Rates of Repeated Colonoscopies to Clean the Colon from Low and High Risk Adenomas - Results from the EPoS trials

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Abstract

Objective

High-quality colonoscopy (adequate bowel preparation, whole-colon visualization, and removal of all neoplastic polyps) is a prerequisite to start polyp surveillance, and is ideally achieved in one colonoscopy. In a large multinational polyp surveillance trial, we aimed to investigate clinical practice variation in number of colonoscopies needed to enroll patients with low-risk and high-risk adenomas in polyp surveillance.

Design

We retrieved data of all patients with low-risk adenomas (one or two tubular adenomas <10mm with low-grade dysplasia) and high-risk adenomas (3-10 adenomas, ≥1 adenoma ≥10mm, high-grade dysplasia or villous components) in the European Polyp Surveillance trials fulfilling certain logistic and methodologic criteria. We analyzed variations in number of colonoscopies needed to achieve high-quality colonoscopy and enter polyp surveillance by endoscopy center, and by endoscopists who enrolled ≥30 patients.

Results

The study comprised 15,581 patients from 38 endoscopy centers in five European countries; 6,794 patients had low-risk and 8,787 had high-risk adenomas. 961 patients (6.2%, 95%CI: 5.8-6.6) underwent two or more colonoscopies before surveillance began; 101 (1.5%, 95%CI: 1.2-1.8) in the low-risk group and 860 (9.8%, 95%CI: 9.2-10.4) in the high-risk group. Main reasons were poor bowel preparation (21.3%) or incomplete colonoscopy/ polypectomy (14.4%) or planned second procedure (27.8%). Need of repeat colonoscopy varied between study centers ranging from 0% to 11.8% in low-risk adenoma patients and from 0% to 63.9% in high-risk adenoma patients). On the second colonoscopy, the two most common reasons for a repeat (third) colonoscopy were piecemeal resection (26.5%) and unspecified reason (23.9%).

Conclusion

There is considerable practice variation in the number of colonoscopies performed to achieve complete polyp removal, indicating need for targeted quality improvement to reduce patient burden. Clinicaltrials.gov: NCT02319928.

Key messages

What is already known on this topic

High-quality colonoscopy is a prerequisite to start polyp surveillance, and is ideally achieved in one colonoscopy. However, little is known about the frequency with which repeated colonoscopies are performed to achieve these high-quality requirements.

What this study adds

Our study shows considerable variation between endoscopy centers and endoscopists in the frequency of repeat baseline colonoscopy for patients with polyps before entering surveillance.

How this study might affect research, practice or policy

Endoscopy services may measure their rate of repeat colonoscopy in patients with polyps to identify potential areas for improvement.

Introduction

Whilst colonoscopy with polypectomy protects against colorectal cancer (CRC), post-polypectomy surveillance is believed to provide additional benefit.[1 2] Thus, colonoscopy surveillance is generally recommended for patients after polyp removal.[3 4]

High-quality colonoscopy is a prerequisite to assign patients to appropriate polyp surveillance schemes and requires adequate bowel preparation, visualization of the whole colon, and detection and complete removal of all neoplastic polyps.[5] Ideally, these goals should be achieved in a single colonoscopy (so-called baseline colonoscopies; colonoscopies before surveillance can start) in most patients.[3 5]

Unwanted variation in clinical practice is variation that can be targeted by quality improvement. It is recognized as a major challenge for health care systems.[6] Unwanted variation analyses describe potential challenges in local quality of care. Following principles of modern quality improvement, services or individual physicians deviating from their peers in key performance indicators are offered follow-up with individualized audits to assess reasons for the observed variation. If challenges in local quality are confirmed, targeted quality improvement measures are implemented to improve service or individual performance, reduce variation, and increase quality of care.[6] Importantly, variation due to non-influenceable variables (such as differences in patient comorbidities which affect outcomes in a tertiary care center as compared to a community practice) are not unwanted variation but confounders of variation analyses and are not target for quality improvement.

