

# Efficacy of Endocuff Vision compared to first-generation Endocuff in adenoma detection rate and polyp detection rate in high-definition colonoscopy: a systematic review and network meta-analysis




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## ABSTRACT

**Background and study aims** Recently, the newer Endocuff Vision (ECV) has been evaluated for improving colonoscopy outcome metrics such as adenoma detection rate (ADR) and polyp detection rate (PDR). Due to lack of direct comparative studies between ECV and original Endocuff (ECU), we performed a systematic review and network meta-analysis to evaluate these outcomes.

**Methods** The following databases were searched: PubMed, Embase, Cochrane, and Web of Sciences to include randomized controlled trials (RCTs) comparing ECV or ECU colonoscopy to high-definition (HD) colonoscopy. Direct as well as network meta-analyses comparing ADR and PDR were performed using a random effects model. Relative-risk (RR) with 95% confidence interval (CI) was calculated.

**Results** A total of 12 RCTs with 8638 patients were included in the final analysis. On direct meta-analysis, ECV did not demonstrate statistically improved ADR compared to HD colonoscopy (RR: 1.12, 95% CI 0.99–1.27). A clinically and statistically improved PDR was noted for ECV compared to HD (RR: 1.15, 95% CI 1.03–1.28) and ECU compared to HD (RR: 1.26, 95% CI 1.09–1.46) as well as improved ADR (RR: 1.22, 95% CI 1.05–1.43) was observed for ECU colonoscopy when compared to HD colonoscopy. These results were also consistent on network meta-analysis. Lower overall complication rates (RR: 0.14, 95% CI 0.02–0.84) and particularly lacerations/erosions (RR: 0.11, 95% CI 0.02–0.70) were noted with ECV compared to ECU colonoscopy.

**Conclusions** Although safe, the newer ECV did not significantly improve ADR compared to ECU and HD colonoscopy. Further device modification is needed to increase the overall ADR and PDR.

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## Introduction

Colorectal cancer (CRC) is the second and fourth leading cause of cancer death in the United States and around the world, respectively [1]. The estimated deaths from CRC in 2019 were 51,020 in the United States, according to the SEER database [2]. The majority of the CRCs (~80%) develop through the well-studied adenoma-carcinoma sequence while a subset of CRCs (~20%) develop through the serrated adenoma pathway [3]. High-definition (HD) colonoscopy identifies adenomas and serrated lesions at early stage and reduces cancer-related morbidity and mortality [4]. Adenoma detection rate (ADR) – defined as proportion of colonoscopies with at least one adenoma detected – is a well-established colonoscopy indicator [4, 5]. An improvement in ADR is associated with a significant reduction in interval CRC and mortality [5]. The ADR  $\geq 30\%$  for men and  $\geq 20\%$  for women is recommended for average risk screening colonoscopies [6].

Current efforts are directed to increase the ADR for endoscopists by using numerous interventions (electronic chromoendoscopy, add-on devices, antispasmodic medications, multiple observers, water-aided methods, second forward exam or retroflexion in right colon, artificial intelligence) [7–13]. Two such add-on devices used in recent times are Endocuff (ECU) and Endocuff Vision (ECV) (Arc Medical Design, Leeds, UK) [14]. The first-generation ECU included two rows of soft finger-like projections in order to flatten the colonic haustral folds while the newer second generation ECV includes only one row of finger-like projections with blunter tips to decrease the incidence of mucosal laceration and erosions [14, 15].

Recent meta-analyses in literature have compared the Endocuff devices to HD colonoscopy and a significantly improved ADR was noted for Endocuff colonoscopy. The major limitation of these meta-analyses is that both ECU and ECV were pooled together for generating outcomes [7, 16–19]. Further, data regarding the comparative efficacy of the two cuffs (i.e. ECU vs ECV) is not available in literature. We conducted an updated systematic review and network meta-analysis of all the available randomized controlled trials (RCTs) to generate the best possible evidence comparing the first- and second-generation Endocuff devices to each other and to HD colonoscopy.

## Methods

A detailed and comprehensive search of the following databases were conducted from inception through March 25, 2020: PubMed/Medline, Embase, Web of Science Core Collection, and Cochrane Central Register of Controlled Trials. The keywords and search terms for the concepts of “colonoscopy”, “adenoma/polyps”, “detection rates”, and “Endocuff” were developed for EMBASE and translated to vocabulary for other databases. The search strategy was created by an experienced librarian (W.L.S.) and reviewed by another investigator (M.A.). Detailed search strategy for EMBASE is provided in **Supplementary Table 1**. Screening of the articles was performed by two independent reviewer (H.H. and M.A.) and discrepancy was resolved through mutual discussion. Preliminary screening was

done using title and abstracts and full texts of relevant articles were obtained. Bibliographies of the included articles were also checked to see any additional articles fulfilled our study criteria. We adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and no restriction to language was applied.

## Study definitions

ADR is defined as the proportion of colonoscopies with at least one adenoma detected in all colonoscopies. Polyp detection rate (PDR) is defined as the proportion of colonoscopies with at least one polyp detected in all colonoscopies. The serrated adenoma detection rate (SADR) is defined as the proportion of colonoscopies with at least one sessile serrated adenoma/polyp (SSA/P) and/or traditional serrated adenoma (TSA) detected in all colonoscopies. The advanced adenoma detection rate (AADR) is defined as proportion of colonoscopies with at least one advanced adenoma (adenomas  $\geq 10$  mm or with villous components or high-grade dysplasia) in all colonoscopies. The neoplasia detection rate (NDR) is defined as proportion of colonoscopies with at least one neoplasia (intramucosal carcinoma and/or adenocarcinoma) in all colonoscopies. The mean adenoma per procedure (MAP) is defined as the total number of adenomas divided by the total number of procedures. The mean polyp per procedure (MPP) is defined as the total number of polyps divided by the total number of procedures. The cecal intubation rate (CIR) is defined as achieving cecal intubation during the insertion phase of colonoscopy.

