B-CLEAN STUDY RESULTS

Alan N. Barkun [1] , Myriam Martel [1] , Ian L. Epstein [2] , Pierre Hallé [3] , Robert J. Hilsden [4], Paul D. James [5] , Alaa Rostom [6], Michael Sey [7], Harminder Singh [8] , Richard Sultanian [9], Jennifer J. Telford [10], Daniel Von Renteln [11], Kristina Candido [1]

[1] Mcgill University Health Center, McGill University, Montreal, QC; [2] Dalhousie University, Halifax, NS; [3] Hôpital Du Saint-sacrement, Québec, QC; [4] University Of Calgary, Calgary, AB; [5] University Health Network , Toronto, ON; [6] University Of Ottawa, Ottawa, ON; [7] Western University, London, ON; [8] University Of Manitoba, Winnipeg, MB, [9] Division Of Gastroenterology, University Of Alberta, Edmonton, AB; [10] University Of British Columbia, Vancouver, BC; [11] University Of Montreal, Montreal, QC, Canada

Name: Dr. Alan Barkun

Conflict of Interest Disclosure

(over the past 24 months)

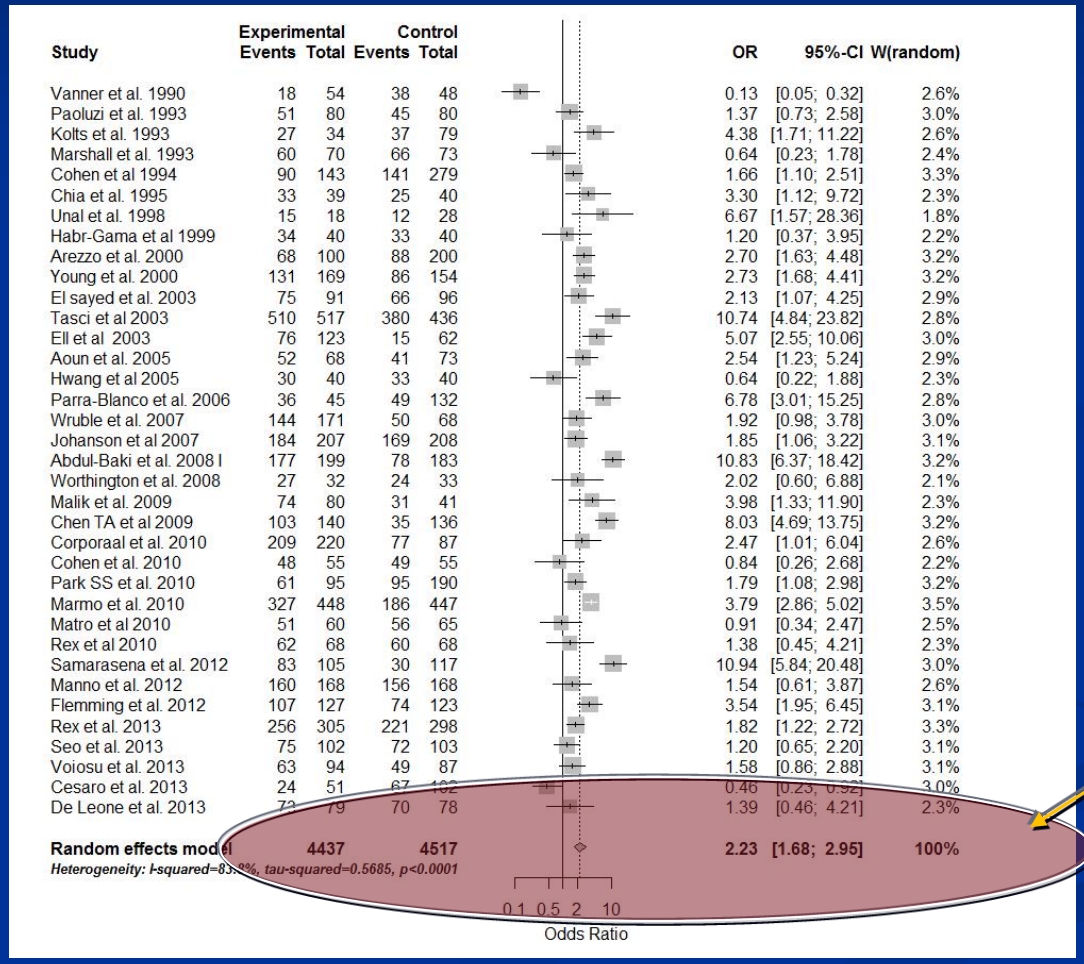
Commercial or Non-Profit Interest	**Relationship**
Cook Medical	advisory board, consultant
Olympus	advisory board, consultant
Pendopharm	advisory board, consultant, research support
ATGEN	advisory board, research support

INTRODUCTION

- Key quality indicators of colonoscopy, cecal intubation rate and polyp/adenoma detection rates, are associated with the quality of bowel cleansing
- An inadequate level of bowel cleansing also results in further costs (1% - 1%)
- The discomfort and inconvenience of bowel preparation may affect the acceptability and uptake of colonoscopy in screening programs

