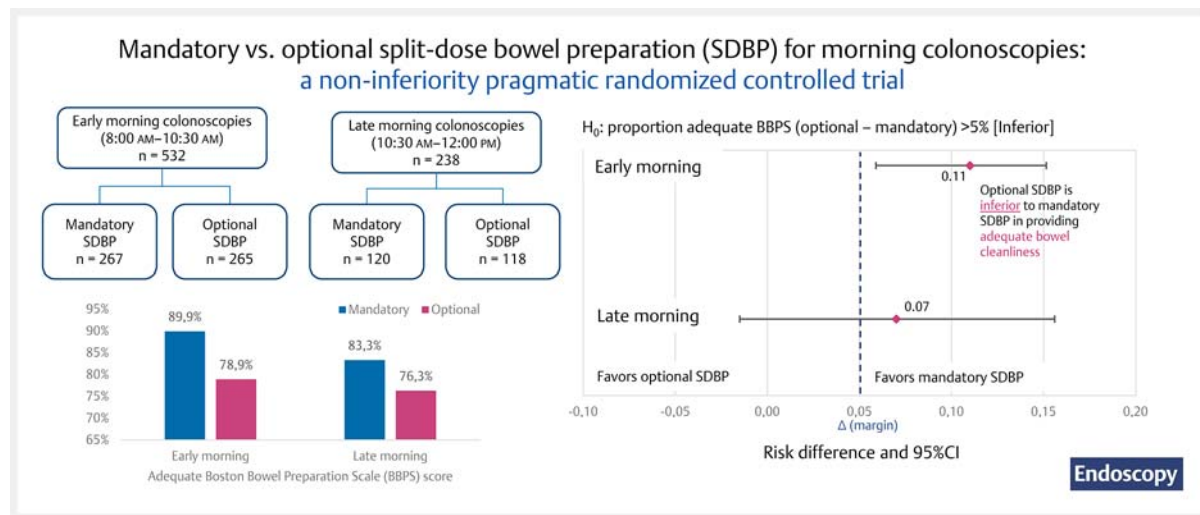


# Mandatory vs. optional split-dose bowel preparation (SDBP) for morning colonoscopies: a pragmatic noninferiority randomized controlled trial

## GRAPHICAL ABSTRACT



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## ABSTRACT

**Background** We compared the effectiveness of optional split-dose bowel preparation (SDBP) with mandatory SDBP for morning colonoscopies in usual clinical practice.

**Methods** Adult patients undergoing outpatient early morning (8:00 AM–10:30 AM) and late morning (10:30 AM–12:00 PM) colonoscopies were included. Written bowel

preparation instructions were provided based on randomization: one group were instructed to take their bowel preparation (4L polyethylene glycol solution) as a split dose (mandatory), while the comparator group was allowed the choice of SDBP or single-dose bowel preparation administered entirely on the day before (optional). The primary end point, using noninferiority hypothesis testing with a 5% margin, was adequate bowel cleanliness measured by the Boston Bowel Preparation Scale (BBPS) and defined by a BBPS score  $\geq 6$ .

**Results** Among 770 randomized patients with complete data, there were 267 mandatory SDBP and 265 optional SDBP patients for early morning colonoscopies, and 120

mandatory SDBP and 118 optional SDBP patients for late morning colonoscopies. Optional SDBP was inferior to mandatory SDBP, with a lower proportion of adequate BBPS cleanliness for early morning colonoscopies (78.9% vs. 89.9%; absolute risk difference [aRD] 11.0%, 95%CI 5.9% to 16.1%), but was not statistically different for late morning colonoscopies (76.3% vs. 83.3%; aRD 7.1%, 95%CI -1.5% to 15.5%).

**Conclusions** Optional SDBP is inferior to mandatory SDBP in providing adequate bowel preparation quality for early morning colonoscopies (8:00 AM–10:30 AM), and probably inferior for late morning colonoscopies (10:30 AM–12:00 PM).

## Introduction

The use of colonoscopy has been increasing continuously worldwide [1, 2]. Colonoscopy is universally accepted as the preferred option for screening and surveillance of people who are at high risk of developing colorectal cancer (CRC), as well as for following up results of other screening tests [3]. Successful visualization and identification of lesions during colonoscopy is contingent on adequate bowel preparation [4]. Unfortunately, bowel cleansing for colonoscopies has been reported to be suboptimal in up to 20%–40% of cases [5]. Poor bowel cleansing can lead to repeat colonoscopies at shorter intervals [6], increased costs to the healthcare system [7], an increased risk of complications, longer procedure times, and a higher likelihood of missed lesions [5, 8].

Traditionally, people undergoing a colonoscopy have been advised to complete a bowel preparation regimen the day before the procedure (i.e. they were instructed to consume the bowel preparation laxatives, most commonly 4L polyethylene glycol [PEG] [9], entirely the day before their colonoscopy). Randomized controlled trials (RCTs) have demonstrated that splitting the volume into two 2-L doses on the day before and morning of the colonoscopy, referred to as split-dose bowel preparation (SDBP), provides better bowel cleansing than the day-before bowel preparation approach [10–12]. SDBP with 3L or more of PEG has been reported to yield greater bowel cleanliness than lower volume split-dose regimens on intention-to-treat (ITT) analysis [10], so continues to be used by many practices.

There have however been concerns raised about the generalizability of the current RCT findings to the general population undergoing colonoscopies [13]. For example, the RCTs do not specifically evaluate early morning colonoscopies, include volunteer participants who may be more adherent to a challenging bowel preparation regimen (e.g. middle of the night intake of bowel preparation for the early morning procedures with SDBP), and involve research personnel who can provide more support and intensive instructions to those undergoing bowel preparation than is feasible in usual clinical practice. Therefore, there continues to be reluctance in using SDBP for

early morning colonoscopies owing to concerns regarding patient compliance and the effectiveness of SDBP in unselected patients in clinical practice [14, 15].

Healthcare providers are worried that routinely splitting the dose for early morning colonoscopies may: (i) discourage patients from undergoing colonoscopy in the early morning owing to a fear of sleep interruption; (ii) risk noncompletion of the bowel preparation prior to transit to the endoscopy facility; (iii) accumulate extra work in terms of patient phone calls about their concerns regarding the procedure, rebooking, and late cancellations; (iv) lead to a lack of adequate adherence to the bowel preparation regimen. As a result, the day-before bowel preparation regimen is still commonly used for early morning colonoscopies. Many practices (including our citywide practice across six busy sites) continue to give patients a choice of SDBP or day-before bowel preparation (optional SDBP) for morning colonoscopies, with the belief that this optional SDBP does not lead to overall markedly worse bowel preparation for early or late morning colonoscopies.

As such, we compared the effectiveness of optional SDBP with mandatory SDBP protocols for morning colonoscopies in a noninferiority pragmatic RCT. We aimed to assess, and powered the study to evaluate, noninferiority (optional SDBP is not substantially worse than mandatory SDBP) for early morning colonoscopies (8:00 AM–10:30 AM) and separately for late morning colonoscopies (10:30 AM–12:00 PM), in two parallel RCTs.

## Methods

### Study population

Adult patients undergoing outpatient morning colonoscopies (before 12:00 PM) between 20 June 2018 and 8 October 2020 in usual clinical practice, performed by any of the four gastroenterologists at a single center, were included in a pragmatic single-blinded RCT. Patients were randomized by the central booking office into two groups, using a computer-generated randomization schedule (1:1 randomization in blocks of 10) and were sent written instructions on bowel preparation for either: (i) mandatory SDBP or (ii) optional SDBP (choice be-

tween SDBP or day-before bowel preparation). The 1:1 randomization was stratified according to early morning (8:00 AM–10:30 AM) and late morning (10:30 AM–12:00 PM) colonoscopies.