## Inclusion/exclusion criteria

We included randomized controlled trials (RCT) that met the following criteria: (A) Population: Adult patients (>18 years) undergoing colonoscopy (B) Intervention: First-generation ECU, and/or second-generation ECV utilization for colonoscopy. (C) Comparison: High-definition (HD) colonoscopy. Studies with colonoscopy performed using older standard definition colonoscopy were excluded. Studies comparing ECU or ECV with other devices (Endocap, Endoring, etc.) were also excluded (D) Outcomes: ADR and PDR. Studies were excluded if patients with obvious underlying pathology were included (inflammatory bowel disease, serrated polyposis syndrome, hyperplastic polyposis syndrome). Other types of studies (single arm, cohort, editorials, case series/reports, review articles) were also excluded. Abstracts were also excluded for the purpose of the manuscript.

## Data extraction and study outcomes

Data from finalized studies including baseline demographics (age, gender, indication for colonoscopy), total study participants, type of intervention, study completion rate, quality indicators (cecal intubation time, withdrawal time), and study outcomes (PDR, ADR, AADR, NDR, SADR, MAP, and MPP) was collected and tabulated on Microsoft Excel (Microsoft, Redmond, Washington, United States) by two independent reviewers (H.H. and M.A.). Any discrepancy in data collection was resolved through mutual discussion. We used the per-protocol

(PP) analysis with detection rates calculated based on actual study completion.

## Data synthesis and statistical analysis

We performed direct meta-analysis to generate direct evidence for studies doing a head-to-head comparison between intervention groups. We also performed a network meta-analysis to generate direct and indirect evidence for the same. DerSimonian-Laird method and random effects model was used to perform a direct meta-analysis on 'Comprehensive Meta-Analysis' software (Biostat, Englewood, New Jersey, United States). Network meta-analysis was conducted using a random-effects model on 'R' package 'Netmeta' (Bell labs, Murray Hill, New Jersey, United States). Relative risk (RR) with 95% confidence interval (CI) for each proportional outcome was calculated. Mean difference (MD) with 95% CI was calculated for continuous variables.  $P < 0.05$  was considered statistically significant. The "frequentist method" was used to rank the intervention and a P score was generated [20]. A higher P score (closer to 1.00) correspond to superior detection rates for respective intervention group. For complications, a higher P score (closer to 1.00) correspond to lower complication rates for respective intervention. Study heterogeneity was assessed using the  $I^2$  statistic defined by the Cochrane Handbook for systematic reviews and value  $> 50\%$  was considered as substantial heterogeneity [21]. Disagreement between direct and indirect evidence was assessed using the node splitting technique [22]. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was utilized for assessing the certainty of evidence and rating of very low, low, moderate and high was determined [23].

## Subgroup analysis

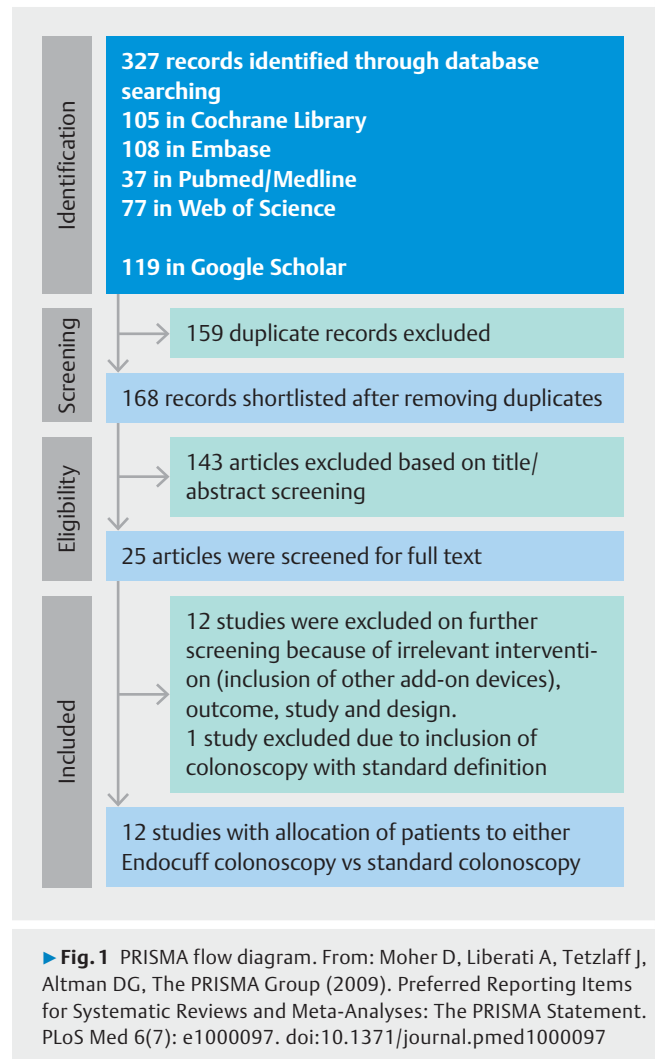
Subgroup analysis was performed based on the ADR for control groups i.e. studies with control ADR  $\leq 40\%$  vs ADR  $> 40\%$  and studies with control ADR  $\leq 30\%$  vs ADR  $> 30\%$ .

## Bias assessment

The bias assessment for included RCTs was evaluated using the methodology outlined in Cochrane handbook for systematic reviews of interventions [24]. Publication bias was visually assessed using funnel plots as well as quantitatively assessed using Egger's regression analysis.  $P < 0.05$  was indicative of substantial publication bias.

