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Drug Class Review: Bowel Preparations

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Purpose for Class Review:
Review the evidence for drugs used in cleansing the bowel prior to diagnostic or therapeutic colonoscopy. Recommend development of a Preferred Drug List (PDL) class with preferred and nonpreferred agents based on safety and efficacy.

Plain Language Summary:

- Colorectal cancer is cancer of the large intestine (colon) or rectum. The risk for having colorectal cancer is highest in people with a family history of colorectal cancer or polyps, which are small early cancer growths that form in the lining of the intestine. Other risk factors for colorectal cancer include a history of Crohn's disease, ulcerative colitis, cigarette smoking, being overweight, or eating a lot of processed meats and high fat meals. It is recommended that people begin screening for colon cancer at 45 years of age.
- The easiest way to screen for colorectal cancer is by testing the stool for blood at home. This test checks for unusual bleeding in the large intestine, but it will not find polyps. A more through physical exam called a colonoscopy can find small polyps. A colonoscopy lets a doctor look inside the large intestine using an instrument called a scope. During this exam, the doctor checks for unusual inflammation, polyps, and ulcers in the large intestine. Polyps can be removed during the colonoscopy, which decreases the odds of developing cancer.
- Before undergoing a colonoscopy, the large intestine must be completely cleaned so the doctor can get a clear view of the intestinal tract lining. Different medicines called laxatives are used to help empty the large intestine before a colonoscopy. Most doctors prescribe polyethylene glycol (PEG) because is safe and effective. This medicine causes watery diarrhea for several hours to remove stool from the large intestine.
- Polyethylene glycol is supplied as 4 liters (approximately 1 gallon) of liquid which must be taken before the procedure. Many people find it difficult to drink an entire gallon of liquid the night before colonoscopy. For this reason, split-dose dosing is now recommended. In split dosing, one-half of the laxative liquid is taken the night before the procedure and the other half is taken the morning of the colonoscopy. Adding a flavor packet, drinking through a straw, and chilling the solution help improve the taste of the medicine and can reduce side effects such as nausea or bloating.
- An alternative to taking one gallon of PEG solution is a salt-based laxative which is available as a liquid or tablet. These products do not require the patient to drink as much fluid as the PEG products and may be easier for some people to swallow. People with heart failure, kidney problems, or liver disease should not use salt-based laxatives because the large amount of salt in these products can cause serious side effects.
- We recommend at least one PEG product and one oral salt-based laxative be available to Oregon Health Plan members. For all other medicines in this class, the provider must explain to the Oregon Health Authority why their patient needs that medicine. This is process is called prior authorization.

Research Questions:

1. What is the comparative efficacy for saline-based laxatives and PEG 3350 for cleansing the bowel prior to colonoscopy and detecting polyps or adenomas?
2. What are the comparative harms of saline-based laxatives and PEG 3350 laxatives?
3. Are there specific populations (i.e., elderly patients, patients with renal or hepatic disease) in which certain laxative formulations are better tolerated or more effective?

Conclusions:

- A literature search for recently published, high-quality evidence on the safety and efficacy of bowel preparation prior to colonoscopy identified 6 systematic reviews[1-5] and 2 clinical practice guidelines.[6,7]
- Ineffective bowel cleansing prior to colonoscopy increases the risk of not detecting precancerous lesions and increases costs related to repeat procedures.[6]
- A 2019 systematic review and meta-analysis evaluated the efficacy of polyp detection of 2 pre-colonoscopy dosing regimens. Single dose administration was compared with splitting the administration of bowel preparations into 2 doses (split-dose).[1] Medications of interest included high- and low-volume PEG solutions, sodium phosphate, oral sulfate solutions, and the combination product of sodium picosulfate, magnesium oxide, and citric acid (SPMC).[1] Pooled data from 4 randomized controlled trials (RCTs) that compared split-dose versus day-before bowel preparation regimens showed an increased detection rate of adenomas in the split-dose groups (risk ratio (RR) 1.26; 95% confidence interval (CI) 1.10 to 1.44; I^2 = 0%; n=1,258).[1] In addition, when split-dose administration was compared with day-before administration, there was increased detection of advanced adenomas (RR 1.53, 95% CI 1.22 to 1.92; 3 RCTs; I^2 = 0%; n=1,155).[1] Compared with day-before bowel preparation regimens, split-dose bowel preparations regimens increased the detection of adenomas and advanced adenomas.[1]
- A 2020 systematic review and meta-analysis evaluated efficacy of bowel preparation prior to colonoscopy with high-volume PEG products (>2 L [liter]) versus low-volume laxatives (≤ 2 L) administered in split-dose regimens.[2] In the pooled analysis of 17 RCTs (n=7528), no significant differences in adequacy of bowel cleansing were identified between the low- versus high-volume split-dose regimens (86.1% vs. 87.4%; RR 1.00; 95% CI 0.98 to 1.02; I^2 = 17%).[2] Compared with high-volume regimens, low-volume regimens had higher odds for patient completion of the prescribed laxative (86.8% vs. 92.8%; RR 1.06; 95% CI 1.02 to 1.10; p<0.01; I^2 = 85%).[2] When adverse effects (AEs) were evaluated, low-volume regimens had less bloating (RR 0.66, 95% CI 0.48 to 0.92), nausea (RR 0.86, 95% CI 0.46 to 1.00), and vomiting (RR 0.68, 95% CI 0.46 to 1.00) compared with high-volume regimens.[2] Abdominal pain was less likely with high-volume regimens compared with low-volume regimens (RR 1.22; 95% CI 0.73 to 2.03).[2]
- A 2022 systematic review evaluated the efficacy of ultra-low volume (< 1 L) bowel preparation products compared with high-volume (> 2 L) and low-volume (1-2 L) products.[3] In single-arm RCTs, bowel preparation with SPMC 300 mL (milliliters), 1 L PEG with ascorbate (PEG-ASC), sodium phosphate 240 mL, and sodium sulfate solution 354 mL was adequate in 75.2%, 82.9%, 81.9%, and 92.1%, of patients, respectively.[3] However, heterogeneity between studies was considerable (I^2 range: 86 to 98%).[3] Ultra-low volume bowel preparation fluids do not always meet the 90% quality standard for adequate bowel preparation as defined by 2017 European Society of Gastrointestinal Endoscopy (ESGE) guidelines.[3,8]
- A 2023 meta-analysis of 9 RCTs evaluated the safety and effectiveness of 1 L PEG-ASC compared with other bowel preparation products.[4] The comparators included: 2 L PEG-ASC, 4 L PEG, a trisulfate product (magnesium, potassium, and sodium salts), SPMC, and SPMC plus PEG.[4] The meta-analysis showed a higher bowel cleansing rate with 1 L PEG-ASC than with the other preparations (odds ratio [OR] 1.50; 95% CI 1.25 to 1.81; p<0.01, I^2 = 0%, n=6,720).[4] In addition, a higher right-colon high-quality cleansing rate was found with 1 L PEG-ASC than with the other preparations (OR 1.67; 95% CI 1.21 to 2.31; p<0.01, I^2 = 43%, n= 3,221).[4] The pooled estimate of the adenoma detection rate did not significantly differ between the 2 groups (OR 1.02; 95% CI 0.87 to 1.20; p=0.79, I^2 = 0%, n=3,984).[4] More patients reported AEs with 1 L PEG-ASC than with the other laxatives (OR 1.51; 95% CI 1.23 to 1.84; p<0.01, I^2 = 0%, n=3,500).[4]

