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META-ANALYSIS

The diagnostic yield of pan-enteric capsule endoscopy in inflammatory bowel disease: A systematic review and meta-analysis

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Abstract

Background and Aim: Capsule endoscopy (CE) is a non-invasive diagnostic modality enabling real time video imaging of the gastrointestinal (GI) mucosa. Pan-enteric capsule endoscopy (PCE) is now able to thoroughly assess the entire GI tract, including for inflammatory bowel disease (IBD). Our aim was to evaluate the diagnostic accuracy of PCEs in IBD.
Methods: We comprehensively searched electronic databases (MEDLINE, SCOPUS, EMBASE, and Cochrane Central Register of Controlled Trials) for studies comparing the diagnostic accuracy of PCE with endoscopic evaluation, intestinal ultrasound or magnetic resonance enterography (MRE). Data were analyzed by calculating forest plots and the use of the I^2 statistic for heterogeneity.
Results: Fourteen studies were identified, with seven studies evaluating PCE diagnostic yield in Crohn's disease (CD) and seven studies in ulcerative colitis (UC). In CD, there was a trend to superiority of PCE over MRE and colonoscopy with a pooled odds ratio (OR) of 1.25 (95% CI, 0.85–1.86%) for the detection of CD. This translates to an increased diagnostic yield of 5% and 7% for PCE compared with MRE and colonoscopy, respectively. PCEs had a diagnostic sensitivity for the detection of UC of 93.8% (95% CI, 87.6–97.0%) and a specificity of 69.8% (95% CI, 38.2–89.6%).
Conclusion: PCEs have a comparable diagnostic yield to colonoscopy and MRE in Crohn's disease. The major difficulty remains standardization of PCE scoring systems and the lack of transmural assessment. In UC, PCE has an excellent diagnostic sensitivity and positive predictive value, but there are limitations to its use including the lack of histologic assessment and poor specificity.

Introduction

The advent of wireless capsule endoscopy in 2000 revolutionized the imaging and diagnosis of disorders of the small intestine.[1,2] It was hoped the subsequent development of colon capsule endoscopy (CCE) would similarly transform imaging of the large bowel and reduce the need for diagnostic colonoscopy.[3] However, the first generation of CCEs had limitations in their ability to detect clinically significant polyps or masses. To address these inadequacies, upgraded technology was incorporated into the 2nd generation of CCE (CCE-2). The addition of adaptive frame rate technology and a wider viewing angle significantly improved the diagnostic capabilities of this device.[4] The most recent iteration of CCE systems, the Pillcam Crohn's (Medtronic, USA), has been developed to detect lesions consistent with inflammatory bowel diseases (IBD). Technological improvements such as reporting software that facilitates temporal monitoring of disease activity, structured Lewis score reporting, improved device localisation and prolonged battery life have been made.[5,6] In this study, we collectively refer to these capsules (CCE-1, CCE-2, and Pillcam Crohn's) as pan-enteric capsule endoscopy systems (PCE) as they can image the entire GI tract and are not limited to the colon.

There are numerous available modalities for the diagnostic assessment of IBD, including small bowel follow through, computed tomographic enterography (CTE), magnetic resonance enterography (MRE), intestinal ultrasound (IUS), capsule endoscopy, and colonoscopy. In the absence of a single, reliable diagnostic test, thorough evaluation of the entire gastrointestinal tract has required the use of two or more modalities. The additive value of a pan-enteric capsule endoscopy is its potential to reduce the duplication of tests, by assessing the small and large bowel in a single procedure without the need for invasive endoscopic assessment. However, the clear limitation of PCE in diagnosis and monitoring of IBD is its inability to collect samples for histological analysis.

Previous meta-analyses have reported that the diagnostic accuracy of small bowel capsule endoscopy in small bowel CD is

equivalent to MRE and IUS and may in fact to be superior to CTE.[7,8] However, unlike studies reporting on colonic polyp detection by CCE or the role of small bowel capsule endoscopy in CD diagnosis, there are fewer studies reporting on the diagnostic accuracy of PCE in IBD. The aim of this systematic review and meta-analysis is to evaluate the available data to determine the accuracy of PCEs in diagnosing and detecting active IBD (CD or UC), and their ability act as a single diagnostic tool in IBD.

Methods

Methods of analysis and inclusion criteria were based on PRISMA recommendations,[9] and the study protocol was prospectively registered with the PROSPERO register.[10]

Eligibility criteria. We considered all clinical studies (involving adult, human subjects), both in abstract form and fully published manuscripts, that evaluated the diagnostic yield of PCE systems in patients with inflammatory bowel disease. The use of a comparator arm (colonoscopy, enteroscopy, IUS, or MRI) was required for the study to be included. Non-English studies, review studies or studies reporting the results of < 10 patients were excluded.

Information sources. Relevant publications were identified from the EMBASE, MEDLINE, SCOPUS, and Cochrane Central Register of Controlled Trials (CENTRAL) databases. Additional publications were identified from searching the references of the extracted studies. The electronic search included all studies up to September 2021, with no other time limitations. A thorough search was conducted including the following pre-specified MeSH and non-MeSH terms: "Inflammatory bowel disease" or "Crohn's disease" or "ulcerative colitis" and "capsule endoscopy" and "diagnostic accuracy" or "diagnostic techniques". Gray literature, unpublished studies and expert opinion papers were not included. References for all retrieved studies were downloaded and stored in a reference management system (Endnote, Clarivate, USA).

