Artificial intelligence–assisted colonoscopy for adenoma and polyp detection: an updated systematic review and meta-analysis

Mohamed G. Shiha, MRCP, Priya Oka, MRCP, Suneil A. Raju, MRCP, Foong Way David Tai, MD, Hey-Long Ching, MD, Mo Thoufeeq, MRCP, Reena Sidhu, MD, Mark E. McAlindon, PhD, David S. Sanders, MD

Sheffield, United Kingdom

Background and Aims: There is a growing interest in the role of artificial intelligence in colonoscopy. The aim of this systematic review and meta-analysis was to evaluate the efficacy of computer-aided detection (CADe) of colorectal adenomas and polyps.

Methods: The MEDLINE, Embase, and Cochrane Central of Controlled Trials (from inception to December 2022) databases were searched for randomized controlled trials comparing colonoscopy with CADe versus standard colonoscopy (SC). We performed a random-effects meta-analysis and reported the results as relative risks (RRs) or mean difference with 95% confidence intervals (CIs).

Results: Twelve randomized controlled trials comprising 11,340 patients were included in the final analysis. The pooled adenoma detection rate was significantly higher in the CADe group compared with the SC group (41.4% vs 33%; RR, 1.26; 95% CI, 1.18-1.35). CADe increased the detection of adenomas regardless of their size (≤5 mm [RR, 1.56; 95% CI, 1.38-1.77], 6-9 mm [RR, 1.24; 95% CI, 1.05-1.47], and ≥10 mm [RR, 1.30; 95% CI, 1.11-1.53]), location (proximal colon [RR, 1.41; 95% CI, 1.26-1.58] and distal colon [RR, 1.44; 95% 1.29-1.61]), or morphology (polypoid [RR, 1.35; 95% CI, 1.17-1.56] and nonpolypoid [RR, 1.55; 95% CI, 1.25-1.93]). There was no difference between the CADe and SC groups in detecting advanced adenomas or sessile serrated lesions. Colonoscopy withdrawal time was longer in the CADe group compared with the SC group (mean difference, .34 minute; 95% CI, .17-.51).

Conclusions: Using CADe during colonoscopy is associated with a significant increase in adenoma detection rate and adenomas per colonoscopy, mainly due to the increased detection of diminutive adenomas. (iGIE 2023;2:333-43.)

Colorectal cancer is the third most common cancer worldwide, with nearly 2 million new cases annually.[1] Colonoscopy prevents colorectal cancer by detecting and removing adenomas, the major precursors of cancer.[2] The adenoma detection rate (ADR) is considered the main quality indicator for colonoscopy effectiveness in preventing cancer.[3] An annual ADR ≥25% is inversely associated with the risk of colorectal cancer and cancer-related deaths.[4] However, wide variations in ADR exist between endoscopists, and recent evidence suggests that 1 in 4 adenomas are missed during colonoscopy.[5] These missed adenomas are responsible for the majority of interval post-colonoscopy colorectal cancer (PCCRC) and share distinct characteristics that challenge human perception such as small size and flat morphology.[6]

Advances in artificial intelligence (AI) and machine learning enabled the development of computer-aided detection (CADe) systems that highlight colorectal polyps to endoscopists in real time via visual or acoustic alarms with high sensitivity and low false-positive rates.[7] Therefore, CADe may reduce the risk of missing adenomas during colonoscopy and the variations in practice between endoscopists.

The initial randomized controlled trials (RCTs) conducted in China showed significant benefits to AI-assisted colonoscopy.[8,9] More recently, several RCTs have been conducted in different settings and more diverse populations. The aim of the current systematic review and meta-analysis was to summarize the latest evidence on the efficacy of AI-assisted colonoscopy with CADe for adenoma and polyp detection compared with standard colonoscopy (SC).

METHODS

This systematic review and meta-analysis was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Supplementary Fig. 1,

available online at www.igiejournal.org). The a priori established study protocol was registered in the International Prospective Register of Systematic Reviews (CRD42022370635; August 11, 2022).

Search strategy and study selection

We conducted a comprehensive literature search in MEDLINE, Embase, and Cochrane Central of Controlled Trials databases from their inception to December 2, 2022, without language restrictions. The full search strategy is provided in Supplementary Table 1 (available online at www.igiejournal.org).

The search results were exported to EndNote 20 (Clarivate Analytics, London, United Kingdom), and duplicate records were removed. Two reviewers (M.G.S. and P.O.) independently screened the titles and abstracts of all citations against the inclusion criteria. The full-text articles of all potentially relevant studies were retrieved and further evaluated in more detail using standardized forms. Any disagreements were resolved by discussion with a third reviewer (S.A.R.). Finally, the bibliographies of the included studies and relevant reviews, including previous meta-analyses, were manually searched for additional eligible studies.

Parallel-group RCTs were included that evaluated the effect of AI-assisted colonoscopy on adenoma and polyp detection by comparing real-time CADe colonoscopy (intervention) with SC (control) in adult patients undergoing colonoscopy for symptomatic, screening, and surveillance purposes. Studies using tandem colonoscopy methodology, not reporting ADR, not conducted as an RCT, or not published in full-text articles were excluded.

Primary and secondary outcomes

The primary outcome was ADR, defined as the proportion of patients with at least 1 adenoma detected during colonoscopy. Secondary outcomes included the following:

- Polyp detection rate (PDR): the proportion of patients with at least 1 polyp detected during colonoscopy.
- Advanced adenomas per colonoscopy: the total number of advanced adenomas detected during colonoscopy divided by the total number of colonoscopies.
- Sessile serrated lesions (SSLs) per colonoscopy: the total number of SSLs detected divided by the total number of colonoscopies.
- Mean adenomas per colonoscopy: the mean number of adenomas detected per colonoscopy.
- Colonoscopy withdrawal time: time spent inspecting the colonic mucosa while withdrawing the colonoscope from the cecum.

Data extraction

Two reviewers (M.G.S. and P.O.) independently extracted data onto a Microsoft Excel spreadsheet (Microsoft, Redmond, Wash, USA). The following data were extracted from each study, where available: country, study design, study period, number of patients, patient demographic characteristics (age and gender), colonoscopy indications, exclusion criteria, endoscopists' characteristics, CADe systems, and outcomes data. The corresponding authors of the included studies were contacted for missing data. Any disagreements were resolved by discussion with a third reviewer (S.A.R.).

Risk of bias and quality assessment

Two reviewers (M.G.S. and P.O.) independently assessed the risk of bias using the Cochrane risk-of-bias tool for randomized trials at the study level based on the following domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding (performance and detection bias), incomplete data (attribution bias), and selective reporting (reporting bias).[10] The Grading of Recommendations, Assessment, Development, and Evaluation criteria were used to assess the quality of evidence.[11] Any disagreements were resolved by discussion with a third reviewer (S.A.R.).

Data synthesis and statistical analysis

We calculated the relative risks (RRs) for dichotomous outcomes and mean differences (MDs) for continuous outcomes with 95% confidence intervals (CIs). Where continuous outcomes were reported as median and interquartile range, the method described by Wan et al[12] was used to calculate the mean and standard deviation. The Mantel-Haenszel method was used to estimate the pooled RR and the inverse variance method to estimate the MD. Heterogeneity was assessed among studies by using the Cochrane Q and I^2 statistics, with values of less than 25%, ≥25% to 50%, and more than 50% representing low, moderate, and high levels of heterogeneity, respectively. The risk of publication bias was visually examined with funnel plots and quantified by using the Harbord regression test.[13] The Duval and Tweedie trim and fill method was used to adjust for potential publication bias.[14] All analyses were performed by using a random-effects model, and a P value $< .05$ was considered statistically significant.

To assess the robustness of the synthesized results for the primary outcome, sensitivity analyses were performed according to study setting, geographical location, and endoscopists' experience. In addition, a leave-one-out analysis was used to examine the influence of each study on the overall effect size estimate.

We also performed prespecified subgroup analyses according to adenoma location (proximal colon and distal colon), size (diminutive, ≤5 mm; small, 6-9 mm; and large ≥10 mm), and morphology (polypoid and nonpolypoid). The Mantel-Haenszel method was used to estimate the differences between subgroups and the Cochrane Q and I^2 statistics for heterogeneity.

All analyses were performed by using Review Manager 5.4 (The Cochrane Collaboration, Oxford, UK) and Stata version 17 (StataCorp, College Station, Texas, USA).

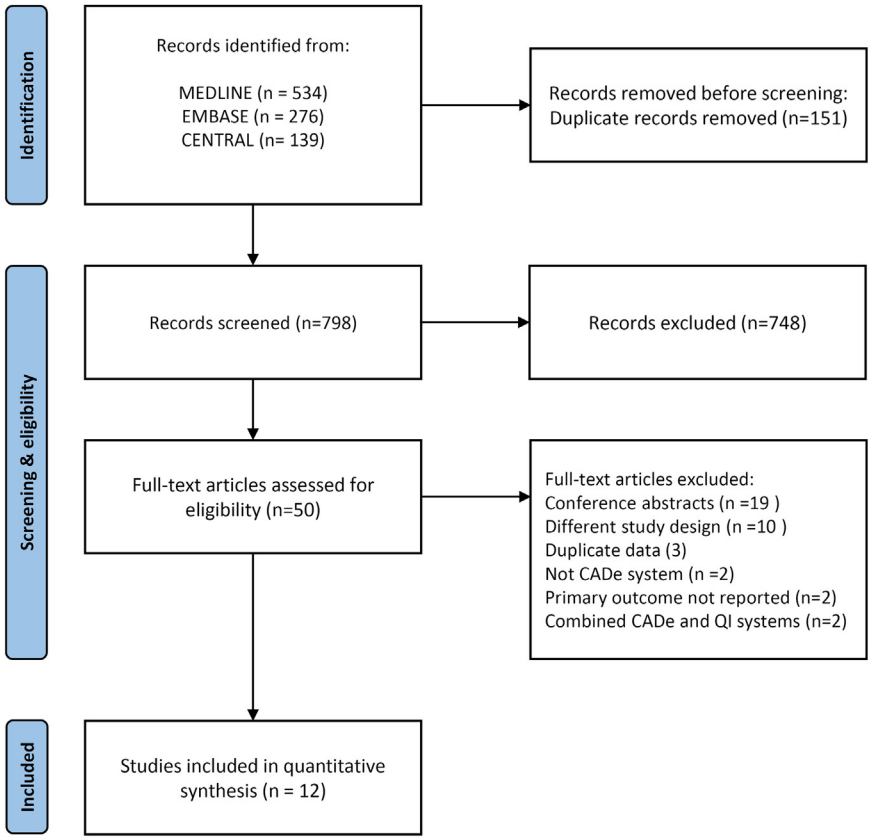

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement flow diagram of study selection. *CENTRAL*, Cochrane Central of Controlled Trials; *CADe*, computer-aided detection; *QI*, quality improvement.