Both SDBP groups (mandatory and optional) received standardized information regarding pre-procedure diet, medication use, and the sedatives and colonoscopy. Both groups were encouraged to visit an informative online platform (<https://mycolonoscopy.ca>), which provides validated patient-education materials focused on SDBP [16]. Patients were aware of the bowel preparation instructions, but the endoscopists were unaware of the bowel preparation instructions that had been provided to the patients.

### Mandatory split-dose bowel preparation

Written instructions sent to the mandatory group instructed patients to take their bowel preparation (4 L PEG) split into two doses of 2 L each (split dose). The instructions required the first 2 L to be taken at 6:00 PM on the day before the colonoscopy, and the second dose to be started 4–5 hours prior to the scheduled time of the colonoscopy. Patients were instructed to ingest aliquots from each of the 2-L doses every 10–15 minutes in 250-mL increments (1 cup) over a 2-hour timespan.

The European and North American guidelines highly recommend the use of SDBP for all colonoscopies [5, 17, 18], so mandatory SDBP was used as the reference for noninferiority hypothesis testing.

### Optional split-dose bowel preparation

The instructions sent to the optional group advised patients on the SDBP (as per the mandatory option), but also included instructions for day-before bowel preparation, in which the bowel preparation is taken entirely during the day before. In the latter case, patients were instructed to start drinking the 4 L PEG in 250-mL increments every 10–15 minutes, beginning at 6:00 PM and finishing within a 4-hour timespan. The instructions highlighted that the SDBP was the optimal and preferred preparation for cleansing the bowel and for visualization of lesions, but that the patient could choose the day-before bowel preparation over the SDBP if they preferred.

### Patient experience with bowel preparation (survey data)

On the day of the procedure, a sample of patients were asked to participate in a survey regarding their experiences with the preparation for colonoscopy. The survey was administered when there was time between check-in and the procedure, and when staff were available to distribute the survey. Those who gave their consent completed the survey prior to their procedure. Patient experience factors included: ability to follow and clarity of instructions, anxiety about the bowel preparation and colonoscopy, willingness to do the same preparation in the future, tolerability, sleep, and incontinence experiences. Patients were also asked whether they agreed to link their survey responses to their procedural data (colonoscopy bowel cleanliness, procedure details, pathology).

### Demographic, procedural, and pathologic characteristics

Demographic characteristics included: age; known inflammatory bowel disease (IBD); and indication for colonoscopy (diagnostic, to assess IBD activity, screening, surveillance). Procedure characteristics included: withdrawal and total procedure times; completeness of colonoscopy (cecal or ileal intubation); need for repeat colonoscopy because of poor bowel preparation; and lesions detected, such as polyps, suspected/definitive tumor, suspected/definitive IBD, and diverticulosis. The histologic analysis (pathology) of the polyps was categorized as advanced adenomas (villous, high grade dysplasia,  $\geq 1$  cm in size), hyperplastic, serrated lesions, or other.

### Primary end point and secondary outcomes

The primary end point for noninferiority hypothesis testing was adequate quality of bowel cleanliness measured by the Boston Bowel Preparation Scale (BBPS) score. The BBPS is recommended as the preferred standard [4], having been validated [19] and used in many studies in order to measure adequate bowel cleanliness [20–22]. The total BBPS score ranges from 0 to 9, with each colon segment receiving a “segment score” from 0 to 3. Adequate cleansing was defined a priori as a BBPS score  $\geq 2$  in all segments [23, 24] (i.e. a total BBPS score  $\geq 6$  among individuals with no prior colonic resection). The total BBPS and segment scores were analyzed continuously as secondary outcomes, whereas adequate BBPS was analyzed as a binary variable (adequate vs. inadequate) and considered the primary end point.

The Ottawa Bowel Preparation Scale (OBPS), although not as frequently used, has also been validated [25] when assessing the quality of bowel cleanliness [26, 27]. The total OBPS score ranges from 0 (excellent) to 14 (inadequate), based on three segment scores of 0 to 4, plus a total colon score for fluid quantity of 0 to 2. Adequate cleanliness was defined as a total OBPS score  $\leq 7$  [16]. OBPS was analyzed continuously (total and segment scores) and categorically (adequate vs. inadequate). Although the OBPS measures bowel cleanliness at the onset of the procedure, the score is not routinely recorded at our center, so it was decided a priori that its documentation would not be compulsory, in contrast to the BBPS; the OBPS was considered a secondary outcome.

Other secondary outcomes included: laxative intake completion; any phone calls received from patients about the bowel preparation; and procedure measures, including withdrawal and total procedure time, and the polyp and adenoma detection rates.

### Statistical analysis

Sample size calculations for the primary outcome (adequate bowel cleanliness) for both the early and late morning colonoscopy groups were based on previous literature [15]. To detect noninferiority for a preset absolute difference of 5% or less, with a power of 0.80 and a *P* value of 0.025 (one-sided) for the comparisons of the optional group (80%) with the mandatory group (85%), a total of 356 patients (178/group) were required.

ed, which increased to 418 patients (n = 209/group) after adding a subject withdrawal rate of 15%.

If a patient was randomized to the mandatory group and ended up ingesting the bowel preparation entirely the day before, they were still analyzed as part of the mandatory group as per ITT. The proportion of missed colonoscopies and BBPS scores not recorded were determined and compared between the two groups. A sensitivity analysis was conducted, assuming all missing BBPS scores were inadequate. All missing colonoscopy procedures and unrecorded BBPS scores were excluded from the final analysis, and therefore the comparisons were analyzed as a modified ITT (mITT) analysis. Demographic characteristics (age, sex, known IBD) were compared between the randomized and non-missing data.

All analyses were conducted for early morning (8:00 AM–10:30 AM) and late morning (10:30 AM–12:00 PM) colonoscopies separately. Descriptive statistics are presented as mean (SD) and proportions. The secondary outcomes and potential predictors are presented using point estimates and 95% CIs around the point estimates.

We assessed the association between SDBP groups and secondary outcomes using bivariate analysis. We also assessed the association between nonrandomized laxative timing (split dose or day before) and adequate bowel cleanliness, and the secondary outcomes listed in the methods section, among those assigned to the optional group. The nonrandomized laxative intake timing was defined by whether a patient actually took the laxative as a split dose or on the day before.

Lastly, we conducted planned subgroup analyses assessing whether the patient experiences of the bowel preparation (survey data) differed: (i) between the mandatory and the optional SDBP groups; and (ii) for nonrandomized split-dose compared with day-before bowel preparation for those assigned to the

optional group. Post hoc exploratory multivariable logistic regression analysis was performed to identify possible predictors for choosing day-before bowel preparation among the optional group.

