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Follow-up endoscopy rates as an indicator of effectiveness in colon capsule endoscopy: a systematic review and meta-analysis

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ABSTRACT

Objective Colon capsule endoscopy (CCE) has emerged as a promising alternative for investigating lower gastrointestinal symptoms. However, its adoption has been limited due to concerns about cost-effectiveness, significantly influenced by follow-up endoscopy rates (FERs). Understanding CCE's FERs is crucial for its integration into routine clinical practice. We synthesised the evidence to evaluate the overall rate of further investigation in CCE.

Design A systematic review and meta-analysis were conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Data sources Medline, Embase, and PubMed were searched through 15 August 2024.

Eligibility criteria Studies included reporting FERs after CCE, including subsequent endoscopic procedures and radiological imaging. There were no language restrictions or limitations in CCE referral indications, patient recruitment criteria, or pathologies investigated.

Data extraction and synthesis All studies were independently screened and extracted two times by four reviewers. A random-effects model was used for meta-analysis and meta-regression to identify key contributing factors.

Results 2850 participants from 19 studies were included in the analysis. Compared with the key performance indicators for FERs in colonoscopy (0.10–0.15) and CT colonography (0.25), the pooled FER for CCE was found to be 0.42 (95% CI 0.34 to 0.50). The meta-regression analysis identified complete transit rates and adequate bowel cleansing quality as factors inversely associated with FERs. Furthermore, the CCE2 capsule demonstrated a higher reinvestigation risk than CCE1, likely due to its improved diagnostic accuracy. Although CCE indications were associated with lower FERs, subgroup analysis did not reach statistical significance with high heterogeneity.

Conclusion This study highlights significant FERs for CCE and identifies key contributing factors, emphasising the importance of appropriate patient selection to reduce reinvestigation needs. Future research should focus on improving completion rates, bowel preparation protocols, and refining CCE indications. This will minimise environmental impact and enhance cost-effectiveness and patient satisfaction.

PROSPERO registration number CRD42024567959.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Colon capsule endoscopy (CCE) offers diagnostic accuracy comparable to colonoscopy for detecting polyps and colorectal cancer. Although high follow-up endoscopy rates after CCE have been reported, these findings have not been systematically reviewed or assessed for their economic and environmental impact.

WHAT THIS STUDY ADDS

⇒ This meta-analysis found that 42% of patients undergoing CCE required a follow-up endoscopy—a rate higher than that observed with colonoscopy or CT colonography. Reinvestigation was more frequent with CCE2 capsules, likely due to improved diagnostic performance. Age and sex did not significantly influence follow-up rates, highlighting persistent uncertainty in individual risk factors.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Refining CCE indications, improving completion rates and bowel preparation, and optimising patient selection could reduce unnecessary follow-up procedures. This identifies a key research gap in CCE and makes clear that the challenge lies not in the tool itself but in how it is applied. These improvements could enhance cost-effectiveness and increase patient satisfaction by minimising invasive testing and streamlining the diagnostic pathway.

INTRODUCTION

Colon capsule endoscopy (CCE) has emerged as a minimally invasive option for lower gastrointestinal (GI) evaluations, serving as a complement to standard methods such as colonoscopy and CT colonography (CTC). Despite accumulating evidence of its diagnostic accuracy over the last decade, scepticism regarding its clinical effectiveness and cost-efficiency continues to hinder widespread acceptance. Extensive studies carried out in Denmark, Scotland, and England amid

the COVID-19 pandemic have contributed to this discussion[1–3] and identified cost-effectiveness as the primary obstacle to sustainable implementation.[4]

While CCE provides a non-invasive method, its drawbacks—such as inadequate bowel preparation, incomplete transit, and the inability to conduct biopsies or therapeutic measures—often require additional evaluations. The follow-up endoscopy rate (FER), which encompass procedures like colonoscopy or flexible sigmoidoscopy, greatly influence the economic viability of CCE. A cost assessment conducted by the Scottish Health Technologies Group (SHTG), derived from the ScotCap study, indicated that minimising follow-up colonoscopies or transitioning to less intensive flexible sigmoidoscopies could result in substantial cost reductions.[5] In addition to its economic effects, FER influences patient experiences and environmental sustainability. Repeated bowel preparation can lead to discomfort, postpone diagnoses and increase the likelihood of non-compliance or refusal of further examinations. Research indicates that keeping FERs under 30% is essential for encouraging patients to prefer CCE over colonoscopy.[6 7] Environmentally, patient travel contributes significantly to CO_2 emissions within the CCE service pathway. Minimising reinvestigations could improve both environmental sustainability and cost-effectiveness.[8]

This underscores the importance of understanding and optimising the FER for the successful integration of CCE into routine clinical practice. Despite its significance, a systematic review of FER in CCE remains absent. This systematic review and meta-analysis aim to evaluate FERs and identify factors influencing these rates to support the effective implementation of CCE.

METHODS

This study protocol was designed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (PRISMA checklist in the online supplemental file)[9] and is registered with the PROSPERO International Prospective Register of Systematic Reviews (registration number: CRD42024567959). The primary aim of the review was to evaluate the FER following CCE. The secondary aims include exploring contributing factors to the FER to guide future research to reduce this rate further. The FER refers to additional urgent colonoscopy or flexible sigmoidoscopy required after initial CCE due to incomplete procedures, inadequate bowel preparation, or the need for therapeutic interventions or histological biopsies.

