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CLINICAL TRIAL

Man Plus Machine: A Randomized Control Trial of Artificial Intelligence Including the Impact of Adjunctive Polyp Detection Techniques

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Keywords: adenoma detection | artificial intelligence | colon polyps | colonoscopy

ABSTRACT

Background and Aims: Computer-aided polyp detection tools (CADe) utilizing artificial intelligence (AI) have been shown to demonstrate benefit with improved polyp detection during colonoscopy. Questions remain around the impact of CADe when combined with additional techniques that improve polyp detection such as lengthening withdrawal time, cecal and rectal retroflexion, dynamic position change, and narrow band imaging (NBI) use.

Methods: A single-center prospective, randomized control trial comparing ENDO-AID AI module to conventional colonoscopy was conducted between October 11, 2023 and March 16, 2024 at Waitakere Hospital. Additional techniques to improve polyp detection were recorded but left to the discretion of participating 26 endoscopists.

Results: Seven hundred seventy-six patients (mean ± SD age, 61.2 ± 13.0 years; 344 females) were recruited, 383 patients allocated to AI and 393 to control. Position change was used in 43%, antispasmodic in 25%, distal cap in 25%, NBI in 21%. Overall, univariate analysis demonstrated a nonsignificant trend towards higher adenoma detection rate (ADR) in the CADe than control group (63.4% vs. 57.3%, $p = 0.08$). AI was most effective in the screening cohort (ADR 79% vs. 68%, average polyp rate 3.7 vs. 2.8 $p < 0.05$). Multivariable analysis demonstrated CADe was independently associated with increased adenoma detection rate (odds ratio [OR], 1.38; 95% confidence interval [CI], 1.01–1.89; $p = 0.042$), as was use of NBI, OR 2.00; (95% CI: 1.23–3.25; $p = 0.006$) and increased withdrawal time, OR 1.11; (95% CI: 1.08–1.15; $p < 0.001$).

Conclusion: ADR was increased by CADe in a cohort of high detectors and was further augmented by traditional techniques known to be beneficial. It is important to incorporate traditional techniques with CADe to maximize ADR.

1 | Introduction

Colonoscopy is a widely performed medical procedure with a rising demand. This increased demand has created pressure on healthcare providers to enhance both the scale and quality of services, while maximizing efficiency.

Real-time computer-aided polyp detection tools (CADe), utilizing artificial intelligence (AI) and deep-learning software have been consistently shown across different modules, endoscopists, and populations to improve adenoma detection rate (ADR) [1, 2]. ADR is the most commonly used measure of quality colonoscopy and is inversely related to the incidence

[Correction added on 10 December 2025, after first online publication: The author list has been re-sequenced to display "Michael T. W. Wang" first, followed by "N. Atkinson".]

of postcolonoscopy interval CRC and CRC-related mortality [3, 4]. Because colonoscopy is operator-dependent, ADR varies significantly among endoscopists, with up to an eightfold difference (8% vs. 68%) between high and low detectors [5]. New Zealand has recently implemented updated polyp surveillance guidelines which now include a 10-year surveillance interval for patients with one to two adenomas [6]. A patient with four adenomas or nine adenomas is offered surveillance in 5 or 3 years, respectively. A patient without any polyp is suggested to wait to undergo fecal immunochemical test (FIT) based screening at the commencement age, which in New Zealand is 60 years old [6]. With these lengthened surveillance intervals, there is a growing emphasis on the critical importance of even small polyp identification and resection to reduce the risk of postcolonoscopy colorectal cancer.

In the 20 years prior to CADe, many techniques, technology, interventions, endoscopist education and feedback have been investigated and demonstrated to improve ADR [7]. Specifically, lengthening withdrawal time, cecal and rectal retroflexion, dynamic patient position change, distal attachment, enhanced imaging technology with narrow band imaging (NBI), involvement of a second observer, and an endoscopist report card to feedback key quality indicators are established [7]. These are known to be implemented variably and often user dependent, but are evidence-based and cost-effective (or free).

CADe studies also report widely variable ADR, ranging from 16% [8] to 61% [9]. Furthermore, despite the use of AI, miss rates of up to 20% are reported in tandem studies [10]. In a post hoc analysis of video of missed lesions reviewed by expert endoscopists, the majority were not visible within the visual field suggesting that polyps missed by CADe are obscured behind folds [11]. It is notable, therefore, that in published CADe studies many interventions traditionally used to improve mucosal exposure and improve ADR are incompletely described, and studies specifically exclude distal attachment devices and image enhancement techniques [12].

A retrospective case-control study from our group in 2022 found CADe improved ADR from 39% to 48% (odds ratio 1.59; 95% CI [1.05–2.41]; $p = 0.03$) but was limited in its retrospective, nonrandomized nature, lack of patients undergoing screening, and vitally in our view, did not record the use of techniques used by endoscopists to improve ADR.

