

ORIGINAL RESEARCH

BowelScope: Accuracy of Detection Using Endocuff Optimisation of Mucosal Abnormalities (the B-ADENOMA Study): a multicentre, randomised controlled flexible sigmoidoscopy trial

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ABSTRACT

Objectives Adenoma detection rate (ADR) is an important quality marker at lower GI endoscopy. Higher ADRs are associated with lower postcolonoscopy colorectal cancer rates. The English flexible sigmoidoscopy (FS) screening programme (BowelScope), offers a one-off FS to individuals aged 55 years. However, variation in ADR exists. Large studies have demonstrated improved ADR using Endocuff Vision (EV) within colonoscopy screening, but there are no studies within FS. We sought to test the effect of EV on ADR in a national FS screening population.

Design BowelScope: Accuracy of Detection Using Endocuff Optimisation of Mucosal Abnormalities was a multicentre, randomised controlled trial involving 16 English BowelScope screening centres. Individuals were randomised to Endocuff Vision-assisted BowelScope (EAB) or Standard BowelScope (SB). ADR, polyp detection rate (PDR), mean adenomas per procedure (MAP), polyp characteristics and location, participant experience, procedural time and adverse events were measured. Comparison of ADR within the trial with national BowelScope ADR was also undertaken.

Results 3222 participants were randomised (53% male) to receive EAB (n=1610) or SB (n=1612). Baseline demographics were comparable between arms. ADR in the EAB arm was 13.3% and that in the SB arm was 12.2% (p=0.353). No statistically significant differences were found in PDR, MAP, polyp characteristics or location, participant experience, complications or procedural characteristics. ADR in the SB control arm was 3.1% higher than the national ADR.

Conclusion EV did not improve BowelScope ADR when compared with SB. ADR in both arms was higher than the national ADR. Where detection rates are already high, EV is unable to improve detection further.

Trial registration numbers NCT03072472, ISRCTN30005319 and CPMS ID 33224.

INTRODUCTION

A total of 16 000 people die in the UK annually from colorectal cancer (CRC), with 1.4 million cases worldwide in 2012.¹ The English National Health

Significance of this study

What is already known on this subject?

- ▶ We searched MEDLINE and PubMed for publications in humans up to July 2019 using the terms 'Endocuff' (EC) and 'Endocuff Vision' (EV). We identified 11 randomised controlled trials (RCTs) and four case series studies. This included our own group's study (the ADENOMA study) published in 2018. Two other RCTs and the ADENOMA study used the EV device, while the remainder used the original EC. The ADENOMA trial demonstrated an increase in adenoma detection rate (ADR) of 4.7% overall, driven by a bowel cancer screening subgroup increase of 10.8%. One EV study demonstrated an improvement in ADR of 7.8%, which was not statistically significant but was accompanied by a significant increased polyp detection rate of 11.9%. A single-centre trial showed no increase in ADR with EV, influenced by an exceptionally high ADR in both trial arms.
- ▶ Of the RCTs which used the original EC device, three showed increases in ADR of 3.3%, 8.9% and 14.7%, respectively; one reported a lower adenoma miss rate of 23.7%, but the rest did not demonstrate any significant difference in ADR. Findings from the case series reported an improved mean number of adenomas detected per procedure and ADRs of up to 44.7%.

Service (NHS) Bowel Cancer Screening Programme (BCSP) delivers two CRC screening programmes: a faecal occult blood test (FOBT)-based programme for people aged 60–74 years and one-off flexible sigmoidoscopy (FS) examination for people aged 55 years (termed BowelScope).² Evidence demonstrates that one-off FS between ages 55 and 64 years can reduce CRC incidence by 23% and deaths by 31%.³ FS and subsequent polypectomy interrupts the adenoma–carcinoma sequence, preventing progression to CRC.⁴ At BowelScope, if >3 adenomas, a polyp with villous histology or high



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Significance of this study

What are the new findings?

► To the best of our knowledge, this is the first trial of EV in a flexible sigmoidoscopy (FS) population, and it is the largest endoscopy randomised controlled device trial ever reported. The trial did not show an increase in ADR in the EV arm of this average risk population; however, both the control arm ADR (12.2%) and the intervention arm ADR (13.3%) were significantly higher than the ADR in the broader national BowelScope programme (9.1%). EV was well tolerated.

