From:	JoAnn.Gallagher-Berndt@ferring.com on behalf of glenn.oneidas@ferring.com
To:	E-OHPSCA2713.EBSA
Cc:	JoAnn.Gallagher-Berndt@ferring.com
Subject:	Attention RIN 1210-AB44
Date:	Thursday, August 26, 2010 11:22:59 AM
Attachments:	Ferring cover letter E-OHPSCA2713 EBSA RIN 1210-AB44. . jgb 8-26-10.pdf Bowel prep consensus document.pdf colorectal_panel_stmt.pdf

---

Ferring Pharmaceuticals Inc. submits these comments to the Interim Final Rules for Group Health Plans and Health Insurance Issuers Relating to Coverage of Preventive Services Under the Patient Protection and Affordable Care Act (RIN 1210–AB44).

The comments request clarification that for purposes of compliance with the regulations, the term "preventive service" includes prescription drugs that are an essential component of a United States Preventive Services Task Force (USPSTF)recommended service, such as the bowel preparation drugs ordered by physician prescription and taken by the patient as an essential first step to a colonoscopy under the USPSTF "Screening for colorectal cancer" recommendation.

Attached please find the following three PDF attachments:
<<Ferring cover letter E-OHPSCA2713 EBSA RIN 1210-AB44. . jgb 8-26-10.pdf>> <<Bowel prep consensus document.pdf>> <<colorectal_panel_stmt.pdf>>

Thank you,
Glenn Oneidas
Senior Director - Managed Care
Ferring Pharmaceuticals Inc.
4 Gatehall Drive, 3rd floor
Parsippany, NJ 07054
Office: 973-796-1680

FERRING
PHARMACEUTICALS

August 26, 2010

Submitted via email to: E-OHPSCA2713.EBSA@dol.gov

Office of Health Plan Standards and Compliance Assistance
Employee Benefits Security Administration
Room N–5653
Department of Labor
200 Constitution Ave., NW
Washington, DC 20210

Attention: RIN 1210–AB44

Summary

Ferring Pharmaceuticals Inc. submits these comments to request that the Final Regulations (to be issued under Section 2713 of the PHS Act, as added by the Affordable Care Act) make clear that for purposes of compliance with the regulations, the term "preventive service" includes prescription drugs that are an essential component of a United States Preventive Services Task Force (USPSTF) recommended service, such as the bowel preparation drugs ordered by physician prescription and taken by the patient as an essential first step to a colonoscopy under the USPSTF "Screening for colorectal cancer" recommendation.

Background

Section 2713 of the Public Health Service Act, as amended by the Patient Protection and Affordable Care Act, requires that a group health plan and a health insurance issuer offering group or individual health insurance coverage provide benefits for and prohibit the imposition of cost-sharing requirements with respect to certain evidence-based items or services in the current recommendations USPSTF.

Screening for colorectal cancer is a USPSTF "Grade A" recommendation. See: http://www.healthcare.gov/center/regulations/prevention/taskforce.html. Grade A recommendations are those that the USPSTF "strongly recommends" clinicians provide to eligible patients because "the USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms." See: http://www.uspreventiveservicestaskforce.org/3rduspstf/ratings.htm.

Rationale for Request

Where a preventive service straddles two different insurance benefit programs, it is important to clarify that the "service" addressed by the Final Rule embraces both programs.

Health insurers often have a different benefit program and administrative structure for prescription drugs (a "Prescription Drug" program) than for all other outpatient services insured under the "Medical Benefit" program. Depending on the insurance plan's structure, some people who have coverage for a colorectal screening pay two co-payments – one under the Medical Benefit for the colonoscopy performed in the imaging suite of a clinic, office or hospital; and another co-payment for the bowel cleansing agent dispensed by a retail pharmacy and self-administered at home prior to the colonoscopy procedure. As published, the Interim Final Rules do not address the issue of whether an outpatient prescription drug that was an essential component of a covered screening procedure, but managed under a different benefit program, should receive the same cost sharing treatment as the covered procedure. In the absence of clear direction on that issue, we expect that some insurers will not apply the co-payment waiver to the prescription drug. As a result, the cost sharing barrier that the Final Rules are designed to break down would be rebuilt by the insurer on the prescription drug side of the insurance package.

Ferring Pharmaceuticals Inc., 4 Gatehall Drive, 3rd Floor, Parsippany, New Jersey 07054, U.S.A.
Telephone: (973) 796-1600 Fax: (973) 796-1660

Example of When the Prescription Drug Is an Essential Component of the "Service"

The first step in performing a colonoscopy is thorough bowel cleansing, most often with a prescription drug cleansing agent approved by the Food and Drug Administration for that purpose. Without adequate bowel cleansing, colonoscopy is useless as a cancer screening tool. The National Institutes of Health recognized that as recently as February 2010 in a "State-of-the-Science" Conference Statement, noting that, "Testing options vary in the amount of preparation and effort required by patients. For example, colonoscopy and computed tomography colonography require preparation to cleanse the colon completely...." (See attached *Final Statement*, NIH State-of-the-Science Conference: Enhancing Use and Quality of Colorectal Screening. February 2–4, 2010 at p. 4).

A consensus statement prepared by the medical specialty societies whose members perform colonoscopies states that, "Diagnostic accuracy and therapeutic safety of colonoscopy depends on the quality of the colonic cleansing or preparation. The ideal preparation for colonoscopy would reliably empty the colon of all fecal material in a rapid fashion with no gross or histologic alteration of the colonic mucosa." (See attached *A consensus document on bowel preparation before colonoscopy: Prepared by a Task Force From The American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)*. Gastrointestinal Endoscopy; vol. 63, no. 7 (2006) at p. 894.)

The consensus statement authors report that, "Inadequate bowel preparation for colonoscopy can result in missed lesions, cancelled procedures, increased procedural time, and a potential increase in complication rates." (Consensus Document at p. 903) The financial consequences of poor preparation resulting in a repeat colonoscopy (and preparation) are reported to be significant. "Specifically, the patient may be required to pay an additional co-pay for each examination and the financial intermediary may deem one or both examinations unnecessary. In these instances, the patient may be responsible for payment in full for both examinations." (Consensus Document at p. 903)

Bowel cleansing typically takes place at home, beginning the day before the colonoscopy procedure. The physician performing the procedure gives the patient comprehensive written instructions on how to prepare and a prescription for one of several cleansing drugs (also known as purgatives). All purgatives that are currently FDA approved for colonoscopy preparation are prescription drugs.

The Objective of the Final Rules Cannot Be Accomplished Without Including Essential Prescription Drugs in the Cost Sharing Waiver

A 2005 study found that average wholesale prices for the least expensive purgative drug ranged from a low of approximately $15 for a flavored solution drunk in large quantities (CoLyte® polyethelyne glycol electrolyte solution) to $66 for the oral tablet formulation of the same drug (Visicol® sodium phosphate monobasic monohydrate, USP, and sodium phosphate dibasic anhydrous, USP tablets). (Consensus Document at pp. 904 - 905). In January 2010, those prices were $35 and $150 respectively (Red Book, 2010 Edition). For a person who would avoid having a colonoscopy because of the cost sharing burden, having to pay the drug cost sharing might well create the same avoidance behavior.

The dollar amount of drug cost sharing depends on the drug tier each insurer assigns to each drug. A study published by the BlueCross BlueShield Association in 2008 found that employer-based plans had average copayments of $11 to $43 per prescription (http://www.bcbs.com/blueresources/mcrg/chapter2/ch2_slide_9.html). We believe that those cost sharing obligations are high enough to prevent many of the people who would otherwise benefit from the Final Rule from having a screening colonoscopy.

We therefore urge the Departments of Labor, Health and Human Services and Treasury to clarify in the Final Rule that **"Preventive Service" includes an outpatient prescription drug that is an essential component of a USPSTF recommended service.**

I can be reached at (973) 796-1680 or my cell (732) 241-3618 and my e-mail is glenn.oneidas@ferring.com.

Respectfully submitted,

Glenn Oneidas
Senior Director, Managed Care

Preamble

The following ''Consensus Document on Bowel Preparation for Colonoscopy'' is the culmination of an exceptional cooperative effort by 3 leading gastrointestinal societies. For over a year, a tripartite task force with representation from the American Society for Gastrointestinal Endoscopy, the American Society of Colon and Rectal Surgeons, and the Society of American Gastrointestinal and Endoscopic Surgeons has worked diligently to prepare this state of the art review. The comprehensive document is evidence based and a valuable resource for all physicians who perform colonoscopy. In addition to a critical scientific review of existent data, the document provides practical information on the manufacturers and pricing of available products used in bowel preparation. The governing bodies of all 3 organizations have reviewed and approved this document, which is to be published contemporaneously by the respective journals of each society. All who worked on this project should be congratulated for this practical contribution that will enhance the quality patient care that the members of all 3 societies provide on a daily basis.

Robert H. Hawes
President
American Society for Gastrointestinal Endoscopy (ASGE)
Ann Lowry
President
American Society of Colon and Rectal Surgeons
Dan Deziel
President
Society of American Gastrointestinal and Endoscopic Surgeons

0016-5107/$32.00
doi:10.1016/j.gie.2006.03.919

A consensus document on bowel preparation before colonoscopy: Prepared by a Task Force From The American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)

Colonoscopy is the current standard method for evaluation of the colon. Diagnostic accuracy and therapeutic safety of colonoscopy depends on the quality of the colonic cleansing or preparation. The ideal preparation for colonoscopy would reliably empty the colon of all fecal material in a rapid fashion with no gross or histologic alteration of the colonic mucosa. The preparation also would not cause any patient discomfort or shifts in fluids or electrolytes and would be inexpensive.[1] Unfortunately, none of the preparations currently available meet all of these requirements.[1,2]

A brief history of the evolution of bowel preparation for colonoscopy will be discussed followed by an evidence-based analysis of the various colonoscopy preparations, dosing regimens, and adjuncts currently used.

Addendum provides manufacturers' information for all products discussed in this document.

0016-5107/$32.00
doi:10.1016/j.gie.2006.03.918

EVOLUTION OF BOWEL PREPARATIONS

Colonoscopy preparations evolved from radiologic and surgical preparations.[3] Early preparations used dietary

limitations, cathartics, and enemas. Although these preparations cleansed the colon, they were time consuming (48-72 hours), uncomfortable for the patient, and associated with fluid and electrolyte disturbances.[4] A rapid preparation used high-volume (7-12 liters) per oral gut lavage with saline/electrolyte solution. This also was associated with severe fluid and electrolyte shifts and poor patient tolerance. In 1980, Davis et al[5] formulated polyethylene glycol (PEG), an osmotically balanced electrolyte lavage solution. The standard 4-liter dosing regimen given the day before the procedure was established as safe and effective.[6-8] PEG quickly became the ''gold standard'' for colonoscopy. However, poor compliance related to the salty taste, the smell from the sulfates, and the large volume of fluids required led to modifications of the PEG solutions and their dosing recommendations and re-evaluations of other osmotic laxatives (eg, sodium phosphate [NaP]).[9-16] Chang et al[17] developed a method of pulsed rectal irrigation combined with magnesium citrate. These regimens and their use continue to evolve.[18-39] More recent studies have focused on identifying the ''ideal'' preparation (Table 1), including parameters such as taste, electrolyte supplementation, and the timing and division of doses.

With this historical background and the precedent of an American Society for Gastrointestinal Endoscopy (ASGE) technology committee report,[40] this document reviews the available evidence to create guidelines for bowel preparation before colonoscopy. The various studies in the literature have been graded according to the Levels of Evidence Grade Recommendation scale proposed by Cook et al[41] (Table 2).

REGIMENS FOR COLONIC CLEANSING BEFORE COLONOSCOPY

Diet

Dosing. Dietary regimens characteristically incorporate clear liquids and low-residue foods during one to four days. Regimens typically incorporate dietary changes, and oral cathartic and/or additional cathartic enemas.[42] A cathartic, such as magnesium citrate or senna extract, often is used on the day before the procedure. Tap water enemas are administered on the morning of and occasionally on the evening before the procedure.

Evidence. Much of the evidence supporting these regimens comes from studies of colon cleansing for radiography. Although the individual components of these preparations vary widely, the combination of dietary restrictions and cathartics has proven to be safe and effective for colonic cleansing for colonoscopy.[6] In a recent study of in-patients undergoing colonoscopy, a clear liquid diet before administration of the bowel preparation was the only diet modification that improved the quality of preparation.[43] Although prolonged dietary restrictions and cathartics are effective, these regimens are less than ideal because of the time commitment required.

Recommendations. Dietary modifications alone, such as a clear liquid diet are inadequate for colonoscopy. However they have proven to be a beneficial adjunct to other mechanical cleansing methods (Grade IIB).

Enemas

Dosing. Tap water or NaP enemas are administered on the evening before or the morning of the procedure. For colonic cleansing, they are usually administered in conjunction with dietary restrictions or cathartics. In patients with poor or incomplete cleansing, one or two NaP enemas are useful in washing out the distal colon. Enemas are useful in washing out the distal segment of bowel in patients with a proximal stoma or a defunctionalized distal colon (eg, Hartmann's). Various commercial enema preparations are discussed in the adjunct section.

Evidence. The evidence is mostly anecdotal with no recent prospective trials (Grade IIIB).

Recommendations. Use enemas in patients who present to endoscopy with a poor distal colon preparation and in patients with a defunctionalized distal colon.

High-volume gut lavage

Dosing. Per oral gut lavage with high volumes (7-12 liters) of saline solution or balanced electrolyte solutions with or without a nasogastric tube have been used for colonic preparation.[2] Mannitol was used in early formulations but abandoned secondary to bacterial fermentation into hydrogen and methane gas, which can cause explosion when electrocautery is used.[1,44]

Evidence. Although these regimens are effective in cleansing the colon, they are poorly tolerated. Administration of high-volume unbalanced solutions can result in dramatic fluid and electrolyte shifts. There also have been anecdotal reports of complications after high-volume infusion through a nasogastric tube.[38,45]

Recommendations. Neither high-volume nor unbalanced solutions, such as mannitol, should be used for colonic preparation (Grade IA). In addition, caution should be taken when using nasogastric tubes for the administration of any bowel preparation infusion (Grade VD).