## Results

A total of 168 articles were screened after removing duplicates and using the search strategy mentioned above. Twelve RCTs were included after rigorous screening of abstracts and full texts with a total of 8638 patients (4285 in HD group, 4353 in Endocuff group) (► Fig. 1) [15, 25–35]. All studies were published after 2014. Study completion rate was 98.4% and 97.1% respectively for HD and Endocuff group.



## Baseline demographics/study outcomes

The groups were similar in terms of age range (55.7–68 vs 55.1–68), male gender (52.9% vs 52.1%) and screening/surveillance indication (60.8% vs 60.7%). Of the Endocuff group, 2627 patients (6 studies) underwent ECV colonoscopy [14, 25, 29, 30, 33, 35] and 1726 patients (6 studies) underwent ECU colonoscopy [26–28, 31, 32, 34] (► Table 1). The outcomes for individual studies are summarized in ► Table 2.

## Direct meta-analysis

A total of six studies assessed ADR and a statistically insignificant but improved detection trend was observed for ECV compared to HD colonoscopy (42.6% vs 36.8%, RR: 1.12, 95% CI 0.99–1.27,  $P = 0.07$ ,  $I^2 = 66.6\%$ ) (► Fig. 2a) [15, 25, 29, 30, 33]. Six studies compared ECU to HD colonoscopy and improved ADR was observed for ECU colonoscopy that was statistically significant (48.3% vs 41.1%, RR: 1.22, 95% CI 1.05–1.43,  $p = 0.01$ ,  $I^2 = 71.4\%$ ) (► Fig. 2b) [26, 27, 28, 31, 32, 34]. A statistically and clinically significant improvement in PDR was noted for ECV colonoscopy compared to HD colonoscopy (52.5% vs 45.5%, RR: 1.15, 95% CI 1.03–1.28,  $P = 0.01$ ,  $I^2 = 67.0\%$ ) (► Fig. 2c) [15, 25, 29, 33]. Similarly, PDR was found to be improved for

► **Table 1** Baseline study characteristics and patient demographics.

Study, year	Tech- niques compared	Total Patients, N	Study comple- tion, N	Mean/ Median Age, n	Male propor- tion, %	Indication for colonoscopy, %		Type of Colonoscope used
						HD	ECU/ECV	
Biecker, 2015 [26]	HD ECU	253 245	249 240	68 65	51.8% 47.8%	S: NR D: NR	S: NR D: NR	Fujifilm EC-590 WM4, EC-590 WL4, Olympus CF-H180 AI
De Palma, 2018 [27]	HD ECU	144 144	137 137	55.7 55.1	52.6% 51.8%	S: 66.4% D: 33.6%	S: 65.0% D: 35.0%	Olympus CF-HQ190, CF-Q180AL/I
Floer, 2014 [28]	HD ECU	248 252	243 249	63 64	44.9% 49.0%	S: NR D: NR	S: NR D: NR	Olympus CF-H180AI/AL, Fujifilm EC-590 WM4/ WL4
Van Doorne, 2017 [31]	HD ECU	533 530	514 486	65 65	53.5% 49.8%	S: 51.8% D: 48.2%	S: 51.9% D: 48.1%	Olympus CF-H180AL, CF-HQ190L, PCF- H180AL, Fujinon EC 350-WL
Wada, 2018 [32]	HD ECU	238 239	237 235	62.2 61.2	48.3% 51.0%	S: 58.0% D: 42.0%	S: 58.6% D: 41.4%	Olympus PCF-H290Z1, CF-HQ290, CF-HQ290Z1
Rex (1), 2018 [34]	HD ECU	316 316	295 299	62.6 63.2	52.9% 52.8%	S: 94.6% D: 5.4%	S: 92.3% D: 7.7%	Olympus H190, H180 series
Bhattacharyya, 2017 [25]	HD ECV	267 267	265 266	67 68	67.9% 60.9%	S: 100% D: 0%	S: 100% D: 0%	Olympus CF-H260
Jacob, 2019 [29]	HD ECV	146 214	138 182	NR NR	50.7% 56.7%	S: NR D: NR	S: NR D: NR	Olympus CF-190 L/I, CF- H180 L/I, PCF-H180AL/I, PCF-H190 L/I
Ngu, 2017 [15]	HD ECV	884 888	884 888	62.1 61.7	56.8% 57.1%	S: 45.6% D: 54.4%	S: 44.4% D: 55.6%	Olympus (details not reported)
Rex (2), 2019 [30]	HD ECV	99 101	99 101	61.7 62.7	42.4% 56.4%	S: NR D: NR	S: NR D: NR	Olympus (details not reported)
Von Figura, 2019 [33]	HD ECV	125 125	122 118	65.3 63.6	62.9% 51.7%	S: 38.5% D: 61.5%	S: 45.8% D: 54.2%	Olympus CF-HQ190
Karsenti, 2020 [35]	HD ECV	1032 1032	1032 1026	57.4 59.3	48.9% 47.4%	S: NR D: NR	S: NR D: NR	Olympus CF-H190, Fuji- film EC-690 WM/EC-600 WM

D, diagnostic/others; ECU, first-generation Endocuff colonoscopy; ECV, Endocuff Vision colonoscopy; HD, high-definition colonoscopy; N, no of patients; n, mean/median; NR, not reported; S, screening/surveillance.

ECU colonoscopy compared to HD statistically and clinically (65.6% vs 52.9%, RR: 1.26, 95% CI 1.09–1.46,  $P=0.002$ ,  $I^2=74.9%$ ) (► **Fig. 2d**) [26, 28, 32, 34].