How might it impact on clinical practice in the foreseeable future?

► EV has not been proven to increase ADR in an average risk population such as those undergoing FS screening. This contrasts with the increase in ADR in individuals at increased risk of adenomas (those who are faecal occult blood positive). Where ADR is high, it is unlikely that EV can increase detection further; however, it may be of value to endoscopists with lower detection rates. Future EV research should focus on which specific endoscopy populations EV will benefit.

grade dysplasia, a polyp of >10 mm in size, >20 hyperplastic polyps above the rectum or a polyp which cannot be removed due to patient factors are found, individuals are referred for full colonoscopy. BowelScope is predicated on the ability of the investigation to maximise detection of adenomas present in the examined part of the colon. Details of BowelScope have been described elsewhere.^{2,5}

The most widely used measure of mucosal visualisation at lower GI endoscopy is adenoma detection rate (ADR).^{6,7} ADR in BowelScope is lower than that in FS trials, varying between centres and endoscopists.^{3,5,8,9} Factors influencing ADR at lower GI endoscopy include withdrawal time, use of antispasmodic medication, quality of bowel preparation and, crucially, adequate visualisation of the proximal aspect of mucosal folds.^{10,11} One approach to improve detection is using devices to hold back folds and to enhance mucosal visualisation. Endocuff Vision (EV) (figure 1) is a polypropylene device mounted onto the distal tip of a colonoscope.¹² EV consists of a fixed portion and a row of eight soft projections which folds backward during insertion but pulls forward during withdrawal to evert and slowly release colonic folds. This is



Figure 1 Endocuff vision (photograph taken by the author).

a second-generation device with the earlier Endocuff (EC) improving ADR in some colonoscopy studies.^{13–15}

A recent multicentre RCT, the ADENOMA trial, undertaken in participants attending for colonoscopy, demonstrated a significant increase in ADR using EV.¹⁶ ADENOMA demonstrated a 4.7% higher ADR in the intervention arm ($p=0.02$) driven by a 10.8% higher ADR ($p<0.001$) in FOBT-positive BCSP participants undergoing colonoscopy. The greatest benefit was in the left colon, considered to be due to its increased tortuosity and prominent folds. No studies have investigated EV in FS. The effects of a device on total procedure time, completion rate, indirect health economic effects of finding more polyps and effect of a device on the experience of participants, particularly procedural comfort, are important. The acceptability of an investigation is vitally important to screening tests.^{17,18} BowelScope: Accuracy of DDetection Using Endocuff OOptimisation of Mucosal Abnormalities (B-ADENOMA) was an RCT comparing FS with and without EV in the English BowelScope screening programme. B-ADENOMA sought to determine the effect of EV on ADR, other detection markers and any other impact on BowelScope procedures.

METHODS

Study design

B-ADENOMA was a multicentre RCT recruiting patients from 16 hospitals in England between February 2017 and February 2018. All hospitals delivered dedicated BowelScope lists. A short learning curve has previously been identified for EV use; therefore, all endoscopists had to complete a minimum of 10 EV procedures prior to the study.^{16,19}

The B-ADENOMA protocol has been published,²⁰ registered with clinicaltrials.gov and International Standard Randomised Controlled Trials, and adopted onto the UK NHS National Institute for Health Research (NIHR) portfolio.

Participants

BowelScope screening invites all 55-year-olds for a one-off procedure; however, individuals between 55 and 61 years may contact screening centres and opt into BowelScope. Participants receive a BowelScope appointment at their closest local screening hospital. B-ADENOMA recruited BowelScope individuals aged 55–61 who were able to give informed, written consent. Exclusion criteria included absolute contraindications to FS, known or suspected bowel obstruction, colonic strictures, polyposis syndromes, known severe diverticular segment, active colitis, anticoagulation precluding polypectomy and pregnancy. BowelScope procedures were done without sedation. Reasons to withdraw participants from the trial after randomisation were withdrawal of consent or new diagnosis of a polyposis syndrome. These individuals were excluded due to the different natural history of development of these polyps and significant malignant potential. All inclusion and exclusion criteria can be found in the protocol summary on the International Standard Randomised Controlled Trial Number (ISRCTN) registry.