RESULTS

Study selection and characteristics

Our search strategy yielded 949 citations, of which 50 articles seemed to be relevant and were eligible for full-text screening (Fig. 1). Fourteen RCTs compared ADR in patients undergoing CADe colonoscopy versus SC. Two studies were excluded because they combined CADe with AI quality improvement systems to monitor withdrawal time and bowel preparation, which may have overestimated the true effect of the CADe systems.[15,16]

Twelve RCTs were included in the meta-analysis comprising 11,340 patients, of whom 5638 were randomized to the CADe group and 5702 were randomized to the SC group.[17-28] Studies were conducted between September 2017 and January 2022 across 6 countries. All but 1 study showed a significant increase in ADR in the CADe group compared with the SC group.[25] Two studies involved 4 parallel groups, including SC, CADe, and computer-aided quality improvement system in Yao et al[23] or mucosal exposure device in Aniwan et al[26]; the fourth group was a combination of both interventions. Only the SC and CADe groups were included in our analyses. All studies excluded patients with contraindications to endoscopy or biopsy, history of colorectal cancer, inflammatory bowel disease, previous failed colonoscopy, and polyposis syndromes. Study characteristics are summarized in Table 1.

Adenoma detection rate

The pooled ADR was significantly higher in the CADe group compared with the SC group (41.4% vs 33%; RR, 1.26; 95% CI, 1.18-1.35), with moderate heterogeneity between studies ($I^2 = 42\%$, $P = .06$) (Fig. 2). Two studies had a larger influence on the overall effect size than the other studies and contributed to between-study heterogeneity.[18,25] Omitting Liu et al[18] decreased the overall effect size (RR, 1.22; 95% CI, 1.16-1.29) and eliminated significant heterogeneity ($I^2 = 1\%, P = .43$), whereas omitting Shaukat et al[25] increased the overall effect size (RR, 1.29; 95% CI, 1.21-1.37) and eliminated significant heterogeneity ($I^2 = 25\%$, $P = .21$). The influence of excluding each study on the overall effect size is shown in Supplementary Figure 2 (available online at www.igiejournal.org).

There was evidence of funnel plot asymmetry (Harbord $z = 2.5$, $P = .01$), indicating possible publication bias or small-study effects. However, the difference in ADR between the CADe and the SC groups remained significant after adjusting for 6 imputed studies using the trim and fill method (RR, 1.17; 95% CI, 1.09-1.27) (Supplementary Fig. 3, available online at www.igiejournal.org).

TABLE 1. Study characteristics

Author (Year)	Country	Design and setting	No. of patients (CADe/SC)	Mean age (CADe/SC), y	Colonoscopy indication	Endoscopists	AI system
Wang et al (2019)[17]	China	Single-center RCT	1058 (522/536)	51.07/49.94	Screening, 84 (7.9%); symptomatic, 974 (92.1%)	2 expert endoscopists (>20,000 colonoscopies); 2 midlevel endoscopists (3000-10,000 colonoscopies); 4 junior endoscopists (100-500 colonoscopies)	EndoScreener (Shanghai Wision AI Co Ltd, China)
Liu et al (2020)[18]	China	Single-center RCT	1026 (508/518)	51.02/50.13	Screening, 66 (6.4%); symptomatic, 960 (93.5%)	Data not provided	CADe system of polyps (Henan Xuanweitang Medical Information Technology Co, Ltd, Zhengzhou City, China)
Wang et al (2020)[19]	China	Single-center RCT	962 (484/478)	49.0/49.0	Screening, 158 (15.1%); symptomatic, 804 (76.9%)	4 expert endoscopists (at least 5 years' experience and 1000 colonoscopies per year)	EndoScreener (Shanghai Wision AI Co Ltd, China)
Repici et al (2020)[20]	Italy	Multicenter RCT	685 (341/344)	64.5/61.1	Screening, 153 (22.3%); FIT+, 207 (30.2%); symptomatic, 161; (23.5%); surveillance, 164 (23.9%)	6 expert endoscopists (>2000 screening colonoscopies)	GI Genius (Medtronic, Minneapolis, Minn, USA)
Liu et al (2020)[21]	China	Single-center RCT	790 (393/397)	49.84/48.79	Screening, 182 (23%); symptomatic, 608 (77%)	4 expert endoscopists; 4 midlevel endoscopists; 3 junior endoscopists	EndoScreener (Shanghai Wision AI Co Ltd, China)
Repici et al (2021)[22]	Italy and Switzerland	Multicenter RCT	660 (330/330)	61.9/62.6	Screening, 192 (29%); FIT+, 48 (7.2%); symptomatic, 175 (26.5%); surveillance, 245 (37.1%)	10 nonexpert endoscopists (<2000 colonoscopies)	GI Genius (Medtronic, Minneapolis, Minn, USA)
Yao et al (2021)[23]	China	Single-center RCT	539 (268/271)	50.69/50.85	Screening, 479 (88.8%); symptomatic, 5 (1%); surveillance, 55 (10.2%)	4 expert endoscopists (>2000 screening colonoscopies)	EndoAngel (Wuhan EndoAngel Medical Technology Company Co, Ltd, Wuhan, China)
Xu et al (2022)[24]	China	Multicenter RCT	2527 (1238/1289)	57.49/57.03*	Screening, 1684 (55%); FIT+, 127 (4.1%); FIT–, 1248 (40.8%)*	12 expert endoscopists (>5000 colonoscopies); 12 nonexpert endoscopists (<5000 colonoscopies)	Eagle Eye version 5.1 (Xiamen Innovision, Xiamen, China)
Shaukat et al (2022)[25]	United States	Multicenter RCT	1359 (682/677)	60.6/59.9	Screening, 894 (65.7%); surveillance, 465 (34.2%)	22 expert endoscopists (>1000 colonoscopies and minimum ADR of 25%)	SKOUT (Iterative Scopes, Cambridge, Mass, USA)
Aniwan et al (2022)[26]	Thailand	Single-center RCT	622 (312/310)	62.8/62	Screening, 554 (89%); FIT+, 68 (11%)	7 expert endoscopists; 10 trainee endoscopists (supervised)	CAD EYE (FUJIFILM, Tokyo, Japan)

(*continued on the next page*)

TABLE 1. Continued

Author (Year)	Country	Design and setting	No. of patients (CADe/SC)	Mean age (CADe/SC), y	Colonoscopy indication	Endoscopists	AI system
Gimeno-García et al (2022)[27]	Spain	Single-center RCT	312 (155/157)	62.99/64.71	Screening, 124 (39.7%); symptomatic, 87 (27.8%); surveillance, 101 (32.3%)	8 expert endoscopists (>2000 colonoscopies)	ENDO-AID (OIP-1) (Olympus, Tokyo, Japan)
Rondonotti et al (2022)[28]	Italy	Multicenter RCT	800 (405/395)	62/61	FIT+, 800 (100%)	Expert endoscopists (>300 colonoscopies/ year, minimum ADR of 25%, and cecal intubation rate of 95%)	CAD EYE (FUJIFILM, Tokyo, Japan)

CADe, Computer-aided detection; *SC*, standard colonoscopy; AI, artificial intelligence; *RCT*, randomized controlled trial; *FIT*, fecal immunochemical test.
*Data from intention-to-treat analysis.

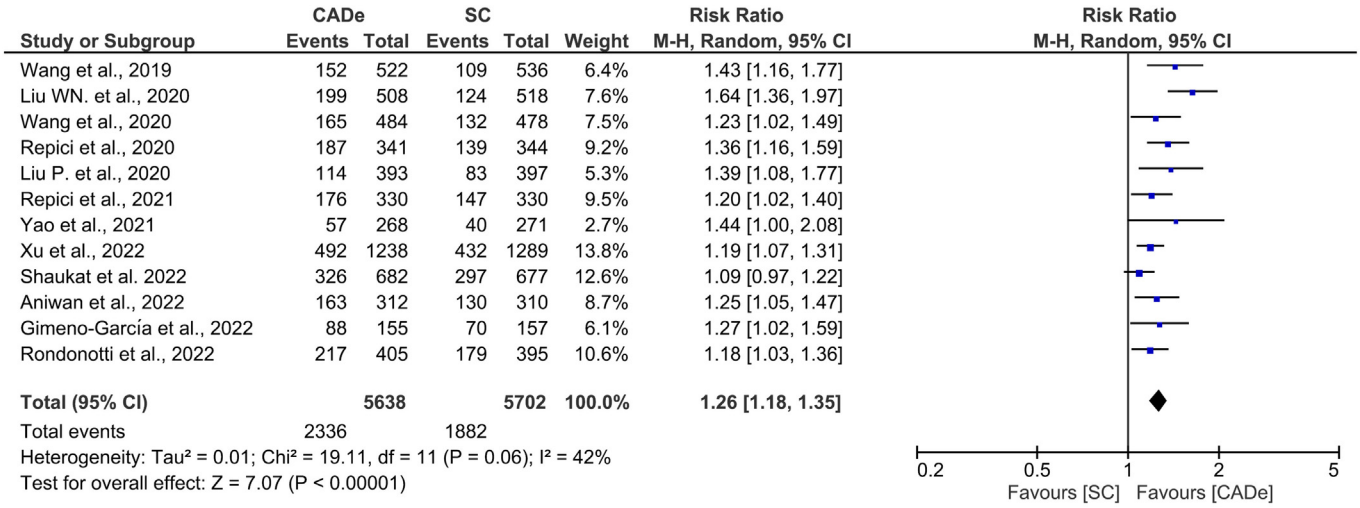

Figure 2. Forest plot for the adenoma detection rate in computer-aided detection (CADe) versus standard colonoscopy (SC). *M-H*, Mantel-Haenszel; *CI*, confidence interval.