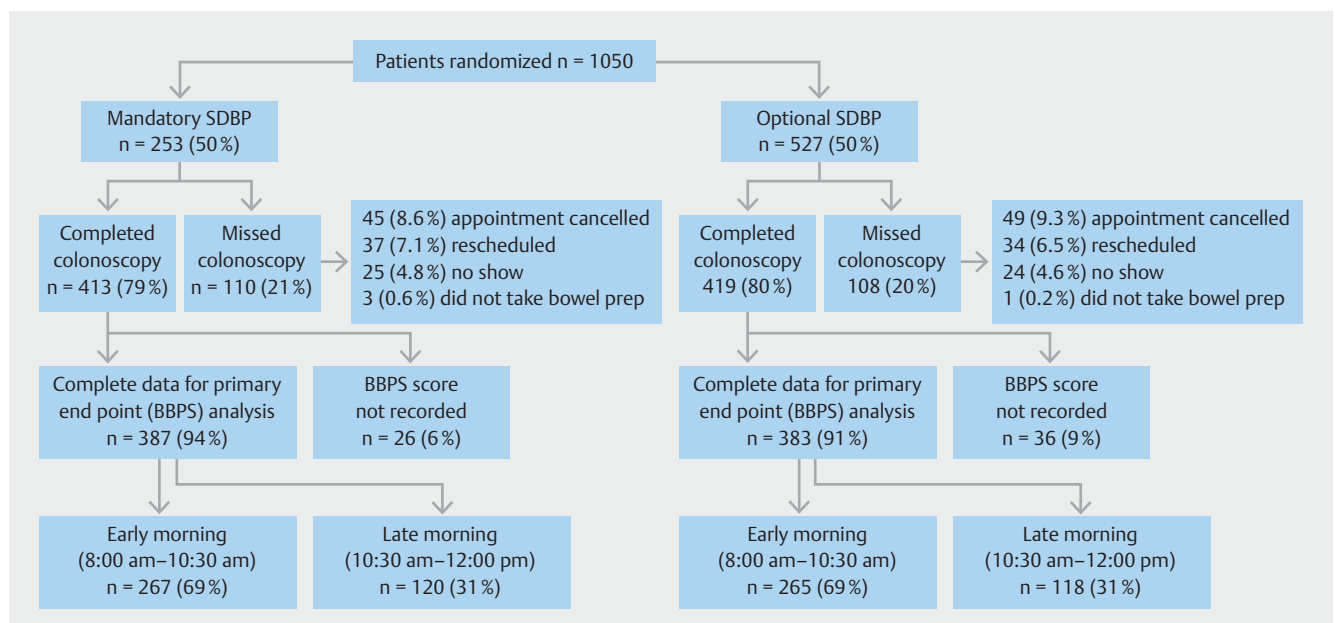
Noninferiority hypothesis testing is presented using the absolute risk difference (aRD) in the proportions (optional SDBP proportion – mandatory SDBP proportion) and 95% CIs for the primary end point (adequate BBPS). Secondary outcomes and potential predictors of choosing day-before bowel preparation were assessed using Fisher's exact test for categorical variables, and *t* test or Wilcoxon signed-rank test for continuous variables, depending on the distribution of the data. *P* values of <0.05 were considered as statistically significant.

In the analysis of bowel cleanliness in the colonic segments, the Bonferroni correction was used with *P* < 0.0125 for four comparisons (BBPS in the three colonic segments and continuous total score) and *P* < 0.01 with five comparisons (OBPS scores). When assessing the many factors regarding patient experiences (survey data) between the SDBP groups, we used the point estimates and 95% CIs; statistical significance between groups was determined if the 95% CIs did not overlap. Analyses were conducted using SAS V9.4 (SAS Institute Inc., Cary, North Carolina, USA).

This study was approved by the Health Research Ethics Board at the University of Manitoba.

## Results

Out of 1050 randomized patients, approximately 50% were randomized to each of the SDBP groups: mandatory (n = 523) and optional (n = 527) (► Fig. 1). The proportions of patients who missed a colonoscopy were similar between the two groups (21.0% for the mandatory compared with 20.5% for



► Fig. 1 Flow chart showing patients randomized to optional or mandatory split-dose bowel preparation (SDBP) with complete Boston Bowel Preparation Scale (BBPS) scores who were included in the overall analysis.

the optional group) and they were excluded from the final analysis. Among patients who underwent a colonoscopy, over 90% in both the mandatory and optional groups had completed BBPS scores. The sensitivity analysis that included unrecorded BBPS observations as inadequate BBPS had no effect on the noninferiority analysis (data available upon request) and therefore these were also excluded from the final analysis. Patient demographic characteristics were similar between: (i) patients who attended a colonoscopy compared with patients who did not attend a colonoscopy, and (ii) patients who attended a colonoscopy and had their BBPS recorded vs. those who did not have their BBPS recorded (Table 1s, see online-only Supplementary material).

After exclusion of incomplete data, there was a total of 770 randomized patients included: for early morning colonoscopies, 267 mandatory SDBP and 265 optional SDBP patients; for late morning colonoscopies, 120 mandatory SDBP and 118 optional SDBP patients. Demographic and clinical characteristics

were similar between the two randomized SDBP groups, among both early and late morning colonoscopies (► Table 1).

Given the choice (optional SDBP group), patients were more likely to choose to complete the laxative intake entirely on the day before: 73.2% for early and 58.8% for late morning colonoscopies. There were no differences in the procedure measures, including withdrawal or procedure times, polyp or adenoma detection rates, completion of laxative intake, or phone calls received by the secretarial team from patients in the mandatory compared with the optional SDBP groups for either early or late morning colonoscopies (► Table 2).

### Bowel cleanliness for early morning colonoscopies

Among early morning (8:00 AM–10:30 AM) colonoscopies, the optional SDBP group had inferior bowel cleanliness compared with the mandatory SDBP group: proportion of adequate BBPS 78.9% vs. 89.9%; aRD 11.0%, 95%CI 5.9% to 16.1% (► Table 2). The lower end of the 95%CI of the aRD exceeded the predefined 5% noninferiority margin (► Fig. 2), therefore the differ-

► **Table 1** Patient and clinical characteristics for the mandatory and optional split-dose bowel preparation (SDBP) groups, stratified by early vs. late morning colonoscopies (n = 770).

	Early morning (8:00 AM–10:30 AM)		Late morning (10:30 AM–12:00 PM)	
	Mandatory (n = 267)	Optional (n = 265)	Mandatory (n = 120)	Optional (n = 118)
<b>Patient</b>				
Sex, female, n (%)	134 (50.2)	139 (52.5)	59 (49.2)	64 (54.2)
Age, mean (SD), years	53.2 (15.6)	54.9 (16.1)	55.2 (16.2)	54.5 (16.6)
Known IBD, n (%) <sup>1</sup>	62 (24.5)	52 (20.8)	29 (25.4)	21 (18.6)
Indication, n (%)				
▪ Diagnostic	128 (47.9)	148 (55.8)	61 (50.8)	56 (47.5)
▪ Assess IBD activity	34 (12.7)	36 (13.6)	19 (15.8)	9 (7.6)
▪ Screening	46 (17.2)	43 (16.2)	19 (15.8)	19 (16.1)
▪ Surveillance	81 (30.3)	61 (23.0)	26 (21.7)	40 (33.9)
<b>Procedure</b>				
Withdrawal time, mean (SD), minutes <sup>2</sup>	9.7 (5.9)	9.4 (6.7)	9.2 (5.5)	8.4 (4.8)
Total procedure time, mean (SD), minutes <sup>3</sup>	17.6 (7.6)	18.2 (9.0)	17.3 (7.2)	17.4 (7.4)
Intubation (cecal or ileal), n (%)	261 (97.8)	258 (97.4)	117 (97.5)	113 (95.8)
Need to repeat colonoscopy, n (%) <sup>4</sup>	11 (4.1)	14 (5.3)	9 (7.5)	13 (11.0)
Lesions, n (%)				
▪ Polyp detection rate	75 (28.1)	72 (27.2)	41 (34.2)	35 (29.7)
▪ Suspected/definitive tumor	3 (1.1)	4 (1.5)	1 (0.8)	–
▪ Suspected/definitive IBD	28 (10.5)	13 (4.9)	10 (8.3)	3 (2.5)
▪ Diverticulosis	55 (20.6)	56 (21.1)	22 (18.3)	20 (16.9)
▪ None	119 (44.6)	127 (47.9)	53 (44.2)	62 (52.5)
<b>Pathology of polyps, n (%)<sup>5</sup></b>				
Adenoma detection rate	41 (15.4)	40 (15.1)	22 (18.3)	21 (17.8)
▪ Advanced adenoma <sup>6</sup>	4 (1.5)	4 (1.5)	2 (1.7)	2 (1.7)