ESGE, Endoscopy, 2013; Johson, GIE/Gastro/AJG, 2014

Superiority of split-dose preprations



Martel, Gastro, 2014

Recommended colonoscopy regimen

- Use of a **split-dose bowel cleansing regimen** is strongly recommended for elective colonoscopy
  (Strong recommendation, high-quality evidence)
- A **same-day regimen** is an acceptable alternative to split dosing, especially if afternoon exam
  (Strong recommendation, high-quality evidence)
- The 2nd dose of split preparation should start **4–6 hours before** the colonoscopy (**end 2hrs pre**; no longer than 4 hours pre [ESGE])
  (Strong recommendation, moderate-quality evidence)

Johnson, GIE, 2014

Split-dose preparations and polyp detection

- N=28, n=8,842
- Split-dose vs day-before (N=7):
  - increased ADR (1.26, 1.10–1.44)
  - Greater advanced adenoma detection (1.53, 1.22–1.92)
  - Higher SSP detection (2.48, 1.21–5.09).
- Split-dose vs same-day (N=8), no differences
- For various split-dose vs split-dose trials (N=14) no superior split-dosing regimen was identified

Zawaly, AJG, 2019

SAME DAY VS SPLIT DOSING

- N=10, n=1807; 3 used Pico, 6 3-day low residue
- Adequate cleansing: Same 85.3% vs Split 86.3% (P=NS)
- Compliance: 89.7% vs 96.6% (P=0.03)
- Sleep disturbance: 13.7% more in Split (P=NS)
- Nausea: 10.5% more in Same group (P=0.01)
- Pico Same cleaned better than Pico Split (not Randomized)
- PEG vs Pico in various regimens: no difference in cleansing, more compliance with Pico

Bucci, Gastro Revs Pract, 2019

PEG vs Pico Sulfate preps

- N=15: Pico resulted in cleaner, better compliance, better tolerated preparations
- But very few split-dosing, limited methodology in 12 studies (concealment of randomization*)
- N=25 RCTs: trend to better preps with PEG (RR 0.93; 0.86-1.01, P = 0.07)
- More likely to complete SPMC (1.08; 1.04-1.13) and willing to repeat (1.44; 1.25-1.67)
- Lower adverse events SPMC (0.78; 0.66-0.93)
- No differences in PDR or ADR

Cheng, Surg Endosc, 2016; Jin, Eur J Clin Pharmacol, 2016

PEG vs Sodium Picosulfate with Magnesium Citrate

- N=13, good quality, large heterogeneity
- SPMC slightly better cleansing than PEG (RR 1.06; 1.02-1.11)
- SPMC better tolerated than PEG
- No differences in effectiveness or tolerability between SPMC and NaP
- Side effects similar, except for dizziness (1.71; 1.32 to 2.21) in favour of PEG, and vomiting (0.35; 0.13 to 0.95) in favour of single-dose SPMC vs. split-dose
- Problem: many studies used single dose PEG

Van Lieshut, UEGJ, 2017

Low residue vs Clear Liquid Diet

- N=9, n=1686 patients (5 w split preps)
- No differences in adequate bowel preparation rates (OR 1.21; 0.64-2.28)
- Greater tolerability with LRD (OR 1.92; 1.36-2.70)
- Greater willingness to repeat with LRD (OR 1.86; 1.34-2.59)
- No differences in adverse effect rates (OR 0.88; 0.58-1.35)
- ?NPO x 2hrs with split-dosing…

Nguyen, GIE, 2016

NPO duration prior to colonoscopy

- Prep within 8 hours of colonoscopy
- N=28 RCTs, 2 controlled, 10 observational studies
- N=6 (n=2,421) reported on aspiration; none found that shorter NPO status prior to colonoscopy increased aspiration risk (but studies not designed to assess this)

Shaukat, Gastro Res Pract, 2017

Use of enhanced instructions

- N=8 RCTs, n=3795
- Better prep quality with enhanced instructions (OR=2.35, 1.65-3.35)
- Results independent of different purgative types, administration methods, or diet restriction
- Also greater willingness to repeat the preparation (1.91; 1.20-3.04)
- Visual aid, Social Media, SMS, telephone, Tel ap, additional explanations, cartoon visual aids, redesigned booklets – written/verbal instructions of both

Guo, GIE, 2017

Use of a smart phone app

- N=6, n=1665,
- Greater adequate prep: 87.5% vs 77.5% (OR=2.67, P=0.05)
- Only a trend if only looking at RCTs (OR 2.66, P=0.07)
- When only using BBPS, mean diff=0.9 (P<0.01)