Eligibility criteria

The search included full-text clinical, retrospective, and prospective trials evaluating the use of CCE in patients with any colonic pathology. There were no language restrictions, and all the non-English articles were screened with the intention of being translated and included if they met the predefined inclusion criteria. Both adult and paediatric studies were considered, provided they offered clear documentation of follow-up investigations after the initial CCE. There were no limitations regarding CCE referral indications, patient recruitment criteria, or pathologies investigated in these studies. However, conference abstracts were excluded due to their high risk of bias. Similarly, review articles, systematic reviews, editorials, study protocols, case reports, and small case series or studies with 10 or fewer participants were excluded.

Information sources

The literature search was conducted across EMBASE, MEDLINE, and PubMed databases. Additional studies were identified through manual searches of reference lists from the selected publications. The electronic search covered studies published between January 2004 and August 2024, as CCE was unavailable before 2004. Both Medical Subject Headings (MeSH) and non-MeSH terms were included in the search strategy, encompassing keywords such as colonoscopy, sigmoidoscopy, CT scan, conversion, and reinvestigation (see online supplemental table A1 for details). The specific search strings for each database are also provided in the online supplemental appendix. Grey literature and unpublished studies were excluded from the review.

Study selection

Titles and abstracts of all retrieved studies were independently screened by pairs of authors, with each set assigned to one of the following pairs: IIL and AR or AA and CT. Discrepancies within each group were resolved through discussion among the respective reviewers. Studies that did not meet the eligibility criteria were excluded. The inclusion criteria for the full-text review were:

1. Follow-up investigations (reinvestigation) prompted by incomplete procedures, poor bowel preparation, or any detected GI pathology in the terminal ileum or colon.
2. Any clinical indication for CCE.
3. Studies with more than 10 participants.
4. The FER did not need to be explicitly stated as the study's primary or secondary endpoint but could be calculated from the available raw data.

Exclusion criteria primarily focused on studies where follow-up investigations were conducted for upper GI findings, as these conditions would not typically be identified during colonoscopy, the gold standard for comparison of CCE FERs. Additionally, studies where all participants underwent both colonoscopy and CCE as part of a diagnostic accuracy study were excluded (see figure 1).

Data compilation

The final selection of studies was reviewed, and data extraction was performed by I.L. The extracted details included the CCE indication, patient selection criteria, sex, mean age, FER, the type of investigation modality,

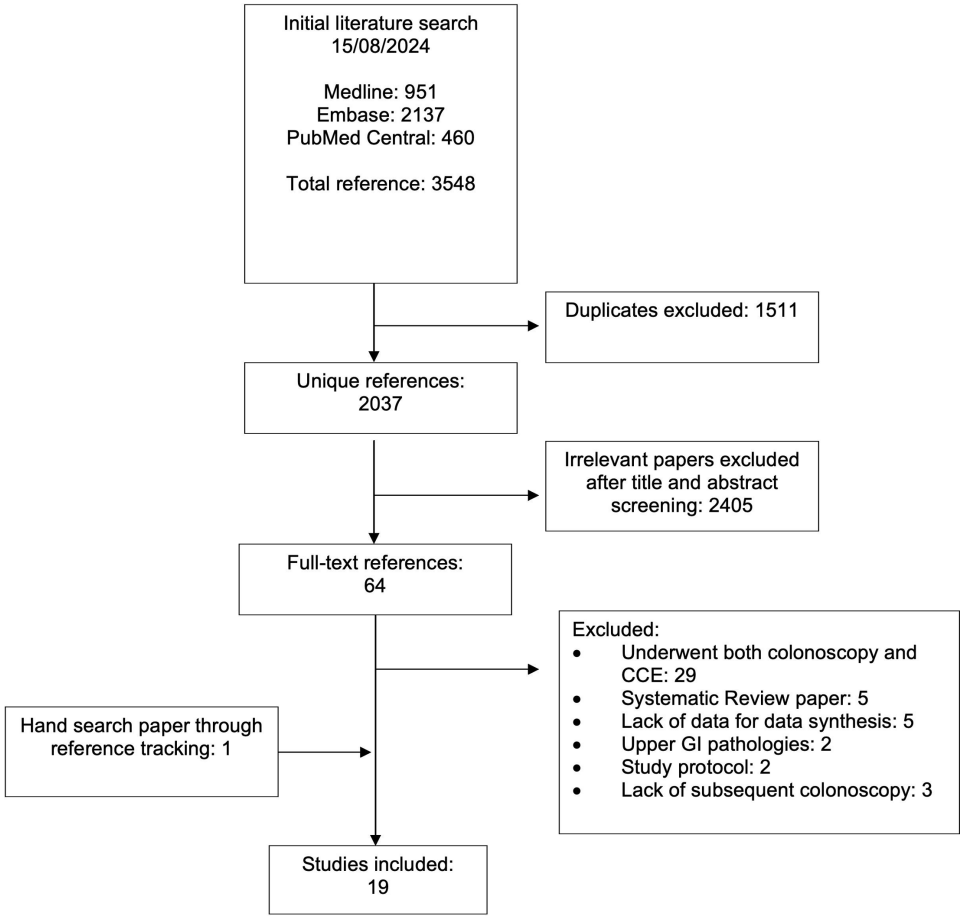

Figure 1 PRISMA flowchart. CCE, colon capsule endoscopy; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

capsule type, bowel preparation regimen (including prokinetic drugs and boosters), study design, sample size, bowel cleansing quality and CCE complete transit rate (see online supplemental tables A2 and A3).