► **Table 1** (Continuation)

	Early morning (8:00 AM–10:30 AM)		Late morning (10:30 AM–12:00 PM)	
	Mandatory (n=267)	Optional (n=265)	Mandatory (n=120)	Optional (n=118)
Hyperplastic	15 (5.6)	23 (8.7)	7 (5.8)	8 (6.8)
Serrated	3 (1.1)	9 (3.4)	5 (4.2)	4 (3.4)
Other	24 (9.0)	20 (7.5)	17 (14.2)	8 (6.8)
▪ Normal tissue	16 (6.0)	9 (3.4)	13 (10.8)	7 (5.9)
<b>Bowel preparation, n (%)</b>				
Laxative intake completed <sup>7</sup>	192 (87.3)	183 (83.9)	80 (87.9)	69 (90.8)
When did the subject take the laxative? <sup>8</sup>				
▪ Split dose	179 (74.3)	58 (24.7)	78 (70.3)	37 (38.1)
▪ Day before colonoscopy	59 (24.5)	172 (73.2)	28 (25.2)	57 (58.8)
▪ Not recorded	3 (1.2)	5 (2.1)	5 (4.5)	3 (3.1)
Phone calls made by patient	24 (9.0)	16 (6.0)	7 (5.8)	7 (5.9)

IBD, inflammatory bowel disease.

Note: there were no statistically significant differences between the groups except for “when the subject took the laxative,” so *P* values are not shown.

<sup>1</sup> Missing data: early (n=29), late (n=11).

<sup>2</sup> Missing data: early (n=58), late (n=22).

<sup>3</sup> Missing data: early (n=47), late (n=19).

<sup>4</sup> Need to repeat colonoscopy owing to inadequate bowel preparation according to endoscopist opinion.

<sup>5</sup> Includes multiple responses as patients may have more than one polyp.

<sup>6</sup> Defined as adenomas (tubular, villous, tubulovillous) with high grade dysplasia, villous or tubulovillous adenoma, or size ≥ 1 cm.

<sup>7</sup> Missing data: early (n=94), late (n=71).

<sup>8</sup> Missing data: early (n=56), late (n=30).

► **Table 2** Comparison of the primary end point (adequate Boston bowel preparation scale [BBPS] score) and secondary outcomes between the mandatory and optional split-dose bowel preparation (SDBP) groups, for early and late morning colonoscopies (n=770).

	Early morning colonoscopies (8:00 AM –10:30 AM)			Late morning colonoscopies (10:30 AM –12:00 PM)		
	Mandatory (n=267)	Optional (n=265)	<i>P</i> value	Mandatory (n=120)	Optional (n=118)	<i>P</i> value
<b>Primary end point</b>						
Adequate BBPS, n (%) <sup>1</sup>	240 (89.9%)	209 (78.9%)		100 (83.3%)	90 (76.3%)	
▪ aRD (95%CI) <sup>2</sup>	11.0% (5.9% to 16.1%)			7.1% (–1.5% to 15.6%)		
<b>Secondary outcomes</b>						
BBPS score, mean (95%CI)						
▪ Total	7.9 (7.7 to 8.1)	7.3 (7.0 to 7.5)	<0.001 <sup>3</sup>	7.4 (6.9 to 7.8)	6.9 (6.4 to 7.3)	0.06
▪ Right	2.6 (2.5 to 2.7)	2.4 (2.3 to 2.5)	0.004 <sup>3</sup>	2.4 (2.3 to 2.6)	2.2 (2.0 to 2.3)	0.02
▪ Transverse	2.7 (2.6 to 2.8)	2.5 (2.4 to 2.6)	<0.001 <sup>3</sup>	2.5 (2.4 to 2.7)	2.4 (2.2 to 2.5)	0.08
▪ Left	2.7 (2.6 to 2.8)	2.5 (2.4 to 2.6)	<0.001 <sup>3</sup>	2.5 (2.4 to 2.7)	2.4 (2.2 to 2.5)	0.06
Procedure times, mean (95%CI), minutes						
Withdrawal <sup>4</sup>	9.7 (8.9 to 10.4)	9.4 (8.5 to 10.3)	0.59	9.2 (8.2 to 10.3)	8.4 (7.5 to 9.4)	0.25
Total procedure <sup>5</sup>	17.6 (16.7 to 18.6)	18.2 (17.0 to 19.3)	0.47	17.3 (16.0 to 18.7)	17.4 (16.0 to 18.8)	0.94
OBPS score, mean (95%CI) <sup>6</sup>						
▪ Total score	4.6 (4.2 to 5.1)	5.6 (5.1 to 6.1)	0.008 <sup>7</sup>	5.8 (5.0 to 6.6)	7.2 (6.4 to 8.1)	0.01
▪ Liquid	1.1 (1.0 to 1.2)	1.3 (1.2 to 1.4)	0.02	1.3 (1.2 to 1.5)	1.5 (1.3 to 1.6)	0.14



► **Table 2** (Continuation)

	Early morning colonoscopies (8:00 AM – 10:30 AM)			Late morning colonoscopies (10:30 AM – 12:00 PM)		
	Mandatory (n = 267)	Optional (n = 265)	P value	Mandatory (n = 120)	Optional (n = 118)	P value
▪ Recto-sigmoid	1.0 (0.8 to 1.1)	1.3 (1.1 to 1.4)	0.01	1.4 (1.2 to 1.7)	1.8 (1.5 to 2.1)	0.05
▪ Right	1.4 (1.3 to 1.6)	1.7 (1.6 to 1.9)	0.003 <sup>7</sup>	1.7 (1.4 to 1.9)	2.0 (1.8 to 2.3)	0.02
▪ Transverse	1.1 (0.9 to 1.2)	1.4 (1.2 to 1.5)	0.01	1.4 (1.2 to 1.7)	1.8 (1.6 to 2.1)	0.03
Adequate OBPS score, n (%) [95%CI] <sup>6,8</sup>	152 (56.9) [51.0 to 62.9]	133 (50.2) [44.1 to 56.2]	0.01 <sup>9</sup>	57 (47.5) [38.5 to 56.5]	36 (30.5) [22.1 to 38.9]	0.02*
Polyp detection rate, n (%) [95%CI]	75 (28.1) [22.7 to 33]	72 (27.2) [21.8 to 33]	0.85	41 (34.2) [25.6 to 43]	35 (29.7) [21.4 to 38]	0.49
Adenoma detection rate, n (%) [95%CI]	41 (15.4) [11.0 to 20]	40 (15.1) [10.8 to 19]	>0.99	22 (18.3) [11.4 to 25]	21 (17.8) [10.8 to 25]	>0.99
Laxative intake completed, n (%) [95%CI] <sup>10</sup>	192 (87.3) [82.9 to 91.7]	183 (83.9) [79.1 to 88.8]	0.34	80 (87.9) [81.1 to 94.7]	69 (90.8) [84.2 to 97.4]	0.62
Phone calls made by patient, n (%) [95%CI]	24 (9.0) [5.5 to 12.4]	16 (6.0) [3.2 to 8.9]	0.25	7 (5.8) [1.6 to 10.1]	7 (5.9) [1.6 to 10.2]	>0.99

aRD, absolute risk difference; OBPS, Ottawa Bowel Preparation Scale.