Standard BowelScope (SB) was undertaken in accordance with standard National Health Service Bowel Cancer Screening Programme (NHSBCSP) procedures.²¹ Data were recorded on the Bowel Cancer Screening System database from which trial data were also reported.

Endocuff Vision-assisted BowelScope (EAB) was performed using the same protocol as SB with the following modifications: once in procedure room, the endoscopist and staff were made

aware of the randomisation outcome and EV was attached to the tip of the endoscope according to manufacturer's instructions.

Removal of EV during BowelScope was advised if the endoscopist felt the device was hindering safe progression. Reasons for this included acute angulation in fixed sigmoid colon, colonic stricture, new diagnosis of malignancy or new diagnosis of active colitis (endoscopist concern over risk of mucosal damage).

Randomisation and masking

Stratified randomisation based on age, sex and hospital site was performed using a dynamic allocation algorithm created by the North Wales Organisation for Randomised Trials in Health Clinical Trials Unit using a computerised internet-based platform.²² It was not possible to blind endoscopists, endoscopy staff, research teams or participants to randomisation allocation as EV was visible on the end of the colonoscope.

Outcomes

The primary outcome was the proportion of participants with one or more colorectal adenomas detected at BowelScope as measured by the ADR.

Secondary outcomes were polyp detection rate (PDR); sessile serrated polyps detection rate; advanced ADR; cancer (cancerous polyps, those found to be cancerous on histological assessment) or endoscopic cancer (lesion felt to be a cancer by the endoscopist) detection rate; mean number of adenomas detected per procedure; mean number of polyps detected per procedure; mean number of advanced adenoma detected per procedure; polyp size (measured in millimetre); polyp morphology (Paris classification); polyp location (transverse colon, splenic flexure, sigmoid colon or rectum); procedure withdrawal time (in minutes, recorded in procedures where no lesions were detected to remove confounder of time taken for lesion removal); procedure completion time (in minutes, recorded in procedures where no lesions were detected to remove confounder of time taken for lesion removal); reach of procedure (transverse colon, splenic flexure, sigmoid colon or rectum); discomfort assessed by patient (0–9 scale); discomfort assessed by nurse (0–4 scale); complication rate (adverse events (AEs) related to the procedure); rate of conversion colonoscopies generated; and rate of EV change (how often the cuff was removed).

Additional explanatory analyses included comparison of ADRs of the first 20% of procedures for each endoscopist with the last 20% of procedures for each endoscopist in each arm to identify changes due to learning curve effect, and comparison of endoscopist ADR pretrial and within trial; post hoc explanatory comparison of ADR within the trial with NHSBCSP data were also undertaken.

The modified Gloucester score was used by nursing staff to record patient comfort as per BowelScope practice, and a truncated Nurse-Assessed Patient Comfort Score (NAPCOMS) was given to participants pre-discharge and for completion at 24 hours.^{23 24} Participants were followed up for 14 days for late complications and to check polyp histology. AEs or serious AEs were defined a priori in the trial protocol and reported to the data monitoring committee (DMC), with severity and relation to EV reviewed by two independent clinicians. A full list of endpoints can be found in the protocol summary on the ISRCTN registry.

Statistical analysis

This trial was powered to detect a difference in ADR at BowelScope between EAB and SB. National BowelScope ADR at trial commencement was 8.8% (BCSP national data). This figure

was used to power the trial; however, subsequent analyses used the more up-to-date published national ADR of 9.1%.⁹ An increase in ADR of 3% was agreed to be clinically significant. Using a two-sided test with 5% significance level and 80% power, the trial required 1611 participants per group to detect a statistically significant difference in the proportion of participants with adenomas, as measured by ADR, between trial arms.

All analyses were conducted on an intention-to-treat basis. Tests of non-inferiority (procedure withdrawal and completion time) were analysed on both per protocol and intention-to-treat basis. Secondary analyses (PDR, polyp location and comfort scores) were adjusted for multiple comparisons using Bonferroni correction. All other analyses, performed using a 5% significance level with 95% CIs, are presented. All statistical tests and CIs were two-sided. A fully defined statistical analysis plan was written and agreed upon prior to completion of data collection. When conducting analysis, trial statisticians were blinded as to which arm was which.

