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# Does i-scan improve adenoma detection rate compared to high-definition colonoscopy? A systematic review and meta-analysis

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## ABSTRACT

**Background and study aims** Recent studies evaluated the impact of i-scan in improving the adenoma detection rate (ADR) compared to high-definition (HD) colonoscopy. We aimed to systematically review and analyze the impact of this technique.

**Methods** A thorough search of the following databases was undertaken: PubMed/Medline, EMBASE, Cochrane and Web of Science. Full-text RCTs and cohort studies directly comparing i-scan and HD colonoscopy were deemed eligible for inclusion. Dichotomous outcomes were pooled and compared using random effects model and DerSimonian-Laird approach. For each outcome, relative risk (RR), 95% confidence interval (CI), and *P* value was generated. $P < 0.05$ was considered statistically significant.

**Results** A total of five studies with six arms were included in this analysis. A total of 2620 patients (mean age 58.6 ± 7.2 years and female proportion 44.8%) completed the study and were included in our analysis. ADR was significantly higher with any i-scan (RR: 1.20, [CI: 1.06–1.34], $P = 0.003$) compared to HD colonoscopy. Subgroup analysis demonstrated that ADR was significantly higher using i-scan with surface and contrast enhancement only (RR: 1.25, [CI: 1.07–1.47], $P = 0.004$).

**Conclusions** i-scan has the potential to increase ADR using the surface and contrast enhancement method. Future studies evaluating other outcomes of interest such as proximal adenomas and serrated lesions are warranted.

## Introduction

Colorectal cancer (CRC) is the second most common cause of cancer death in the United States and the third most common cause of cancer in both men and women [1]. The majority of colorectal cancers begin as adenomatous polyps, therefore, endoscopic excision of adenomas can reduce the chance of developing CRC [2, 3]. Colonoscopy is the gold standard for adenoma and neoplasia detection [4]. However, no endoscopist is perfect and all endoscopists have an adenoma "miss rate." This miss rate, which may potentially account for 3.7 % of interval CRC, is a major clinical concern (95 % confidence interval (CI): 2.8 %-4.9 %) [5]. Concern about missed polyps drive the development of new technologies to help detect polyps during colonoscopy [6, 7].

Poor colon prep, the existence of an obstructing lesion in the colon, and the fact that normal white light may be unable to identify some small or flat lesions, which are most common in the right side of the colon, are all significant factors affecting the adenoma detection rate (ADR) [8–10]. Extended withdrawal time, as well as operator experience, can only partially compensate for these challenges. Endoscopists can overlook up to 26 % of adenomas and 9 % of advanced adenomas [11].

Changes in procedural methods, such as inspection time, and more concerted efforts to search behind colonic folds, are among the initiatives to improve endoscopic identification of adenomatous polyps [12, 13]. Another method would be to strengthen optical processes, such as increasing the endoscopic system's resolution and contrast. High-definition (HD) endoscopy, introduced two decades ago, offers more than 650 lines of resolution and 1 to 2 million pixels, which practically provides native resolution display [14]. HD colonoscopy has shown its superiority in quality markers like ADR compared to standard definition colonoscopy [15]. Narrowband imaging, autofluorescence imaging, blue laser imaging, and linked color imaging are examples of virtual chromoendoscopy tested and demonstrated some efficacy in previous randomized controlled trials (RCTs) and meta-analyses [12, 16, 17].

i-scan (Pentax Medical, Japan), a post-processing software filter designed to enhance tissue contrast through three distinct algorithm modes, has been studied recently in colonoscopy. The various modes, which include surface enhancement (SE), tone enhancement (TE), and contrast enhancement (CE), attempt to highlight multiple mucosal abnormalities simultaneously [18]. SE increases light-dark contrast, which aids in visualizing the boundaries between normal and pathological mucosa and has been suggested as a strategy to assist in polyp detection. CE produces a slightly blue-tinged image due to the suppression of specific red and green wavelengths in the white light spectrum, which helps to augment differences with regards to mucosa depth. Finally, TE dampens the dominant red light wavelengths, allowing enhanced definition of subtle vascular irregularities and vessel structures [18, 19].

