Second-generation distal attachment cuff improves adenoma detection rate: meta-analysis of randomized controlled trials

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Background and Aims: Multiple randomized controlled trials (RCTs) using the second-generation distal attachment cuff device (Endocuff Vision; Olympus America, Center Valley, Pa, USA) have reported conflicting results in improving adenoma detection rate (ADR) compared with standard high-definition colonoscopy without the distal attachment. We conducted a systematic review and meta-analysis of RCTs to compare outcomes between second-generation cuff colonoscopy (CC) versus colonoscopy without the distal attachment (standard colonoscopy [SC]).

Methods: An electronic literature search was performed using PubMed, Google Scholar, Embase, and Cochrane Library through May 2020. The primary outcome was reporting of ADR, and secondary outcomes were polyp detection rate (PDR), mean withdrawal time, mean adenomas per colonoscopy (APC), sessile serrated lesion detection rate, and adverse events. Pooled rates and risk ratios (RRs) with 95% confidence intervals were reported.

Results: Eight RCTs with 5695 patients were included in the final analysis, with 2862 patients (mean age, 62.8 years; 52.9% men) in the CC group and 2833 patients (mean age, 62.6 years; 54.2% men) in the SC group. Compared with SC, use of CC was associated with a significant improvement in ADR (49.8% vs 45.6%, respectively; RR, 1.12; $P = .02$), PDR (58.1% vs 53%, respectively; RR, 1.12; $P = .009$), and APC ($P < .01$). Furthermore, use of CC had a .93-minute lower mean withdrawal time ($P < .01$) when compared with SC. The difference in ADR was larger in the screening/surveillance population (6.5%, $P = .02$) and when used by endoscopists with ADRs <30% (9.4%, $P = .03$).

Conclusions: The results of this meta-analysis of randomized trials show a significant improvement in ADR and APC with shorter withdrawal times using the second-generation cuff device compared with SC. (Gastrointest Endosc 2021;93:544-53.)

Abbreviations: ADR, adenoma detection rate; APC, mean adenomas per colonoscopy; A-ADR, advanced adenoma detection rate; CC, cuff colonoscopy; FOBT+, fecal occult blood test–positive; D-ADR, distal adenoma detection rate; NNT, number needed to treat; PDR, polyp detection rate; P-ADR, proximal adenoma detection rate; RCT, randomized controlled trial; RR, risk ratio; SC, standard colonoscopy; SDR, sessile serrated lesion detection rate.

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Despite steadily decreasing trends in the incidence of colorectal cancer over the last 5 years, colorectal cancer still ranks second in the United States for cancer-related mortality.[1] Colonoscopy, as a screening procedure, is a useful tool in detecting tumors at an earlier and more treatable stage and also facilitates the timely removal of precancerous lesions or adenomas.[2] Adenoma detection rate (ADR) has been proposed as a benchmark and a reportable colonoscopy quality measure by the Centers for Medicare & Medicaid Services.[3-6] ADR has been shown to be inversely associated with the risk of interval colorectal cancer.[3,4] ADR can be improved by technique or devices that improve mucosal exposure or by tools that highlight flat colonic lesions.

A number of distal attachments have been tested to improve ADR, including a transparent cap, cuff, or rings. The cuff is attached to the tip of the colonoscope, and the fingers are used to flatten colonic folds, leading to increased mucosal visualization. Although a number of studies and analyses have been published, they had mostly used the first-generation cuff (Endocuff, UK).[7-13] More recently, a second-generation cuff (Endocuff Vision; Olympus America, Center Valley, Pa, USA) has been evaluated in several randomized controlled trials (RCTs) showing divergent results in improving ADR. Compared with the first-generation device, the Endocuff Vision has only 1 row of flexible arms that are softer, 2 mm longer, and available in 4 different sizes for different types of colonoscopes. The aim of this systematic review and meta-analysis was to compare the outcomes of cuff colonoscopy (CC) using the more recent and widely available second-generation device with standard high-definition white-light colonoscopy (SC) without any distal attachment.

METHODS

This systematic review and meta-analysis along with the eligibility criteria and analyses were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement[14] (Supplementary Table 1, available online at www.giejournal.org).

Search strategy

A comprehensive electronic literature search was conducted in PubMed/MEDLINE, Google Scholar, EMBASE, Cochrane, and major conference proceedings to identify eligible articles, from the beginning of indexing for each database through May 10, 2020. The following text words and Medical Subject Heading/Entrée terms were searched: "Endocuff vision," "Endocuff," "distal attachment," "adenoma detection rate," "ADR," "adenoma," "polyp detection rate," "PDR," "screening," "surveillance," "withdrawal," and "adverse events" (Supplementary Table 2, available online at www.giejournal.org).

Inclusion and exclusion criteria

The retrieved articles were screened for eligibility by 2 independent reviewers (H.K.P. and V.T.C.), and any disagreement was resolved by consensus with a third author (P.S.). The inclusion criteria for this analysis were studies reporting ADR using CC and SC, prospective enrollment of patients undergoing colonoscopy, and randomized study design. Exclusion criteria were studies not reporting ADR for either CC or SC in the same study; studies including patients with polyposis syndrome and inflammatory bowel disease; retrospective studies, prospective single-arm studies, case reports, and case series; and studies conducted using the first-generation cuff device.

Data extraction and quality assessment

The following data were extracted from each study in each group: study author, study design, age, gender, number of patients, ADR, total number of adenomas, polyp detection rate (PDR), sessile serrated lesion detection rate (SDR), advanced adenoma detection rate (A-ADR), proximal and distal ADR (P-ADR, D-ADR), cecal intubation rate, ileal intubation rate, mean adenomas per colonoscopy (APC), withdrawal times, and adverse events.

Definitions and outcomes

ADR was defined as the number of patients with at least 1 adenoma (tubular, villous, or tubulovillous adenoma based on histopathology) divided by the total number of patients. PDR was defined as the number of patients with at least 1 polyp divided by the total number of patients. SDR was defined as the number of patients with at least 1 sessile serrated lesion (sessile serrated or traditional serrated adenoma) divided by the total number of patients. A-ADR was defined as the total number of patients with at least 1 advanced adenoma (adenoma $\geq$10 mm in size, villous features, or high-grade dysplasia). P-ADR was defined as the number of patients with adenoma in the proximal colon (cecum, ascending colon, hepatic flexure, and transverse colon) divided by the total number of patients. D-ADR was defined as the number of patients with adenoma in the distal colon (splenic flexure, descending colon, sigmoid colon, and rectum) divided by the total number of patients. APC was defined as the number of adenomas detected in total divided by the number of patients who underwent colonoscopy. Cecal intubation rate was defined as the proportion of patients who had a successful intubation of the cecum. Mean withdrawal time was calculated by the time measured from reaching the cecum until examination of the colon was complete with withdrawing of the scope and termination of the procedure, excluding the time required for polypectomy. Serious adverse events recorded during the procedure included the incidence of bleeding and perforation.

The primary outcome of interest was comparing the ADR between the CC and SC groups. Secondary outcomes

were PDR, SDR, A-ADR, P-ADR, D-ADR, APC, cecal intubation rate, ileal intubation rate, mean withdrawal time, and rate of adverse events. If there was moderate to high heterogeneity, subgroup and sensitivity analyses were performed as follows: (1) outcomes for screening and surveillance patients only, (2) outcomes for screening and surveillance patients after excluding the U.K. Bowel Cancer Screening Program fecal occult blood test–positive patients (FOBT+), and (3) comparison of ADR between the 2 groups for studies reporting <30%, <40%, <50%, and > 50% ADR in the SC group (control arm).