Rectal pulsed irrigation

Per rectal pulsed irrigation in combination with per oral ingestion of 10 oz of magnesium citrate the night before the colonoscopy is another potential preparation. The patient is given a 30-minute infusion of short pulses of warm tap water via the rectum through a rectal tube immediately before the colonoscopy. Disadvantages to this regimen are that it is time consuming and requires skilled nursing to administer, making it expensive to use.

Evidence. Chang et al[17] developed this regimen and compared it with PEG. No significant differences in quality

TABLE 1. Randomized, Controlled trials

Study (y) (reference)	No. of patients	Study groups	Main outcome
Cohen et al (1994) (13)	422	4l PEG vs 4l PEG (sulfate-free) vs 90 ml NaP	NaP better prep, better tolerated
Church (1998) (24)	317	4l PEG (night before) vs 4l PEG (day of procedure)	PEG day of procedure with better prep
El-Sayed et al (2003) (25)	187	3l PEG + liquid diet vs 3l PEG (split dose) + bisacodyl + minimal diet restriction	Split-dose PEG with better prep, better tolerated
Adams et al (1994) (26)	382	4l PEG vs 2l PEG + bisacodyl	PEG + bisacodyl better tolerated, prep equal
Henderson et al (1995) (27)	242	4l PEG vs 90 ml NaP	Prep similar, NaP better tolerated
Young et al (2000) (28)	323	2l PEG + bisacodyl vs 90 ml NaP	NaP better prep, better tolerated
Poon et al (2003) (19)	200	2l PEG vs 90 ml NaP	Prep + tolerance similar
Barclay (2004) (29)	256	135 ml NaP vs 90 ml NaP	135 ml NaP better prep, poorer tolerance
Law et al (2004) (30)	299	2–4l PEG vs 45 ml NaP vs 90 ml NaP	90 ml NaP best prep, better tolerated
Schmidt et al (2004) (31)	400	Na picosulfate vs NaP	Prep equal, Na picosulfate better tolerated
Golub et al (1995) (32)	329	4l PEG vs 4l PEG + metoclopramide vs 90 ml NaP	Preps equal, NaP better tolerated
Balaban et al (2003) (33)	101	90 ml NaP (liquid) vs 40 tabs NaP (tablet)	Liquid NaP better prep, better tolerated
Aronchick et al (2000) (34)	305	4l PEG vs 90 ml NaP vs 24–32 tabs NaP	Preps equal, NaP tabs better tolerated
Kastenberg et al (2001) (21)	845	4l PEG vs 40 tabs NaP	Prep equal, NaP tabs better tolerated

TABLE 1 (*continued*)

Study (y) (reference)	No. of patients	Study groups	Main outcome
Afridi et al (1995) (20)	147	4l PEG vs 90 ml NaP + bisacodyl	Prep equal, NaP + bisacodyl better tolerated
Frommer (1997) (14)	486	3l PEG vs 90 ml NaP (day before) vs 90 ml NaP (day before, day of procedure)	NaP day of procedure best prep, NaP better tolerated than PEG
Ell et al (2003) (35)	185	4l PEG (standard) vs 4l PEG (sulfate-free) vs 90 ml NaP	Standard PEG best prep, tolerance similar
Martinek et al (2001) (36)	187	4l PEG vs 90 ml NaP (with/without cisapride)	PEG better prep, NaP better tolerated
Vanner et al (1990) (37)	102	4l PEG vs 90 ml NaP	NaP better prep, better tolerated
Marschall and Bartels (1993) (38)	143	4l PEG vs 90 ml NaP	Prep equal, NaP better tolerated
Kolts et al (1993) (39)	113	4l PEG vs 90 ml NaP vs 60 ml Castor Oil	NaP best prep, better tolerated than PEG

PEG, Polyethylene glycol; *NaP*, sodium phosphate; *tabs*, tablets; *prep*, preparation.

of colonic cleansing were demonstrated between these two methods.

Recommendations. Rectal pulsed irrigation administered immediately before the procedure combined with magnesium citrate given the evening before the procedure is a reasonable alternative to full-volume (4-liters) PEG in those individuals who cannot tolerate per oral administration of PEG (Grade IIB).

PEG (electrolyte lavage solution)

PEG is a nonabsorbable solution that should pass through the bowel without net absorption or secretion. Significant fluid and electrolyte shifts are therefore avoided. Large volumes (4 liters) are required to achieve a cathartic effect.

Products.

1. Colyte® (Flavors: Cherry, Citrus-Berry, Lemon-Lime, Orange, Pineapple)
2. GoLYTELY® (Flavor: Pineapple)

Dosing. No solid food for at least two hours before ingestion of the solution; 240 ml (8 oz) every ten minutes until rectal output is clear or 4 liters are consumed. Dosage for nasogastric administration is 20 to 30 ml per minute (1.2–1.8 l/hr).[45]

Evidence. PEG is more effective and better tolerated than the diet combined with cathartic regimens that were used before 1980.[6-8,46,47] PEG also is safer and more effective than high-volume balanced electrolyte solutions.[48] PEG is safer (less production of hydrogen gas), more effective, and better tolerated by patients than mannitol-based solutions.[49] Although PEG is generally well tolerated, 5 percent to 15 percent of patients do not complete the preparation because of poor palatability and/or large volume.[32,50] The additional use of enemas does not offer any improvement in the efficacy of PEG solutions, yet increases patient discomfort.[51] The timing of PEG doses has proven to be important to the quality of the bowel preparation. PEG taken in divided doses (3 liters the evening before and 1 liter the morning of the procedure) was demonstrated to be as effective as and better tolerated than the standard 4-liter dose given one day before the procedure.[52] The timing of the preparation in relation to the colonoscopy also is

TABLE 2. Levels of evidence and grade recommendation[41]

Level	Source of Evidence
I	Meta-analysis of multiple well-designed, controlled studies, randomized trials with low-false positive and low-false negative errors (high power)
II	At least one well-designed experimental study; randomized trials with high false-positive or high false-negative errors or both (low power)
III	Well-designed, quasi experimental studies, such as nonrandomized, controlled, single-group, preoperative-postoperative comparison, cohort, time, or matched case-control series
IV	Well-designed, nonexperimental studies, such as comparative and correlational descriptive and case studies
V	Case reports and clinical examples
Grade	Grade of Recommendation
A	Evidence of Type I or consistent findings from multiple studies of Type II, III, or IV
B	Evidence of Type II, III, or IV and generally consistent findings
C	Evidence of Type II, III, or IV but inconsistent findings
D	Little or no systematic empirical evidence

significant. In one study, consumption of the PEG solution less than 5 hours before the procedure resulted in better preparation than when given more than 19 hours before the procedure.[24] Additional studies have continued to show that divided-dose regimens are superior to single-dose regimens. One recent study suggests that the method and/or timing of administration is more important in determining quality of the preparation than is dietary restriction.[53] The addition of prokinetic agents to PEG administration has not been shown to improve patient tolerance or colonic cleansing.[36,54,55] Similarly, bisacodyl administration does not significantly improve colonic cleansing or overall patient tolerance when used as an adjunct with full-volume (4 liters) PEG.[56] PEG is relatively safe for patients with electrolyte imbalance and for patients who cannot tolerate a significant fluid load (renal failure, congestive heart failure, or advanced liver disease with ascites).[38] In addition, PEG gut lavage has proven to be the preferred method for colonic cleansing in infants and children.[57-59]

Recommendations. PEG is a faster, more effective, and better-tolerated method for cleansing the colon than a restricted diet combined with cathartics, high-volume gut lavage, or mannitol (Grade IA). PEG is safer than osmotic laxatives/NaP for patients with electrolyte or fluid imbalances, such as renal or liver insufficiency, congestive heart failure, or liver failure and is, therefore, preferable in these patient groups (Grade IA). Divided-dose PEG regimens (2–3 liters given the night before the colonoscopy and 1–2 liters on the morning of procedure) are acceptable alternative regimens that enhance patient tolerance (Grade IIB). Cleansing preparations for colonoscopies performed in the afternoon should instruct that at least part of the PEG solution be given the morning before the procedure (Grade IIB). Enemas, bisacodyl, and metaclopramide as adjuncts to the full volume of PEG have not been demonstrated to improve colonic cleansing or patient tolerance and are, therefore, unnecessary (Grade IIB).

Sulfate-free PEG (SF-PEG)

PEG-based lavage solution without sodium sulfate was developed by Fordtran et al[60] in an attempt to improve the smell and taste of PEG solutions. The improved taste was the result of a decrease in potassium concentration, increase in chloride concentration, and complete absence of sodium sulfate. The elimination of sodium sulfate results in a lower luminal sodium concentration. Therefore, the mechanism of action is dependent on the osmotic effects of PEG.[61]

Products.

1. NuLYTELY® (Flavors: Cherry, Lemon-lime, Orange, Pineapple)
2. TriLyte® (Flavors: Cherry, Citrus-Berry, Lemon-lime, Orange, Pineapple)

Dosing. No solid food for at least two hours before taking the solution; 240 ml (8 oz) every 10 minutes until rectal output is clear or 4 liters are consumed. Dosage for nasogastric administration is 20 to 30 ml per minute (1.2–1.8 liters per hour). Pediatric (older than aged 6 months) dose is 25 ml/kg per hour until rectal effluent is clear.[45]

Evidence. SF-PEG is less salty, more palatable, and comparable to PEG in terms of effective colonic cleansing and overall patient tolerance.[9]

Recommendations. SF-PEG is comparable to PEG in terms of safety, effectiveness, and tolerance. SF-PEG is better tasting, but still requires the consumption of 4 liters in its standard regimen. SF-PEG is an acceptable alternative lavage solution when a PEG-based lavage solution is required (Grade IIB).

Low-volume PEG/PEG-3350 and bisacodyl delayed-release tablets

Low-volume PEG solutions were developed in an attempt to improve patient tolerance. To reduce the amount of volume of lavage solution required and reduce volume-related symptoms, such as bloating and cramping, while maintaining efficacy, bisacodyl and magnesium citrate are administered.

Product.

1. Halflytely® (Flavor: Lemon-lime)

Dosing: Only clear liquids on the day of the preparation. Dosage is four bisacodyl delayed-release tablets

(5 mg) at noon. Wait for bowel movement or maximum of six hours; 240 ml (8 oz) every ten minutes until 2 liters are consumed.[45]

Evidence. Multiple studies have compared full-volume (4 liters) PEG with low-volume (2 liters) PEG combined with magnesium citrate or bisacodyl. These studies have demonstrated equal efficacy of colonic cleansing but with improved overall patient tolerance.[26,62]

Low-volume PEG without any dietary restrictions has been recently suggested to provide better quality colon cleansing than the whole-dose regimen with no significant impact on tolerability or adverse effects.[53]

Recommendations. Two-liter PEG regimens combined with bisacodyl (ie, HalfLytely®) or magnesium citrate are equally effective compared with standard 4-liter PEG regimens but appear to be better tolerated and therefore a more acceptable alternative to the 4 liter PEG regimens (Grade IA). However, the safety of the reduced dose PEG in patients who may not tolerate fluids is still unknown. Additional studies comparing 2-liter regimens with NaP would be beneficial.

Low-volume PEG-3350 and bisacodyl delayed-release tablets

An additional low-volume PEG-3350 without electrolytes administered with adjuncts, such as bisacodyl, also has been used.

Product.

1. Miralax®

Dosing. Clear liquids only the day of the preparation. Dosage is four bisacodyl delayed-release tablets (5 mg) at noon. Wait for bowel movement or maximum of six hours; 240 ml (8 oz) of clear liquid containing one capful of Miralax® every ten minutes until 2 liters are consumed.

Evidence. Studies that have compared full-volume (4-liter) PEG with low-volume (2-liter) PEG-3350 combined with bisacodyl have clearly demonstrated an equal efficacy in terms of colonic cleansing and improved overall patient tolerance.

Recommendations. Two-liter PEG 3350 regimens combined with bisacodyl (ie, Miralax®) are equally effective compared with standard 4-liter PEG (Grade IA).

Aqueous NaP

Aqueous NaP is a low-volume hyperosmotic solution that contains 48 g (400 mmol) of monobasic NaP and 18 g (130 mmol) of dibasic NaP per 100 ml.[63] The NaP osmotically draws plasma water into the bowel lumen to promote colonic cleansing. Significant fluid and electrolyte shifts can occur. NaP must be diluted before drinking to prevent emesis and must be accompanied by significant oral fluid to prevent dehydration. Patients with compromised renal function, dehydration, hypercalcemia, or hypertension with the use of angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs) have experienced phosphate nephropathy after use of oral NaP solutions.[64] The effects seem to be age-related and dose-related. Linden and Waye[65] described the pharmacologic properties of NaP. The mean onset of bowel activity was 1.7 hours after the first dose and 0.7 hours after the second dose. The mean duration of action was 4.6 hours after the first dose and 2.9 hours after the second dose. Bowel activity ceased within four hours in 83 percent of patients and within five hours in 87 percent.

Product.