Desai, Endo Int, 2019

Predictors of poor bowel preparation

Table 1. Summary of patient-related factors to poor bowel preparation

Patient characteristics	
Age	• Higher risk of inadequate bowel preparation in patients 65 or older
	• Patients seem to tolerate well the bowel preparation intake
	• Higher rate on non-compliance
	• 30-min walk during preparation intake may increase motility
	• No optimal bowel preparation was found
Gender	• Male patients had higher risk of inadequate bowel cleanliness compared to females
Socio-economic status	• Patients with Medicare programs, low education status and low income are at higher risk of inadequate bowel preparation
	• Higher rate of non-compliance
Other	• American Society of Anesthesiology was not found to be associated to inadequate bowel preparation in the general population
Co-morbidities	
Inflammatory bowel disease	• Patients with repeated colonoscopy with required excellent quality of cleanliness to evaluate the mucosa
	• Higher level of anxiety
	• No preparation was found to be better, but sodium phosphate should be avoided due to potential superficial mucosal abnormalities and in rare cases nephrotoxicity
In-patients	• Hospitalized patients have higher risk of poor bowel preparation compared to outpatients
	• Higher prevalence of comorbidities such as hypertension, diabetes, and chronic kidney disease and ischemic heart disease
	• Indications where less for screening and constipation but more often for anemia and positive occult blood testing
	• No optimal bowel preparation was found
	• Positive impact of ward nurse education on patient compliance and bowel cleanliness
Body mass index (BMI)	• Higher BMI was found in some study to be associated with poor bowel cleanliness but not in all studies
Diabetes mellitus	• Patients with slower gastric emptying and higher risk of constipation
	• Higher rate of inadequate bowel cleanliness
	• RCT did not demonstrate 6-L PEG to be more
	• Addition of 10 mg magnesium citrate was more efficient than without (combined with 4-L PEG) and another RCT suggested multimodal strategy including an educational intervention, a low-fiber diet for 3 days followed by a 24-h liquid diet before the colonoscopy with accompanied adjustments of glucose-lowering agents
Cirrhosis	• Higher inadequate bowel cleanliness in cirrhosis patients
	• Water-salt imbalance in liver disease patients affects intestinal fluid permeability during standard colonic preparation and may be responsible for a suboptimal bowel cleanliness
Constipation	• Higher inadequate bowel cleanliness in constipated patients
	• Patients with slower colonic transit time
	• No optimal bowel preparation was found but probiotic treatment for 2 weeks prior to colonoscopy was found to be effective in one trial
Neurological condition	• Higher inadequate bowel cleanliness in patients with Parkinson or dementia/stoke

Martel, Curr Treat Opt Gastro, 2019

Predictors of poor bowel preparation

- N=24, n=49,868; world region variations; significant predictors (*if split-dosing):
  - Age (OR: - 1.20)
  - Male sex (OR: 0.85); Race* (OR: 0.93)
  - Inpatient status (OR: 0.57)
  - Diabetes mellitus (OR: 0.58)
  - Hypertension (OR: 0.58)
  - Cirrhosis (OR: 0.49)
  - Narcotic use (OR: 0.59)
  - Constipation (OR: 0.61)
  - Stroke (OR; 0.51)*
  - TCA use (0.51)*

Mahmood; Eur Gastro Hepato, 2018

Current status of bowel preps

- Split-dosing superior
- Yet limited data on using split-dose vs day before
- Many still use day before for AM patients
- Limited data on same-day vs split-dosing
- Limited data on 2L vs 4L split-dose PEG
- Limited RCT data from Canada on PEG preparations

THE BCLEAN INITIATIVE

10 participating Canadian Centres

BCLEAN studies at DDW

- Sa 1748 – Day before vs split-dose preps
- Mo 1068 - Same-day preps
- Mo 1662 - Hi vs Lo split-dose PEG preps
- Dr. H Singh: Sa 1754 - Sleep disturbances and travel interruption

The Bowel CLEAnsing: a National initiative (B-CLEAN)

- Multicenter blinded* randomized study across Canada
- Main outcome: bowel cleanliness
- Objectives: To address issue of
  - Timing of colonoscopy : morning vs. afternoon
  - High vs. low volume
  - Timing of preparation, incl. same day
  - Influence of diet (clear liq. vs. no residue)

Timing of endoscopy

- *Early colonoscopy:* 7:30 AM to 10h30 AM
- *Later colonoscopy:* 10:30 AM to 4:30 PM

Bowel preparation regimens

- High volume PEG split-dose
  - Colyte® or PegLyte®
  - 1st dose: 2L starting at 7:00 PM the day before the procedure at a rate of 240 mL every 10 minutes.
  - 2nd dose: 2L of preparation the morning of the colonoscopy starting 4-5 hours prior to the planned procedural time at a rate of 240 mL every 10 minutes.

Bowel preparation regimens

- Low volume PEG split-dose
  - Bi-PegLyte®
  - 15mg Bisacodyl at 2:00 PM the day before the procedure. (use of antacids is not permitted within one hour)
  - 1st dose: after the first bowel movement (or within 6 hours of taking the Bisacodyl), 1L at a rate of 240 mL every 10 minutes.
  - 2nd dose: 1L of preparation the morning of the colonoscopy starting 4-5 hours prior to the procedure at a rate of 240 mL every 10 minutes.

Bowel preparation regimens

- High volume PEG non split, day before
  - Colyte® or PegLyte®
  - 4L starting at 6:00 PM the day before the procedure, at a rate of 240 mL every 10 minutes until completed.

- Low volume PEG non split, same day
  - Bi-PegLyte®
  - 15mg Bisacodyl at 2:00 PM the day before the procedure. (use of antacids is not permitted within one hour)
  - 2L of preparation the morning of the colonoscopy starting 4 hours prior to the procedure at a rate of 240 mL every 10 minutes.

