Supplementary Material

**Supplementary table 1**: definition of dysplasia used by pathologist reading WATS samples.

| Study               | Dysplasia reported | Both positive | Only FB + WATS | Only FB + only WATS | Both negative |
|---------------------|--------------------|---------------|----------------|----------------------|---------------|
| Anandasabapathy 2011| LGD/HGD/AC         | 15            | 23             | 16                   | 97            |
| Johanson 2011       | LGD/HGD/AC         | 4             | 8              | 7                    | 372           |
| Smith 2019          | HGD/AC             | 1             | 2              | 6                    | 2478          |
| Bisschops 2020      | HGD/AC             | 25            | 10             | 14                   | 98            |
| Dunkle 2020         | HGD/AC             | 2             | 5              | 1                    | 94            |
| Vennalaganti 2018   | HGD/AC             | 6             | 7              | 29                   | 70            |
**Supplementary table 2**: tabular presentation for QUADAS-2 results

| Study               | Publication type | PATIENT SELECTION | INDEX TEST | REFERENCE STANDARD | FLOW AND TIMING | PATIENT SELECTION | INDEX TEST | REFERENCE STANDARD |
|---------------------|------------------|-------------------|------------|--------------------|----------------|-------------------|------------|--------------------|
| Vennalaganti 2018   | Manuscript       | ☺                 | ☺          | ☺                  | ☺              | ☺                 | ☺          | ☺                  |
| Anandasabapathy 2011| Manuscript       | ☇                 | ☺          | ☺                  | ☺              | ☺                 | ☺          | ☺                  |
| Johanson 2011       | Manuscript       | ☺                 | ☇          | ☇                  | ☇              | ☺                 | ☇          | ☺                  |
| Gross 2018          | Manuscript       | ☺                 | ☇          | ☮                  | ☺              | ☺                 | ☇          | ☺                  |
| Smith 2019          | Manuscript       | ☺                 | ☺          | ☺                  | ☮              | ☺                 | ☺          | ☺                  |
| Raphael 2019        | Manuscript       | ☔                 | ☔          | ☔                  | ☔              | ☔                 | ☔          | ☔                  |

- ☺ Low Risk
- ☇ High Risk
- ☔ Unclear Risk
**Supplementary figure 1:** Forest plots of the additional yield in Barrett’s esophagus (BE) detection

| Study name       | Risk ratio | Lower limit | Upper limit | p-Value |
|------------------|------------|-------------|-------------|---------|
| Johanson 2011    | 1.71       | 1.43        | 2.05        | 0.000   |
| Gross 2018       | 1.83       | 1.67        | 2.00        | 0.000   |
| Smith 2019       | 2.53       | 2.40        | 2.66        | 0.000   |
| Srinivasan 2019  | 1.32       | 1.09        | 1.61        | 0.005   |

Meta Analysis

```
0.1 0.2 0.5 1 2 5 10
```
**Supplementary figure 2:** (a) funnel plot of standard of error by Log risk ratio for studies assessing the additional yield of all dysplasia in WATS compared to forceps biopsies; (b) forest plot of the additional yield of all dysplasia with one study removed at a time; (c) sensitivity analysis of the additional yield of all dysplasia when an outlier study was included; (d) sensitivity analysis of the additional yield of all dysplasia stratified by study design; and (e) sensitivity analysis of the additional yield of all dysplasia stratified by publication type (abstract vs. manuscript).
### Supplementary material

#### (c)

| Study name             | Risk ratio | Lower limit | Upper limit | p-Value |
|------------------------|------------|-------------|-------------|---------|
| Vennalaganti 2018      | 1.83       | 1.29        | 2.59        | 0.001   |
| Anandasabapathy 2011   | 1.42       | 1.00        | 2.01        | 0.048   |
| Dunkle 2020            | 2.44       | 1.17        | 5.09        | 0.017   |
| Raphael 2019           | 1.67       | 1.04        | 2.66        | 0.033   |
| Elden 2020             | 9.40       | 3.77        | 23.44       | 0.000   |
| Johanson 2011          | 1.58       | 0.78        | 3.22        | 0.204   |
| Gross 2018             | 1.92       | 1.21        | 3.07        | 0.006   |
| Smith 2019a            | 1.65       | 0.91        | 2.99        | 0.100   |
|                         | 1.94       | 1.47        | 2.55        | 0.000   |