To address these limitations, we conducted a prospective, real-world randomized trial to elucidate the benefit of CADe compared to conventional colonoscopy, in the context of adjunctive techniques and their impact on ADR.

2 | Patients and Methods

We performed a single-center, prospective, single-blinded randomized control trial at Waitakere Hospital, Auckland, New Zealand. This is a secondary center with three endoscopy rooms performing general gastroscopy and colonoscopy including screening procedures. Inclusion criteria included consecutive patients aged over 18 years requiring colonoscopy for colorectal cancer screening (via a positive FIT test cut off 200 ng Hb/mL of buffer, screening commencement at age 60 years old), surveillance, or investigation of symptoms. Patients were excluded if there was contraindication or conditions precluding polyp resection, the procedure was for a scheduled polypectomy, or a history of inflammatory bowel disease or previous bowel resection. Agreement to participate was obtained in all cases via standard written consent.

Randomization was stratified by gender and indication (surveillance, screening, or symptoms). Allocation was done using concealed envelopes. Treatment allocation was known to the patients, staff in the room and endoscopists, but not the reporting pathologist.

Patients were randomized to either the ENDO-AID (OIP-1, Olympus Medical Systems Inc, Tokyo, Japan) system, or standard high-definition white light (HD-WL) colonoscopy in the control group. All practicing endoscopists agreed to participate. This included 14 consultant gastroenterologists, five consultant surgeons, seven fellows (three gastro, four surgical), and one nurse endoscopist. The ENDO-AID device was activated upon reaching the cecum if the patient was randomized to the intervention arm. ENDO-AID processes colonoscopy images in real time, superimposing a green box over suspected polyps. Detection Type A preset (sensitive) was used in all cases. Additional use of techniques to enhance polyp detection remained at the endoscopist's discretion, recorded at the conclusion of the procedure. NBI was recorded if utilized during some or all of the withdrawal for lesion detection. Patient position change was recorded only if applied on withdrawal to optimize views. Antispasmodics included either hyoscine butylbromide or glucagon.

The primary outcome was ADR, defined as the proportion of patients with at least one histologically proven adenoma or carcinoma. Secondary outcomes included sessile serrated lesion detection rate (SSLDR), polyp detection rate (PDR), left and right hemicolon ADR and PDR, size categorization and withdrawal time.

All patients used Glycoprep-C, large volume split bowel preparation. Bowel preparation was evaluated and graded by the endoscopist performing the exam using the Boston bowel preparation scale (BBPS) [13]. All procedures were completed in two rooms with the same equipment, including high-definition colonoscopes (HQ 190 with EVIS X1 video column; Olympus, Tokyo, Japan). All colonoscopies were performed using conscious sedation with fentanyl and midazolam. Patient comfort scores were recorded by nurses using Gloucester comfort score descriptors, from 1 (*No discomfort, resting comfortably throughout*) to 5 (*Extreme discomfort, experienced frequently during the procedure*) [14].

Withdrawal time was measured by nursing staff from the time of cecal intubation to removal of the colonoscope from the colon. Polyps were classified by the endoscopist and included estimation of size, location, and morphology (polypoidal: Paris 0-Ip or nonpolypoidal: Paris 0-IIa, Paris 0-IIb, and Paris 0-Is) [15]. Location was considered right colon if proximal to the splenic flexure, and left colon if distal to this, excluding the rectum, which was recorded separately. The final decision for polyp resection was at the discretion of the endoscopist. Polyps were

TABLE 1 | Baseline and procedural characteristics of patients by intervention group. Data are presented as mean ± SD, or number of participants (% of participants).