Study selection. Titles and abstracts of all retrieved studies were reviewed by two reviewers (A. G. T. and S. P.), and studies not meeting inclusion criteria were excluded. Full text review of the remaining studies was conducted to evaluate whether they met the following inclusion criteria: (i) prospective study with ≥ 10 patients; (ii) use of a pan-enteric capsule endoscopy device system; (iii) detection or diagnosis of IBD-related inflammation as a study endpoint; and (iv) use of a comparator arm (colonoscopy/enteroscopy, MRI, or IUS were all accepted). Exclusion criteria included (i) use of small bowel capsule endoscopy devices only and (ii) primary endpoints other than the assessment of IBD-related inflammation. Data were extracted and tabulated by two reviewers (A. G. T. and S. P.) and checked by another reviewer (R. L.). Any disagreements were resolved by consensus.

Data collection. Once the final list of studies was confirmed, the reviewers extracted relevant data from each study, including the type PCE used and the comparator arm, the type and volume of bowel preparation, prokinetic agents and boosters used, the criteria used to assess active disease and remission, the numbers of patients included in the efficacy analysis, the number of patients and/or intestinal segments with active disease, and those in remission. The full data collection table used is included (Table S1).

Risk of bias. To identify potential bias and evaluate the quality of the retrieved studies, the Quality Assessment of Diagnostic Accuracy in Systematic Reviews-2 (QUADAS-2) tool was used.[25] Studies which were classified as low risk for all four assessed domains were deemed low risk of bias studies. Studies which scored a high risk of bias for any of the tested domains were deemed high risk of bias studies. The applicability of the included studies to this review was assessed by the same tool.

Outcome measures and prioritization. The primary endpoints of this study were (i) per-patient diagnostic yield of pan-enteric capsule endoscopy devices for detection of active CD and (ii) per-patient sensitivity of pan-enteric capsule endoscopy devices for detection of active UC.

Statistical analysis. Standard measures of diagnostic test accuracy were calculated from the data provided in each individual study. For UC studies these tests included: sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio and diagnostic odds ratio. For the CD studies, calculating diagnostic test accuracy as outlined above was not possible for most of the studies because an accepted gold standard test does not exist for the detection of CD. Therefore, any positive finding for capsule endoscopy or the comparator test was considered a true positive. Diagnostic yield was calculated as the number of patients with active disease divided by the number of patients who underwent that test. Per-segment analysis was performed by dividing the number of intestinal segments with active disease by the total number of intestinal segments analyzed (this was calculated only for PCE and colonoscopy for the terminal ileum and the colon, there were insufficient numbers to analyze the proximal small bowel). Odds ratios were calculated using these diagnostic yields, and forest plots were formulated comparing capsule endoscopy against the comparator tests.

A random effects model was used for the meta-analysis and forest plot calculations. The inter-study heterogeneity was calculated using the inconsistency index, I^2. Significant heterogeneity was defined as $I^2 > 50\%$. Meta-regression was performed to analyze pre-specified sub-groups, including older *versus* newer generation PCE systems and comparison of PCE against individual comparators (endoscopy or MRE). A meta-analysis of proportions was performed to determine incremental differences in diagnostic yield between the imaging modalities for CD. Meta-analysis was performed using R packages (mada and metafor package).[26,27]

Results

The systematic review flow chart is shown in Figure 1. From a total of 1580 non-duplicate studies retrieved, 14 studies were included in the qualitative analysis (Table 1), and 11 studies were included in the quantitative meta-analysis[11,13,16–18,20–24,28] as three studies did not have adequate data to perform the relevant