Numerous RCTs have attempted to demonstrate the efficacy of i-scan in improving colonoscopy outcomes. This meta-analysis aims to compare HD colonoscopy to i-scan and assess outcomes including ADR, polyp detection rate (PDR), adenoma per subject (APS), polyps per subject (PPS), and procedure times. Further, we attempted subgroup analysis based on the specific features of the i-scan.

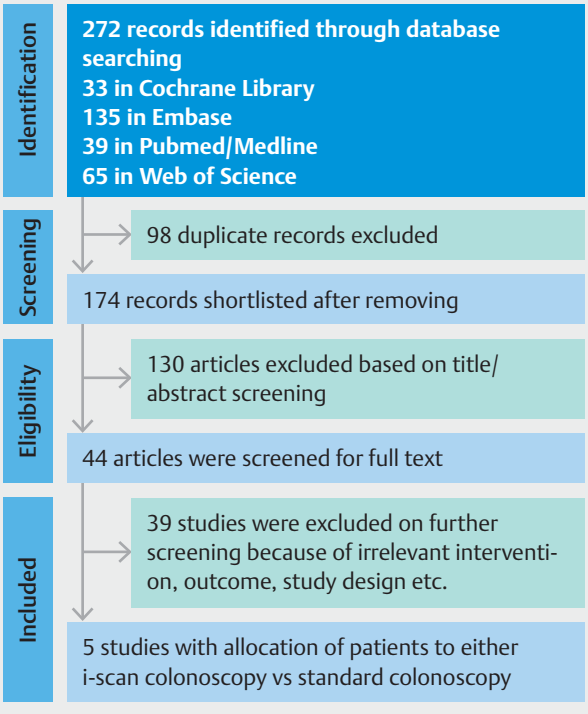
## Methods

### Search strategy

We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) criteria to perform our study. From inception till June 17, 2021, a comprehensive search of the following databases was conducted: PubMed/Medline, EMBASE, Web of Science Core Collection, and Cochrane Register of Controlled Trials. The research investigator (M.A.) devised the initial search criteria which was expanded, modified, and conducted by an experienced librarian (W.L.-S.), utilizing controlled vocabularies applicable to distinct databases. An example search strategy using EMBASE is highlighted in **Supplementary Table 1**. Our search was not limited to a single language.

### Study definitions

ADR is defined as the proportion of procedures where at least one adenoma is detected. PDR is defined as the proportion of procedures where at least one polyp is detected. APS is defined as the total number of adenomas divided by total number of colonoscopies. PPS is defined as the total number of polyps divided by total number of colonoscopies. Cecal intubation time (CIT) is defined as the time to reach the cecum after insertion




▶ **Fig. 1** PRISMA flow diagram. 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.

▶ **Table 1** Study details and demographics of patients included in the study.