For the primary binary outcome, of whether an adenoma was detected or not, logistic regression was employed to compare the difference in primary outcome between groups, taking into account randomisation stratification variables (endoscopy site, sex and age group). Similarly, for secondary outcomes of PDRs, sessile serrate polyps, advanced adenoma and cancer, logistic regression was employed to compare the differences between the EAB and SB groups, adjusting for the effects of the randomisation stratification variables (endoscopy site, sex and age).

The secondary outcomes based on the number of adenomas, polyps and advanced adenomas detected were analysed using analysis of variance (ANOVA) models, which adjusted for the effects of randomisation stratification variables. Secondary outcomes concerning characteristics of the detected polyps (polyp size, morphology and location) were compared between the EAB and SB groups. For polyp size, an ANOVA was conducted, and for polyp morphology and location, multinomial logit regressions were conducted.

Non-inferiority testing for withdrawal and completion times involved using an ANOVA and a non-inferiority margin of 1 min, which was deemed a minimal clinically important difference. To determine whether the examination extent of the EAB group was inferior to SB, descriptive analysis was used where the proportion of procedures for each extent of examination was calculated for both groups, and clinician judgement was used to determine if they were inferior. A χ^2 test was also undertaken to compare the examination extent between the two groups. Non-inferiority testing for participant experience of comfort involved conducting ANOVAs using a non-inferiority margin of one point for participant experience of comfort. Non-inferiority testing for complication rates involved conducting a logistic regression with a non-inferiority margin of 10%.

Logistic regression was employed to compare the rate of conversion colonoscopies generated by the EAB and SB groups. Repeated measures t-tests were used to compare the ADR for the first 20% of procedures with the ADR for the last 20% of procedures for each endoscopist.

Dropouts were defined as patients who were randomised to enter the study but for some reason did not complete it (ie, withdrew). Given the low percentage of missing data, the complete case approach to dealing with missing data was employed in line with the recent recommendations of best practice.²⁵ As this trial was aimed to detect differences in detection rates at BowelScope as affected by EV, the detection rates for subsequent colonoscopy procedures were not measured.

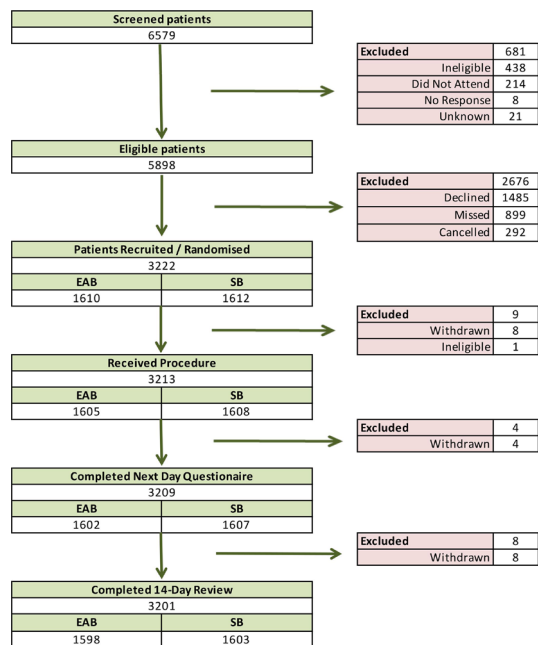


Figure 2 Consort flow diagram. EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

Patient and public involvement

Patient and public involvement informed the development, conduct and reporting of this study with a patient representative on the trial steering committee. Input was also obtained from local patient groups and patient and public representation on the National Cancer Research Institute CRC screening and prevention group.

RESULTS

A total of 6579 individuals were identified and assessed for trial eligibility between 14 February 2017 and 13 February 2018 (figure 2). A total of 3357 individuals were excluded, with the most common reasons being ineligibility (438), not attending for BowelScope (214), declining the study (1485) and individuals who were not recruited at procedure, for example, unavailable research staff (899) and procedure cancellation (292). A total of 3222 individuals were randomised into the study, with one found to be ineligible postrandomisation.

Patient demographics were balanced across arms. The mean age of the participants was 55 years. Fifty-three per cent of the participants were male and 22% had prior abdominal surgery (table 1).