Unwanted variation in number of patients in need of repeat baseline colonoscopies before entering polyp surveillance increase costs and add to patient burden. Possible reasons for a patient to undergo more than one baseline colonoscopy before surveillance can start may be suboptimal endoscopist performance or inadequate colonoscopy center services. Examples of

inadequate colonoscopy center services include handling of patients with needs related to literacy, compliance or comorbidities resulting in poor bowel cleansing or anticoagulation therapy that is not discontinued before colonoscopy, or inappropriate time schedules, work-flow or staff communication.[7]

There is limited evidence regarding clinical practice variation for treatment of patients with colorectal polyps to meet high-quality requirements for baseline colonoscopy as recommended in current guidelines.[4 7] Thus, needs and opportunities for improvement are unknown. With more than 10 million estimated screening colonoscopies yearly performed in the United States alone,[8] unwanted variation in need of repeat colonoscopies to meet high-quality requirements may have important consequences for patients and payers.

We took advantage of the European Polyp Surveillance (EPoS) project which includes three large, randomized trials of polyp surveillance in eight European countries with a homogenous group of patients with high-risk and low-risk adenomas. We investigated variations in the need of repeated baseline colonoscopies to meet high-quality requirements before enrolment of patients in polyp surveillance.

Methods

The EPoS project

The EPoS project includes three clinical trials performed in eight European countries (Austria, Denmark, Norway, Poland, Portugal, Spain, Sweden and The Netherlands) investigating the impact of different surveillance intervals on CRC incidence during 10-years follow-up. The rationale and design of the EPoS project have been described in detail elsewhere.[9]

Briefly, from April 2015 through March 2020, patients aged 40-74 years who had colorectal polyps removed at participating endoscopy centers were invited to participate in EPoS.

Patients with one or two tubular adenomas <10 mm in diameter with low-grade dysplasia at baseline colonoscopy were classified as low-risk, enrolled in the EPoS I trial and randomized to surveillance after 5 and 10 years, or surveillance after 10 years only.

Patients with 3-10 adenomas, one or more adenoma ≥10 mm in diameter, or one or more adenoma with high-grade dysplasia or villous growth pattern at baseline colonoscopy were classified as high-risk, enrolled in EPoS II trial and randomized to surveillance after 3, 5 and 10 years, or surveillance after 5 and 10 years only.[9]

Patients with more than 10 adenomas, genetic cancer syndromes (adenomatous or serrated polyposis syndrome; Lynch or Lynch-like syndrome), inflammatory bowel disease, history of surgical colon resection for any reason, severe co-morbidity with reduced life expectancy (NYHA 3-4), ongoing cytotoxic treatment or radiotherapy for malignant disease, long-lasting attention and nursing services, non-retrieval of any polyp (EPoS I trial) or non-retrieval of any polyp ≥10 mm (EPoS II trial) were not eligible for the EPoS trials.

The current report does not include data from the EPoS III trial, a single-arm trial for patients with serrated polyps, because of smaller number of included patients and more heterogeneous polyp characteristics than in EPoS trials I and II.[9]

To be enrolled in the EPoS trials, high-quality baseline colonoscopy was required, defined according to current guidelines[3] by adequate bowel cleansing as assessed by a Boston Bowel Preparation Scale[10] score of two or higher in all colon segments, full visualization of all colon segments, and complete removal of all detected polyps as assessed by the endoscopist.

If high-quality colonoscopy could not be achieved in a single procedure, one or more repeat baseline colonoscopies within 52 weeks were allowed before patients could be enrolled in one

of the EPoS trials. For all enrolled patients, details of all baseline colonoscopies were reported to the EPoS project database.

For the present study, we retrieved data from the EPoS project database for all baseline colonoscopies in patients enrolled in EPoS trial I or II. The main outcome variable was the number of baseline colonoscopies per patient needed to achieve high-quality assessment and enter surveillance in EPoS for each participating endoscopist, endoscopy center and country.

Study concept and analyses

Because eligibility for EPoS is defined by strict inclusion and exclusion criteria, the included patients share polyp and patient characteristics across endoscopy centers. Conceptually, performance differences are therefore not justifiable (they do not represent unwanted variation) for the number of baseline colonoscopies needed to achieve high-quality assessment.