Further sensitivity analyses revealed a larger effect size in the studies conducted in Asia (RR, 1.33; 95% CI, 1.21-1.46) compared with the studies conducted in Europe and the United States (RR, 1.20; 95% CI, 1.11-1.29) (Supplementary Fig. 4, available online at www.igiejournal.org). Single-center studies also had a larger effect size (RR, 1.36; 95% CI, 1.25-1.48) compared with multicenter studies (RR, 1.18; 95% CI 1.11-1.26) (Supplementary Fig. 5, available online at www.igiejournal.org). Finally, there was no significant difference between the studies that included expert endoscopists only (RR, 1.21; 95% CI, 1.12-1.31) and those that included expert and/or nonexpert endoscopists (RR, 1.24; 95% CI, 1.15-1.33) (Supplementary Fig. 6, available online at www.igiejournal.org).

Polyp detection rate

Nine studies provided data for PDR. The pooled PDR was significantly higher in the CADe group compared with the SC group (56.3% vs 43.5%; RR, 1.32; 95% CI, 1.19-1.47), with high heterogeneity between studies (I^2 = 81%, P < .00001) (Supplementary Fig. 7, available online at www.igiejournal.org).

Per colonoscopy analyses

The added benefit of CADe was more marked for diminutive (≤5 mm) adenomas (RR, 1.56; 95% CI, 1.38-1.77) compared with small (6-9 mm) adenomas (RR, 1.24; 95% CI, 1.05-1.47) and large (≥10 mm) adenomas (RR, 1.30; 95% CI, 1.11-1.53) (Fig. 3). Furthermore, CADe increased the detection of adenomas regardless of their location (proximal colon [RR, 1.41; 95% CI, 1.26-1.58] and distal colon [RR, 1.44; 95% CI, 1.29-1.61]) (Fig. 4) or morphology (polypoid [RR, 1.35; 95% CI, 1.17-1.56] and nonpolypoid [RR, 1.55; 95% CI, 1.25-1.93]) (Fig. 5).

Mean adenomas per colonoscopy was significantly higher in the CADe group compared with the SC group

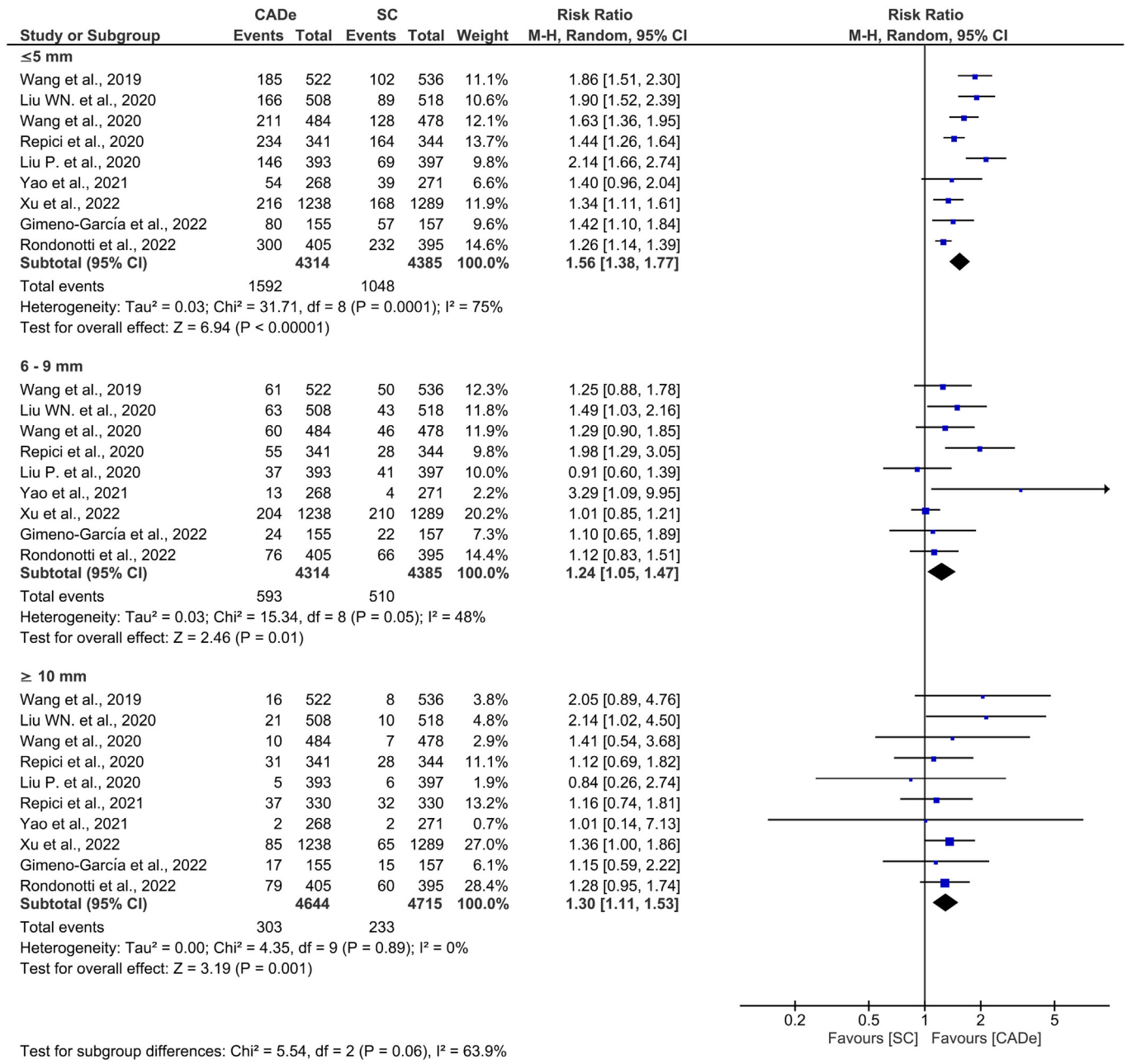

Figure 3. Forest plot for adenomas per colonoscopy in computer-aided detection (CADe) versus standard colonoscopy (SC) subgrouped according to adenoma size. *M-H*, Mantel-Haenszel; *CI*, confidence interval.

(MD, .22; 95% CI, .12-.32), with high heterogeneity between studies (I^2 = 64%, P = .01) (Supplementary Fig. 8, available online at www.igiejournal.org).

There was no statistically significant difference in advanced adenoma detection between the CADe group and the SC group (RR, 1.11; 95% CI, .96-1.27), with no evidence of heterogeneity between studies (I^2 = 0%, P = .73) (Supplementary Fig. 9, available online at www.igiejournal.org). Similarly, CADe did not increase SSL detection compared with SC colonoscopy (RR, 1.14; 95% CI, .84-1.56), with high heterogeneity between studies (I^2 = 67%, P = .0009) (Supplementary Fig. 10, available online at www.igiejournal.org).

Colonoscopy withdrawal time

Six studies provided data for the total colonoscopy withdrawal time, and 11 studies provided data for the no-biopsy withdrawal time. The mean total withdrawal time was significantly longer in the CADe group compared with the SC group (MD, .34 minute; 95% CI, .17-.51), with high heterogeneity between studies (I^2 = 64%, P = .02). When excluding biopsy time, withdrawal time was still significantly longer in the CADe group compared with the SC group (MD, .22 minute; 95% CI, .10-.33), with high heterogeneity between studies (I^2 = 59%, P = .006) (Fig. 6).