Statistical analyses

The pooled proportions were calculated including the frequency of events over the total number of patients along with 95% confidence limits. The random-effects model described by DerSimonian and Laird was used for analysis. Risk ratios (RRs) were calculated by comparison of the pooled proportions. A $P < .05$ was considered statistically significant. The corresponding forest plots were constructed with the weights of individual studies representing the size of individual squares. Heterogeneity among the studies was assessed using the inconsistency index (I^2-statistic). I^2-values of 0% to 30%, 31% to 60%, 61% to 75%, and 76% to 100% were reflective of low, moderate, substantial, and considerable heterogeneity, respectively. Comparison of APC and withdrawal times were performed by calculating the mean difference with standard error. Publication bias was assessed by funnel plot, and asymmetry was tested using the Rucker test. The number needed to treat (NNT) for detecting 1 additional patient with an adenoma was calculated as the inverse of the difference of ADR between the 2 groups. All analyses were performed using Open Meta analyst (CEBM; Brown University, Providence, RI, USA) and Review Manager version 5.3 (The Nordic Cochrane Center, Copenhagen, Denmark) statistical software.

Quality of evidence assessment

The risk of bias in individual studies was assessed using the Cochrane Collaboration tool.[15] The quality of body of evidence was assessed using the Grading of Recommendations, Assessment and Evaluation approach.[16] Two independent researchers (H.K.P. and V.T.C.) graded risk of bias, indirectness, inconsistency, imprecision, and publication bias, and the quality was deemed high, moderate, low, or very low using GRADEPro (GRADEpro GDT; GRADEpro Guideline Development Tool, McMaster University, 2015 (developed by Evidence Prime, Inc).

RESULTS

Four hundred sixty-nine articles were retrieved based on the initial search, and after exclusions, 21 studies were reviewed in detail, of which 8 RCTs were included in the final analysis (Fig. 1).[12,13,17-22] Of 5695 patients, 2862 were in the CC group (52.9% men; mean age, 62.8 ± 2.9 years) and 2833 in the SC group (54.2% men; mean age, 62.6 ± 3.4 years). There were no differences in the proportion of men or mean age between the 2 groups. The indications for colonoscopy in most studies were varied (screening, surveillance, and/or diagnostic), but 5 of 8 studies[12,13,17,21,22] reported outcomes on screening and surveillance patients also. Of the 8 studies, 2 were from the United Kingdom (2306 patients),[12,13] and 1 each from France (2058),[21] United States (200),[17] Germany (240),[19] Portugal (170),[20] Thailand (404),[22] and Australia (320).[18] Two studies were multicenter[13,17] and 6 were single-center experiences.[12,18-22] Six studies were in full text format[12,13,17-19,21] and 2 were abstracts.[20,22] Of 4 studies that reported the information, endoscopists were experienced in all but 1 study (EVASTA)[19] in using CC before initiation of the trial. Detailed characteristics of each study with their demographics are reported in Table 1. Risk of bias assessment using Cochrane Collaboration tool is provided in Supplementary Figure 1 (available online at www.giejournal.org).

Primary outcome: ADR

All 8 studies reported ADR in the CC and SC groups (5695 patients) and was reported as the primary outcome in 4 of 8 studies[13,18,21,22] (Table 2, Fig. 2, Supplementary Table 3, available online at www.giejournal.org). The Rucker's coefficient for publication bias in these studies was $P = .294$, indicating no publication bias existed for the primary outcome between the 8 studies (Supplementary Fig. 2, available online at www.giejournal.org). The pooled ADR in the CC group was 49.8% (95% CI, 42.3%-57.3%) and in the SC group was 45.6% (95% CI, 36.3%-54.8%). The use of CC was associated with a statistically significant ∼4.2% improvement in ADR when compared with SC (RR, 1.12; 95% CI, 1.02-1.23; $P = .02$; $I^2 = 53\%$).

If ADR calculation was restricted to the subgroup of patients undergoing either screening or surveillance colonoscopies[12,13,17,21,22] (n = 3294), the values were as follows: CC 55.8% (95% CI, 46.7%-64.9%) and SC 49.3% (95% CI, 37.7%-61%) (RR, 1.15; 95% CI, 1.03-1.28; $P = .02$; $I^2 = 59\%$) (Fig. 2, Supplementary Table 4, available online at www.giejournal.org). The NNT was calculated at 24 for all 8 studies and at 15 if the calculation was restricted to only screening/surveillance studies. Further sensitivity analysis for the average-risk screening and the surveillance population, after excluding 2 studies that included FOBT+ patients,[12,13] yielded the following results: 51.7% versus 44.2% (RR, 1.21; 95% CI, 1.09-1.34; $P = .0004$; $I^2 = 3\%$; NNT, 13), respectively, for CC versus SC[17,21,22] (Fig. 2, Supplementary Table 5, available online at www.giejournal.org).

Further subgroup analysis of ADR based on the baseline ADR of endoscopists involved in the RCTs yielded the following results (Supplementary Fig. 3, available online at www.giejournal.org; Supplementary Table 5). For operators with low baseline ADR <30% (ie, low

