Artificial intelligence for colorectal neoplasia detection during colonoscopy: a systematic review and meta-analysis of randomized clinical trials

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Summary

Background The use of artificial intelligence (AI) in detecting colorectal neoplasia during colonoscopy holds the potential to enhance adenoma detection rates (ADRs) and reduce adenoma miss rates (AMRs). However, varied outcomes have been observed across studies. Thus, this study aimed to evaluate the potential advantages and disadvantages of employing AI-aided systems during colonoscopy.

Methods Using Medical Subject Headings (MeSH) terms and keywords, a comprehensive electronic literature search was performed of the Embase, Medline, and the Cochrane Library databases from the inception of each database until October 04, 2023, in order to identify randomized controlled trials (RCTs) comparing AI-assisted with standard colonoscopy for detecting colorectal neoplasia. Primary outcomes included AMR, ADR, and adenomas detected per colonoscopy (APC). Secondary outcomes comprised the poly missed detection rate (PMR), poly detection rate (PDR), and poly detected per colonoscopy (PPC). We utilized random-effects meta-analyses with Hartung-Knapp adjustment to consolidate results. The prediction interval (PI) and I^2 statistics were utilized to quantify between-study heterogeneity. Moreover, meta-regression and subgroup analyses were performed to investigate the potential sources of heterogeneity. This systematic review and meta-analysis is registered with PROSPERO (CRD42023428658).

Findings This study encompassed 33 trials involving 27,404 patients. Those undergoing AI-aided colonoscopy experienced a significant decrease in PMR (RR, 0.475; 95% CI, 0.294–0.768; I^2 = 87.49%) and AMR (RR, 0.495; 95% CI, 0.390–0.627; I^2 = 48.76%). Additionally, a significant increase in PDR (RR, 1.238; 95% CI, 1.158–1.323; I^2 = 81.67%) and ADR (RR, 1.242; 95% CI, 1.159–1.332; I^2 = 78.87%), along with a significant increase in the rates of PPC (IRR, 1.388; 95% CI, 1.270–1.517; I^2 = 91.99%) and APC (IRR, 1.390; 95% CI, 1.277–1.513; I^2 = 86.24%), was observed. This resulted in 0.271 more PPCs (95% CI, 0.144–0.259; I^2 = 65.61%) and 0.202 more APCs (95% CI, 0.144–0.259; I^2 = 68.15%).

Interpretation AI-aided colonoscopy significantly enhanced the detection of colorectal neoplasia detection, likely by reducing the miss rate. However, future studies should focus on evaluating the cost-effectiveness and long-term benefits of AI-aided colonoscopy in reducing cancer incidence.

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Keywords: Artificial intelligence; Computer-aided detection; Colonoscopy; Adenoma detection rate; Adenoma miss rate; Meta-analysis

Research in context

Evidence before this study

A comprehensive electronic literature search was performed in Embase, Medline, and the Cochrane Library using MeSH terms and keywords until October 04, 2023. Additionally, reference lists of relevant studies, guidelines, and reviews were manually searched, and forward citation tracking via Web of Science was utilized to identify additional relevant studies.

Added value of this study

The analysis of 33 studies involving 27,404 randomized patients revealed significant findings. Individuals undergoing AI-aided colonoscopy experienced a 50.5% and 52.5% relative decrease in AMR and PMR, respectively, Moreover, there was a relative increase of 24.2% and 23.8% in ADR and PDR and a 39% and 38.8% relative increase in the rate of APC and PPC. Additionally, this resulted in an increment of 0.202 more APCs and 0.271 more PPCs, with a mean inspection time increase of 20 s.

Implications of all the available evidence

Our study demonstrates that AI-aided colonoscopy significantly enhances the detection of patients with advanced adenomas, especially those with non-neoplastic lesions. Moreover, we observed a significant increase in the detection of diminutive and small adenomas, potentially influencing surveillance strategies and reducing the risk of interval Colorectal cancer. Our findings suggest that endoscopists with lower ADR (or PDR) and shorter inspection times, as well as patients with lower BMI and younger age, tend to benefit more from AI-aided colonoscopy. Furthermore, factors such as bowel preparation, anesthesia, and the time of day also exhibited some influence on the efficacy of AI-aid colonoscopy.

Introduction

Colorectal cancer (CRC) is the third most prevalent cancer globally, representing a significant cause of cancer-related deaths.[1,2] The pivotal approach to reducing CRC incidence and mortality involves the detection and removal of adenomatous polyps during colonoscopy.[3–6] Every 1% increase in the adenoma detection rate (ADR), the primary quality indicator of colonoscopy, correlated with a 3% decrease in the risk of interval CRC.[7,8] Nevertheless, wide variability exists in ADR Among different endoscopy services, with up to 27% of adenomatous polyps potentially being overlooked due to technical and cognitive limitations associated with the standard colonoscope.[9–11]

Several artificial intelligence (AI)-aided systems have been developed to standardize polyp detection among endoscopists and mitigate human error.[12–14] However, the impact of these AI tools on colonoscopy outcomes has been shown inconsistent across studies. Concerns include the potential negative effects on endoscopic training, endoscopist distraction, and the risk of polyp overdiagnosis,[15,16] which could lead to increased cost and patient burden without significant additional benefits.[16,17] Thus, more reliable evidence is essential for supporting the clinical application of AI-aided colonoscopy.

Recent meta-analyses have highlighted significantly improved detection rates using AI-aided systems.[18–31] However, certain limitations undercut the strength of their conclusions. Many meta-analyses encompassed only a few small RCTs,[18–21,24,25,27,29,30] and some studies even incorporated non-RCTs,[22,23,26,28,30] leading to underpowered and unreliable pooled estimates. Moreover, the pooled outcomes reported in previous studies exhibit substantial and unexplained heterogeneity.[18–31] Notably, while meta-analysis aims to provide pooled estimates, understanding variance amidst considerable heterogeneity is equally critical, with the summary effect becoming less significant.[32] Furthermore, most published studies disregarded other important colonoscopy quality indicators, such as the adenoma miss rate (AMR),[18–21,23–25,27–30] which better reflects the clinical utility of this emerging technology.[9,33]

To address the limitations of previous studies and extend our knowledge of AI-aided colonoscopy on colorectal neoplasia, we conducted a comprehensive systematic review and meta-analysis of randomized controlled trials (RCTs) to evaluate the potential advantages and disadvantages of AI-aided systems during colonoscopy compared to standard colonoscopy. This comprehensive meta-analysis aims to increase statistical power, reduce bias, explore potential heterogeneity sources, and facilitate exploratory analyses to formulate hypotheses for future research.[34]

Method

Registration

This systematic review and meta-analysis is registered with PROSPERO (CRD42023428658) and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Assessing the Methodological Quality of Systematic Reviews (AMSTAR) guidelines.[35,36] This study was independently conducted by two authors (SHL and FQD), with any disagreements resolved through

consensus. In cases of unresolved disagreements, a third reviewer (WJS) was consulted.