Three studies compared ECU to HD colonoscopy and increased MPP was noted for ECU statistically and clinically (MD: 0.53, 95% CI 0.39–0.67,  $P<0.001$ ,  $I^2=0%$ ) (**Supplementary Fig. 1a**) [26, 28, 32]. No clinical and statistically significant difference in MPP was observed for ECV group compared to HD (MD: -0.13, 95% CI -0.31–0.05,  $P=0.16$ ,  $I^2=4.4%$ ) (**Supplementary Fig. 1b**) [25, 29, 33]. Four studies assessed MAP for ECU and HD colonoscopy and improved MAP was noted for ECU group clinically and statistically (MD: 0.31, 95% CI 0.19–0.44,  $P<0.001$ ,  $I^2=0%$ ) (**Supplementary Fig. 1c**) [28, 31, 32, 34]. The MAP was not clinically and statistically different for ECV group when compared to HD colonoscopy (MD: 0.14, 95%

CI -0.01–0.28,  $p=0.06$ ,  $I^2=53.1%$ ) (**Supplementary Fig. 1d**) [15, 23, 28, 35].

### Network meta-analysis

The results for network meta-analysis are summarized in table 3 and demonstrated using network forest plots (► **Fig. 3a**, ► **Fig. 3b**, ► **Fig. 3c**, ► **Fig. 3d**, ► **Fig. 3e**, ► **Fig. 3f**, ► **Fig. 3g**, ► **Fig. 3h**). Network diagrams for respective forest plots are shown in **Supplementary Fig. 2**. Overall improved PDR was seen with ECU compared to HD colonoscopy (RR: 1.25, 95% CI 1.10–1.43) as well as ECV compared to HD colonoscopy (RR: 1.14, 95% CI 1.02–1.29). Improved ADR was noted for ECU colonoscopy compared to HD colonoscopy (RR: 1.22, 95% CI: 1.06–1.40). These results were both statistically and clinically significant. ADR improvement was not statistically significant

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

Study, year	Techniques compared	Outcomes							
		Total Polyps, n	Total Adenomas, n	ADR, n (%)	PDR, n (%)	AADR, n (%)	SADR, n (%)	NDR, n (%)	CIR, n (%)
Biecker, 2015 [26]	HD ECU	246 388	NR NR	69 (27.7%) 87 (36.3%)	106 (42.6%) 138 (57.5%)	NR NR	NR NR	NR NR	NR NR
De Palma, 2018 [27]	HD ECU	NR NR	129 176	39 (28.5%) 38 (27.7%)	NR NR	NR NR	NR NR	NR NR	NR NR
Floer, 2014 [28]	HD ECU	189 312	88 144	50 (20.6%) 87 (34.9%)	93 (38.3%) 138 (55.4%)	NR NR	NR NR	NR NR	229 (94.2%) 238 (95.6%)
Van Doorne, 2017 [31]	HD ECU	883 982	610 700	271 (52.7%) 260 (53.5%)	NR NR	111 (21.6%) 103 (21.2%)	NR NR	NR NR	518 (97.2%) 508 (96.0%)
Wada, 2018 [32]	HD ECU	197 312	158 263	93 (39.2%) 132 (56.2%)	117 (49.4%) 148 (63.0%)	11 (4.6%) 18 (7.7%)	NR NR	7 (3.0%) 5 (2.1%)	237 (99.6%) 235 (98.3%)
Rex (1), 2018 [34]	HD ECU	NR NR	445 543	166 (56.3%) 191 (63.9%)	226 (76.6%) 247 (82.6%)	NR NR	36 (12.2%) 33 (11.0%)	NR NR	295 (100.0%) 299 (100.0%)
Bhattacharyya, 2017 [25]	HD ECV	470 436	359 336	167 (63.0%) 162 (60.9%)	185 (69.8%) 187 (70.3%)	49 (18.5%) 45 (16.9%)	NR NR	15 (5.7%) 14 (5.3%)	NR NR
Jacob, 2019 [29]	HD ECV	NR NR	NR NR	40 (29.0%) 67 (36.8%)	48 (34.8%) 97 (53.3%)	NR NR	NR NR	NR NR	NR NR
Ngu, 2017 [15]	HD ECV	NR NR	NR NR	320 (36.2%) 362 (40.8%)	424 (50.0%) 480 (54.1%)	NR NR	10 (1.1%) 20 (2.3%)	20 (2.3%) 36 (4.1%)	852 (95.9%) 858 (96.6%)
Rex (2), 2019 [30]	HD ECV	NR NR	NR NR	52 (52.5%) 62 (61.4%)	NR NR	NR NR	11 (11.1%) 20 (19.8%)	NR NR	99 (100.0%) 101 (100.0%)
Von Figura, 2019 [33]	HD ECV	211 169	97 87	52 (42.6%) 45 (38.1%)	64 (52.5%) 64 (54.2%)	NR NR	NR NR	NR NR	122 (100.0%) 118 (100.0%)
Karsenti, 2020 [35]	HD ECV	NR NR	557 800	304 (29.4%) 402 (39.2%)	389 (37.7%) 474 (46.2%)	95 (9.2%) 114 (11.1%)	NR NR	NR NR	NR NR

AAADR, advanced adenoma detection rate; ADR, adenoma detection rate; CIR, cecal intubation rate; ECU, first-generation Endocuff colonoscopy; ECV, Endocuff-vision colonoscopy; HD, high-definition colonoscopy; n, total numbers (polyps/adenomas/patients); NDR, neoplasia detection rate; PDR, polyp detection rate; SADR, serrated adenoma detection rate.

for ECV colonoscopy compared to HD colonoscopy (RR: 1.12, 95% CI: 0.98–1.29). No statistically significant difference was noted between ECV and ECU colonoscopy in terms of ADR, PDR, NDR, AADR, CIR and MAP. ECV was found to have statistically higher SADR compared to both HD (RR: 1.87, 95% CI 1.13–3.11) and ECU (RR: 2.07, 95% CI 1.06–4.06) colonoscopy. Lower MPP was noted with ECV group compared to ECU colonoscopy (MD: -0.65, 95% CI -0.87– -0.43). This was both statistically and clinically significant.