- A 2016 systematic review and meta-analysis evaluated the safety and efficacy of SPMC versus PEG-based regimens for colonoscopy preparation.[5] In the meta-analysis of 21 RCTs, adequate bowel preparation favored PEG compared with SPMC (RR 0.93; 95% CI 0.86 to 1.01; p=0.07; I^2 = 87%).[5] Pooled data from 7 RCTs showed no difference between SPMC and PEG in adenoma detection rate (RR 0.88; 95% CI 0.74 to 1.05; p=0.16; I^2 = 37%).[5] Pooled data from 13 RCTs showed less AEs with SPMC compared with PEG (RR 0.78; 95% CI 0.66 to 0.93; p=0.004; I^2 = 88%).[5] When analyzing individual AEs, more patients in the PEG group had nausea, vomiting and abdominal bloating while more patients in the SPMC group developed dizziness. There was no significant difference between the two groups in the incidence of abdominal pain.[5]
- A 2022 meta-analysis of 8 RCTs evaluated the efficacy of oral sulfate solution versus PEG-based solutions (volume ranged from 1L to 4L)for polyp and adenoma detection during colonoscopy.[9] Meta-analysis of 6 RCTs suggested that oral sulfate solutions increased the polyp detection rate compared with PEG-based laxatives (47.34% vs. 40.14%, RR 1.13, 95% CI 1.03 to 1.24; p=0.01; I^2 = 69%).[9] In pooled data from 5 RCTs, the adenoma detection rate was higher with oral sulfate solutions compared with PEG-based laxatives (44.60% vs. 38.14%; RR 1.17; 95% CI 1.03 to 1.33; p=0.01; I^2 = 73%).[9]
- Guidance for adequate bowel preparation prior to colonoscopy was published in 2014 by a multi-society task force comprised of the American College of Gastroenterology, the American Gastrological Association, and the American Society for Gastrointestinal Endoscopy.[6] Strong recommendations based on moderate- to high quality-evidence include:
    - Use of a split-dose bowel cleansing regimen is strongly recommended for elective colonoscopy (strong recommendation, high-quality evidence).[6]
    - A same-day regimen is an acceptable alternative to split dosing, especially for patients undergoing an afternoon examination (strong recommendation, high-quality evidence).[6]
    - The second dose of split preparation ideally should begin 4–6 hours before the time of colonoscopy with completion of the last dose at least 2 hours before the procedure time (strong recommendation, moderate-quality evidence).[6]
    - Selection of a bowel-cleansing regimen should take into consideration the patient's medical history, medications, and, when available, the adequacy of bowel preparation reported from prior colonoscopies (strong recommendation, moderate-quality evidence).[6]
- In 2019, the European Society Of Gastrointestinal Endoscopy (ESGE) Guideline Committee updated 2013 guidance on the efficacy and safety of bowel preparation products prior to endoscopy.[7] Most of the recommendations are similar to the 2014 U.S. multi-task force guidance, but include data for the safety and efficacy of formulations which received FDA-approval after 2013. Strong recommendations based on low- to high-quality evidence include:
    - The use of high-volume or low-volume PEG-based regimens as well as that of non-PEG-based agents that have been clinically validated for routine bowel preparation are recommended.[7] In patients at risk for electrolyte disturbances, the choice of laxative should be individualized (strong recommendation, moderate-quality evidence).[7]
    - Do not routinely use oral sodium phosphate for bowel preparation (strong recommendation, low-quality evidence).[7]
    - High volume or low volume PEG-based bowel preparations are recommended in patients with inflammatory bowel disease (strong recommendation, high-quality evidence).[7]
- Both guidelines recommend the selection of a bowel preparation product should take into consideration patient risk factors. For most people, PEG-electrolyte lavage solutions (ELS) are preferred.[6,7] For people that cannot tolerate the large volume of solution that must be consumed, saline-based laxatives are available. Saline-based laxatives are recommended for use in people under 65 years of age without risk factors for electrolyte disturbances (i.e., heart failure, renal impairment, end-stage hepatic disease).[6,7] Products that contain magnesium should be avoided in older patients, patients with renal disease and people taking medications (i.e., diuretics) that impact renal blood flow or electrolyte excretion.[7] The PEG- electrolyte lavage solutions (ELS) formulations that contain ascorbic acid should be avoided in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency, as ascorbic acid can trigger hemolysis.[10]
- Colorectal cancer disease burden varies across racial groups, with the highest incidence and mortality rates in Blacks, American Indians, and Alaska Natives.[11]

Health-care providers should make extra efforts to promote access for these populations to get the follow-up they need, including access to clear information and colonoscopy.[12]

Recommendations:

- Create a PDL class entitled "Bowel Preparations" and include PEG 3350 products and saline-laxatives approved for colonoscopy preparation in this drug class.
- Make at least one PEG product and one saline-laxative preferred on the PDL.
- Evaluate drug costs in executive session.

Background:

According to the World Health Organization, colorectal cancer has the fourth highest incidence of non-cutaneous cancer worldwide, affecting 32.3 per 100,000 people in 2020.[13] By the year 2070, colorectal cancer is projected to be the most common cancer globally with 4.7 million expected cases.[14] In the U.S., colorectal cancer is the second leading cause of cancer death, leading to 50,000 deaths annually.[15] Colorectal cancer disease burden varies across racial groups, with the highest incidence and mortality rates in Blacks, American Indians, and Alaska Natives.[11] Colorectal cancer can be prevented by the detection and removal of precancerous polyps, and survival is significantly better when colorectal cancer is diagnosed early, while still localized.[16]

Colorectal cancer screening includes guaiac-based fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy.[16] Fecal blood testing can be completed at home, but only indicates the presence of blood in the rectum or intestine, as polyps cannot be detected with this test. Sigmoidoscopy can be performed with a simple bowel preparation, without sedation, and by a variety of practitioners including nurses and physician assistants in office-based settings.[16] The major limitation of sigmoidoscopy is that it only examines a portion of the large intestine (i.e., the rectum, sigmoid, and descending colon).[16] Colonoscopy requires extensive bowel preparation, patient sedation, and is conducted in a hospital or outpatient surgical setting by a specialist. In contrast to sigmoidoscopy, colonoscopy allows direct mucosal inspection of the entire colon and biopsy sampling or polypectomy in the case of precancerous polyps and some early-stage cancers.[16] Indications for colonoscopy include screening for colon cancer, evaluating signs and symptoms of possible colonic disease, assessing a response to treatment in patients with known colonic disease (e.g., inflammatory bowel disease), evaluating unexplained gastrointestinal bleeding, and evaluating abnormalities found on imaging studies.[17] Therapeutic indications for colonoscopy include stricture dilation, stent placement, colonic decompression, and foreign body removal.[17]

A successful colonoscopy requires cleansing of the large bowel to permit clear visualization of the mucosal surface.[16] Current options for bowel preparation include polyethylene glycol-electrolyte lavage solutions (PEG-ELS) and various saline laxatives.[18] Polyethylene glycol-electrolyte lavage solutions are isosmotic, which minimizes fluid exchange across the colonic membrane.[19] Some PEG-ELS formulations (i.e., MOVIPREP, PLENVU) contain ascorbic acid to improve palatability.[18] These products should be avoided in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency, as ascorbic acid can trigger hemolysis.[20] Some PEG-ELS products contain magnesium (i.e., SUFLAVE) and should be avoided in patients with renal impairment.[21] In 2016, the Food and Drug Administration (FDA) issued a safety communication due the risk of phosphate-induced nephropathy associated with oral sodium phosphate products used for bowel preparation.[22] As of 2019, oral sodium phosphate tablets and liquids have been removed from the U.S. market due to safety concerns. **Table 1** provides a list of bowel preparation products which are FDA-approved prior to colonoscopy. A summary of relevant drug information is included in **Appendix 2**, which includes pharmacology, pharmacokinetics, contraindications, warnings and precautions.

Table 1. FDA-Approved Bowel Preparations Prior to Colonoscopy.

Generic Drug Name (BRAND NAME)	FDA-Approved Indication(s)	How Supplied	Total Volume of Adult Dose and Additional Fluid Requirements	Total Volume of Pediatric Dose and Additional Fluid Requirements	Comments
Polyethylene Glycol Laxatives					
PEG 3350 with 4 Electrolytes (Potassium Chloride; Sodium Bicarbonate; Sodium Chloride; Sodium Sulfate) (COLYTE, GOLYTELY)[23]	-Barium Enema Preparation -Colonoscopy Preparation	• Oral Powder for Solution. • Reconstitute with water to a final volume of 4000 mL.	• Laxative dose: 4000 mL • No additional fluids are required.	• Safety and efficacy not established in pediatrics	• Gold standard for bowel preparation efficacy.
PEG 3350 with 3 Electrolytes (Potassium Chloride; Sodium Bicarbonate; Sodium Chloride) (NULYTELY)[24]	Colonoscopy Preparation	• Oral Powder for Solution. • Reconstitute with water to a final volume of 4000 mL.	• Laxative dose: 4000 mL • No additional fluids are required.	• Approved in pediatric patients 6 months and older. • Drink at a rate of 25 mL/kg/hour orally or via NGT until stool is watery, clear and free of solid matter (usually within 4 hours). Total dose not included in prescribing information.	• Gold standard for bowel preparation efficacy.
PEG 3350/Sodium Ascorbate/Ascorbic Acid with 3 Electrolytes (Potassium Chloride; Sodium Chloride; Sodium Sulfate) (MOVIPREP, PLENVU)[10]	Colonoscopy Preparation	• Oral Powder for Solution. • Supplied in 2 separate pouches, which are combined and reconstituted with water to a final volume of 960 mL.	• Laxative dose: 1920 mL (Two 960 mL doses) • Additional total volume of clear liquids: 960 mL (Two 480 mL doses)	• Safety and efficacy not established in pediatrics	• Avoid in people with G6PD deficiency due to ascorbic acid component, which can cause hemolysis.
PEG 3350/Magnesium Sulfate with 3 Electrolytes (Potassium Chloride; Sodium Sulfate; Sodium Chloride) (SUFLAVE)[21]	Colonoscopy Preparation	• Oral Powder for Solution. • Supplied as active ingredients and flavor packet, which are combined and reconstituted with water to a final volume of 1000 mL.	• Laxative dose: 2000 mL (Two 1000 mL doses) • Additional total volume of water: 960 mL (Two 480 mL doses)	• Safety and efficacy not established in pediatrics	• Use with caution in people with renal impairment due to magnesium component.