We performed crude analyses without adjustment for patient and polyp variables between endoscopist and endoscopy center, and present descriptive statistics of the following variables: indication for first baseline colonoscopy (clinical sign or symptoms; colonoscopy screening; colonoscopy after a positive screening test (i.e.: Fecal Immunochemical Test (FIT)); other (e.g. family history of CRC)); Boston Bowel Preparation score (dichotomized into adequate (score two or higher in all segments) or not adequate (score one or lower in any segment); complete colonoscopy (proportion with cecum intubation); number of polyps removed; size of largest polyp removed; number of adenomas removed; size of largest adenoma removed; indication for repeat baseline colonoscopy (endoscopists were asked to choose the most appropriate alternative: anticoagulant or antiplatelet therapy; incomplete

colonoscopy; incomplete polypectomy; piecemeal polyp resection (e.g. to assess a polypectomy scar); polyps left in situ; poor bowel cleansing; unspecified reason).

As high-quality assessment should be achieved in one colonoscopy for the majority of patients before entering polyp surveillance,[3] we categorized patients into two groups;

A. Patients in need of one colonoscopy
B. Patients in need of two or more colonoscopies

We calculated the primary outcome measure as the proportion of repeat baseline colonoscopies (number of patients in group B. divided by the total patient number (group A. plus group B.)) of all enrolled EPoS trial patients for each endoscopy center and country, as well as for each participating endoscopist who had performed the first baseline colonoscopy in at least 30 EPoS patients. EPoS I and EPoS II trial patients were analyzed separately. For endoscopists working at more than one EPoS study center, we applied the endoscopist's total number of first baseline colonoscopies. The EPoS trials' case report forms allowed one indication for repeat baseline colonoscopy to be registered for each repeat procedure,

Categorical data are presented as absolute numbers with percentages. Proportion of repeat baseline colonoscopy are presented with 95% exact binomial (Clopper-Pearson) confidence intervals (CI). Continuous data are presented as medians with interquartile ranges. We used Stata 17.0 (StataCorp, College Station, TX, USA) for all analyses.

Considerations on possible multivariate mediation analyses

There may be differences between endoscopists and endoscopy centers regarding service routines and clinical colonoscopy practice, such as time schedules and time set aside per colonoscopy, bowel cleansing regimens and patient information, colonoscopist skills and

training, or other clinical procedures. One may therefore be inclined to analyze our data using multivariate logistic or linear regression analyses embedded in mediation analysis of causal inference[11]. However, for the following reasons, we believe such analyses would not have been valid for our study and thus did not perform them:

1. Mediation analyses require detailed knowledge and assumptions about the nature and relationship of the abovementioned variables at play in the study. This relates to the understanding of what type of variable a variable is (a mediator, a moderator, a confounder etc.), what relationship the variables have on the exposure and the outcome of our study, and of the relationships between the different variables. We do not know what category the variables at hand actually represent, we do not know their relationship to each other and to the exposure and outcome of the study. E.g. our measured variable "indication for colonoscopy" may influence the exposure in the study (the exposure is the baseline colonoscopy), because at some centers in EPoS, certain extra measures are taken for patients that are exposed (i.e. have a baseline colonoscopy) due to one indication as compared to another. Examples of such variables would be "time available for colonoscopy" or "endoscopist skills", which are not available and thus not measured in our study. Thus, the variable "indication for colonoscopy" may affect exposure not immediately but through unmeasured variables such as "time available" or "endoscopist skills". As we do not know the nature and value of these unmeasured variables that are behind the variable we know and measure ("indication for colonoscopy"), and we do not know the precise action of the unmeasured variables behind the known variable, it is difficult or indeed impossible to interpret mediation analyses[11].
2. Our study is a quality assurance study for clinical practice variation. The purpose of such studies is not to understand and analyze the causal pathways of different

variables (such as the ones described above) between the exposure (baseline colonoscopy) and the outcome (number of colonoscopies until all polyps are completely removed). The purpose of a study like ours is to document variations in clinical practice among patients who are so similar that one would not expect large variations if services were of the same, good quality. For such studies, two principles of modern quality assurance in medicine apply: firstly that the main interest is in outliers and not in the variation itself or the mean or median values, and secondly that reasons for variation in identified outliers cannot be established by statistical analyses such as regression or mediation[11]. They must be established locally, through observation, audits, and root cause analysis. Thus, this report represents the important first step of a quality improvement process, as described above.[6]

Ethics and trial registration

The EPoS project has been approved by the ethical committees at each participating center and is registered at ClinicalTrials.gov (NCT02319928). All patients provided written informed consent before enrolment. All authors had access to the study data and reviewed and approved the final manuscript.