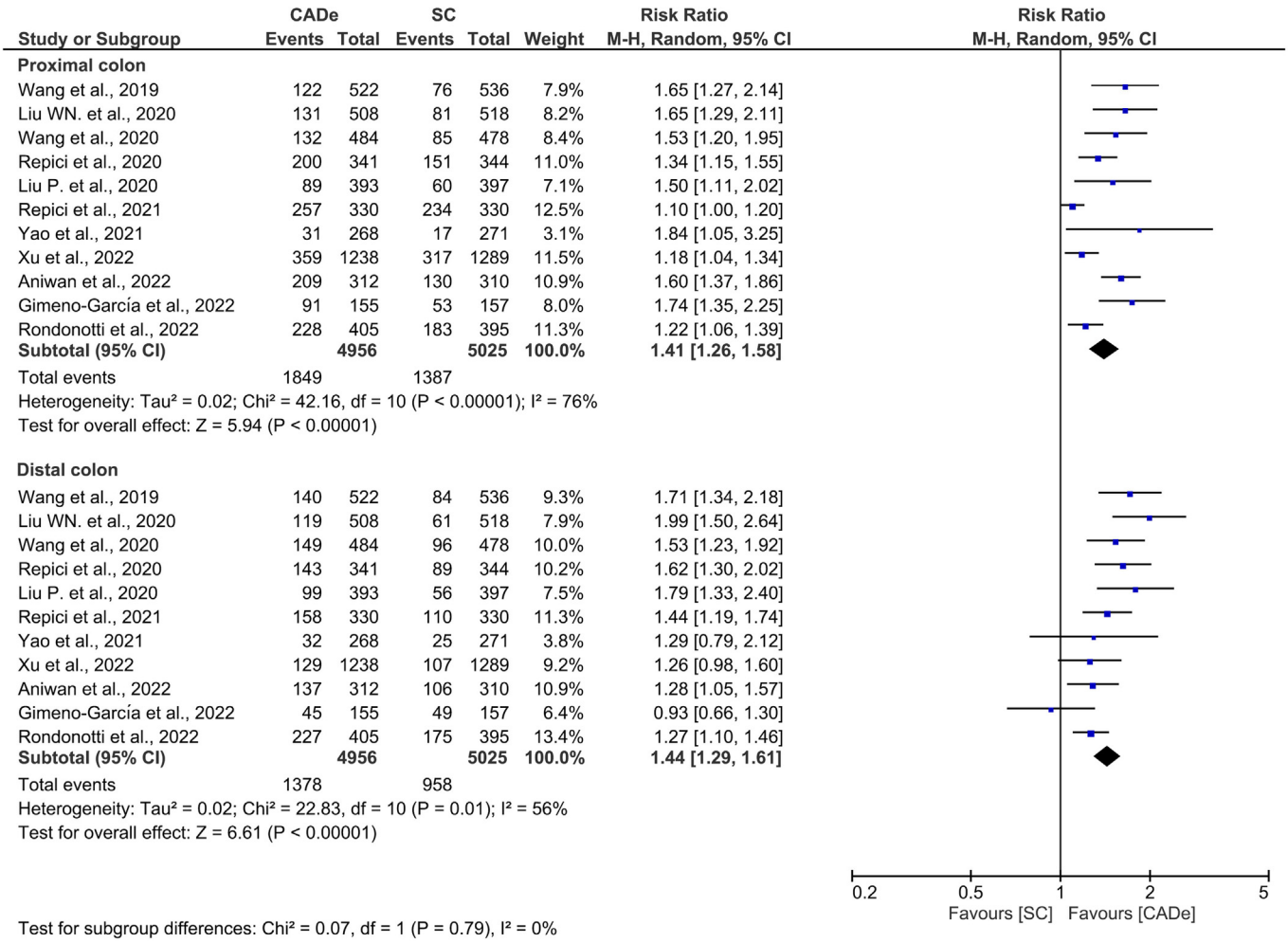

Figure 4. Forest plot for adenomas per colonoscopy in computer-aided detection (CADe) versus standard colonoscopy (SC) subgrouped according to adenoma location. *M-H*, Mantel-Haenszel; *CI*, confidence interval.

Risk of bias and certainty of the evidence

Only one study used a sham system to blind endoscopists to treatment allocation, and it had a low risk of bias across all domains.[19] All other studies were rated at high risk of performance and detection bias due to the lack of blinding of endoscopists. One study did not report the randomization and allocation sequence process and had the highest risk of bias compared with the other studies.[18] The risk of bias assessment summary is reported in Supplementary Fig. 11 (available online at www.igiejournal.org). The overall certainty of the evidence was moderate due to serious risk of bias (Supplementary Table 2, available online at www.igiejournal.org).

DISCUSSION

In this systematic review and meta-analysis of 12 RCTs including 11,340 patients, CADe significantly increased ADR, PDR, and adenomas per colonoscopy regardless of adenoma characteristics. Although CADe was associated with a longer colonoscopy withdrawal time compared with SC, the mean difference between groups was negligible. AI-assisted colonoscopy with CADe was associated with a 26% relative increase in ADR, from 33% to 41.1%.

The relative increase in ADR in the current meta-analysis is lower than the 52% and 44% previously reported in meta-analyses of the early studies conducted in China.[8,9] These studies included mostly symptomatic patients, had a low ADR in the control groups,[17-19] and 2 studies used AI systems to monitor withdrawal time and colonoscopy quality in addition to the CADe systems.[15,16] Therefore, the overall effect of CADe on ADR may have been overestimated in previous meta-analyses. However, considering that each 1% increase in ADR is associated with a 3% decrease in the risk of interval colorectal cancer,[3] the 8% difference in ADR between the CADe and the SC groups is of a great clinical significance, and it could lead to a considerable reduction in the risk of interval cancer and cancer-related deaths; long-term follow-up studies are needed, however, to confirm this hypothesis.

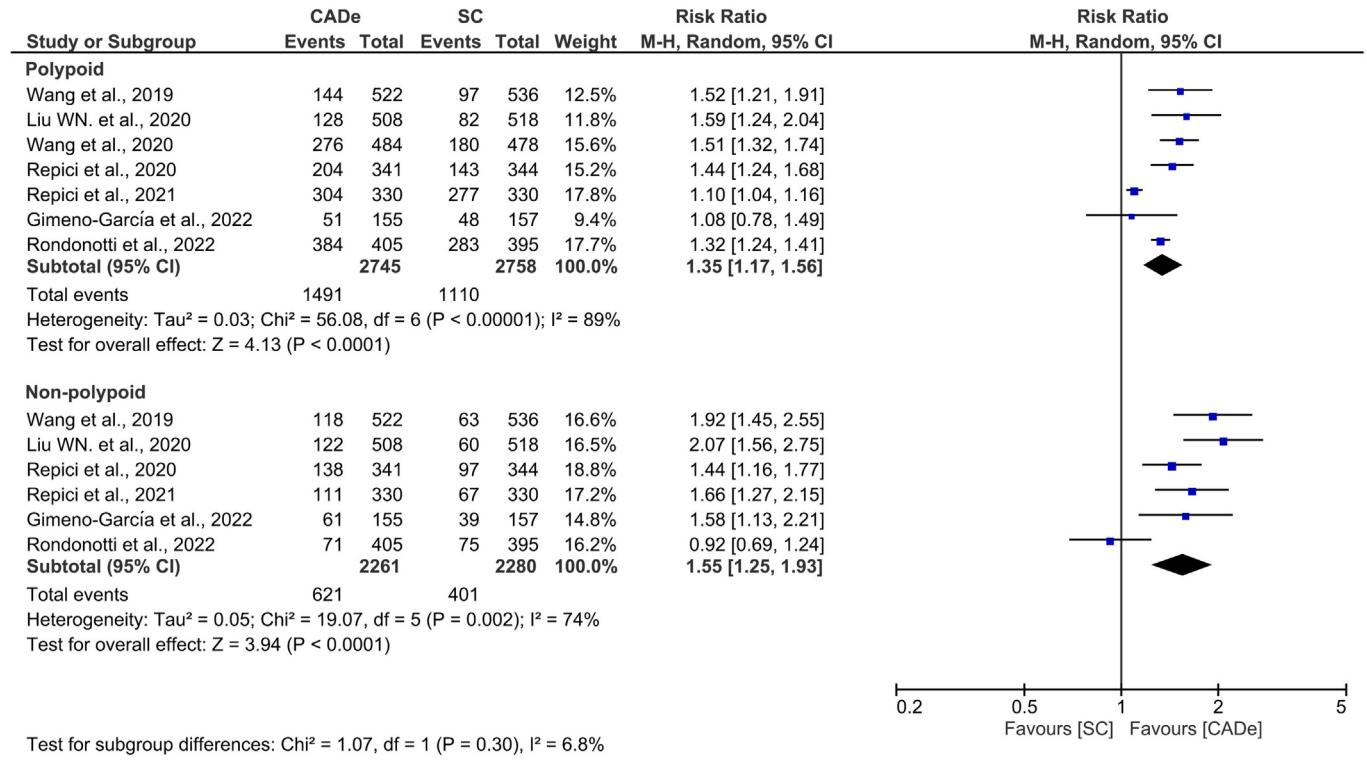

Figure 5. Forest plot for adenomas per colonoscopy in computer-aided detection (CADe) versus standard colonoscopy (SC) subgrouped according to adenoma morphology. *M-H*, Mantel-Haenszel; *CI*, confidence interval.

The incremental increase in ADR with CADe remained consistent and significant after several sensitivity analyses but showed a higher relative increase in the studies conducted in Asia (33%; from 27.6% to 36%) compared with the studies conducted in Europe and the United States (20%; from 43.7% to 51.9%), and in single-center studies (36%; from 25.7% to 35.5%) compared with multicenter studies (18%; from 39.3% to 46.6%). This again reflects the differences in patient populations and study design between the Eastern and Western studies. The latter were mostly multicenter studies including older patients undergoing colonoscopy for screening and surveillance purposes with a relatively high ADR in the control groups. Although we could not directly compare the differences in ADR between expert and nonexpert endoscopists, a pooled analysis of 2 studies showed that CADe but not the endoscopists' experience was the major influence on ADR.[22] Hence, using CADe may bridge the experience gap and variations in colonoscopy practice between expert and nonexpert endoscopists.

Our subgroup analysis showed that the increased adenomas per colonoscopy in the CADe group was mainly attributable to the increased detection of diminutive adenomas. Although diminutive adenomas carry a low risk of cancer or high-grade dysplasia,[29] patients with more than 2 diminutive adenomas have a higher risk of developing metachronous advanced adenomas compared with those with 2 or fewer diminutive adenomas.[30] Therefore, detecting more diminutive adenomas may have an impact on the recommendations of colonoscopy surveillance. A recent pooled analysis of RCTs reported that using AI in colonoscopy increased the proportion of patients requiring early colonoscopy surveillance by nearly 20% and 35% according to the European and American guidelines, respectively.[31]

The increased detection of proximal and flat adenomas using CADe is also clinically significant as these adenomas are more frequently missed during SC. A meta-analysis including more than 15,000 colonoscopies showed high adenoma miss rates for proximal advanced adenomas (14%; 95% CI, 16-40) and flat adenomas (34%; 95% CI, 24-45).[5] Indeed, PCCRCs are 4 times more likely to be proximally located and 2 times more likely to be flat than prevalent colorectal cancers.[6] Thus, CADe may improve the overall protective effect of colonoscopy against colorectal cancer and reduce the incidence of PCCRCs.