<sup>1</sup> Defined as  $\geq 2$  in all colonic segments.

<sup>2</sup> Defined as: percentage adequate BBPS in optional group – percentage adequate BBPS in mandatory group.

<sup>3</sup>  $P < 0.0125$  using Bonferroni correction with four comparisons.

<sup>4</sup> Missing data: early (n = 58), late (n = 22).

<sup>5</sup> Missing data: early (n = 47), late (n = 19).

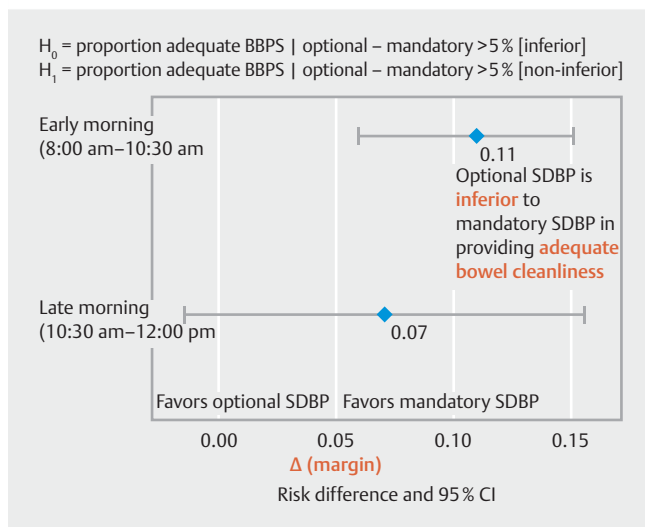
<sup>6</sup> Missing data: early (n = 147), late (n = 73).

<sup>7</sup>  $P < 0.01$  using Bonferroni correction with five comparisons.

<sup>8</sup> Defined as a score  $\leq 7$ .

<sup>9</sup>  $P < 0.05$ .

<sup>10</sup> Missing data: early (n = 94), late (n = 71).



► **Fig. 2** Absolute risk difference and 95% CIs for adequate Boston Bowel Preparation Scale (BBPS) score in the mandatory vs. optional split-dose bowel preparation (SDBP) groups for early morning and late morning colonoscopies.

ence is statistically significant and clearly demonstrates inferiority.

Similarly, adequate OBPS was less frequent in the optional SDBP group (50.2%, 95%CI 44.1% to 56.2%) than in the mandatory SDBP group (56.9%, 95%CI 51.0% to 62.9%;  $P = 0.01$ ). The mean BBPS and OBPS total scores showed lower adequacy in the optional group compared with the mandatory group (a lower score being better with the OBPS) (► **Table 2**).

### Bowel cleanliness for late morning colonoscopies

The proportion of patients with adequate BBPS for late morning (10:30 AM–12:00 PM) colonoscopies was lower in the optional group (76.3%) vs. the mandatory group (83.3%) (► **Table 2**); however, the 95%CI for the aRD included the predefined noninferiority margin (► **Fig. 2**) and was therefore not statistically different, and did not reject the noninferior hypothesis: aRD 7.1%, 95%CI  $-1.5\%$  to  $15.6\%$ . Adequate OBPS was however less frequent with optional SDBP (30.5%, 95%CI 22.1% to 38.9%) compared with mandatory SDBP (47.5%, 95%CI 38.5% to 56.5%;  $P = 0.02$ ).

Among the optional group, patient characteristics and study outcomes were similar for those individuals who took the bowel preparation the day before compared with those who took the laxative as SDBP for both early and late morning colonoscopies (► **Table 3**).

► **Table 3** Associations with split-dose vs. day-before laxative intake (nonrandomized analyses) among those assigned to the optional group for early morning and late morning colonoscopies.

	Early morning (n = 230)			Late morning (n = 94)		
	Day before (n = 172)	Split dose (n = 58)	P <sup>1</sup>	Day before (n = 57)	Split dose (n = 37)	P <sup>1</sup>
<b>Demographic data, n (%) [95%CI]<sup>2</sup></b>						
Sex, female, n (%) [95%CI]	96 (55.8) [48.3 to 63.3]	28 (48.3) [35.3 to 61.2]	0.36	33 (57.9) [44.8 to 71.0]	23 (62.2) [46.2 to 78.1]	0.83
Age, mean (95%CI), years	54.9 (52.3 to 57.4)	54.8 (50.8 to 58.7)	0.97	55.0 (50.9 to 59.1)	53.3 (47.8 to 58.8)	0.62
Known IBD <sup>3</sup>	39 (24.2) [17.6 to 30.9]	9 (16.1) [6.4 to 25.8]	0.21	11 (19.6) [9.0 to 30.3]	6 (18.2) [4.8 to 31.6]	0.54
<b>Indication</b>						
Diagnostic	93 (54.1) [46.6 to 61.6]	32 (55.2) [42.3 to 68.1]	>0.99	27 (47.4) [34.2 to 60.6]	20 (54.1) [37.7 to 70.4]	0.67
Assess IBD activity	27 (15.7) [10.2 to 21.2]	9 (15.5) [6.1 to 24.9]	>0.99	4 (7.0) [0.3 to 13.8]	5 (13.5) [2.3 to 24.7]	0.31
Screening	29 (16.9) [11.2 to 22.5]	10 (17.2) [7.4 to 27.0]	>0.99	10 (17.5) [7.5 to 27.6]	6 (16.2) [4.1 to 28.3]	>0.99
Surveillance	40 (23.3) [16.9 to 29.6]	14 (24.1) [13.0 to 35.2]	0.86	19 (33.3) [20.9 to 45.8]	9 (24.3) [10.2 to 38.4]	0.49
<b>Primary outcome, n (%) [95%CI]</b>						
Adequate BBPS	139 (80.8) [74.9 to 86.7]	46 (79.3) [68.8 to 89.8]	0.85	39 (68.4) [56.1 to 80.7]	30 (81.1) [68.2 to 93.9]	0.23
<b>Secondary outcomes, n (%) [95%CI]<sup>2</sup></b>						
Adequate OBPS <sup>4</sup>	86 (68.3) [60.0 to 76.5]	29 (67.4) [53.3 to 81.6]	>0.99	15 (38.5) [22.8 to 54.2]	12 (52.2) [31.2 to 73.2]	0.43
Laxative intake completed <sup>5</sup>	135 (84.9) [79.3 to 90.5]	46 (82.1) [72.0 to 92.3]	0.67	43 (95.6) [89.4 to 100]	25 (86.2) [73.4 to 99.1]	0.20
Phone calls made by patient	9 (5.2) [1.9 to 8.6]	5 (8.6) [1.3 to 15.9]	0.35	3 (5.3) [0.0 to 11.2]	4 (10.8) [0.6 to 21.0]	0.43
Withdrawal time, mean (95%CI), minutes <sup>6</sup>	9.2 (8.0 to 10.4)	9.7 (8.3 to 11.1)	0.60	8.3 (6.9 to 9.7)	8.9 (7.2 to 10.5)	0.60
Total procedure time, mean (95%CI), minutes <sup>7</sup>	17.7 (16.3 to 19.2)	19.2 (16.6 to 21.7)	0.31	18.1 (15.9 to 20.3)	17.2 (15.1 to 19.3)	0.58
Polyp detection rate	49 (28.5) [21.7 to 35]	14 (24.1) [13.0 to 35]	0.61	18 (31.6) [19.3 to 44]	11 (29.7) [14.7 to 45]	>0.99
Adenoma detection rate	27 (15.7) [10.2 to 21]	8 (13.8) [4.9 to 23]	>0.99	11 (19.3) [8.9 to 30]	6 (16.2) [4.1 to 28]	0.79

IBD, inflammatory bowel disease; BBPS, Boston Bowel Preparation Scale; OBPS, Ottawa Bowel Preparation Scale.