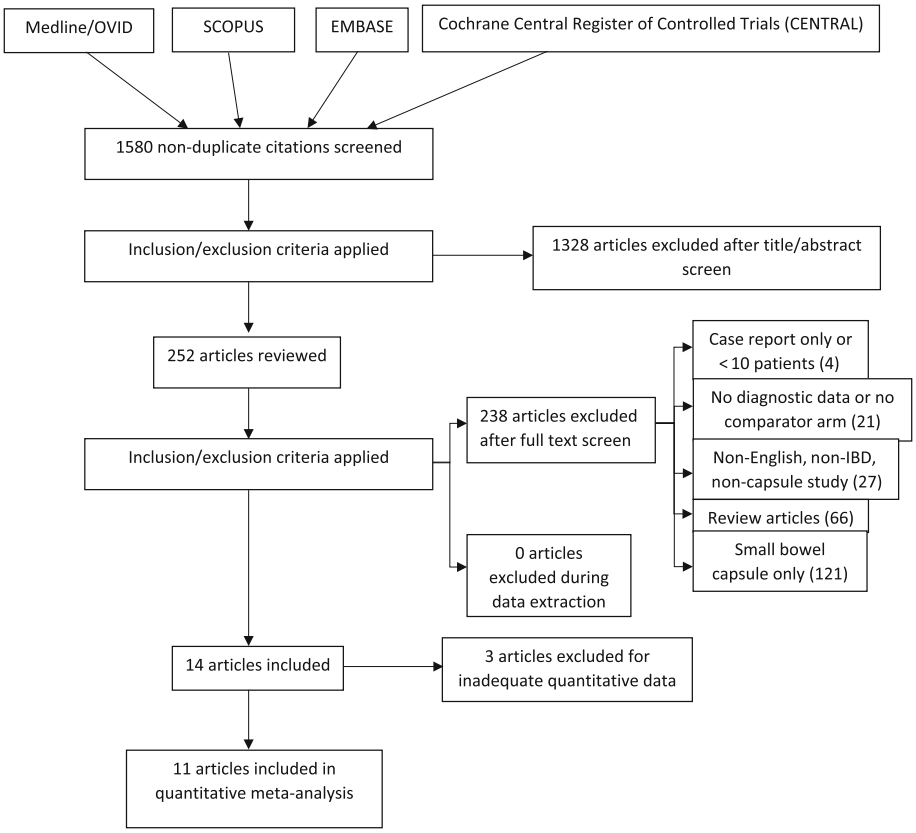


Figure 1 Flow chart of the systematic review.

Table 1 Characteristics of included studies

Author	Year	Design	Capsule	Comparator arm	UC/CD	Patients enrolled	Number per protocol analysis
Adler *et al.*[11]	2019	Prospective, multi-center	Pillcam Crohn's	colonoscopy	UC	30	23
Hosoe *et al.*[12]	2013	Prospective, single center	Pillcam Colon 2	colonoscopy	UC	30	29
Juan-Acosta *et al.*[13]	2014	Prospective, single center	Pillcam Colon 1 and 2	colonoscopy	UC	42	42
Ye *et al.*[14]	2013	Prospective, single center	Pillcam Colon 1	colonoscopy	UC	25	25
Meister *et al.*[15]	2013	Prospective, single center	pillcam colon 1	colonoscopy	UC	13	13
Shi *et al.*[16]	2017	Prospective, single center	Pillcam Colon 2	colonoscopy	UC	150	108
Sung *et al.*[17]	2012	Prospective, multi-center	Pillcam colon	colonoscopy	UC	96	96
Hausmann *et al.*[18]	2017	Prospective, multi-center	Pillcam Colon 2	colonoscopy	CD	17	CE = 12, colonoscopy = 15
Leighton *et al.*[19]	2017	Prospective, multi-center	Pillcam Crohn's	colonoscopy	CD	114	66
Bruining *et al.*[20]	2020	Prospective, multi-center	Pillcam Crohn's	colonoscopy and MRE	CD	119	99
D'Haens *et al.*[21]	2015	Prospective, multi-center	Pillcam Colon 2	colonoscopy	CD	40	40
Gonzalez-Suarez *et al.*[22]	2018	Prospective, single center	Pillcam Colon 2	MRE	CD	47	PCE = 26, MRE = 47
Hall *et al.*[23]	2015	Prospective, single center	CCE2	colonoscopy	CD	10	10
Yamada *et al.*[24]	2021	Prospective, single center	CCE2	DBE	CD	22	20

calculations. All three studies excluded from the meta-analysis investigated the diagnostic accuracy of PCE in UC.[12,14,15]

Study characteristics

Participants and interventions. The included studies were published between 2012 and 2021, with total patient enrolment of 797. Individual studies enrolled between 10–158 patients. There were seven studies examining PCE accuracy in CD, with two studies utilizing the Pillcam Crohn's system and five studies using CCE-2 (Pillcam Colon 2). Six studies had adequate data to be included in the primary (per-patient) analysis, while the final study could only be included as part of the per-segment analysis.

There were seven studies examining PCE accuracy in UC, with one study using the Pillcam Crohn's system, two studies using CCE-2 (Pillcam Colon-2), three studies using CCE-1 (Pillcam Colon 1), and one study using a combination of CCE-1 and CCE-2. There were four studies that were able to be quantitatively analyzed in the meta-analysis. Two studies only reported concordance values between capsule endoscopy findings and colonoscopy, without reporting absolute values, so diagnostic sensitivity could not be calculated. One study reported mean disease severity scores (± standard deviation) but without concordance to colonoscopy, and thus, we were unable to calculate accurate sensitivity and specificity values.

Comparator and scoring criteria. Eleven studies used colonoscopy as the comparator arm, one study compared PCE against MRE and colonoscopy, one study used combined anterograde and retrograde double balloon enteroscopy, and one study used MRE alone as the comparator.

There was significant heterogeneity in the disease activity scoring criteria. Of the seven CD studies, capsule endoscopy Crohn's disease activity index (CECDAI) was used in two studies, the Lewis score was used in two studies, the Rutgeert's score in one study, the capsule index of severity in one study and one study used established colonoscopy scoring systems (SES-CD and CDEIS).

Of the seven UC studies, the Mayo endoscopic score was used in three studies (one of which also used the UC endoscopic index of severity [UCEIS]), while the Matts endoscopic score, the Baron score and Rachmilewitz score were used in one study each.