1. Fleet®

Dosing. Only clear liquids can be consumed on the day of preparation. Two doses of 30 to 45 ml (2-3 tbsp) of oral solution are given at least 10 to 12 hours apart. Each dose is taken with at least 8 oz of liquid followed by an additional minimum of at least 16 oz of liquid. The second dose must be taken at least three hours before the procedure.[45]

Evidence. NaP has been compared with full-volume (4-liter) PEG in multiple studies and has generally been found to be more or equally effective and better tolerated. Colonoscopists also were more likely to rate NaP as more acceptable than PEG-based solutions.[15] A divided-dose NaP regimen in which the first dose is given the evening before the procedure and the second is given 10 to 12 hours later on the morning of the procedure has proven to be more effective than a regimen using two doses of NaP given the day before the procedure or a regimen using full-volume (4-liter) PEG.[14] This finding is consistent with the pharmacologic properties of NaP discussed above. A second split-dose method for morning colonoscopies was demonstrated to be equally effective and as tolerable as standard 4-liter PEG.[20] The split dose of NaP was given at 1600 and 1900 hours on the day before a morning colonoscopy. Bisacodyl was used as an adjunct in this regimen and given at 2200 hours the evening before the colonoscopy. In one study, NaP was demonstrated to be more effective in colonic cleansing than Picolax® (sodium picosulfate + magnesium citrate).[66] However, a second study offered conflicting data.[31] Because of its osmotic mechanism of action, NaP can result in potentially fatal fluid and electrolyte shifts, especially in elderly patients, patients with bowel obstruction, small intestine disorders, poor gut motility, renal or liver insufficiency, congestive heart failure, or liver failure.[67] Nephrocalcinosis, as described previously, also is a concern, particularly in those patients who are being treated with ACE inhibitor or ARB.[64] NaP can cause colonic mucosal lesions and ulcerations that may mimic inflammatory bowel disease.[68] Although contraindicated in children younger than age five years, several studies have assessed NaP in the pediatric population and found the efficacy of NaP similar to PEG.[58,69] The efficacy of NaP in the elderly is similar to younger adults and comparable to PEG.[70,71] The addition of cisapride does not result in any improvement in colon cleansing or patient tolerance.[36] Agents that counteract the fluid and electrolyte shifts of NaP have proven to be

successful, at least to a limited degree. In one study, the addition of a carbohydrate electrolyte rehydration solution resulted in less intravascular volume contraction.[72] In another study, E-Lyte® solution was shown to enhance both patient tolerance and the overall efficacy of NaP.[73] The addition of any carbohydrates to a bowel preparation may increase the production of explosive gases. Compared with the 40-tablet NaP regimen, aqueous NaP is better tolerated and more effective.[32] Further studies comparing the newer 28 and 32 tablet regimens with aqueous NaP are pending publication.

Recommendations. Aqueous NaP colonic preparation is an equal alternative to PEG solutions except for pediatric and elderly patients, patients with bowel obstruction, and other structural intestinal disorders, gut dysmotility, renal failure, congestive heart failure, or liver failure (Grade IA). Dosing of aqueous NaP should be 45 ml in divided doses, 10 to 12 hours apart with one of the doses taken on the morning of the procedure (Grade IIB). Aqueous NaP is the preferable form of NaP at this time (Grade IIB). Apart from anecdotal reports, the addition of adjuncts to the standard NaP regimen has not demonstrated any dramatic effect on colonic cleansing preparation. Carbohydrate-electrolyte solutions such as E-Lyte® may improve safety and tolerability.

Tablet NaP

The tablet form of NaP was designed to improve the taste and limit the volume of liquid required. The results of two large, identically designed, Phase III, multicenter, randomized, investigator-blinded trials that compared tablet NaP with 4-liter PEG regimens[21] were the basis for FDA approval in 2000. Each 2 g tablet contains 1500 mg of active ingredients (monobasic and dibasic NaP) and 460 mg of microcrystalline cellulose as a tablet binder. The amount of active ingredient in this regimen is comparable to the standard aqueous NaP regimen. Microcrystalline cellulose is a nonabsorbable inert polymer and is therefore insoluble in the gastrointestinal tract.[23] The remnants of this polymer can be visualized during colonoscopy and may interfere with the examination of the bowel mucosa. Therefore, reduced amounts of microcrystalline cellulose may help visualize the colonic mucosa. In 2001, a laboratory study demonstrated the beneficial effects of ginger ale when administered with Visicol® tablets. This study attempted to provide a scientific basis for the clinical observation that ginger ale facilitates the removal of microcrystalline cellulose from the colon after the administration of Visicol® before colonoscopy.[74]

Product.

1. Visicol®

Dosing. Dosage is 32 to 40 tablets: 20 tablets on the evening before the procedure and 12 to 20 tablets the day of the procedure (3–5 hours before). The 20 tablets are taken as 4 tablets every 15 minutes with 8 oz of clear liquid.[45] Bisacodyl is prescribed by some physicians as an adjunct.

Evidence. The Phase III trials in which tablet NaP regimens were compared with 4-liter PEG regimens demonstrated equal colon cleansing with fewer side effects.[21,23] Tablet NaP has been compared with aqueous NaP in multiple studies. Balaban et al[33] found that liquid or aqueous NaP is better tolerated and more effective than tablet NaP. Aronchick et al[34] found that tablet NaP is as safe and effective as Colyte® and aqueous NaP and greatly preferred by patients. Two problems were identified with the initial 40-tablet regimen. First, the inactive ingredient microcrystalline cellulose produces a residue that obscures the mucosal surface. Second, a large number of tablets (n = 40) needs to be ingested in a short period of time. These problems have been overcome by the reduction in the amount of microcrystalline cellulose per tablet [22] by a reduction in the number of tablets needed to complete the preparation from 40 to between 28 and 32 tablets.[23] Studies comparing liquid NaP and a 2-liter PEG regimen with NaP tablets are pending publication; studies on adjunct therapies are currently lacking.

Recommendations. The improved taste and palatability of tablet NaP compared with aqueous NaP has not translated into improved overall patient tolerance (Grade IA). The reduced amount of microcrystalline cellulose allows for better visualization of the colonic mucosa with less need for colonic irrigation (Grade IVB). Efficacy is maintained despite decreasing the number of tablets required to complete the preparation (Grade IIB), significantly improving patient tolerance.

ADJUNCTS TO COLONIC CLEANSING BEFORE COLONOSCOPY

Flavoring

There have been many attempts to improve the flavor of both PEG-electrolyte solutions and NaP solutions. As a result, PEG-electrolyte solutions are available in multiple flavors, such as cherry, citrus-berry, lemon-lime, orange, and pineapple. In addition, the sulfate salts have been removed from HalfLytely® and NuLYTELY®, resulting in a less salty taste and avoidance of the ''rotten egg'' smell. Gatorade®, CrystalLite®, and carbohydrate-electrolyte solutions have been used to improve palatability in both PEG and NaP solutions. Ginger ale and water are used with NaP to improve the taste. However, improved flavor does not necessarily equate to improved tolerance.[75] Special care must be taken to avoid altering the osmolarity of the preparation or adding substrates to the preparation, which can metabolize into explosive gases[45,73] or alter the amount of water and salts absorbed.

Nasogastric/orogastric tube administration of colonic preparations

Nasogastric tubes have been used to instill colonic preparations, primarily PEG solutions, in both children and adults. In addition to the potential complications

related to placement of the nasogastric tube, case reports have demonstrated the potential for severe life-threatening complications, such as aspiration.[38]

Carbohydrate-electrolyte solutions

Products.

1. Gatorade®
2. E-Lyte®
3. Generic formulations of carbohydrate-electrolyte solutions also are available.

Carbohydrate-electrolyte solutions have been used in combination with both PEG and NaP solutions to make the preparation more palatable and, in the latter, to avoid the severe electrolyte/fluid shifts. Combining PEG-3350 laxative powder (Miralax®) and Gatorade® has been shown to improve the taste and tolerability of the preparation.[76] E-Lyte® combined with NaP was demonstrated to improve overall tolerability and reduce the degree of volume contraction, hypokalemia, and the need for intravenous rehydration.[73] Although beneficial, the addition of these carbohydrate-based solutions is associated with a theoretical risk of cautery-induced explosion if these carbohydrates are metabolized by colonic bacteria into explosive gases.

Enemas

Products.

1. Tap Water
2. Soap Suds
3. Fleet®
4. Fleet® Bisacodyl
5. Fleet® Mineral Oil

Before the development of PEG, enemas were an essential component of colonic preparation. However, conclusive evidence has demonstrated that enemas do not improve the quality of bowel cleansing, yet significantly increase patient discomfort.[51] Enemas may still play a role in the patient who presents for colonoscopy with a poor preparation.

Metaclopramide

Products.

1. Reglan®
2. Generic formulations also are available.

Metaclopramide is a dopamine antagonist gastroprokinetic that sensitizes tissues to the action of acetylcholine. This results in increased amplitude of gastric contraction, increased peristalsis of the duodenum and jejunum, and does not change colonic motility. Metaclopramide used as an adjunct with PEG has been shown to reduce nausea and bloating but not improve colonic cleansing.[54] However, a second study did not reveal any advantage with regards to colonic cleansing or patient tolerance.[55]

Simethicone

Products.

1. Gas-X®
2. Mylicon®
3. Mylanta®
4. Generic formulations also are available.

Simethicone is an anti-flatulent, anti-gas agent that has been used as an adjunct to colonoscopy preparations. The use of simethicone as an adjunct to PEG-electrolyte solution to eliminate foam formation after colonoscopy preparation and improve visualization during colonoscopy has been studied.[77] Simethicone reduced foaming and improved tolerability and improved efficacy (*i.e.,* reduction in residual stool at time of colonoscopy). However, the mechanism of action of simethicone was unclear. A subsequent study also showed a reduction in bubble formation seen during colonoscopy and an improvement in overall tolerability.[78]

Bisacodyl

Bisacodyl is a poorly absorbed diphenylmethane that stimulates colonic peristalsis.[35] Bisacodyl used as an adjunct with high-volume balanced solution shortened the duration of whole gut irrigation, although no significant difference in colon cleansing was identified.[79] Bisacodyl, when used as an adjunct with PEG, has demonstrated no significant difference in the quality of the preparation or amount of residual colonic fluid during colonoscopy.[56,80] Bisacodyl and magnesium citrate are used as adjuncts to PEG solutions and have allowed for less volume of PEG necessary for colonic cleansing.[18,26] Afridi et al[20] studied bisacodyl as an adjunct with NaP given in split doses the evening before the procedure. This combined regimen was found to be equally effective and tolerable as standard 4-liter PEG. Anecdotally, bisacodyl has been used as an adjunct for aqueous and tablet NaP, although further studies are necessary.

Saline Laxatives

Products.

1. Magnesium citrate
2. Picolax® (sodium picosulfate/magnesium citrate)

Magnesium citrate is a hyperosmotic saline laxative that increases intraluminal volume resulting in increased intestinal motility. Magnesium also stimulates the release of cholecystokinin, which causes intraluminal accumulation of fluid and electrolytes and promotes small bowel and, possibly, colonic transit. Because magnesium is eliminated from the body solely by the kidney, magnesium citrate should be used with extreme caution in patients with renal insufficiency or renal failure. Two studies by Sharma et al[18,62] used magnesium citrate as an adjunct to PEG. The addition of magnesium citrate allowed for less PEG solution (2 liters) to be used to achieve the same result. Thus, the 2-liter volume PEG regimen was significantly better tolerated by patients.

Saline laxatives that use sodium picosulfate and magnesium citrate as the active ingredients are available primarily in the United Kingdom. Bowel preparations with this regimen have been compared with both PEG[81] and NaP.[65] Picolax® was found to be equally effective as PEG in terms

of quality of preparation but more tolerable (less nauseating and easier to finish). Conflicting data concerning NaP compared with Picolax® have been published.[31,65]

Senna

Products.

1. X-Prep®
2. Senakot

Senna laxatives contain anthraquinone derivatives (glycosides and sennosides) that are activated by colonic bacteria. The activated derivatives then have a direct effect on intestinal mucosa, increasing the rate of colonic motility, enhancing colonic transit, and inhibiting water and electrolyte secretion.[39] Senna has been used as an adjunct to PEG regimens in a manner similar to that of bisacodyl.[82] No differences were found between senna and bisacodyl when used as an adjunct in combination with PEG.[80] The adjunctive use of senna with PEG solutions has been demonstrated to improve the quality of bowel preparation[82] and to reduce the amount of PEG required for effective bowel preparation.[83]

EFFICACY

To assess the efficacy of bowel preparation, one must assess the relatively subjective appearance of the prepared colonic mucosa to a relatively objective parameter. Toward that end, several colonic cleansing systems have been proposed[11,34,84]; however, no single system seems ideal in all situations.

SAFETY

The safety of the various bowel preparation protocols currently available for use before colonoscopy is related to the safety profile of the base agent, PEG or NaP. Generally, all of the preparations detailed in this document have been demonstrated safe for use in otherwise healthy individuals without significant comorbid conditions.[21,85,86] Caution should be taken in selecting a bowel preparation for patients with significant hepatic, renal, or cardiac dysfunction, and for those at the extremes of age.

The administration of isotonic PEG solution does not result in significant physiologic changes as measured by patient weight, vital signs, serum electrolytes, blood chemistries, and complete blood counts.[7,56,60] Isotonic PEG has been safely used in patients with serum electrolyte imbalances, advanced hepatic dysfunction, acute and chronic renal failure, and congestive heart failure. PEG does not alter the histologic features of colonic mucosa and may be used in patients suspected of having inflammatory bowel disease without obscuring the diagnostic capabilities of colonoscopy or biopsy analysis.[87]

Rare adverse events in patients receiving PEG have been reported and include nausea with and without vomiting, abdominal pain, pulmonary aspiration, Mallory-Weiss tear, PEG-induced pancreatitis and colitis, lavage-induced pill malabsorption, cardiac dysrhythmia, and the syndrome of inappropriate antidiuretic hormone.[2,88-90] An increase in plasma volume has been shown to occur in some individuals with concomitant disease states that predispose them to fluid retention.[91,92] Adverse effects may occur less frequently in association with preparation regimens that use a reduced volume of PEG.[93] Some drug interaction databases raise concerns when PEG solutions, especially HalfLytely®, are prescribed for patients taking ACE inhibitors and/or potassium-sparing diuretics because of the small amount of potassium present in this preparation solution. Although this problem raises a theoretic concern for hyperkalemia in these patients, no clinical reports of adverse outcomes were available as of this writing.