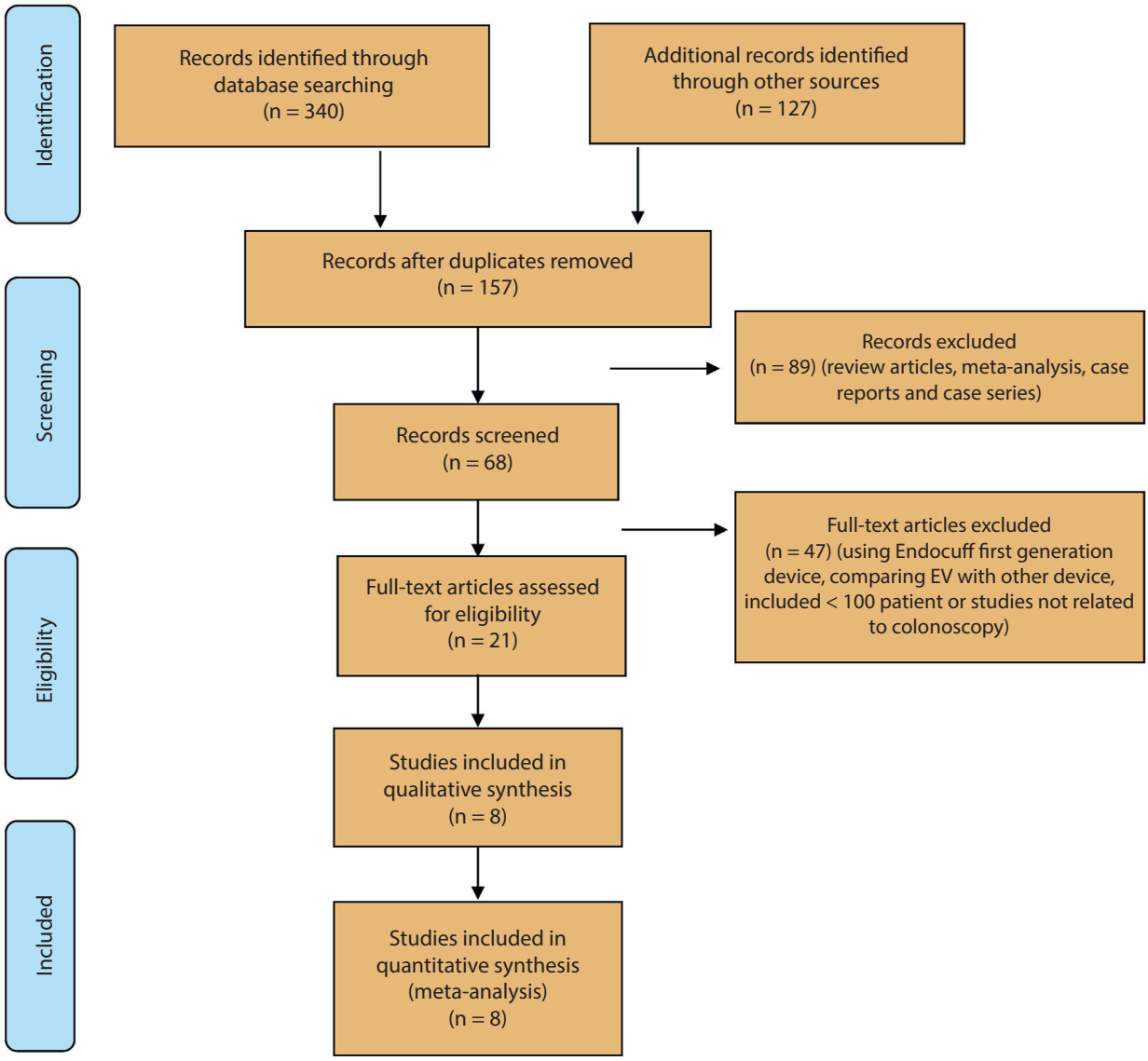

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of study selection process.

detectors, n = 2378),[18,21] 38.8% versus 29.4% (RR, 1.32; 95% CI, 1.18-1.48; $P < .01$; $I^2 = 0\%$); baseline ADR <40% (n = 4150),[13,18,21] 39.7% versus 31.9% (RR, 1.23; 95% CI, 1.09-1.39; $P = .0009$; $I^2 = 45\%$); baseline ADR <50% (n = 4390),[13,18,19,21,22] 41.4% versus 36.7% (RR, 1.16; 95% CI, 1.03-1.31; $P = .01$; $I^2 = 51\%$); and baseline ADR >50% (ie, very high detectors, n = 901),[12,17,20] 64% versus 60.8% (RR, 1.03; 95% CI, .93-1.14; $P = .51$; $I^2 = 0\%$). Thus, ADR improved in the CC group for detectors up to 50% but no difference was seen beyond that. The NNT further decreased to 11 for baseline ADR <30% (Fig. 4).

Restricting the analysis further to include only the 3 studies that reported withdrawal time,[13,17,21] the ADR was higher with CC versus SC: 41% versus 33.5% (RR, 1.21; 95% CI, 1.08-1.36; $P = .001$; $I^2 = 0\%$), respectively (NNT, 13). If the population was limited to screening/surveillance subgroup in those 3 studies, the difference in ADR was further higher with CC versus SC: 50.9% versus 40.9% (RR, 1.24; 95% CI, 1.14-1.35; $P < .0001$; $I^2 = 0\%$), respectively (NNT, 10) (Supplementary Fig. 4, available online at www.giejournal.org; Supplementary Table 5).

Secondary outcomes

Sessile serrated lesion detection rate. Five studies reported the SDR (n = 4520)[13,17,18,20,21] (Table 2, Fig. 3, Supplementary Table 3). The CC and SC groups had individual pooled rates of 8.8% (95% CI, 3.1%-14.4%) and 6.1% (95% CI, .7%-11.5%), respectively, with no statistically significant difference in the SDR (RR, 1.21; 95% CI, .90-1.61; $P = .20$; $I^2 = 18\%$). If analysis was

TABLE 1. Study characteristics with demographics and indications

Study and year	Duration	Type of study and center	No. of patients (CC; SC)	Mean age (y) (CC; SC)	Men (%) (CC; SC)	Primary outcome	Screening ± surveillance population (%) (CC; SC)	Pretrial experience of using Endocuff Vision
Bhattacharya et al,[12] 2017	2015-2016	Parallel, 1 center	266; 265	68; 67	60.9; 67.9	Mean polyp per patient	100; 100 (FOBT+)	NA
Ngu et al,[13] 2018	2014-2016	Parallel, 7 centers	888; 884	61.7; 62.1	57.1; 56.8	ADR	45.4; 44.6	20 procedures
Rex et al,[17] 2019	2017-2018	Parallel, 2 centers	101; 99	62.7; 61.7	56.4; 42.4	Withdrawal time	100; 100	Highly experienced
Jacob et al,[18] 2019	2016-2017	Parallel, 1 center	182; 138	NA	56.7; 59.3	ADR	NA	4 procedures
Von Figura et al,[19] 2019	2017-2019	Parallel, 1 center	118; 122	63.6; 65.3	51.7; 62.3	Polypectomy duration	45.8; 38.5	None
Costa Santos et al,[20] 2019*	2018-2019	Parallel, 1 center	81; 89	62.4 (total)	57.4 (total)	Mean sessile serrated lesion per colonoscopy	100; 100	NA
Karsenti et al,[21] 2020	2017-2018	Cluster-randomized, crossover, 1 center	1026; 1032	59.2; 57.4	47.4; 49	ADR	64.3; 62.2	NA
Vanduangden et al,[22] 2020*	NA	Parallel, 1 center	200; 204	NA	NA	ADR	100; 100	NA

CC, Cuff colonoscopy; *SC*, standard colonoscopy; *ADR*, adenoma detection rate; *FOBT*, fecal occult blood test; *NA*, not available.
*Abstracts.

TABLE 2. Outcomes of meta-analysis comparing cuff colonoscopy and standard colonoscopy

Outcomes (no. of studies)	Cuff colonoscopy (%)	Standard colonoscopy (%)	Risk ratio (95% CI; *P* value; I^2)	Quality of evidence per Grading of Recommendations, Assessment and Evaluation
ADR (8)	49.8 (42.3-57.3)	45.6 (36.3-54.8)	1.12 (1.02-1.23; .02; 53%)	Low
Polyp detection rate (5)	58.1 (49 .5-66.8)	53 (40.7-65.4)	1.13 (1.03-1.23, .009, 54%)	Low
Sessile serrated lesion detection rate (5)	8.8 (3.1-14.4)	6.1 (.7-11.5)	1.21 (.90-1.61; .20; 18%)	Low
Advanced ADR (3)	11.4 (7.5-15.4)	10.8 (6.5-15.2)	1.11 (.93-1.33; .49, 0%)	Low
Proximal ADR (3)	29.9 (20.1-39.7)	25.5 (21.9-29)	1.26 (.94-1.68; .12; 81%)	NA
Distal ADR (3)	25.2 (23.2-27.3)	18.2 (13.7-22.8)	1.31 (1.09-1.58; .004; 41%)	NA
Ileal intubation rate (3)	50 (21.9 - 78.1)	58.7 (22.6-94.8)	.83 (.68-1.02; .07; 81%)	NA
Cecal intubation rate (7)	97.8 (96.4-99.2)	98.7 (97.7-99.7)	.99 (.98-1.01; .46; 68%)	NA
Adverse events (7)	.4 (-.7)	.6 (-1.1)	.70 (.35-1.38; .66; 0%)	NA

Values in parentheses are 95% confidence interval unless otherwise defined.
ADR, Adenoma detection rate; *NA*, not applicable.

restricted to the screening/surveillance population only (n = 2299),[13,17,21] the SDR was significantly higher in the CC group: 12.1% versus 8.3% (RR, 1.28; 95% CI, 1.01-1.64; $P = .04$; $I^2 = 0\%$) for CC and SC, respectively (Supplementary Table 4).

Mean adenomas per colonoscopy. Seven studies reported the APC in the CC group and SC group (Supplementary Table 3): 1.18 ± .33 (n = 2680 patients) and 1.05 ± .36 (n = 2695 patients), respectively.[12,13,17,19-22] The mean difference between the 2 groups was statistically significantly higher for the CC group, detecting .13 more adenomas compared with SC group (standard error, .009; 95% CI, .11-.15; $P < .0001$).