Search strategy

Using Medical Subject Headings (MeSH) terms and keywords, a comprehensive electronic literature search was performed in Embase, Medline, and the Cochrane Library until October 04, 2023. The detailed search strategy is provided in File S1. Additionally, reference lists of relevant studies, guidelines, and reviews were manually searched, and forward citation tracking using the Web of Science database was conducted to identify additional pertinent studies.

Eligibility criteria

To be included in this study, trials had to meet the following inclusion criteria: (1) Enrollment of patients undergoing colonoscopy for primary screening, surveillance, or symptoms; (2) Comparison of real-time AI-aided colonoscopy with conventional colonoscopy; (3) Reporting of outcomes of interest; (4) Conducted as RCTs.

Excluded studies were those that: (1) Presented no original data; (2) Had no full text available; and (3) Were conducted in patients with inflammatory bowel disease or hereditary polyposis syndromes. No restrictions were imposed on language, publication date, study location, or sample size.

Study selection

All citations identified during the literature search were imported into reference management software, with automatic removal of duplicates. Titles and abstracts were initially screened for relevance, and full-text articles were reviewed for final inclusion. In cases where multiple reports existed for a single study, the most recent publication was used, supplemented with the complete version if necessary.

Outcomes of interest

Primary outcomes included AMR, ADR, and adenomas detected per colonoscopy (APC). A separate analysis for the primary outcomes stratified by pathology, morphology, size, and location was performed when data were available. Secondary outcomes consisted of the poly missed rate (PMR), poly detection rate (PDR), poly detected per colonoscopy (PPC), procedure time, adverse events, and false alarms. A detailed definition of the terms can be found in Table S1.

Data extraction

Data were extracted using standardized forms, encompassing study characteristics, patient characteristics, intervention characteristics, characteristics of detected adenomas and polyps, and outcomes of interest. Data about only the first colonoscopy for tandem trials were extracted to avoid a carryover effect. Data were obtained through direct extraction or indirect calculation.[37] In cases of missing data, corresponding authors were contacted via e-mail.

Statistics

The Cochrane tool was used to assess the risk of bias,[38] while publication bias was evaluated using Egger's weighted regression test.[39] If publication bias was detected, the trim-and-fill method was used to estimate its potential impact on the overall effect sizes.[40] The quality of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[41]

For dichotomous outcomes, we calculated risk ratios (RRs) or incidence rate ratios (IRRs), and for continuous outcomes, we computed mean differences, along with 95% confidence intervals (CIs). Given the anticipated considerable between-study heterogeneity, we utilized a random-effects model.[42] The Sidik–Jonkman estimator with Hartaung-Knapp (HK) adjustments was employed to pool effect sizes.[43,44]

Between-study heterogeneity was assessed using Cochran's Q test, I^2 statistics, and prediction intervals.[45–48] Meta-regression and subgroup analyses were performed to investigate potential sources of heterogeneity. The meta-regression analysis employed a random-effects model using the random effect maximum likelihood (REML) method with HK adjustment.[49] Furthermore, subgroup interactions were tested with the chi-square test.

Sensitivity analyses were performed initially using the leave-one-out approach to assess the influence of individual trials on the overall effect estimate. Additionally, sensitivity analyses were performed to examine the robustness of findings by restricting analyses to (1) trials with data obtained by direct extraction or (2) trials with a low risk of bias.

Statistical analyses were conducted using Stata (version 17) and Comprehensive Meta-Analysis software (version 3.3.070). A two-tailed *P-value* of 0.05 was considered as the threshold for statistical significance.

Role of the funding source

This work was supported by the Heilongjiang Provincial Natural Science Foundation of China (LH2023H096), the Postdoctoral research project in Heilongjiang Province (LBH-Z22210), the National Natural Science Foundation of China's General Program (82072640), and the Outstanding Youth Project of Heilongjiang Natural Science Foundation (YQ2021H023).

The funders of this study played no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Result

Study selection

An initial search identified 1959 potential studies from the electronic databases, along with three additional

studies via hand-searching reference lists. After eliminating duplicates, 1612 studies underwent title and abstract screening. Subsequently, 66 articles were selected for full-text review, from which 33 full-text articles were further excluded due to being study protocols, conference abstracts, or not RCTs. Finally, 33 unique RCTs were included in this meta-analysis.[50–82] The study screening and selection process is depicted in Fig. 1.

Study characteristics

Of the 27,404 individuals across the 33 included trials (sample size range: 96–3213), 13,580 patients underwent AI-aided colonoscopy, while 13,824 underwent standard colonoscopy. All studies were published between 2019 and 2023. Among these, 8 studies were designed as tandem studies, 18 were single-center experiences, and 14 were conducted in Western settings. Most studies utilized AI algorithms designed for colorectal lesion identification. Notably, two studies focused on assessing the colonoscopy quality by monitoring the withdrawal time and scope speed, while two others used the algorithm for both lesion detection and quality assurance. Study characteristics are summarized in Table 1 and Table S2, and the geographical distribution of the 33 trials is depicted in Fig. 2.

Risk of bias assessment

The revised Cochrane risk of bias (RoB 2) tool was employed to assess the risk of bias for the included studies. As shown in Fig. 3, seven out of the 33 trials exhibited at least one criterion for potential bias concerns, with issues primarily observed in the randomization process (n = 4), measurement of outcomes (n = 1), and selection of reported results (n = 5).