PEG 3350 OTC product (MIRALAX)	Constipation *Off-Label Indication: Colonoscopy Preparation*	• Oral Powder for Solution.	• Laxative dose: Dilute 238 g in 2000 mL of a sports drink (Two 1000 mL doses) • No additional fluids are required	• Safety and efficacy not established in pediatrics	• May precipitate severe hyponatremia because not osmotically balanced.
Saline-Based Laxatives					
Sodium Sulfate; Potassium Sulfate; Magnesium Sulfate (SUPREP)[25]	Colonoscopy Preparation	• Oral Solution supplied in adult (180 mL) and pediatric (135 mL) doses. • Each 180 mL dose must be diluted with water to a final volume of 480 mL • Each 135 mL dose diluted to a final volume of 360 mL.	• Laxative dose: 960 mL (Two 480 mL doses) • Additional total volume of water: 1920 mL (Two 960 mL doses)	• Approved in pediatric patients aged 12 years and older. • Laxative dose: 720 mL (Two 360 mL doses) • Additional total volume of water: 1440 mL (Two 720 mL doses)	• If taking tetracycline or fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, or penicillamine, take these medications at least 2 hours before and not less than 6 hours after administration.
Sodium Picosulfate; Magnesium Oxide; Citric Acid (CLENPIQ)[26]	Colonoscopy Preparation	• Oral Solution supplied as 175 mL	• Laxative dose: 350 mL (Two 175 mL doses) • Additional total volume of clear liquids: 1920 mL (Two 960 mL doses)	• Approved in pediatric patients aged 9 years and older. • Pediatric dosing is the same as the adult dose.	• If taking tetracycline or fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, or a penicillamine, take these medications at least 2 hours before and not less than 6 hours after administration. • Avoid in severe renal impairment (Cr Cl < 30 mL/min.
Sodium Sulfate; Magnesium Sulfate; Potassium Chloride (SUTAB)[27]	Colonoscopy Preparation	• Oral Tablets • 1 dose = 12 tablets. Total dose = 24 tablets.	• Laxative dose: 12 tablets. • Additional total volume of water: 2800 mL (Two 1400 mL doses)	• Safety and efficacy not established in pediatrics	• If taking tetracycline or fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, or penicillamine, take these medications at least 2 hours before and not less than 6 hours after administration.
Abbreviations: Cr Cl = creatinine clearance**;** FDA = Food and Drug Administration**;** G = grams; G6PD = glucose-6-phosphate dehydrogenase; kg = kilogram; L = liter; min = minute; mL = milliliter; NGT = nasogastric tube; OTC = over-the-counter; PEG = polyethylene glycol					

Up to one-quarter of patients who present for colonoscopies have inadequate bowel preparation.[28] Proper bowel cleansing is defined as one that allows the detection of colonic polyps 5 millimeters (mm) or larger.[29] In 2017, the Quality Committee of the European Society of Gastrointestinal Endoscopy (ESGE) recommended the minimum standard for adequate bowel preparation achieve least 90% or greater stool cleansing.[8] Insufficient bowel preparation may result in: an increased risk of adverse events related to the procedure; increased procedure time; reduced interval between procedures; and reduced adenoma detection rates.[30] Medical predictors of inadequate bowel preparation include: previous failed preparation, obesity, chronic constipation, use of constipating medications (i.e. opioids, tricyclic antidepressants), people with diabetes, and previous colonic resection.[30] People with low health literacy may not be equipped to follow the bowel preparation instructions which could lead to inadequate bowel preparation.[30]

Other factors which may influence the quality of the bowel cleansing include volume of the bowel preparation medication, timing of medication administration, and dietary factors.[30] Poor patient adherence prompted recommendations to split the dose administration of large volume PEG (> 3 L) products into 2 doses.[30] Dose splitting consists of taking half the preparation the evening before and the remaining half on the day of the procedure.[30] Day before bowel preparations instruct the patient to consume up to 4 L of the medication the day before the colonoscopy. A shorter interval between the last dose of bowel preparation and the examination is associated with improved bowel preparation quality.[31] To maximize preparation quality, colonoscopy should be performed within 3 to 5 hours of the last dose of preparation.[31] Every hour the interval is extended is associated with a 10% decrease in adequate bowel preparation.[31]

Five scoring systems have been used to assess the quality of bowel preparation.[32] The Aronchick Bowel Preparation Scale provides a single score reflecting the overall quality of the bowel preparation (i.e., excellent, good, fair, poor, or inadequate) depending on the volume of clear liquid or stool present in the intestine and the percentage of intestinal surface that can be observed during the procedure.[33] The Ottawa Bowel Preparation Scale uses 3 separate colonic segment scores which are rated 0 to 4 and summed as part of a total score ranging from 0 (excellent) to 14 (inadequate).[34] Cleanliness and fluid volume are separately assessed in this instrument and then combined into the total score. The Boston Bowel Preparation Scale (BBPS), provides scores ranging from 0 (unprepared colon) to 3 (entire segment of colon well seen) for 3 individual segments of the colon (right, transverse, and left) for a total score of 0 to 9 points.[35] Adequate preparation is defined as an overall BBPS score of 6 or greater, with each segment scored 2 points or greater.[35] The BBPS has been validated in multiple clinical studies.[32] The reliability and validation data for BBPS is more extensive compared with the Aronchick and Ottawa Bowel Preparation scales and include good supporting data correlating scores with key clinical outcomes.[32] Other instruments that have been validated, but are less commonly used, include the Harefield Cleansing Scale and the Chicago Bowel Preparation Scale.[32] A comparison of all 5 instruments is presented in **Table 2**.

Table 2. Instruments for Quality of Bowel Preparation Assessment.[32]

Scale Name	Score/Rating Description	Other Scale Properties
Aronchick Bowel Preparation Scale	*Total Colon:* 1. Excellent: Small volume of liquid; > 95% of mucosa seen 2. Good: Clear liquid covering 5-25% of mucosa, but >90% of mucosa seen 3. Fair: Semisolid stool could not be suctioned or washed away, but 90% of mucosa seen 4. Poor: Semisolid stool could not be suctioned or washed away and < 90% of mucosa seen 5. Inadequate: Repeat preparation/screening needed	• Total score range: Minimum 1 (excellent) to maximum 5 (inadequate). • Scoring performed before washing or suctioning. • No separate ratings for segments; global colon rating only. • No threshold for adequate/inadequate provided.
Ottawa Bowel Preparation Scale	*By Colon Segment:* 0. Excellent: Mucosal detail clearly visible, almost no stool residue; if fluid present, it is clear, almost no stool residue.	• Total score (obtained by adding scores for each segment + total colon fluid score) range: Minimum 0 (excellent) to

	1. Good: Some turbid fluid or stool residue, but mucosal detail still visible without need for washing/suctioning. 2. Fair: Some turbid fluid of stool residue obscuring mucosal detail; however, mucosal detail becomes visible with suctioning, washing not needed. 3. Poor: Stool present obscuring mucosal detail and contour; a reasonable view is obtained with suctioning and washing. 4. Inadequate: Solid stool obscuring mucosal detail and not cleared with washing and suctioning. *Total Colon Fluid:* 0. Small amount of fluid 1. Moderate amount of fluid 2. Large amount of fluid	maximum 14 (inadequate due to solid stool throughout with lots of fluid). • Scoring performed before washing or suctioning. • Rates cleansing by colon segment: Right colon, mid-colon, and rectosigmoid colon. • No threshold for adequate/inadequate provided.
Boston Bowel Preparation Scale (BBPS)	*By Colon Segment:* 0. Unprepared colon segment with mucosa not seen because of solid stool that cannot be cleared. 1. Portion of mucosa of the colon segment seen, but other areas of segment not well seen because of staining, residual stool, and/or opaque liquid. 2. Minor amount of residual staining, small fragments of stool, and/or opaque liquid, but mucosa of colon segment is well seen. 3. Entire mucosa of colon segment well seen, with no residual staining, small fragments of stool, or opaque liquid.	• Total score (obtained by adding scores for each segment) range: Minimum 0 (very poor) to maximum 9 (excellent). • Scoring performed after washing or suctioning. • Segments separately rated: Right colon (including cecum and ascending colon); transverse (includes hepatic and splenic flexures); and left colon (descending and sigmoid colon, and rectum). • Optimal threshold is a total score of ≥ 6 AND ≥ 2 per segment.

Harefield Cleansing Scale	*By Colon Segment:*
	0. Irremovable, heavy, hard stools
	1. Semisolid, only partially removable stools
	2. Brown liquid/fully removable semi-solid stools
	3. Clear liquid
	4. Empty and clean
		• Total score (obtained by adding scores for each segment) range: Minimum 0 (very bad) to maximum 20 (very good).
		• Scoring performed after washing or suctioning.
		• Segments separately rated: Rectum, sigmoid, left, transverse, right colon.
		• Threshold for successful cleansing:
		  ○ Successful cleansing:
		  ▪ Grade A: no segment scored < 3 or 4 or
		  ▪ Grade B: ≥ 1 segment scored 2 but no segment < 2
		  ○ Unsuccessful cleansing:
		  ▪ Grade C: ≥ 1 segment scored 1 but no segment < 1 or
		  ▪ Grade D: ≥ 1 segment scored 0

Chicago Bowel Preparation Scale	*Total Colon:* 0. Little fluid (≤ 50 mL) 1. Minimal amount of fluid (51-150 mL) 2. Moderate amount of fluid (151-300 mL) 3. Large amount of fluid (> 300 mL)	• Total score range: Minimum 0 (little fluid) to maximum 3 (large amount of fluid). • Scoring performed before washing or suctioning. • No threshold for adequate/inadequate provided. • Not incorporated into total score for segments.

Methods:
A Medline literature search for new systematic reviews and RCTs assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 4**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, Canadian Agency for Drugs and Technologies in Health (CADTH), and Scottish Intercollegiate Guidelines Network (SIGN), resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

Systematic Reviews:
Efficacy of Split-Dose Bowel Preparations
A 2019 systematic review and meta-analysis evaluated the efficacy of polyp detection for split-dose bowel preparation versus single dose administration.[1] Literature was searched through June 2017 for RCTs conducted in adults aged 18 to 85 years of age undergoing elective outpatient colonoscopy.[1] Studies that were limited to inpatients, pediatrics, or people with inflammatory bowel disease were excluded from the review.[1] Medications of interest included high- and low-volume PEG solutions, sodium phosphate, oral sulfate solutions, and the combination product of sodium picosulfate, magnesium oxide, and citric acid (SPMC).[1] Although oral sodium phosphate solutions are no longer recommended for bowel preparation in the U.S., they continued to be available through 2019.