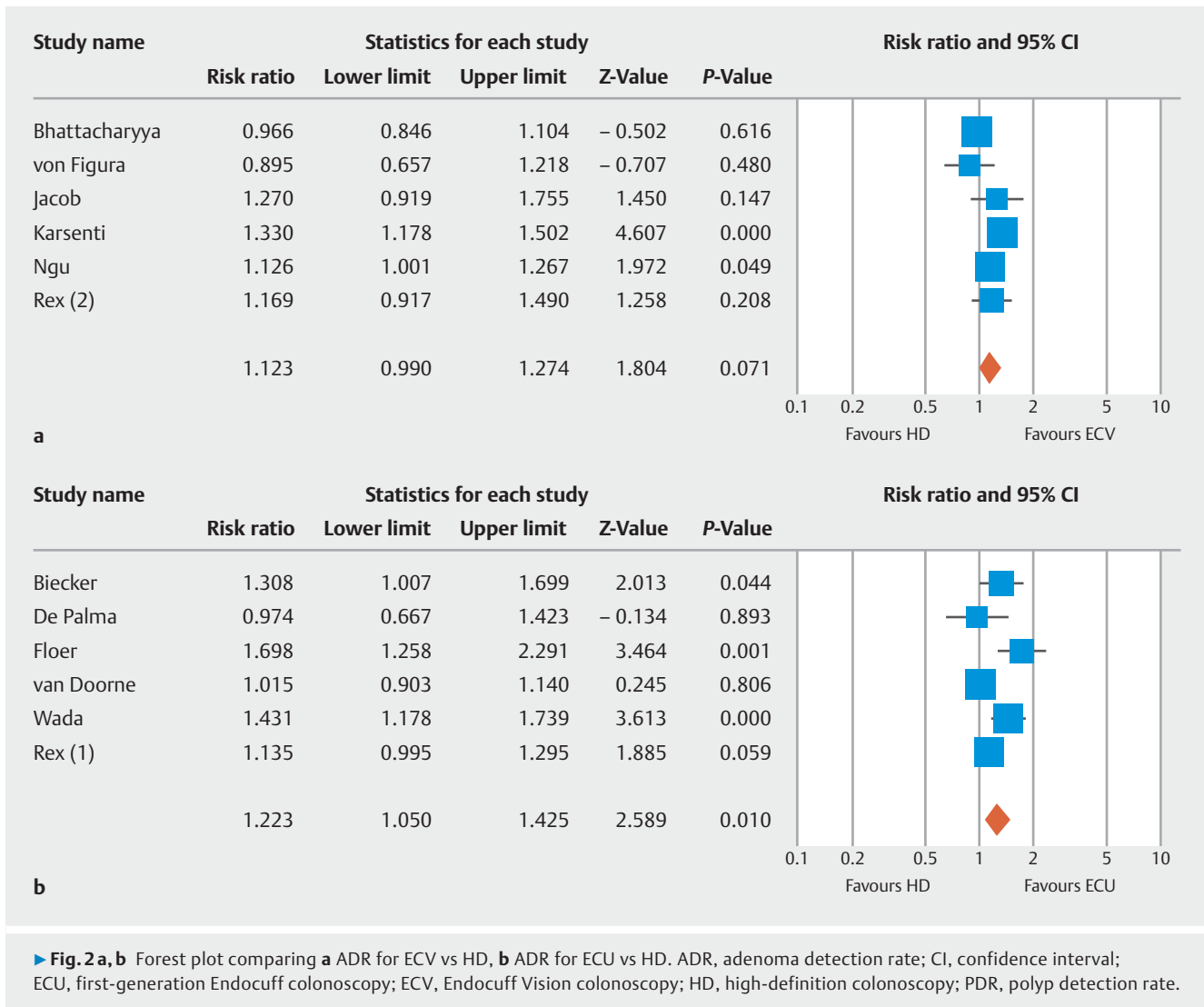
A subgroup analysis was performed for low detectors using control ADR of  $\leq 40\%$  and  $\leq 30\%$  as reference. The ADR for both ECV and ECU showed improvement for endoscopist when control ADR was  $\leq 40\%$  (RR: 1.22 and RR: 1.37, respectively for ECV and ECU) and  $\leq 30\%$  (RR: 1.31 and RR: 1.33, respectively for ECV and ECU) (► **Table 3**).

## Adverse events

Lower rates of overall complications (RR: 0.20, 95% CI 0.08–0.50) and particularly lacerations/erosions (RR: 0.12, 95% CI 0.05–0.29) were noted with HD colonoscopy compared to ECU colonoscopy. Similarly, lower overall complication rates (RR: 0.14, 95% CI 0.02–0.84) and particularly lacerations/erosions (RR: 0.11, 95% CI 0.02–0.70) were also noted for ECV colonoscopy when compared to ECU colonoscopy. The adverse events are compared and summarized in **Supplementary Table 2**.

## Ranking of interventions

Based on frequentist approach, ECU was better compared to ECV in terms of PDR, ADR, AADR, MAP and MPP. ECV was found to be better compared to ECU in terms of NDR, SADR, and lower rates for complications (overall, lacerations, perforations, and major bleeding) (**Supplementary Fig. 3**).



### Risk of bias/inconsistency

The visual assessment of funnel plot based on ADR for all studies revealed visible symmetry (**Supplementary Fig. 4**). No significant publication bias was observed based on Egger's regression analysis ( $P=0.47$ ). The risk of bias for individual studies are highlighted in **Supplementary Table 3**. High risk of bias was observed for all studies as the endoscopists were not blinded to intervention groups as well as outcomes. Inconsistency between direct and indirect evidence was not applicable due to lack of number of study designs.