<sup>1</sup> Statistical significance at  $P < 0.05$

<sup>2</sup> Unless otherwise specified.

<sup>3</sup> Missing data: early (n = 13), late (n = 5).

<sup>4</sup> Missing data: early (n = 61), late (n = 32).

<sup>5</sup> Missing data: early (n = 15), late (n = 20).

<sup>6</sup> Missing data: early (n = 29), late (n = 11).

<sup>7</sup> Missing data: early (n = 18), late (n = 8).



► **Table 4** Patient experiences for mandatory compared with optional split-dose bowel preparation (SDBP) groups for early and late morning colonoscopies for those who responded to the survey (n = 444).

	Early morning (8:00 AM–10:30 AM)		Late morning (10:30 AM–12:00 PM)	
	Mandatory (n = 160)	Optional (n = 159)	Mandatory (n = 66)	Optional (n = 59)
<b>Adequate scores, n (%) [95%CI]</b>				
BBPS <sup>1</sup>	<b>130 (90.9)</b> [86.2 to 95.7]	<b>104 (77.0)</b> [69.9 to 84.2]	53 (85.5) [76.6 to 94.4]	39 (73.6) [61.5 to 85.6]
OBPS <sup>2</sup>	78 (77.2) [69.0 to 85.5]	64 (64.6) [55.1 to 74.1]	<b>32 (71.1)</b> [57.6 to 84.6]	<b>16 (42.1)</b> [26.1 to 58.1]
<b>Survey questions, n (%) [95%CI]<sup>3</sup></b>				
<b>Demographic data</b>				
Sex, female	87 (54.7) [46.9 to 62.5]	85 (53.5) [45.7 to 61.3]	33 (50.8) [38.4 to 63.1]	37 (62.7) [50.2 to 75.2]
Age (years), mean (95%CI)	53.7 (51.4 to 56.0)	54.1 (51.6 to 56.6)	54.0 (49.9 to 58.2)	54.0 (49.9 to 58.0)
Education				
▪ Less than high school	22 (13.9) [8.5 to 19.4]	31 (19.5) [13.3 to 25.7]	7 (10.8) [3.1 to 18.4]	5 (8.8) [1.3 to 16.2]
▪ High school or greater	136 (86.1) [80.6 to 91.5]	128 (80.5) [74.3 to 86.7]	58 (89.2) [81.6 to 96.9]	52 (91.2) [83.8 to 98.7]
Marital status				
▪ Married/common law	43 (27.0) [20.1 to 34.0]	62 (39.0) [31.4 to 46.6]	12 (18.5) [8.9 to 28.0]	22 (38.6) [25.8 to 51.4]
▪ Single/widowed	116 (73.0) [66.0 to 79.9]	97 (61.0) [53.4 to 68.6]	53 (81.5) [72.0 to 91.1]	35 (61.4) [48.6%–74.2]
Previous colonoscopy				
▪ <5 years ago	65 (58.6) [49.3 to 67.8]	58 (55.2) [45.7 to 64.8]	25 (59.5) [44.3 to 74.7]	22 (59.5) [43.3 to 75.6]
▪ >5 years ago	46 (41.4) [32.2 to 50.7]	47 (44.8) [35.2 to 54.3]	17 (40.5) [25.3 to 55.7]	15 (40.5) [24.4 to 56.7]
<b>Clinical questions</b>				
How were you able to follow the instructions for bowel prep?				
▪ Well or less (poorly, very poor)	44 (27.5) [20.5 to 34.5]	52 (32.7) [25.4 to 40.0]	18 (27.3) [16.4 to 38.2]	14 (23.7) [12.7 to 34.7]
▪ Very well	116 (72.5) [65.5 to 79.5]	107 (67.3) [60.0 to 74.6]	48 (72.7) [61.8 to 83.6]	45 (76.3) [65.3 to 87.3]
How clear were the instructions for the bowel prep?				
▪ Very clear	100 (62.9) [55.3 to 70.4]	109 (68.6) [61.3 to 75.8]	46 (69.7) [58.5 to 80.9]	40 (67.8) [55.7 to 79.9]
▪ Quite clear	39 (24.5) [17.8 to 31.3]	33 (20.8) [14.4 to 27.1]	11 (16.7) [7.6 to 25.8]	15 (25.4) [14.2 to 36.7]
▪ Moderately or less clear	20 (12.6) [7.4 to 17.8]	17 (10.7) [5.9 to 15.5]	9 (13.6) [5.2 to 22.0]	4 (6.8) [0.3 to 13.3]
How worried were you about the bowel prep?				
▪ Moderately or less	122 (76.3) [69.6 to 82.9]	128 (80.5) [74.3 to 86.7]	55 (83.3) [74.2 to 92.4]	49 (83.1) [73.3 to 92.8]
▪ Worried/extremely	38 (23.8) [17.1 to 30.4]	31 (19.5) [13.3 to 25.7]	11 (16.7) [7.6 to 25.8]	10 (16.9) [7.2 to 26.7]

► **Table 4** (Continuation)