Risk of bias

The studies included in this analysis underwent a risk of bias assessment utilising the Risk of Bias In Non-randomized Studies of Exposure (ROBIN-E) tool across seven domains due to mixed included study types.[10] The risk of bias for each domain was classified as low, moderate, critical, or no information available. Studies receiving a critical risk rating in any domain were considered to have a high risk of bias (see online supplemental table A4).

Statistical analysis

A random-effects model was employed for meta-analysis and forest plot generation to account for both within-study and between-study variability. Statistical significance was set at the 0.05 level, and 95% CIs were calculated. All pooled estimates were calculated from the patient data of included studies using Freeman-Tukey double arcsine transformation, which stabilises variances in proportion data for reliable pooling. Interstudy heterogeneity was assessed using the I^2 statistic, with I^2=50%–75% indicating substantial heterogeneity while >75% indicating considerable heterogeneity.[11] The meta-analysis used the 'meta' R package, specifically employing the 'metaprop' function, which calculates study-level effect sizes based on raw proportions.[12]

To explore potential sources of heterogeneity, meta-regression was performed, analysing prespecified subgroups or covariates, including capsule type, different CCE indications, age, sex, and the proportion of participants with adequate bowel cleansing (%) and complete transit rates (%). Both univariate and multivariate random-effects meta-regression models were applied to identify covariates significantly contributing to variability across studies. Further subgroup meta-analyses were performed for covariates demonstrating statistical significance in the meta-regression, and results were visualised using forest to illustrate subgroup effects. Additionally, bubble plots, generated through the 'ggplot2' R package,[13] were performed to demonstrate the relationships between covariates and effect sizes. Sensitivity analysis included a 'leave-one-out' approach, where each study was sequentially removed to assess its impact on the overall results. Additionally, studies with a high risk of bias were excluded to evaluate their influence on pooled estimates. Meta-regression, sensitivity analysis and

publication bias assessment (Egger's test) were conducted using the 'metafor' R package.[14]

RESULTS

Literature search and study selection

A systematic literature search conducted on 15 August 2024, yielded 3548 articles across three databases. After removing duplicates and irrelevant studies through title and abstract screening, 64 articles were reviewed in full. A Chinese systematic review was identified during the abstract screening stage; however, none of its referenced studies met the inclusion criteria and were therefore excluded.[15] Of these, 46 were excluded for reasons detailed in figure 1, with the most common exclusion being that participants underwent both CCE and colonoscopy as part of diagnostic accuracy studies. Additionally, one study identified through hand-searching was included, resulting in a total of 19 studies[1 2 16–32] with 2850 participants included in the meta-analysis. Among these, one study was retrospective, while the rest were prospective.

The risk of bias assessments, performed using the ROBIN-E tool, are summarised in online supplemental table A4. Two studies, Triantafyllou *et al*[24] and Otani *et al*,[26] were identified as having a high risk of bias, primarily due to biases related to FERs rather than their primary outcomes. Eleven studies were assessed as having a moderate risk of bias in specific domains. Common sources of bias included unclear patient selection criteria, significant patient attrition or loss to follow-up, preselection of cases with good or excellent bowel preparation, retrospective inclusion of high-risk patients with obstructive lesions, variability in bowel preparation protocols, and unclear definitions of CCE indications. The two high-risk studies were included in a sensitivity analysis to assess their impact on the overall findings (see online supplemental figure A4).

Overall results

The result yielded a pooled FER of 0.42 (95 CI 0.34 to 0.50) with high heterogeneity (I^2=93.6%) and a 95% prediction interval of 0.06–0.78, suggesting a wide range of possible true pooled rates. This is summarised in the Forest plot in figure 2. In addition, Egger's test showed a regression intercept at 0.123 (95 CI −0.4579 to 0.7064) with a p value=0.216, indicating no statistically significant evidence of asymmetry. The funnel plot also demonstrates a balanced distribution of effect sizes, suggesting that missing or unpublished studies are unlikely to have systematically influenced the results. Therefore, there is no evidence of publication bias (see online supplemental figure A1).

Meta-regression

The influence of covariates on the FER of CCE is summarised in online supplemental table A5. Meta-regression analysis identified two significant factors: complete transit rate (β=−0.020; 95% CI −0.038 to −0.0016; p=0.033) and adequate bowel cleansing rate (β=−0.031; 95% CI −0.06 to −0.0014; p=0.04). Both factors were inversely associated with FERs, indicating that higher complete transit and bowel cleansing rates correspond to lower FERs. This relationship is visually illustrated in the bubble plots shown in figure 3, where a clear inverse trend is observed using linear regression models.