PMR, PDR, and PPC

An AI-aided colonoscopy showed a 52.5% decrease (19% risk difference) in the PMR (RR, 0.475; 95% CI, 0.294–0.768; Figure S1), a 23.8% increase (9.9% risk difference) in the PDR (RR, 1.238; 95% CI, 1.158–1.323;

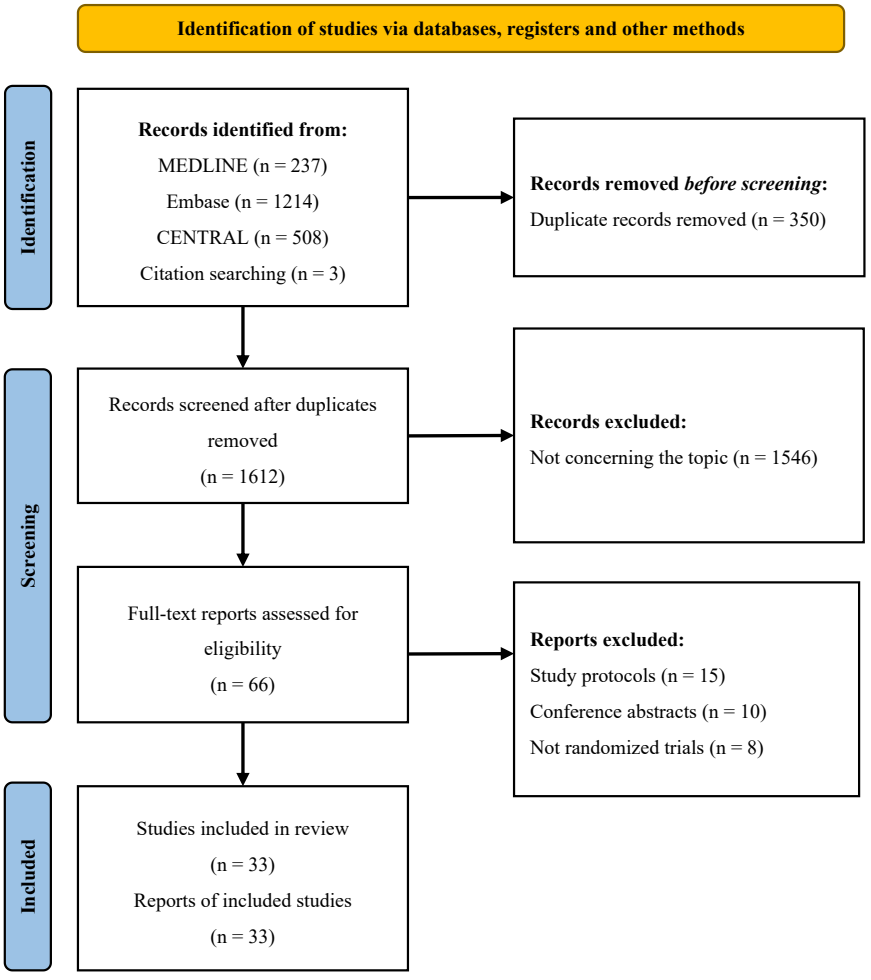

Fig. 1: PRISMA flowchart of study.

Study, year	Study design	No. of center	Study region	AI system		Indication (%)				Sample size			Sex (Male, %)		Age (mean, years)		
				Name	Function	Screening	Surveillance	Symptomatic	FIT positive	AI	Control	Total	Male	%	AI	Control	Total
Ahmad 2023	Parallel	1	Western	GI-Genius	CADe				100.00%	308	306	614	208	33.88%	66.2	66.4	66.30
Aniwan 2023	Parallel	1	Asia	CAD-EYE	CADe	88.75%			11.25%	312	310	622	266	42.77%	62.8	62	62.40
Engelke 2023	Parallel	1	Western	GI-Genius	CADe	3.88%	7.76%	88.36%		122	110	232	113	48.71%	63.54	65.24	64.35
Gimeno-García 2023	Parallel	1	Western	ENDO-AID	CADe	6.09%	32.37%	27.88%	33.65%	155	157	312	165	52.88%	62.99	64.71	63.86
Glissen 2022	Tandem	4	Western	EndoScreener	CADe	59.64%	40.36%			113	110	223	122	54.71%	61.18	60.51	60.85
Gong 2020	Parallel	1	Asia	ENDOANGEL	CAQ	17.47%	5.11%	77.42%		355	349	704	345	49.01%	48.25	47.25	47.75
Hüneburg 2023	Parallel	1	Western	CAD-EYE	CADe					50	46	96	41	42.71%	50.3	46.3	48.38
Kamba 2021	Tandem	4	Asia	Locally system	CADe	46.76%	35.77%		17.47%	178	177	355	272	76.62%	61.63	61.44	61.54
Karsenti 2023	Parallel	1	Western	GI-Genius	CADe	14.94%	43.47%	26.10%	7.10%	1003	1012	2015	979	48.59%	58.4	58.4	58.40
Liu PX 2020	Parallel	1	Asia	EndoScreener	CADe	23.04%		76.96%		393	397	790	374	47.34%	49.84	48.79	49.31
Liu WN 2020	Parallel	1	Asia	Locally system	CADe	6.43%		93.57%		508	518	1026	551	53.70%	51.02	50.13	50.57
Lui 2023	Tandem	3	Asia	Locally system	CADe	54.17%		45.83%		108	108	216	104	48.15%	62	61.4	61.70
Mangas-Sanjuan 2023	Parallel	6	Western	GI-Genius	CADe				100.00%	1610	1603	3213	1717	53.44%	60.7	60.6	60.65
Nakashima 2023	Tandem	1	Asia	CAD-EYE	CADe	7.71%	38.07%		54.22%	207	208	415	298	71.81%	54.9	55.9	55.40
Repici 2020	Parallel	3	Western	GI-Genius	CADe	22.34%	23.94%	23.50%	30.22%	341	344	685	337	49.20%	61.5	61.1	61.30
Repici 2022	Parallel	5	Western	GI-Genius	CADe	29.09%	37.12%	26.52%	7.27%	330	330	660	330	50.00%	61.9	62.6	62.25
Rondonotti 2022	Parallel	5	Western	CAD-EYE	CADe				100.00%	405	395	800	409	51.13%	62	61	61.51
Shaukat 2022	Parallel	5	Western	Locally system	CADe	65.78%	34.22%			682	677	1359	723	53.20%	60.6	59.9	60.25
Shen 2021	Parallel	1	Asia	Locally system	CADe					64	64	128	62	48.44%	58.6	59	58.80
Su 2020	Parallel	1	Asia	Locally system	CADe and CAQ	34.67%		65.33%		308	315	623	307	49.28%	50.54	51.63	51.09
Vilkoite 2023	Parallel	1	Western	ENDO-AID	CADe					194	206	400	193	48.25%	50.1	51.2	50.67
Wallace 2022	Tandem	8	Western	GI-Genius	CADe	35.65%	64.35%			116	114	230	157	68.26%	63	64.6	63.79
Wang 2019	Parallel	1	Asia	EndoScreener	CADe	7.94%		92.06%		522	536	1058	512	48.39%	51.07	49.94	50.50
Wang 2020-a	Tandem	1	Asia	EndoScreener	CADe	30.63%	8.67%	60.70%		184	185	369	179	48.51%	47.72	47.19	47.45
Wang 2020-b	Parallel	1	Asia	EndoScreener	CADe	16.42%		83.58%		484	478	962	495	51.46%	49.35	48.40	48.88
Wang 2022	Parallel	1	Asia	Locally system	CADe					200	200	400	191	47.75%	49.29	47.21	48.25
Wang 2023	Parallel	4	Asia	EndoScreener	CADe	16.97%	5.55%	77.48%		636	625	1261	690	54.72%	45.56	46.3	45.93
Wei 2023	Parallel	4	Western	EndoVigilant	CADe	71.78%	28.22%			387	382	769	392	50.98%	58	57.6	57.80
Xu 2021	Parallel	6	Asia	Locally system	CADe	8.55%		91.45%		1177	1175	2352	1198	50.94%	50.9	51.7	51.30
Xu 2023	Parallel	6	Asia	Eagle-Eye	CADe	95.85%			4.15%	1519	1540	3059	1435	46.91%	57.49	57.03	57.26
Yamaguchi 2023	Tandem	3	Asia	CAD-EYE	CADe	20.78%	12.12%	9.96%	50.65%	113	118	231	124	53.68%	63.1	63.3	63.20
Yao 2022	Parallel	1	Asia	ENDOANGEL	CAQ	88.89%	10.00%	1.10%		269	271	540	241	44.63%	49.91	50.85	50.38
Yao 2023	Tandem	3	Asia	ENDOANGEL	CADe and CAQ	63.80%	8.18%	28.02%		227	458	685	357	52.12%	50.63	49.86	50.12