Clear Liquid Diet

- Starting the morning before the colonoscopy (no normal breakfast)

ALLOWED: Clear Liquid Diet	**NOT ALLOWED:**
Example: • Clear soup, broth or bouillon • Sports drinks (Gatorade) or soft drinks (7-Up, Ginger Ale, etc.) • Clear fruit juices such as apple juice, white grape or white cranberry juice • Kool-Aid, Jello (not red, purple, blue or green) • Tea, coffee (without milk or cream) • Popsicles (not red, purple, blue or green) • Water	**NO RED, PURPLE, BLUE or GREEN colored liquids** • Orange, pineapple or red grape juice • Milk or dairy products • Milk shakes • Malt • Alcoholic drinks • Dark colored soft drinks such as Coke or Pepsi **NO liquids containing PULP**

Low residue diet

- Starting the morning, the day before your colonoscopy (no normal breakfast) until bedtime

ALLOWED

Example:

- Well-cooked, tender meat and fish
- Limited servings of steamed well-cooked vegetables that do not include skins
- Canned fruit, grapes without skins, honeydew melon, peaches without skins, watermelon
- White bread, buns, melba toast,
- White rice or refined pasta and noodles
- Tofu, smooth nut butters, eggs

Consume a lot of clear fluids, including:

- Clear soup, broth or bouillon
- Sports drinks (Gatorade) or soft drinks (7- Up, Ginger Ale, etc.)
- Clear fruit juices such as apple juice, white grape or white cranberry juice
- Kool-Aid, Jello (not red, purple, blue or green)
- Tea, coffee (without milk or cream)
- Popsicles (not red, purple, blue or green)
- Water

Low residue diet cont

NOT ALLOWED

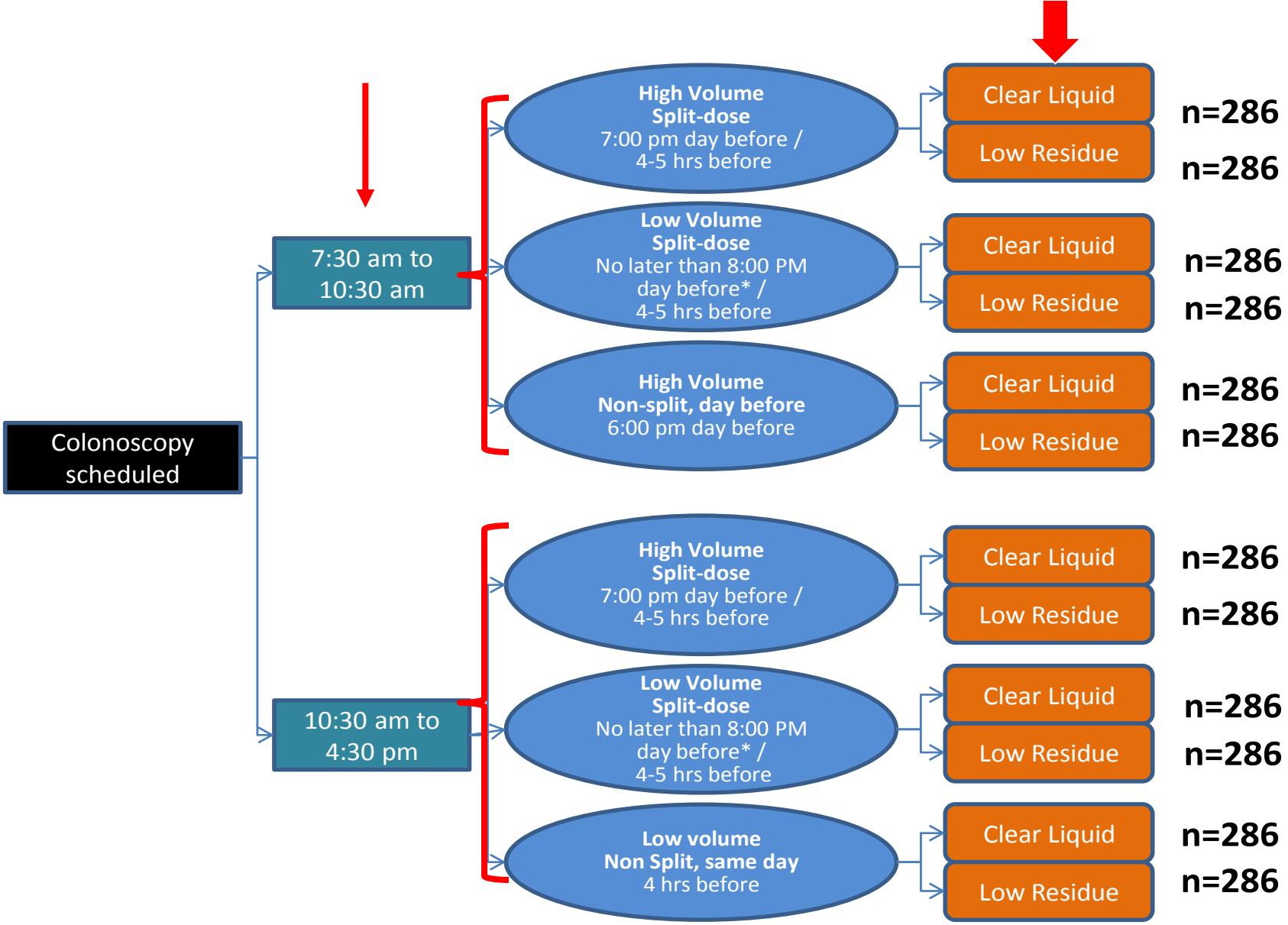
- Salami, sausages, cold cuts
- Any raw vegetables, corn, tomato seeds, vegetables from the cruciferous family such as broccoli, cauliflower, brussels sprouts, cabbage, kale, swiss chard, etc (even if cooked)
- All other fruit
- Whole grain, sesame seeds, flax
- Whole wheat (brown), quinoa, wild rice, multigrain
- Beans, lentils, peas, chunky nut butters
- Dairy products