Additionally, the analysis revealed that the CCE2 capsule type was linked to an increased risk of reinvestigation, whereas CCE indication was associated with a reduced

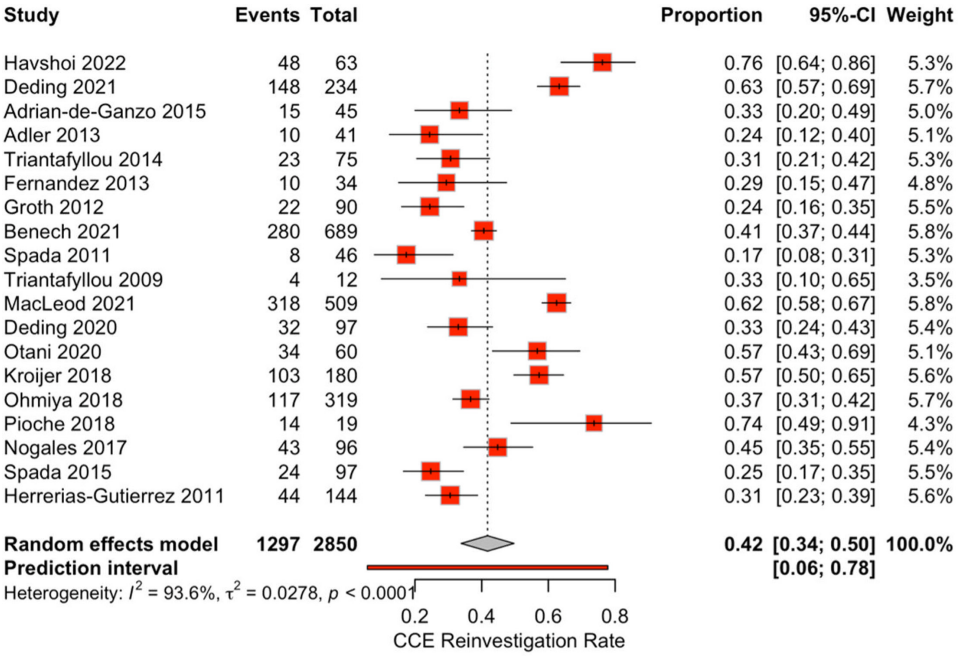

Figure 2 The forest plot of the overall CCE reinvestigation rate. CCE, colon capsule endoscopy.

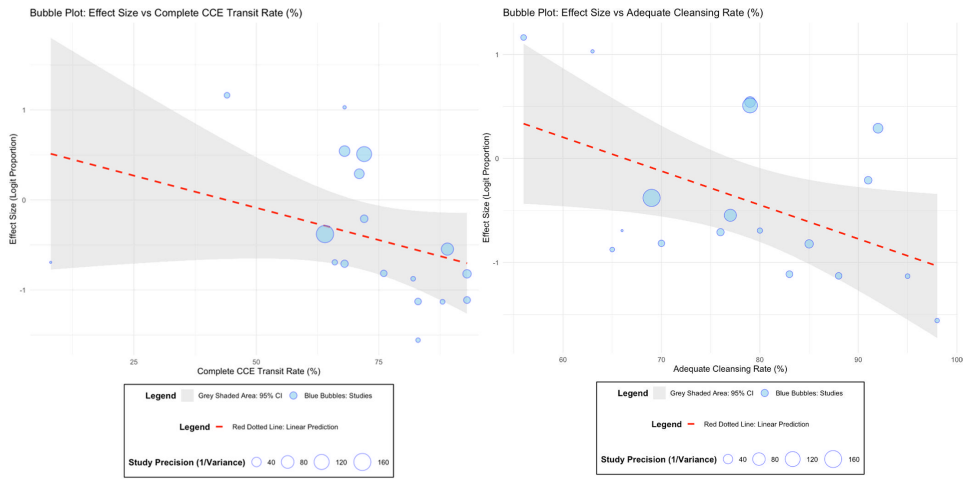

Figure 3 Bubble plot illustrating the relationship between effect size and CCE complete transit rate (left) and adequate bowel cleansing rate (right). Both plots demonstrate an inverse trend, indicating that as the CCE complete transit rate or bowel cleansing rate increases, the reinvestigation rate decreases. CCE, colon capsule endoscopy.

reinvestigation risk. In a multivariate meta-regression model assessing five CCE indication subgroups, only the 'All Indications' subgroup demonstrated a statistically significant reduction in reinvestigation risk (β=−0.93; 95% CI −1.66 to −0.19; p=0.013). While not reaching statistical significance, marginal trends were suggesting an increased reinvestigation risk in the 'Symptomatic and/or Surveillance' (β=1.013; 95% CI −0.0757 to 2.101, p=0.0682) and 'CRC Screening' (β=1.00; 95% CI −0.137 to 2.136, p=0.0837) subgroups.

The sensitivity analysis using both leave-one-out analysis and filtered out the two high-risk studies showed consistent effect size estimates across all iterations. No single study disproportionately influenced the overall results (see online supplemental figures A2 and A3), demonstrating the robustness of the meta-analysis.