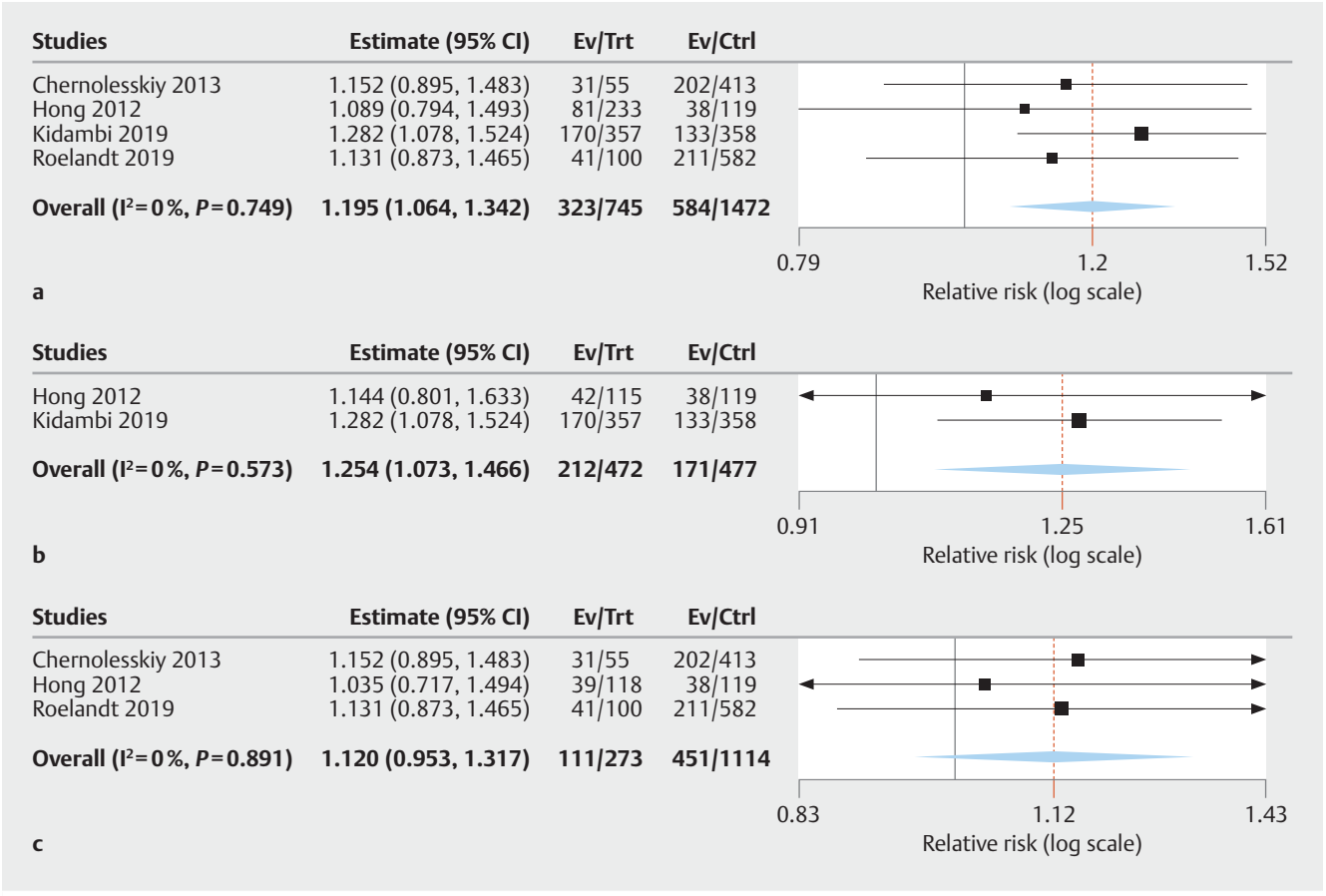
| | Kidambi et al. 2019 | Shan et al. 2017 | Roelandt et al. 2019 | Chernolesskiy et al. 2013 | Hong et al. 2012 |
|---|---|---|---|---|---|
| Techniques compared | HD vs i-scan1 | HD vs i-scan1 | HD vs i-scan2 | HD vs i-scan2 | HD vs i-scan1 vs i-scan2 |
| Total patients enrolled, n | 740 (HD: 371 i-scan 1: 369) | 403 (HD: 202 i-scan 1: 201) | 765 (HD: 653 i-scan 2: 112) | 483 (HD: 425 i-scan 2: 58) | 356 (HD: 120 i-scan 1: 117 i-scan 2: 119) |
| Study Completion rate, n (%) | 715 (96.6 %) (HD: 358 i-scan 1: 357) | 403 (100.0 %) (HD: 202 i-scan 1: 201) | 682 (89.2 %) (HD: 582 i-scan 2: 100) | 468 (96.9 %) (HD: 413 i-scan 2: 55) | 352 (98.9 %) (HD: 119 i-scan 1: 115 i-scan 2: 118) |
| Mean age (SD), years | HD: 60.8 (7.6) i-scan1: 61.4 (7.5) | HD: 49.7 (13.1) i-scan1: 48.9 (13.4) | HD: 60.8 (12.1) i-scan2: 61.3 (13) | HD: 66.3 (4.3) i-scan2: 65.8 (4.7) | HD: 48.9 (10.7) i-scan1: 50.4 (11.4) i-scan2: 49.6 (11.3) |
| Female Proportion, % | HD: 50.4 % i-scan1: 50.1 % | HD: 39.1 % i-scan1: 41.6 % | HD: 48.1 % i-scan2: 54.0 % | HD: 42.1 % i-scan2: 36.4 % | HD: 35.3 % i-scan1: 34.8 % i-scan2: 34.7 % |
| Indication for colonoscopy, % | Scr/Sur: 98.4 % Diag: 1.6 % | Scr/Sur: 5.7 % Diag: 94.3 % | Scr/Sur: 68.3 % Diag: 31.7 % | Scr/Sur: 100 % Diag: 0 % | Scr/Sur: 100 % Diag: 0 % |