The use of NaP is associated with physiologically significant, although rarely clinically meaningful, changes in volume status and electrolyte abnormalities. NaP is contraindicated in patients with serum electrolyte imbalances, advanced hepatic dysfunction, acute and chronic renal failure, recent myocardial infarction, unstable angina, congestive heart failure, ileus, malabsorption, and ascites.[20,27,37,91,94-98] NaP preparations have been shown to alter both the macroscopic and microscopic features of intestinal mucosa, and induce aphthoid erosions similar to those seen in inflammatory bowel disease, which may obscure the diagnosis of inflammatory bowel disease.[68,99,100] For this reason, many clinicians avoid using NaP preparations in patients undergoing diagnostic colonoscopy for suspected inflammatory bowel disease or microscopic colitis.

NaP is available as a bowel preparation for colonoscopy in both liquid and solid tablet form. The following adverse events are characteristic of both formulations. Serum electrolyte abnormalities and extracellular fluid volume is altered, initially by increasing fluid retention, and then causing significant losses of both fluid and electrolytes in the stool effluent.[39,101] The significant volume contraction and resultant dehydration seen in some patients using NaP preparations may be lessened by encouraging patients to drink fluids liberally during the days leading up to their procedure, especially during their preparation.[94] Although usually asymptomatic, hyperphosphatemia is seen in as many as 40 percent of healthy patients completing NaP preparations, and may be significant in patients with renal failure.[58,102] As many as 20 percent of patients using NaP preparations develop hypokalemia; in addition, NaP has been shown to cause elevated blood urea nitrogen levels, decreased exercise capacity, increased plasma osmolality, hypocalcemia,[101,103] and significant hyponatremia and seizures.[104] These significant blood chemistry abnormalities are more profound in children; therefore, NaP should not be used in children with acute and chronic renal failure, congestive heart failure, ileus, and ascites. Rare adverse events, such as nephrocalcinosis with acute renal failure, also have been reported after NaP preparation for

colonoscopy particularly in those patients with hypertension receiving ACE inhibitors or ARBs.[64,105]

SPECIAL CONSIDERATIONS

Inadequate bowel preparation

Inadequate bowel preparation for colonoscopy can result in missed lesions, cancelled procedures, increased procedural time, and a potential increase in complication rates. One study examined the possible causes for poor preparations.[106] Surprisingly, less than 20 percent of patients with an inadequate colonic preparation reported a failure to adequately follow preparation instructions. Independent predictors of an inadequate colon preparation included a later colonoscopy starting time, failure to follow preparation instructions, inpatient status, procedural indication of constipation, use of tricyclic antidepressants, male gender, and a history of cirrhosis, stroke, or dementia. Anecdotally, a poor preparation after a PEG preparation is usually liquid and more easily managed than a preparation after NaP, which tends to be thick and tenaciously adhered to the mucosa. There is no published information on the management of the patient who has received a colonoscopy preparation that has been deemed inadequate. Regardless of the preparation selected, the patient and physician must be aware of potential financial obligations of a repeat colonoscopy and preparation. Specifically, the patient may be required to pay an additional co-pay for each examination and the financial intermediary may deem one or both examinations unnecessary. In these instances, the patient may be responsible for payment in full for both examinations. The following are recommendations (Grade VD) on management of this clinical predicament. Identify whether or not the patient has consumed the preparation as prescribed. If not, it would be reasonable to repeat the same preparation, although not within 24 hours using NaP because of the risk of toxicity. If the patient has properly consumed the preparation, reasonable options include repeating the preparation with a longer interval of dietary restriction to clear liquids, switching to an alternate but equally effective preparation (if the patient received PEG, change to NaP or vice versa), adding another cathartic, such as magnesium citrate, bisacodyl, or senna, to the previous regimen, or double administration of the preparation during a two-day period (with the exception of NaP). Combining preparations, for example PEG solution and NaP solution, also has been described with some success.[18]

Selection of bowel preparation based on comorbidities

Elderly patients. Elderly patients tend to have poorer preparations, although one study found no difference in the adequacy of the colonic preparation between PEG and NaP solutions.[107] They are at an increased risk for phosphate intoxication because of decreased kidney function, concomitant medication use, and systemic and gastrointestinal diseases. Administration of NaP causes a significant rise in serum phosphate,[108] even in patients with normal creatinine clearance.[109] Hypokalemia is more prevalent in frail patients.[110] However, NaP preparations may be safe in selected healthy elderly patients.[71,72]

Possible underlying inflammatory bowel disease. NaP preparations may cause mucosal abnormalities that mimic Crohn's disease.[68,100,111] However, the frequency of this problem is rare and may not mitigate against using NaP. This caveat is most important in the initial colonoscopic evaluation of patients with symptoms suspect for colitis.

Diabetes mellitus. One study showed that patients with diabetes have significantly poorer preparations with PEG solutions than patients without diabetes, although there is no evidence that NaP preparations are superior in this group.[112]

Pregnancy. The need for colonoscopy is uncommon during pregnancy, therefore, the safety and efficacy of colonoscopy in these individuals is not well studied. However, invasive procedures are justified when it is clear that by not doing so could expose the fetus and/or mother to harm. The safety of PEG electrolyte isotonic cathartic solutions has not been studied in pregnancy. PEG solutions are FDA Category C for use in pregnancy, as defined in the FDA Current Category for Drug Use in Pregnancy, wherein no adequate and well-controlled studies have been undertaken in pregnant females and a limited number of animal studies have shown an adverse effect. The common use of PEG solutions, such as Miralax®, to manage constipation associated with pregnancy supports its safety as a bowel preparation. NaP preparations, which are also FDA Category C, may cause fluid and electrolyte abnormalities and should be used with caution.[35]

Recommendations. If the potential benefit of colonoscopy outweighs the small but potential risks, patients may be cleansed with PEG solutions or, in select patients, a NaP preparation may be used (Grade VD).

Pediatric population. Although there are no ''national standards'' per se for pediatric bowel preparations for colonoscopy, review of the literature documents the three most commonly used preparations. The least commonly used preparation is the administration of two pediatric Fleet® enemas and X-Prep® (for age). A more widely used preparation includes Miralax® at 1.25 mg/kg per day for four days, the last day of which the child is maintained on clear liquids. This regimen is mild, well tolerated, and relatively simple to administer. The simplest preparation, both for the parents and the child, is the administration of a sugar-free, clear-liquid diet the day before and then nil by mouth for eight hours before the colonoscopy. This regimen is combined with Fleet® Phospho-soda® at a dosage of

TABLE 3. Cost of bowel preparation agents

Product	Quantity	Average wholesale price*
Colyte®		
flavored	3785 mL	$16.16
nonflavored	3785 mL	$13.89
GlycoLax™	255 g	$19.54
	527 g	$39.06
GoLYTELY®		
flavored	4000 mL	$19.70
nonflavored	4000 mL	$18.45
MiraLax™	255 g	$21.73
	527 g	$43.45
NuLYTELY®		
flavored	4000 mL	$25.65
nonflavored	4000 mL	$25.65
TriLyte®†		
flavored	4000 mL	$25.63
Oral sodium phosphate (aqueous)	45 mL	$1.48
Fleet® Phospho-soda	90 ml	$2.65
Oral sodium phosphate (tablet) Visicol™	100s	$160.22 ($1.60/tablet, $44-$66/preparation)
Bisacodyl (tablet) 5 mg (Amkas)	100s	$9.85 ($0.10/tablet)
Magnesium citrate (liquid) (AmerisourceBergen)	300 mL	$1.43
Senna (AmerisourceBergen)	100s	$8.99 ($0.09/tablet)
Senna/Docusate (tablet)	100s	$11.13 ($0.11/tablet)
Senna Plus®		
(American Health)		
Metoclopramide (tablet) 5 mg (Pliva)	100s	$32.00 ($0.32/tablet)
Fleet® Enema	135 mL	$0.80
Fleet® Bisacodyl		
ECT, po 5 mg	25s	$2.90 (each)
SUP, RC, 10 mg	4s	$1.83 (each)
Fleet® Bisacodyl Enema 10 mg/1.25 oz	37.5 mL	$1.12
Fleet® Mineral Oil	480 mL	$1.88
Fleet® Mineral Oil Enemas	135 mL	$1.45
Enemeez® Mini Enema (replacement for Therevac®-SB)	5 ml (30s)	$72.99‡
Gas-X® (80 mg)	12s	$1.88
	36s	$4.67
Mylicon® Infant Drops	15 mL	$6.22
40 mg/0.6 ml	30 mL	$10.36

TABLE 3 (*continued*)

Product	Quantity	Average wholesale price*
Simethicone 80 mg	100s	$6.30 (each)
(Rugby) 125 mg	60s	$5.02 (each)
Mylanta®	150 mL	$2.63
	360 mL	$4.45
	720 mL	$8.00
X-Prep® Syrup 8 mg/5 mL	75 ml	$13.59
X-Prep® Bowel Evacuant Kit-1, with Senokot-S	1 kit	$19.32 (each)
HalfLytely® and Bisacodyl Tablet Bowel Prep Kit	1 kit	$48.75 (each)
E-Lyte®	20 oz	$20.00‡

*Product pricing provided by manufacturers as listed in July 2005 (2003 Red Book®, American Academy of Pediatrics, Elk Grove Village, IL).
†Only TriLyte® with Flavor Packs was listed in the Red Book®.
‡Price listed on the internet.

1.5 tablespoons for children weighing less than 15 kg and 3 tablespoons for children weighing 15 kg or more, the afternoon and then again the evening before the colonoscopy. Each of these preparations is safe and will adequately prepare the child's colon for colonoscopy (Grade IA).[113,114]

COST

Table 3 shows the cost of bowel preparation agents listed as average wholesale price (AWP), which is provided by the ''Red Book'' July 2005. As can be seen, the least expensive solution is oral NaP and the most expensive is the tablet form of NaP. The various PEG preparations are intermediate in cost. None of the bowel preparation agents has an associated CPT code that would allow for separate payment reimbursed by the patients' insurance company or Medicare in an outpatient setting. In an inpatient setting, the reimbursement for these agents would be included in the DRG payment. Of note, patients' compliance and adequacy of bowel preparation agents can affect the direct cost for colonoscopic examination. A cost analysis has shown that inadequate bowel preparation could prolong the procedure time and increase the chance for an aborted examination and repeat colonoscopy earlier than suggested or required by current practice standards.[115] In one study, inadequate bowel preparation led to a 12 percent increase in costs at a university hospital setting and a 22 percent increase at a public hospital setting.[116] A meta-analysis performed on eight colonoscopist-blinded trials showed that the direct costs of colonoscopic examination (excluding the cost of bowel preparation agents) were $465 for NaP and $503 for PEG, assuming that the rates of re-examination secondary to incomplete bowel preparation for NaP and PEG were 3 and 8 percent, respectively. The results suggest that NaP is less costly than PEG with a more easily completed preparation.[15]

SUMMARY

Colonoscopy is the most commonly used technique for inspection of the colonic mucosa. The safety and effectiveness of colonoscopy in identifying important colonic pathology is directly impacted by the quality of the bowel preparation performed in anticipation of the procedure. Physicians favor preparations associated with the best patient compliance to achieve the best results. Patients favor preparations that are low in volume, palatable, have easy to complete regimens, and are reimbursed by health insurance or are inexpensive. Both patients and physicians favor preparations that are safe to administer in light of existing comorbid conditions and those that will not interact with previously prescribed medications. Aqueous NaP solutions, NaP tablets, and PEG solutions, especially low-volume solutions, are all accepted and well tolerated by the majority of patients undergoing bowel preparation for colonoscopy. Physicians are advised to select a preparation for each patient based on the safety profile of the agent, NaP or PEG, in light of the overall health of the patient, their comorbid conditions, and currently prescribed medications. In certain circumstances, such as bowel preparation in children, elderly patients, patients with renal insufficiency, and those with hypertension who are receiving ACE inhibitors or ARBs, it may be advisable to adhere to PEG-based solutions because of the risks of occult physiologic disturbances that may potentially contraindicate the use of NaP-based regimens. A variety of other preparations, none of which seems as popular because of inferior efficacy and/or patient acceptance, remain available for use in other circumstances in which bowel preparation is necessary.

Many adjuncts to bowel preparation have been proposed but remain largely inefficacious and therefore cannot be recommended for routine use.

ACKNOWLEDGEMENT

The authors and the governing bodies of the three respective societies thank Ms. Elektra McDermott for her assistance in all phases of data collection and manuscript preparation and Dr. Thomas Lobe for his expert contributions regarding bowel preparation in pediatric patients.

DISCLOSURE

Steven D. Wexner, MD, Scientific Advisory Panel to C.B. Fleet, David E. Beck, MD, Consultant, Braintree Salix, Todd H. Baron, MD, None, Robert D. Fanelli, MD, None, Neil Hyman, MD, None, Bo Shen, MD, Consultant to Salix, Visicol, Kevin E. Wasco, MD, None.

APPROVAL STATEMENT

This document was reviewed and approved by the SAGES Board of Governors, the ASCRS Standards Committee and Executive Council, and the ASGE Governing Board.