Despite the clear benefits of CADe on adenoma detection per patient and per colonoscopy, using CADe did not increase the detection of advanced adenomas. This was a surprising finding as CADe led to an increased detection of large adenomas per colonoscopy, which constitute the majority of advanced adenomas. This discrepancy could be due to imprecision owing to the small number of events or variability in defining advanced adenomas between studies. Similarly, using CADe did not improve the detection of SSLs per colonoscopy. The SSL detection rates were low and highly variable between studies in both the

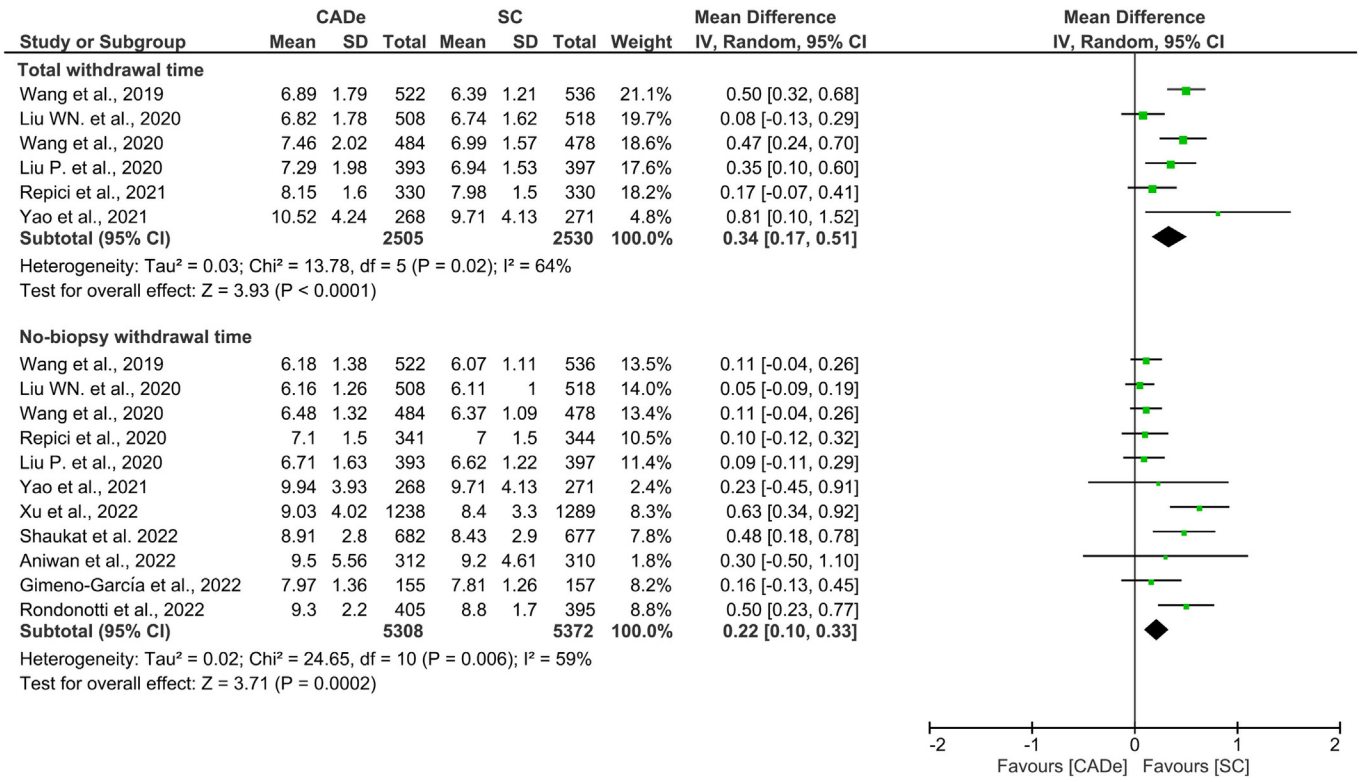

Figure 6. Forest plot for the colonoscopy withdrawal times in computer-aided detection (CADe) versus standard colonoscopy (SC) including and excluding biopsy time. *M-H*, Mantel-Haenszel; *CI*, confidence interval.

CADe and SC groups. The lack of added benefit with CADe on SSL detection is likely related to the relatively small number of SSLs in the training data sets of the included CADe systems and the interpathologist variation in reporting SSLs.[32] These findings underscore the challenges of detecting SSLs that are easily missed during colonoscopy and increasingly recognized as a cause of PCCRC.[33] Future RCTs should focus on advanced adenomas and SSL detection as primary end points to determine whether CADe could improve the detection of these lesions.

Withdrawal time is an important colonoscopy quality metric that is directly associated with ADR and the risk of interval colorectal cancer. Current guidelines recommend a minimum mean withdrawal time of 6 minutes,[34] which was met in all the included studies. The pooled mean colonoscopy withdrawal time in the CADe group was approximately 20 seconds longer than in the SC group. This mean difference, albeit statistically significant, is clinically insignificant, which precludes the notion that using AI in colonoscopy may negatively affect the efficacy of endoscopy service provision.

The current meta-analysis has several strengths. First, we conducted a comprehensive and systematic literature search with stringent inclusion and exclusion criteria based on the a priori registered protocol. We only included RCTs using a similar methodology to assess the effect of CADe on adenoma detection, thus providing more precise estimates of the true effect of CADe without the confounding synergetic effect of AI systems that influenced withdrawal time or other colonoscopy quality measures. Second, we performed rigorous subgroup and sensitivity analyses to explore the causes of heterogeneity and to assess the robustness of synthesized results. Third, the included RCTs evaluated the effect of CADe across different countries and populations and included endoscopists of various levels of experience, thus adding to the generalizability of our findings. Finally, we used validated methods to assess the risk of bias and the certainty of the evidence.

This study still had limitations. Because most of the studies did not report the intention-to-treat analysis, our analyses were based on the per-protocol analysis of the included studies. However, we do not expect this approach to have had a significant influence on the final outcomes. Another limitation is that the endoscopists were not blinded to the intervention in all but one study, which may have influenced the endoscopists' performance and introduced a risk of bias. Nonetheless, the results of the double-blind RCT by Wang et al[19] are consistent with our pooled results, indicating that the performance bias was trivial.

The adoption of any new technology is often hampered by unforeseen consequences. As such, with the great potential benefits of CADe comes novel risks. A recent retrospective study in Israel compared endoscopists' ADR in two 6-month periods before and after implementing CADe in

their colonoscopy practice.[35] Surprisingly, using CADe was associated with a significant reduction in ADR (30.3% vs 35.2%, $P < .001$). However, procedure time was significantly shorter in the CADe period, suggesting that endoscopists may have over-relied on CADe, which influenced their withdrawal time and overall colonoscopy quality. These real-world data offer important insights into endoscopists' attitude and behavior in response to AI and highlight the need for awareness of the limitations of CADe. Computer-aided quality improvement systems that monitor colonoscopy withdrawal time and colonoscopy quality have been shown to increase ADR when combined with CADe and may mitigate the risks of overreliance on CADe.[15,16] Moreover, CADe can only detect lesions present in the visual field of the endoscopists, which reduces the risk of missing lesions due to recognition failure but does not address the risk of missed lesions due to exposure failure. Hence, using a mucosal exposure device such as Endocuff (Olympus America, Center Valley, Penn, USA) with CADe provides a complementary effect leading to an additional increase in ADR than each intervention alone.[26]

In conclusion, our study shows that CADe significantly increases ADR and adenomas per colonoscopy compared with SC in various settings and populations, and regardless of the endoscopists' experience or the adenoma characteristics. Long-term longitudinal studies are required to evaluate the effect of CADe on the risk of interval colorectal cancer and cancer-related deaths.

ACKNOWLEDGMENTS

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DISCLOSURE

All authors disclosed no financial relationships.

Abbreviations: ADR, adenoma detection rate; AI, artificial intelligence; CADe, computer-aided detection; CI, confidence interval; MD, mean difference; PCCRC, post-colonoscopy colorectal cancer; PDR, polyp detection rate; RCT, randomized controlled trial; RR, relative risk; SC, standard colonoscopy; SSL, sessile serrated lesion.

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Current affiliation: Academic Unit of Gastroenterology, Sheffield Teaching Hospitals, and Department of Infection, Immunity & Cardiovascular Disease, University of Sheffield, Sheffield, UK.

Reprint requests: David S. Sanders, MD, Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield S10 2JF, United Kingdom. E-mail: david.sanders1@nhs.net.

SUPPLEMENTARY TABLE 1. Search strategy

MEDLINE	
1	exp intestinal neoplasms/ or exp cecal neoplasms/ or exp colorectal neoplasms/ or exp colonic neoplasms/ or exp rectal neoplasms/ 258292
2	adenoma/ or exp adenomatous polyps/ 60116
3	exp intestinal polyps/ or exp colonic polyps/ 16090
4	(colo* adenoma or colo* polyp* or colo* cancer).tw,kw. 171206
5	or/1-4 352375
6	exp artificial intelligence/ or exp machine learning/ or exp deep learning/ 160502
7	exp diagnosis, computer-assisted/ or exp image processing, computer-assisted/ 309675
8	(cade or cad* or computer aided detection or computer aided system or intelligent system or Artificial intelligent assist* or computer assist* or automatic detection or (automat* and detect*) or neural networks).tw,kw. 354467
9	or/6-8 750743
10	5 and 9 8752
11	randomized controlled trial.pt. 580856
12	controlled clinical trial.pt. 95102
13	randomized.ab. 573719
14	randomly.ab. 391428
15	trial.ab. 614350
16	or/11-15 1481517
17	exp animals/ not humans.sh. 5065587
18	16 not 17 1350754
19	10 and 18 **534**
Embase	
1	colorectal adenoma/ or adenoma/ or benign intestine tumor/ or colorectal tumor/ 68446
2	exp intestine polyp/ or polyp/ or colon polyp/ or colorectal polyp/ 56358
3	colorectal cancer/ or colon cancer/ or colorectal disease/ or rectum cancer/ 278078
4	(colo* adenoma or colo* polyp* or colo* cancer).tw,kw. 260052
5	or/1-4 431752
6	artificial intelligence/ or exp machine learning/ or exp deep learning/ 374538
7	diagnosis, computer-assisted/ or exp image processing, computer-assisted/ 152642
8	(cade or cad* or computer aided detection or computer aided system or intelligent system or Artificial intelligent assist* or computer assist* or automatic detection or (automat* and detect*) or neural networks).tw,kw. 479183
9	or/6-8 904853
10	5 and 9 12014
11	randomized controlled trial/ 739940
12	controlled clinical trial/ 467632
13	randomized.ab. 847821
14	randomised.ab. 167509
15	randomly.ab. 525232
16	trial.ab. 917655
17	groups.ab. 3405208
18	or/11-17 4901158
19	limit 10 to randomized controlled trial 276
20	10 and 18 1768
21	19 and 20 **276**