	Early morning (8:00 AM–10:30 AM)		Late morning (10:30 AM–12:00 PM)	
	Mandatory (n = 160)	Optional (n = 159)	Mandatory (n = 66)	Optional (n = 59)
How worried were you about the colonoscopy?				
▪ Moderately or less	121 (75.6) [68.9 to 82.3]	130 (81.8) [75.7 to 87.8]	55 (83.3) [74.2 to 92.4]	48 (81.4) [71.3 to 91.4]
▪ Worried/extremely	39 (24.4) [17.7 to 31.1]	29 (18.2) [12.2 to 24.3]	11 (16.7) [7.6 to 25.8]	11 (18.6) [8.6 to 28.7]
How worried were you about the results of the colonoscopy?				
▪ Moderately or less	129 (80.6) [74.5 to 86.8]	132 (83.0) [77.2 to 88.9]	58 (87.9) [79.9 to 95.9]	48 (81.4) [71.3 to 91.4]
▪ Worried/extremely	31 (19.4) [13.2 to 25.5]	27 (17.0) [11.1 to 22.8]	8 (12.1) [4.1 to 20.1]	11 (18.6) [8.6 to 28.7]
<b>Tolerability</b>				
Please indicate if the following symptoms were moderate or severe:				
▪ Unpleasant taste	57 (35.6) [28.2 to 43.1]	61 (38.4) [30.8 to 46.0]	23 (34.8) [23.2 to 46.5]	19 (32.2) [20.1 to 44.3]
▪ Excess thirst	24 (15.0) [9.4 to 20.6]	13 (8.2) [3.9 to 12.5]	3 (4.5) [0.0 to 9.6]	6 (10.2) [2.3 to 18.0]
▪ Nausea	30 (18.8) [12.7 to 24.8]	33 (20.8) [14.4 to 27.1]	11 (16.7) [7.6 to 25.8]	13 (22.0) [11.3 to 32.8]
▪ Vomiting	12 (7.5) [3.4 to 11.6]	13 (8.2) [3.9 to 12.5]	6 (9.1) [2.1 to 16.1]	3 (5.1) [0.0 to 10.8]
▪ Bloating	15 (9.4) [4.8 to 13.9]	21 (13.2) [7.9 to 18.5]	6 (9.1) [2.1 to 16.1]	6 (10.2) [2.3 to 18.0]
▪ Abdominal Pain	13 (8.1) [3.9 to 12.4]	17 (10.7) [5.9 to 15.5]	4 (6.1) [0.2 to 11.9]	4 (6.8) [0.3 to 13.3]
▪ Headache	28 (17.5) [11.6 to 23.4]	27 (17.0) [11.1 to 22.8]	13 (19.7) [10.0 to 29.4]	8 (13.6) [4.7 to 22.4]
▪ Dizziness	5 (3.1) [0.4 to 5.8]	9 (5.7) [2.0 to 9.3]	1 (1.5) [0.0 to 4.5]	2 (3.4) [0.0 to 8.1]
▪ Sleep distress	52 (32.5) [25.2 to 39.8]	41 (25.8) [18.9 to 32.6]	16 (24.2) [13.8 to 34.7]	13 (22.0) [11.3 to 32.8]
▪ Anal irritation	34 (21.3) [14.9 to 27.6]	30 (18.9) [12.8 to 25.0]	9 (13.6) [5.2 to 22.0]	12 (20.3) [9.9 to 30.8]
▪ Chills	45 (28.1) [21.1 to 35.1]	45 (28.3) [21.3 to 35.3]	18 (27.3) [16.4 to 38.2]	16 (27.1) [5.6 to 38.6]
If required future colonoscopy, would you be willing to use the same bowel prep instructions again?				
▪ No	20 (12.5) [7.3 to 17.7]	19 (11.9) [6.9 to 17.0]	8 (12.3) [4.2 to 20.4]	9 (15.5) [6.1 to 25.0]
▪ Yes	104 (65.0) [57.6 to 72.4]	108 (67.9) [60.6 to 75.2]	44 (67.7) [56.2 to 79.2]	34 (58.6) [45.8 to 71.5]
▪ Don't know	36 (22.5) [16.0 to 29.0]	32 (20.1) [13.9 to 26.4]	13 (20.0) [10.1 to 29.9]	15 (25.9) [14.4 to 37.]
Tolerance, mean (95 %CI) <sup>4</sup>	7.3 (6.9 to 7.7)	6.9 (6.5 to 7.3)	7.6 (7.03 to 8.1)	7.0 (6.3 to 7.7)
Tolerance scale				
▪ ≤5	41 (25.6) [18.8 to 32.4]	52 (32.7) [25.4 to 40.0]	13 (20.0) [10.1 to 29.9]	18 (31.0) [19.0 to 43.1]

► **Table 4** (Continuation)

	Early morning (8:00 AM–10:30 AM)		Late morning (10:30 AM–12:00 PM)	
	Mandatory (n = 160)	Optional (n = 159)	Mandatory (n = 66)	Optional (n = 59)
▪ >5	119 (74.4) [67.6 to 81.2]	107 (67.3) [60.0 to 74.6]	52 (80.0) [70.1 to 89.9]	40 (69.0) [56.9 to 81.0]
<b>Sleep, mean (95%CI)</b>				
▪ Last night, number of times woke up during the night	2.6 (2.1 to 3.1)	2.5 (2.1 to 2.9)	2.5 (2.0 to 3.1)	2.6 (1.9 to 3.2)
▪ Last night, number of times woke because of bowel movement	1.8 (1.4 to 2.1)	2.1 (1.7 to 2.5)	2.1 (1.5 to 2.6)	2.2 (1.5 to 2.8)
▪ How many times do you usually wake up?	1.4 (1.2 to 1.6)	1.3 (1.1 to 1.5)	1.4 (1.0 to 1.7)	1.3 (1.0 to 1.6)
▪ How many hours did you sleep last night?	4.1 (3.9 to 4.4)	4.5 (4.2 to 4.8)	5.1 (4.6 to 5.5)	4.9 (4.5 to 5.4)
▪ How many hours do you usually sleep?	7.1 (6.9 to 7.3)	7.1 (6.9 to 7.3)	6.8 (6.4 to 7.1)	7.2 (6.9 to 7.5)
<b>Bowel movement information</b>				
How much time before colonoscopy was your last bowel movement?				
▪ <1 hour	38 (23.8) [17.1 to 30.4]	28 (17.8) [11.8 to 23.9]	14 (21.5) [11.4 to 31.7]	10 (18.5) [8.0 to 29.0]
▪ 1–2 hours	70 (43.8) [36.0 to 51.5]	76 (48.4) [40.5 to 56.3]	25 (38.5) [26.5 to 50.5]	22 (40.7) [27.4 to 54.0]
▪ 2–3 hours	22 (13.8) [8.4 to 19.1]	28 (17.8) [11.8 to 23.9]	10 (15.4) [6.5 to 24.3]	12 (22.2) [11.0 to 33.5]
▪ >3 hours	30 (18.8) [12.7 to 24.8]	25 (15.9) [10.2 to 21.7]	16 (24.6) [14.0 to 35.2]	10 (18.5) [8.0 to 29.0]
Stopped for bowel movement during travel to clinic/hospital	7 (4.4) [1.2 to 7.6]	7 (4.4) [1.2 to 7.6]	4 (6.3) [0.2 to 12.3]	7 (12.1) [3.6 to 20.6]
Urgent bowel movement <sup>5</sup>	113 (70.6) [63.5 to 77.7]	114 (71.7) [64.7 to 78.7]	46 (71.9) [60.7 to 83.0]	42 (72.4) [60.7 to 84.1]
Incontinence <sup>6</sup>	27 (17.0) [11.1 to 22.8]	27 (17.0) [11.1 to 22.8]	11 (17.2) [7.8 to 26.6]	15 (26.3) [14.7 to 37.9]

BBPS, Boston Bowel Preparation Scale; OBPS, Ottawa Bowel Preparation Scale.

Note: bold values indicate that the 95% CIs between the two groups do not overlap.

<sup>1</sup> Calculated for those with complete BBPS data who agreed to link to retrospective data: total early (n = 278); mandatory early (n = 143); optional early (n = 135); total late (n = 115); mandatory late (n = 62); optional late (n = 53).

<sup>2</sup> Calculated for those with complete OBPS data who agreed to link to retrospective data: total early (n = 200); mandatory early (n = 101); optional early (n = 99); total late (n = 83); mandatory late (n = 45); optional late (n = 38).

<sup>3</sup> Unless otherwise stated.

<sup>4</sup> Scale 1 (not tolerated at all) to 10 (totally tolerated).

<sup>5</sup> In the time period between starting to take the bowel preparation medication and the colonoscopy, did you have one or more times when you had an urgent bowel movement?

<sup>6</sup> Did you have any incontinence (accident) episodes between the start of taking the first dose of bowel preparation liquid and the time of your colonoscopy?

## Patient experiences with bowel preparation (survey data)

Demographic and clinical characteristics for the patient experiences with bowel preparation (survey) data are presented in ► **Table 4**. A total of 444 patients (58.0%) participated in the survey and agreed to link their responses to their procedural data. The proportions with adequate BBPS for the optional compared with the mandatory SDBP group were similar to the

proportions found for the entire cohort. The patient demographic characteristics were similar between the groups (data available upon request).