Diag, diagnostic; HD, high definition; i-scan1, i-scan with surface and contrast enhancement; i-scan 2, i-scan with surface, contrast and tone enhancement; n, number of patients; SD, standard deviation; Scr/Sur, screening/surveillance.

▶ **Table 2** Outcomes for individual studies.

| | Kidambi et al. 2019 | Shan et al. 2017 | Roelandt et al. 2019 | Chernolesskiy et al. 2013 | Hong et al. 2012 |
|---|---|---|---|---|---|
| Mean CIT (SD), mins | HD: 6.1 (4.2) i-scan1: 6.7 (5.3) | HD: NR i-scan1: NR | HD: NR i-scan2: NR | HD: 11.1 (6.6) i-scan2: 11.6 (7.5) | HD: NR i-scan1: NR i-scan2: NR |
| WT (SD), mins | HD: 9 (4.9) i-scan1: 9.2 (4) | HD: 8.4 (1.7) i-scan1: 8.2 (1.5) | HD: NR i-scan2: NR | HD: 15.6 (8.2) i-scan2: 14.7 (8) | HD: 7.8 (2.3) i-scan1: 7.8 (1.7) i-scan2: 8.4 (1.8) |
| PDR, n (%) | HD: NR i-scan1: NR | HD: 107 (53.0 %) i-scan1:103 (51.2 %) | HD: NR i-scan2: NR | HD: 239 (57.9 %) i-scan2: 37 (67.3 %) | HD: 50 (42.0 %) i-scan1: 60 (52.2 %) i-scan2: 53 (44.9 %) |
| ADR, n (%) | HD: 133 (37.2 %) i-scan1: 170 (47.6 %) | HD: NR i-scan1: NR | HD: 211 (36.3 %) i-scan2: 41 (41.0 %) | HD: 202 (48.9 %) i-scan2: 31 (56.4 %) | HD: 38 (31.9 %) i-scan1: 42 (36.5 %) i-scan2: 39 (33.1 %) |
| APS (SD) | HD: 0.69 (1.4) i-scan1: 0.81 (1.2) | HD: NR i-scan1: NR | HD: NR i-scan2: NR | HD: 1 (1.54) i-scan2: 1.07 (1.27) | HD: 0.54 (1.19) i-scan1: 0.63 (1.06) i-scan2: 0.61 (1.04) |
| PPS (SD) | HD: NR i-scan1: NR | HD: NR i-scan1: NR | HD: NR i-scan2: NR | HD: 1.42 (1.96) i-scan2: 1.58 (1.73) | HD: 0.83 (1.43) i-scan1: 0.99 (1.34) i-scan2: 0.92 (1.27) |

ADR, adenoma detection rate; APS, adenoma per subject; CIT, cecal intubation time; HD, high definition; i-scan 1, i-scan with surface and contrast enhancement; i-scan 2, i-scan with surface, contrast and tone enhancement; n, number of patients; PDR, polyp detection rate; PPS, polyps per subject; SD, standard deviation; WT, withdrawal time.




▶ **Fig. 2** Adenoma detection rate (ADR) for i-scan. **a** Overall any i-scan. **b** i-scan1 (with SE and CE). **c** i-scan 2 (with SE, CE and TE).

of colonoscope at the anal verge. Withdrawal time (WT) is defined as the time spent while examining the colon after achieving cecal intubation until the end of colonoscopy.