NO RED, PURPLE, BLUE or GREEN colored liquids

- Orange, pineapple or red grape juice
- Milk or dairy products; Milk shakes
- Malt
- Alcoholic drinks
- Dark colored soft drinks such as Coke or Pepsi

NO liquids containing PULP

- Starting the morning, the day before the colonoscopy: clear liquid diet



*** See complete description in section 4.2**

Note 1: Patients per group to detect a non inferiority of 10% (power of 0.80), alpha=0.05. One sided test

Note 2: All proportions were calculated considering a 15% drop-off

Note 3: Poor evidence for all comparisons resulting in a limitation for sample size precision

* With a Power of 80%, a true difference will be missed 20% the time

Primary objective and endpoint

- **The primary objective of this clinical study was to determine the cleansing efficacy of different bowel preparations for outpatients while varying**
  - assigned diet,
  - method of administration and
  - volume of the PEG solution

stratified according to time of scheduled colonoscopy (10:30 AM vs later)

- **The primary endpoint was to evaluate the bowel cleansing score rate for a total of BBPS score ≥6 and/or all BBPS score ≥6 and/or each segment ≥2 as rated by the blinded endoscopist**
- **The second primary endpoint was the bowel cleansing score rated by the blinded endoscopist using the Boston Bowel Preparation Scale (BBPS) dichotomized using a cut-off of 7 or greater**

Secondary endpoints (I)

- Subject willingness to repeat the preparation (%)
- Withdrawal time and total procedural time (mn)
- Cecal or ileal intubation rate for colonoscopies (%)
- Polyp detection and polypectomy rate (%)
- Right colon polyp detection rate (%)
- Specific lesional rates identified according to pathology (adenoma, hyperplastic, sessile serrated polyp, advanced neoplasia, cancer) (%)

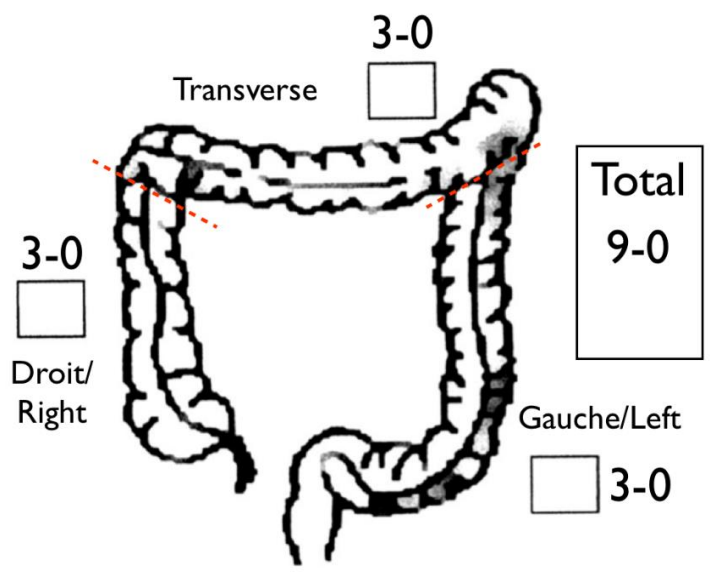
Secondary endpoints (II)

- Subject product completion (% of total required intake and time to complete mn)
- Subject travel time to endoscopy unit (hrs) and any incontinence (%)
- Assess other potential predictors of
  - clean preparation or
  - willingness to repeat
- These include
  - age
  - gender
  - comorbidities
  - indication
  - social economic status
  - use of a patient support tool
  - endoscopist profile
  - concomitant medications
  - time between end of last dose and endoscopy
  - previous failed colonoscopy due to preparation and
  - constipation

Secondary endpoints (III)

- Montreal score compared to Boston Bowel Preparation Score
- Ottawa Bowel Preparation Scores