AI, artificial intelligence; FIT, fecal immunochemical test; CADe, computer assisted detection; CAQ, computer assisted quality.

Table 1: **Characteristics of included studies.**

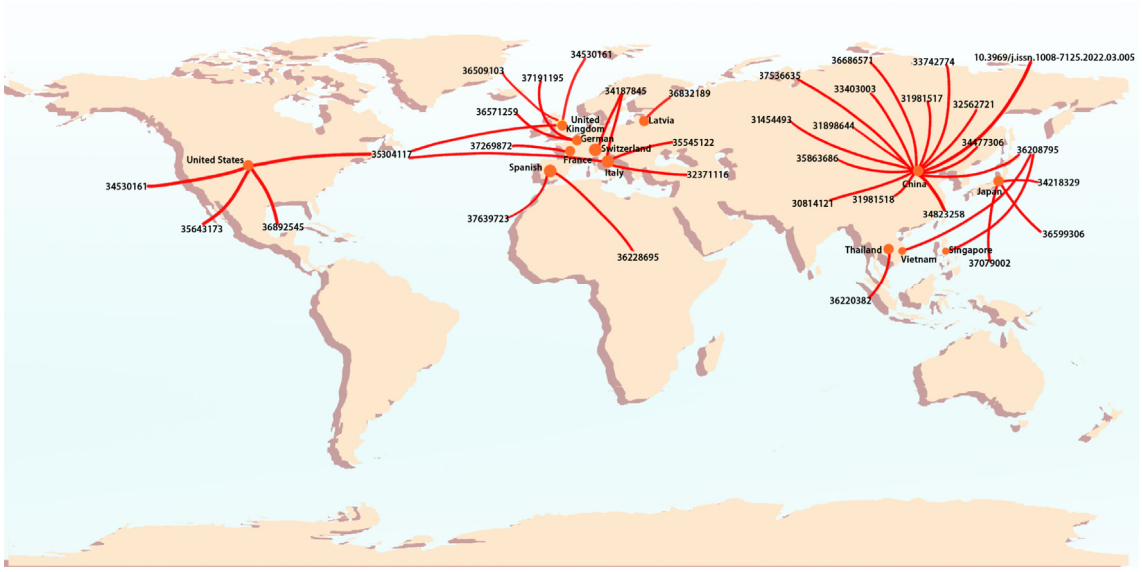

Fig. 2: Geographical distribution of the 33 trials. Note: the number or words in map means the PMID or DOI of every trial.

Figure S2), a 38.8% increase (37.1% rate difference) in PPC rate (IRR, 1.388; 95% CI, 1.270–1.517; Figure S3), and 0.271 more number of PPC (95% CI, 0.144–0.398; Figure S4) compared to standard colonoscopy (Table 2).

Substantial heterogeneity was observed for most polyp-related outcomes. The 95% prediction intervals crossed the no-effect line for PMR (0.135–1.679), PDR (0.922–1.662) and PPC rate (0.892–2.160), indicating the potential for negative intervention effects in future studies. Additionally, potential publication bias was identified for PDR (Figure S5). However, correcting for the possibility of publication bias would not change the conclusion.

AMR, ADR, and APC

Individuals who intervened with the AI-aided systems experience a 50.5% decrease (17.5% risk difference) in AMR (RR, 0.495; 95% CI, 0.390–0.627; Figure S6), a 24.2% increase (7.4% risk difference) in ADR (RR, 1.242; 95% CI, 1.159–1.332; Figure S7), a 39% increase (19.9% rate difference) in APC rate (IRR, 1.390; 95% CI, 1.277–1.513; Figure S8), and 0.202 more number of APC (95% CI, 0.144–0.259; Figure S9) compared to standard colonoscopy (Table 2).

Substantial heterogeneity was observed for ADR and APC. Moreover, the 95% prediction intervals crossed the no-effect line for ADR (RR, 0.886–1.742) and APC (IRR, 0.909–2.126), indicating that AI-aided colonoscopy may not benefit adenoma detection in certain populations. Publication bias was identified for ADR (Figure S10) and APC (Figure S11 for rate ratio and Figure S12 for mean difference), yet it did not affect the overall conclusions.

Separate analysis for AMR, ADR, and APC

As shown in Table 3, the advanced AMR and sessile serrated lesion (SSL) miss rate in the AI-aided group was not statistically significant compared to the control group. Based on available data, there were no statistically significant interactions between AMR and pathology types.

For the detection rate of adenomas per patient, we found that AI-aided colonoscopy could identify more patients with advanced adenomas, polypoid and non-polypoid adenomas, diminutive (0–5 mm) and small adenomas (6–10 mm), proximal and distal adenomas. However, interaction analyses for subgroup differences determined that the performance of AI-aided colonoscopy in significantly improving ADR was confirmed irrespectively from adenoma pathology, morphology, size, and location.