## Inclusion/exclusion criteria

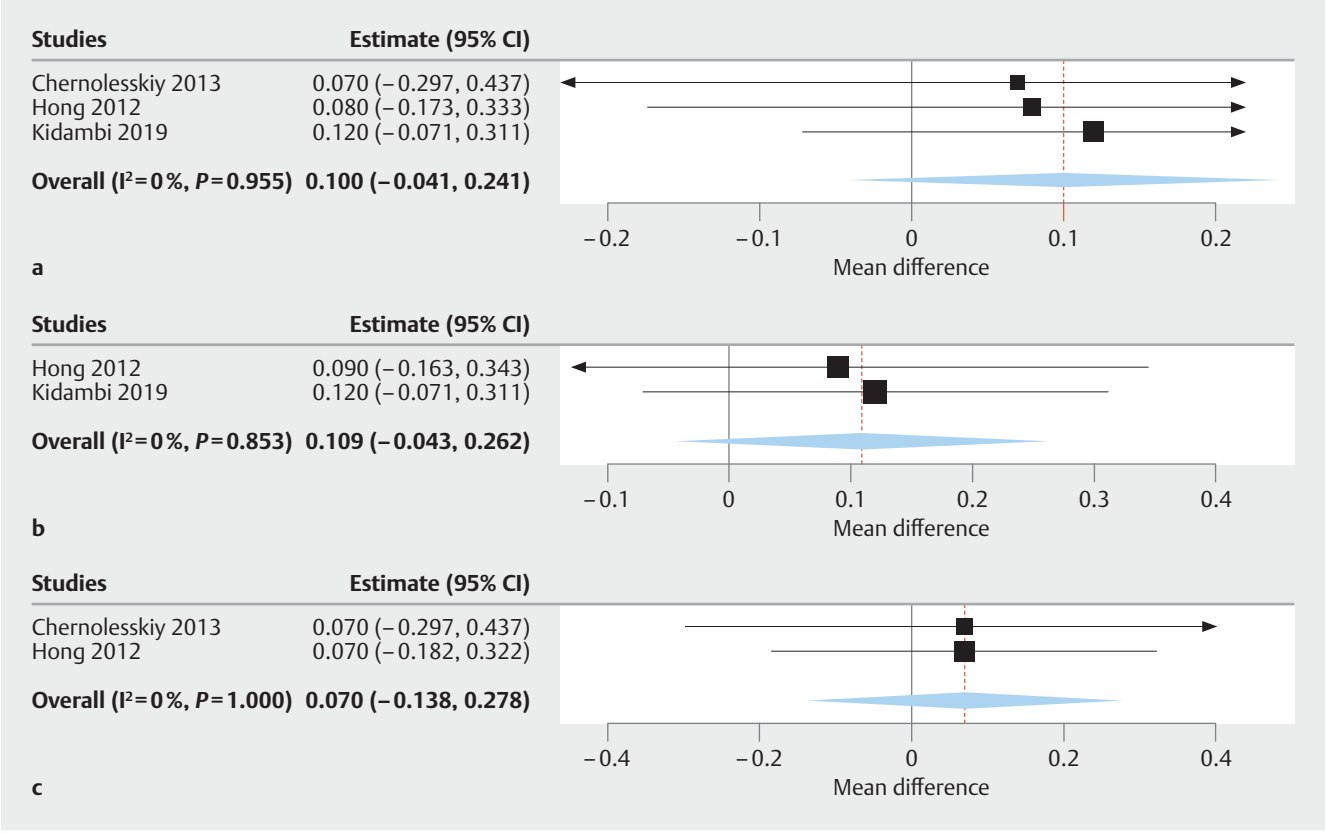
We used the following parameters for study inclusion: 1) Patients – enrolled in study for undergoing colonoscopy for any indication; 2) Intervention – use of i-scan during colonoscopy; 3) Control – Use of HD colonoscopy; and 4) Outcomes – ADR and PDR. We only included full-length RCTs and prospective/retrospective studies. All other study designs including case-control, cross-sectional, case series, case reports, review articles, guidelines, and letter to the editor were excluded. We also excluded abstracts as bias assessment is difficult, given the lack of details regarding study methodology.

## Screening and data collection

The studies were screened by two independent reviewers (H.H. and M.A.). The initial screening was based on titles and abstracts, with the full-text screening of relevant publications following. Two independent reviewers extracted the data (H.H. and M.A.). Discrepancy in study selection and data extraction was resolved through mutual discussion. Data on demographics (age, gender), indication for procedure (diagnostic, screening/surveillance), features of i-scan (CE, SE, and/or TE) and outcomes (primary – ADR, PDR and secondary – CIT and WT) were collected and summarized using Microsoft Excel (Microsoft, Redmond, Washington, United States). Per-protocol data were used for all studies.