REFERENCES

1. DiPalma JA, Brady CE. Colon cleansing for diagnostic and surgical procedures: polyethylene glycol-electrolyte lavage solution. Am J Gastroenterol 1989;84:1008-16.
2. Tooson JD, Gates LK Jr. Bowel preparation before colonoscopy. Choosing the best lavage regimen. Postrgrad Med 1996;100:203-14.
3. Beck DE, Harford FJ, DiPalma JA. Comparison of cleansing methods in preparation for colonic surgery. Dis Colon Rectum 1985;28:491-5.
4. Zmora O, Wexner SD. Bowel preparation for colonoscopy. Clin Colon Rectal Surg 2001;14:309-15.
5. Davis GR, Santa Ana CA, Morawski SG, et al. Development of a lavage solution with minimal water and electrolyte absorption or secretion. Gastroenterology 1980;78:991-5.
6. DiPalma JA, Brady CE 3rd, Stewart DL, et al. Comparison of colon cleansing in preparation for colonoscopy. Gastroenterology 1984; 86:856-60.
7. Ernstoff JJ, Howard DA, Marshall JB, et al. A randomized blinded critical trial of a rapid colonic lavage solution compared with standard preparation for colonoscopy and barium enema. Gastroenterology 1983;84:1512-6.
8. Thomas G, Brozisky S, Isenberg JI. Patient acceptance and effectiveness of a balanced lavage solution (Golytely) versus the standard preparation for colonoscopy. Gastroenterology 1982;82:435-7.
9. DiPalma JA, Marshall JB. Comparison of a new sulfate-free polyethylene glycol lavage solution versus a standard solution for colonoscopy cleansing. Gastrointest Endosc 1990;36:285-9.
10. Froehlich F, Fried M, Schnegg JF, et al. Palatability of a new solution compared with standard polyethylene glycol solution for gastrointestinal lavage. Gastrointest Endosc 1991;37:325-8.
11. Froehlich F, Fried M, Schnegg JF, et al. Low sodium solution for colonic cleansing: a double blind, controlled, randomized prospective study. Gastrointest Endosc 1992;38:579-81.
12. Raymond JM, Beyssac R, Capdenat E, et al. Tolerance, effectiveness, and acceptability of sulfate-free electrolyte lavage solution for colon cleansing before colonoscopy. Endoscopy 1996;28:555-8.
13. Cohen SM, Wexner SD, Binderow SR, et al. Prospective, randomized endoscopist-blinded trial comparing precolonoscopy bowel cleansing methods. Dis Colon Rectum 1994;37:689-96.
14. Frommer D. Cleansing ability and tolerance of three bowel preparations for colonoscopy. Dis Colon Rectum 1997;40:100-4.
15. Hsu CW, Imperiale TF. Meta-analysis and cost comparison of polyethylene glycol lavage versus sodium phosphate for colonoscopy preparation. Gastrointest Endosc 1998;48:276-82.
16. Hookey LC, Depew WT, Vanner S. The safety profile of oral sodium phosphate for colonic cleansing before colonoscopy in adults. Gastrointest Endosc 2002;56:895-902.
17. Chang KJ, Erickson RA, Schandler S, et al. Per-rectal pulsed irrigation versus per-oral colonic lavage for colonoscopy preparation: a randomized, controlled trial. Gastrointest Endosc 1991;37:444-8.
18. Sharma VK, Chockalingham SK, Ugheoke EA, et al. Prospective, randomized, controlled comparison of the use of polyethylene glycol electrolyte lavage solution in four-liter versus two-liter volumes and pretreatment with either magnesium citrate or bisacodyl for colonoscopy preparation. Gastrointest Endosc 1998;47:167-71.
19. Poon CM, Lee DW, Mak SK, et al. Two liters of polyethylene glycol-electrolyte solution versus sodium phosphate as bowel cleansing regimen for colonoscopy: a prospective randomized controlled trial. Endoscopy 2002;34:560-3.
20. Afridi SA, Barthel JS, King PD, et al. Prospective, randomized trial comparing a new sodium phosphate-bisacodyl regimen with conventional PEG-ES lavage for outpatient colonoscopy preparation. Gastrointest Endosc 1995;41:485-9.
21. Kastenberg D, Chasen R, Choudhary C, et al. Efficacy and safety of sodium phosphate tablets compared with PEG solution in colon cleansing: two identically designed, randomized, controlled, parallel group multicenter Phase III trials. Gastrointest Endosc 2001;54:705-13.
22. Rex DK, Chasen R, Pochapin MB. Safety and efficacy of two reduced doing regimens of sodium phosphate tablets for preparation before colonoscopy. Aliment Pharmacol Ther 2002;16:937-44.
23. Khashab M, Rex DK. Efficacy and tolerability of a new formulation of sodium phosphate tablets and a reduced sodium phosphate dose, in colon cleansing: a single-center open-label pilot trial. Aliment Pharmacol Ther 2005;21:465-8.
24. Church JM. Effectiveness of polyethylene glycol antegrade gut lavage bowel preparation for colonoscopy-timing is the key. Dis Colon Rectum 1998;41:1223-5.
25. El Sayed AM, Kanafani ZA, Mourad FH, et al. A randomized single-blind trial of whole versus split-dose polyethylene glycol-electrolyte solution for colonoscopy preparation. Gastrointest Endosc 2003;58:36-40.
26. Adams WJ, Meagher AP, Lubowski DZ, et al. Bisacodyl reduces the volume of PEG solution required for bowel preparation. Dis Colon Rectum 1994;27:229-33.
27. Henderson JM, Barnett JL, Turgeon DK, et al. Single-day, divided-dose oral sodium phosphate laxative versus intestinal lavages as preparation for colonoscopy: efficacy and patient tolerance. Gastrointest Endosc 1995;42:238-43.
28. Young CJ, Simpson RR, King DW, et al. Oral sodium phosphate solution is a superior colonoscopy preparation to polyethylene glycol with bisacodyl. Dis Colon Rectum 2000;43:1568-71.
29. Barclay RL. Safety, efficacy, and patient tolerance of a three-dose regimen of orally administered aqueous sodium phosphate for colonic cleansing before colonoscopy. Gastrointest Endosc 2004;60:527-33.
30. Law WL, Choi HK, Chu KW, et al. Bowel preparation for colonoscopy: a randomized controlled trial comparing polyethylene glycol solution, one dose and two doses of oral sodium phosphate solution. Asian J Surg 2004;271:20-4.

31. Schmidt LM, Williams P, King D, et al. Picoprep-3 is a superior colonoscopy preparation to Fleet: a randomized, controlled trial comparing the two bowel preparations. Dis Colon Rectum 2004;47:238-42.
32. Golub RW, Kerner BA, Wise WE Jr. Colonoscopic preparations-which one? A blinded, prospective, randomized trial. Dis Colon Rectum 1995;58:594-7.
33. Balaban DH, Leavell BS Jr, Oblinger MJ, et al. Low-volume preparation for colonoscopy: randomized, endoscopist-blinded trial of liquid sodium phosphate versus tablet sodium phosphate. Am J Gastroenterol 2003;98:827-32.
34. Aronchick CA, Lipshutz WH, Wright SH, et al. A novel tableted purgative for colonoscopic preparation: efficacy and safety comparisons with Colyte and Fleet Phospho-Soda. Gastrointest Endosc 2000;52:346-52.
35. Ell C, Fischbach W, Keller R, et al. A randomized, blinded, prospective trial to compare the safety and efficacy of three bowel-cleansing solutions for colonoscopy (HSG-01*). Endoscopy 2003;35:300-4.
36. Martinek J, Hess J, Delarive J, et al. Cisapride does not improve the precolonoscopy bowel preparation with either sodium phosphate or polyethylene glycol electrolyte lavage. Gastrointest Endosc 2001; 54:180-5.
37. Vanner SJ, MacDonald PH, Paterson WG, et al. A randomized prospective trial comparing oral sodium phosphate with standard polyethylene glycol-based lavages solution (Golytely) in the preparation of patients for colonoscopy. Am J Gastroenterol 1990;85:422-7.
38. Marschall H-U, Bartels F. Life-threatening complications of nasogastric administration of polyethylene glycol-electrolyte solutions (Golytely) for bowel cleansing. Gastrointest Endosc 1998;47:408-10.
39. Kolts BE, Lyles WE, Achem SR, et al. A comparison of the effectiveness and patient tolerance of oral sodium phosphate, castor oil, and standard electrolyte lavage for colonoscopy or sigmoidoscopy preparation. Am J Gastroenterol 1993;88:1218-23.
40. Nelson DB, Barkun AN, Block KP, et al. ASGE Technology Committee. Technology Status Evaluation Report: Colonoscopy Preparations. Gastrointest Endosc 2001;54:829-32.
41. Cook DJ, Guyatt GH, Laupacis A, et al. Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1992; 102(Suppl 4):305S–11S.
42. Berry MA, DiPalma JA. Orthograde gut lavage for colonoscopy. Aliment Pharmacol Ther 1994;8:391-5.
43. Reilly T, Walker G. Reasons for poor colonic preparation for inpatients. Gastroenterol Nurs 2004;27:115-7.
44. Bigard MA, Gaucher P, Lassalle C. Fatal colonic explosion during colonoscopic polypectomy. Gastroenterology 1979;77:1307-10.
45. Panton ON, Atkinson KG, Crichton EP, et al. Mechanical preparation of the large bowel for elective surgery. Comparison of whole gut lavage with conventional enema and purgative technique. Am J Surg 1985;149:615-9.
46. Chan CH, Diner WC, Fontenot E, et al. Randomized single-blind clinical trial of a rapid colonic lavage solution versus standard preparation for barium enema and colonoscopy. Gastrointest Radiol 1985;10:378-82.
47. Burke DA, Mannin AP, Murphy L, et al. Oral bowel lavage preparation for colonoscopy. Postgrad Med J 1988;64:772-4.
48. Adler M, Quenon M, Even-Adin D, et al. Whole gut lavage for colonoscopy: A comparison between two solutions. Gastrointest Endosc 1984;30:65-7.
49. Beck DE, Fazio VW, Jagleman DG. Comparison of oral lavage methods for preoperative colon cleansing. Dis Colon Rectum 1986;29:699-703.
50. Marshall JB, Pineda JJ, Barthel JS, et al. Prospective, randomized trial comparing sodium phosphate solution with polyethylene glycol electrolyte lavage for colonoscopy preparation. Gastrointest Endosc 1993;39:631-4.
51. Lever EL, Walter MH, Condon SC, et al. Addition of enemas to oral lavage preparation for colonoscopy is not necessary. Gastrointest Endosc 1992;38:369-72.
52. Rosch T, Classen M. Fractional cleansing of the large bowel with Golytely for colonoscopic preparations: a controlled trial. Endoscopy 1987;19:198-200.
53. Aoun E, Abdul-Baki H, Azar C, et al. A randomized single-blind trial of split-dose PEG-electrolyte solution without dietary restriction compared with whole dose PEG-electrolyte solution with dietary restriction for colonoscopy preparation. Gastrointest Endosc 2005;62:213-8.
54. Rhodes JB, Engstrom J, Stone KE. Metoclopramide reduces the distress associated with colon cleansing by an oral electrolyte overload. Gastrointest Endosc 1978;24:162-3.
55. Brady CE III, DiPalma JA, Pierson WP. Golytely lavage: is metoclopramide necessary? Am J Gastroenterol 1985;80:180-4.
56. Brady CE 3rd, DiPalma JA, Beck DE. Effect of bisacodyl on gut lavage cleansing for colonoscopy. Am Clin Res 1987;19:34-8.
57. Sondheimer JM, Sokol RJ, Taylor SF, et al. Safety, efficacy, and tolerance of intestinal lavage in pediatric patients undergoing diagnostic colonoscopy. J Pediatrics 1991;119:148-52.
58. Gremse DA, Sacks AI, Raines S. Comparison of oral sodium phosphate to polyethylene-glycol-based solution for bowel preparation in children. J Pediatric Gastroenterol Nutr 1996;23:586-90.
59. Tolia V, Fleming S, Dubois R. Use of Golytely in children and adolescents. J Pediatr Gastroenterol Nutr 1984;3:468-70.
60. Fordtran JS, Santa Ana CA, Cleveland MvB. A low-sodium solution for gastrointestinal lavage. Gastroenterolgy 1990;98:11-6.
61. Schiller LR, Emmett M, Santa Ana CA, et al. Osmotic effects of polyethylene glycol. Gastroenterology 1988;94:933-41.
62. Sharma VK, Steinberg EN, Vasudeva R, et al. Randomized, controlled study of pretreatment with magnesium citrate on the quality of colonoscopy preparation with polyethylene glycol electrolyte lavage solution. Gastrointest Endosc 1997;46:541-3.
63. Schiller LR. Clinical pharmacology and use of laxatives and lavage solutions. J Clin Gastroenterol 1988;28:11-8.
64. Markowitz GS, Stokes MB, Radhakrishnan J, et al. Acute phosphate nephropathy following oral sodium phosphate bowel purgative: an underrecognized cause of chronic renal failure. Am Soc Nephrol 2005;16:3389-96.
65. Linden TB, Waye JD. Sodium phosphate preparation for colonoscopy: onset and duration of bowel activity. Gastrointest Endosc 1999;50: 811-3.
66. Yoshioka K, Connolly AB, Ogunbiyi OA, et al. Randomized trial of oral sodium phosphate compared with oral sodium picosulfate (Picolax) for elective colorectal surgery and colonoscopy. Dig Surg 2000;17: 66-70.
67. Curran MP, Plosker GL. Oral sodium phosphate solution: A review of its use as a colonic cleanser. Drugs 2004;64:1697-714.
68. Rejchrt S, Bures J, Siroky M, et al. A prospective, observational study of colonic mucosal abnormalities associated with orally administered sodium phosphate for colon cleansing before colonoscopy. Gastrointest Endosc 2004;59:651-4.
69. da Silva MM, Briars GL, Patrick MK, et al. Colonoscopy preparation in children: safety efficacy, and tolerance of high versus low volume cleansing methods. J Pediatr Gastroenterol Nutr 1997;24:33-7.
70. Thomson A, Naidoo P, Crotty B. Bowel preparation for colonoscopy: a randomized prospective trial comparing sodium phosphate to polyethylene glycol in predominantly elderly population. J Gastroenterol Hepatol 1996;11:103-7.
71. Seinela L, Pehkonen E, Laasanen T, et al. Bowel preparation for colonoscopy in very old patients: a randomized prospective trial comparing oral sodium phosphate and polyethylene glycol electrolyte lavage solution. Scand J Gastroenterol 2003;38:216-20.
72. Barclay RL, Depew WT, Vanner SJ. Carbohydrate-electrolyte rehydration protects against intravascular volume contraction during colonic cleansing with orally administered sodium phosphate. Gastrointest Endosc 2002;56:633-8.
73. Tjandra JJ, Tagkalidis P. Carbohydrate-electrolyte (E-Lyte®) solution enhances bowel preparation with oral Fleet® Phospho-soda. Dis Colon Rectum 2004;47:1181-6.
74. InKine confirms effect of ginger ale on Visicol tablets. Business Wire, November 5, 2001; Available at: http://static.elibrary.com/b/businesswire/november052001/.