Subgroup analysis

A subgroup analysis was conducted based on statistically significant findings from the meta-regression. Figure 4

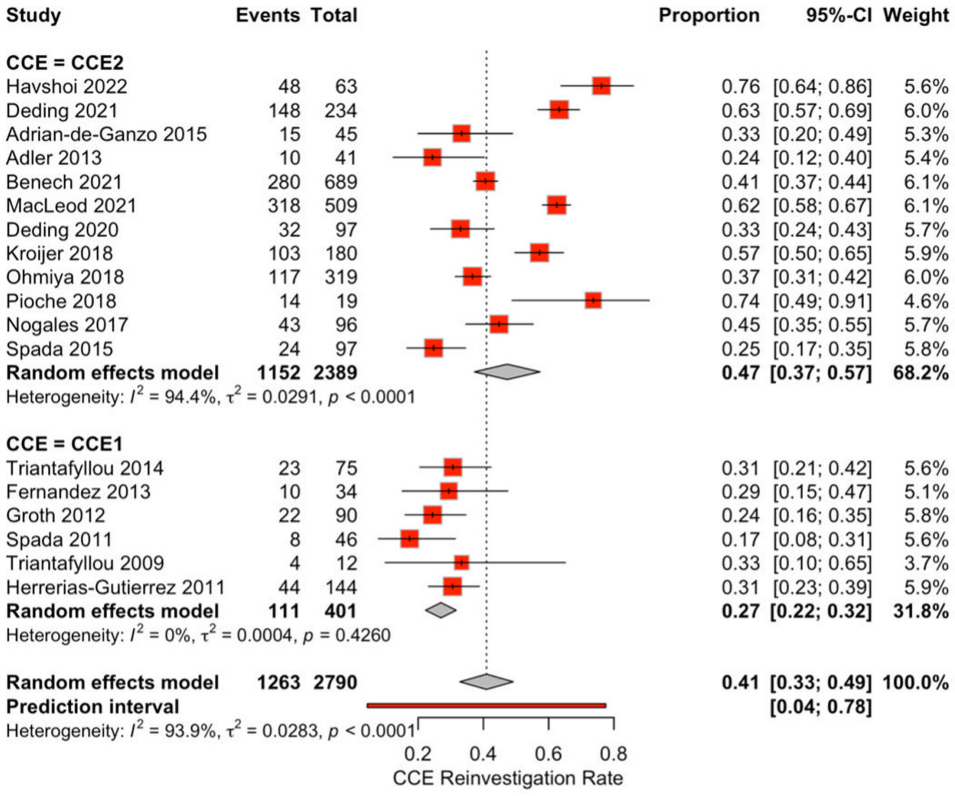

Figure 4 Forest plot illustrating the overall CCE reinvestigation rate, stratified by subgroup analysis according to CCE generation 1 versus generation 2. Test for subgroup differences: Q=15.41, df=1, P<0.0001. CCE, colon capsule endoscopy.

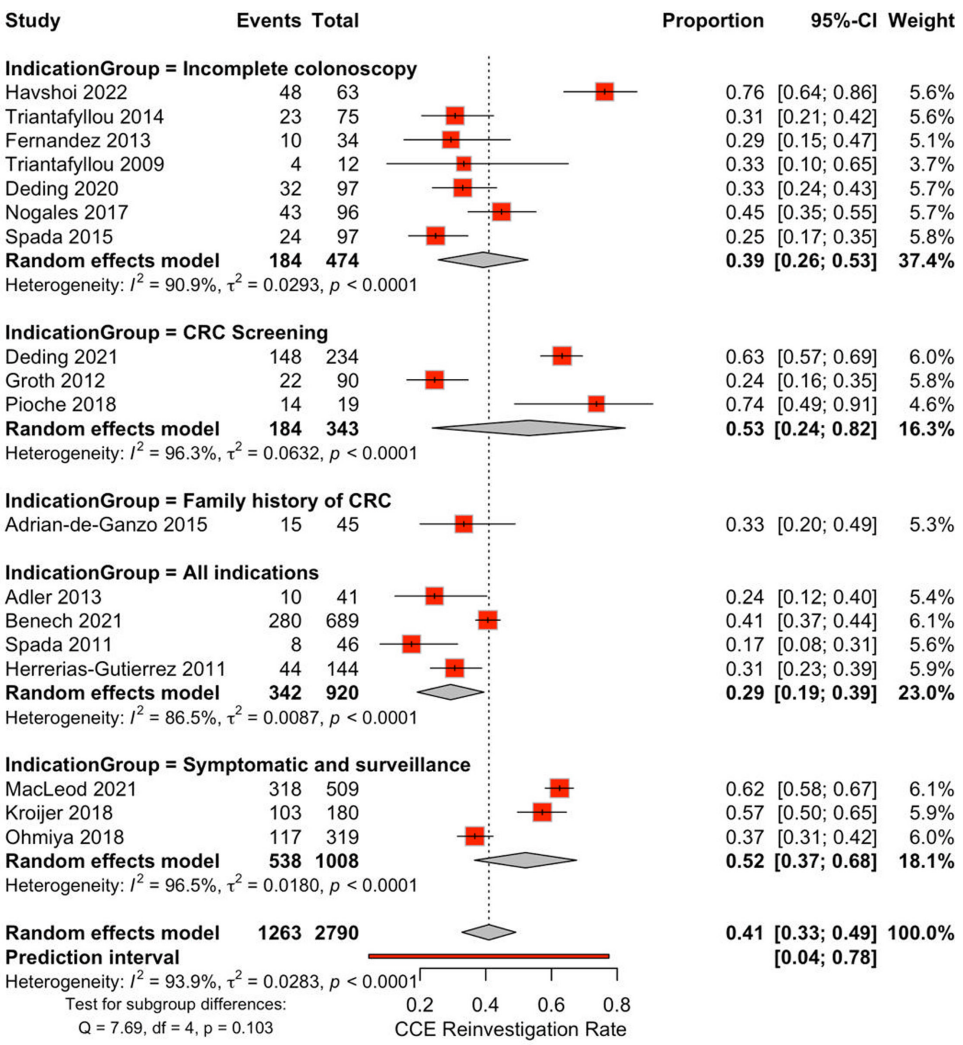

Figure 5 Forest plot illustrating the overall CCE reinvestigation rate, stratified by subgroup analysis according to different CCE indications: incomplete colonoscopy, CRC screening, symptomatic and surveillance and all other indications. CCE, colon capsule endoscopy; CRC, colorectal cancer.

