer. Oncology Letters 17(6): 5481-5486 | - Study design not relevant to this review protocol<br><br>*case control study comparing narrow band imaging with white light images as control (unclear if patients underwent both procedures)* |
| Suzuki, H., Saito, Y., Ikehara, H. et al. (2009) Evaluation of visualization of squamous cell carcinoma of esophagus and pharynx using an autofluorescence imaging videoendoscope system. Journal of Gastroenterology & Hepatology 24(12): 1834-9 | - Population not relevant to this review protocol<br><br>*squamous cell carcinoma* |

| Study | Exclusion reason |
|---|---|
| Tanaka, T., Niwa, Y., Tajika, M. et al. (2014) Prospective evaluation of a transnasal endoscopy utilizing flexible spectral imaging color enhancement (FICE) with the Valsalva maneuver for detecting pharyngeal and esophageal cancer. Hepato-Gastroenterology 61(134): 1627-34 | - Population not relevant to this review protocol<br><br>*investigation of head and neck cancer with squamous cell carcinoma* |
| Thota, P. N., Zuccaro Jr, G., Vargo, Ii J. J. et al. (2005) A randomized prospective trial comparing unsedated esophagoscopy via transnasal and transoral routes using a 4-mm video endoscope with conventional endoscopy with sedation. Endoscopy 37(6): 559-565 | - Study design not relevant to this review protocol<br><br>*general investigation for multiple gastro-oesophageal conditions* |
| Tokai, Y., Yoshio, T., Aoyama, K. et al. (2020) Application of artificial intelligence using convolutional neural networks in determining the invasion depth of esophageal squamous cell carcinoma. Esophagus 17(3): 250-256 | - Population not relevant to this review protocol<br><br>*Squamous cell carcinoma* |
| Tomie, A., Dohi, O., Yagi, N. et al. (2016) Blue Laser Imaging-Bright Improves Endoscopic Recognition of Superficial Esophageal Squamous Cell Carcinoma. Gastroenterology Research and Practice 2016 (no pagination) | - Population not relevant to this review protocol<br><br>*squamous cell carcinoma* |
| Tsoi, E. H., Fehily, S., Williams, R. et al. (2019) Diffuse endoscopically visible, predominantly low grade dysplasia in Barrett's esophagus (with video). Endoscopy International Open 7(12): E1742-E1747 | - Study design not relevant to this review protocol<br><br>*non comparative study* |
| Uedo, N., Iishi, H., Tatsuta, M. et al. (2005) A novel videoendoscopy system by using autofluorescence and reflectance imaging for diagnosis of esophagogastric cancers. Gastrointestinal Endoscopy 62(4): 521-8 | - Data not reported in an extractable format or a format that can be analysed<br><br>*incomplete data reported* |
| Ueyama, H., Kato, Y., Akazawa, Y. et al. (2021) Application of artificial intelligence using a convolutional neural network for diagnosis of early gastric cancer based on magnifying endoscopy with narrow-band imaging. Journal of Gastroenterology & Hepatology 36(2): 482-489 | - Population not relevant to this review protocol<br><br>*investigation for gastric cancer* |
| Van Der Sommen, F., Zinger, S., Curvers, W. L. et al. (2016) Computer-aided detection of early neoplastic lesions in Barrett's esophagus. Endoscopy 48(7): 617-624 | - Incorrect target condition: not dysplasia |