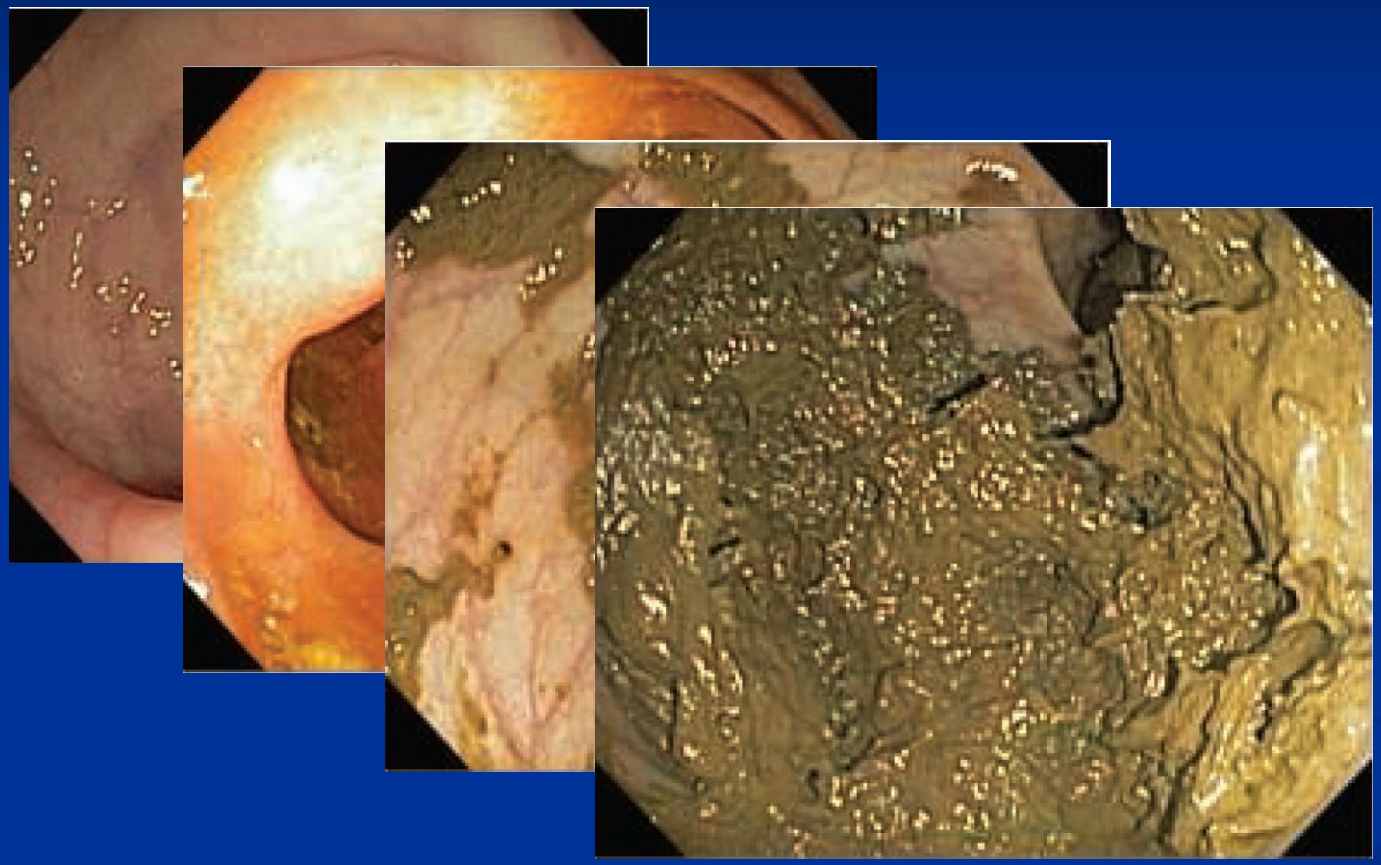
BOSTON:
Score 3 segments after cleaning: Right + Transverse (include both flexures) + Left
Score pour 3 segments après nettoyage: Droit + Transverse (inclus les deux angles) + Gauche



Write NA if segment surgically removed
Inscrire mention NA si segment chirurgicalement manquant

Visual description/ Description visuelle	BBPS score
Entire mucosa of colon segment seen well with no residual staining, small fragments of stool, or opaque liquid/ Muqueuse du segment de colon parfaitement bien vue, sans aucun résidus de selles ou de liquide teinté	3
Minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well/ Résidus minimes de selles et/ou de liquide teinté, mais la muqueuse du segment de colon est globalement bien vue	2
Portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen because of staining, residual stool, and/or opaque liquid/ Des portions de muqueuse du segment de colon sont vues tandis que d'autres ne sont pas vues à cause de matières solides et/ou de liquide teinté	1
Unprepared colon segment with mucosa not seen because of solid stool that cannot be cleared/ Segment de colon non préparé avec muqueuse non visualisée à cause de matières solides qui ne peuvent pas être aspirées	0

BOSTON BOWEL PREP SCORE



Score possible de 0-9

Lai, GIE, 2009

Inclusion Criteria

- Outpatients
- 18 years or older
- Able to comprehend the trial
- Have an indication for full colonoscopy