Patient and Public Involvement Statement

There was no patient involvement in concept, design or analysis of this study.

Results

Study cohort

A total of 17,916 patients were enrolled in EPoS trials I and II (figure 1). For the present study, we excluded all patients from Austria and Portugal due to few included patients (56 patients); all patients from the Netherlands because for logistic reasons most of the Dutch centers did not include patients to the EPoS project if they had more than one baseline colonoscopy (1,275 patients); all patients from Poland with polyps ≥20 mm in diameter because per country policy in Poland they were all called back for repeat colonoscopy (399 patients); patients recruited through sigmoidoscopy screening at two Norwegian centers (494 patients); and 111 patients with missing data for polyp characteristics in the EPoS project database (figure 1).

Thus, our analyses are based on 15,581 patients from five countries and 38 endoscopy centers; 6,794 enrolled in EPoS I and 8,787 in EPoS II trials. The median patient age was 61.0 years and 38.6% of patients were women (table 1). Screening colonoscopy was the most common indication for first baseline colonoscopy in EPoS I trial (51.2%), while most patients in EPoS II trial were recruited after a positive screening test other than colonoscopy (i.e., fecal testing) (63.6%), table 1. The indications for first baseline colonoscopies in each country are shown in supplementary table S1.

Table 1: Characteristic of included patients in EPoS I and EPoS II trials by number of baseline colonoscopies

	EPoS I (Low-risk adenomas)			EPoS II (High-risk adenomas)		
	Total	**One baseline colonoscopy**	**≥2 baseline colonoscopies**	**Total**	**One baseline colonoscopy**	**≥2 baseline colonoscopies**
All patients	6,794	6,693	101	8,787	7,927	860
Female	2,964 (43.6%)	2,921 (43.6%)	43 (42.6%)	3,057 (34.8%)	2,769 (34.9%)	288 (33.5%)
Male	3,830 (56.4%)	3,772 (56.4%)	58 (57.4%)	5,730 (65.2%)	5,158 (65.1%)	572 (66.5%)
Patient age (median years)	61	61	61	62	62	63
Indication first colonoscopy						
Clinical sign or symptom	1,481 (21.8%)	1,443 (21.6%)	38 (37.6%)	2,095 (23.8%)	1,777 (22.4%)	318 (37.0%)
Screening colonoscopy	3,477 (51.2%)	3,459 (51.7%)	18 (17.8%)	941 (10.7%)	911 (11.5%)	30 (3.5%)
Other positive screening test	1,717 (25.3%)	1,674 (25.0%)	43 (42.6%)	5,588 (63.6%)	5,115 (64.5%)	473 (55.0%)
Other	119 (1.8%)	117 (1.7%)	2 (2.0%)	163 (1.9%)	124 (1.6%)	39 (4.5%)
*Bowel cleansing quality**						
Adequate BBPS**	6,735 (99.1%)	6,693 (100.0%)	42 (41.6%)	8,505 (96.8%)	7,927 (100.0%)	578 (67.2%)
Non-adequate BBPS**	59 (0.9%)	n/a	59 (58.4%)	282 (3.2%)	n/a	282 (32.8%)
Complete first colonoscopy	6,752 (99.4%)	6,693 (100.0%)	59 (58.4%)	8,671 (98.7%)	7,927 (100.0%)	744 (86.5%)
Number of polyps						
1-2	6,159 (90.7%)	6,079 (90.8%)	80 (79.2%)	3,734 (42.5%)	3,476 (43.9%)	258 (30.0%)
3-4	540 (7.9%)	525 (7.8%)	15 (14.9%)	3,305 (37.6%)	3,045 (38.4%)	260 (30.2%)
5 or more	95 (1.4%)	89 (1.3%)	6 (5.9%)	1,748 (19.9%)	1,406 (17.7%)	342 (39.8%)
Size of largest polyp						
< 10 mm	6,794 (100.0%)	6,693 (100.0%)	101 (100.0%)	4,741 (54.0%)	4,501 (56.8%)	240 (27.9%)
10-19 mm	n/a	n/a	n/a	3,504 (39.9%)	3,129 (39.5%)	375 (43.6%)
≥ 20 mm	n/a	n/a	n/a	542 (6.2%)	297 (3.7%)	245 (28.5%)
Number of adenomas						
1-2	6,794 (100.0%)	6,693 (100.0%)	101 (100.0%)	4,538 (51.6%)	4,152 (52.4%)	386 (44.9%)
3-4	n/a	n/a	n/a	3,308 (37.6%)	3,034 (38.3%)	274 (31.9%)