For the number of APC, while more polypoid adenomas were detected via AI-aided colonoscopy, no significant interactions were found between APC and morphology. Tests for subgroup differences determined that the number of APC detected in the AI-aided colonoscopy group was significantly higher for small adenomas (<10 mm) and adenomas at the proximal colon.

Furthermore, for the rate of APC, no significant difference was observed between the AI-aided and control groups regarding the rate ratios of advanced adenomas, SSLs, colorectal cancers, and large adenomas (>10 mm). Of note, although AI-aided colonoscopy did not identify more patients with non-neoplastic lesions (RR, 1.163; 95% CI, 0.976–1.386), it showed a greater rate of non-neoplastic lesions per colonoscopy (IRR, 1.632; 95% CI, 1.389–1.916).

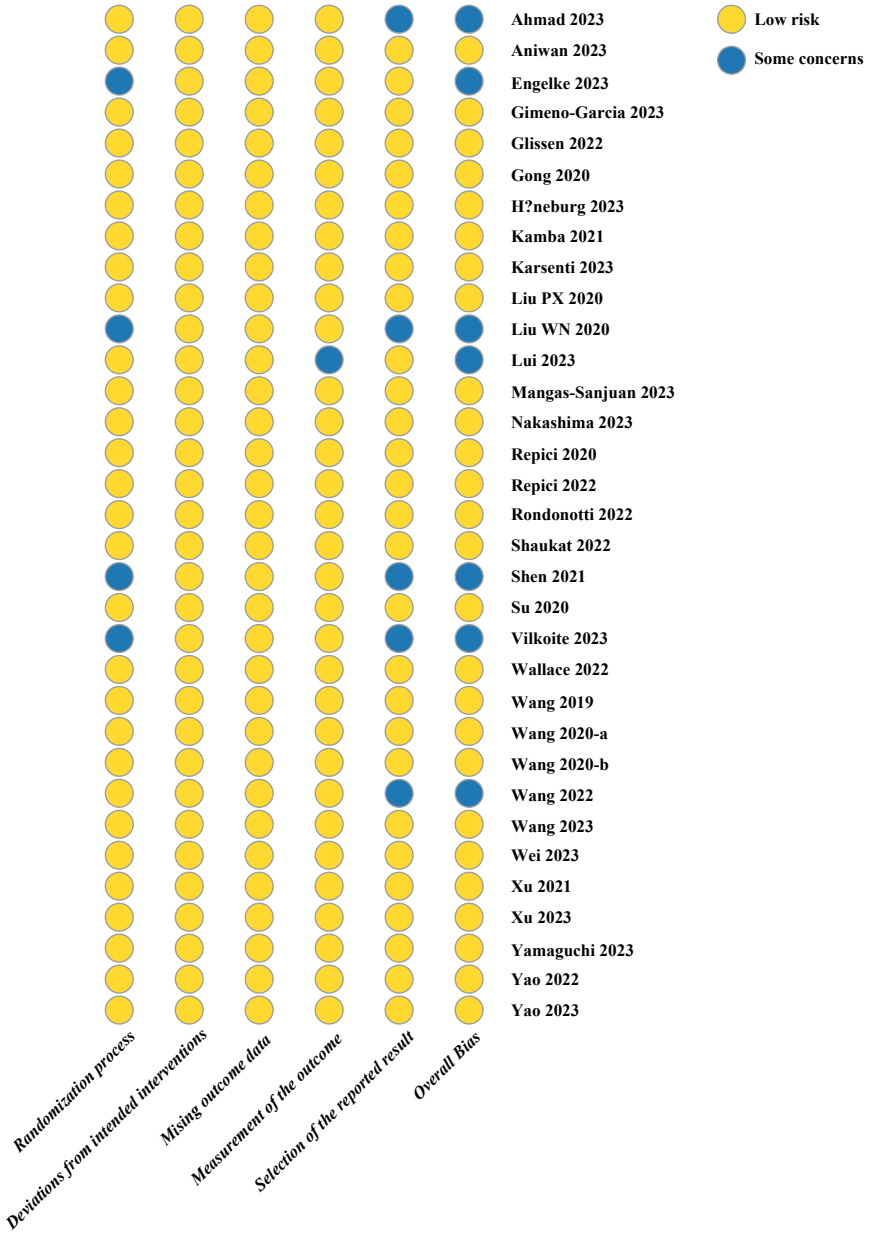

Fig. 3: Risk of bias graph.

Procedure time, adverse events, and false alarms

As shown in Table 2, no statistically significant differences were observed between the AI-aided and standard colonoscopy groups for the insertion time (WMD, –0.090 min; 95% CI, –0.234 to 0.053 min; Figure S13). However, the inspection time was 20 s longer with AI-aided colonoscopy (WMD, 0.330 min; 95% CI, 0.087–0.573 min; Figure S14) than with standard colonoscopy.

In 17 out of the 20 included studies that reported data on adverse events, no adverse events occurred. There was no statistically significant difference in adverse event risk between the two groups (RR, 0.837; 95% CI, 0.629–1.114; Figure S15).

In eight trials, the reported number of false negatives was zero. However, these eight trials also reported false positives, ranging between 7.1% and 20.1%, and the pooled proportion of false positives on AI-aided colonoscopy was 12.2% (95% CI, 7.5%–16.9%; Figure S16).

Significant heterogeneity was observed for the inspection time, and the wide 95% prediction interval indicated that AI-aided colonoscopy might reduce

	Studies	Effect size and 95% CI				Heterogeneity				Publication bias				
		Effect size	95% CI		*P-value*	I^2	95% PI		*P-value*	Egger test	Missed study	Adjusted values		
Adenoma outcomes														
Adenoma miss rate (RR)	7	0.495	0.390	0.627	***0.00030***	48.76%	0.286	0.857	*0.080*	*0.65*	NA			
Adenoma detection rate (RR)	29	1.242	1.159	1.332	***<0.0001***	78.87%	0.886	1.742	***<0.0001***	***0.00080***	9	1.144	1.048	1.249
Adenoma per colonoscopy (IRR)	29	1.390	1.277	1.513	***<0.0001***	86.24%	0.909	2.126	***<0.0001***	***0.00040***	5	1.311	1.184	1.451
Adenoma per colonoscopy (WMD)	19	0.202	0.144	0.259	***<0.0001***	68.15%	−0.017	0.420	*0.089*	***0.017***	6	0.155	0.075	0.235
Polyp outcomes														
Polyp miss rate (RR)	5	0.475	0.294	0.768	***0.013***	87.49%	0.135	1.679	***<0.0001***	*0.57*	NA			
Polyp detection rate (RR)	24	1.238	1.158	1.323	***<0.0001***	81.67%	0.922	1.662	***<0.0001***	***0.0026***	7	1.155	1.071	1.245
Poly per colonoscopy (IRR)	27	1.388	1.270	1.517	***<0.0001***	91.99%	0.892	2.160	***<0.0001***	*0.073*	NA			
Poly per colonoscopy (WMD)	10	0.271	0.144	0.398	***0.00090***	65.61%	−0.107	0.649	*0.14*	*0.96*	NA			
Procedure time														
Insertion time (WMD)	13	−0.090	−0.234	0.053	*0.20*	29.82%	−0.502	0.321	*0.70*	*0.94*	NA			
Inspection time (WMD)	18	0.330	0.087	0.573	***0.012***	93.15%	−0.647	1.307	***<0.0001***	*0.68*	NA			
Adverse event														
Adverse event rate (RR)	20	0.837	0.629	1.114	*0.21*	0.94%	0.536	1.305	*1.0*	*0.46*	NA			