Data from participants who dropped out and those with missing data are reported in table 1 but were not analysed further. Dropout rates were comparable across arms EAB (0.4%,

n=7) and SB (0.3%, n=5). The percentage of missing data was 0.33%. These missing data were in 53 patients, spread evenly across both trial arms; thus, complete case analyses were undertaken on 1578 patients in each arm.

No significant difference was demonstrated in the primary outcome. ADRs in the EAB and SB arms were 13.3% and 12.2%, respectively. Results of logistical regression analyses for other detection markers were adjusted to account for randomisation stratification variables (age group, sex and endoscopy site) and are summarised in table 2.

Results of the number of lesions detected using ANOVA and adjusted to account for randomisation stratification variables (age group, gender and endoscopy site) are summarised in table 3.

Regarding the characteristics of the detected polyps, no statistically significant differences were observed between the EAB and SB groups for the size of polyps detected (4.68 mm vs 4.79 mm, mean difference = -0.11, p=0.635, 95% CI 0.58 to 0.35). Similarly, there were no statistically significant differences between the EAB and SB groups for polyp morphology ($\chi^2(6)=8.04$, p=1; table 4) and polyp location ($\chi^2(4)=3.88$, p=1; table 5).

Analyses of withdrawal time and overall procedure time (in procedures where no lesions were detected) demonstrated no inferiority of EAB relative to SB. The difference in withdrawal duration between the EAB group (mean=3.32, SD=2.05) and the SB group (mean=3.44, SD=2.00) was -0.11 min (95% CI -0.25 to 0.03), which did not cross the specified non-inferiority boundary of 1 min. The difference in procedure duration between the EAB group (mean=7.80, SD=3.49) and the SB group (mean=8.03, SD=3.69) was -0.23 min (95% CI -0.48 to 0.03), which also did not cross the specified non-inferiority boundary of 1 min. Intention to treat and per protocol analyses were comparable since there were only five protocol deviations: three in EAB and two in SB.

The reach of the procedures for the EAB and SB groups is summarised in table 6. There was a statistically significant difference in the extent reached, as judged by endoscopist, between the EAB and SB groups ($\chi^2(4)=18.99$, p<0.001), with further extent reached in the SB arm. Post hoc testing showed that there were statistically significant differences between the EAB and SB groups for sigmoid, ($\chi^2(1)=9.81$, p=0.002), splenic flexure ($\chi^2(1)=6.72$, p=0.010) and transverse ($\chi^2(1)=6.13$, p=0.013) extent.

Analyses of comfort demonstrated non-inferiority of EAB compared with SB. Greater discomfort was reported by the patients (+0.26 point, 95% CI 0.1 to 0.43) and the endoscopy nursing staff (+0.11 point, 95% CI 0.03 to 0.19) in the EAB arm compared with the SB arm; however, although these differences

Table 1 Summary of participant characteristics

	EAB (n=1609) (%)	SB (n=1612) (%)
Sex		
Female	757 (47)	758 (47)
Male	852 (53)	854 (53)
Previous abdominal surgery		
No	1243 (77.3)	1276 (79.2)
Yes	365 (22.7)	334 (20.7)
Unknown	1 (0.1)	2 (0.1)

EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

Table 2 Summary of detection rate results from the logistic regression and adjusted to account for randomisation stratification variables (age group, gender and endoscopy site)

	EAB % (n*) n=1578	SB % (n*) n=1578	OR	95% CI	P value
Adenoma detection rate	13.3 (209)	12.2 (193)	1.11	0.90 to 1.37	0.353
Polyp detection rate	28.6 (451)	26.6 (420)	1.11	0.89 to 1.39†	1.0†
Sessile serrated polyps	0.3 (5)	0.3 (4)	1.32	0.34 to 5.42	0.686
Advanced adenoma	6.1 (95)	5.0 (80)	1.23	0.90 to 1.69	0.200
Cancer	0.2 (3)	0.4 (6)	0.48	0.10 to 1.85	0.292

*Raw frequency.
†In accordance with the predefined statistical analysis plan, only the key secondary analyses were adjusted for multiple comparisons.
EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