### Certainty of evidence

The evidence based on direct meta-analysis for all outcomes assessed was MODERATE. The evidence was downgraded due to high risk of bias in the included studies. The evidence based on network meta-analysis for outcomes (ADR, PDR, MAP, MPP, and CIR) assessed was LOW. The evidence was rated down due to indirectness of results and high risk of study bias. Evidence for other outcomes (SADR, NDR, and AADR) based on network meta-analysis was rated VERY LOW. The evidence was rated

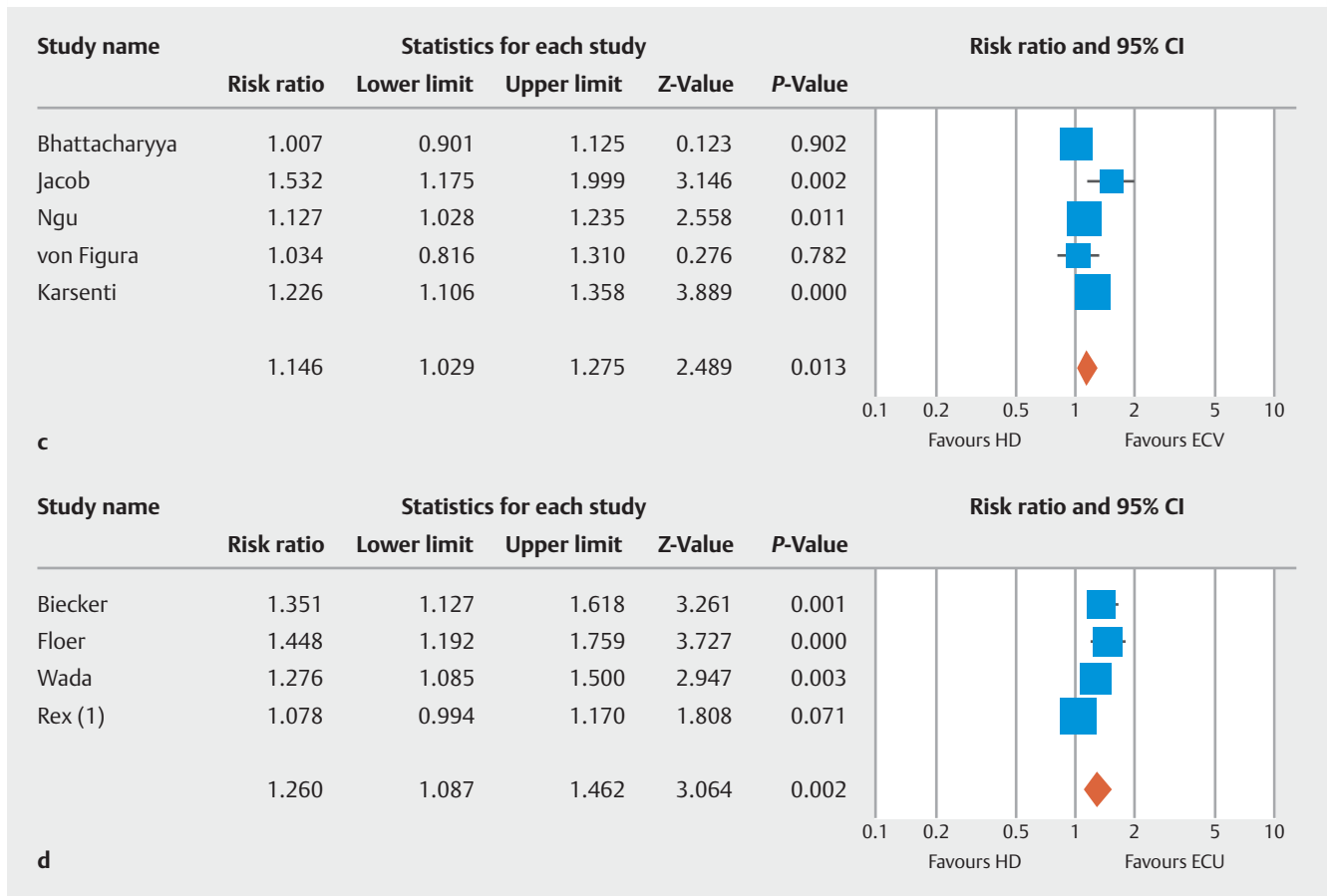
down due to indirectness of results, high risk of study bias, and imprecision due to low number of studies.

### Discussion

The results of our direct and network meta-analysis suggest the relative lack of efficacy of ECV in terms of ADR, AADR, NDR, MAP and MPP when compared to HD colonoscopy. Significantly lower MPP was observed when ECV was compared to ECU using the network meta-analysis model.

ADR is a well-established colonoscopy quality indicator and has been inversely linked with incidence CRC (i. e. increase ADR leading to decrease CRC) [5, 36]. Corley et al. demonstrated a reduction of CRC mortality by 5% for every 1% increment in ADR [5]. Add-on devices (such as Endocap, Endocuff, EndoRing, G-EYE, AmplifEYE) are thought to assist with increasing ADR by flattening the mucosal fold on withdrawal leading to a thorough examination [14]. Evidence of increased ADR was observed with original ECU compared to HD colonoscopy based on previous RCTs and current meta-analysis, the device was re-





► **Fig. 2c, d** Forest plot comparing **c** PDR for ECV vs HD, and **d** PDR for ECU vs HD. ADR, adenoma detection rate; CI, confidence interval; ECU, first-generation Endocuff colonoscopy; ECV, Endocuff Vision colonoscopy; HD, high-definition colonoscopy; PDR, polyp detection rate.

placed with the newer ECV due to significant adverse events particularly lacerations and erosions [27, 32]. There was also the lack of efficacy of improving overall MAP and MPP using ECV in addition to ADR. Although the safety profile of ECV was similar to HD colonoscopy and significantly better compared to ECU, the relative lack of improved efficacy in terms of major outcome metrics such as ADR, MAP and MPP compared to HD colonoscopy makes the device less cost effective. However, the use of ECV maybe justified for low detectors as we demonstrated significantly improved ADR when control ADR for endoscopist was  $\leq 30\%$  and  $\leq 40\%$  respectively.