CI, confidence interval; PI, prediction interval; RR, risk ratio; IRR, incidence rate ratios; WMD, weighted mean difference; NA, not applicable.

Table 2: **Summary of results.**

inspection time by 39 s (95% prediction interval, −0.647 to 1.307 min) in some populations. Notably, no publication bias was detected.

Meta-regression analyses

Given the substantial heterogeneity in adenoma- and polyp-relevant outcomes, REML univariate meta-regression analyses with HK adjustment were performed to explore the sources of heterogeneity. As shown in Table S3, four aspects were explored as sources of heterogeneity. As for study characteristics, more involved centers were significantly associated with reduced differences in ADR, APC, PDR, and PPC.

Regarding patient characteristics, increased age was significantly associated with decreased differences in ADR, APC, PDR, and PPC. A higher proportion of symptomatic patients was significantly associated with increased differences in APC, PDR, and PPC. A higher proportion of fecal immunochemical test-positive patients were significantly associated with a reduced ADR difference. Moreover, a better bowel preparation, assessed by the Boston bowel preparation score, was significantly associated with increased inspection times and reduced ADR, PDR, and PPC differences. Additionally, a higher proportion of patients with adequate cleaning (Boston bowel preparation score >6) was significantly associated with reduced APC and PDR differences.

In terms of intervention characteristics, a higher proportion of patients who received anesthesia were significantly associated with an increased difference in PPC. Moreover, a higher proportion of patients who underwent colonoscopy in the morning were significantly associated with an increased difference in ADR, APC, and PPC. A longer inspection time was also significantly associated with a decreased difference in ADR, APC, PDR, and PPC.

As for endoscopist experience, a higher baseline ADR for standard colonoscopy was significantly associated with a reduced difference in ADR, APC, PDR, PPC, and inspection time. Similarly, a higher baseline PDR for routine colonoscopy was significantly associated with decreased ADR, APC, PDR, and PPC differences.

Subgroup analyses

Consistent with the meta-regression analyses, subgroup analyses also supported similar findings. Results from single-center studies showed more favorable outcomes compared to multiple-center studies. Additionally, endoscopists with low ADR (ADR <25%) appeared better than those reported with high ADR (ADR <25%). Moreover, bowel preparation and inspection time may also play a significant influencing role on the effect of AI-aided colonoscopy for polyp-relevant outcomes (Table S4).

Of note, subgroup analyses further determined that results obtained from China seem better than those reported in other countries; patients younger than screening (age <50 years) may benefit more from the AI-aided colonoscopy; overweight individuals (BMI >25) seem to benefit less from AI-aided colonoscopy.

Sensitivity analyses

The sensitivity analyses, detailed in Table S5, validated the consistency of the main findings. First, our results remained unchanged in leave-one-out analyses. Second, all conclusions were robust when only considering trials with data obtained by direct extraction. Third, results

	Studies	Effect size and 95% CI				Heterogeneity				Test for subgroup difference
		Effect size	95% CI		*P-value*	I^2	95% PI		*P-value*	
Adenoma miss rate (RR)										
Pathology										
Advanced adenoma miss rate (RR)	4	0.702	0.127	3.876	*0.56*	32.28%	0.015	33.429	*0.32*	*0.59*
Sessile serrated lesion miss rate (RR)	4	0.456	0.111	1.876	*0.18*	37.70%	0.018	11.426	*0.23*	
Adenoma detection rate (RR)										
Pathology										
Advanced adenoma	13	1.132	1.016	1.261	***0.028***	38.33%	0.804	1.593	*0.59*	*0.64*
Sessile serrated lesion	12	1.001	0.849	1.180	*0.99*	31.66%	0.624	1.605	*0.67*	
Non-neoplastic lesion	7	1.163	0.976	1.386	*0.079*	50.71%	0.764	1.771	*0.13*	
Colorectal cancer	8	1.441	0.702	2.955	*0.27*	62.30%	0.203	10.237	*0.40*	
Morphology										
Polypoid	6	1.230	1.050	1.441	***0.020***	63.37%	0.768	1.969	*0.46*	*0.27*
Non-polypoid	8	1.419	1.204	1.671	***0.0015***	57.63%	0.864	2.330	*0.46*	
Size category										
0–5 mm	9	1.269	1.133	1.421	***0.0013***	62.34%	0.928	1.733	***0.037***	*0.99*
6–10 mm	9	1.238	1.009	1.520	***0.043***	75.76%	0.630	2.436	*0.39*	
<10 mm	3	1.308	0.878	1.950	*0.10*	52.20%	0.163	10.488	*0.34*	
>10 mm	11	1.287	0.984	1.684	*0.063*	83.66%	0.468	3.543	*0.28*	
Location										
Proximal colon	7	1.187	1.134	1.242	***0.00010***	9.79%	1.090	1.293	*0.90*	*0.30*
Distal colon	6	1.291	1.092	1.526	***0.011***	50.91%	0.866	1.925	*0.24*	
Adenoma per colonoscopy (WMD)										
Pathology										
Sessile serrated lesion	4	0.001	−0.030	0.032	*0.94*	6.76%	−0.076	0.077	*0.91*	*NA*
Morphology										
Polypoid	5	0.131	0.076	0.185	***0.0026***	4.21%	0.044	0.217	*0.91*	*0.97*
Non-polypoid	5	0.133	−0.053	0.319	*0.11*	84.87%	−0.335	0.621	***0.0012***	
Size category										
0–5 mm	3	0.223	−0.481	0.927	*0.31*	90.45%	−3.675	4.121	***0.0060***	***0.027***
6–10 mm	3	0.031	−0.017	0.079	*0.11*	7.29%	−0.154	0.216	*0.68*	
<10 mm	5	0.175	0.031	0.319	***0.028***	48.07%	−0.137	0.487	*0.085*	
>10 mm	6	0.017	−0.005	0.040	*0.10*	13.61%	−0.024	0.059	*0.78*	
Location										
Proximal colon	8	0.191	0.107	0.275	***0.0010***	63.19%	−0.019	0.402	***0.00060***	***0.027***
Distal colon	5	0.073	−0.028	0.173	*0.12*	52.62%	−0.154	0.299	*0.092*	
Adenoma per colonoscopy (IRR)										
Pathology										
Advanced adenoma	19	1.057	0.856	1.304	*0.59*	76.86%	0.411	2.716	*0.47*	***0.012***
Sessile serrated lesion	16	1.133	0.895	1.434	*0.28*	72.60%	0.435	2.952	***0.014***	
Non-neoplastic lesion	14	1.632	1.389	1.916	***<0.0001***	81.43%	0.928	2.87	***<0.0001***	
Colorectal cancer	4	2.061	0.196	21.625	*0.40*	52.11%	0.005	808.073	*0.25*	
Morphology										
Polypoid	13	1.453	1.262	1.673	***0.00010***	78.86%	0.868	2.433	***0.0023***	*0.80*
Non-polypoid	13	1.517	1.18	1.95	***0.0035***	80.25%	0.578	3.981	***0.0019***	
Size category										
0–5 mm	12	1.576	1.288	1.929	***0.00040***	89.00%	0.783	3.173	***<0.0001***	*0.076*
6–10 mm	11	1.204	1.08	1.343	***0.0035***	24.57%	0.93	1.559	*0.61*	
<10 mm	13	1.416	1.266	1.583	***<0.0001***	77.27%	0.982	2.041	***<0.0001***	
>10 mm	13	1.223	0.979	1.528	*0.072*	64.18%	0.59	2.534	*0.29*	
Location										
Proximal colon	15	1.433	1.258	1.634	***<0.0001***	78.73%	0.895	2.296	***<0.0001***	*0.97*
Distal colon	13	1.438	1.255	1.648	***0.00010***	72.36%	0.922	2.243	***<0.0001***	