75. Matter SE, Rice PS, Campbell DR. Colonic lavage solutions: plain versus flavored. Am J Gastroenterol 1993;88:49-52.
76. Pashankar DS, Uc A, Bishop WP. Polyethylene glycol 3350 without electrolytes: a new safe, effective, and palatable bowel preparation for colonoscopy in children. J Pediatr 2004;144:358-62.
77. Shaver WA, Storms P, Peterson WL. Improvement of colonic lavage with supplemental simethicone. Dig Dis Sci 1988;33:185-8.
78. Lazzaroni M, Petrillo M, Desideri S, et al. Efficacy and tolerability of polyethylene glycol-electrolyte lavage solution with and without simethicone in the preparation of patients with inflammatory bowel disease for colonoscopy. Aliment Pharmacol Ther 1993;7:655-9.
79. Rings EH, Mulder CJ, Tytgat GN. The effect of bisacodyl on whole-gut irrigation in preparation for colonoscopy. Endoscopy 1989;21:172-3.
80. Ziegenhagen DJ, Zehnter E, Tacke W, et al. Senna versus bisacodyl in addition to GoLytely lavage for colonoscopy preparation: A prospective randomized trial. Z Gastroenterol 1992;30:17-9.
81. Hamilton D, Mulcahy D, Walsh D, et al. Sodium picosulphate compared with polyethylene glycol solution for large bowel lavage: a prospective randomized trial. Br J Clin Pract 1996;50:73-5.
82. Ziegenhagen DJ, Zehnter E, Tacke W, et al. Addition of Senna improves colonoscopy preparation with lavage: a prospective randomized trial. Gastrointest Endosc 1991;37:547-9.
83. Iida Y, Miura S, Asada Y, et al. Bowel preparation for the total colonoscopy by 2000 ml of balanced lavage solution (GoLytely) and sennoside. Gastroenterol Jpn 1992;27:728-33.
84. Huppertz-Hauss G, Bretthauer M, Sauar J, et al. Polyethylene glycol vs sodium phosphate in bowel cleansing for colonoscopy: a randomized trial. Endoscopy 2005;37:537-41.
85. Eschinger EJ, Littman JJ, Meyer K, et al. Safety of sodium phosphate tablets in patients receiving propofol-based sedation for colonoscopy. J Clin Gastroenterol 2004;38:425-8.
86. Reddy DN, Rao GV, Sriram PV. Efficacy and safety of oral sodium phosphate versus polyethylene glycol solution for bowel preparation for colonoscopy. Indian J Gastroenterol 2002;21:219-21.
87. Pockros PJ, Foroozan P. Golytely lavage versus a standard colonoscopy preparation: effect on normal colonic mucosal histology. Gastroenterology 1985;88:545-8.
88. Gabel A, Muller S. Aspiration: a possible severe complication in colonoscopy preparation by orthograde intestine lavage. Digestion 1999; 60:284-5.
89. Franga DL, Harris JA. Polyethylene glycol-induced pancreatitis. Gastrointest Endosc 2000;52:789-91.
90. Schroppel B, Segerer S, Keuneke C, et al. Hyponatremic encephalopathy after preparation for colonoscopy. Gastrointest Endosc 2001;53: 527-9.
91. Granberry MC, White LM, Gardner SF. Exacerbation of congestive heart failure after administration of polyethylene glycolelectrolyte lavage solution. Ann Pharmacother 1995;29:1232-5.
92. Turnage RH, Guice KS, Gannon P, et al. The effect of polyethylene glycol gavage on plasma volume. J Surg Res 1994;57:284-8.
93. DiPalma JA, Wolff BG, Meagher A, et al. Comparison of reduced volume versus four liters sulfate-free electrolyte lavage solutions for colonoscopy colon cleansing. Am J Gastroenterol 2003;98:2187-91.
94. Huynh T, Vanner S, Paterson W. Safety profile of 5-h oral sodium phosphate regimen for colonoscopy cleansing: lack of clinically significant hypocalcemia or hypovolemia. Am J Gastroenterol 1995;90: 104-7.
95. Ehrenpreis ED, Wieland JM, Cabral J, et al. Symptomatic hypocalcemia, hypomagnesemia, and hyperphosphatemia secondary to Fleet's Phospho-soda colonoscopy preparation in a patient with jejunoileal bypass. Dig Dis Sci 1997;42:858-60.
96. Campisi P, Badhwar V, Morin S, et al. Postoperative hypocalcemic tetany caused by Fleet Phospho-soda preparation in a patient taking alendronate sodium: report of a case. Dis Colon Rectum 1999;42: 1499-501.
97. Fass R, Do S, Hixson LJ. Fatal hyperphosphatemia following Fleet phospho-soda in a patient with colonic ileus. Am J Gastroenterol 1993;88:929-32.
98. Ullah N, Yeh R, Ehrinpreis M. Fatal hyperphosphatemia from a phosphosoda bowel preparation. J Clin Gastroenterol 2002;34:457-8.
99. Hixson LJ. Colorectal ulcers associated with sodium phosphate catharsis. Gastrointest Endosc 1995;42:101-2.
100. Zwas FR, Cirillo NW, el-Serag HB, et al. Colonic mucosal abnormalities associated with oral sodium phosphate solution. Gastrointest Endosc 1996;43:463-6.
101. Clarkston WK, Tsen TN, Dies DF, et al. Oral sodium phosphate versus sulfate-free polyethylene glycol electrolyte lavage solution in outpatient preparation for colonoscopy: a prospective comparison. Gastrointest Endosc 1996;43:42-8.
102. Lieberman DA, Ghormley J, Flora K. Effect of oral sodium phosphate colon preparation on serum electrolytes in patients with normal serum creatinine. Gastrointest Endosc 1996;43:467-9.
103. Holte K, Neilsen KG, Madsen JL, et al. Physiologic effects of bowel preparation. Dis Colon Rectum 2004;47:1397-402.
104. Frizelle FA, Colls BM. Hyponatremia and seizures after bowel preparation: report of three cases. Dis Colon Rectum 2005;48:393-6.
105. Markowitz GS, Nasr SH, Klein P, et al. Renal failure due to acute nephrocalcinosis following oral sodium phosphate bowel cleansing. Hum Pathol 2004;35:675-84.
106. Ness RM, Manam R, Hoen H, et al. Predictors of inadequate preparation for colonoscopy. Am J Gastroenterol 2001;96:1797-802.
107. Lukens FJ, Loeb DS, Machicao VI, et al. Colonoscopy in octogenarians: a prospective outpatient study. Am J Gastroenterol 2002;97:1722-5.
108. Ainley EJ, Winwood PJ, Begley JP. Measurement of serum electrolytes and phosphate after sodium phosphate colonoscopy bowel preparation: an evaluation. Dig Dis Sci 2005;50:1319-23.
109. Gumurdulu Y, Serin E, Ozer B, et al. Age as a predictor of hyperphosphatemia after oral phosphosoda administration for colon preparation. J Gastroenterol Hepatol 2004;19:68-72.
110. Beloosesky Y, Grinblat J, Weiss A, et al. Electrolyte disorders following oral sodium phosphate administration for bowel cleansing in elderly patients. Arch Intern Med 2004;163:803-8.
111. Wong NA, Penman ID, Campbell S, et al. Microscopic focal cryptitis associated with sodium phosphate bowel preparation. Histopathology 2000;36:476-8.
112. Taylor C, Schubert ML. Decreased efficacy of polythelyene glycol lavage solution (Golytely) in the preparation of diabetic patients for outpatient colonoscopy: a prospective and blinded study. Am J Gastroenterol 2001;96:710-4.
113. Dahshan A, Lin CH, Peters J, et al. A randomized, prospective study to evaluate the efficacy and acceptance of three bowel preparations for colonoscopy in children. Am J Gastroenterol 1999;94:3497-501.
114. Trautwein AL, Vinitski LA, Peck SN. Bowel preparation before colonoscopy in the pediatric patient: a randomized study. Gastroenterol Nurs 1996;19:137-9.
115. Chilton AP, O'Sullivan M, Cox MA, et al. A blinded randomized comparison of a novel low dose triple regimen with Fleet® phosophoda: a study of colon cleanliness, speed, and success of colonoscopy. Endoscopy 2000;32:37-41.
116. Rex DK, Imperiale TF, Latinovich DR, et al. Impact of bowel preparation on efficacy and cost of colonoscopy. Am J Gastroenterol 2002; 97:1696-700.

This article appears simultaneously in the June 2006 issues of *Diseases of the Colon and Rectum, Gastrointestinal Endoscopy*, and *Surgical Endoscopy*.

Steven D. Wexner, MD[1]
Task Force, Chair
David E. Beck, MD (ASCRS)[2]
Todd H. Baron, MD (ASGE)[3]
Robert D. Fanelli, MD (SAGES)[4]
Neil Hyman, MD (ASCRS)[5]
Bo Shen, MD (ASGE)[6]
Kevin E. Wasco, MD (SAGES)[7]
[1]Department of Colorectal Surgery, Cleveland Clinic Florida, Weston, Fla.
[2]Department of Colon and Rectal Surgery, Ochsner Clinic Foundation, New Orleans, La.
[3]Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, Minn.
[4]Surgical Specialists of Western New England, PC/Department Surgery, Berkshire Medical Center, Pittsfield, Mass.
[5]Department of Surgery, University of Vermont College of Medicine, Burlington, Vt.
[6]Department of Gastroenterology/Hepatology, Cleveland Clinic Foundation, Cleveland, Ohio.
[7]Surgical Associates of Neenah, S.C., Neenah, Wis.

Reprint requests: Steven D. Wexner, MD, Department of Colorectal Surgery, Cleveland Clinic Florida, 2950 Cleveland Clinic Blvd., Weston, FL 33331. Email: mcderme@ccf.org

ADDENDUM

Products and Manufacturers

Product	Manufacturer	City, State
Colyte®	SchwarzPharm	Mequon, WI
GoLYTELY®	Braintree Laboratories	Braintree, MA
NuLYTELY®	Braintree Laboratories	Braintree, MA
TriLyte®	SchwarzPharm	Mequon, WI
HalfLytely®	Braintree Laboratories	Braintree, MA
Miralax®	Braintree Laboratories	Braintree, MA
Fleet® Phospho-soda	C.B. Fleet Company	Lynchburg, VA
Picolax®	Ferring Pharmaceuticals	Berkshire, UK
E-Lyte®	C.B. Fleet Company	Lynchburg, VA
Visicol®	Salix Pharmaceuticals	Morrisville, NC
Gatorade®	Gatorade International	Chicago, IL
CrystalLite®	Kraft Foods	Northfield, IL
Fleet® Bisacodyl	C.B. Fleet Company	Lynchburg, VA
Fleet® Mineral Oil	C.B. Fleet Company	Lynchburg, VA
Reglan®	Robins Pharmaceutical	Eatontown, NJ
Gas-X®	Novartis Consumer Health, Inc.	Broomfield, CO
Mylicon®	J&J/Merck Pharmaceuticals	Fort Washington, PA
Mylanta®	J&J/Merck Pharmaceuticals	Fort Washington, PA
X-Prep®	Purdue Frederick	Norwalk, CT

ADDENDUM

Immediately following publication of ''Wexner SD (Task Force Chair), Beck DE, Baron TH, Fanelli RD, Hyman N, Shen B, Wasco KE. A consensus document on bowel preparation before colonoscopy: prepared by a Task Force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) (Gastrointest Endosc 2006;63:894-909),'' the Food and Drug Administration (FDA) issued an alert regarding the use of oral sodium phosphate (OSP) products for bowel preparation. The three sponsoring societies (ASCRS, ASGE, and SAGES) wish to add the following FDA warning to the consensus document.

Ann Lowry, Immediate Past President, ASCRS
Robert Hawes, Immediate Past President, ASGE
Daniel Deziel, Immediate Past President, SAGES

''Acute phosphate nephropathy, a type of acute renal failure, is a rare, but serious event associated with the use of oral sodium phosphate (OSP) for bowel cleansing. Documented cases of acute phosphate nephropathy include 21 patients who used an OSP solution (such as Fleet Phospho-soda or Fleet ACCU-PREP) and one patient who used OSP tablets (Visicol). No cases of acute phosphate nephropathy or acute renal failure have been associated with OsmoPrep, an OSP tablet bowel preparation recently approved. Individuals at increased risk of acute phosphate nephropathy include: those of advanced age, those with kidney disease or decreased intravascular volume, and those using medicines that affect renal perfusion or function [diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and possibly nonsteroidal anti-inflammatory drugs (NSAIDs)].

0016-5107/$32.00
doi:10.1016/j.gie.2006.05.016

NATIONAL INSTITUTES OF HEALTH
STATE-OF-THE-SCIENCE CONFERENCE STATEMENT
NIH State-of-the-Science Conference:
Enhancing Use and Quality of Colorectal Screening
February 2–4, 2010

National Institutes of Health (NIH) consensus and state-of-the-science statements are prepared by independent panels of health professionals and public representatives on the basis of (1) the results of a systematic literature review prepared under contract with the Agency for Healthcare Research and Quality (AHRQ), (2) presentations by investigators working in areas relevant to the conference questions during a 2-day public session, (3) questions and statements from conference attendees during open discussion periods that are part of the public session, and (4) closed deliberations by the panel during the remainder of the second day and morning of the third. This statement is an independent report of the panel and is not a policy statement of NIH or the Federal Government.