## Data synthesis and statistical analysis

Given the presumed heterogeneity in studies, the random effects model and DerSimonian-Laird approach was used as a priori to pool and compare outcomes [20]. Risk ratios (RR) with 95 % CI and *P* values were determined for binary outcomes. Mean difference (MD), 95 % CI, and *P* values were obtained for continuous outcomes. The $I^2$ statistic, as defined by the Cochrane handbook for systematic reviews, was used to measure heterogeneity across trials. Significant heterogeneity was described as a percentage of $I^2$ greater than 50 %. Subgroup analysis was performed based on the modes of i-scan used (SE, TE and/or CE). Subgroup analysis was also performed based on study design i. e. RCTs and cohort studies where applicable. For all the outcomes studied, $P<0.05$ was considered statistically significant [21]. Open Meta Analyst was used to compute the results (CEBM, University of Oxford, Oxford, United Kingdom).




▶ **Fig. 3** Adenoma per subject (APS) for i-scan. **a** Overall any i-scan. **b** i-scan1 (with SE and CE). **c** i-scan 2 (with SE, CE and TE).

### Bias assessment

The Cochrane Risk of Bias tool was used to subjectively assess bias in included RCTs. The Newcastle-Ottowa score was used to assess bias in cohort studies. Publication bias was measured qualitatively and quantitatively using funnel plot and Egger's regression analysis respectively. $P<0.05$ was considered significant for publication bias.

## Results

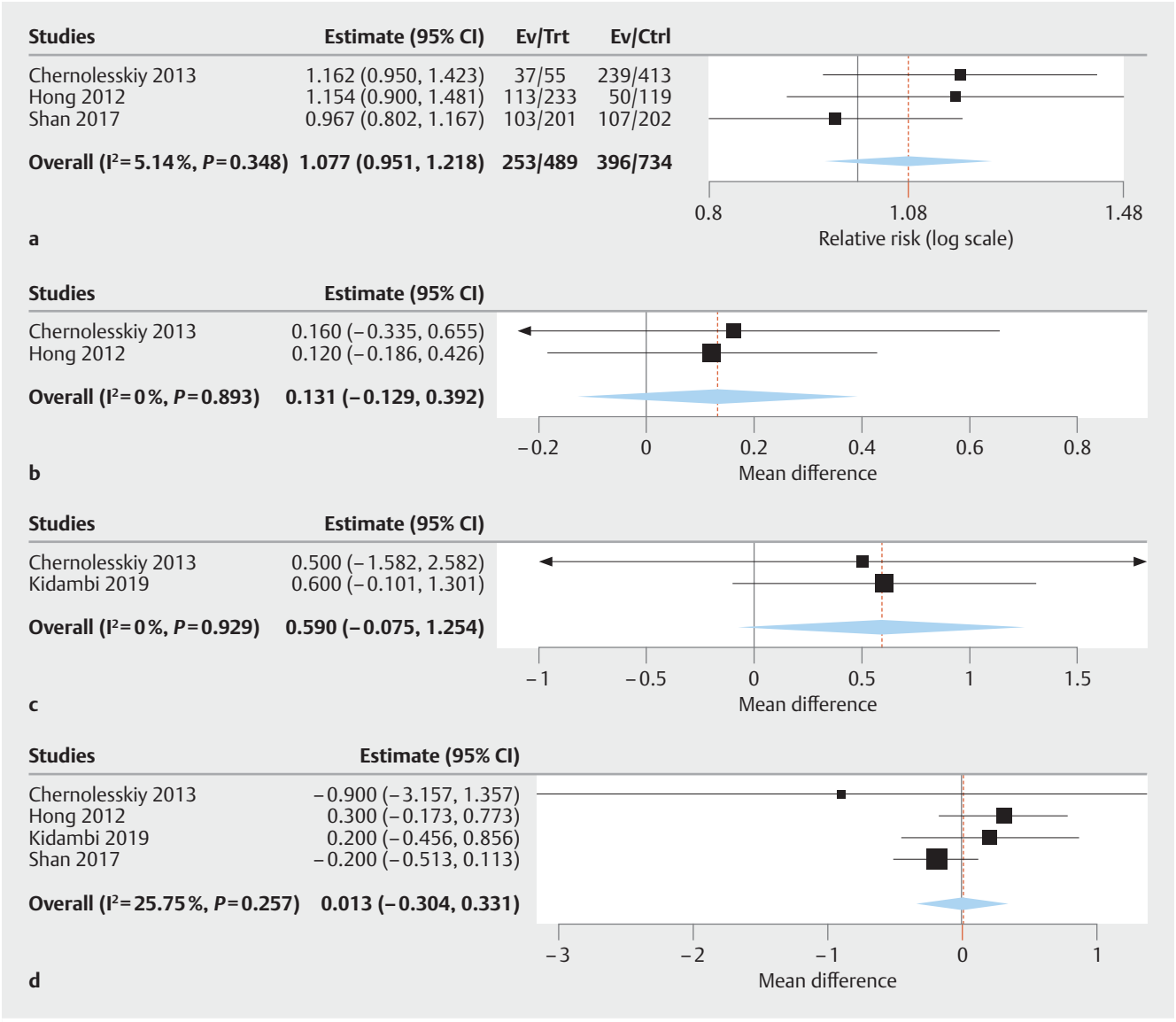
After applying the inclusion and exclusion criteria, a total of four RCTs and one retrospective study with 2747 patients were included. The details of study selection are highlighted in the PRISMA flow diagram (▶ **Fig. 1**). From 2747 patients a total of 2620 (95.4%) completed the procedures and were included in the study. The mean age of included patients was 58.6 ± 7.2 years and female proportion was 44.8%. The indication for colonoscopy was as follows: screening/surveillance 77.0% and diagnostic 23.0%. Two studies used i-scan with CE and SE (i-scan1) [22, 23], two studies used i-scan with CE, SE, and TE (i-scan2) [24, 25], and one study compared both i-scan1 and i-scan2 to HD colonoscopy.[26] Study details and demographics of included patients are shown in ▶ **Table 1**. The outcomes for individual studies are shown in ▶ **Table 2**.