Bowel cleansing and capsule completion rates. Bowel preparation protocols were reported in all included studies. Most studies used a polyethylene glycol (PEG)-based bowel preparation followed by post-capsule ingestion boosters. Two of the 14 studies included in the qualitative analysis did not report on the adequacy of bowel cleansing and one further study only reported on small bowel cleansing, not colonic cleansing. The rates of adequate bowel cleansing, based on a 4-point scale of poor, fair, good or excellent for each colonic segment and an overall score,[19] ranged from 29.3% to 90%. Capsule completion rates were reported in 13 out of 14 studies and ranged from 69% to 100%. The type of bowel preparation used and associated bowel cleansing and capsule completion rates are shown in Table 2.

Risk of bias assessments. The quality of the included studies and the associated risk of bias are shown in Supplementary Table 2. Four studies were found to have a low risk of bias, while one study was found to have a high risk of bias. The remaining nine studies had an overall low risk of bias, however most had an "unclear" risk of bias rating in at least one of the tested domains. The most common reasons for an unclear risk of bias classification included lack of clarity regarding subject recruitment (i.e. whether consecutive recruitment was used) and the degree of blinding used when interpreting the index and reference tests.

Diagnostic yield: Crohn's disease. The pooled per-patient OR of PCE in the detection of active CD was 1.25 (95% CI, 0.85–1.86%) when compared against all comparator tests (MRE, colonoscopy, and enteroscopy) (Fig. 2). When compared only against endoscopic comparator tests (colonoscopy or double balloon enteroscopy) the pooled OR increased marginally to 1.30 (95% CI, 0.85–1.98%). There was no detectable heterogeneity in either calculation (I^2 = 0%). When assessed against MRE alone, capsule endoscopy performed well, with a pooled OR of 1.32 (95% CI, 0.79–2.20%). Notably, two out of three studies using the older generation of PCEs had ORs of < 1, suggesting the trend to superiority of PCE was driven by the newer capsule devices. A meta-analysis of proportions showed these pooled results convert to an incremental increase in diagnostic yield for PCE devices of 5% compared with MRE and 7% compared with colonoscopy.

The per-segment analysis included three studies with a total of 273 intestinal segments analyzed. The pooled ORs for diagnostic yield of PCE compared with colonoscopy in the terminal ileum and the colon were 1.19 (95% CI, 0.78–1.79%), and 1.14 (95% CI, 0.76–1.71%) respectively (Figs S1 and S2).

Diagnostic yield: ulcerative colitis. The per-patient sensitivity of PCE in the detection of active UC was reported in four out of the seven included studies. The pooled diagnostic sensitivity was 93.8% (95% CI, 87.6–97.0%), which was associated with a very low inter-study heterogeneity (I^2 = 12%). The pooled diagnostic specificity was 69.8% (95% CI, 38.2–89.6%), although significant inter-study heterogeneity was noted (I^2 = 83%). As the majority of the heterogeneity appeared to be arising from a single study,[16] repeat sensitivity analysis was performed without this study and the I^2 for this re-calculation was 0. The sensitivity and specificity are shown as forest plots in Figure 3.

The pooled positive predictive value was 88.8% (95% CI, 82.6–92.9%), while the pooled negative predictive value was 80.1% (95% CI, 59.4–91.8%). The diagnostic odds ratio was 24.0 (95% CI, 10.4–55.3%).

Earlier versus newer generation capsules. To determine whether newer PCE devices had improved diagnostic accuracy compared with previous iterations, we performed a sub-group analysis (Fig. 4). For CD, CCE2 was defined as the older generation and Pillcam Crohn's as the newer generation. None of the included studies investigated the diagnostic accuracy of CCE1 in CD, so it was not included in this analysis. There were 156 patients who underwent Pillcam Crohn's in two studies, with a

Table 2 Bowel preparation, cleansing rates and capsule completion rates

Author	Capsule type	PEG	Volume (L)	Prokinetic	Booster	Volume	Adequate cleansing level	Completion rate
Adler *et al.*[11]	Crohn's	Yes	1 + 2	Metoclopramide (optional)	Suprep	88 mL + 88 mL (+ 88 mL optional)	no absolute value given	76.70%
Hosoe *et al*[12]	CCE2	Nil	Nil	Mosapride	PEG	2 L	29.30%	69.00%
Hausmann *et al.*[18]	CCE2	Yes	2 + 1	Domperidone	Nil	Nil	no absolute value given	100%
Juan-Acosta *et al.*[13]	CCE1 & 2	Yes	2 + 2	Domperidone	NaP	30 mL + 15 mL	80%	85.70%
Ye *et al.*[14]	CCE1	Yes	2 + 1	Itopride	NaP	30 mL + 15 mL	80%	100%
Meister *et al.*[15]	CCE1	Yes	1 + 0.75	Domperidone	PEG	500 mL + 250 mL	90%	77%
Leighton *et al.*[19]	Crohn's	Yes	2 + 2	Metoclopramide (optional)	Suprep	88 mL + 88 mL	48%	93%
Bruining *et al.*[20]	Crohn's	Yes	2 + 2	metoclopramide or erythromycin	Suprep	88 mL + 88 mL	79% (prox SB), 91% (TI), 64% colon	85%
Shi *et al.*[16]	CCE2	Yes	3 + 1	Metoclopramide (optional)	NaP	30 mL + 15 mL	66%	72%
D'Haens *et al.*[21]	CCE2	Yes	2 + 2	Nil	NaP	30 mL	84%	75%
Sung *et al.*[17]	CCE1	Yes	3 + 1	metoclopramide	NaP	30 mL	64%	80%
Gonzalez-Suarez *et al.*[22]	CCE2	Yes	1 + 1	Nil	PEG	500 mL	100% (SB only), colon not reported	91% SB completion not reported
Hall *et al.*[23]	CCE2	Yes	2 + 2	Nil	NaP	1 packet NaP	Not reported	
Yamada *et al.*[24]	CCE2	Yes	1 + Mg citrate	Mosapride	PEG/ castor oil/ sodium picosulfate	**1)** 1 L PEG + 30 mL castor oil **2)** Sodium pico-sulfate 48 mg + 30 mL castor oil **3)** Mg citrate 50 mg	80%	75%