#### (d)

| Group by Study design  | Study name     | Risk ratio | Lower limit | Upper limit | p-Value |
|------------------------|----------------|------------|-------------|-------------|---------|
| Prospective            | Vennalaganti 2018 | 1.83       | 1.29        | 2.59        | 0.001   |
| Prospective            | Anandasabapathy 2011 | 1.42       | 1.00        | 2.01        | 0.048   |
| Prospective            | Johanson 2011    | 1.58       | 0.78        | 3.22        | 0.204   |
| Prospective            | Gross 2018       | 1.92       | 1.21        | 3.07        | 0.006   |
| Prospective            | Smith 2019a      | 1.65       | 0.91        | 2.99        | 0.100   |
| Retrospective          | Dunkle 2020      | 2.44       | 1.17        | 5.09        | 0.017   |
| Retrospective          | Raphael 2019     | 1.67       | 1.04        | 2.66        | 0.033   |
| Retrospective          | Smith 2019a      | 1.65       | 0.91        | 2.99        | 0.100   |
| Retrospective          | Smith 2019a      | 1.79       | 1.29        | 2.49        | 0.001   |

#### (e)

| Group by Design        | Study name     | Risk ratio | Lower limit | Upper limit | p-Value |
|------------------------|----------------|------------|-------------|-------------|---------|
| Abstract               | Dunkle 2020    | 2.44       | 1.17        | 5.09        | 0.017   |
| Abstract               | Smith 2019a    | 1.65       | 0.91        | 2.99        | 0.100   |
| Abstract               | Johanson 2011  | 1.58       | 0.78        | 3.22        | 0.204   |
| Manuscript             | Vennalaganti 2018 | 1.83       | 1.29        | 2.59        | 0.001   |
| Manuscript             | Anandasabapathy 2011 | 1.42       | 1.00        | 2.01        | 0.048   |
| Manuscript             | Raphael 2019   | 1.67       | 1.04        | 2.66        | 0.033   |
| Manuscript             | Johanson 2011  | 1.58       | 0.78        | 3.22        | 0.204   |
| Manuscript             | Gross 2018     | 1.92       | 1.21        | 3.07        | 0.006   |
| Manuscript             | Gross 2018     | 1.67       | 1.38        | 2.02        | 0.000   |
**Appendix 1**: search strategy and terms for each search engine.

Cochrane Library (Wiley Online Library)/CENTRAL

### Search Name: Qumseya Barrett's Esophagus, WATS

| ID | Search                                                                 | Hits                                                                 |
|----|------------------------------------------------------------------------|----------------------------------------------------------------------|
| #1 | MeSH descriptor: [Barrett Esophagus] explode all trees                 |                                                                      |
| #2 | (barrett esophag* OR barrett's esophag* OR barretts esophag* OR barrett oesophag* OR barrett's oesophag* OR barretts oesophag*):ti,ab,kw |                                                                      |
| #3 | #1 OR #2                                                               |                                                                      |
| #4 | (wide NEAR/2 area):ti,ab,kw                                           |                                                                      |
| #5 | (WATS* or 3D?WATS or EndoCDx or Endo?CDx or CDx or brush or transepithelial or trans?epithelial or WATS3D or "WATS-3D" or "WATS 3D"):ti,ab,kw |                                                                      |
| #6 | (brush NEAR/2 biops*):ti,ab,kw                                        |                                                                      |
| #7 | MeSH descriptor: [Specimen Handling] explode all trees                 |                                                                      |
| #8 | MeSH descriptor: [Biopsy] explode all trees                            |                                                                      |
| #9 | MeSH descriptor: [Image Interpretation, Computer-Assisted] explode all trees |                                                                |
| #10| MeSH descriptor: [Electronic Data Processing] explode all trees         |                                                                      |
#11  #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
#12  #3 AND #11

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Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily

1  exp Barrett Esophagus/

2  (barrett* esophag* or barrett* oesophag*).ti,ab,kw.