CI, confidence interval; PI, prediction interval; RR, risk ratio; IRR, incidence rate ratios; WMD, weighted mean difference; NA, not applicable.

Table 3: **Separate analysis for the primary outcomes.**

based on studies with a low risk of bias also suggest that the outcomes were robust, although the effect sizes became small.

Quality of evidence

Based on the GRADE approach, the overall quality of available evidence ranged from very low to moderate. The downgrade in the level of evidence for RCTs was primarily due to (1) the risk of bias of the included RCTs (assessed via the RoB 2 tool), (2) inconsistency attributed to the study (e.g., number of study centers and study region), and patient characteristics (e.g., age and indications for colonoscopy), (3) insufficient sample size and a small number of events, (4) the potential publication bias (Table S6).

Discussion

According to our study, the 52.5% and 50.5% relative decrease in PMR and AMR, 23.8% and 24.2% relative increase in PDR and ADR, 38.8% and 39% relative increase in the rate of PPC and APC, as well as 0.271 more number of PPC and 0.202 more number of APC, respectively, underscore the benefit of employing of adding AI-aided systems during colonoscopy without significantly affecting the efficiency of the procedure, as evidenced by similar procedure times and adverse event rates in both groups.

With 33 studies involving 27,404 randomized patients, our meta-analysis is the most extensive to date in this field. Our sample size is far more than the latest study published on August 29, 2023, which included 21 randomized trials on 18,232 patients in their research.[31] Our large sample size allowed for inferring potential benefits in detecting clinically significant, albeit infrequent, lesions like advanced adenomas and SSLs. The comprehensive size and nature of this study enhance the reliability of the evidence and its applicability in real-world clinical settings.[34]

Our study is the first to provide evidence regarding the significant contribution of AI-aided colonoscopy to the detection of more patients with advanced adenomas, which have the highest potential for malignancy. Consequently, identifying this factor could greatly reduce CRC risk.[83] In other words, AI-aided colonoscopy is more effective in identifying people at a high risk of CRC.

Previous meta-analyses have also reported positive outcomes of AI-aided colonoscopy.[18–31] However, owing to the limited sample size of each study, they often focused on small, non-advanced lesions, especially diminutive adenomas. Consistent with prior studies,[18–30] our study observed a significant increase in the detection of diminutive and small adenomas during AI-aided colonoscopy. Notably, diminutive and small lesions are often missed during colonoscopy screening.[84] Previous studies have demonstrated that diminutive and small lesions show high-grade dysplasia and malignancy at rates between 0.6% and 5.6%.[85,86] Moreover, an increased risk of metachronous cancer has been reported when three or more non-advanced diminutive adenomas are present.[87,88] Although not all small lesions were up to the criteria for clinical treatment, their potential to develop CRC in the future cannot be ruled out. Overall, these positive detections could change the surveillance strategy for individuals, thus reducing the risk of interval CRC.

Despite the additional detection of advanced adenomas at a per-patient level (ADR), consistent with the latest study,[31] our study failed to show an increase in the detection of advanced adenomas at a per-polyp level (APC). This discrepancy could be attributed to various reasons. One is that advanced lesions are larger and rarely overlooked by the human eye. Another is that the meta-analyses were underpowered to detect advanced adenomas, compared to conventional adenomas, owing to the low incidence of these lesions. Similarly, although AI-aided colonoscopy did not show an increase in the detection of non-neoplastic lesions at a per-patient level, we observed a greater number of non-neoplastic lesions at a per-polyp level. Such discrepancies are not unexpected, considering that not all AI-rescued missed neoplasia necessarily correspond to the only single neoplasia that characterizes a patient as neoplasia-bearing.

Of note, most findings of the latest study are in line with our results.[31] Additionally, this study used several other key quality indicators as secondary endpoints to comprehensively assess the clinical utility of this emerging technology of colorectal neoplasia detection.[89] The significant improvement of all these indicators in the current meta-analysis provides more compelling evidence for the potential of AI in colonoscopy. Moreover, the special subgroup and meta-regression analyses provide satisfactory explanations for the substantial heterogeneity among the outcomes, allowing for a better characterization of the patient population that is most likely to benefit from AI-aided colonoscopy.