illustrates a forest plot comparing the two colon capsule generations (CCE1 and CCE2). Studies using CCE1 reported a pooled FER of 0.27 (95% CI 0.22 to 0.32) with low heterogeneity (I^2=0%). In contrast, studies using CCE2 demonstrated a significantly higher rate of 0.48 (95% CI 0.39 to 0.57) with substantial heterogeneity (I^2=94%). This difference was statistically significant (p<0.0001), highlighting a notable increase in FERs with CCE2. Studies achieving a completion rate ≥80%, the recommended standard for CCE, exhibited a lower FER of 0.28 (95% CI 0.22 to 0.33) with moderate heterogeneity (I^2=60%), compared with 0.50 (95% CI 0.40 to 0.60) with high heterogeneity (I^2=93%) for completion rates <80% (see online supplemental figure A2). For bowel cleansing scores ≥80%, FERs showed a modest improvement to 0.35 (95% CI 0.25 to 0.45), although with high heterogeneity (I^2=92%) (see online supplemental figure A3).

Subgroup analysis of CCE indications included five categories (figure 5). The 'All Indications' subgroup exhibited the lowest pooled FER of 0.29 (95% CI 0.19 to 0.39), consistent with meta-regression results. However, substantial heterogeneity persisted (I^2=86.5%), and the χ^2 test for subgroup differences yielded a p value of 0.103, indicating no statistically significant variation in FERs across the CCE indication subgroups. These findings limit the conclusiveness of the CCE indication subgroup analysis.

DISCUSSION

Despite the non-invasive nature and lack of sedation requirements associated with CCE, its adoption remains limited, as highlighted in the recently published EU CAPTURE study.[33] A key barrier to widespread implementation is its economic cost-effectiveness, which is heavily influenced by the FER.[5] The pooled FER in our study was 42%, which appears relatively high when compared with benchmarks in related procedures like colonoscopy and CTC. While no universal threshold defines a 'high' FER in CCE, insights can be drawn from established key performance indicators (KPIs) for similar procedures.

For colonoscopy, repeat procedures due to inadequate bowel preparation range from 5%–60%, with a median of 25%, and incomplete procedures, measured by caecal intubation failure rates, range from <1% to 13%.[34–38] Professional guidelines in the US and EU recommend KPIs of >95% for caecal intubation rates and >90% for adequate bowel preparation.[39–41] However, the absence of reported reinvestigation rates in colonoscopy highlights a gap in the literature, underscoring the need for future research to enable a fair comparison with CCE. In the context of CTC, cost-effectiveness is significantly reduced when FERs exceed 30% (16). The Royal College of Radiologists in the UK recommends a reinvestigation threshold of <25% as a KPI.[42] When compared with these benchmarks, the 42% FER in our study underscores the need for targeted strategies to mitigate factors contributing to this high rate. Addressing these issues is essential to enhance the clinical efficiency, patient experience, and cost-effectiveness of CCE.

Our analysis identified that FERs in CCE are significantly influenced by complete transit rates and bowel preparation quality, both closely tied to patient selection. Poor bowel cleansing or incomplete procedures elevate the risk of missed pathology, increasing the need for follow-up investigations. This finding mirrors colonoscopy studies, where inadequate bowel preparation and incomplete procedures are associated with reduced adenoma detection rates.[38 43] Encouragingly, the introduction of prucalopride has improved CCE completion rates. In a study by Deding *et al*, patients receiving prucalopride showed a prevalence ratio of 1.32 for complete CCE compared with those on a standard booster regimen.[44] In terms of bowel preparation, it remains a challenge without a universally effective protocol established. Since colonoscopy and CCE are fundamentally different diagnostic modalities, the lack of washing and suctioning in CCE requires more stringent bowel preparation. However, despite this limitation, CCE provides extensive colonic visualisation. The capsule can linger in segments sometimes for hours, offering a more prolonged and detailed assessment than minutes of examination during a colonoscopy. This unique feature may partially compensate for the lack of washing but also introduces greater subjectivity,[45] sometimes revealing hidden areas behind residual stool that may not be visible from a single perspective.

A meta-analysis by Bjørsum-Meyer *et al* reported an acceptable bowel cleanliness rate of 0.77 across 46 studies,[46] which is significantly below the >90% benchmark set by colonoscopy guidelines.[39–41] Our analysis also highlights considerable variability in bowel preparation protocols among the included studies, with differences in booster types, doses and regimens (see online supplemental table A3). Notably, only 4 of the 19 studies adhered to a standardised preparation and booster protocol, reflecting the heterogeneity in clinical practice and the need for optimised and standardised regimens in CCE.