3  1 or 2

4  (wide adj2 area).ti,ab,kw.

5  (WATS* or 3D?WATS or EndoCDx or Endo?CDx or CDx or brush or 
  transepithelial or trans?epithelial or WATS3D or "WATS-3D" or "WATS 
  3D").ti,ab,kw.

6  (brush adj2 biops*).ti,ab,kw.

7  exp specimen handling/ or exp biopsy/

8  exp image interpretation, computer-assisted/ or Automatic Data Processing/

9  7 or 8

10  4 or 5 or 6 or 9

11  exp Esophagus/

12  (esophag* OR oesophag*).ti,ab,kw.

13  11 or 12

14  3 and 10 and 13

15  sensitiv:.mp.
16 diagnos:.mp.
17 di.fs.
18 or/15-17
19 animals/
20 humans/
21 19 not (19 and 20)
22 18 not 21
23 14 and 22

Filter: Haynes RB, Wilczynski NL. Optimal search strategies for retrieving scientifically strong studies of diagnosis from Medline: analytical survey. BMJ. 2004;328(7447):1040. Also at http://hiru.mcmaster.ca/hiru/HIRU_Hedges_MEDLINE_Strategies.aspx

PubMed
***
"Barrett Esophagus"[Mesh] OR barrett esophag*[tiab] OR barrett's esophag*[tiab] OR barretts esophag*[tiab] OR barrett oesophag*[tiab] OR barrett's oesophag*[tiab] OR barretts oesophag*[tiab]
wide-area[tiab] OR WATS*[tiab] OR WATS[tiab] OR "3D WATS"[tiab] OR "3D-WATS"[tiab] OR WATS3D[tiab] OR WATS-3D[tiab] OR "WATS 3D"[tiab] OR EndoCDx[tiab] OR Endo-CDx[tiab] OR CDx[tiab] OR brush[tiab] OR transepithelial[tiab] OR trans-epithelial[tiab] OR "trans epithelial"[tiab] OR "wide area"[tiab] OR ("Specimen Handling"[Mesh:NoExp] OR "Biopsy"[Mesh] OR "Automatic Data Processing"[Mesh:NoExp] OR "Image Interpretation, Computer-Assisted"[Mesh])

("Esophagus"[Mesh] OR esophag*[tiab] OR oesophag*[tiab])

sensitiv*[tiab] OR sensitivity and specificity[Mesh] OR diagnos*[tiab] OR diagnosis[MeSH:noexp] OR diagnostic* [MeSH:noexp] OR diagnosis,differential[MeSH:noexp] OR diagnosis[Subheading:noexp]

#1 AND #2 AND #3 AND #4

NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))

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Embase (Elsevier)

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Review

Supplementary material

(barrett* NEXT/1 esophag*):ab,ti OR (barrett* NEXT/1 oesophag*):ab,ti OR 'Barrett esophagus'/exp

WATS*:ab,ti OR WATS:ab,ti OR '3D WATS':ab,ti OR '3D-WATS':ab,ti OR WATS3D:ti,ab OR WATS-3D:ti,ab OR "WATS 3D":ti,ab OR EndoCDx:ab,ti OR Endo?CDx:ab,ti OR CDx:ab,ti OR (brush NEAR/2 biops*):ab,ti OR transepithelial:ab,ti OR trans?epithelial:ab,ti OR ('sampling'/exp OR 'biopsy'/exp) AND ((computer NEAR/1 assist*):ab,ti OR (3?dimensional:ab,ti OR three?dimensional:ab,ti OR 3?D:ab,ti OR threedimensional:ab,ti) OR 'computer analysis'/exp)

'Esophagus'/exp OR esophag*:ab,ti OR oesophag*:ab,ti

#1 AND #2 AND #3

-------------------

Web of Science (Clarivate Analytics)