Parameter	CADe group ($n = 383$)	Control group ($n = 393$)
Age group (years)		
< 20	2 (0.5%)	1 (0.3%)
20 to 39	32 (8.4%)	30 (7.6%)
40 to 59	127 (33.2%)	127 (32.3%)
60 to 79	204 (53.3%)	215 (54.7%)
≥ 80	18 (4.7%)	20 (5.1%)
Male sex	216 (56.4%)	216 (45.0%)
Ethnicity		
European	266 (69.5%)	261 (66.4%)
Asian	76 (19.8%)	77 (19.6%)
Māori	16 (4.2%)	21 (5.3%)
Pacific	19 (5.0%)	24 (6.1%)
Other	6 (1.6%)	10 (2.5%)
Indication		
Diagnostic	148 (38.6%)	148 (37.7%)
Surveillance	77 (20.1%)	85 (21.6%)
Screening	158 (41.3%)	160 (40.7%)
Diagnostic indication		
Anemia	33 (22.3%)	30 (20.3%)
Bleeding	39 (26.4%)	33 (22.3%)
Diarrhea	16 (10.8%)	21 (14.2%)
Constipation	5 (3.4%)	5 (3.4%)
Change in bowel habit	8 (5.4%)	15 (10.1%)
Abnormal imaging	8 (4.7%)	11 (7.4%)
Weight loss	11 (7.4%)	7 (4.7%)
Pain	25 (16.9%)	17 (11.5%)
Boston bowel preparation scale	8.4 ± 1.2	8.4 ± 1.2
Bowel preparation		
Excellent	229 (59.8%)	231 (58.8%)
Good	84 (21.9%)	87 (22.1%)
Fair	19 (5.0%)	26 (6.6%)
Inadequate	5 (1.3%)	6 (1.5%)
Admission status		
Outpatient	379 (99.0%)	390 (99.2%)
Inpatient	4 (1.0%)	3 (0.8%)
Clinician		
Gastroenterology specialty	339 (88.5%)	346 (88.0%)
Consultant	298 (77.8%)	308 (78.4%)
Colonoscopy times (minutes)		
Insertion time	8.9 ± 0.70	9.8 ± 0.77
Noninterventional withdrawal time	10.7 ± 0.63	9.7 ± 0.40
Interventional withdrawal time	18.8 ± 1.2	18.5 ± 1.1
Extent reached		
Terminal ileum	337 (88.0%)	337 (85.8%)
Cecum	376 (98.2%)	387 (98.5%)
Incomplete	7 (1.8%)	6 (1.5%)
Gloucester comfort score (GCS)		
GCS 1	263 (68.7%)	258 (65.6%)
GCS 2	75 (19.6%)	81 (20.6%)
GCS 3	36 (9.4%)	42 (10.7%)
GCS 4	9 (2.3%)	11 (2.8%)
GCS 5	0 (0.0%)	1 (0.3%)
Sedation		
Midazolam (mg)	2.7 ± 0.12	2.7 ± 0.12
Fentanyl (μg)	67.9 ± 2.9	67.5 ± 2.7
Techniques		
Cecal retroflexion	199 (52.0%)	207 (52.7%)
Rectal retroflexion	275 (71.8%)	283 (72.0%)
Narrow band imaging during withdrawal	43 (11.2%)	84 (21.4%)
Position change	161 (42.0%)	175 (44.5%)
Antispasmotics	124 (32.4%)	150 (38.2%)
Clear cap	106 (27.7%)	93 (23.7%)

fixed in formalin solution and reported according to Vienna classification [16].

The ENDO-AID equipment from Olympus was loaned free of charge. Olympus Australia also provided a grant to assist with the running of the study. The funder had no input in study design, nor access to results during the study. The study was approved by the NZ Ethics Committee (2021FULL11946), Australian New Zealand Clinical Trials Registry number: ACTRN12622000866707, Universal Trial Number (UTN): U1111-1278-0636.

TABLE 2 | Polypectomy characteristics and histology detection rates of patients by intervention group. Data are presented as median (IQR), or number of participants (% of participants). Asterisks denote statistically significant values ($p < 0.05$).

Parameter	CADe group ($n = 383$)	Control group ($n = 393$)	p
Polyp characteristics			
Number of polyps	2 (1–4)	2 (0–4)	0.006*
Polyp detection rate	298 (77.8%)	286 (72.8%)	0.11
Right polyp detection rate	204 (53.3%)	198 (50.4%)	0.43
Left polyp detection rate	154 (40.2%)	130 (33.1%)	0.04*
Rectal polyp detection rate	75 (19.6%)	71 (18.1%)	0.65
> 10-mm polyp	57 (14.9%)	70 (17.8%)	0.29
Pedunculated morphology rate	24 (6.3%)	31 (7.9%)	0.40
Sessile morphology rate	246 (64.2%)	231 (58.8%)	0.12
Polyp histology characteristics			
Adenoma detection rate	243 (63.4%)	225 (57.3%)	0.08
Sessile serrated lesion detection rate	90 (23.5%)	61 (15.5%)	0.006*
Combined adenoma and sessile serrated lesion detection	260 (67.9%)	237 (60.3%)	0.03*
Villous morphology	7 (1.8%)	15 (3.8%)	0.13
High-grade dysplasia	8 (2.1%)	9 (2.3%)	> 0.99
Adenocarcinoma	23 (6.0%)	20 (5.1%)	0.64
Hyperplastic	116 (30.3%)	103 (26.2%)	0.23

3 | Statistics

Power calculations (NCSS PASS 2002, Utah, USA) showed that a minimum of 373 patients per arm was required to discriminate a clinically significant intergroup difference in ADR of 10%, with 80% power ($\beta = 0.2$), and a two-sided statistical significance level of 5% ($\alpha = 0.05$). The expected ADR of the control group is estimated at 35%.[1]