Table 3 Summary of the quantity of lesions detected results

	EAB (mean, SD, n)	SB (mean, SD, n)	Mean difference	95% CI	P value
Mean number of adenomas	0.23, 0.47, 1578	0.21, 0.43, 1578	0.02	-0.01 to 0.05	0.153
Mean number of polyps	0.53, 0.92, 1578	0.49, 0.85, 1578	0.04	-0.02 to 0.12	0.190
Mean number of advanced adenomas	0.07, 0.28, 1578	0.06, 0.25, 1578	0.01	-0.02 to 0.10	0.216

EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

were statistically significant, they did not reach the level of clinical significance as agreed upon pretrial, which was set at 1 point of difference on both assessment scales.

Complication rates (AEs related to the procedure) were identical between the EAB (0.3%) and SB (0.3%) groups; hence, non-inferiority of EAB compared with SB was demonstrated.

Logistic regression adjusting for randomisation stratification variables revealed no statistically significant differences in the number of conversion colonoscopies generated between the EAB (8.4%) and SB (6.8%) groups (OR=1.27, 95% CI 0.97 to 1.67). As a consequence, there was also no difference in workload of colonoscopy or surveillance generated based on polyp follow-up by guidelines.²⁶ The rate of EV exchange in the EAB group was 4.21% (95% CI 2.97 to 5.95). Endoscopists performed procedures using both SB and EAB, and the distribution of number of procedures performed is depicted in figure 3.

There was no difference at the level of individual endoscopists between ADR 6 months pretrial and the ADR of those endoscopists in the control arm (SB) of the trial (10.1% vs 11.4%, $t(44)=0.93$, $p=0.355$, mean difference=1.3%, 95% CI -0.01% to 0.04%). For the EAB arm, there was a statistically significant difference in ADR for the first 20% of patients compared with the last 20% of patients per endoscopist (8.6% vs 16.6%, $t(51)=2.23$, $p=0.030$, mean difference=8.0%, 95% CI 0.81% to 15.09%). For the SB arm, there was no statistically significant difference in ADR for the first 20% of patients compared with the last 20% of patients per endoscopist (9.2% vs 14.2%, $t(51)=1.77$, $p=0.083$, mean difference=5.0%, 95% CI -0.68% to 10.59%). However, although this difference was not statistically significant, it is substantial, especially given that a difference of 3% or greater had been deemed clinically significant. Furthermore, further explorative analysis (shown in figure 4) strongly suggests that there is evidence for a trial progression effect in the both the EAB and SB groups; that is, in both arms, the ADR rose as recruitment to the trial proceeded.

DISCUSSION

B-ADENOMA was a multicentre RCT delivered across 16 English endoscopy units. To our knowledge, this is the largest endoscopy device trial ever conducted. There are no other trials examining the use of EV during FS. The trial did not demonstrate a significant difference in ADR detection between EAB and SB in the English

NHS BowelScope Flexible Sigmoidoscopy Cancer Screening Programme.

EV previously demonstrated improved detection at colonoscopy in the ADENOMA trial, but only among participants recruited through the BCSP and thus FOBt positive,¹⁶ that is, a population with high rates of pathology. No increase in detection was demonstrated in an average risk population in the ADENOMA trial. BowelScope invites unselected asymptomatic 55 year olds who are at average population risk of colorectal neoplasia.

It is important to explore why EV improves detection in some settings and not others. ADR in the control arm of this study was much higher than in SB practice, and it is likely that the high detection rates of pathology in the control arm could not be improved on with EV. At the beginning of this study, ADR in the national BowelScope programme was 8.8% (Public Health England figures) and, more recently, several years into the programme, had only risen to 9.1%.⁹ The high control arm ADR of 12.2% in this trial is well above (3.1% higher) national ADR, and it is likely that this high ADR meant that EV was unable to confer additional improvements in ADR. In contrast to the ADENOMA trial, a single-centre UK EV study demonstrated no difference in ADR using EV in FOBt-positive screening patients undergoing colonoscopy.¹⁹ In that trial, ADR in the control arm was much higher (63%) than national figures. Similarly, a Netherlands study, while using the original EC, found a higher than expected ADR in the control arm (52%) and did not see an increase in ADR when EC was used.²⁷ These results demonstrate a consistent pattern: where control arm ADR is high (higher than reported ADR in those populations), the intervention arm (EV) does not demonstrate an increase in ADR. In any population endoscoped, there will be a ceiling where all present polyps have been detected and the addition of a device or technology to improve detection will not be able to raise that ceiling and increase detection further. In three other trials using the original EC where baseline ADRs were comparatively low (13.5%, 20.7% and 26.3% respectively), ADR improvements were demonstrated.¹³⁻¹⁵ EV and the original EC are not the same device, so direct comparisons are not possible; however, these findings reinforce the same message that low ADR may be improved, but there will be a level at which further improvement is not possible.