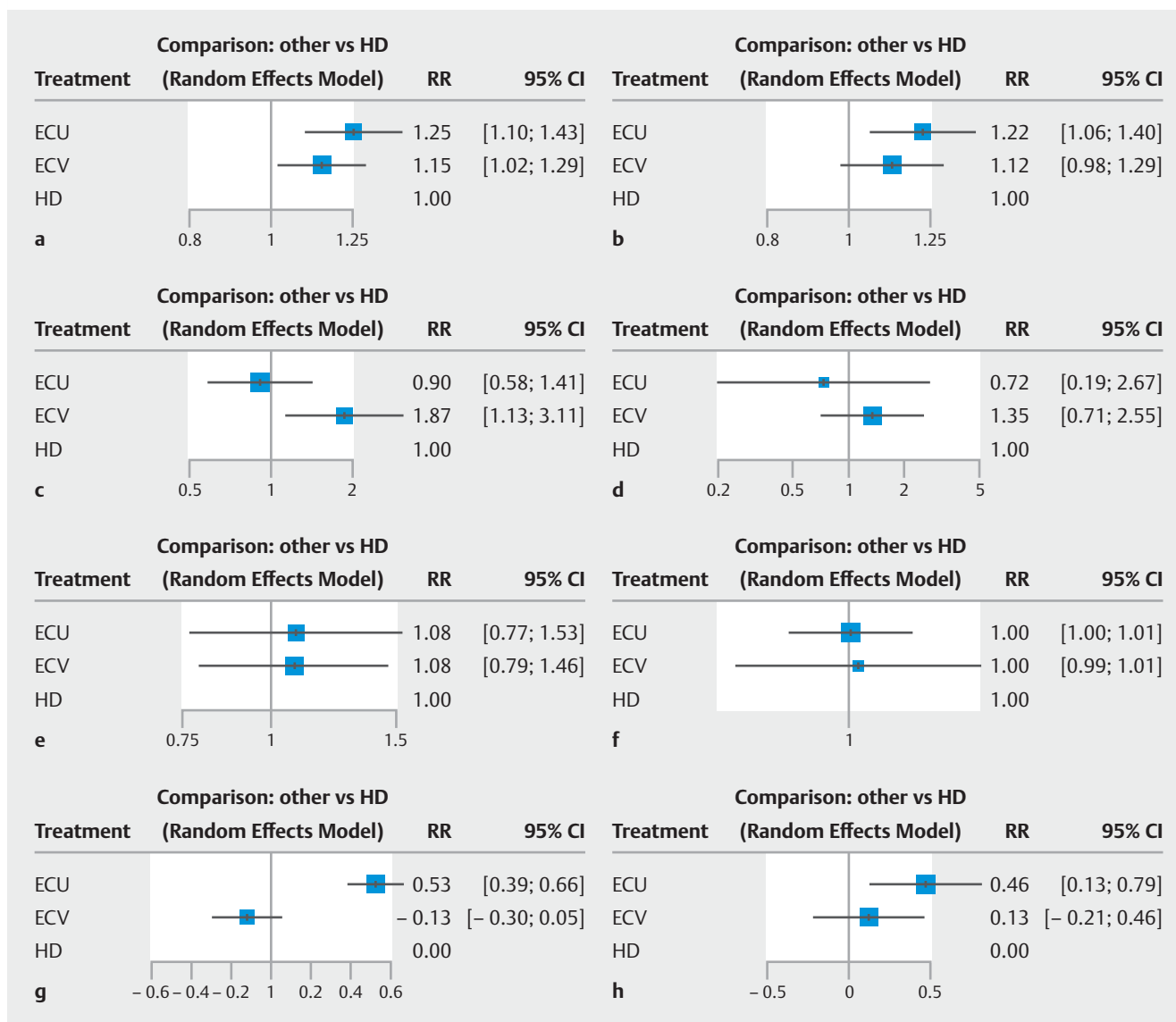
Recently, there has been interest in improving the SADR [37, 38]. The culprit lesions, i.e. SSAs/polyps and traditional serrated adenomas, are attributed to interval CRC through the serrated adenoma pathway [3]. Interestingly, we found significantly improved SADR using ECV compared with HD colonoscopy (RR: 1.87, 95% CI 1.13–3.11) as well as ECU colonoscopy (RR: 2.07, 95% CI 1.06–4.06). These results are limited as only three studies (1 comparing ECU to HD and 2 comparing ECV to HD) evaluated this effect.

Previous meta-analyses demonstrated significant improvement in ADR using Endocuff colonoscopy. Williet et al. (RR: 1.20, 95% CI 1.06–1.36), Facciorusso et al. (Odds ratio (OR): 1.22, 95% CI 1.04–1.44), Chin et al. (OR: 1.49, 95% CI 1.23–

1.80), Jian et al. (OR: 1.37, 95% CI 1.15–1.62), and Triantafyllou et al. (RR: 1.18, 95% CI 1.05–1.32) showed improved detection of adenoma using Endocuff colonoscopy compared to HD colonoscopy. These analyses have serious limitation as all the Endocuff devices (ECU and ECV) were pooled together to demonstrate significantly improved colonoscopy outcome metrics [7, 16–19]. Although somewhat similar, these devices are still different and should be evaluated as such. Further, these meta-analyses included RCTs published as abstracts or conference proceedings which somewhat limit the validity of the overall results as it is hard to assess the study quality based on abstracts alone [7, 16]. As newer RCTs were published, we excluded the abstracts to generate the best evidence and provided separate analysis for each device to help guide the clinician regarding the utility and efficacy of these devices.

An important observation to note here is the improvement in ADR for low detectors using both ECU and ECV compared with HD. The use of Endocuff can perhaps be justified for low detectors as is evident from the results.