Statistical analysis was performed using IBM SPSS Statistics version 26.0 (New York, USA). Univariate intergroup comparisons were performed using the unpaired t-test, where normal distribution had been confirmed by Shapiro–Wilk testing ($p > 0.05$). Nonnormally distributed data were analyzed using the Mann–Whitney U test and categorical data using the chi-squared or Fisher's exact test. Preliminary univariate logistic or Poisson regression analysis was used to identify potential confounding factors for outcome measures. The association between artificial intelligence use and outcome measures was then assessed using multivariable logistic or Poisson regression, incorporating relevant variables with a univariate association threshold of $p < 0.15$. The number of variables used in the multivariable regression analysis was approximately limited to the number of adverse events divided by 10, to avoid overfitting. All tests were two-tailed, and $p < 0.05$ was considered statistically significant.

4 | Results

Between October 11, 2023 and March 16, 2024, a total of 776 patients (mean ± SD age, 61.2 ± 13.0 years; 432 males and 344 females) were recruited, of which 383 patients were allocated to the intervention (CADe) group and 393 patients to the control group. Baseline and procedural characteristics of patients by intervention group are summarized in Table 1; 41% of procedures were performed for screening. Bowel preparation scores and endoscopist specialty (gastroenterologist or surgeon) were well matched between the two groups. Cecal intubation was achieved in 763 (98.3%) cases, and the mean ± SD interventional withdrawal time was 18.6 ± 1.1 min. There was no difference between groups in medications administered (Fentanyl 67.9 ± 2.9 mcg + Midazolam 2.7 ± 0.12 mg) or comfort during the procedure (87.2% GCS ≤ 2).

Techniques to improve polyp detection were similar between groups. Cecal and rectal retroflexion was performed 52% and 72% of the time in both arms, respectively. Dynamic patient position change was used in 43.3% of cases, antispasmodic in 35.3%, and a clear distal cap in over 25.6% of colonoscopies; 21% of endoscopists in the HD-WLE group used NBI on withdrawal, compared to 11% using CADe.

Polypectomy characteristics and histology detection rates of patients by intervention group are presented in Tables 2 and 3. Overall, univariate analysis demonstrated a nonsignificant trend towards higher ADRs in the CADe than control group (63% vs. 57%, $p = 0.08$). There was also no difference in PDR (73% vs. 78%, $p = 0.11$). A greater number of polyps ($p = 0.006$), detection rate of sessile serrated lesions (24% vs. 16%), and detection rate of adenoma and sessile serrated lesions were seen in the CADe group (both $p < 0.05$). There was no difference between groups for advanced lesions; > 10 mm, villous histology, high-grade dysplasia, or adenocarcinoma. ADR was significantly higher in the screening patients between CADe and control groups (79% vs. 68%, $p = 0.03$) as was SSLDR (26% vs. 14%, $p = 0.008$).

Multivariable regression analysis of polyp, adenoma, and sessile serrate lesion detection rate, and the number of polyps detected is presented in Tables A1–A4. Multivariable analysis demonstrated that CADe was independently associated with increased ADR (odds ratio [OR], 1.38; 95% confidence interval [CI], 1.01–1.89; $p = 0.042$).

TABLE 3 | Subgroup analysis of polypectomy characteristics and histology detection rates of patients by intervention group and indication. Data are presented as median (IQR), or number of participants (% of participants). Asterisks denote statistically significant values ($p < 0.05$).