The statement reflects the panel's assessment of medical knowledge available at the time the statement was written. Thus, it provides a "snapshot in time" of the state of knowledge on the conference topic. When reading the statement, keep in mind that new knowledge is inevitably accumulating through medical research.

Introduction

Colorectal cancer is the third most common cancer, and the second leading cause of cancer deaths, in the United States. Each year, nearly 150,000 people are newly diagnosed with colorectal cancer and 50,000 die. Polyps are abnormal growths of tissue along the lining of the colon. Many polyps are harmless, but a common type of polyp, the adenoma, can develop over time into a colorectal cancer. An effective way to reduce mortality from colorectal cancer is to screen for it and its precursor, the adenoma. Although screening methods have been available for decades and new methods continue to develop, screening rates remain low. The purpose of this conference was to analyze national screening rates for colorectal cancer, identify the barriers to screening, and propose solutions to increase screening rates. Evaluating or establishing the comparative effectiveness of the various colorectal cancer screening options was beyond the scope of this conference and not part of the charge to this panel. Nonetheless, the panel recognized that high-quality evidence about the comparative effectiveness of the various current and emerging screening modalities is needed and must be a scientific priority.

Screening is defined as the testing of individuals for a disease prior to the onset of any symptoms. The goal of colorectal cancer screening is to reduce disease-specific mortality through prevention and early detection.

Colorectal cancer screening, as with any screening test, is most effective when it is applied to a large percentage of eligible people and utilized appropriately. Major published guidelines describe the eligible target population for colorectal cancer population-based screening as persons over age 50 at average risk of colorectal cancer (i.e., those who do not have

family history, genetic predisposition, or underlying disease that predisposes to colorectal cancer). When a polyp is detected by any method, subsequent follow-up by colonoscopy is referred to as surveillance.

To provide health care providers, public health practitioners, policymakers, and the general public with a comprehensive assessment of how colorectal cancer screening and surveillance are most appropriately implemented, monitored, and evaluated for U.S. populations at average risk, the National Cancer Institute and the Office of Medical Applications of Research of the National Institutes of Health convened a State-of-the-Science Conference on February 2-4, 2010, to assess the available scientific evidence. The key questions that the panel were asked to address were the following:

- What are the recent trends in the use and quality of colorectal cancer screening?
- What factors influence the use of colorectal cancer screening?
- Which strategies are effective in increasing the appropriate use of colorectal cancer screening and follow-up?
- What are the current and projected capacities to deliver colorectal cancer screening and surveillance at the population level?
- What are the effective approaches for monitoring the use and quality of colorectal cancer screening?
- What research is needed to make the most progress and have the greatest public health impact in promoting the appropriate use of colorectal cancer screening?

During the first 2 days of the conference, experts presented information on each of the key questions. After weighing the scientific evidence—including the data presented by the speakers, input from attendees, and a formal evidence report commissioned through the Agency for Healthcare Research and Quality (AHRQ)—an independent panel prepared and presented a draft of this State-of-the-Science Statement addressing the conference questions. The evidence report prepared for the conference is available at: http://www.ahrq.gov/clinic/tp/crcprotp.htm.

1. What are the recent trends in the use and quality of colorectal cancer screening?

In the United States, colorectal cancer screening is underused. (Underuse is defined as the circumstances in which people are not screened or are screened at a lower rate than recommended by applicable guidelines.) Data regarding colorectal cancer screening rates arise from multiple sources including patient and population surveys, administrative data, and chart reviews from health systems and medical practices. Unfortunately, a central registry with uniform data guidelines is lacking, thus limiting more detailed analysis. In general, there has been a slow, steady upward trend in colorectal cancer screening rates within the target population (adults age 50 and older), with overall screening rates increasing from 20 to 30 percent in 1997

to nearly 55 percent in 2008. Despite this positive trend, millions of eligible people are not screened by any method.

Table 1. Colorectal cancer screening recommendations from the U.S. Preventive Services Task Force and the American Cancer Society-U.S. Multisociety Task Force

Screening Test	Description	United States Preventive Services Task Force (USPSTF)	American Cancer Society–U.S. Multi-Society Task Force (ACS-USMSTF)
Fecal occult blood test (FOBT)* and fecal immunochemical test (FIT)*	Examination of the stool for traces of blood not visible to the naked eye	Recommends high-sensitivity FOBT and FIT annually for ages 50-75	Recommends high-sensitivity FOBT and FIT annually for ages ≥ 50
Sigmoidoscopy*	Internal examination of the lower part of the large intestine	Recommends every 5 years with high-sensitivity FOBT and every 3 years for ages 50 - 75	Age ≥ 50, every 5 years
Double-contrast barium enema*	X-ray examination of the colon	--	Age ≥ 50, every 5 years
Colonoscopy	Internal examination of the entire large intestine	Recommends every 10 years for ages 50-75	Age ≥ 50, every 10 years
Computed tomography colonography*	Examination of the colon and rectum using pictures obtained using a computed tomography scanner	--	Age ≥ 50, every 5 years
Fecal DNA*	Examination of the stool for traces of colorectal cancer DNA	--	Age ≥ 50, interval uncertain

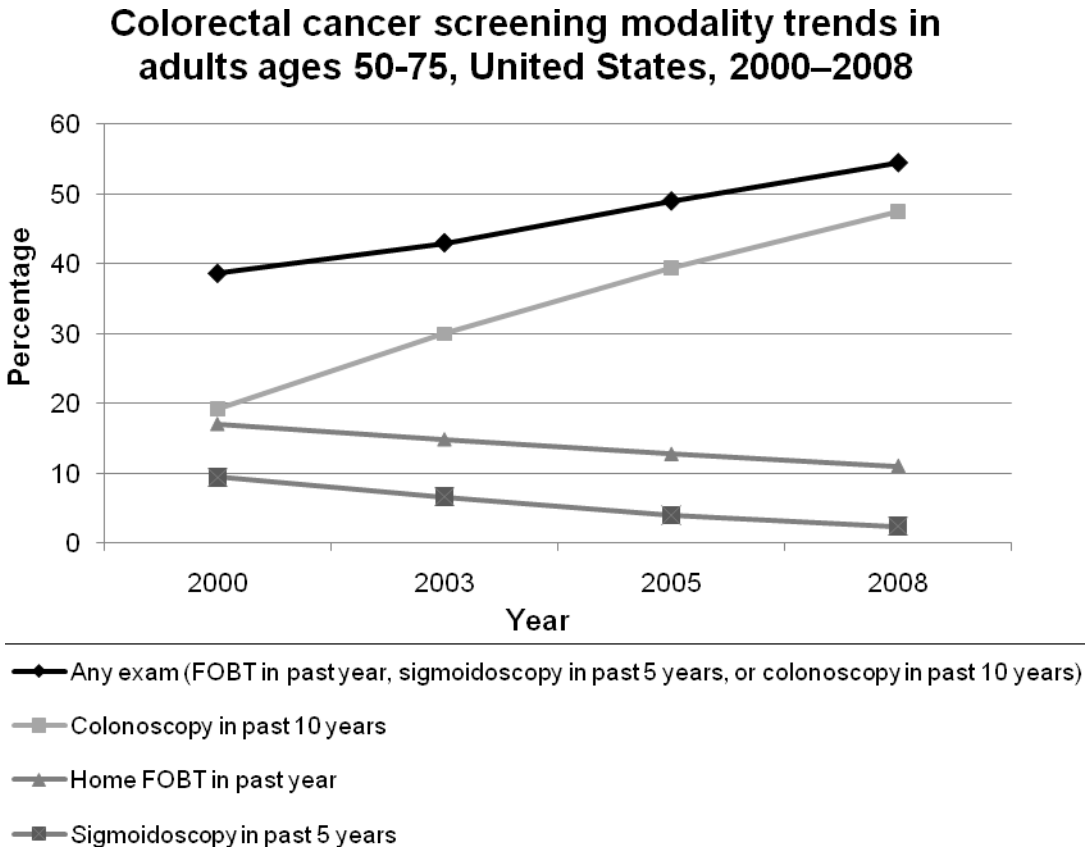
* *Positive findings require follow-up colonoscopy.*

Major national guideline-making bodies, including the USPSTF and ACS-MSTF, recommend various efficacious tests for colorectal cancer screening (see Table 1). These include annual high sensitivity fecal occult blood testing (FOBT) including immunochemical tests, flexible sigmoidoscopy or double-contrast barium enema every 5 years, and colonoscopy every 10 years. The ACS-MSTF also includes computed tomography colonography every 5 years as a screening option. A positive result of an FOBT, flexible sigmoidoscopy, double-contrast barium enema, or computed tomography colonography should be followed by a colonoscopy.

Before the emergence of colonoscopy, FOBT and flexible sigmoidoscopy were the most widely used screening tests for the general population. Colonoscopy soon replaced these tests as the most used screening method, and its use increased rapidly after Medicare initiated coverage for screening colonoscopies in July 2001; it continues to be the most widely used test today. Conversely, since 2001, a nearly reciprocal decrease has occurred in the number of flexible sigmoidoscopies (see Figure 1). Double-contrast barium enema has fallen out of favor over the same time, and fewer radiologists now perform this exam. Overall use of FOBT has declined

more gradually, and immunochemical testing has increased relative to guaiac testing. These stool tests remain widely utilized in the U.S. Department of Veterans Affairs (VA) system and some managed care systems nationwide.

Because the federally funded clinical trial demonstrating the accuracy of computed tomography colonography for the detection of large adenomas and cancers was only recently completed, the use of computed tomography colonography is rapidly changing. Therefore, national usage trend data for that screening test are not yet available.



Source: National Health Interview Survey Public Use Data File 2000, 2003, 2005, and 2008. National Center for Health Statistics, Centers for Disease Control and Prevention. Data synthesis courtesy of Carrie Klabunde.

Figure 1. Testing options vary in the amount of preparation and effort required by patients. For example, colonoscopy and computed tomography colonography require preparation to cleanse the colon completely, which takes time and is inconvenient and unpleasant. FOBT requires patients to collect stool samples at home and return them to their provider. Testing costs also vary among testing options.

Although a primary emphasis of this conference involved analyzing and exploring ways to increase colorectal cancer screening rates, some problematic issues with the use of colorectal cancer screening are not to be overlooked.

For example, screening is overused when patients with severe comorbidities and limited life expectancy who are unlikely to benefit from prevention or early detection are screened, or when colonoscopies are performed more frequently than most guidelines recommend.

Misuse involves screening that is conducted in a suboptimal way such that the potential benefits are not achieved—for example, an FOBT test conducted using in-office stool samples rather than the recommended home technique. Methods to address these quality issues are discussed later in this report.

Finally, some of the most sensitive techniques for colorectal cancer and polyp detection carry risks for adverse events. For example, colonoscopy requires sedation and carries the risk of colon perforation, which, although uncommon, is potentially serious. Computed tomography colonography carries a theoretical risk from radiation exposure. Optimal performance of these procedures requires adequate training and should be monitored.

2. What factors influence the use of colorectal cancer screening?

For the purposes of this report, the factors associated with the use of colorectal cancer screening are characterized as patient-related factors, physician-related factors, and system-related factors.

What Is Known

Patient Factors. The most important factors related to being screened for colorectal cancer are having insurance coverage, access to a usual source of health care, or both. In addition, two socioeconomic characteristics—income and education level—are important correlates of screening. These factors are all highly correlated; for example, compared to the average person, one who is more educated is likely to be more knowledgeable about the risks and benefits of colorectal cancer screening, to have a higher income, to have health insurance, and to have a usual source of care. Nevertheless, each of these factors has an independent effect on screening rates.

There are differences in screening rates across racial and ethnic groups. Relative to non-Hispanic whites, blacks and Hispanics are less likely to be screened. Once socioeconomic characteristics are taken into account, the differences in screening rates are attenuated. Within given racial or ethnic groups, differences occur in screening across subgroups. For example, among Asians, Koreans have lower rates of screening, and among whites, those living in Appalachia have lower rates of screening.

People who were born abroad and have shorter residency in the United States or who do not speak English as their primary language (less acculturated) are less likely to be screened. Gender has a complex relationship to colorectal cancer screening. Overall there is no difference

between genders, however, in some ethnic/age subgroups, men have lower screening rates; in other subgroups women have lower rates. Older patients (age 60-75 years) are more likely to be screened than younger patients (age 50-59 years). People who have had more contact with the health care system are more likely to be screened. People who have been screened for other types of cancer (breast, cervical, or prostate cancer) are more likely to be screened for colorectal cancer.

Additional patient factors positively associated with being screened are a person's knowledge about the test, a perceived risk of developing colorectal cancer, a positive attitude about screening tests in general, and a belief that the test is safe. Those attitudes associated with not being screened include the invasiveness of endoscopy, anxiety about test outcomes, and a belief that healthy people do not need to have the test.

Physician Factors. A recommendation from a physician is the only physician-related factor consistently predicting colorectal cancer screening. The relationship between physician characteristics such as age, gender, years of training, and specialty and screening rates in populations has not been well established.

Systems Organization. Only a limited number of studies have looked at whether the way a practice is organized has an effect on whether patients are screened. However, some research suggests that those practices that have electronic medical record reminder systems, ancillary personnel who can facilitate follow-up arrangements, and patient navigators have had the most success.

Establishing a screening program is difficult because it has many components. However, the data suggest a number of effective programs. One set of examples exists within integrated systems of care: for example, Kaiser Permanente has screening rates of 75 percent in the Medicare population, and the VA has screening rates of 80 percent. These programs were based on FOBT that incorporated direct mailing, focused reminders, and careful follow-up of positive results with colonoscopy.