Twenty-eight RCTs (n=8,842) met inclusion criteria.[1] Seven RCTs (n=1,834) evaluated split-dose versus day-before preparation, 7 trials (n=1,587) evaluated split-dose versus same-day preparation, and 14 trials (n=5,496) compared different split-dose regimens.[1] Most of the trials (16 of 28) had a low risk of bias.[1] Twelve trials had an unclear risk of bias; of these 12 trials, 8 did not describe the measures taken to prevent bias in the allocation assignment, 5 trials did not report whether there were withdrawals, 3 trials did not describe how a random sequence generation occurred, and 1 trial did not describe a method to ensure the endoscopist remained blinded to the intervention.[1]

Detection of adenomas was the primary outcome for the meta-analysis, measured as the number of patients with at least one adenoma detected.[1] In 4 RCTs comparing split-dose versus day-before bowel preparation regimens, there was an increased detection rate of adenomas in the split-dose groups (RR 1.26; 95% CI 1.10 to 1.44; I^2 = 0%; n = 1,258).[1] Eleven patients would be required to use a split-dose bowel preparation regimen for 1 patient to have an adenoma detected that otherwise would not have been detected through the use of a day-before, single-dose regimen.[1] A meta-analysis of 3 RCTs showed there was an increased rate of adenomas detected among participants who received a split-dose regimen of 2 L PEG compared with 2 L PEG the day before the procedure (RR 1.22; 95% CI 1.00–1.48; I^2 = 57%; n= 1,155).[1]

One small RCT (n=103) evaluated a split-dose regimen of 4 L PEG with 2 L PEG the day before colonoscopy and found no evidence of a statistically significant difference between groups for the number of adenomas detected.[1] Pooled estimates from 8 trials (n=1,587) evaluating split-dose versus same-day bowel preparations yielded no evidence of statistical difference in adenoma detection.[1] For 14 RCTs (n=5,496) which evaluated split-dose versus other split-dose regimens (i.e., PEG split high-volume (≥3 L) vs. PEG split low-volume (<3 L); PEG split high-volume (≥3 L) vs. split PEG 3350 + sports drink; PEG split high-volume (≥3 L) vs. sodium phosphate split; PEG split vs. SPMC split; and PEG split vs. oral sulfate solution split), no superior split-regimen was identified to detect adenomas.[1]

Secondary outcomes were detection of advanced adenomas and sessile serrated polyp (SSPs). Sessile serrated polyps are believed to be responsible for a higher proportion of interval colorectal cancers (cancers occurring between surveillance colonoscopies) than sporadic cancers.[1] This may be due to the challenging phenotypic characteristics of SSPs because they are often located in the right colon (where bowel preparation is often worse than when compared with the left colon), or slightly elevated above the colonic mucosa and covered in mucus, which makes them difficult to detect.[1] When split-dose administration was compared with day-before administration, there was increased detection of advanced adenomas (RR 1.53; 95% CI 1.22 to 1.92; 3 trials; I^2 = 0%; n=1,155).[1] Twelve patients would be required to use a split-dose regimen of 2 L PEG to detect an advanced adenoma in 1 patient, that otherwise would not have been detected through the use of a 2 L PEG day-before regimen.[1] Split-dose regimens also improved SSP detection (RR 2.48; 95% CI 1.21 to 5.09; 2 RCTs; I^2 = 0%; n=1,045).[1] No trials reported advanced adenoma detection or SSP detection for a split-dose regimen versus a different split-dose regimen.[1]

In summary, this review found that compared with day-before bowel preparation regimens, split-dose bowel preparations regimens increase the detection of adenomas, advanced adenomas, and have the greatest benefit in SSP detection.[1]

Efficacy Of High- Versus Low-Volume Split Dose PEG Bowel Cleansing Regimens for Colonoscopy

A 2020 systematic review and meta-analysis evaluated efficacy of high-volume PEG laxatives (> 2 L) versus low-volume laxatives (≤ 2 L) administered in split-dose regimens for bowel preparation prior to colonoscopy.[2] Literature was searched through January 2019 for RCTs that included adults undergoing elective colonoscopy.[2] Trials that included pediatric patients, patients with a history of colorectal resection, patients with inflammatory bowel disease, or patients with previous poor bowel preparation we excluded.[2] Low volume laxatives included: 2 L PEG-ASC (9 RCTs), a combination of 2 L PEG with citrate and simethicone in 4 studies (with the addition of oral bisacodyl in 2 RCTs), SPMC (3 RCTs), and oral sulfate solution (2 RCTs).[2] Excluded products were sodium phosphate and over-the-counter (OTC) PEG regimens.[2] After review, 17 RCTs (n=7,528) met inclusion criteria.[2] Baseline characteristics in terms of age and gender were comparable between the 2 groups.[2] Risk of bias was low for all except for allocation concealment (i.e., blinding of endoscopists at randomization) and incomplete outcome data (i.e., for excluded patients).[2] The overall quality of evidence was moderate.[2]

The primary outcome was bowel preparation efficacy in the overall colon and the right colon based on validated instruments (see **Table 2**).[2] In the pooled analysis of 17 RCTs, comprising 7,528 patients, no significant differences in adequacy of bowel cleansing were identified between the low- versus high-volume split-dose regimens (86.1% vs 87.4%; RR 1.00; 95% CI 0.98 to 1.02; p=0.2; I^2 = 17%).[2] In the RCTs reporting on right colon cleansing (10 studies, n=5,288), no difference in efficacy between low-volume PEG and non-PEG versus high-volume PEG regimens was found in the meta-analysis (91.2% vs 89.6%; RR 1.01; 95% CI 0.99 to 1.03; I^2 = 18%; p=0.2).[2] In 13 RCTs (n=6,593) that compared split-dose 2 L PEG-ASC with high-volume split-dose PEG, in differences were observed in the percentage of patients who presented with adequate bowel preparation (84.9% vs 86.3%; RR 1.0; 95% CI 0.95 to 1.02; I^2 = 38%; p=0.09).[2]

Secondary outcomes included adenoma detection rates, regimen compliance (defined as consumption of 75 to 100% of the prescribed solution) and AEs such as abdominal bloating, nausea, vomiting, and abdominal pain.[2] In pooled data from 4 RCTs (n=5,399), no difference in adenoma detection rate between low- and high-volume split dose regimens was found (RR 0.96; 95% CI 0.87–1.08; p-value not reported; I^2 = 0%).[2] Compared with high-volume split-dose regimens, low-volume split-dose regimens had higher odds for compliance of regimen completion (86.8% vs 92.8%; RR 1.06; 95% CI 1.02 to 1.10; p<0.01; I^2 = 85%).[2] For AEs, low-volume split dose-regimens had less risk for bloating (RR 0.66, 95% CI 0.48 to 0.92), nausea (RR 0.86, 95% CI 0.46 to 1.00), and vomiting (RR 0.68, 95% CI 0.46 to 1.00) compared with high-volume split dose regimens.[2] Abdominal pain was not statistically different with high-volume regimens compared with low-volume split dose regimens(RR 1.22; 95% CI 0.73 to 2.03).[2]

In summary, this review did not find statistically significant differences in bowel cleansing and adenoma detection rates between low- and high-volume regimens, when split-dose administration is adopted.[2] Low-volume regimens had higher odds of patient adherence to regimen completion and less incidence of bloating, nausea, and vomiting.[2]

Efficacy Of Ultra-Low Volume Bowel Preparation Fluids

A 2022 systematic review evaluated the efficacy of ultra-low volume bowel preparation products (< 1 L) compared with high-volume (> 2 L) and low-volume (1 to 2 L) products.[3] Literature was searched through April 2020 for RCTs that evaluated comparative efficacy of ultra-low volume bowel preparation products.[3] Forty-three studies met inclusion criteria.[3] All RCTS were single or multi-center assessor-blinded trials in outpatients with various indications for colonoscopy.[3] Of the 43 included studies, 26 RCTs evaluated SPMC, 12 RCTs evaluated 1 L PEG-ASC, 4 RCTs evaluated oral sulfate solution, 4 RCTs evaluated oral sodium phosphate solution, 2 RCTs evaluated sennosides, and one RCT evaluated magnesium citrate.[3] The small number of studies evaluating sennosides and magnesium citrate reflects their limited use in clinical practice.[3] The mean age of the included patients ranged from 47 years to 62 years.[3] Other patient demographics were not described in the report. Fourteen studies were sponsored by pharmaceutical companies.[3] The overall risk of bias was low in 58.1%, intermediate in 23.3%, and high in 16.3% of the included studies.[3]

The primary endpoint for this systematic review was the proportion of patients with adequate bowel cleansing for each studied product.[3] Adequate bowel cleansing was defined using validated bowel preparation instruments (see **Table 2**). If the outcome was reported with more than one preparation scale, BBPS and Ottawa Bowel Preparation Scores were preferred over the Aronchick Scale, as previous studies have shown better interrater consistency with these scales.[3] Additionally, BBPS was preferred over the Ottawa Bowel Preparation Scale because of more extensive validation and more frequent use in clinical practice with this instrument.[32] Secondary outcomes included adenoma detection rate and AEs.