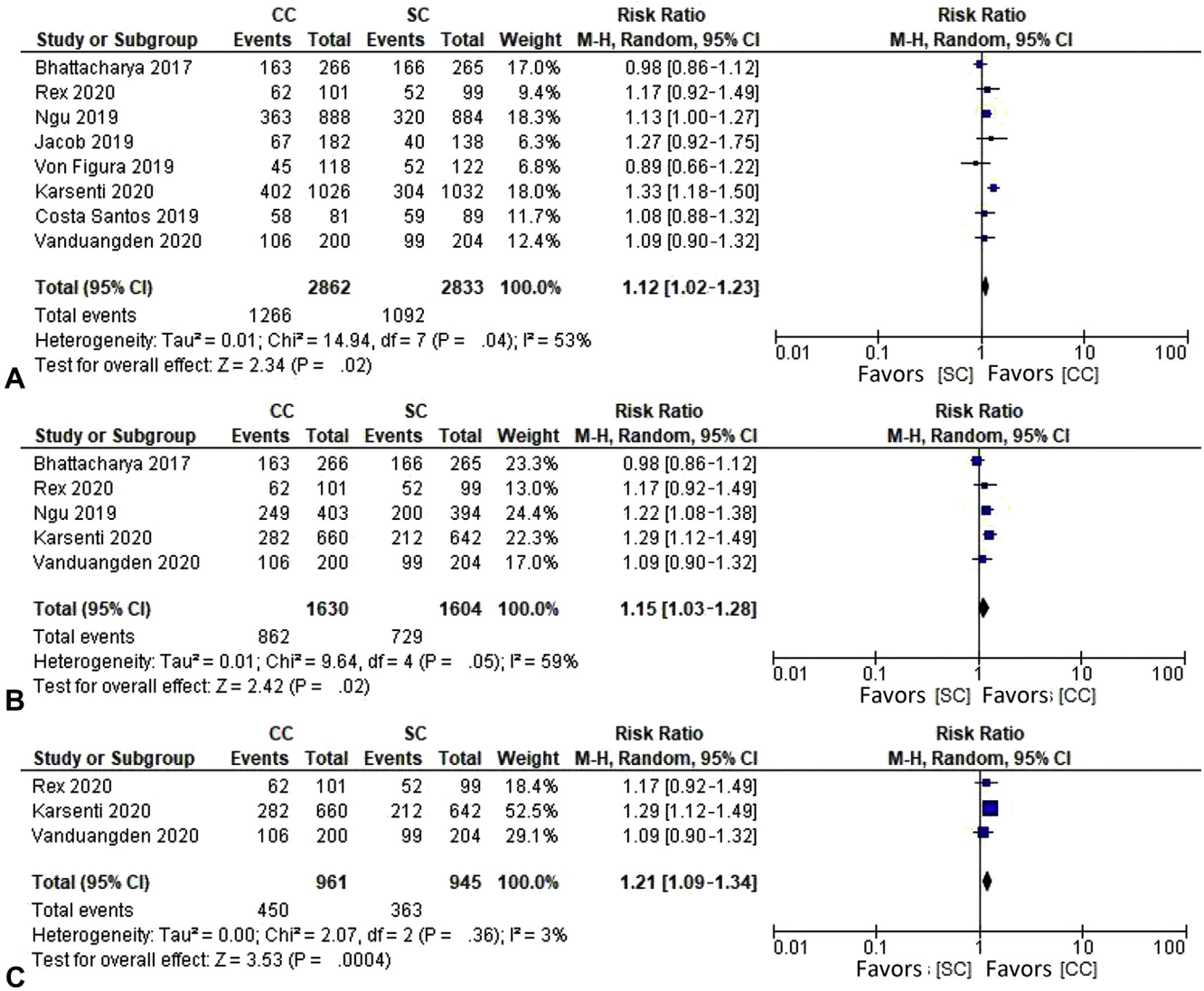

Figure 2. Comparison of adenoma detection rate between cuff-assisted colonoscopy (CC) and standard colonoscopy (SC) in the form of a risk ratio forest plot. **A,** All 7 RCTs. **B,** Five RCTs reporting screening/surveillance population. **C,** Exclusion of fecal occult blood test–positive population from the screening/surveillance subgroup. *CI*, Confidence interval.

Advanced ADR. A-ADR was reported in only 3 of 8 studies (n = 4361)[12,13,21] (Table 2, Fig. 3, Supplementary Table 3). The use of CC did not show any statistically significant increase in A-ADR when compared with the SC group: 11.4% (95% CI, 7.5%-15.4%) versus 10.8% (95% CI, 6.5%-15.2%), respectively (RR, 1.11; 95% CI, .93-1.33; $P = .499$, $I^2 = 0\%$).

Proximal and distal ADR. The P-ADR and D-ADR were reported by 3 of 8 studies.[13,18,21] The use of CC did not improve the P-ADR but did improve the D-ADR compared with SC (Table 2, Fig. 3, Supplementary Table 3): 29.9% (95% CI, 20.1%-39.7%) versus 25.5% (95% CI, 21.9%-29%) (RR, 1.26; 95% CI, .94-1.68; $P = .12$; $I^2 = 81\%$) for P-ADR and 25.2% (95% CI, 23.2%-27.3%) versus 18.2% (95% CI, 13.7%-22.8%) (RR, 1.31; 95% CI, 1.09-1.58; $P = .004$; $I^2 = 41\%$) for D-ADR, respectively. In the screening/surveillance population from 2 studies (n = 2099),[13,21] again there was no difference in P-ADR between the CC and SC groups (Supplementary Table 4): 39.9% (95% CI, 36.9%-42.8%) versus 29.7% (95% CI, 20.7%-38.6%) (RR, 1.24; 95% CI, .96-1.58; $P = .09$), but CC resulted in detection of more distal adenomas than SC: 32.1% (95% CI, 16.8%-47.3%) versus 25.6% (95% CI, 10.3%-40.9%), respectively (RR, 1.26; 95% CI, 1.10-1.45; $P < .01$).

Polyp detection rate. Five studies reported the PDR (n = 4921)[12,13,18,19,21] (Table 2, Fig. 3, Supplementary Table 3). The PDR for CC was significantly higher than SC: 55.5% (95% CI, 47.4%-63.6%) versus 49.8% (95% CI, 38.8%-60.8%) (RR, 1.13; 95% CI, 1.03-1.23; $P = .009$; $I^2 = 54\%$), respectively. When the analysis was restricted to only screening/surveillance population (n = 2630),[12,21] the difference was still significant and greater (Supplementary Table 4): 62% (95% CI, 42%-82%) versus