	Diagnostic			Screening			Surveillance		
	CADe group ($n = 139$)	Control group ($n = 152$)	p	CADe group ($n = 160$)	Control group ($n = 161$)	p	CADe group ($n = 84$)	Control group ($n = 80$)	p
Polypectomy characteristics									
Number of polyps	1 (0–4)	1 (0–3)	< 0.001*	3 (1–5)	2 (1–3)	< 0.001*	3 (1–5)	3 (1–5)	0.40
Polyp rate	91 (65.5%)	90 (59.2%)	0.28	136 (85.0%)	131 (81.4%)	0.46	71 (84.5%)	65 (81.3%)	0.68
Right polyp rate	68 (48.9%)	66 (43.4%)	0.41	85 (53.1%)	82 (50.9%)	0.74	51 (60.7%)	50 (62.5%)	0.87
Left polyp rate	42 (30.2%)	39 (25.7%)	0.43	80 (50.0%)	63 (39.1%)	0.057	32 (38.1%)	28 (35.0%)	0.75
Rectal polyp rate	16 (11.5%)	22 (14.5%)	0.49	43 (26.9%)	33 (20.5%)	0.19	16 (19.0%)	16 (20.0%)	> 0.99
> 10-mm polyp rate	12 (8.6%)	12 (7.9%)	0.83	42 (26.3%)	52 (32.3%)	0.27	3 (3.6%)	6 (7.5%)	0.32
Pedunculated rate	3 (2.2%)	4 (2.6%)	> 0.99	20 (12.5%)	26 (16.1%)	0.43	1 (1.2%)	1 (1.3%)	> 0.99
Sessile rate	76 (54.7%)	78 (51.3%)	0.64	107 (66.9%)	98 (60.9%)	0.30	63 (75.0%)	55 (68.8%)	0.39
Histology detection rates									
Adenoma	65 (46.8%)	66 (43.4%)	0.63	127 (79.4%)	110 (68.3%)	0.03*	51 (60.7%)	49 (61.3%)	> 0.99
Sessile serrated lesion	24 (17.3%)	18 (11.8%)	0.24	42 (26.3%)	23 (14.3%)	0.008*	24 (28.6%)	20 (25.0%)	0.72
Villous	5 (3.6%)	12 (7.9%)	0.14	0 (0.0%)	1 (0.6%)	> 0.99	2 (2.4%)	2 (2.5%)	> 0.99
Combined adenoma and sessile serrated lesion detection	75 (54.0%)	71 (46.7%)	0.24	127 (79.4%)	110 (68.3%)	0.03*	58 (69.0%)	56 (70.0%)	> 0.99
High-grade dysplasia	0 (0.0%)	2 (1.3%)	0.50	8 (5.0%)	7 (4.3%)	0.79	0 (0.0%)	0 (0.0%)	> 0.99
Adenocarcinoma	6 (4.3%)	7 (4.6%)	> 0.99	17 (10.6%)	13 (8.1%)	0.45	0 (0.0%)	0 (0.0%)	> 0.99
Hyperplastic	33 (23.7%)	29 (19.1%)	0.39	47 (29.4%)	46 (28.6%)	0.90	36 (42.9%)	28 (35.0%)	0.34

Additional factors improving ADR included use of NBI, OR 2.00; (95% CI: 1.23,3.25; $p = 0.006$) and increased withdrawal time, OR 1.11; (95% CI: 1.08,1.15; $p < 0.001$). CADe was also significantly associated with increased SSLDR and the number of polyps detected (both $p \leq 0.001$).

5 | Discussion

This is the first study utilizing CADe to document and report all of the additional techniques used by endoscopists that are known to enhance the ADR. This is especially significant as our study reports the highest ADR seen in the randomized CADe literature to date. With such a high control group ADR (57%), we only demonstrated a trend towards statistical significance for ADR improvement with CADe overall ($p = 0.08$); however, this improvement was significant on multivariate analysis ($p = 0.04$), and when narrowed to screening patients ($p = 0.03$).

One high detector study, conducted by a single expert endoscopist with a known high ADR, showed an 8% increase in ADR for a total of 61%, and reported similar results when stratified to screening patients [9]. In contrast, our overall cohort demonstrated a 6% increase, bringing the ADR to 63%. A large Spanish screening program study reported an increase from 62% to 64% [17]. Ahmed et al. studying primarily screening patients or those with large or multiple adenomas detected during flexible sigmoidoscopy, reported an increase in ADR from 65% to 71% ($p = 0.09$) [18]. In comparison, our cohort of screening patients showed an increase in ADR from 68% to 79% ($p < 0.05$) with the use of CADe. It is notable that the Ahmed et al. study also reported a very high use of ENDOCUFF VISION (> 70%), which they suggest may enhance visibility and detection, potentially minimizing any additional benefit from the CADe system. Subsequently, several authors have explored the combination of Endocuff with CADe to improve mucosal exposure, including randomized controlled trials (RCTs) [19–22], which have demonstrated significant improvements in ADR. One such study demonstrated a 17% increase in ADR, with notable improvements in the detection of proximal and advanced adenomas [22].

A well-recognized limitation of traditional CADe systems has been their inability to improve mucosal exposure. They are obviously only able to identify lesions on mucosa that are exposed to the camera, then prompt endoscopists to the presence and location of suspected polyps within this field of view. AI attempts to improve this include a study that combined CADe with a speed dashboard on the monitor, which alerted endoscopists if the withdrawal speed was considered too fast [23]. This led to a significant ADR increase over just CADe of 9%. Another study developed an AI-based system for measuring fold examination quality of colonoscopic withdrawal technique [24]. This study showed significantly poorer quality of fold examination in low detectors compared to high detectors, which was also associated with a reduced withdrawal time.