Due to the higher rate of missed proximal adenoma detection,[90] interval CRCs are more common in the proximal colon.[91,92] To evaluate the accurate effect of AI-aided tools for colorectal adenoma detection with different characteristics, we conducted separate analyses based on the size, location, and morphology of adenomas. Our results indicated that AI-assisted colonoscopy has the potential to identify a greater number of APC for diminutive and small adenomas at the proximal colon, offering a potential method to decrease the incidence of proximal interval cancers.

Concerns regarding increased procedure time and complication risk with AI-aided colonoscopy were not substantially supported by our findings. Although there was a significant increase in the mean inspection time, the 20-s increased time might not be clinically

significant. Thus, adding an AI-aided system will not significantly affect the colonoscopy workflow. The increased inspection time with AI-aided colonoscopy could be mainly attributed to improved lesion detection. Moreover, since the pooled proportion of false positives on AI-aided colonoscopy was 12% (95% CI, 7%–18%) in our study, the increased inspection time could also be partially attributed to the number of false positives.[93]

However, a concern arises about the increased rate of unnecessary resections for non-neoplastic lesions per colonoscopy, although without increasing the detection of patients with non-neoplastic lesions. Most of these resections were likely due to small hyperplastic polyps that are generally not associated with risk for interval CRC.[85,94] Improved detection of these non-neoplastic lesions may ultimately result in overdiagnosis and overtreatment, raising concerns about the real benefit of AI-aided colonoscopy.[95] However, recently published microsimulation studies suggested that the adoption of AI-aided tools has the potential to be cost-effective.[96–98] Thus, the effect of such resections on the cost-effectiveness of AI-aided colonoscopy remains inconclusive and warrants further investigation.

An essential aspect of the clinical applications of AI-aided systems is understanding the factors influencing their effectiveness cost-effectively. To our knowledge, this is the first meta-analysis assessing and exploring the reasons behind heterogeneity. Similarly, this study is the first to provide evidence that endoscopists with lower ADR (or PDR), shorter inspection time, patients with lower BMI, and younger age will benefit more from AI-aided colonoscopy. Meanwhile, bowel preparation, anesthesia, and time of day also affect the effect of AI-aid colonoscopy to a certain extent.

Of note, results from China seem better than those reported in other countries, mainly attributed to the young age and low ADR for studies done in China. We have shown a negative correlation between age and the effect of AI-aided colonoscopy. Moreover, patients of younger age are known to have a lower risk of colorectal neoplasia, which may partly explain the low ADR in the control group for studies in China. Also, the low ADR may be attributed to genetic, dietary, lifestyle, and habitus differences, as well as the incidence of colorectal neoplasia between the different populations.[60] Regarding studies coming from China, the indication of colonoscopy in the majority of patients was included for diagnostic purposes. This is problematic as true ADR should be accounted for screening colonoscopies only. This issue may explain the low ADR in the control group across the studies. Thus, the effect difference of AI-aided colonoscopy between China and other countries warrants further investigation via multicenter international trials.

This study has several limitations. First, the included studies varied in quality, but sensitivity analyses involving studies with a low risk of bias affirmed the robustness of the pooled results. Second, while the exclusion of studies with direct extraction data did not significantly alter the results in sensitivity analyses, it may reduce the strength of evidence. Third, potential publication bias, though addressed, could still affect the findings Fourth, some analyses did not reveal statistical differences, but caution is necessary due to the low statistical power. Finally, despite the identified associations in meta-regression and subgroup analyses, there might be unexplained confounding factors. Moreover, the associations identified in these studies may not translate to the individual level. Thus, some caution is warranted in extrapolating our findings in the subgroup and meta-regression analyses at individual patient levels.

The study findings suggest that AI-aided colonoscopy effectively improves the detection of colorectal neoplasia, especially adenomas, potentially mitigating the effects of suboptimal bowel preparation and short inspection time. Since small increments in colonoscopy quality could substantially affect net gains from any large-scale CRC screening program,[99] the application of AI systems has the potential to maintain high quality and homogeneity of colonoscopies and further improve endoscopist performance in large screening programs and centers with high workloads.

This study also provides several implications for future research. (1) Although ADR is an important outcome of screening colonoscopy, wherein it is inversely related to CRC incidence and mortality,[7,8] ADR remains a surrogate for CRC prevention. Concerning the long-term effectiveness of AI systems, clinical studies providing evidence on the AI-driven increased detection of colorectal neoplasia contributing to CRC prevention are lacking. Therefore, future studies with longitudinal follow-up are needed to confirm the potential benefit of AI-aided colonoscopy for the morbidity and mortality of CRC. (2) Although microsimulation studies suggested that adopting AI-aided tools may be cost-effective,[96–98] further high-quality studies are needed to evaluate the cost-effectiveness of AI systems in different global regions to support their use in clinical practice. (3) Based on our subgroup analyses and meta-regression analyses, future studies should verify the performance of AI in different conditions, exploring the most applicable situation for AI-aided colonoscopy. (4) Further studies are required to improve the existing AI systems. Importantly, AI systems should undergo dedicated training with a large dataset of SSLs and advanced adenomas to increase the sensitivity and specificity for the detection of these high-risk precancerous lesions.[100,101] Additionally, AI systems should undergo dedicated training with enough samples, including feces, fecal residue, wrinkled mucosa, and other false detections, to reduce false positives.

In conclusion, our study confirmed the role of AI-aided colonoscopy in safely improving the detection of

colorectal neoplasia, particularly for low-risk lesions and advanced adenomas, without significant delays in procedure time. AI-aided colonoscopy might be most beneficial in endoscopists with lower ADRs and shorter inspection times and in younger patients with fair bowel preparation. Yet, to assess the long-term benefits and cost-effectiveness of reducing CRC, future studies are needed.

Contributors

Project development: Shenghan Lou, Fenqi Du, Wenjie Song, Binbin Cui, Yanlong Liu, and Peng Han. Data collection or management: Shenghan Lou, Fenqi Du, Wenjie Song, Yixiu Xia, Xinyu Yue, and Da Yang. Data analysis: Shenghan Lou, Fenqi Du, Wenjie Song, and Peng Han. Manuscript writing/editing: Shenghan Lou, Fenqi Du, Wenjie Song, Yixiu Xia, Xinyu Yue, Da Yang, Binbin Cui, Yanlong Liu, and Peng Han. Shenghan Lou, Fenqi Du, Wenjie Song, Binbin Cui, Yanlong Liu, and Peng Han have verified the underlying data. All authors read and approved the final version of the manuscript.

Data sharing statement

This systematic review extracted data from publicly available literature. Upon request, the authors can share these data with qualified researchers.

Declaration of interests

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2023.102341.

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