Exclusion Criteria

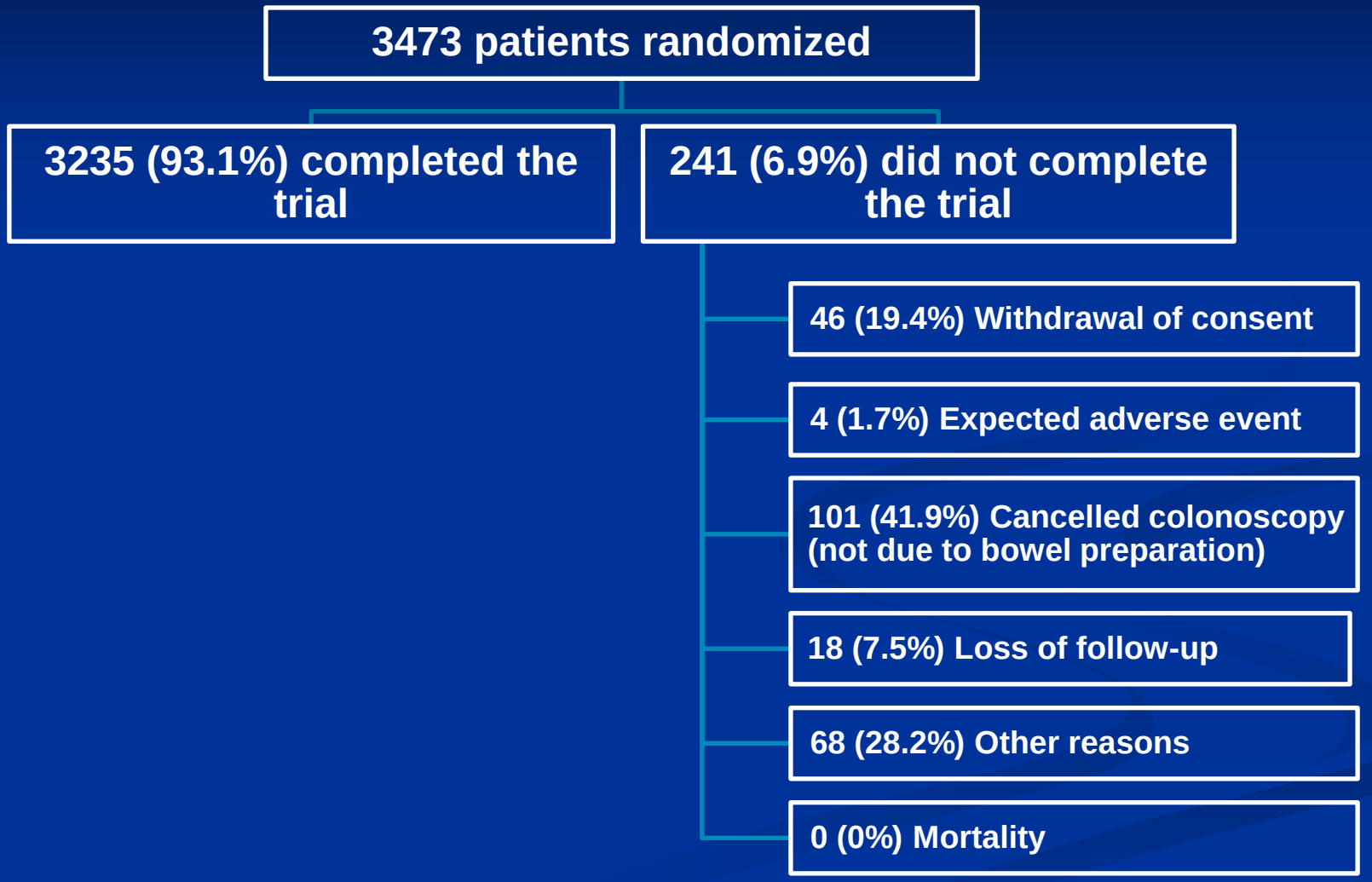
General exclusion criteria:

- Subject refusal
- Previous bowel preparation in the last 14 days
- Pregnancy or breastfeeding
- Reduced mobility
- Known allergy to preparation constituent

Medical/Endoscopic exclusion criteria:

- Suspected or diagnosed with bowel obstruction
- Any colonic surgery
- Toxic megacolon
- Ileus
- Ischemic colitis
- Decompensated heart failure
- Severe acute renal failure
- Severe electrolyte imbalance

Flow diagram



Results – Patient demographics

	All patients N=3473
Age	56.3 ± 13.3
Female	53.2%
BMI	27.8 ± 14.4
Help required for preparation directive	1.0%
Known IBD	7.3%
Received colonoscopy in the past	58.1%
Previous failed colonoscopy	4.0%
Narcotic use in the last 24 hours	3.3%
Chronic laxative use or known medication induced constipation	9.5%
Functional constipation*	9.8%
Indication	
Non screening	37.8%
Screening	37.4%
Surveillance	24.8%

*According to the ROME III classification

Results comparisons

- #1 Split-dose high-volume PEG compared to split-dose low-volume PEG with Bisacodyl
- #2 Same-day low-volume PEG versus split-dose high-volume PEG versus split-dose low-volume PEG with Bisacodyl (PM patients only)
- #3 Day before high-volume PEG versus split-dose high-volume and/or split-dose low-volume PEG with Bisacodyl (for AM patients only)

#1 Split-dose high-volume PEG compared to split-dose low-volume PEG with Bisacodyl

	Split-dose High-volume N=1157 AM+PM	Split-dose Low-volume N=1157 AM+PM	
Withdrawal time	8.3 ± 3.2	8.4 ± 3.5	0.742
Total Boston preparation score	7.4 ± 1.7	7.0 ± 1.9	0.003
BBPS Adequate*	90.8%	88.1%	0.041
Patient willing to repeat the preparation	66.9%	91.9%	<0.001
Patient Tolerance (1-10 scale)	7.2 ± 2.3	8.1 ± 1.9	<0.001
Caecal intubation	97.4%	95.6%	0.023
Polyp detection rate	49.0%	45.8%	0.137
Functional constipation**	9.4%	10.4%	0.422

* Boston Bowel Preparation Scale (BBPS) dichotomized using a cut-off of ≥6 and/or all segment ≥2 scores
** According to the ROME III classification
NB: incontinence was evaluated in a sub-study by Dr Singh et al.,