High ADRs seen in the control group arms of the current and previous trials may be influenced by high ability of endoscopists operating in centres participating in clinical research or influenced by research causing a change in practice.^{19 27} Individuals who agree to participate as endoscopists in research may self-select

Table 4 Summary of the modal polyp morphology for each procedure as a function of group

	EAB (%)	SB (%)
lp	31 (6.8)	30 (7.0)
lps	36 (7.9)	28 (6.6)
ls	244 (53.6)	209 (48.9)
0-IIa	136 (29.9)	156 (36.5)
0-IIa/c	2 (0.4)	3 (0.7)
0-IIb	5 (1.1)	1 (0.2)
0-IIc	0 (0)	0 (0)
0-IIc/IIa	1 (0.2)	0 (0)

EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

Table 5 Summary of the modal polyp location for each procedure as a function of group

	EAB (%)	SB (%)
Rectum	184 (40.3)	176 (41.0)
Sigmoid	232 (50.1)	212 (49.4)
Descending	35 (7.7)	33 (7.7)
Splenic flexure	6 (1.3)	7 (1.6)
Transverse	0 (0)	1 (0.2)

EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

Table 6 Anatomical location, as judged by endoscopist, reached during procedure as a function of group

	EAB (%)	SB (%)
Rectum	7 (0.4)	7 (0.4)
Sigmoid	372 (23.2)	301 (18.7)
Descending	762 (47.6)	738 (45.9)
Splenic flexure	367 (22.9)	432 (26.9)
Transverse	93 (5.8)	129 (8.0)

EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

and be detectors with higher performance levels. This principle was suggested by the Netherlands study,²⁷ where it was noted that endoscopists who had a high ADR prior to the use of EC benefitted little from addition of the device. Change in behaviour among practitioners participating in trials is well recognised. While the Hawthorne effect refers to changes in behaviour of individuals when they are being studied, it may be that endoscopists participating in research change practice and become more thorough in their mucosal inspection with or without device enhancement leading to above-normal performance.^{28, 29} It is also possible that endoscopists performing both control and intervention endoscopies change their technique both with and without the EV. This effect was suggested in a pilot study where an increase in ADR using EV in a colonoscopy screening population persisted when EV was no longer used when compared with the period before introduction of the device, although this difference did not achieve statistical significance.¹² The current trial demonstrates an ongoing rise in ADR throughout the study, providing evidence that endoscopist practice changed throughout the trial.

A number of patient factors are known to affect polyp prevalence including sex, age, ethnicity, smoking and obesity.^{9, 30} This was a multisite study of 16 centres across wide English geography with equivalent characteristics across the two arms, so this is unlikely to have influenced the outcome. We have no evidence to suggest the population studied was unrepresentative of the English BowelScope screened population with pretrial ADR for participating sites comparable to national figures. By randomising by participants and not endoscopists, this trial has demonstrated the effect of EV on detection. An alternative could have been to employ a cluster methodology whereby endoscopists rather than participants were randomised and only performed either EAB or SB. This could potentially have limited the influence of practice changes using a device being employed without the device; however, this could have introduced other confounders around endoscopist characteristics, and we believe the current trial design to be better. If the true difference between the groups was smaller than anticipated (eg, 1.1% as seen rather than the 3% used for power calculation), the study would not have been adequately powered to demonstrate