pooled OR of 1.46 (95% CI, 0.82–2.59%). There were 65 patients who underwent CCE2 in three studies with a pooled OR of 0.96 (95% CI, 0.37–2.41%).

For UC, CCE1 was defined as the earlier generation and CCE2 + Pillcam Crohn's were collectively defined as the newer generation. There were 150 patients who underwent the newer generation PCEs, and there were 119 patients who underwent the older generation PCE. The pooled sensitivity of the newer generation capsules was 97.2% (95% CI, 91.6–99.1%), while for the earlier generation of capsules it was 89.1% (95% CI, 81.0–94.1%). However, the specificity for the newer capsules was substantially lower, 46% (95% CI, 12.4–83.6%) compared with the earlier generation, 82.6% (95% CI, 68.9–91.1%).

Discussion

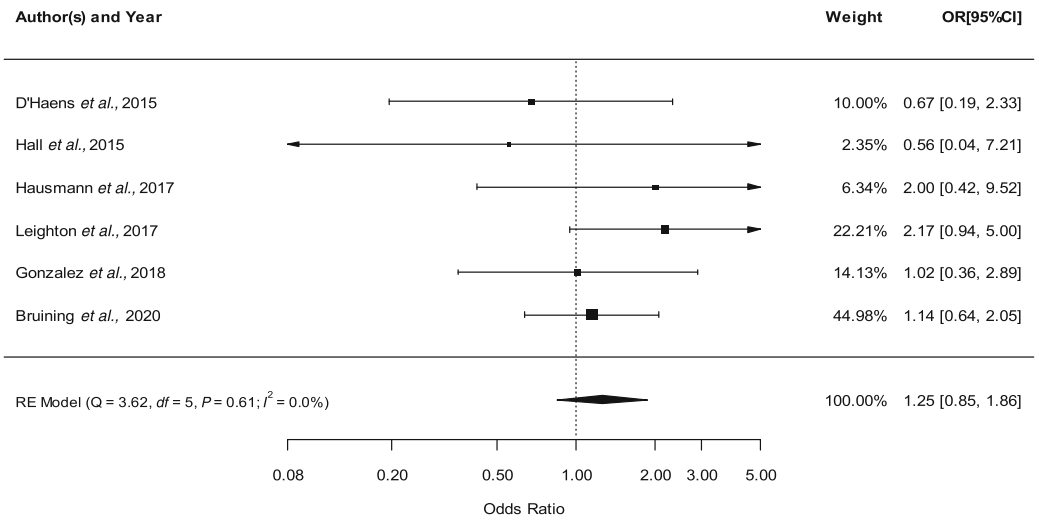
In the two decades since the development and first clinical use of small bowel capsule endoscopy, the use of capsule endoscopy in obscure small bowel bleeding and polyp screening has been well demonstrated,[4] as well as its role in small bowel CD diagnosis and monitoring.[7,8] However, there are far fewer studies reporting on the accuracy of PCE in the diagnosis and detection of ileocolonic or colonic IBD. To the authors' knowledge, there are no published meta-analyses that quantitatively analyze the current data.

According to our meta-analysis results, the diagnostic accuracy of PCE in the detection of CD was equivalent to MRE and endoscopic assessment on both per-patient and per-segment analyses. In fact, the pooled per-patient ORs for CD showed a trend to superiority over endoscopy and MRE. For UC, our meta-analysis shows that PCE has a diagnostic sensitivity and specificity of 94% and 70% respectively for the detection of active UC, with a diagnostic odds ratio of 24.0. As might have been expected, these results were primarily driven by newer PCE systems, which outperformed older devices in sub-group analyses for both CD and UC.