#2 Same-day low-volume PEG versus split-dose high-volume PEG versus split-dose low-volume PEG with Bisacodyl –

- (for PM patients only) -

	Same-day low-volume N=583 PM	Split-dose high-volume N=582 PM		Split-dose low-volume N=585 PM		Same-day low-volume vs Split-dose high or low volume N=1167 PM	
Withdrawal time	8.4 ± 4.1	8.2 ± 3.3	0.591	8.3 ± 3.2	0.609	8.2 ± 3.3	0.528
Total BBPS	7.5 ± 1.7	7.4 ± 1.6	0.523	7.1 ± 1.8	<0.001	7.3 ± 1.73	0.012
BBPS Adequate*	90.5%	92.2%	0.338	87.9%	0.173	90.1%	0.764
Patient willing to repeat the preparation	91.0%	68.9%	<0.001	92.5%	0.395	81.2%	<0.001
Patient Tolerance (1-10 scale)	8.1 ± 1.9	7.2 ± 2.3	<0.001	8.2 ± 1.9	0.652	7.7 ± 2.1	0.001
Caecal intubation	97.0%	97.6%	0.549	87.9%	0.232	96.6%	0.673
Polyp detection rate	47.0%	47.7%	0.823	48.4%	0.656	48.1%	0.699

* Boston Bowel Preparation Scale (BBPS) dichotomized using a cut-off of ≥6 and/or all segment ≥2 scores
NB: incontinence was evaluated in a sub-study by Dr Singh et al.,

#3 Day before high-volume PEG versus split-dose high-volume PEG and/or split-dose low-volume PEG with Bisacodyl

- (for AM patients only) -

	Day before high-volume N=579	Split-dose high-volume N=575		Split-dose low-volume N=572		(High or Low) split-dose N=1147	
Withdrawal time	8.8 ± 3.8	8.4 ± 3.1	0.203	8.4 ± 3.2	0.203	8.5 ± 3.4	0.208
Total BBPS	6.2 ± 2.0	7.3 ± 1.7	<0.001	7.2 ± 1.8	<0.001	7.2 ± 1.8	<0.001
BBPS Adequate*	71.8%	89.4%	<0.001	88.2%	<0.001	88.8%	<0.001
Boston ≥ 7	42.9%	65.5%	<0.001	66.2%	<0.001	63.8%	<0.001
Patient willing to repeat the preparation	59.6%	64.8%	0.107	91.2%	<0.001	78.5%	<0.001
Patient Tolerance (1-10 scale)	7.0 ± 2.3	7.2 ± 2.4	0.106	8.0 ± 1.8	<0.001	7.6 ± 2.1	<0.001
Caecal intubation	94.4%	97.2%	0.023	95.6%	0.394	96.4%	0.068
Polyp detection rate	43.5%	50.3%	0.026	43.1%	0.909	46.7%	0.222

* Boston Bowel Preparation Scale (BBPS) dichotomized using a cut-off of ≥6 and/or all segment ≥2 scores
NB: incontinence was evaluated in a sub-study by Dr Singh et al.,

Conclusion 1

Split-dose high-volume PEG (2L+2L) compared to split-dose low-volume PEG (1L+1L) with bisacodyl (15mg)

- **Split-dose high-volume PEG - Independent of time of procedure (AM or PM) or diet (clear liquid or low residue diet)**
  - **Improved bowel cleansing according to the BBPS**
  - **Improved cecal intubation**
  - **Improved polypectomy rates**
- **However,**
  - **Lower patient willingness to repeat the bowel preparation**
  - **Lower patient tolerance**

Conclusion 2

Same-day low-volume PEG (2L) compared split-dose high-volume PEG (2L+2L) and/or split-dose low-volume (1L+1L) PEG with bisacodyl (15mg)

- Low volume PEG given the day of the colonoscopy - independent of diet (clear liquid or low residue)
  - Similar bowel cleanliness compared to split-dose high-volume PEG
  - "Better bowel cleanliness" compared to split-dose low volume PEG

- Same-day low-volume PEG
  - Greater willingness-to-repeat compared to split-dose high-volume PEG
  - No different willingness-to-repeat compared to split-dose low-volume PEG

Conclusion 3

Day before high-volume PEG (4L) versus split-dose high-volume PEG (2L+2L) and/or split-dose low-volume PEG (1L+1L) with Bisacodyl (15mg)

- **Day before high-volume PEG - independent of diet (clear liquid or low residue)**
  - **Worse bowel cleanliness compared to split-dose high volume PEG**
  - **Worse bowel cleanliness compared to split-dose low volume PEG**
  - **Lower patient willingness to repeat compared to the split-dose low-volume PEG**
  - **Not significantly different patient willingness to repeat compared to the split-dose high-volume PEG**
  - **Inferior cecal intubation and polyp detection vs split-dose high-volume PEG**

DAY BEFORE PREPARATIONS ARE OUT

Acknowledgments

- Myriam Martel,
- Ian L. Epstei, Pierre Hallé, Robert J. Hilsden, Paul D. James, Alaa Rostom, Michael Sey, Harminder Singh, Richard Sultanian, Jennifer J. Telford, Daniel Von Renteln,
- Kristina Candido, Meaghan Smith
- Pendopharm Inc. – at arms length funding of this investigator-initiated trial