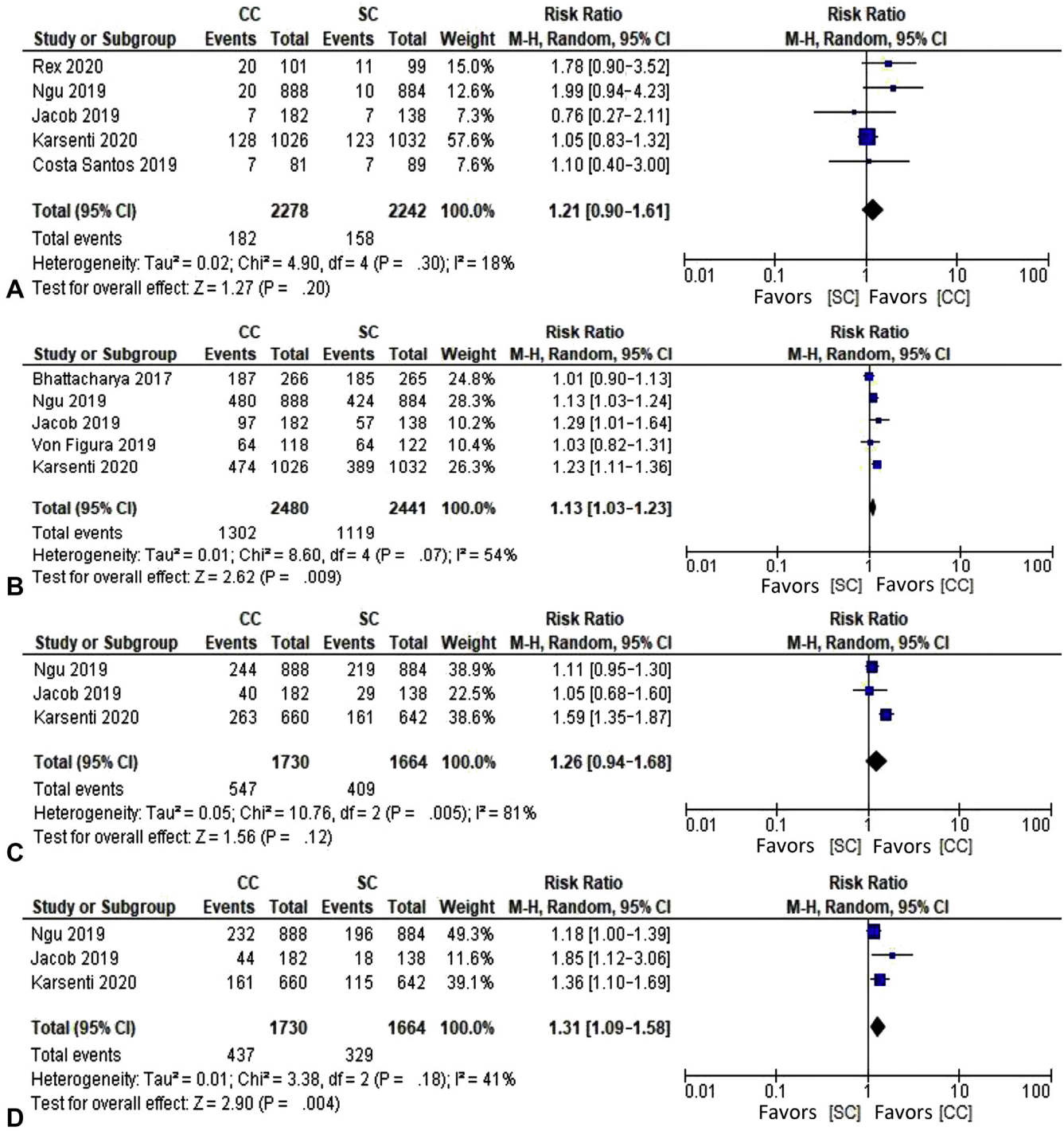

Figure 3. Comparison of outcomes between cuff-assisted colonoscopy (CC) and standard colonoscopy (SC) in the form of a risk ratio forest plot. **A,** Polyp detection rate. **B,** Sessile serrated lesion detection rate. **C,** Proximal adenoma detection rate. **D,** Distal adenoma detection rate. *CI*, Confidence interval.

53.2% (95% CI, 30.7%-75.7%) (RR, 1.14; 95% CI, 1.07-1.21; $P < .01$), respectively.

Mean withdrawal time and other outcomes. The mean withdrawal time was reported by 3 studies[13,17,21] and was significantly lower in the CC group (7.19 ± .62 minutes; 2015 patients) compared with the SC group (8.12 ± .30 minutes; 2015 patients) with a significant mean difference of .93 minutes (standard error, .02; 95% CI, .89-.97; $P < .0001$) (Table 2). For additional secondary outcomes, including the cecal intubation rate, ileal intubation rate, and adverse events, there was no significant difference between the 2 groups. Table 2 reports individual pooled rates and RR for all detection endpoints.

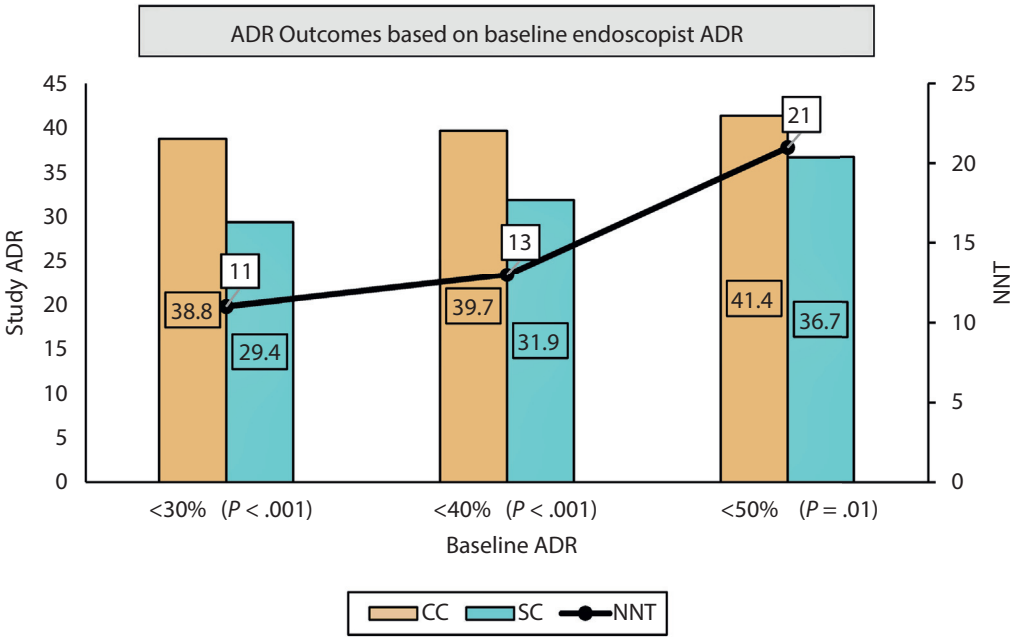

Figure 4. Comparison of adenoma detection rate (ADR) between cuff-assisted colonoscopy (CC) and standard colonoscopy (SC) based on baseline endoscopist ADR. *NNT*, Number needed to treat.

Quality assessment by Grading of Recommendations, Assessment and Evaluation estimate. The quality of evidence based on the Grading of Recommendations, Assessment and Evaluation approach was found to be moderate for ADR for the screening and surveillance population and low for ADR, PDR, SDR, A-ADR, APC, and mean withdrawal time (Table 2, Supplementary Table 6, available online at www.giejournal.org). The level of evidence was downgraded by 2 levels primarily because of concerns for risk of bias because endoscopists were not blinded to the study groups or outcomes and of presence of indirectness because of different study populations and indications for procedure. Overall, the quality of evidence based on the estimates was considered to be low.

DISCUSSION

This systematic review and meta-analysis of RCTs reports quality measure outcomes in patients undergoing colonoscopy using either a distal cuff attachment versus no attachment. The results of 8 RCTs[12,13,17-22] demonstrate a 4.2% increase in ADR (RR, 1.12; $P = .02$), a 5.1% increase in PDR (RR, 1.13; $P = .009$), and a .13 increase in APC along with an approximate 1 minute shorter withdrawal time when the second-generation cuff device was used compared with an SC without any distal attachment. The D-ADR was also significantly higher in the CC group by 7% (25.2% vs 18.2%), but there was no significant difference in the serrated lesion ADR, cecal intubation rates, or the P-ADR between the 2 groups. Prior meta-analyses have been published on the utility of distal attachment devices such as cap and cuff; however, the cuff results were based primarily on the first-generation tip device.