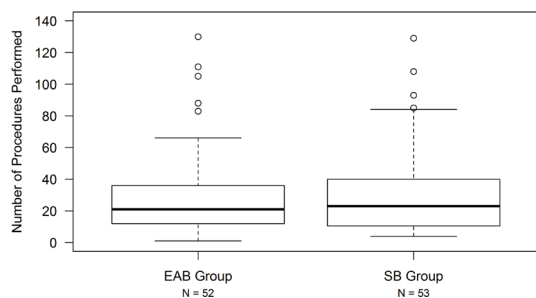


Figure 3 Total number of procedures performed by an endoscopist for each group. EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

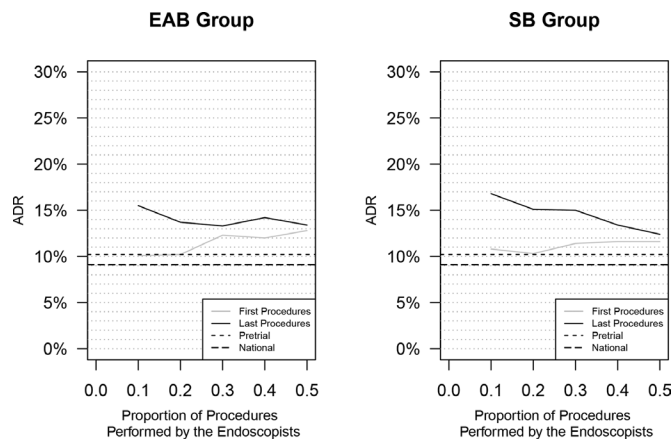


Figure 4 ADR for the first proportions of procedures versus ADR for the last proportions of procedures as a function of split size and group allocation. ADR, adenoma detection rate; EAB, Endocuff Vision-assisted BowelScope; SB, Standard BowelScope.

statistical significance. However, were this to be the case, the clinical significance of a 1% increase in ADR would be small, and the authors would consider this not to be a clinically important value.

Comfort, procedural time and complication rates are crucial to the success of screening procedures, which must be effective, safe and acceptable to the screened population.^{17, 18} In our study, EV was associated with a statistically significant increase in participant and endoscopy nurse-reported discomfort. However, this was not deemed clinically significant as set out by pretrial levels for non-inferiority analysis of 1 point on the modified NAPCOMS of 0–9 points used by participants and the modified Gloucester scale of 0–4 points used by endoscopy nursing staff. EV demonstrated a trend towards shorter withdrawal and overall procedural times, consistent with other studies. EV was not associated with an increase in complications.^{12, 27}

We summarise that EV does not increase detection in an average risk population among endoscopists who already have high ADRs. It is possible that endoscopists with ADRs more consistent with or below national detection rates might benefit from EV use, but we are unable to prove that assertion. It should be noted that while EV did not enhance detection, although the extent of the procedure was less with EV, this did not equate to a reduction in ADR. EV was safe and not associated with any increase in complication rates. Patient comfort was not adversely affected significantly.

To our knowledge, B-ADENOMA is the largest endoscopy device trial ever reported, and it recruited from 16 units in half the anticipated time of 9 rather than 18 months. This study demonstrates the ability of a well-motivated network of endoscopy units to achieve rapid large-scale recruitment.

CONCLUSION

The B-ADENOMA trial did not demonstrate increased detection with EV in an average risk population undergoing FS. The ADRs in both the control arm and the intervention arm were significantly higher than those in the SB FS screening practice.

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Correction notice This article has been corrected since it published Online First. The arrow alignment in figure 2 has been corrected.

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Contributors CJR: designed the study, contributed to the running of study, recruited patients to the study, analysed results, and reviewed and contributed to the writing of manuscript; AB, WSN and ZH: contributed to the study design, reviewed the analysis, and reviewed and contributed to the writing of the manuscript; CS: managed trial sites and reviewed and contributed to the writing of the manuscript; NT: contributed to the study design, data custodian during the trial conduct, reviewed the analysis, and reviewed and contributed to the writing of the manuscript; PB, MDR, AMV and TJL: contributed to running of the study, recruited patients to the study, analysed the results, and reviewed and contributed to the writing of the manuscript; LS: analysed the results, reviewed and contributed to the writing of the manuscript; AB: contributed to running of the study, assisted in the analysis of the results, and reviewed and contributed to the writing of the manuscript; MW: contributed to the study design, ran the study, recruited patients to the study, analysed the results, and reviewed contributed to the writing of the manuscript.

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