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Cochrane Central of Controlled Trials		
ID	Search	Hits
#	colorectal adenoma in Trials (Word variations have been searched)	1942
#2	colorectal polyp in Trials (Word variations have been searched)	2020
#3	intestinal polyps in Trials (Word variations have been searched)	829
#4	colonic polyps in Trials (Word variations have been searched)	2088
#5	#1 OR #2 OR #3 OR #4	3013
#6	artificial intelligence in Trials	1431
#7	computer aided detection in Trials	210
#8	cad in Trials	6013
#9	#6 OR #7 OR #8	7496
#10	#5 AND #9	**139**

SUPPLEMENTARY TABLE 2. Summary of findings table and grades of recommendation

Outcome	No. of participants (studies)	Anticipated absolute effects (95% confidence interval)		Certainty of the evidence
		Risk with standard colonoscopy	Risk with AI-assisted colonoscopy	
ADR	11,340 (12 RCTs)	330 per 1000	416 per 1000 (389 to 446)	⨁⨁⨁◯* Moderate
PDR	7391 (9 RCTs)	436 per 1000	575 per 1000 (519 to 641)	⨁⨁⨁◯* Moderate
Diminutive APC (≤5 mm)	8699 (9 RCTs)	239 per 1000	373 per 1000 (330 to 423)	⨁⨁⨁◯* Moderate
Proximal APC	9981 (11 RCTs)	276 per 1000	389 per 1000 (348 to 436)	⨁⨁⨁◯* Moderate
Nonpolypoid APC	4541 (6 RCTs)	176 per 1000	273 per 1000 (220 to 339)	⨁⨁⨁◯* Moderate
AAs per colonoscopy	9981 (11 RCTs)	69 per 1000	76 per 1000 (66 to 87)	⨁◯◯◯† Very low
SSLs per colonoscopy	10,718 (11 RCTs)	66 per 1000	75 per 1000 (56 to 103)	⨁◯◯◯† Very low

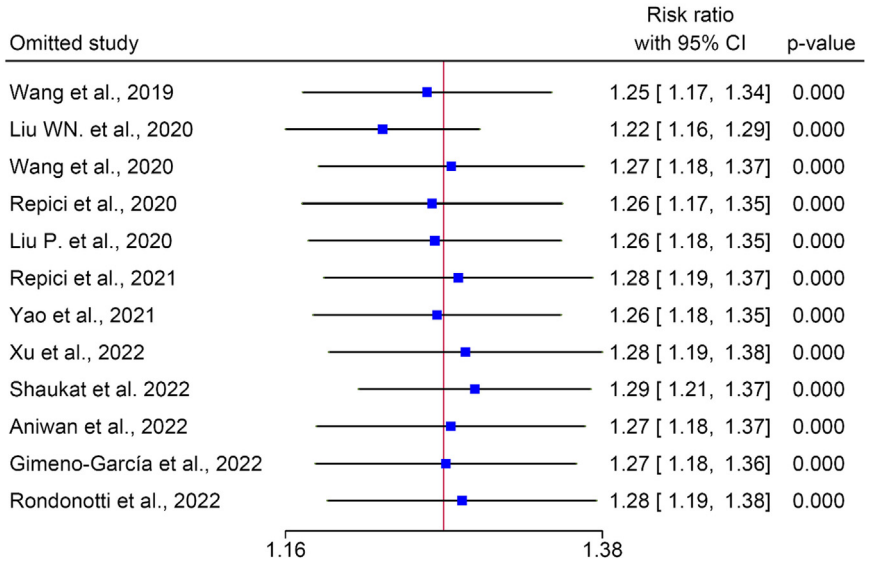
AI, Artificial intelligence; *ADR*, adenoma detection rate; RCTs, randomized controlled trials; *PDR*, polyp detection rate, *APC*, adenomas per colonoscopy; *AAs*; advanced adenomas; *SSLs*, sessile serrated adenomas.

*Downgraded due to serious risk of bias (lack of blinding of endoscopists); although the risk of publication bias could not be fully excluded for ADR, its influence was insufficient to downgrade the certainty of the evidence.

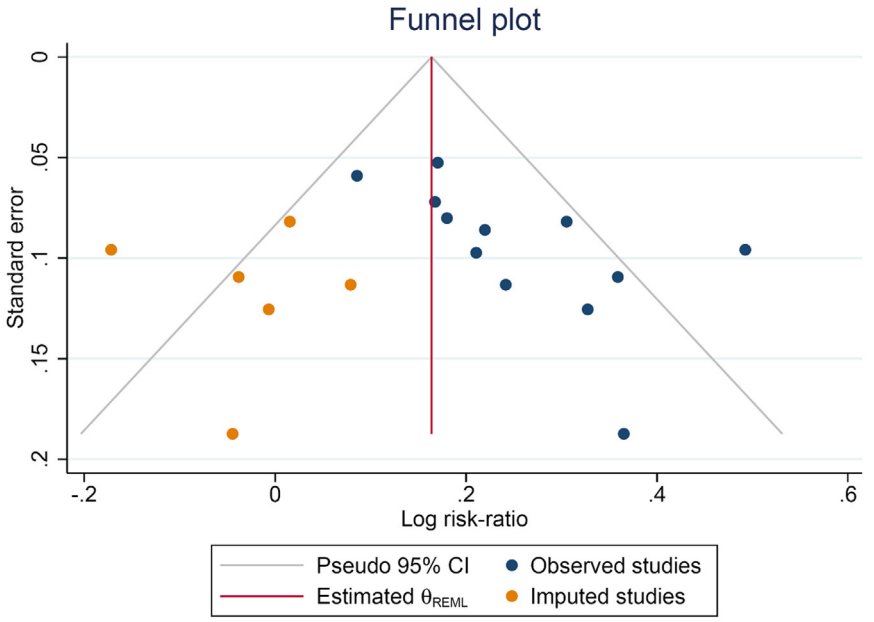
†Downgraded due to serious risk of bias (lack of blinding), inconsistency (differences in defining advanced adenomas and sessile serrated lesions between studies), and imprecision (small number of events and wide confidence intervals).

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2 – 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 5,28, S3-S5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 7
Section and Topic	**Item #**	**Checklist item**	**Location where item is reported**
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 7 - 8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 7 – 8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 7 – 8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 7 – 8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 7 – 8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 7 – 8
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 7 – 8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 7 - 8
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 9
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 9
Study characteristics	17	Cite each included study and present its characteristics.	Page 9, 25 - 27
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page S16
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 10 – 12, 29 – 33, S10 – S15
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 10 – 12, 29 – 33, S10 – S15
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 10
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 10
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 12
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 12, S9
Section and Topic	**Item #**	**Checklist item**	**Location where item is reported**
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 13 – 17
	23b	Discuss any limitations of the evidence included in the review.	Page 16
	23c	Discuss any limitations of the review processes used.	Page 16
	23d	Discuss implications of the results for practice, policy, and future research.	Page 13 - 17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 1
Competing interests	26	Declare any competing interests of review authors.	Page 1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 34

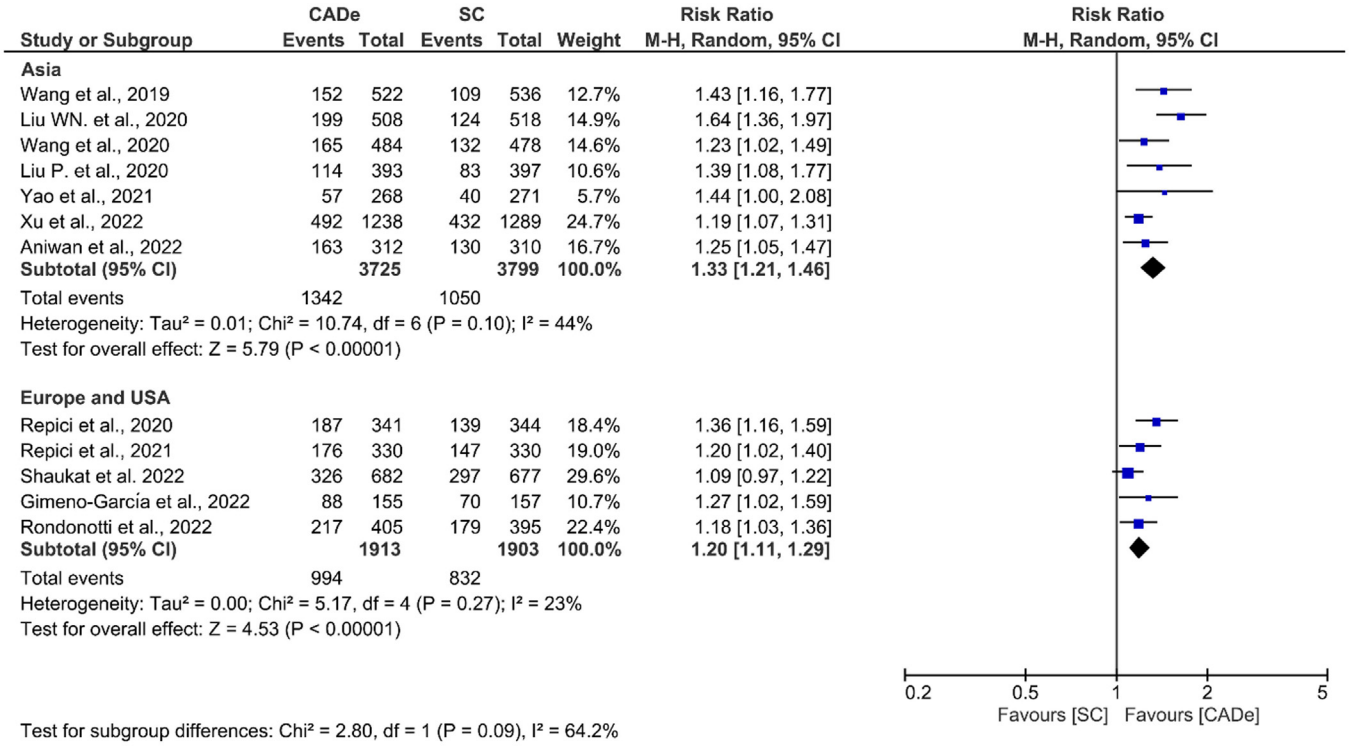
Supplementary Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) checklist.[36]