Factors associated with choosing day-before bowel preparation over SDBP in the optional group are presented in **Table 2s**. Among the 209 patients in the optional group, day-before bowel preparation was chosen by 104/153 (68.0%) for early morning colonoscopies and 34/56 (60.7%) for late morning colonos-

copies. There were no differences in the patient experiences related to the bowel preparation (ability to follow/clarity of instructions, anxiety, tolerability, sleep, incontinence). Multivariable logistic regression analysis identified no significant predictors associated with choosing day-before bowel preparation over SDBP among early morning colonoscopies (**Table 3s**).

## Discussion

We found that optional SDBP was inferior to mandatory SDBP in providing adequate bowel cleanliness (adequate BBPS) for early morning (8:00 AM–10:30 AM) colonoscopies. It also numerically less frequently provided adequate bowel cleanliness (measured by the BBPS) among late morning (10:30 AM–12:00 PM) colonoscopies, although the difference for late morning colonoscopies did not reach statistical significance. The data collection period extended partially into the COVID-19 pandemic, which meant we stopped the study before we had reached the intended sample size ( $n=209$ ) for both the mandatory and optional SDBP groups for late morning colonoscopies, which may have influenced statistical significance. Adequate OBPS for late morning procedures was significantly less frequent in the optional SDBP group compared with the mandatory SDBP group. Giving patients a choice (optional SDBP) did not improve patient experiences of bowel preparation compared with the mandatory SDBP group for early or late morning colonoscopies.

The literature continues to provide evidence to support SDBP being a better regimen than the day-before bowel preparation approach [10–12, 28, 29], yet endoscopists have been hesitant to mandate SDBP for early morning procedures owing to concerns regarding patient compliance, comfort [15], and efficacy in clinical practice [30]. A study that surveyed trusts in the UK [31] suggested most did not provide instructions optimizing the timing (split dose) of bowel preparation prior to colonoscopy procedures, which resulted in an increased rate of inadequate cleansing. As many centers use day-before rather than split-dose regimens for early morning colonoscopies, patients may be unaware and lack knowledge of the advantages that split dosing provides. Therefore, in these centers, the uptake of split dosing for early morning colonoscopies is likely to be even lower than the 25% uptake observed in our study. Consequently, the rate of inadequate bowel preparation may be higher than we have reported.

When we compared those who took the laxative as a split dose versus those who took the laxative the day before among those assigned to the optional group, we found no differences in the clinical characteristics for either early or late morning procedures. However, the sample size was limited, so more research is needed to identify any patient factors that predict patients' choice of day-before bowel preparation.

We have shown that, regardless of whether procedures are early or late morning, when given a choice (optional SDBP), patients are more likely to choose to take the laxative entirely the day before. This finding is not surprising as we have previously shown in a survey of 1336 respondents that unclear bowel preparation information (odds ratio [OR] 1.86, 95%CI 1.21–2.85) and high bowel preparation anxiety (OR 2.02, 95%

CI 1.35–3.02) are predictors of patient reluctance to use early morning bowel preparation [32]. Our studies suggest the need to provide additional information to patients, highlighting the benefits of SDBP. We have recently reported how the use of an informative online platform is associated with an increased use of SDBP [33].

Our previous study that assessed patients' opinions about waking early for bowel preparation [32] found that almost three-quarters of patients did not express reluctance to get up early for bowel preparation; however, 27% did. Results from another study, consistent with our findings, assessing patients' willingness to undergo SDBP for early morning procedures, scheduled between 7 AM and 9 AM, found that a substantial minority of patients do not comply with SDBP [34] (85% stated they would be willing to get up, with 78% actually awakening early to take the second dose). Additional efforts should be made to reduce the likelihood of patients continuing to be reluctant to take laxatives early in the morning, although acknowledging SDBP may not be feasible for those travelling long distances on the day of their colonoscopy [35].

Dissemination of our current study results could allay some of the patient anxiety associated with the early morning intake of bowel preparation. In our current study, we found that there was no difference in patient experiences relating to anxiety (worried about bowel preparation, colonoscopy, results of the colonoscopy), tolerability, sleep, or incontinence between the mandatory and optional SDBP groups, or between those who chose day-before bowel preparation over SDBP for early morning colonoscopies.

Our study provides evidence that optional SDBP is inferior to mandatory SDBP in terms of adequate bowel cleanliness for early morning colonoscopies, and possibly also for late morning procedures. In addition, the mandatory SDBP group did not show a higher proportion of missed colonoscopies, workload in terms of phone calls for nurses, or proportion of incomplete laxative intake, or differ in the procedural measures compared with the optional SDBP group for early or late morning procedures. These findings should be reassuring to centers that have switched to or are considering switching to mandatory SDBP for morning colonoscopies. As a net result of this study, our regional citywide endoscopy program is now moving toward mandatory SDBP for most patients; we believe other jurisdictions who are still using optional SDBP or day-before bowel preparation should do so as well.

The greatest advantage of our study is its adoption of a pragmatic (i.e. real world) setting, as it is more generalizable to usual practice [36]. As a result of this, we did have a high proportion of incomplete colonoscopies and some unrecorded BBPS scores. Other studies have reported similar or lower rates of attendance for colonoscopies [37–39]. Patient characteristics (including survey response results) and subgroup analysis suggest robustness of our results. A further limitation is that, among the mandatory SDBP group, 25% of patients ingested the bowel preparation entirely the day before rather than in two split doses. We did not ask patients why they did not complete the intended SDBP; however, it has been previously reported that 15%–22% of patients do not comply with SDBP

[15,34]. In addition, high volume PEG is not considered the standard in many countries, which may limit the external validity of our study findings. Similarly to other studies, our secondary end points and post-hoc analysis are exploratory and should be interpreted with caution. This was also a single-center study, albeit from a center that provides care to a wide spectrum of patients. In addition, sample size was small in many of the subgroup analyses.

Our study suggests that patients undergoing morning colonoscopy should not be offered the option of day-before high volume PEG, as an alternative to split-dose high volume PEG. Patients reasoning and the predictors for ingesting the bowel preparation laxatives entirely on the day before when mandatory SDBP instructions have been provided need further investigation. Facilitators of SDBP use in usual clinical practice should be assessed and implemented. The implications of our study findings in settings where low volume bowel preparation is the standard needs evaluation.

In conclusion, our study results suggest bowel preparation quality is inferior with optional compared with mandatory SDBP for early morning (8:00 AM–10:30 AM) and possibly for late morning (10:30 AM–12:00 PM) colonoscopies. Patient experience, compliance for colonoscopies, and workload for clinical staff in terms of phone calls, rescheduling, and cancellations does not differ between these groups. Given the choice, the majority of patients choose the day-before bowel preparation method, which results in inferior cleanliness. Our study results suggest that the day-before option needs to be eliminated and the mandatory SDBP regimens need to be promoted for most patients, including those undergoing early morning colonoscopies. Switching to mandatory SDBP will need to be optimized through appropriate physician and patient education.

## Competing interests

A.N. Barkun has been on advisory boards/consulted for Pendopharm Inc. H. Singh has been on advisory boards/consulted for Amgen Canada, Roche Canada, Sandoz Canada, Takeda Canada, Pendopharm Inc, and Guardant Health, Inc. C. Dolovich, C. Unruh, D.C. Moffatt, C. Loewen, B. Kaita, and M. Martel declare that they have no conflicts of interest.

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## Clinical trial

Trial Registration: ClinicalTrials.gov | Registration number (trial ID): NCT03650725 | Type of study: Pragmatic Randomized Controlled Trial

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