The E-CAP study by Bhattacharyya et al[12] was the first randomized study comparing CC and SC where all patients enrolled in the study were FOBT+ from the U.K. Bowel Cancer Screening Program. Contrary to the results of this meta-analysis, there was no significant difference in endpoints (ADR, APC, and PDR) between both groups from this study. One possible explanation could be the high baseline ADR of endoscopists (58.5%) in the U.K. study and higher ADR in FOBT+ patients compared with other populations,[23] making it difficult to improve ADR further with the use of any distal attachment device. However, Karsenti et al[21] reported that the ADR with CC significantly improved in the high-detector group. However, the cutoff for high ADR in their study was >25%, which overlaps with the low-detector group in prior meta-analyses and prior RCTs. Consequently, high-ADR endoscopists will probably not benefit from the use of CC or any other attachment device; this was shown in our current analysis based on baseline ADR. Stratifying studies into groups based on ADR from the SC arm (control arm) as <30%, <40%, <50%, and ≥50%, we showed that operators with baseline ADR <30%[18,21] benefit from the use of CC (NNT, 11), whereas the very high baseline detectors (ADR >50%)[12,17,20] did not (no or low heterogeneity in this population).

Rex et al[17] highlighted the significance of withdrawal times. As reported in prior studies, they suggested that CC helps reduce procedural times and technical success without compromising the endpoints for outcomes.[24,25] However, that study was not adequately powered to

report significant differences in ADR, PDR, and APC. The current meta-analyses included 2 large studies[13,21] that constituted most patients. Ngu et al,[13] with a large sample size of 1772 patients, reported improved ADR, PDR, SDR, D-ADR, and APC but no difference in mean withdrawal time using CC (Supplementary Table 3). Karsenti et al,[21] in a large cluster randomized crossover trial (n = 2058), reported close to a 10% improvement in ADR and significantly lower withdrawal times using CC. Given the differences in the above studies, our meta-analysis reports important results of improvement in ADR and APC while reducing the mean withdrawal time in the CC compared with SC group.

To minimize the influence of the outcomes from nonscreening or nonsurveillance procedures, we performed a subgroup analysis based on indications for colonoscopy including patients undergoing a screening or surveillance colonoscopy (n = 3234).[12,13,17,21,22] There was a statistically significant improvement in ADR,[12,13,17,21,22] SDR,[13,17,21] and D-ADR.[13,21] The NNT based on the ADR for this subgroup was 15. An interesting observation was the significant increase in the SDR in this subgroup with the use of CC over SC: 12.1% versus 8.3% (RR, 1.28; $P = .04$). However, there was still a high heterogeneity in this subgroup for the primary outcome of ADR ($I^2 = 59\%$). Thus, we performed a further sensitivity analysis by excluding 2 studies that included an FOBT+ population and found persistent improvement in the ADR with minimal heterogeneity ($I^2 = 3\%$), further reducing the NNT to 13.

Finally, our results show that an attachment with flexible arms at the tip of the endoscope did not translate into increased adverse events. A meta-analysis with the first-generation cuff compared with SC by Chin et al[26] showed more adverse events and specifically mucosal abrasions when compared with SC. On the contrary, studies with the second-generation device have not shown similar results, and our meta-analysis reaffirms these results.

The strength of the current analysis lies in the inclusion of only RCTs with more than 5500 patients. This meta-analysis specifically focuses on all outcomes only for the second-generation cuff device compared with screening colonoscopy, which have not been reported before. Most outcomes reported in our study had only mild or moderate heterogeneity. The potential reasons for heterogeneity were studies performed in different countries with different patient populations, varying expertise and experience of endoscopists, and variations in bowel preparation and withdrawal time. In case of moderate to high heterogeneity, we performed further subgroup and sensitivity analyses to successfully identify and reduce or eliminate the heterogeneity for most outcomes. However, there are limitations to the study. The endoscopists in both groups were not blinded, which is common to most endoscopic studies designed for assessment of external attachments. Data on polyp size, adenoma miss rate, and cancer outcomes were limited because there were no follow-up data in these studies, and we could not perform an analysis for these outcomes. There were different scales used for grading the quality of bowel preparation across different studies, making it difficult to generalize the outcomes, but individual studies did not have significant difference in bowel preparation between both groups; thus, the results from our analysis holds good, even if we were unable to analyze outcomes based on bowel preparation. One study reported industry funding for the RCT, making it difficult to eliminate funding bias.[13]

In conclusion, the use of the second-generation cuff distal attachment device was associated with a significant improvement in ADR and APC and a reduction in the mean withdrawal time without any increase in adverse events compared with standard high-definition colonoscopy without any distal attachment. The benefit in ADR was more pronounced in patients undergoing screening and/or surveillance colonoscopy and for endoscopists with baseline low ADR. Future studies with stratification of outcomes based on polyp size and evaluation of cost-effectiveness are needed.