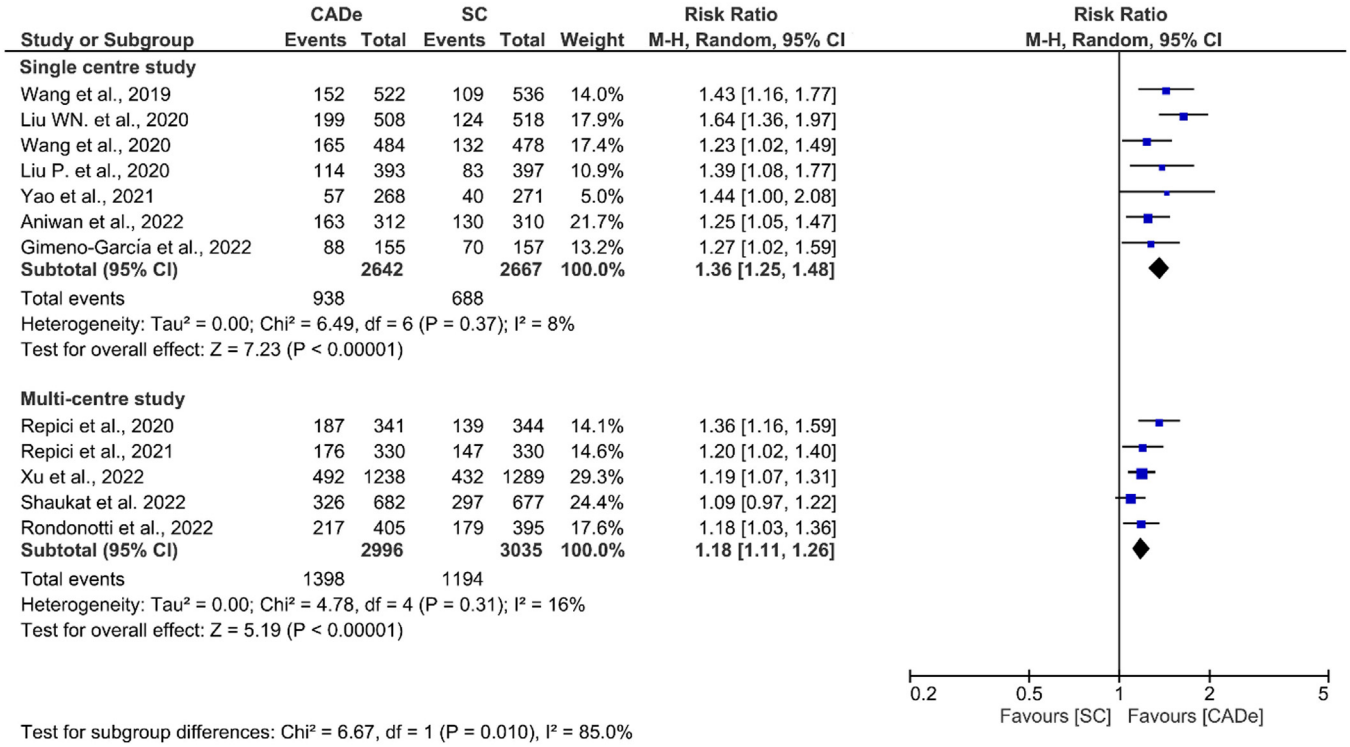
Supplementary Figure 2. Leave-one-out analysis for adenoma detection rate. *CI*, Confidence interval.



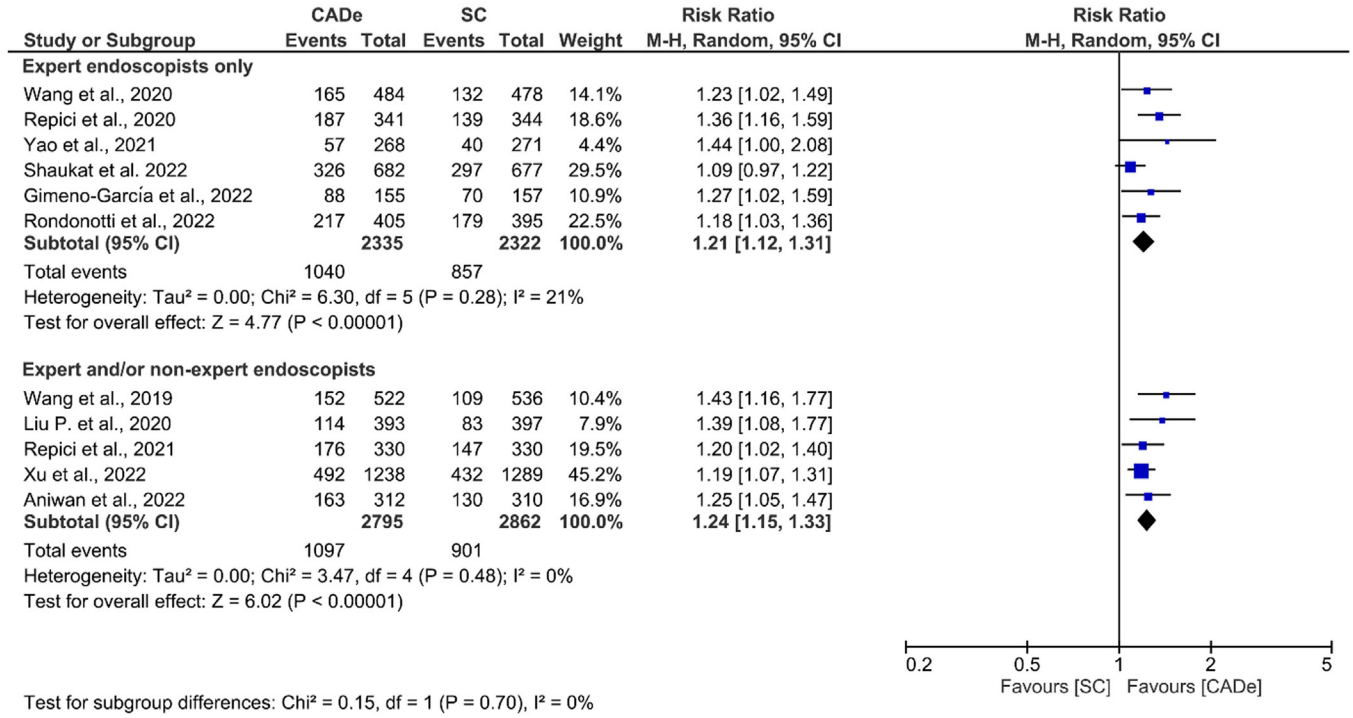
Supplementary Figure 3. Funnel plot for adenoma detection rate, including the observed studies and the imputed studies using trim and fill analysis. *CI*, Confidence interval.



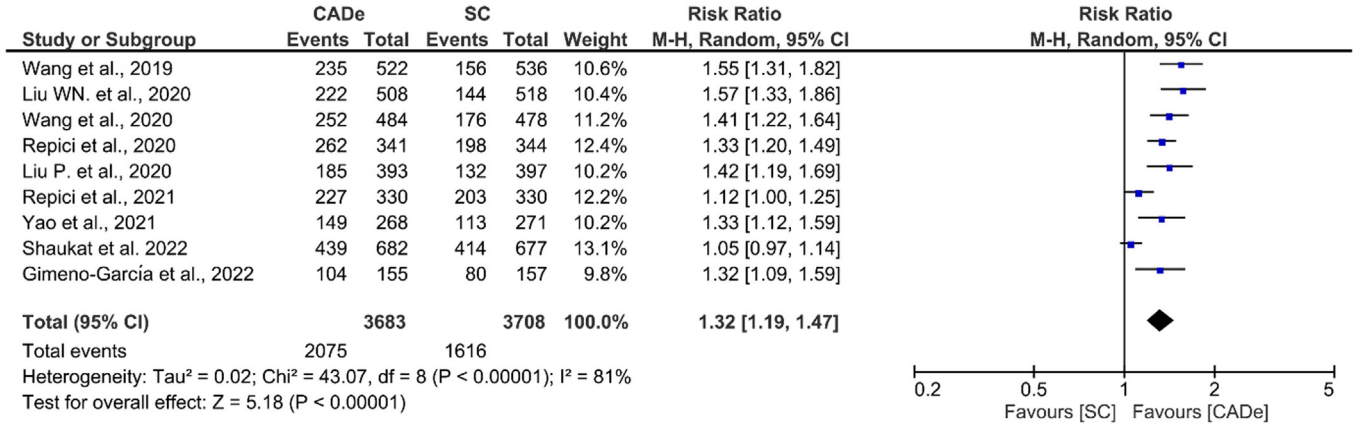
Supplementary Figure 4. Forest plot for the adenoma detection rate in computer-aided detection (CADe) versus standard colonoscopy (SC) according to study geographical location. *M-H*, Mantel-Haenszel; *CI*, confidence interval.