Our meta-analysis is not without limitations. The biggest one was the lack of studies directly comparing ECU with ECV. Another important limitation worth mentioning was that majority of the studies included patients other than for a screening indication. This limits the overall conclusion as “true ADR”



**▶ Fig. 3** Forest plots for network meta-analysis **a** PDR, **b** ADR, **c** SADR, **d** NDR, **e** AADR, **f** CIR, **g** MPP, and **h** MAP. AADR, advanced adenoma detection rate; ADR, adenoma detection rate; CIR, cecal intubation rate; ECU, first-generation Endocuff; ECV, Endocuff Vision; HD, high-definition colonoscopy; MAP, mean adenoma per procedure; MPP, mean polyp per procedure; NDR, neoplasia detection rate; PDR, polyp detection rate. Note: Line represents a direct comparison, width of line corresponds to weight, overall effect and number of studies).

should be accounted for screening colonoscopies, and hence our results should be interpreted keeping in mind this limitation [39]. A high risk of bias was noted as it is virtually impossible to blind the endoscopist to treatment allocation and outcome assessment. This brings into play performance and detection biases. Finally, factors related to the endoscopist (training level, experience, fatigue factor) and patient (family history, ethnicity, bowel preparation) can have an influence on the outcome of colonoscopy and were not accounted in the current study. This may account for the heterogeneity seen in our study.

Despite these limitations, we included RCTs with a robust number of study population. We provided both direct and indirect evidence regarding the outcomes of particular intervention. We further provided subgroup analysis result based on

control ADR of the studies to assess if these devices had impact on low detectors.

## Conclusions

In conclusion, the utility of ECV is somewhat limited in terms of improving the outcome metrics, including ADR, AADR, NDR, MAP and MPP. Although improved SADR was noted, that is limited due to the low number of studies reporting this outcome. ECV can perhaps be best justified for low detectors to improve ADR and PDR. Further device modification is needed to improve outcome metrics as well as keeping the safety profile as demonstrated by ECV.



► **Table 3** Outcomes based on network meta-analysis

Study outcome	No. of Studies compared	ECU vs HD	ECV vs HD	ECV vs ECU	
		Relative risk (95% CI)			I <sup>2</sup>
Overall PDR	9	1.25 (1.10–1.43) <sup>1</sup>	1.14 (1.02–1.29) <sup>1</sup>	0.92 (0.77–1.09)	70.9%
PDR <sup>2</sup>	3	1.08 (0.99–1.17)	1.01 (0.91–1.12)	0.94 (0.82–1.07)	0%
PDR <sup>3</sup>	6	1.35 (1.20–1.52) <sup>1</sup>	1.21 (1.10–1.33) <sup>1</sup>	0.90 (0.77–1.04)	34.5%
PDR <sup>4</sup>	5	1.14 (1.01–1.29) <sup>1</sup>	1.06 (0.96–1.18)	0.93 (0.80–1.09)	47.8%
PDR <sup>5</sup>	4	1.40 (1.20–1.63) <sup>1</sup>	1.29 (1.13–1.47) <sup>1</sup>	0.92 (0.75–1.13)	23.7%
Overall ADR	12	1.22 (1.06–1.40) <sup>1</sup>	1.12 (0.98–1.29)	0.92 (0.76–1.12)	69.2%
ADR <sup>2</sup>	5	1.07 (0.96–1.19)	1.00 (0.88–1.13)	0.93 (0.79–1.10)	22.8%
ADR <sup>3</sup>	7	1.37 (1.16–1.61) <sup>1</sup>	1.22 (1.07–1.42) <sup>1</sup>	0.90 (0.72–1.12)	45.3%
ADR <sup>4</sup>	7	1.16 (0.99–1.34)	1.05 (0.91–1.20)	0.90 (0.74–1.11)	63.0%
ADR <sup>5</sup>	5	1.33 (1.06–1.67) <sup>1</sup>	1.31 (1.05–1.64) <sup>1</sup>	0.99 (0.72–1.36)	42.5%
AADR	4	1.09 (0.77–1.53)	1.08 (0.79–1.46)	0.99 (0.63–1.58)	38.1%
SADR	3	0.90 (0.58–1.41)	1.87 (1.13–3.11) <sup>1</sup>	2.07 (1.06–4.06) <sup>1</sup>	0%
NDR	3	0.72 (0.19–2.67)	1.34 (0.71–2.55)	1.87 (0.44–8.02)	52.1%
CIR	7	1.00 (0.99–1.01)	1.00 (0.99–1.01)	1.00 (0.99–1.01)	0%
		Mean difference (95% CI)			
Overall MPP	6	0.53 (0.39–0.66) <sup>1</sup>	-0.13 (-0.30–0.05)	-0.65 (-0.87–-0.43) <sup>1</sup>	0%
Overall MAP	9	0.46 (0.13–0.79) <sup>1</sup>	0.12 (-0.21–0.46)	-0.34 (-0.81–0.13)	92.5%

AAADR, advanced adenoma detection rate; ADR, adenoma detection rate; CI, confidence interval; CIR, cecal intubation rate; ECU, first-generation Endocuff colonoscopy; ECV, Endocuff Vision colonoscopy; HD, high-definition colonoscopy; MAP, mean adenoma per procedure; MPP, mean polyp per procedure; NDR, neoplasia detection rate; PDR, polyp detection rate; SADR, serrated adenoma detection rate.

<sup>1</sup> P < 0.05 for the study estimate

<sup>2</sup> Denotes studies with control ADR > 40%

<sup>3</sup> Denotes studies with control ADR ≤ 40%

<sup>4</sup> Denotes studies with control ADR > 30%

<sup>5</sup> Denotes studies with control ADR ≤ 30%

## Competing interests

The authors declare that they have no conflict of interest.

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