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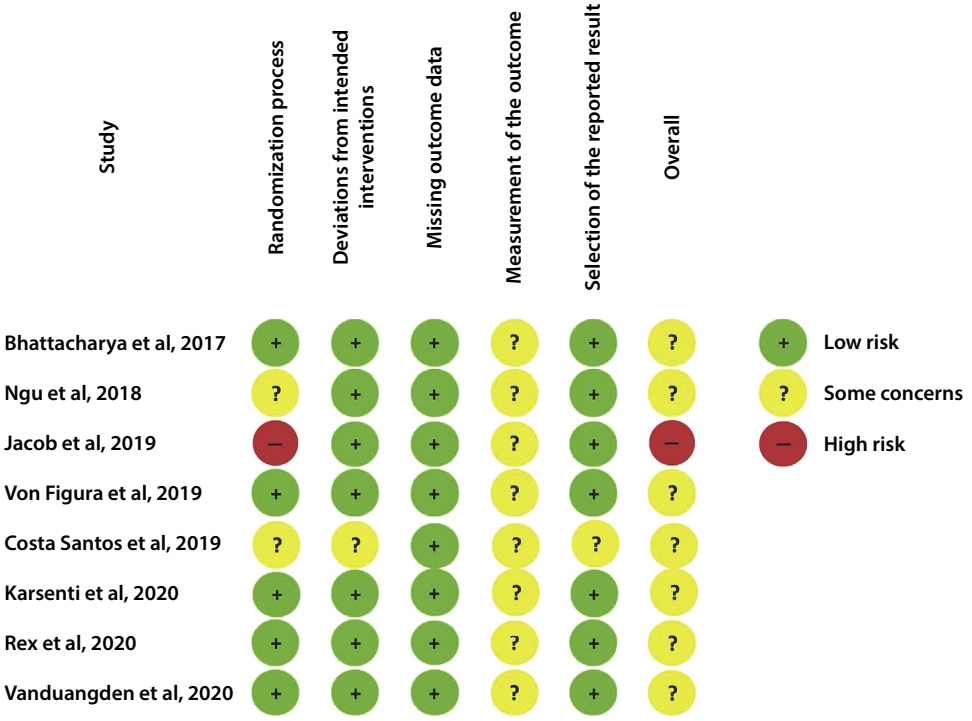
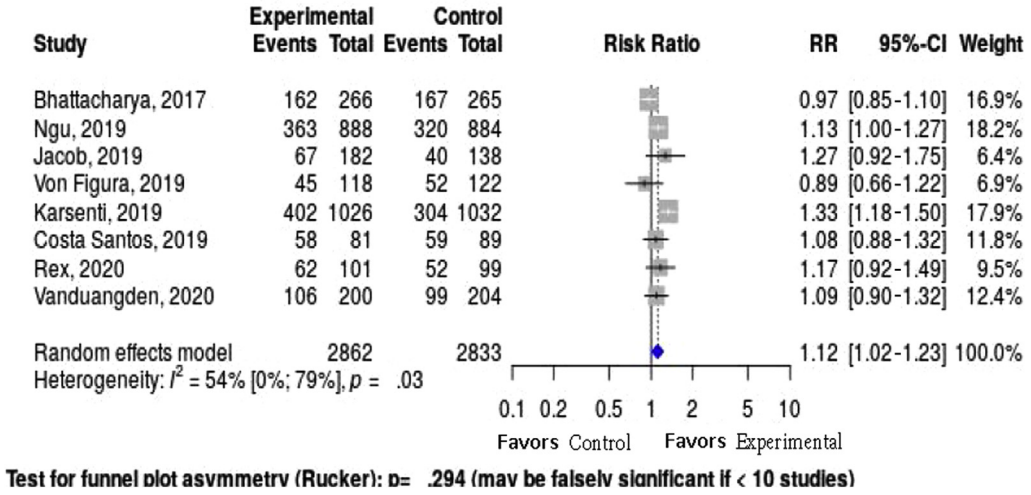
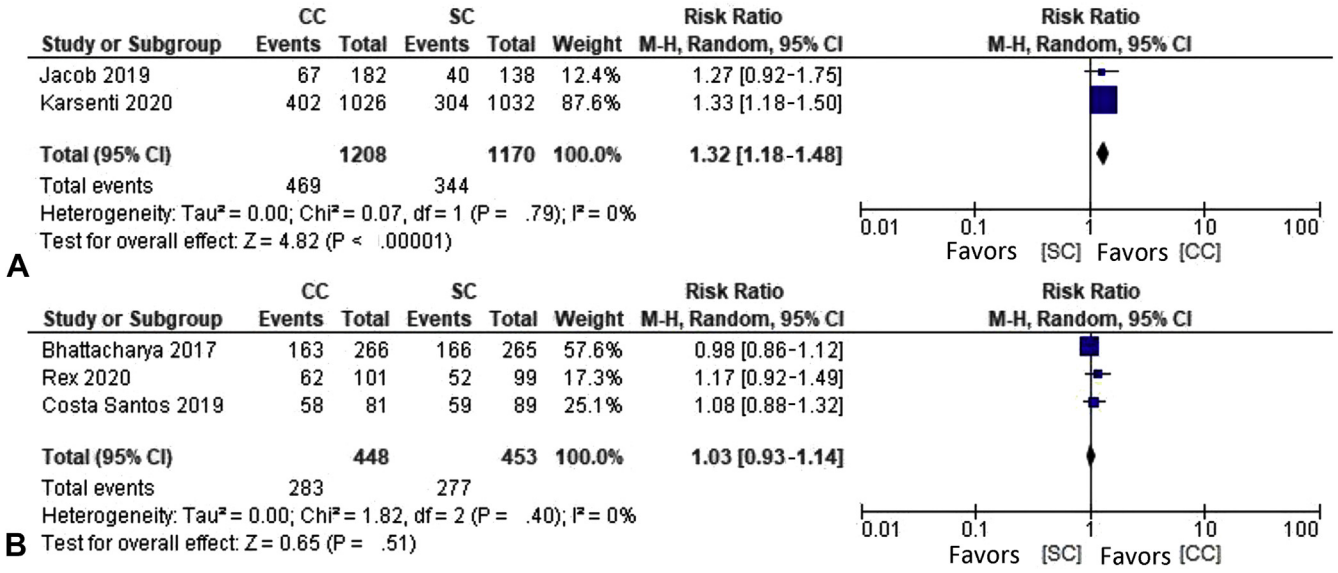


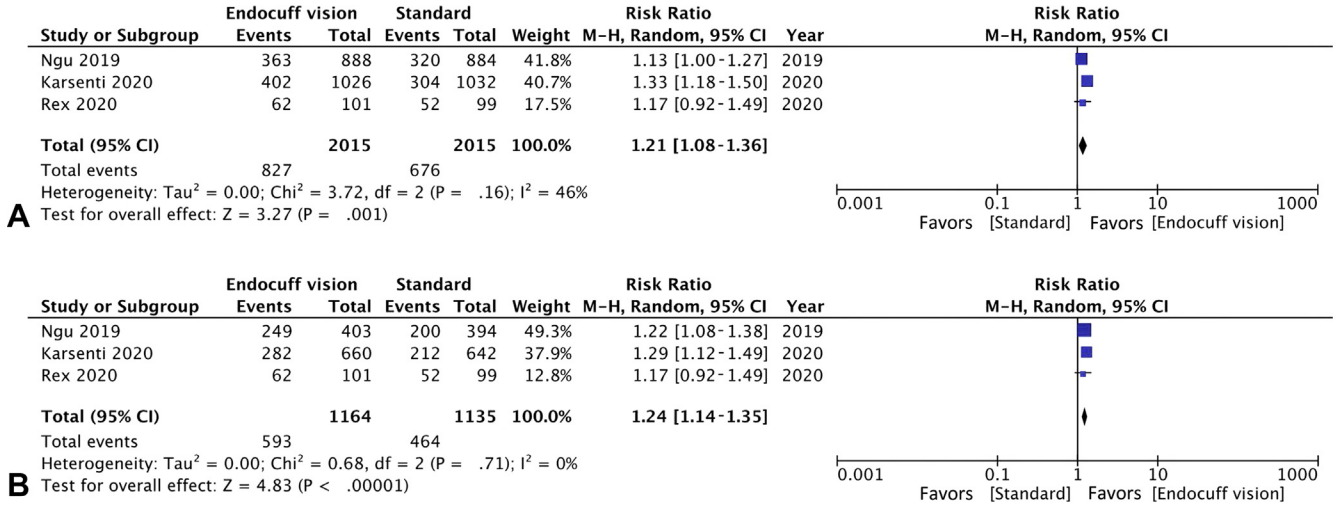
Supplementary Figure 1. Risk of bias assessment using the Cochrane Collaboration tool.



Supplementary Figure 2. Rucker's coefficient for publication bias for the primary outcome of adenoma detection rate. *RR*, Relative risk; *CI*, confidence interval.



Supplementary Figure 3. Comparison of outcomes between cuff colonoscopy (CC) and standard colonoscopy (SC) in form of a risk ratio forest plot. **A,** Baseline adenoma detection rate <30%. **B,** Baseline adenoma detection rate >50%. *CI*, Confidence interval.



Supplementary Figure 4. Comparison of adenoma detection rate between cuff colonoscopy and standard colonoscopy in the form of risk ratio forest plot only including studies that reported withdrawal time. **A,** Entire cohort. **B,** Screening/surveillance population. *CI*, Confidence interval.