Thirty-two RCTs were included in single arm meta-analyses of adequate bowel cleansing rates.[3] For SPMC 300 mL, the percentage of adequately cleaned patients was reported in 19 studies comprising 10,287 patients, with a pooled percentage of 75.2% (95% CI 67.6 to 81.4, I^2 = 96%).[3] Ten studies (n=1,717) reported the proportion of adequately prepared patients using 1 L PEG-ASC, with a pooled percentage of 82.9% (95% CI 74.4 to 90.1, I^2 = 94%).[3] Two studies (n=621) reported the efficacy of sodium phosphate, with a pooled percentage of adequately prepared patients equal to 81.9% (95% CI 36.7 to 97.2, I^2 = 98%).[3] For oral sodium sulfate, 3 studies (n=597) reported on the primary endpoint, with a pooled percentage of 92.1% (95% CI 79.7 to 97.2, I^2 = 86%).[3] The pooled outcome did not change significantly for any of the formulations when excluding the studies classified as high risk of bias, except for the 1 L PEG-ASC group, as a drop from 83.0% (95% CI 74.4 to 90.1) to 75.3% (95% CI 73.0 to 77.3) was identified.[3] In summary, bowel preparation with SPMC, 1 L PEG-ASC, sodium phosphate, and oral sulfate solution was adequate in 75.2%, 82.9%, 81.9%, and 92.1% of patients, respectively.[3] However, heterogeneity between studies was considerable (I^2 range: 86 to 98%).[3]

Adenoma detection rate was reported in 10 SPMC studies with a pooled detection rate of 31.0% (95% CI 25.6 to 36.7, I^2 = 83%).[3] The pooled adenoma detection rate with 1 L PEG was 32.4% (95% CI 26.6 to 38.4, I^2 = 83%, 8 RCTs). Adenoma detection rate was reported in one study in the sodium phosphate group and was 30.4% (95% CI 20.6 to 41.2). Adenoma detection rate was reported in 2 studies in the sodium sulfate group with a pooled adenoma detection rate of 40.9% (95% CI 28.3 to 54.2, I^2 = 81%).[3] Temporary electrolyte changes were seen with all ultra-low volume bowel preparation fluid solutions but without sustained effects in most patients.[3] All included studies reported gastrointestinal symptoms such as abdominal pain and distention, anal irritation, nausea, and to a lesser extent vomiting as most frequent adverse events.[3] Headache, dizziness, and general malaise were reported with the use of all fluids.[3]

The authors concluded ultra-low volume bowel preparation fluids do not always meet the 90% quality standard for adequate bowel preparation as defined by 2017 ESGE guidelines.[3,8] However, ultra-low volume products may be considered in patients intolerant for higher-volume laxatives and without risk factors for inadequate bowel preparation or dehydration-related complications.[3] Hyperosmotic ultra-low volume laxatives may be less suitable for elderly patients or patients with renal dysfunction.[3]

Effectiveness and Safety of 1-Liter Polyethylene Glycol Plus Ascorbate Versus Other Bowel Preparations for Colonoscopy

A 2023 meta-analysis evaluated the safety and effectiveness of 1 L PEG-ASC compared with other bowel preparation products.[4] Literature was searched through July 2022, and 9 RCTs met inclusion criteria.[4] In all included studies, cleansing success was defined as a total BBPS score of ≥6 with a partial BBPS score of ≥2 in each segment.[4] Right colon high-quality cleansing was defined as a partial BBPS score of 3.[4] The adenoma detection rate was defined as the percentage of patients with at least one adenoma in the analyzed population.[4] Safety of the preparations was assessed through occurrence of AEs.

Two different dosing regimens were used: split-dosing regimen in 8 RCTs and day-before regimen in one RCT.[4] One L PEG-ASC was compared with 2 L PEG-ASC in 5 RCTs , 4 L PEG in one RCT, trisulfate (magnesium, potassium, and sodium) solution in one RCT, SPMC in one RCT, and SPMC plus PEG in one RCT.[4] None of the studies were of poor methodological quality.[4] The assignment to the intervention domain remained at a low risk of bias, although all studies reported absence of patient blinding for the intervention owing to differences between the treatments.[4] All other domains were at a low risk of bias.[4] The mean body mass index (BMI) of the patients across the included studies ranged from 24.1 to 29.8 kg/m^2 while the mean age of the patients across the included studies ranged from 45.6 to 70.9 years.[4] Additional patient demographics (i.e., race, ethnicity) were not described in the report.

The meta-analysis showed a significantly higher cleansing success rate with 1 L PEG-ASC than with the other preparations both in the overall group (OR 1.50; 95% CI 1.25 to 1.81; p<0.01; I^2 = 0%; n=6,720) and split-dosing regimen subgroup (OR 1.44; 95% CI 1.16 to 1.80; p<0.01; I^2 = 0%; n=5,958).[4] Similar to the cleansing success rate, a significantly higher right colon HQC rate was found with 1 L PEG-ASC than with the other preparations both in the overall group (OR 1.67; 95% CI 1.21 to 2.31; p<0.01; I^2 = 43%; n= 3,221) and split-dosing regimen subgroup (OR 1.59; 95% CI 1.17 to 2.14; p<0.01; I^2 = 38%; n=2,708).[4] The pooled estimate of the adenoma detection rate did not significantly differ between the two groups either in the overall (OR 1.02; 95% CI 0.87 to 1.20; p=0.79; I^2 = 0%; n=3,984) or split-dosing regimen subgroup analysis (OR 0.99; 95% CI 0.84 to 1.18; p=0.94; I^2 = 0%; n=3,381).[4]

More patients with AEs were observed with 1 L PEG-ASC than with the other preparations (OR 1.51; 95% CI 1.23 to 1.84; p<0.01; I^2 = 0%; n=3,500).[4] A similar result was observed when only the studies with the split-dosing regimen were considered (OR 1.46; 95% CI 1.18 to 1.81; p<0.01; I^2 = 0%; n=2960).[4] When analyzing number and type of AEs, more nausea and vomiting were associated with 1 L PEG-ASC than with the other for specific AEs: nausea (incidence risk ratio [IRR] 1.45; 95% CI 1.24 to 1.70; p <0.01; I^2 = 0%, n=6720) and vomiting (IRR 2.22; 95% CI 1.60 to 3.07; p <0.01; I^2 = 8%, n=5962).[4] The incidence of abdominal pain was similar between 1 L PEG-ASC and other preparations (IRR 1.02; 95% CI 0.78 to 1.33; p <0.90; I^2 = 0%, n=4594).[4] No serious AEs or deaths were reported.[4]

In summary, compared to other preparations, 1-L PEG-ASC yielded higher overall cleansing success rates, higher right-colon high-quality cleansing rates, and similar adenoma detection rates.[4] The number of patients with AEs and incidence of AEs were higher with 1-L PEG-ASC compared with other products.[4] Nausea and vomiting occurred with 1 L PEG-ASC more often than with other products, while the incidence of abdominal pain was similar between the two groups.[4]

Sodium Picosulfate-Magnesium Citrate Versus PEG Laxatives for Colonoscopy Preparation

A 2016 systematic review and meta-analysis evaluated the safety and efficacy of SPMC with PEG-based regimens for colonoscopy preparation.[5] Literature was searched through July 2015 for RCTs that enrolled adult patients undergoing elective colonoscopy.[5] Twenty-five, single-blinded (due to differences in

administration schedules and product packaging) RCTs met inclusion criteria.[5] Ten RCTs compared full-dose SPMC versus full-dose PEG, 6 RCTs compared split-dose SPMC versus split-dose PEG, one RCT compared split-dose SPMC versus full-dose PEG, 4 RCTs evaluated full-dose SPMC versus split-dose PEG, and 4 RCTs evaluated multiple administration schedules.[5] The primary outcome was bowel cleanliness as defined as the proportion of patients attaining a satisfactory preparation.[5] Satisfactory preparation was specified based on validated instrument scores (see **Table 2**).[5] If 2 bowel preparation scales were both used in one study, the authors selected BBPS or the Ottawa Preparation Scale as the preferred instrument.[5] Secondary outcomes included adenoma detection rate, patient tolerability, and AEs.[5] The quality of evidence of RCTs was evaluated as high-quality.[5]

Bowel cleanliness was examined in all 25 trials, regardless of dosage, administration, and preparation cleanliness scale.[5] However, data of satisfactory preps could not be extracted from 4 RCTs according to the defined parameters.[5] In the meta-analysis of 21 RCTs, no differences in adequate bowel preparation were found with PEG compared with SPMC (RR 0.93; 95% CI 0.86 to 1.01; p=0.07; I^2 = 87%).[5] Pooled data from 7 RCTs showed no differences between SPMC and PEG in adenoma detection rate (RR 0.88; 95% CI 0.74 to 1.05; p=0.16; I^2 = 37%).[5]

Pooled data from 13 RCTs showed less AEs with SPMC compared with PEG (RR 0.78; 95 % CI 0.66 to 0.93; p=0.004; I^2 = 88%).[5] When analyzing individual AEs, more patients in the PEG group reported nausea (RR 0.63; 95% CI 0.51 to 0.77; p<0.001; I^2 = 70%), vomiting (RR 0.48; 95% CI 0.33 to 0.69; p<0.001; I^2 = 54 %), and abdominal bloating (RR 0.60; 95% CI 0.48 to 0.76; p<0.001; I^2 = 72 %) while more patients in the SPMC group developed dizziness (RR 1.64; 95% CI 1.34 to 2.01; p<0.001; I^2 = 0%). No significant difference was found between the two groups in development of abdominal pain (RR 0.83; 95% CI 0.65 to 1.07; p=0.15; I^2 = 66%).[5]

In summary, no differences in adequate bowel preparation or adenoma detection rate were found with PEG over SPMC. More patients reported nausea, vomiting, and abdominal bloating with PEG, while more patients developed dizziness with SPMC.