### Adenoma detection rate

ADR was higher with any i-scan and was statistically significant (43.4% vs 39.7%, RR: 1.20, [CI: 1.06–1.34], $P=0.003$, $I^2=0\%$) (▶ **Fig. 2a**) compared to HD colonoscopy. Subgroup analysis demonstrated that ADR was higher and statistically significant in two studies that used i-scan1 (44.9% vs 35.8%, RR: 1.25, [CI: 1.07–1.47], $P=0.004$, $I^2=0\%$) (▶ **Fig. 2b**) and not statistically significant for three studies that utilized i-scan2 (40.7% vs 40.5%, RR: 1.12, [CI: 0.95–1.32], $P=0.18$, $I^2=0\%$) (▶ **Fig. 2c**). Subgroup analysis of only RCTs (3 studies) showed higher and statistically significant ADR for i-scan group compared to HD colonoscopy (42.3% vs 36.1%, RR: 1.21, [CI: 1.06–1.38], $P=0.005$, $I^2=0\%$).

### Adenoma per subject

The APS with any i-scan was numerically higher compared to HD colonoscopy but the mean difference was not statistically significant (MD: 0.10, [CI: −0.04–0.24], $P=0.15$, $I^2=0\%$) (▶ **Fig. 3a**). Subgroup analysis for APS showed consistent results with i-scan1 (MD: 0.11, [CI: −0.04–0.26], $P=0.16$, $I^2=0\%$) (▶ **Fig. 3b**) and i-scan2 (MD: 0.07, [CI: −0.14–0.28], $P=0.16$, $I^2=0\%$) (▶ **Fig. 3c**). Subgroup analysis on only RCTs (2 studies) showed similar results (MD: 0.11, [CI: −0.05 – 0.26], $P=0.18$, $I^2=0\%$).




▶ **Fig. 4** Comparing any i-scan and HD colonoscopy for: **a** PDR, **b** PPS, **c** CIT, **d** WT. CIT, cecal intubation time; PDR, polyp detection rate; PPS, polyp per subject; WT, withdrawal time.