SUPPLEMENTARY TABLE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline checklist

Section/topic	Number	Checklist item	Reported on page number
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable, background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (eg, web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (eg, PICOS, length of follow-up) and report characteristics (eg, years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (eg, databases with dates of coverage, contact with study authors to identify additional studies) in the search, and date last searched.	4
Search	8	Present full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (ie, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (eg, piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (eg, PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (eg, risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (eg, I^2) for each meta-analysis.	6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (eg, publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (eg, sensitivity or subgroup analyses, meta-regression), if done, indicating which were prespecified.	6
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (eg, study size, PICOS, follow-up period) and provide the citations.	7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7,8,9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7, 8,9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15).	7

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Section/topic	Number	Checklist item	Reported on page number
Additional analysis	23	Give results of additional analyses, if done (eg, sensitivity or subgroup analyses, meta-regression [see item 16]).	7,8,9
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (eg, healthcare providers, users, and policy makers).	10,11,12
Limitations	25	Discuss limitations at study and outcome level (eg, risk of bias), and at review-level (eg, incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (eg, supply of data); role of funders for the systematic review.	15

SUPPLEMENTARY TABLE 2. PubMed search strategy

Search	Query	Items found
No. 3	No. 1 AND No. 2	58
No. 2	ADR OR adenoma detection rate OR adenoma	129,660
No. 1	Endocuff OR Endocuff vision OR distal attachments	559

SUPPLEMENTARY TABLE 3. Comparison of outcomes of cuff colonoscopy and standard colonoscopy for individual studies

Study and year	ADR (%) (CC; SC)	Polyp detection rate (%) (CC; SC)	Mean adenomas per patient (CC; SC)	Sessile serrated lesion detection rate (%) (CC; SC)	Advanced ADR (%) (CC; SC)	Proximal ADR (%) (CC; SC)	Distal ADR (%) (CC; SC)	Cecal intubation rate (%) (CC; SC)	Withdrawal time (min) (CC; SC)	Adverse events (CC; SC)
Bhattacharya et al,[12] 2017	60.9; 63	70.3; 69.8	1.3; 1.4	NA	16.9; 18.5	NA	NA	93.6; 100	16.9; 19.5	0; 1
Ngu et al,[13] 2019	**40.9; 36.2**	**54.1; 48**	**.95; .75**	**2.3; 1.1**	7.9; 6.9	27.5; 24.8	**26.1; 22.2**	96.7; 96.4	8; 8.25	11; 12
Rex et al,[17] 2020	61.4; 52.5	NA	1.4; 1.07	19.8; 11.1	NA	NA	NA	100; 100	**6.49; 8.42**	0; 0
Jacob et al,[18] 2019	36.8; 29	**53; 41.1**	NA	3.7; 5.1	NA	22; 21	24.1; 13	92.8; 90.5	7.9; 7.4	0; 0
Von Figura et al,[19] 2020	38.1; 42.6	54.2; 52.5	.84; .97	NA	NA	NA	NA	**100; 100**	12; 13.5	0; 2
Costa Santos et al,[20] 2019*	72; 67	NA	1.8; 1.7	9; 2	NA	NA	NA	99; 94	12.3; 13.1	1; 1
Karsenti et al,[21] 2020	**39.2; 29.4**	**46.2; 37.7**	.78; .54	12.5; 11.9	11.1; 9.2	NA	NA	99.4; 100	7.1; 7.7	1; 0
Vanduangden et al,[22] 2020*	53; 48.5	NA	1.19; .95	NA	NA	NA	NA	NA	NA	NA

Results in bold are all statistically significant ($P < .05$).
ADR, Adenoma detection rate; *CC*, cuff colonoscopy; *SC*, standard colonoscopy; *NA*, not applicable.
*Abstracts.

SUPPLEMENTARY TABLE 4. Comparison of outcomes of cuff colonoscopy and standard colonoscopy for screening/surveillance population

Outcomes (no. of studies)	Cuff colonoscopy (%)	Standard colonoscopy (%)	Risk ratio (95% confidence interal; *P*-value; I^2)
ADR (5)	55.8 (46.7-64.9)	49.3 (37.7-61)	1.16 (1.03-1.28; .02; 59%)
Polyp detection rate (3)	62 (42-82)	53.2 (30.7-75.7)	1.14 (1.07-1.21; <.001; 71%)
Sessile serrated lesion detection rate (3)	12.1 (.7 - 23.5)	8.3 (.9 - 17.4)	1.28 (1.01-1.64; .04; 0%)
Proximal ADR (2)	39.9 (36.9-42.8)	29.7 (20.7-38.6)	1.24 (.96-1.58; .09; 79%)
Distal ADR (2)	32.1 (16.8-47.3)	25.6 (10.3-40.9)	1.26 (1.10-1.45; .001; 0%)

Values in parentheses are 95% confidence interval unless otherwise defined.
ADR, Adenoma detection rate.

SUPPLEMENTARY TABLE 5. Comparison of ADR of cuff colonoscopy and standard colonoscopy for special subgroups based on baseline ADR, after excluding fecal occult blood test–positive population from the screening/surveillance subgroup and for studies reporting the withdrawal time

Subgroups (no. of studies)	Cuff colonoscopy ADR (%)	Standard colonoscopy ADR (%)	Risk ratio (95% confidence interval; *P* value; I^2)	Number needed to treat
Baseline endoscopist ADR				
ADR <30% (2)	38.8	29.4	1.32 (1.18-1.48; <.001; 0%);	11
ADR <40% (3)	39.7	31.9	1.23 (1.09-1.39; .0009; 45%)	13
ADR <50% (5)	41.4	36.7	1.16 (1.03-1.31; .01; 51%)	21
ADR >50% (3)	64	60.8	1.03 (.93-1.14; .51; 0%)	
Excluding fecal occult blood test–positive population from the screening/surveillance subgroup (3)	51.7	44.2	1.21 (1.09-1.34; <.001; 3%)	13
Studies reporting withdrawal time (3)				
Entire cohort	41	33.5	1.21 (1.08-1.36; .001; 0%)	13
Screening/surveillance population	50.9	40.9	1.24 (1.14-1.35; <.0001; 0%)	10

ADR, Adenoma detection rate.

SUPPLEMENTARY TABLE 6. Quality of body of evidence with certainty assessment and summary of findings comparing Endocuff Vision with standard colonoscopy (Grading of Recommendations, Assessment and Evaluation guidelines)

Certainty assessment							No. of patients
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Endocuff Vision
Adenoma detection rate							
8	Randomized trials	Serious	Not serious	Serious	Not serious	None	1266/2862 (44.2%)
Polyp detection rate							
5	Randomized trials	Serious	Not serious	Serious	Not serious	None	1302/2480 (52.5%)
Adenomas per colonoscopy							
7	Randomized trials	Serious	Not serious	Serious	Not serious	None	2680
Mean withdrawal time							
3	Randomized trials	Serious	Not serious	Serious	Not serious	None	2015
Sessile serrated lesion detection rate							
5	Randomized trials	Serious	Not serious	Serious	Not serious	None	182/2278 (8.0%)
Advanced adenoma detection rate							
3	Randomized trials	Serious	Not serious	Serious	Not serious	None	229/2180 (10.5%)
Adenoma detection rate only for screening studies without fecal occult blood test							
3	Randomized trials	Serious	Not serious	Not serious	Not serious	None	450/961 (46.8%)

MD, Mean difference.

SUPPLEMENTARY TABLE 6. Continued

No. of patients	Effect			
Standard colonoscopy	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
1092/2833 (38.5%)	Risk ratio 1.12 (1.02-1.23)	46 more per 1000 (from 8 more to 89 more)	⊕⊕◯◯ LOW	
1119/2441 (45.8%)	Risk ratio 1.13 (1.03-1.23)	60 more per 1000 (from 14 more to 105 more)	⊕⊕◯◯ LOW	
2695	Not applicable	MD .13 higher (.11 higher to .15 higher)	⊕⊕◯◯ LOW	
2015	Not applicable	MD .93 higher (.89 higher to .97 higher)	⊕⊕◯◯ LOW	
158/2242 (7.0%)	Risk ratio 1.21 (.90-1.60)	15 more per 1000 (from 7 fewer to 42 more)	⊕⊕◯◯ LOW	
205/2181 (9.4%)	Risk ratio 1.11 (.93-1.33)	10 more per 1000 (from 7 fewer to 31 more)	⊕⊕◯◯ LOW	
363/945 (38.4%)	Risk ratio 1.21 (1.09-1.34)	81 more per 1000 (from 35 more to 131 more)	⊕⊕⊕◯ MODERATE	