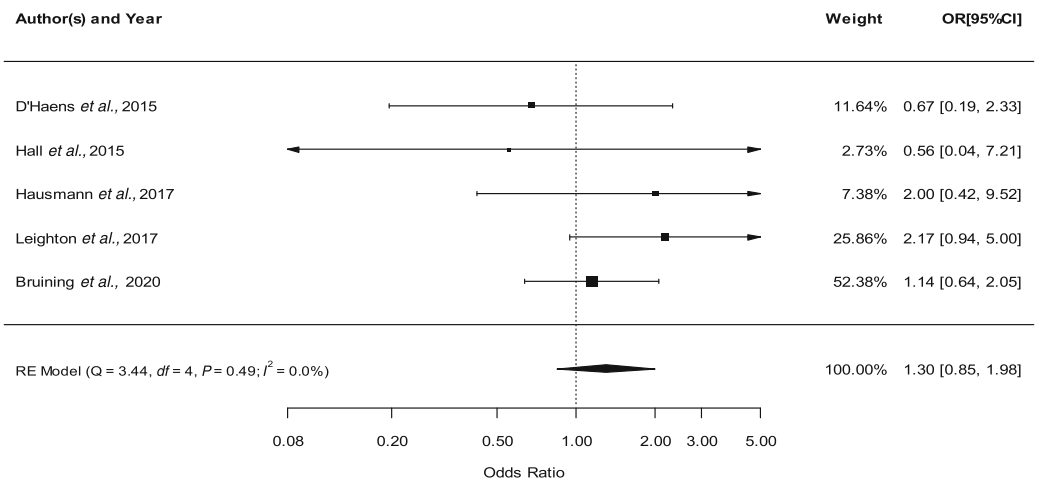
While the comparable diagnostic yield between PCE and colonoscopy (in CD) may partially be explained by detection of small bowel disease beyond the reach of colonoscopy, it should be noted that the per-segment performance of PCE in the terminal ileum and colon was also impressive. The pooled ORs of 1.19 (terminal ileum) and 1.14 (colon) indicate equivalent, or greater, diagnostic yield for PCE in segments accessible by colonoscopy. Of note, most studies defined the terminal ileum as the 10 min of the PCE video preceding the first caecal image, or the last 10 cm of the terminal ileum on colonoscopy. It is possible that PCEs were able to examine more than 10 cm of small bowel during those 10 min, hence potentiallydetecting more disease.

We can only postulate as to the reasons for the colonic findings. Colonic transit time of capsules is often significantly longer than the standard colonoscopy withdrawal time, and this may improve detection of subtle mucosal abnormalities. Additionally, as was seen with the UC cohort, the excellent diagnostic yield may come from a higher rate of false positives or detection of clinically

a Pooled odds ratio for PCE against all comparators



b Pooled odds ratio for PCE against endoscopic assessment



c Pooled odds ratio for PCE against MRE

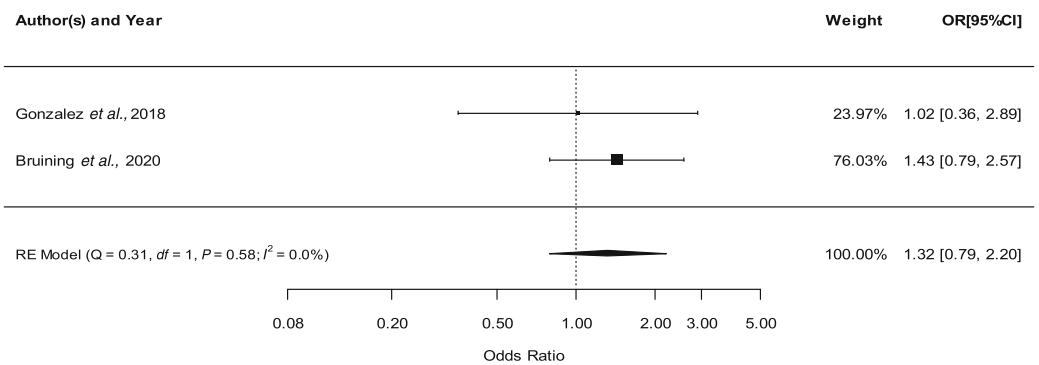


Figure 2 Diagnostic yield for PCE in CD (per patient).