In our study, additional techniques commonly used by endoscopists to improve mucosal exposure included retroflexion, dynamic patient position changes, and the use of clear distal attachments—all of which have well-established evidence for enhancing ADR [7]. Antispasmodics were also frequently used, though the evidence supporting their benefit is mixed with largely inconsistent benefit, outside of multimodal approaches [25]. NBI, which is known to significantly improve ADR by 14% [26] compared to white light endoscopy by enhancing contrast against the background mucosa, was the least frequently used adjunct in our study. Notably, it was used less often in the CADe group compared to the standard colonoscopy group (11% vs. 21%), likely because the ENDO-AID system does not function when NBI is in use. These results therefore may even underestimate the true effect of CADe but reflect real-world practice with endoscopists who are familiar with all three imaging modalities (white light, NBI, and CADe) and chose the best for their situation in their experience. We believe that endoscopists in the CADe group used the two approaches in separate passes of colonic segments. Despite this, NBI use still improved ADR in multivariate regression analysis (OR 2.00, $p = 0.0006$) suggesting complementary assistance to the general endoscopist.

We attribute this high ADR and polyp detection to the long withdrawal time, which we feel indicates careful and thorough inspection by endoscopists. The withdrawal time in the other high detector study was 14.5 min [18], as compared to 19 min if polypectomy was performed and 10 min without any intervention in our cohort. Our study confirmed an 11% increase in ADR per minute longer of withdrawal time, highlighting the importance of this aspect. Large observational studies also note longer withdrawal times were associated with higher ADR (3.6% per minute; 95% confidence interval: 2.4% to 4.8%; $p < 0.0001$) [27]. A further study also noted withdrawal time as the most significant predictor of the proportion of the CADe effect on ADR [28]. There have been concerns raised with regard to false positive activations and therefore increased procedure and withdrawal time, even increased sedative medication requirement or patient discomfort. Our study confirms this not to be the case, with no difference in any of these patient-comfort parameters.

However, this ADR cannot simply be explained by the withdrawal time alone, with other studies reporting similar or longer noninterventional withdrawal times [12, 17, 23, 29–31]. We hypothesize that it is the combination of techniques that is driving this high ADR, which is further amplified and augmented by CADe. In addition broader systems-based approaches to improved operator performance in our unit are relevant. Not measured in this study, our nurse assistants are trained, encouraged, and empowered to assist with polyp detection, which has been shown to increase ADR by 19% [32]. Over the past 10 years in our hospital, regular "report cards" have been produced as part of clinical audit and distributed to endoscopists, including ADR, cecal intubation rate, complications, and missed cancers. We hypothesize that this long-term, consistent, recurrent feedback has also contributed to the high ADR seen in our study, consistent with a known 10 to 15% absolute increase in ADR in hospitals with a report card system [33].

Studies that have looked at the utility of CADe compared with some traditional techniques, including a network meta-analysis, suggested CADe may have a nearly two times higher ADR than competing strategies, including a 4.4% higher ADR than chromoendoscopy, and a 4.1% higher ADR than mucosal exposure devices [34]. Despite successes with CADe, ADRs of 16% [8] and adenoma miss rates up to 20% are still reported despite its use [10].

Given our unexpectedly high ADR, we suggest that techniques with different mechanisms of action to increase ADR should be viewed as complementary rather than competing strategies, and that a combined approach using traditional mucosal exposure techniques alongside CADe may yield the greatest effect. Further trials are needed to confirm these assumptions, with analyses investigating the different variables possibly affecting the impact of CADe largely limited to patient demographic factors, colonoscopy indication, and withdrawal time, but not including endoscopist adjunctive techniques. We believe this may explain some of the substantial levels of heterogeneity found in colonoscopy quality performances [28]. We therefore recommend that future studies on CADe report the use of these adjunctive techniques to assess their impact on reported ADR.

It is thought that ENDO-AID has been trained on more images than other AI detection systems although transparency regarding training datasets on the software is lacking. Only four other studies have reported on the use of the Olympus ENDO-AID module [12, 21, 35, 36], with an overall ADR relative risk (RR) of 1.27 (95% CI 1.15, 1.39), $p < 0.05$ [1]. This is notably higher than the EndoScreener, CAD EYE, and GI-Genius CADe systems [1]. A well-described limitation of CADe systems is the detection of SSLs, which may be more subtle and difficult to detect. Meta-analyses of parallel studies showed no significant difference in SSLDR using CADe (RR, 1.10; 95% CI, 0.93–1.30; $p = 0.27$) [1]. However, when the three ENDO-AID trials reporting SSLDR were reviewed separately [12, 21, 36], there was an overall improved detection of 60% (RR, 1.60; 95% CI, 1.21–2.13; $p = 0.01$), with no difference in the five studies using the GI-Genius system [1]. We also found a significantly improved SSLDR; OR 1.87 (95% CI 1.28–2.75), $p = 0.001$, with the highest overall SSLDR in the reported CADe literature (an increase to 24%).