| Study | Exclusion reason |
|---|---|
| Vazquez-Iglesias, J. L., Alonso-Aguirre, P., Diz-Lois, M. T. et al. (2007) Acetic acid allows effective selection of areas for obtaining biopsy samples in Barrett's esophagus. European Journal of Gastroenterology & Hepatology 19(3): 187-93 | - Comparator in study does not match that specified in this review protocol<br><br>*unclear if white light imaging was used as a reference standard for comparison* |
| Verna, C., Feyles, E., Lorenzi, L. et al. (2014) I-SCAN targeted versus random biopsies in Barrett's oesophagus. Digestive and Liver Disease 46(2): 131-134 | - Data not reported in an extractable format or a format that can be analysed<br><br>*only reports inter-observer agreement* |
| Visaggi, P., Barberio, B., Gregori, D. et al. (2022) Systematic review with meta-analysis: artificial intelligence in the diagnosis of oesophageal diseases. Alimentary pharmacology & therapeutics | - Systematic review used as source of primary studies |
| Wang, F., Liu, P., Zhao, K. et al. (2016) Magnifying endoscopy combined with narrow-band imaging for targeted biopsy of superficial lesions in esophagus. Chinese journal of gastroenterology 21(10): 597-601 | - Study not reported in English |
| Wang, Y. K., Syu, H. Y., Chen, Y. H. et al. (2021) Endoscopic Images by a Single-Shot Multibox Detector for the Identification of Early Cancerous Lesions in the Esophagus: A Pilot Study. Cancers 13(2): 17 | - Population not relevant to this review protocol<br><br>*Squamous cell carcinoma* |
| Watanabe, A., Taniguchi, M., Tsujie, H. et al. (2008) The value of narrow band imaging endoscope for early head and neck cancers. Otolaryngology - Head & Neck Surgery 138(4): 446-51 | - Study does not contain an intervention relevant to this review protocol<br><br>*rhinolaryngo-videoscopic examinations for head and neck cancers* |
| Waxman, I., Raju, G. S., Critchlow, J. et al. (2006) High-frequency probe ultrasonography has limited accuracy for detecting invasive adenocarcinoma in patients with Barrett's esophagus and high-grade dysplasia or intramucosal carcinoma: a case series. American Journal of Gastroenterology 101(8): 1773-9 | - Data not reported in an extractable format or a format that can be analysed<br><br>*some data given, but unclear of diagnostic data for calculation* |
| Wo, J. M., Ray, M. B., Mayfield-Stokes, S. et al. (2001) Comparison of methylene blue-directed biopsies and conventional biopsies in the detection of intestinal metaplasia and dysplasia in Barrett's esophagus: a preliminary study. Gastrointestinal Endoscopy 54(3): 294-301 | - Population not relevant to this review protocol<br><br>*mixed population of patients with heartburn (investigation) and some Barrett's (surveillance)* |

| Study | Exclusion reason |
|---|---|
| Wu, C. C. H., Namasivayam, V., Li, J. W. et al. (2021) A prospective randomized tandem gastroscopy pilot study of linked color imaging versus white light imaging for detection of upper gastrointestinal lesions. Journal of Gastroenterology and Hepatology (Australia) | - Population not relevant to this review protocol<br>*not investigating for barrett's oesophagus* |
| Wu, I. C., Syu, H. Y., Jen, C. P. et al. (2018) Early identification of esophageal squamous neoplasm by hyperspectral endoscopic imaging. Scientific Reports 8(1): 13797 | - Population not relevant to this review protocol<br>*Squamous cell carcinoma* |
| Yang, S, Wu, S, Huang, Y et al. (2012) Screening for oesophageal cancer. Cochrane Database of Systematic Reviews | - Systematic review used as source of primary studies |
| Yang, X. X., Li, Z., Shao, X. J. et al. (2020) Real-time artificial intelligence for endoscopic diagnosis of early esophageal squamous cell cancer (with video). Digestive Endoscopy 04: 04 | - Population not relevant to this review protocol<br>*Squamous cell carcinoma* |
| Yokoyama, A., Ichimasa, K., Ishiguro, T. et al. (2012) Is it proper to use non-magnified narrow-band imaging for esophageal neoplasia screening? Japanese single-center, prospective study. Digestive Endoscopy 24(6): 412-418 | - Population not relevant to this review protocol<br>*mixed results with squamous cell carcinoma, high grade and low grade neoplasia* |
| Yoshimizu, S., Yamamoto, Y., Horiuchi, Y. et al. (2018) Diagnostic performance of routine esophagogastroduodenoscopy using magnifying endoscope with narrow-band imaging for gastric cancer. Digestive Endoscopy 30(1): 71-78 | - Population not relevant to this review protocol<br>*gastric cancer* |
| Zhang, Q. W., Teng, L. M., Zhang, X. T. et al. (2017) Narrow-band imaging in the diagnosis of deep submucosal colorectal cancers: a systematic review and meta-analysis. Endoscopy 49(6): 564-580 | - Population not relevant to this review protocol<br>*SR for studies related to colorectal cancer* |
| Zhang, S. M.; Wang, Y. J.; Zhang, S. T. (2021) Accuracy of artificial intelligence-assisted detection of esophageal cancer and neoplasms on endoscopic images: A systematic review and meta-analysis. Journal of Digestive Diseases 22(6): 318-328 | - 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 H – Research recommendations