Efficacy of Oral Sulfate Solution versus PEG-Based Solutions for Polyp and Adenoma Detection During Colonoscopy

A 2022 meta-analysis of RCTs evaluated the efficacy of oral sulfate solution versus PEG-based solutions for polyp and adenoma detection during colonoscopy.[9] Literature was searched through October 2021 and 8 RCTs (n=2,059) meet inclusion criteria.[9] Most of the RCTs were conducted in Korea (6 of 8); the other 2 RCTs were conducted in the U.S. and India.[9] The sample size of all eligible RCTs ranged between 167 and 556, with a total sample size of 2,059.[9] Two RCTs specifically enrolled elderly individuals, 5 RCTs used 2 L PEG-ASC, 2 RCTs used 4 L PEG- ASC and one RCT used 1 L PEG-ASC as comparators.[9] Three RCTs were conducted in patients scheduled for a morning colonoscopy, and 4 RCTs specifically considered outpatients.[9]

Six RCTs clearly reported the methods to generate a random sequence, but only 2 RCTs clearly reported the approaches of concealing allocation.[9] Seven studies blinded investigators but not participants and were therefore judged as unclear risk in performance bias except for one RCT, which did not blind either investigators or participants.[9] Regarding outcome assessment, 5 studies were judged as low risk of bias because it was evaluated by either blinded independent trained central readers or blind investigators; however, another 3 studies did not clearly describe detailed information on outcome assessment and were therefore rated as unclear risk.[9] For the remaining items, all RCTs were considered as low risk.[9]

The primary outcome was polyp and adenoma detection. Meta-analysis of 6 RCTs suggested that oral sulfate solution significantly increased the polyp detection rate compared with PEG-based laxatives (47.34% vs. 40.14%, RR 1.13, 95% CI 1.03 to 1.24; P=0.01; I^2 = 69%).[9] In the pooled data from 5 RCTs, the adenoma detection rate was higher with oral sulfate solution compared with PEG-based laxatives (44.60% vs. 38.14%; RR 1.17; 95% CI 1.03 to 1.33; P=0.01; I^2 = 73%).[9]

A secondary outcome was effective bowel preparation using the Ottawa Preparation Scale or BBPS.[9] Pooled analyses suggested that, compared with the PEG-based solutions group, the BBPS in the oral sulfate group was greater (mean difference [MD] 0.32, 95% CI 0.03 to 0.62; P=0.03; 5 RCTs), and the Ottawa Preparation Scale in the oral sulfate group was lower (MD −1.28; 95% CI −1.95 to -0.62, P< 0.001; 2 RCTs), demonstrating that the quality of bowel preparation in the oral sulfate group was better than that of PEG-based solutions group.[9]

In summary, compared with PEG-based regimens, the oral sulfate solution bowel preparation regimen increased the polyp and adenoma detection rates and effectiveness of bowel preparation in patients undergoing colonoscopy.[9] However, there was substantial heterogeneity between trials, and AEs were not assessed in this analysis.

After review, 5 systematic reviews were excluded due to poor quality (e.g., network meta-analyses), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). [36-40]

Guidelines:

Optimizing Adequacy of Bowel Cleansing for Colonoscopy: Recommendations from an American Multi-Society Task Force on Colorectal Cancer

Guidance for adequate bowel preparation was published in 2014 by a multi-society task force comprised of the American College of Gastroenterology, the American Gastrological Association, and the American Society for Gastrointestinal Endoscopy.[6] This publication was supported in part by resources from the U.S. Veterans Health Administration.[6] Ineffective bowel cleansing for colonoscopy results in missed precancerous lesions and increased costs related to early repeat procedures.[6] The rate of adequate bowel cleansing should be at least 85%, and higher whenever possible.[6] Evidence and rationale for strong recommendations are summarized below.

- *Use of a split-dose bowel cleansing regimen is strongly recommended for elective colonoscopy (strong recommendation, high-quality evidence).*[6] Six trials showed significantly increased cleanliness for the PEG-ELS split-dose regimen (2 L + 2 L) compared with the PEG-ELS same-day dose (OR, 4.38; 95% CI, 1.88–10.21).[6] Consistent data show superior efficacy with a split dose compared with the traditional regimen of administering the preparation the day before the procedure.[41-43] Split dosing leads to higher adenoma detection rates.[44] Four previously published guidelines endorsed split dosing of preparations for colonoscopy.[45-48]

- *A same-day regimen is an acceptable alternative to split dosing, especially for patients undergoing an afternoon examination (strong recommendation, high-quality evidence).*[6] Several studies have shown that same-day bowel cleansing is an effective alternative to split dosing for patients with an afternoon colonoscopy.[6] One single-blind, prospective study in 277 participants showed same-day preparation provided better mucosal cleansing, less sleep disturbance, better tolerance, less impact on activities of daily living, and greater patient preference scores compared with split dosing.[49]

- *The second dose of split preparation ideally should begin 4–6 hours before the time of colonoscopy with completion of the last dose at least 2 hours before the procedure time (strong recommendation, moderate-quality evidence).*[6] This recommendation is based upon guidance from the American Society of Anesthesiologists, which states that ingestion of clear liquids until 2 hours before sedation does not affect residual gastric volume.[50] Two endoscopic studies found that ingestion of bowel cleansing agents on the day of colonoscopy did not affect residual gastric volumes, indicating that the rate of gastric emptying of bowel preparations is similar to other clear liquids.[51,52]

- *Selection of a bowel-cleansing regimen should take into consideration the patient's medical history, medications, and, when available, the adequacy of bowel preparation reported from prior colonoscopies (strong recommendation, moderate-quality evidence).*[6]

Because they are isosmotic, PEG-ELS regimens often are considered preferred regimens in patients who are less likely to tolerate fluid shifts, including patients with renal insufficiency, congestive heart failure, and advanced liver disease.[6] When sodium picosulfate was compared to PEG-ELS in 10 RCTs, the sodium picosulfate preparation showed similar efficacy in bowel cleansing to PEG-ELS formulations (OR 0.92; 95% CI 0.63 to 1.36).[6] At the time of this guideline publication, 2 comparative studies were available that evaluated oral sulfate solutions with 4 L and 2 L PEG-ELS products. The combined results of 923 patients found that oral sulfate solutions showed no difference in bowel cleanliness compared with PEG-ELS (OR 1.12; 95% CI, 0.77 to 1.62).[6] The use of magnesium-based preparations in patients with chronic kidney disease should be avoided because of possible magnesium toxicity.[6]

PEG-3350 powder (MIRALAX), an over-the-counter (OTC) laxative marketed for constipation, is available as an 8.3-oz bottle (238 g). When used for a pre-colonoscopy bowel preparation, the contents of 1 bottle often are mixed with 64 ounces of Gatorade (PepsiCo, Chicago, IL) to create a 2-L PEG formulation.[6] In some instances, clinicians prescribe bisacodyl tablets or magnesium citrate in conjunction with the PEG-3350 powder.[6] Five randomized controlled trials (total, 1556 patients) compared OTC PEG-3350 powder, either alone or combined with an adjunct, with 4 L PEG-ELS.[6] In one study, satisfactory colon cleansing was less frequent with OTC PEG-3350 powder than with 4 L PEG-ELS (68% vs. 83%; p=0.018).[6] In the remaining 4 studies, including 1 study that used 306 g rather than 238 g, the proportion of patients with adequate bowel preparation was comparable with OTC PEG-3350 powder and 4 L PEG-ELS.[6] Reports of hyponatremia have occurred when OTC PEG-3350 powder was administered the evening before, but not with split-dose regimens.[6] Widespread use of OTC PEG-3350 for bowel preparation seems to have been remarkably safe, but additional evaluation of safety and is warranted.[6]

- *Recommendations for Specific Populations:*
    - *Pediatrics*: There is insufficient evidence to recommend specific bowel preparation regimens for children and adolescents undergoing colonoscopy (strong recommendation, very-low quality evidence).[6]
    - *Pregnancy*: Strongly consider deferring colonoscopy until second trimester and consider risks of bowel preparation regimen.[6] Tap water enemas should be used to prepare the colon for sigmoidoscopy in pregnant women (strong recommendation, very low-quality evidence).[6]

Bowel Preparation For Colonoscopy: European Society Of Gastrointestinal Endoscopy

In 2019, the ESGE Guideline Committee updated 2013 guidance to incorporate additional evidence on the efficacy and safety of bowel preparation prior to endoscopy.[7] Most of the recommendations are similar to the 2014 U.S. multi-task force guidance, but are based upon more recently published evidence not evaluated in the U.S. guidance. The rate of adequate bowel cleansing should be at least 90%, and higher whenever possible.[8] Recommendations regarding selection and administration of medications are summarized below.