We did not observe a superiority in detecting advanced adenomas, likely due to the lower incidence of these lesions in our cohort, as well as the larger sample sizes that would be needed to adequately power this outcome. One larger study, including 3059 patients, did report a statistically significant increase in advanced adenoma detection with CADe (6.6% vs. 4.9%, $p = 0.04$) [37]. However, questions do remain about the effect of CADe on clinically relevant outcomes, particularly given the incremental increases in ADR at already extremely high baseline detection rates. Some data suggest that protection against postcolonoscopy colorectal cancer continues to improve as ADRs increase up to 50% [27, 38]. However, a recent observational study indicated that improvements in ADR over time were associated with a reduced risk of colorectal cancer, but only among patients whose physician had a baseline ADR of less than 26% [39].

It could be argued that our high ADR and SSLDR may limit the generalizability of the findings. However, we feel the primary strength of this study is its cohort, which includes a diverse group of generalist endoscopists including unsupervised fellows as well as an independent nurse endoscopist. This is the first randomized study to include a nurse, whose outcomes were consistent with the whole cohort. Additionally, the senior endoscopist cohort encompasses a wide range of experience levels, reflecting a real-world setting in a secondary care center with a wide variety of colonoscopy practices and indications. The main limitations of this study are related to potential bias in operator performance and outcome detection, which is unavoidable due to the unblinded design of the trial. While true double-blinding can technically be achieved in these studies (e.g., by having a second reviewer review on a separate monitor), we felt this would not eliminate (and may even amplify) performance bias, as participants may alter their usual behavior given they are being so closely observed by a human colleague.

6 | Conclusion

We found CADe increased ADR within a cohort of high detectors in a general hospital setting. Despite CADe use, ADR was further augmented by the traditional factors known to be beneficial, highlighting the synergy of mucosal exposure and mucosal identification. Therefore, it is important to continue emphasizing, documenting, and reporting traditional techniques that we believe herald the optimal synergistic approach with CADe, combining man, system, and machine to maximize ADR.

Ethics Statement

The study was approved by the NZ Ethics Committee (2021FULL11946), Australian New Zealand Clinical Trials Registry number: ACTRN12622000866707, Universal Trial Number (UTN): U1111-1278-0636.

Conflicts of Interest

The authors declare no conflicts of interest.

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Appendix A

TABLE A1 | Per polyp multivariable Poisson regression of number of polyps detected by intervention group, adjusted for confounding variables meeting univariate association threshold of $p < 0.15$. Asterisks denote statistically significant values ($p < 0.05$).

	Univariate regression		Multivariate regression	
Parameter	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
CADe	1.22 (1.12–1.32)	< 0.001*	1.29 (1.18–1.40)	< 0.001*
Age (per year)	1.02 (1.02–1.03)	< 0.001*	1.02 (1.02–1.03)	< 0.001*
Male sex	1.19 (1.09–1.29)	< 0.001*	1.17 (1.07–1.27)	< 0.001*
Indication				
Diagnostic versus screening	0.73 (0.66–0.80)	< 0.001*	0.75 (0.68–0.83)	< 0.001*
Surveillance versus screening	1.06 (0.96–1.18)	0.24	1.03 (0.92–1.14)	0.65
Clinician				
Gastroenterology specialty	1.32 (1.14–1.52)	< 0.001*	1.21 (1.04–1.42)	0.01*
Techniques				
Antispasmotic agent	1.30 (1.19–1.42)	< 0.001*	1.28 (1.17–1.40)	< 0.001*
Right colon retroflexion	1.27 (1.17–1.39)	< 0.001*	1.09 (0.98–1.21)	0.12
Rectum retroflexion	1.38 (1.24–1.52)	< 0.001*	1.14 (1.00–1.30)	0.052
Position changed	1.28 (1.17–1.38)	< 0.001*	0.98 (0.88–1.08)	0.65
Narrow band imaging	1.47 (1.34–1.63)	< 0.001*	1.41 (1.26–1.58)	< 0.001*
Complete extent reached	1.32 (1.15–1.52)	< 0.001*	1.21 (1.03–1.41)	0.02*
Withdrawal time (per minute)	1.32 (1.25–1.39)	< 0.001*	1.31 (1.24–1.38)	< 0.001*

TABLE A2 | Per patient multivariable logistic regression of polyp detection rate by intervention group, adjusted for confounding variables meeting univariate association threshold of $p < 0.15$. Asterisks denote statistically significant values ($p < 0.05$).