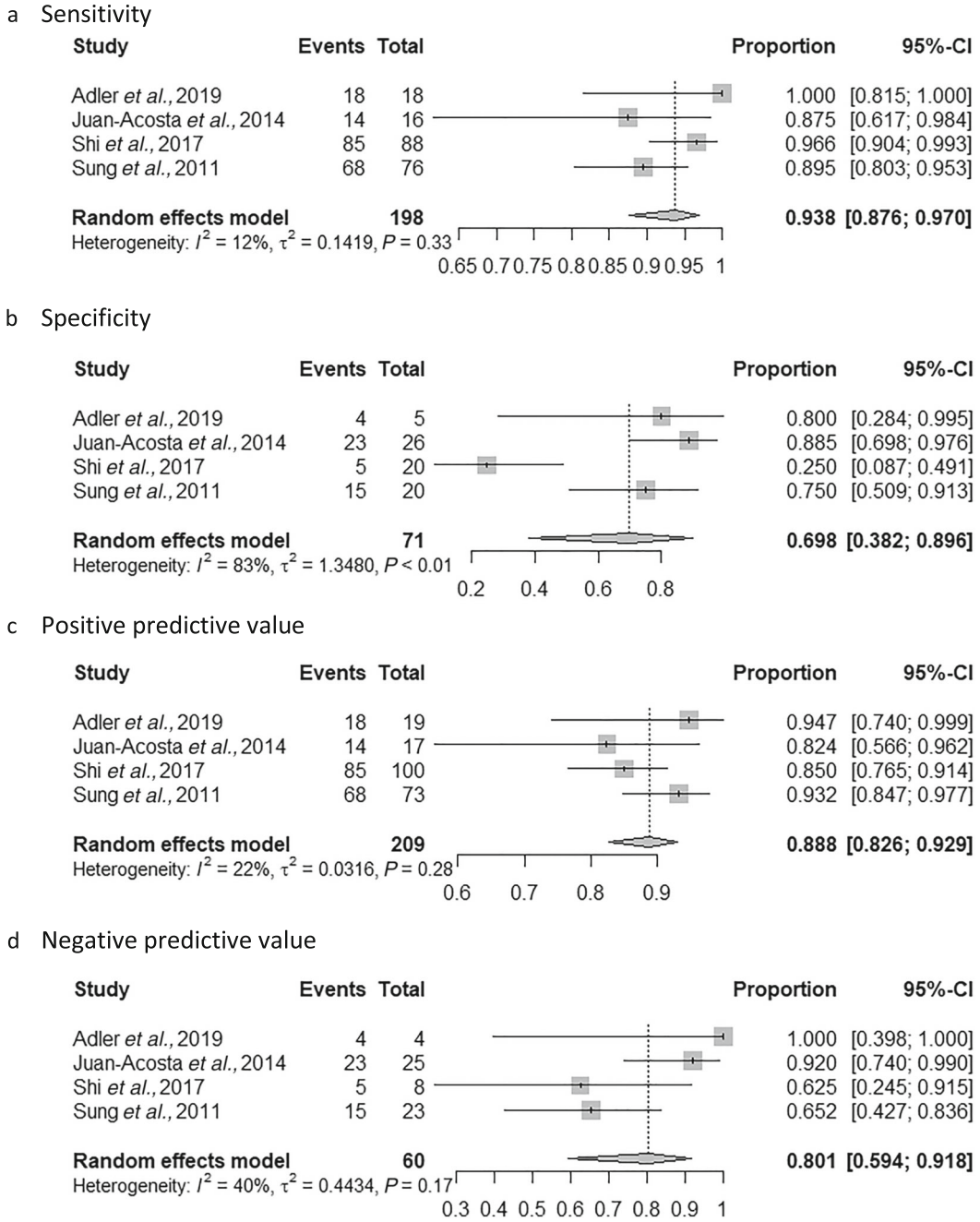


Figure 3 Diagnostic accuracy of PCE in UC.

insignificant mucosal lesions. Determining whether a detected lesion is truly diagnostic of CD is difficult without an accepted reference standard or longitudinal follow up. Future studies evaluating the diagnostic yield of PCE systems should incorporate longer prospective follow up periods, to determine the clinical impact of any purported improved diagnostic yield.

To overcome the limitations of not having a gold standard diagnostic assessment, one study in our meta-analysis used an expert consensus reference panel as the accepted gold standard to compare against, thereby allowing the calculation of diagnostic accuracy values.[20] This method asks an expert panel to determine the true disease state for each patient or intestinal segment. The tested modalities are then compared with this reference standard. However, this method is not without its own flaws such as incorporation bias.

Another potential confounder is the absence of standardization in disease severity scores. The heterogeneity in the scoring criteria used limits the ability to stringently compare disease activity between studies. This was an issue in both UC and CD studies, and particularly for capsule endoscopy and colonoscopy. In