## Endoscopic surveillance

What is the diagnostic accuracy of different endoscopic surveillance techniques including high resolution endoscopy and chromoendoscopy for use in adults?

### Why this is important

Chromoendoscopy, electronic imaging and more recently artificial intelligence have all shown considerable promise in enriched patient populations but their utility in a surveillance population is unclear. In order for image enhanced endoscopy based surveillance protocols to be implemented robust data in a low risk Barrett's surveillance population (i.e. patients who have no history of previous dysplasia or cancer) is needed from high quality fully powered studies.

Large scale studies in patients undergoing endoscopic surveillance are therefore recommended for assessing clinical and cost effectiveness of image enhanced endoscopy in surveillance of Barrett's oesophagus. Narrow band imaging, acetic acid and artificial intelligence are considered as most appropriate for clinical trials.

### Rationale for research recommendation

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| Importance to 'patients' or the population | There is a clinical need to improve upon the current approach of Mapping biopsies in Barrett's surveillance, which is expensive, time consuming and misses pathology. Image enhanced endoscopy has the potential to offer improved surveillance leading to better outcomes for people with Barrett's oesophagus. The clinical and cost effectiveness of this in a Barrett's surveillance population has not been demonstrated by healthcare research to date. |
| Relevance to NICE guidance | Good quality research in this area supporting the effectiveness of image enhanced endoscopy techniques could allow NICE to recommend them for surveillance, reducing the number of missed pathologies and in-turn improving health outcomes for patients. |
| Relevance to the NHS | An image enhanced endoscopy protocol could make Barrett's surveillance more effective with a reduction in missed pathology and greater cost effectiveness. |
| National priorities | None. |
| Current evidence base | There is evidence for acetic acid chromoendoscopy and narrow band imaging in high risk 'enriched' populations to suggest that both of these techniques are effective at identifying neoplasia. Most of these are cohort studies. There has been a pilot NIHR funded randomized crossover endoscopy study of acetic acid in a surveillance population which |

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| | suggested the feasibility of conducting a fully powered trial this patient group. This included qualitative data on patient experience suggesting that patients felt this kind of work was acceptable and necessary. To date, published evidence on the effectiveness of artificial intelligence in people with Barrett's oesophagus has been very limited. |
| Equality considerations | None. |

### H.1.1 Modified PICO table

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| Population | Adults undergoing surveillance for Barrett's oesophagus with no history of previous dysplasia or cancer of the oesophagus. |
| Intervention | Image enhanced endoscopy or artificial intelligence targeted biopsy protocol |
| Comparator | Seattle protocol mapping biopsies |
| Outcome | Neoplasia yield (low grade dysplasia high grade dysplasia and cancer) using each technique. Cost per neoplasia and cost difference of Barrett's surveillance between surveillance techniques adverse events; reoperation for mesh exposure; reoperation for stress urinary incontinence |
| Study design | Multi-centre randomized endoscopy study with Cross-over design |
| Timeframe | Long term |
| Additional information | None |