- *ESGE recommends split-dose bowel preparation for elective colonoscopy (strong recommendation, high quality evidence).*[7] A meta-analysis (47 RCTs, 13, 478 patients) found that split-dose regimens, regardless of the type and dose of the cleansing agent, provided excellent/good colon cleansing more frequently than day-before bowel preparation (OR 2.51 95% CI 1.86 to 3.39).[53] This result was confirmed in sub-analyses restricted to PEG (OR 2.60, 95 % CI 1.46 to 4.63), sodium phosphate (OR 9.34, 95 % CI 2.12 to 41.11), and picosulfate (OR 3.54, 95 % CI 1.95 to 6.45).[53] Split dosing was associated with a higher proportion of patients willing to repeat the preparation (OR 1.90, 95 % CI 1.05 to 3.46).[53]

- *ESGE recommends, for patients undergoing afternoon colonoscopy, a same-day bowel preparation as an acceptable alternative to split dosing (strong recommendation, high quality evidence).*[7] Two meta-analyses (11 and 14 RCTs) compared split-dose with same-day bowel preparation and showed similar results regarding the quality of bowel preparation, patient willingness to repeat it, and overall tolerability.[54,55] Patients taking the same-day

regimen reported less bloating (OR 0.68, 95% CI 0.40 to 0.94)[54] and better sleep quality (OR 0.44, 95% CI 0.24 to 0.82).[55] The adverse effect rate was similar for the two regimens.[54] Most of the people enrolled in the included studies were scheduled for afternoon procedures.[7]

- *ESGE recommends to start the last dose of bowel preparation within 5 hours of colonoscopy, and to complete it at least 2 hours before the beginning of the procedure (strong recommendation, moderate quality evidence).*[7] A meta-regression analysis of 29 RCTs comparing split versus day-before regimens showed that the clinical gain of the split-dose regimen was highest within 3 hours from last dose intake, progressively decreased after 4 to 5 hours, and became statistically not significant at 5 hours.[56]

- *ESGE recommends the use of high volume or low volume PEG-based regimens as well as that of non-PEG-based agents that have been clinically validated for routine bowel preparation. In patients at risk for electrolyte disturbances, the choice of laxative should be individualized (strong recommendation, moderate quality evidence).*[7]
  In a 2015 meta-analysis, split-dose high volume (≥3 L) PEG appeared to be superior to split-dose low volume PEG (6 studies; 1305 patients; OR 1.89, 95% CI 1.01 to 3.46).[53] This confirmed a previous meta-analysis showing the superiority of split-dose high volume PEG versus other alternatives (9 studies; 2477 patients; OR 3.46, 95 % CI 2.45 to 4.89) including low volume PEG with different adjuvants and sodium phosphate, regardless of the adoption of the split regimen.[43] After the meta-analyses were published, several trials compared high-volume PEG vs. low-volume PEG or non-PEG split regimens.[7] Overall, such trials showed an equivalence or superiority of the high-volume versus low-volume PEG or non-PEG regimens in terms of efficacy, while confirming the worse tolerability of the high volume PEG regimens.[7] Studies have not demonstrated significant alterations in vital or biochemical parameters (e. g., sodium, potassium, chloride, bicarbonates) linked to these formulations.[7]

  In order to reduce the volume of PEG solutions, with the aim of improving tolerability, a formulation of 2 L PEG-ASC was developed.[7] One meta-analysis, including 11 RCTs comparing 2 L PEG plus ascorbate versus 4 L PEG preparations for elective colonoscopies, showed noninferior efficacy for bowel cleansing (OR 1.08, 95% CI 0.98 to 1.28) but better compliance for 2 L PEG-ASC (OR 2.23, 95% CI 1.67 to 2.98), with reduced nausea and vomiting.[57] Solutions containing aspartame and ascorbate are contraindicated in patients with phenylketonuria or G6PD deficiency.[7] These products are not recommended in patients with renal insufficiency and creatinine clearance less than 30 mL/min and in patients with New York Heart Association (NYHA) III or IV congestive heart failure.[7] A high rate of hypernatremia has been observed following the administration of 1 L PEG plus ascorbate, primarily due to the sodium content of the product.[7] For this reason, additional clear liquids are recommended. Hyponatremia cases have been described with 2 L PEG-ASC; this prompted caution in patients at risk of electrolyte disturbances.[7]

  Sodium picosulfate, magnesium oxide, and citric acid was compared with PEG and with oral sodium phosphate in two meta-analyses, including 6 and 13 studies.[58,59] In the smaller meta-analysis, SPMC provided satisfactory colon cleansing in a similar proportion of patients compared with PEG, with less frequent adverse events. However oral sodium phosphate produced better colon cleansing than SPMC.[59] In the second meta-analysis, which included only RCTs in which colon cleansing was rated according to a validated scale, SPMC provided a slightly better quality of bowel cleansing compared with PEG (RR 1.06, 95% CI 1.02 to 1.11); this was lost, however, when SPMC was compared with 4 L PEG only.[59] In addition, SPMC was better tolerated than PEG, with a higher probability of completing the preparation.[59] In the most recent meta-analysis, including 25 RCTs that compared SPMC with PEG (but with different regimens), no difference was found in colon cleansing or polyp detection rate.[5] However AEs, including nausea, vomiting, bloating, but not dizziness, were less frequent in the SPMC group (RR 0.78, 95 % CI 0.66 to 0.93), and a higher proportion of patients were likely to complete the SPMC regimen (RR 1.08, 95 %CI 1.04 to 1.13) and willing to repeat the same regimen (RR 1.44, 95% CI, 1.25 to 1.67).[5] Because of hyperosmolarity and

magnesium content, solutions containing SPMC are contraindicated in patients with congestive heart disease, hypermagnesemia, rhabdomyolysis, gastrointestinal ulcerations, and severe impairment of renal function, which can lead to magnesium accumulation.[7]

There is insufficient evidence to recommend a specific product for elderly people. Osmotically balanced PEG solutions are theoretically the safest, and are preferred in these patients.[7] However, high volume products are thought to be particularly poorly tolerated in elderly patients.[7] Hyperosmotic saline laxatives may increase the risk of dehydration and electrolyte imbalances in at-risk populations, such as patients with chronic renal insufficiency, congestive heart failure, or liver failure with ascites.[7] Although the majority of RCTs exclude such patients, PEG solutions with osmotically balanced electrolytes are often selected, on account of their safety profiles, for patients in these categories.[7]

- *ESGE recommends against the routine use of oral sodium phosphate for bowel preparation (strong recommendation, low quality evidence).*[7] Between January 2006 and December 2007, 171 cases of renal failure were reported to the U.S. FDA following the use of oral sodium phosphate and 10 cases were reported following the use of PEG.[60]

- *ESGE recommends high volume or low volume PEG-based bowel preparation in patients with inflammatory bowel disease (strong recommendation, high quality evidence).*[7] In an RCT of patients without colitis, sodium phosphate- or sodium picosulfate-based preparations resulted in a 10-fold increase in mucosal inflammation compared to PEG-based bowel preparation.[61] However, limited comparative data are available for bowel preparation efficacy and tolerability in colitis.[7]

- *ESGE found insufficient evidence to determine for or against the use of specific regimens in pregnant/breastfeeding women. However, if colonoscopy is strongly indicated, PEG regimens may be considered, with tap water enemas preferred for sigmoidoscopy. (Insufficient evidence to determine net benefits or risks).*[7] The use of PEG in pregnancy has not been extensively studied and it is unknown whether it can cause fetal harm; when used for treating constipation during pregnancy it is considered relatively safe.[7]

After review, 3 guidelines were excluded due to poor quality.[62-64]

Randomized Controlled Trials:
A total of 296 citations were manually reviewed from the initial literature search. After further review, 294 citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). The remaining 2 trials are summarized in the table below. Full abstracts are included in **Appendix 2**.

Table 3. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Primary Outcome	Results	Notes/Limitations
Enestvedt BK, et al.[65] Single-center, single-blinded RCT Duration: 7/1/2009 to 6/29/2010	1. PEG 236 g dissolved in 4 L water administered as a split dose (n=103) vs. 2. PEG 238 g dissolved in 2 L sports drink administered as a split dose + 4 bisacodyl 5 mg tablets the day before the procedure (n=87)	Adult patients 50 yo and older undergoing routine outpatient colorectal screening Exclusions: -Chronic constipation -Use of chronic narcotics N=190	Excellent bowel preparation as assessed by the BBPS score as 8 or 9 on 10-point scale ranging from 0 to 9 points	Percent of patients achieving BBPS score of 8 or 9 1. 70% (n=72) 2. 55% (n=48) Difference: 25% P=0.036 *Confidence intervals not reported	-PEG 236 g in 4 L provided effective bowel cleansing prior to colonoscopy compared with PEG 238 in 2 L -Small sample size -Side effects such as electrolyte changes and kidney function were not assessed -Bowel cleansing is a surrogate endpoint for polyp detection -Patients not blinded to treatment assignment due to differences in products and volume of fluids
Hjelkrem M, et al.[66] Single-center, single-blinded RCT Duration: 7/1/2009 to 7/1/2010	1. PEG 236 g dissolved in 4 L water administered as a split dose (n=102) vs 2. PEG 238 g dissolved in 2 L sports drink administered as a split dose (n=100) vs 3. PEG 238 g dissolved in 2 L sports drink administered as a split dose + lubiprostone 24 mcg the day before the procedure (n=101) vs. 4. PEG 238 g dissolved in 2 L sports drink administered as a split dose + bisacodyl 10 mg	Adult patients 18 yo and older undergoing routine outpatient colorectal screening Exclusions: -Congestive heart failure -Kidney disease -Solid organ transplant -Bowel obstruction N=404	Excellent bowel preparation as assessed by the OBPS score less than 5 points on 15-point scale ranging from 0 to 14 points	Mean total OBPS score 1. 5.1 2. 6.9 3. 6.3 4. 6.8 1 vs. 2: Difference = 1.8; P<0.001 1 vs. 3: Difference = 1.2; P<0.001 1 vs. 4: Difference = 1.7; P<0.001 *Confidence intervals not reported Percent of patients achieving OPBS score <5 1. 49% (n=40) 2. 15% (n=15) 3. 19% (n=20) 4. 20% (n=21) P <0.001 for all comparisons with PEG 4 L	-No differences were found in the number of polyps detected with each regimen (p=0.346) -No differences were reported in adverse event reporting

	the day before the procedure (n=101)				
Abbreviations: BBPS = Boston Bowel Preparation Scale; g = grams; L = liters; mcg = micrograms; OBPS = Ottawa Bowel Preparation Scale; PEG = polyethylene glycol; yo = years old					