Science Citation Index Expanded (SCI-EXPANDED) --1900-present

Conference Proceedings Citation Index- Science (CPCI-S) --1993-present

Search run June 2019

184 Records

***
1 TS="barrett esophag*" OR "barrett’s esophag*" OR "barretts esophag*" OR "barrett oesophag*" OR "barrett's oesophag*" OR "barretts oesophag*"

2 TS=(wide NEAR/2 area)

3 TS=(brush NEAR/2 biops*)

4 TS=(computer NEAR/2 assist*)

5 TS=(WATS* OR WATS OR "3D WATS" OR "3D-WATS" OR WATS3D OR WATS-3D OR "WATS 3D" OR EndoCDx OR Endo-CDx OR transepithelial OR trans-epithelial OR "trans epithelial" OR 3-dimensional OR three-dimensional OR 3-D OR 3D)

6 #2 OR #3 OR #4 OR #5

7 TS=(esophag* OR oesophag*)

8 # 1 AND #6 AND #7

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ClinicalTrials.gov

***
Supplementary material

(barrett's OR barrett OR barretts) AND (esophagus OR oesophagus OR esophageal OR oesophageal) | Phase 2, 3, 4

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World Health Organization International Clinical Trials Registry Platform (WHO ICTRP)
Search run June 2019
47 Records
***

Condition: (barrett's OR barrett OR barretts) AND (esophag* OR oesophag*) | Phase 2, 3, 4
| Section and Topic | Item # | Checklist item                                                                 | Location where item is reported |
|------------------|--------|-------------------------------------------------------------------------------|---------------------------------|
| **TITLE**        | 1      | Identify the report as a systematic review.                                  | 1                               |
| **ABSTRACT**     | 2      | See the PRISMA 2020 for Abstracts checklist.                                  | 4-5                             |
| **INTRODUCTION** | 3      | Describe the rationale for the review in the context of existing knowledge.   | 6                               |
|                  | 4      | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 6                               |
| **METHODS**      | 5      | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 7                               |
|                  | 6      | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | 7                               |
|                  | 7      | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Appendix                        |
|                  | 8      | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | 7                               |
|                  | 9      | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | 8                               |
|                  | 10a    | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | 8-9                             |
|                  | 10b    | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | 8-9                             |
|                  | 11     | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | 10                              |
|                  | 12     | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | 8-10                            |
|                  | 13a    | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | 7                               |
|                  | 13b    | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | 7-9                             |
|                  | 13c    | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | 10-11                           |
|                  | 13d    | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | 10-11                           |
|                  | 13e    | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | 9-11                            |
|                  | 13f    | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | 10                              |
| **Reporting bias assessment** | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | 11                              |
| **Certainty assessment** | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | 9-11                            |
### PRISMA 2020 Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|-------------------|--------|----------------|---------------------------------|
| **RESULTS**       |        |                |                                 |
| Study selection   | 16a    | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | 15 |
|                   | 16b    | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | 15 |
| Study characteristics | 17   | Cite each included study and present its characteristics. | Table 1 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Supp table 2 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots. | 11-13 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | 11-15 |
|                   | 20b   | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | 11-15 |
|                   | 20c   | Present results of all investigations of possible causes of heterogeneity among study results. | 15 |
|                   | 20d   | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | 15 |
| Reporting biases  | 21    | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | 14-15 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | 11-12 |
| **DISCUSSION**    |        |                |                                 |
| Discussion        | 23a    | Provide a general interpretation of the results in the context of other evidence. | 15 |
|                   | 23b    | Discuss any limitations of the evidence included in the review. | 18-20 |
|                   | 23c    | Discuss any limitations of the review processes used. | 18-20 |
|                   | 23d    | Discuss implications of the results for practice, policy, and future research. | 20-21 |
| **OTHER INFORMATION** |        |                |                                 |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | NA |
|                   | 24b    | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | 7 |
|                   | 24c    | Describe and explain any amendments to information provided at registration or in the protocol. | None |
| Support           | 25    | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | 2 |
| Competing interests | 26  | Declare any competing interests of review authors. | 2 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | NA |

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed.1000097

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