Another important factor affecting the FER was the type of version of capsule used. The FER rose significantly from 0.27 (95% CI 0.22 to 0.32) with CCE1 to 0.48 (95% CI 0.39 to 0.57) with CCE2 (p<0.0001), as shown in figure 4. This increase can be attributed to the improved diagnostic accuracy and enhanced detection capabilities of CCE2. The CCE2 system features a significantly higher frame rate (35 vs 4 images per second), wide-angle cameras for nearly 360° coverage, enhanced image quality, and an extended battery life. Additionally, it demonstrated superior sensitivity, achieving 84% for polyps ≥6 mm and 88% for polyps ≥10 mm, compared with the CCE1 system's 58%–64% and 64%–69%, respectively.[47] While this improved detection enhances diagnostic accuracy, it also increases the identification of polyps and pathology, leading to a greater number of follow-up procedures, such as biopsies and polypectomies.

Regarding the effect of different CCE indications on FERs, the meta-regression analysis revealed that 'All Indications' had significantly lower FERs than other subgroups of indications. However, further subgroup meta-analysis did not show a statistically significant difference (p=0.103), primarily due to high heterogeneity between studies (see figure 5). Despite the lack of statistical significance, colorectal cancer (CRC) screening appeared to have the highest FER. This may be because high-risk populations are often preselected through significantly elevated quantitative faecal immunochemical test results (different thresholds for different countries), resulting in an increased likelihood of significant pathology requiring further biopsy or therapeutic intervention. The absence of statistical significance is also likely due to the limited number of studies within each subgroup, highlighting the need for additional research to better understand and validate these trends across different CCE indications.

In addition, the expected risk factors that would lead to increase reinvestigation rate were age and sex. The ScotCap study conducted by MacLeod *et al* found that younger patients had higher CCE success rates and better bowel preparation.[48] This may be due to better adherence to bowel preparation and booster regimens among younger patients compared with older individuals. Additionally, ageing has been linked to delayed gastric emptying and slower colonic transit time, possibly due to age-related nerve dysfunction.[47 48] Consequently, poorer bowel preparation is more common in the elderly population.[49] However, findings on age and CCE completion rates remain inconsistent. A study by Moen *et al* reported that older participants had a higher CCE completion rate,[50] contradicting the expectation that advancing age negatively impacts CCE outcomes. Similarly, in our study, age was not a significant factor influencing reinvestigation rates (p=0.21, see online supplemental table A5). Another key factor is the higher prevalence of polyps and advanced neoplasia in older patients,[51 52] which increases the need for follow-up colonoscopies for polypectomy.

In terms of sex differences, previous studies have shown that men generally have faster colonic transit time than women.[53] However, a CCE-specific transit study by Moen *et al* reported a marginally slower gastric transit in men (p=0.07), contradicting existing literature. In our study, male sex did not significantly reduce reinvestigation rates, reflecting ongoing uncertainty. This may be attributed to the higher prevalence of polyps and advanced neoplasia in men compared with women.[54 55] This increased polyp burden in men may have offset the potential benefits of faster transit and higher completion rates, leading to no difference in follow-up colonoscopies.

From a cost-effectiveness perspective, one of the key studies included was the Scotcap study, which conducted a comprehensive cost-effectiveness analysis using large-scale data from Scotland, led by Healthcare Improvement Scotland (SHTG).[1 5] The study compared the total cost per CCE procedure (£747 or €900 at list price) with the cost of a colonoscopy (£900 or €1085), based on National Services Scotland microcosting data. Using colonoscopy as the standard reference, the findings revealed that using CCE in a surveillance population remains cost-incurring, with an additional expense of £64.75 (€79.41) per patient. However, CCE was marginally cost saving in a symptomatic population, reducing £6.71 (€8.23) per patient. Fewer colonoscopies and the downgrading of some urgent colonoscopies to non-urgent flexible sigmoidoscopies largely drove these cost savings. This benefit is most achievable in healthcare systems equipped with flexible sigmoidoscopy services. In the ScotCap study, 35% of reinvestigations were performed using flexible sigmoidoscopy, highlighting its substantial contribution to overall cost savings.

Beyond cost-effectiveness, CCE offers a significant potential benefit by freeing up endoscopy capacity for patients in urgent need of colonoscopy. A recent large-scale UK study by Turvill *et al*[56] demonstrated that CCE functioned effectively as a filter diagnostic test, with 86% of patients avoiding urgent colonoscopy for suspected CRC after being downgraded to non-urgent pathways. This significantly increases endoscopy capacity, though the cautious interpretation around the higher follow-up investigation rate must be considered in context. As outlined in our follow-up letter to the editor, multiple factors contribute to this rate, warranting further evaluation.[57] Nevertheless, this prioritisation role of CCE could be crucial in CRC screening programmes, reducing the number of patients on waiting lists and shortening colonoscopy wait times, particularly in an already strained healthcare system. Additionally, the long-term cost savings from early CRC detection through increased screening uptake remain uncertain but could reduce the financial burden of late-stage CRC treatment. Further research is needed to evaluate these economic impacts.