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Appendix 1: PDL Status: Laxatives, Bowel Preparation

Generic Name	Brand Name	Form	PDL Status
peg3350/sod sul/NaCl/KCl/asb/C	PEG3350-SOD SUL-NACL-KCL-ASB-C	POWD PACK	
peg3350/sod sul/NaCl/KCl/asb/C	MOVIPREP	POWD PACK	
peg3350/sod sul/NaCl/KCl/asb/C	PLENVU	POWD PK SQ	
peg3350/sod sulf, bicarb, Cl/KCl	PEG-3350 AND ELECTROLYTES	SOLN RECON	
peg3350/sod sulf, bicarb, Cl/KCl	GOLYTELY	SOLN RECON	
peg3350/sod sulf, bicarb, Cl/KCl	GAVILYTE-G	SOLN RECON	
peg3350/sod sulf, bicarb, Cl/KCl	GAVILYTE-C	SOLN RECON	
sod picosulf/mag ox/citric ac	CLENPIQ	SOLUTION	
sod sulf/pot chloride/mag sulf	SUTAB	TABLET	
sodium chloride/NaHCO3/KCl/peg	NULYTELY	SOLN RECON	
sodium chloride/NaHCO3/KCl/peg	PEG 3350-ELECTROLYTE	SOLN RECON	
sodium chloride/NaHCO3/KCl/peg	GAVILYTE-N	SOLN RECON	
sodium phosphate, mono-dibasic	PREPARATION CLEANSING	LIQUID	
sodium, potassium, mag sulfates	SOD SULF-POTASS SULF-MAG SULF	SOLN RECON	
sodium, potassium, mag sulfates	SUPREP	SOLN RECON	

Appendix 2: Specific Drug Information

Clinical Pharmacology and Pharmacokinetics:
Almost all of the FDA-approved bowel preparation products are osmotic laxatives and not absorbed systemically; therefore, pharmacokinetic properties have not been assessed. The only product that contains an osmotic laxative and stimulant laxative is CLENPIQ. The sodium picosulfate component acts as a stimulant laxative while the magnesium oxide serves as the osmotic laxative.[26]

Summary of Warnings and Precautions:
All of the FDA-approved bowel preparations carry similar precautions. Because MOVIPREP contains sodium ascorbate and ascorbic acid, it should be used cautiously in patients with G6PD deficiency, especially in patients with active infection, history of hemolysis, or concomitant use of medication known to precipitate hemolytic reaction.[10] MOVIPREP also contains phenylalanine 2.33 mg per treatment, so it should be used cautiously in patients with phenylketonuria.[10] CLENPIQ is contraindicated in patients with severe renal impairment (creatinine clearance < 30 mL/min) as magnesium accumulation may occur.[26]

<u>Precautions:</u>
- Fluid and electrolyte disturbances may occur and can lead to cardiac arrhythmias, seizures and renal impairment; correct abnormalities prior to use.
- Patients with a history of QT prolongation, uncontrolled arrhythmias, recent myocardial infarction, unstable angina, congestive heart failure, or cardiomyopathy are at increased risk of serious arrhythmias; monitoring is recommended.
- Patients with impaired renal function or those taking concomitant drugs that may affect renal function (e.g., diuretics, ACE inhibitors, angiotensin receptor blockers, or NSAIDs) are at increased risk for adverse effects. Maintain adequate hydration; monitoring is recommended.

<u>Contraindications:</u>
- Bowel perforation
- Gastric retention
- Gastrointestinal obstruction
- Ileus
- Toxic colitis
- Toxic megacolon
- Severe acute inflammatory bowel disease

Appendix 3: Abstracts from Comparative Randomized Controlled Trials

Miralax Vs. Golytely - A Controlled Study Of Efficacy And Patient Tolerability In Bowel Preparation For Colonoscopy[65]

BACKGROUND: MiraLAX is gaining acceptance as a bowel cleanser for colonoscopy. We hypothesize that MiraLAX/Gatorade is as efficacious for bowel cleansing as Golytely and is more tolerable for patients undergoing screening colonoscopy.
AIM: To compare bowel preparation scores of MiraLAX/Gatorade vs. Golytely and examine differences in patient tolerability.
METHODS: Patients undergoing screening colonoscopy were randomized to 4 L Golytely or 238 g MiraLAX in 64 ounces Golytely and four bisacodyl tablets. Efficacy in bowel cleansing was assessed using the Boston Bowel Preparation Scale (BPPS). Subjects completed a brief survey assessing patient tolerability.
RESULTS: A total of 190 patients were enrolled (85 male, 105 female; mean age 56.9 years, s.d. 6.3); 87 were randomized to MiraLAX, 103 to Golytely. There was no difference in age, gender or timing of colonoscopy between the bowel preparation groups. Golytely's median total BBPS score was significantly higher than that of MiraLAX [9 (IQR 7-9) vs. 8 (IQR 6-9), P = 0.034]. Golytely had a higher rate of an excellent equivalent BBPS score of 8 or 9 than MiraLAX (70% vs. 55%, P = 0.036). There was no difference in patient tolerability (P = 0.857).
CONCLUSIONS: Golytely was more efficacious than MiraLAX/Gatorade in bowel cleansing; both preparations were equally tolerated by patients.

Miralax Is Not As Effective As Golytely In Bowel Cleansing Before Screening Colonoscopies[66]

BACKGROUND & AIMS: Successful colonoscopies require good bowel preparations-poor bowel preparations can increase medical costs, rates of missed lesions, and procedure duration. The combination of polyethylene glycol (PEG) 3350 without electrolytes (MiraLAX; Schering-Plough Healthcare Products, Inc, Kenilworth, NJ) and 64 oz of Gatorade (PepsiCo, Inc, Purchase, NY) has gained popularity as a bowel preparation regimen. However, the efficacy and tolerability of this approach has not been compared with standard bowel preparations in clinical trials. We compared split-dose (PEG) 3350 with electrolytes (GoLytely; Braintree Laboratories, Inc, Braintree, MA) with split-dose MiraLAX alone and in combination with pretreatment medications (bisacodyl or lubiprostone) to determine the efficacy and patient tolerability of MiraLAX as an agent for bowel preparation.
METHODS: We performed a prospective, randomized, blinded, controlled trial at a tertiary care center. Patients (n=403) were randomly assigned to groups given GoLytely, MiraLAX, MiraLAX with bisacodyl (10 mg), or MiraLAX with lubiprostone (24 mug). MiraLAX was combined with 64 oz of Gatorade. All patients were surveyed regarding preparation satisfaction and tolerability. The Ottawa bowel preparation scale was used to grade colon cleanliness.
RESULTS: GoLytely was more effective at bowel cleansing (average Ottawa score, 5.1) than MiraLAX alone (average Ottawa score, 6.9) or in combination with lubiprostone (average Ottawa score, 6.8), or bisacodyl (average Ottawa score, 6.3) (P<.001). MiraLAX was associated with a trend toward longer procedure duration (P=.096). Groups given MiraLAX rated the overall experience as more satisfactory than those given GoLytely (P<.001). There were no differences between polyp detection rates (P=.346) or adverse events (P=.823).
CONCLUSIONS: Split-dose MiraLAX in 64 oz of Gatorade is not as effective as 4 L split-dose GoLytely in bowel cleansing for screening colonoscopies.

Appendix 4: Medline Search Strategy

Ovid MEDLINE(R) 1996 to November Week 4 2023; Ovid MEDLINE(R) In-Process & In-Data-Review Citations 1946 to November 29, 2023

1	sodium phosphate.mp.	4638
2	Picolines/ or sodium picosulfate.mp.	913
3	moviprep.mp.	53
4	golytely.mp.	100
5	colyte.mp.	19
6	miralax.mp.	52
7	suprep.mp.	10
8	sodium sulfate.mp.	3900
9	polyethylene glycol electrolyte lavage.mp. or Therapeutic Irrigation/	8817
10	Polyethylene Glycols/	49705
11	Laxatives/	1515
12	Cathartics/	3132
13	Colonoscopy/	28197
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	70339
15	13 and 14	1581
16	limit 15 to (english language and humans)	1448
17	limit 16 to (guideline or meta-analysis or practice guideline or "systematic review")	70
18	limit 16 to (comparative study or controlled clinical trial)	296

Appendix 5: Key Inclusion Criteria

Population	Children and Adults
Intervention	Sodium Salts, Polyethylene Glycol Lavage Solutions
Comparator	Other bowel preparation products
Outcomes	Successful bowel preparation
Timing	Split-dose versus one dose the evening prior to procedure
Setting	Outpatients