	Univariate regression		Multivariate regression	
Parameter	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
CADe	1.32 (0.95–1.81)	0.10	1.39 (0.98–1.97)	0.07
Age (per year)	1.04 (1.03–1.06)	< 0.001*	1.04 (1.03–1.06)	< 0.001*
Male sex	1.27 (0.92–1.76)	0.14	1.13 (0.79–1.60)	0.51
Indication				
Diagnostic versus screening	0.34 (0.24–0.50)	< 0.001*	0.41 (0.28–0.62)	< 0.001*
Surveillance versus screening	1.03 (0.63–1.68)	0.92	1.23 (0.72–2.11)	0.45
Clinician				
Gastroenterology specialty	1.48 (0.92–2.37)	0.10	1.12 (0.64–1.95)	0.69
Techniques				
Antispasmotic agent	1.38 (0.99–1.97)	0.06	1.49 (1.00–2.21)	0.048*
Right colon retroflexion	1.55 (1.12–2.14)	0.008*	1.22 (0.78–1.93)	0.39
Rectum retroflexion	1.54 (1.09–2.18)	0.02*	1.18 (0.73–1.90)	0.51
Narrow band imaging	1.61 (1.00–2.59)	0.050	1.49 (0.87–2.55)	0.14
Complete extent reached	2.27 (1.47–3.49)	< 0.001*	2.16 (1.28–3.66)	0.004*
Withdrawal time (per minute)	1.04 (1.03–1.05)	< 0.001*	1.04 (1.03–1.05)	< 0.001*

TABLE A3 | Per patient multivariable logistic regression of adenoma detection rate by intervention group, adjusted for confounding variables meeting univariate association threshold of $p < 0.15$. Asterisks denote statistically significant values ($p < 0.05$).

	Univariate regression		Multivariate regression	
Parameter	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
CADe	1.30 (0.97–1.73)	0.08	1.38 (1.01–1.89)	0.042*
Male sex	1.43 (1.07–1.91)	0.02*	1.35 (0.99–1.84)	0.06
Indication				
Diagnostic versus screening	0.29 (0.21–0.41)	< 0.001*	0.24 (0.16–0.35)	< 0.001*
Surveillance versus screening	0.55 (0.37–0.83)	0.004*	0.44 (0.28–0.68)	< 0.001*
Clinician				
Gastroenterology specialty	1.42 (0.92–2.20)	0.12	1.15 (0.68–1.94)	0.60
Consultant	1.30 (0.92–1.84)	0.13	1.12 (0.81–1.65)	0.43
Techniques				
Right colon retroflexion	1.55 (1.16–2.07)	0.003*	0.99 (0.66–1.48)	0.97
Rectum retroflexion	1.63 (1.18–2.23)	0.003*	1.56 (0.98–2.48)	0.06
Position changed	1.28 (0.96–1.72)	0.09	0.91 (0.62–1.32)	0.61
Narrow band imaging	1.60 (1.06–2.40)	0.03*	2.00 (1.23–3.25)	0.006*
Complete extent reached	2.57 (1.68–3.94)	< 0.001*	2.36 (1.42–3.91)	< 0.001*
Withdrawal time (per minute)	1.11 (1.08–1.14)	< 0.001*	1.11 (1.08–1.15)	< 0.001*

TABLE A4 | Per patient multivariable logistic regression of sessile serrated lesion detection rate by intervention group, adjusted for confounding variables meeting univariate association threshold of $p < 0.15$. Asterisks denote statistically significant values ($p < 0.05$).

	Univariate regression		Multivariate regression	
Parameter	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
CADe	1.67 (1.17–2.40)	0.005*	1.87 (1.28–2.75)	0.001*
Male sex	0.57 (0.40–0.81)	0.002*	0.55 (0.38–0.80)	0.002*
Indication				
Diagnostic versus screening	0.66 (0.43–1.02)	0.06	0.70 (0.44–1.13)	0.14
Surveillance versus screening	1.44 (0.93–2.24)	0.10	1.43 (0.86–2.34)	0.17
Clinician				
Gastroenterology specialty	1.87 (0.97–3.60)	0.06	1.60 (0.79–3.24)	0.20
Consultant	1.52 (0.95–2.43)	0.08	1.26 (0.73–2.20)	0.41
Techniques				
Anti-spasmotic agent	1.45 (1.01–2.09)	0.04*	1.34 (0.90–1.98)	0.15
Narrow band imaging	1.50 (0.96–2.35)	0.08	1.50 (0.91–2.49)	0.10
Complete extent reached	2.17 (1.13–4.16)	0.02*	1.91 (0.95–3.84)	0.07
Withdrawal time (per minute)	1.05 (1.03–1.07)	< 0.001*	1.06 (1.04–1.08)	< 0.001*