5 or more	n/a	n/a	n/a	941 (10.7%)	741 (9.3%)	200 (23.3%)
Size of largest adenoma						
< 10 mm	6,794 (100.0%)	6,693 (100.0%)	101 (100.0%)	4,834 (55.0%)	4,570 (57.7%)	264 (30.7%)
10-19 mm	n/a	n/a	n/a	2,921 (33.2%)	2,682 (33.8%)	239 (27.8%)
≥ 20 mm	n/a	n/a	n/a	1,032 (11.7%)	675 (8.5%)	357 (41.5%)

* Numbers differ from numbers presented in table 2 because the EPoS case report forms required bowel cleansing quality from all colonoscopies, but only one indication for repeat baseline colonoscopy (e.g. poor bowel preparation).

** Boston Bowel Preparation Scale (1 to 3 in each of three colon segments, where 3 is best bowel preparation): Adequate score: ≥2 in all segments; non-adequate score: <2 in any segment.

Repeat colonoscopies

A total of 101 patients (1.5%, 95% CI: 1.2%-1.8%) in EPoS I trial and 860 patients (9.8%, 95% CI: 9.2%-10.4%) in EPoS II trial underwent two or more baseline colonoscopies (table 1). Of these, 57.4% of patients in EPoS I trial and 31.6% in EpoS II trial had poor bowel cleansing at first baseline colonoscopy (Boston Bowel Preparation Score less than two in at least one segment) (table 1). Patients who had repeat baseline colonoscopies also had more polyps and larger polyps at first baseline colonoscopy, as compared to patients who had one baseline colonoscopy (table 1).

The indications for repeat baseline colonoscopy are displayed in table 2. The two most common reasons for repeat colonoscopy were polyps left in situ and poor bowel preparation. Indications for repeat colonoscopy differed between countries; the indication was polyps left in situ for 17.3% of repeat colonoscopies in Spain and 63.3% in Poland, and poor bowel preparation was the indication for 7.2% of repeat colonoscopies in Norway and 29.0% in Spain (supplementary table S2).

Nine patients in EPoS I and 146 patients in EPoS II underwent three or more baseline colonoscopies. Most of these patients were in Spain (67 patients) or Norway (60 patients). The two most common reasons to repeat a (3rd) colonoscopy were piecemeal resection (26.5%) and unspecified reason (23.9%).

Table 2: Indications for repeat baseline colonoscopy in the EPoS I and II trials*

	Total	EPoS I (Low-risk adenomas)	EPoS II (High-risk adenomas)
All patients	961	101	860
Anticoagulant or antiplatelet therapy	69 (7.2%)	12 (11.9%)	57 (6.6%)
Incomplete colonoscopy	53 (5.5%)	10 (9.9%)	43 (5.0%)
Incomplete polypectomy	86 (8.9%)	2 (2.0%)	84 (9.8%)
Piecemeal resection of polyps	120 (12.5%)	1 (1.0%)	119 (13.8%)
Polyps left in situ	267 (27.8%)	33 (32.7%)	234 (27.2%)
Poor bowel preparation	205 (21.3%)	32 (31.7%)	173 (20.1%)
Unspecified reason	161 (16.8%)	11 (10.9%)	150 (17.4%)

*The EPoS case report forms allowed one indication for repeat baseline colonoscopy for each repeat procedure (displayed in table), although more than one reason for suboptimal performance may have been present (such as poor bowel preparation and polyps left in situ).