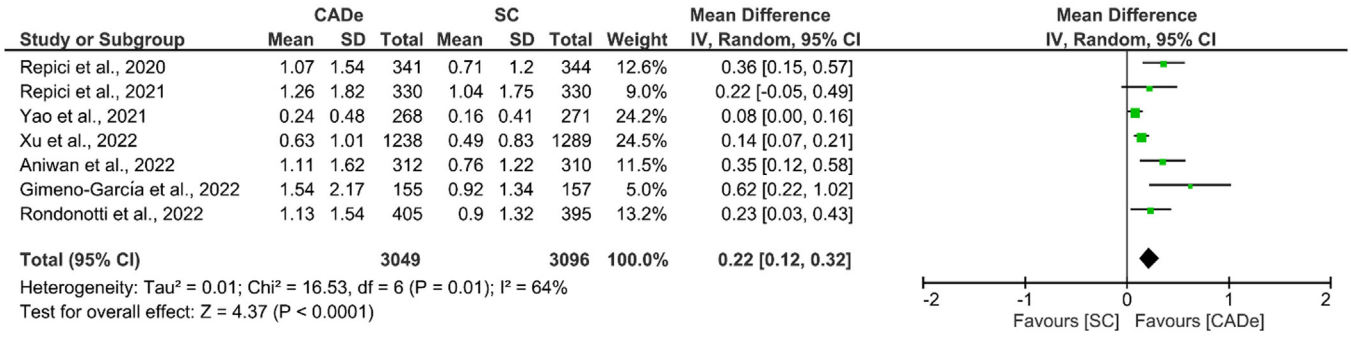
Supplementary Figure 5. Forest plot for the adenoma detection rate in computer-aided detection (CADe) versus standard colonoscopy (SC) according to the study setting. *M-H*, Mantel-Haenszel; *CI*, confidence interval.



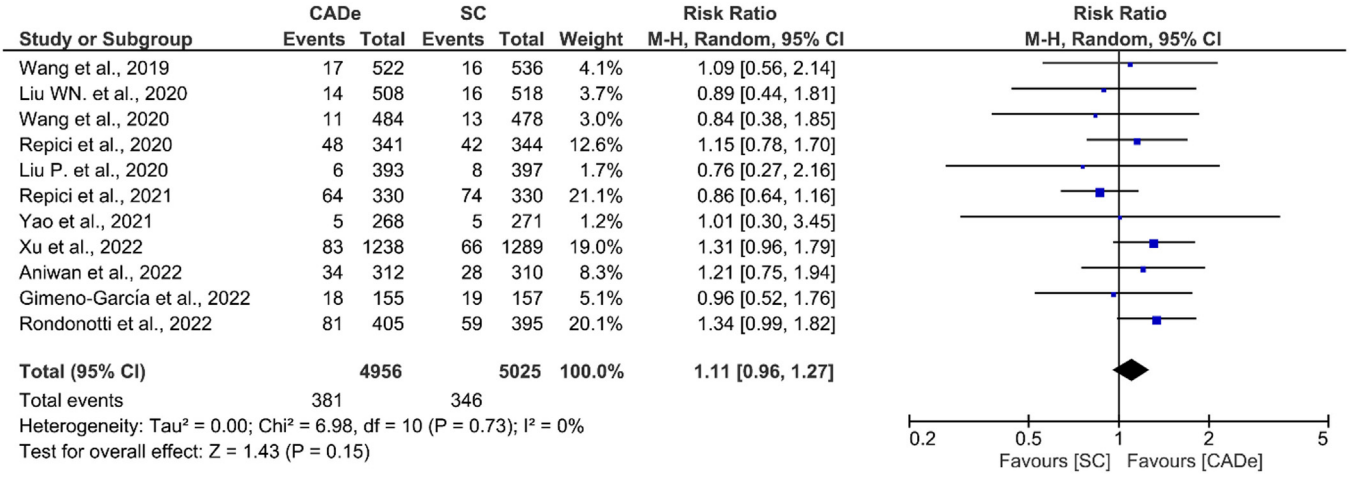
Supplementary Figure 6. Forest plot for the adenoma detection rate in computer-aided detection (CADe) versus standard colonoscopy (SC) according to the endoscopists' experience. *M-H*, Mantel-Haenszel; *CI*, confidence interval.



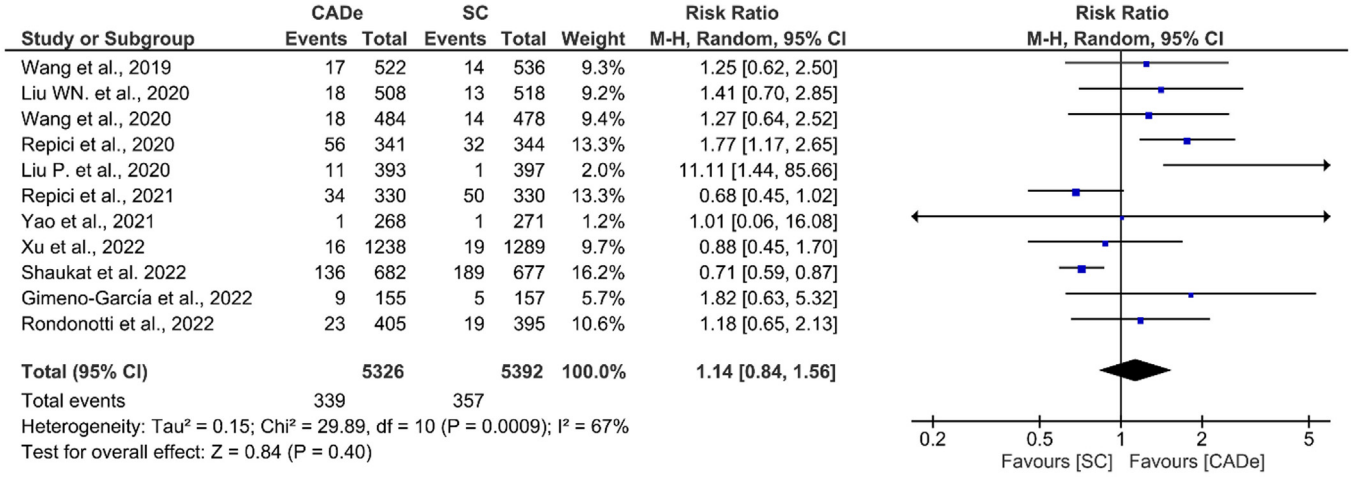
Supplementary Figure 7. Forest plot for the polyp detection rate in computer-aided detection (CADe) versus standard colonoscopy (SC). *M-H*, Mantel-Haenszel; *CI*, confidence interval.



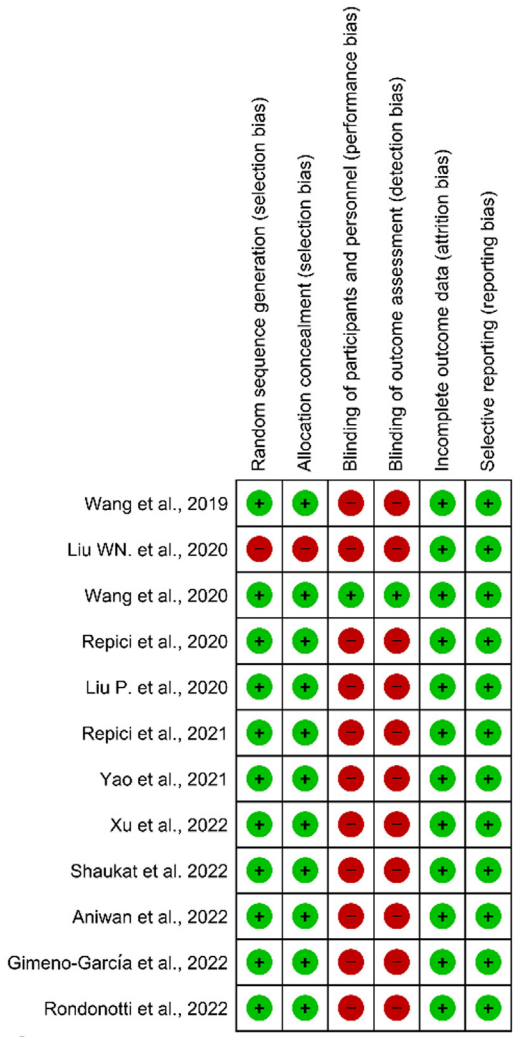
Supplementary Figure 8. Forest plot for mean adenoma per colonoscopy in computer-aided detection (CADe) versus standard colonoscopy (SC). *M-H*, Mantel-Haenszel; *CI*, confidence interval.

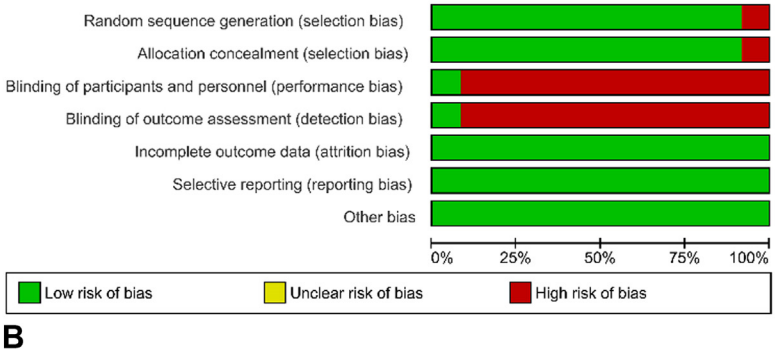


Supplementary Figure 9. Forest plot for advanced adenoma per colonoscopy in computer-aided detection (CADe) versus standard colonoscopy (SC). *M-H*, Mantel-Haenszel; *CI*, confidence interval.



Supplementary Figure 10. Forest plot for sessile serrated lesion per colonoscopy in computer-aided detection (CADe) versus standard colonoscopy (SC). *M-H*, Mantel-Haenszel; *CI*, confidence interval.





Supplementary Figure 11. Risk of bias assessment. **A,** Risk of bias summary for each included study. **B,** Risk of bias graph for each risk of bias domain presented as percentages across all included studies.