For comparison, Sawhney *et al* conducted a cost-effectiveness analysis on CTC for CRC screening, demonstrating a 22% cost savings over colonoscopy. Notably, only 14.5% of patients required a follow-up colonoscopy, contributing to the overall cost savings. The average cost per screened patient was US$307, with each referred colonoscopy costing US$2114, highlighting the economic advantage of CTC in reducing the need for direct colonoscopic evaluation.[58] Additionally, the low rate of follow-up colonoscopy after CTC may be attributed to patient selection, as CTC is often reserved for clinically frail patients.[59] In such cases, the threshold for recommending further invasive investigations may be different and possibly more conservative. Given the similarities between CCE and CTC, along with CCE's superior diagnostic accuracy,[60] these findings suggest that CCE could be a viable option for CRC screening. However, the rate of follow-up endoscopic investigations is expected to be higher, as CCE is more commonly used in younger patients[33] who have fewer contraindications for invasive endoscopic procedures and a higher likelihood of pathology detection due to CCE's superior sensitivity. In fact, some evidence suggests that CCE detects more polyps than colonoscopy.[61] This higher detection, suggesting greater sensitivity, could be viewed as an improved gold standard in polyp recognition and detection. Therefore, optimising follow-up investigation rates is essential to ensure that CCE remains a cost-effective screening option.[56]

The number of publications on CCE and green endoscopy has grown significantly, with a joint consensus from the British Society of Gastroenterology, Joint Advisory Group and the Centre for Sustainable Healthcare endorsing CCE as a viable alternative to colonoscopy for green endoscopy, especially in bowel cancer screening.[62] This recommendation is based on CCE's potential to be conducted in primary care or via telemedicine, reducing patient travel and associated CO_2 emissions. A study by Nia *et al* demonstrated the feasibility of remote CCE deployment using 5G technology and a Smartbox system, highlighting potential environmental benefits with different delivery models.[8] However, current in-hospital CCE practices have a higher carbon footprint than conventional endoscopy, primarily due to equipment return logistics. Additionally, the single-use capsule design and lack of recycling pathways raise environmental concerns, as manufacturing these devices is linked to significant CO_2 emissions. Strategies to reduce CCE's carbon footprint include minimising follow-up endoscopies, reducing patient travel, and adopting cloud-based reporting systems, though these remain theoretical without supporting data.[63]

A high FER potentially increases healthcare costs, CO_2 emissions, and impacts patient comfort, particularly due to repeat bowel preparation, which is consistently identified as one of the most burdensome aspects of CCE.[60 64 65] Recent studies highlighted that patients experience more discomfort from bowel preparation than the procedure itself, unlike colonoscopy, where the procedure is perceived as the most uncomfortable part.[66 67] Consequently, patients with non-urgent findings from CCE may hesitate to repeat bowel preparation for follow-up colonoscopy, potentially delaying necessary

care, compromising clinical outcomes, and reducing patient satisfaction.[17]

To ensure clarity, it may be necessary to distinguish reinvestigation rates from FERs. For colonoscopy, reinvestigation typically refers to urgent repeat procedures due to poor bowel preparation, incomplete exams, or therapeutic needs in challenging cases. In contrast, routine surveillance colonoscopies (eg, at 6 months or 3 years) are part of the planned care pathway. A similar approach should be adopted for CCE, with 'urgent' colonoscopies following initial CCE classified as reinvestigations and routine 1-year or 3-year surveillance categorised as planned follow-up. Additionally, repeat CCE could be considered as a follow-up option, reducing reliance solely on invasive endoscopic procedures.

Finally, this study has several limitations. The first is the high heterogeneity in the results. Despite applying meta-regression and subgroup analysis, heterogeneity remained substantial. This was primarily driven by multiple confounding variables within each covariate, including the lack of a standardised bowel preparation and booster regimen, variability in CCE indications, differing exclusion criteria, and inconsistencies in national referral thresholds due to variations in guidelines, such as the NHS England CCE guidance[68 69] and ESGE 2012 guideline[70] (see online supplemental tables A2–A4 and A6). Similar challenges were previously highlighted in the EU CAPTURE study.[33] In addition, CCE indications were not consistently documented across all included studies, and subgrouping them during the meta-analysis process may have introduced bias. Furthermore, the limited number of studies, particularly within subgroup analyses, may have reduced statistical power, preventing definitive conclusions. For the indication of 'incomplete colonoscopy', the FER might be lower than other indications. This is because, in many cases, the left colon would have already been partially examined during the initial colonoscopy, even if the procedure was incomplete. As a result, the combined coverage from the initial colonoscopy and the subsequent CCE procedure, even if incomplete, often provides a more comprehensive assessment of the colon, reducing the need for further reinvestigation. Moreover, while inflammatory bowel disease (IBD) is a common indication for CCE,[33] there were no studies that specifically investigated the FER in IBD patients in our literature search. Some studies actively excluded IBD patients due to concerns about structuring disease. This highlights a notable gap in the literature and underscores the need for further research to understand FERs in IBD populations.

CONCLUSION

This study revealed a significant FER for CCE and identified several key contributing factors, including complete transit rates, bowel cleansing quality, CCE capsule type, and CCE indications. To enhance the reliability, cost-effectiveness and environmental sustainability of CCE, further research is needed to reduce CCE FERs. This will be essential for improving patient outcomes, optimising resource utilisation, and ensuring CCE becomes a viable and widely adopted service in clinical practice.

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