Clinical practice variation

The proportion of participants who underwent repeat baseline colonoscopies in the EPoS I trial ranged from 0.5% (95% CI: 0.3%-0.8%) in Poland to 5.2% (95% CI: 3.8%-6.9%) in Denmark. In the EPoS II trial, repeat baseline colonoscopies ranged from 2.3% (95% CI: 1.3%-3.9%) in Poland to 15.9% (95% CI: 14.0%-17.8%) in Norway (supplementary table S3).

Frequency of repeat colonoscopy by study center ranged from 0% to 11.8% (95% CI: 1.5-36.4) for patients in the EPoS I trial, and from 0% to 63.9% (95% CI: 46.2%-79.2%) in the EPoS II trial (figure 2).

There were 933 endoscopists registered in the study. Among them, 43 endoscopists in EPoS I trial and 74 in EPoS II trial performed 30 or more first baseline colonoscopies; these were included in endoscopist analyses (figure 3). In the EPoS I trial, repeat colonoscopies ranged from 0% to 5.9% between endoscopists. In the EPoS II trial repeat colonoscopies ranged from 0% to 30%.

Discussion

Our study shows considerable variation between countries, endoscopy centers and endoscopists in the frequency of repeat baseline colonoscopy for patients with polyps before entering surveillance, which may indicate unwanted variation and thus areas for improvement.

As expected and explainable (and thus not indicating unwanted variation), more patients with high-risk adenomas needed more than one baseline colonoscopy than patients with low-risk adenomas (9.8% versus 1.5%). Patients with high-risk adenomas have more and larger polyps

that may be difficult to remove, or require piecemeal resection where repeat baseline colonoscopy is recommended.[3]

More surprising was the variation in repeat baseline colonoscopies among patients within the same polyp risk group (EPoS I and EPoS II trials, respectively). Given the homogeneity between countries in patient and polyp characteristics and the strict inclusion and exclusion criteria in the EPoS trials, this variation seems to be due to differences in endoscopy services' routines and clinical practice.

Unless high quality as defined by key quality indicators is achieved in a single colonoscopy, repetition is recommended.[4] Failure to achieve high quality colonoscopy may result from a single quality indicator not being met, or a combination of factors including endoscopists´ skills, endoscopy service procedures, and patient characteristics such as comorbidities.[4 7]

Unwanted variation in clinical practice is recognized as a major challenge for many health care systems around the World.[6] Unwanted variation in quality of colonoscopies has a variety of reasons[6 7] and identified variation needs to be addressed in context, for the individual endoscopist, the local endoscopy center, and country service level. For example, as compared to a center performing mostly primary colonoscopy screening, a center with a large proportion of colonoscopy patients from a fecal testing-based screening program may have higher proportions of patients on anticoagulation therapy (because such therapy increases the likelihood of positive fecal testing results). The latter center may thus argue to need more repeat baseline colonoscopies after anticoagulation pause to remove polyps after positive fecal screening testing. Other reasons for repeat colonoscopy may be more amendable and thus should be targets for quality audits and subsequent tailored improvement strategies.

As table 2 indicates, common reasons for repeated colonoscopy were technical (polyps left in situ, incomplete or piecemeal polypectomies) or related to inadequate bowel cleansing. The

root cause for the observed differences may be multifactorial, and they may be different at different endoscopy centers. For example, they may be related to differences in endoscopist skills (some are skilled to remove large polyps, while others will not and thus patients need to be rescheduled), or because of re-imbursement or timing reasons, some centers may have policy to limit the number of polyps removed in a single session.

Our paper may provide the first step for local quality assessment by documenting differences and outliers in performance. This study is one of the first which may serve, we hope, to spark a discussion in the field about the observed variations and may start processes of local quality assurance, looking for new solutions to explore areas for improvement and decrease suboptimal performance, if confirmed by local audit.