## Polyp detection rate

Only three studies assessed PDR for any i-scan which was not statistically significant (51.7% vs 53.9%, RR: 1.08, [CI: 0.95–1.22], $P=0.24$, $I^2=5.1\%$) (▶ **Fig. 4a**). Subgroup analysis was consistent for both i-scan1 (51.6% vs 48.9%, RR: 1.07, [CI: 0.84–1.37], $P=0.57$, $I^2=54.0\%$) and i-scan2 (52.0% vs 54.3% RR: 1.13, [CI: 0.96–1.34], $p=0.15$, $I^2=0\%$). Consistent result was obtained for subgroup analysis of only RCTs (2 studies, 49.8% vs 48.9%, RR: 1.04, [CI: 0.88–1.23], $P=0.68$, $I^2=0.68$).

## Polyps per subject

Only two studies assessed PPS and this was not statistically significant (MD: 0.13, [CI: −0.13–0.39], $P=0.32$, $I^2=0\%$) (▶ **Fig. 4b**). Subgroup analysis based on type i-scan and study type was not applicable.

## Procedural times

The procedural times for i-scan and HD colonoscopy were not statistically significant for CIT (MD: 0.59, [CI: −0.08–1.25], $P=0.08$, $I^2=0\%$) and WT (MD: 0.013, [CI: 0.304–0.331], $P=0.935$, $I^2=25.5\%$) (▶ **Fig. 4c**, ▶ **Fig. 4d**).

## Bias assessment

All included RCTs were noted to have high risk as lack of blinding of endoscopists to study intervention was impractical. The only cohort study had a score of 6 (maximum score that can be achieved was 6) The publication bias could not be assessed given the low number of studies.

## Discussion

We evaluated the utility of using i-scan in improving ADR compared to HD colonoscopy. This analysis demonstrates that colonoscopy examinations performed with i-scan1 or i-scan with surface and CE showed higher ADR compared to HD. Other outcomes of interest, including APS, PDR, and PPS, did not achieve statistical significance. Procedure times, such as WT and CIT, did not show statistically significant differences.

ADR is a high-quality indicator with previous studies validating it as a predictor for interval CRC [27, 28]. The U.S. Multi-Society Task Force set ADR benchmarks of ≥ 25 % overall (≥ 20 % in women and ≥ 30 % in men) among colonoscopists to achieve high-quality examinations [29]. Numerous interventions and techniques including use of distal attachments (cap, cuff, rings), virtual chromoendoscopy, water-based techniques, having a second observer, premedication with peppermint oil, optimizing bowel prep and ensuring good examination techniques have been proposed previously to improve ADR during colonoscopy [12, 13, 30–34]. Our study demonstrated the potential use of i-scan with surface and CE as an additional modality that can be employed to improve the ADR [22, 35].

PDR, APS, and PPS showed numerically higher rates of detection, however, statistical significance was not achieved; this may have been due to the low number of studies assessing these outcomes. We were also unable to perform analysis based on size of lesions, appearance of lesions (sessile vs pedunculated), location in colon (proximal vs distal), and serrated lesions. Future studies should focus on these outcomes to further explore the efficacy of i-scan in improving these quality metrics.

Our study is not without limitations. First, only five studies were available to assess the impact of i-scan on ADR. Of these, only three arms were available for each, i-scan 1 and i-scan 2. Second, not all studies assessed the outcomes (ADR, PDR, APS, and PPS) further limiting our analysis. Third, all RCTs were at high risk of bias because of lack of blinding of endoscopists to study intervention. In addition, we could not account for factors that could influence the results such as different levels of training and/or experience of endoscopists, adequacy of bowel prep, and timing of colonoscopy. Likewise, not all studies enrolled patients for screening/surveillance indication and hence the ADR assessed in our study is not reflective of a “true screening ADR.” Despite these limitations, our study was conducted using a stringent search criterion and included a robust number of study applicants. We were able to perform subgroup analysis based on the type of i-scan used. Our results also had low heterogeneity.

## Conclusions

The results of our study highlight the potential benefit of using i-scan technology to improve ADR, but not other associated outcomes of importance.

## Competing interests

The authors declare that they have no conflict of interest.

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