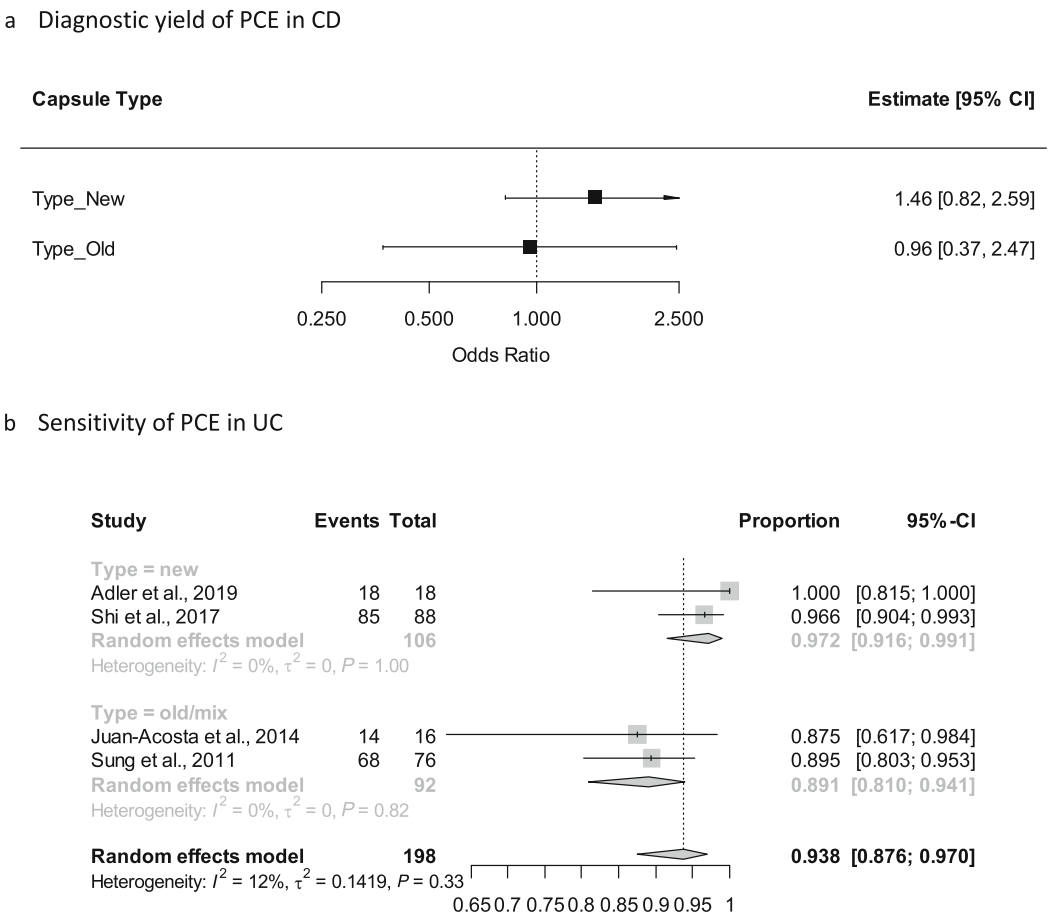


Figure 4 Sub-group analysis (newer generation *vs* older generation capsules).

contrast, the MaRIA score was used in all studies with an MRE comparator arm. We were able to overcome this in our analysis by agreeing upon accepted definitions of active and inactive disease for each scoring criteria. Regardless, developing and uniformly applying an accepted and validated capsule endoscopy scoring system in future prospective studies will substantially reduce bias and heterogeneity and allow for more informative analyses.[29]

Previous meta-analyses have primarily investigated the role and accuracy of capsule endoscopy in the detection of small bowel CD. A recent meta-analysis of 13 studies reported that small bowel capsule endoscopy is comparable in its diagnostic yield to MRE and small intestinal contrast ultrasound (SICUS), with pooled ORs of 1.17 and 0.88, respectively.[8] Prior to that, a meta-analysis of 19 studies reported that capsule endoscopy had a superior diagnostic yield to CTE, small bowel radiography and push enteroscopy in established CD.[7] Our meta-analysis shows similarities to these data, with ORs of 1.35 and 1.32 compared against endoscopic assessment and MRE, respectively. This is a significant finding, particularly the comparable diagnostic yield in the terminal ileum and colon where colonoscopy is presumed to have superior accuracy. Additionally, our data speak to the additive value that PCE, as a single, minimally-invasive diagnostic assessment, can have over the currently accepted modalities (colonoscopy, MRE or small bowel capsule endoscopy).

Our results for PCE systems in UC are significant given the high sensitivity and positive predictive value. Several studies have shown that capsule endoscopy has good concordance with colonoscopy for the evaluation of UC disease severity and extent.[12,14,16,17] There is also high patient acceptance of PCE despite the need for bowel preparation, due to limited discomfort and not requiring sedation, with patients generally preferring capsule endoscopy over colonoscopy.[21] However, studies to date, including our meta-analysis, have generally reported low specificity and negative predictive values for PCE, suggesting PCEs are not suited for the confirmation of mucosal healing or remission. This seems to be a result of PCE being somewhat indiscriminate in its detection of mucosal lesions and not correctly excluding non-IBD lesions, such as NSAID enteropathy, lesions related to bowel preparation or other etiologies. While the current literature and our meta-analysis results would not support PCE replacing fecal biomarkers or colonoscopy in UC diagnostic assessment, perhaps there remains a role for its use in patients with indeterminate fecal calprotectin results and/o those in whom colonoscopy is contra-indicated or high risk.

Our study reports numerous significant results and is, to the authors' knowledge, the first meta-analysis to report on the diagnostic utility of pan-enteric capsule endoscopy systems in IBD. The main limitations of our meta-analysis are a lack of a clearly defined gold standard for Crohn's disease diagnosis and a paucity of studies. For Crohn's disease studies, there is a potential for selection bias due to the exclusion of the stricturing CD phenotype, due to the risk of capsule retention. This may skew results favorably towards capsule endoscopy, as stricturing disease would be better assessed by MRE (or CTE). However, the main hurdle preventing PCE occupying a more prominent role in the IBD diagnostic algorithm is its inability of collect samples for histology and the absence of cross-sectional anatomical detail, the latter point being particularly crucial in a transmural condition, such as CD. The inability of PCE to detect dysplasia or obtain histology to exclude other pathology (i.e. CMV co-infection) limits PCE use in patients with UC.

In conclusion, our meta-analysis shows that PCE has an equivalent diagnostic yield to MRE and colonoscopy in non-stricturing CD and has high diagnostic sensitivity in UC. These results support the use of PCE in the diagnosis and monitoring of CD, potentially as a single diagnostic or monitoring tool given its pan-enteric assessment capacity. For UC, PCE has excellent diagnostic sensitivity but is not suggested to be a replacement for fecal calprotectin or colonoscopy. PCE may have a role in UC in certain patient groups, and its use should be tailored to individual clinical circumstances.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Pooled OR for PCE against colonoscopy in terminal ileum.
Figure S2. Pooled OR for PCE against colonoscopy in the colon.

Table S1. Data collection table.
Table S2. QUADAS-2 risk of bias summary.