In line with current concepts of quality improvement in health care, a root cause analysis of unwanted variation is needed to reveal the reason for variation in performance related to context of the service.[6 12] The purpose of our study is not to disentangle these reasons for variation in care for polyp patients, but to identify possible suboptimal performance and thus enable audit and analyses to clarify cause and initiate improvement measures. However, after we performed the current study, the EPoS principal investigators contacted centers with most repeat colonoscopies and advised them on root-cause analysis locally. Such root-cause analyses revealed that the most common reason at all centers for many repeat colonoscopies were non-compliance of individual endoscopists with evidence-based recommendations for follow-up after polypectomies. These endoscpists tended to be overcautious and wanted a "check just to be sure" before surveillance. Team-based education and supervision locally then lead to improvements with less repeat colonoscopies at these centers for patients with polyps. In this way, our study had positive impact on quality of the colonoscopy service at participating centers.

For a colonoscopy center with many FIT-based colonoscopies, such as in the example above, this may include individualized patient information related to anticoagulant therapy before colonoscopy to avoid repeat procedures and thus reduce patient burden and health care resources. At other centers, early repeat colonoscopy may be related to incomplete polypectomy, and thus improvement of endoscopist training would need priority. If polyps are frequently left in situ, time slots for colonoscopy may be too short. Or finally, if bowel preparation is often suboptimal, patient information or bowel preparation procedures and regimens should be improved.

Our findings underscore the need for continuous measurement of performance indicators to uncover potential unwanted variation, followed by audit and root cause analyses with data evaluation at all levels, and rigorous evaluation of reasons for suboptimal performance.[7] This requires dedicated leadership and recognition of prioritization for quality improvement as an integrated part of the colonoscopy service. Without comparative evaluation of performance such as in our study, potential areas for improvement remain unnoticed.

The strengths of this study are the large sample size and the design with a well-defined study population and rigorous, standardized data recording that allow for comparisons between countries, centers and endoscopists with low risk of confounding.

Limitations of the study include generalization to patients not included in the EPoS trials, lack of detailed information about reason for repeated colonoscopy (e.g., if polyps were left in situ due to large size, cancer suspicion or lack of time during colonoscopy), lack of data on endoscopist experience, and small number of colonoscopies performed for some endoscopists. The indication for first colonoscopy varied between countries. Endoscopists were only allowed to choose one reason (e.g., polyps left in situ) for repeated colonoscopies. Although patient and polyp characteristics where similar within EPoS trials I and II, we cannot exclude

that there are small differences between country, center and endoscopist characteristics that could influence our results. Also, the Polish results may be influenced by exclusion of polyps 20mm and larger in this country although the contribution of patients with such polyps in the other countries was only 6.2% (table 1). Finally, we do not know whether repeat colonoscopy at baseline will be of benefit for the study patients through reduced colorectal cancer incidence. These data will be available at the end of the EPoS trials in 10 years' time.

In conclusion, we discovered considerable clinical practice variation in use of repeat baseline colonoscopy before entering polyp surveillance.

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Supplementary materials

Supplementary Table S1: *Indication first baseline colonoscopy per country in EPoS I and II trials.*

Supplementary Table S2: *Indications for repeat baseline colonoscopy per country in EPoS I and II trials.*

Supplementary Table S3: *Proportion of patients with ≥2 baseline colonoscopies, by country and site.*

Conflict of interest

Nothing to declare.

Contributorship statement

RJ and MB planned the study. SKBF, MB, MK and FEJ had the idea of the current manuscript. FEJ, EN, PW and ML analysed the data. FEJ, EN, KG and MB prepared the first draft of the manuscript. All authors reviewed the manuscript and approved the final version before submission.

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FIGURE LEGENDS

Figure 1: Study flow chart of patients included for analysis

Figure 2: Proportion of patients in EPoS I (low-risk adenomas, panel A) and EPoS II (high-risk adenomas, panel B) trials with two or more baseline colonoscopies at different endoscopy centers in participating countries. *Number of centers per country: Denmark 4, Norway 13, Poland 3, Spain 15, Sweden* 3.

Figure 3: Proportion of patients in EPoS I (low-risk adenomas, panel A) and EPoS II (high-risk adenomas, panel B) trials with two or more baseline colonoscopies for participating endoscopists. *Number of endoscopists: EPoS I: 43, EPoS II: 74.*

Panel A: EPoS I trial. Inlet displays differences on smaller scale on y-axis.

Panel B: EPoS II trial.