What Needs To Be Learned

As noted above, colonoscopy use has increased substantially since 2001, while use of FOBT has declined. It is important to know more about the factors that lead physicians to recommend, or patients to choose, one test over another. Financial considerations, such as differential reimbursement rates for different tests, may affect physicians' decisions to recommend lower endoscopy. A likely factor affecting patient choices is cost sharing. Another factor affecting both groups is a perception that colonoscopy is the gold standard, despite the absence of randomized clinical trial evidence supporting the test's relationship to morbidity and mortality. Studies of screening usually characterize the population as insured or uninsured. However, the structure of health insurance is highly variable. When studying insurance, it would be better to have a more detailed characterization. For example, among persons with Medicare, those with supplemental policies are more likely to be screened.

Since the National Committee for Quality Assurance (NCQA) implemented Healthcare Effectiveness Data and Information Set (HEDIS) measures for colorectal cancer screening, screening rates have increased for enrollees of commercial managed care plans, but not for those of the Medicare managed care plans. More information is needed about the potential of public reporting to affect use and quality.

Based on the Centers for Disease Control and Prevention's (CDC) experience with the National Breast Cancer and Cervical Cancer Early Detection Program (BCCEDP), the CDC has launched a new program to expand colorectal cancer screening for uninsured and underinsured persons in certain states. It is too early to assess the impact of this new program.

Although race/ethnicity, socioeconomic factors, awareness, and insurance are associated with colorectal cancer screening, the specific reasons for these associations are little understood. What drives the association between race, gender, and screening rates? How do we determine the components necessary for informed and preference concordant decision-making (e.g., awareness of the prevalence of colorectal cancer, harms and benefits of screening, pros and cons of each test)?

3. Which strategies are effective in increasing the appropriate use of colorectal cancer screening and follow-up?

What Is Known

The literature documents three broad areas that show some evidence of effective interventions at the patient, provider, and health system level. However, a limited number of studies have examined the effectiveness of health care provider-based interventions.

Effective patient-level interventions include reducing structural barriers (e.g., direct-mailing of FOBT kits), one-on-one interaction with a health care provider or health educator, and patient reminders (e.g., telephone calls, postcards). For some other patient-level interventions, such as group education and small-scale media campaigns, there is insufficient evidence to determine effectiveness.

Although few studies have assessed the effectiveness of provider interventions, the VA system has successfully increased colorectal cancer screening with a multimodality approach that includes provider trainer, computerized reminders, audit and feedback, as well as coordinated care between primary care physicians and gastroenterologists.

Effective interventions at the health care system level refer to the implementation of system-based changes to increase the number of referrals for screening. Studies conducted within integrated health care systems—such as VA, Kaiser Permanente, and the National Health Service in the United Kingdom—have found that organized approaches to screening dramatically increased colorectal cancer screening rates. In addition, some studies have documented the effectiveness of patient navigators (or similar approaches) when used as part of a health care system's intervention.

What Needs To Be Learned

There is limited knowledge regarding the effectiveness of colorectal cancer screening interventions across racial/ethnic, socioeconomic, and geographic groups. Moreover, it is unclear whether interventions targeting one group can be implemented successfully in other groups or whether various cultural groups require specially tailored interventions.

The scientific evidence is mixed regarding the effectiveness of community-based interventions for increasing colorectal cancer screening. In most cases, these interventions are a constellation of multiple efforts—for example, multimedia educational campaigns (e.g., billboards, radio ads), town hall-type meetings, and community health workers. However, the design of these studies often makes it challenging to identify which of these components (or which combination) is effective.

There is also a need to understand more about what health education or mass media messaging strategies would be most effective in motivating patients to participate in screening efforts. It is unclear how the effectiveness of these messages may differ among screening modalities.

The effect of patient preferences on colorectal cancer screening rates has not been well studied. We know very little about how preferences for screening modalities are formed; how they are related to knowledge, beliefs, and cultural norms; and whether these preferences vary across sociodemographic groups. It is also unknown whether patient preferences change vary over time; it is also unknown what factors may influence that change. Given the multiple options for colorectal cancer screening, interventions that provide decision support and incorporate patient preferences may be effective at increasing colorectal cancer screening rates across diverse populations.

Financial incentives have been shown to influence patient and provider behavior in other diseases; yet little research is available on the impact of financial incentives on colorectal cancer screening rates. In the era of pay for performance, it is important to understand how financial incentives to providers or practices affect colorectal cancer screening rates. Similarly, more information is needed on how incentives directed at patients are likely to impact screening rates. In addition, more information is needed on optimal levels of incentives at both patient and provider levels as well as on effective implementation and monitoring strategies.

There are multiple screening options for colorectal cancer, unlike for other cancers. This increases complexity for both patients and providers. It is unknown how the complexity of colorectal cancer screening affects screening rates.

Some of the gaps in knowledge regarding effective interventions for increasing colorectal cancer screening rates—especially in ethnic minority, underserved, and uninsured populations—are partly due to limitations of existing research methodology. Randomized clinical trials have been adopted as the "gold standard" for assessing the effectiveness of interventions; yet in some instances, these trials may be impractical or unethical. Therefore, well-designed interventions

that propose alternative methods (e.g., quasi-experimental designs, community-based participatory research, times series) should be encouraged.

4. What are the current and projected capacities to deliver colorectal cancer screening and surveillance at the population level?

In planning the implementation of population-based screening programs, the current and future capacity to provide the various recommended screening modalities must be considered. Capacity involves not only laboratory and endoscopic facilities and providers, but also support for informed decision-making as well as the primary care resources needed to coordinate screening services, to communicate results effectively, and to track and follow up positive screening findings.

What Is Known

Few studies, primarily conducted in the early 2000s, have addressed the topic of capacity to deliver colorectal cancer screening. Furthermore, the available data focus on endoscopic capacity. These data are limited by the uncertain validity of self-reported data from provider or facility endoscopits on current practice volume and available capacity, the lack of standard definitions, and the lack of distinction between screening and surveillance colonoscopy. Notably, these studies have produced widely variable results, likely reflecting differences in assumptions about uptake, the size of the eligible population, and the available workforce and facilities. In addition, they fail to account for the resources needed to reach the large numbers of individuals who are currently unscreened.

Different resources are needed for different screening modalities. Although sampling for FOBT is self-administered, laboratory facilities are needed to analyze and interpret results; endoscopy requires dedicated facilities with highly trained providers and staff and expensive equipment. It is important to note that although multiple screening strategies are available, positive results of FOBT, flexible sigmoidoscopy, flexible sigmoidoscopy/FOBT, and computed tomography colonography all require subsequent colonoscopy. If FOBT were used as the primary screening strategy, estimates suggest that there is currently sufficient colonoscopy capacity to follow up positive FOBT results. If flexible sigmoidoscopy or flexible sigmoidoscopy/FOBT were used as the primary screening strategy, it is unlikely that current flexible sigmoidoscopy capacity is sufficient; however, current colonoscopy capacity may be sufficient to follow up positive flexible sigmoidoscopy results. If colonoscopy were the primary screening strategy, there is substantial uncertainty that current colonoscopy capacity would be sufficient. Some modeling estimates suggest that colonoscopy capacity may be sufficient if screening targets are achieved over a 5- to 10-year period.

What Needs To Be Learned

Given the uncertainty of the available evidence and the wide variability across studies, additional data are needed to generate more precise estimates of the current and projected endoscopic capacity, the projected demand, and the impact of overuse and misuse on capacity estimates. Also needed is a better understanding of other aspects of capacity, including provider

training, required personnel, and other resources needed to maximize appropriate use of screening and surveillance and to monitor quality. One aspect of this involves developing strategies to ensure that individuals have the resources and support necessary to make informed choices about screening modalities that are most consistent with their preferences.

Because it is unlikely that current capacity is sufficient for strategies other than universal FOBT screening, expansion of endoscopic capacity may be needed. A first step may be to examine the feasibility of increasing productivity or efficiency of existing facilities. Expanding high-quality endoscopy training to more providers, including non-physicians, may also be warranted. Such expansion would require careful consideration of quality and patient satisfaction. Also needed is evaluation of the role of incentives, disincentives, and third-party payment policies for performing endoscopy.

It is clear that capacity varies widely by geographic region and urban/rural location, and therefore, national capacity may not reflect local capacity. The needs of communities vary; identifying strategies to match capacity with need is critical. For example, evaluation is needed to understand whether incentives for providing screening services in underserved areas will ameliorate the uneven distribution of resources.

As additional screening strategies are developed and become more widely adopted, their role in the delivery of population-based colorectal cancer screening and the impact on overall capacity must be considered. Capacity estimates must be responsive to new evidence about the comparative effectiveness of screening strategies, changes in screening recommendations, and shifts in preferences for various tests.

5. What are the effective approaches for monitoring the use and quality of colorectal cancer screening?

At present, no comprehensive system in the United States effectively monitors the use or quality of colorectal cancer screening across a range of populations and for all approved modalities. Effective monitoring of screening is complicated by the variety of screening methods and the varying intervals for screening among methods (e.g., 10 years for colonoscopy vs. annually for FOBT). This variety of modalities also complicates monitoring because some approaches (e.g., colonoscopy) require more resources than others (e.g., FOBT). Ultimately, a robust system should be usable for setting and monitoring population-based goals and should contribute to improved understanding of the relative benefits of different screening strategies as well as factors associated with optimal use of each approach. The system should be of a sufficient scale to provide accurate estimates of underuse, overuse, misuse, and quality, and it should be timely, flexible, and affordable.

Current sources of population-based data that are available for monitoring colorectal cancer screening in the United States are inadequate for estimating rates and essentially nonexistent for assessing appropriate use. Assessment of quality on a population level is limited to a few measures, such as frequency of major complications, polyp detection rate, and missed cancers following colonoscopy. Other measures—such as the percentage of patients undergoing colonoscopy with adequate bowel preparation, colonoscopic withdrawal times, and the

percentage of FOBT cards with an adequate sample—are not widely available on a population basis. Ideally, both use and quality should be measured in the same population; however, most available data address one or the other, but not both.

What Is Currently Done

Population-based surveys, such as the National Health Interview Survey (NHIS) and the Behavioral Risk Factor Surveillance System (BRFSS), include questions about colorectal cancer screening modality and timing and are the major source of information about trends in colorectal cancer screening rates. Compared with reviews of patient records, however, such surveys may not accurately distinguish colonoscopy from sigmoidoscopy and may overestimate the rate of screening. The surveys do not include questions about overuse, misuse, or outcomes of screening.

The HEDIS measures for colorectal cancer screening are based on the experience of persons enrolled in selected managed care plans and are reported in aggregate by plan. Current reporting does not permit the assessment of screening rates by age, race, or gender. The measures do not specify which screening modality was used, and they include no information about quality, complication rates, or follow-up.

Administrative data sets, such as Medicare data or data from health plans, can be used to measure rates of screening and follow-up medical care. The data are most accurate for assessing use of colonoscopy or flexible sigmoidoscopy and least accurate for measuring use of FOBT. The long period of coverage needed (10 years) to determine that someone is nonadherent to screening recommendations is a limiting factor. Administrative data are a good source of information on the rate and nature of complications related to colorectal cancer screening (e.g., colon perforation) that require specific treatment (e.g., hospitalization, surgery).

Electronic medical records provide detail that is not available in administrative databases, but these records rarely cover an entire population. Few electronic medical record systems are designed for population monitoring, and their use for these purposes generally relies on text fields and complex algorithms that draw information from clinical notes and laboratory reports. Electronic medical records have the potential for assessing the indication for a test, results, time to follow-up, and complications.

What Could Be Done

Given the reported link between increased rates of colorectal cancer screening and both decreased incidence of colorectal cancer and earlier stage at diagnosis, cancer registries might be used to monitor the incidence and stage of colorectal cancer in population subgroups to identify regions with relatively low rates of colorectal cancer screening. The value of cancer registries could be extended if they were to collect information on whether a tumor was detected as a result of screening or evaluation of symptoms.

Data on use and quality should be collected by state and local programs to monitor the rate and quality of colorectal cancer screening.

A colorectal cancer screening registry analogous to the Breast Cancer Surveillance Consortium should be established to monitor rates of colorectal cancer screening, overuse, quality, and complications.

Expansion and analysis of existing data sources and collaborative databases relating to colorectal cancer screening and quality should be supported. These sources include the Clinical Outcomes Research Initiative (CORI) endoscopy database, the Cancer Research Network (CRN), and the Computed Tomography Colonography Registry.

An ideal monitoring system should be able to estimate rates of screening regardless of a patient's insurance status and demographic characteristics and to assess use, appropriateness, and outcomes. A variety of strategies will likely need to be combined to obtain a relatively complete picture of colorectal cancer screening and quality.

6. What research is needed to make the most progress and have the greatest public health impact in promoting the appropriate use of colorectal cancer screening?

Evidence to guide colorectal cancer screening practice and policy is essential. The systematic review of available evidence reveals substantial and significant gaps. There will have to be a greater investment in research on the effectiveness of alternative approaches to engage the population in screening, to support the delivery of screening services, and to enhance systems of care to facilitate access to screening and appropriate follow-up. The recommendations for each of the key questions addressed in this document follow.

Tracking Trends in Colorectal Cancer Screening. The panel recommends the development of an infrastructure for capturing information concerning colorectal cancer screening, follow-up, and cancer outcomes. This infrastructure could be patterned on the existing Breast Cancer Surveillance Consortium. The system should include existing screening modalities and allow for adding new screening techniques. In addition, the proposed monitoring system could include expansions, extensions, and greater use of the BRFSS, the Medicare Current Beneficiary Survey, the Medical Expenditure Panel Survey, NHIS, and administrative data that will allow tracking of population screening by subgroups as well as by screening method.

Factors Influencing Use of Colorectal Cancer Screening. The panel recommends research (1) to study patient preferences and other factors influencing informed and shared decision-making regarding the choice of a colorectal cancer screening modality; (2) to better understand and reduce barriers (e.g., insurance coverage, out-of-pocket costs) to timely and appropriate colorectal cancer screening; (3) to study physician recommendations to the patient regarding the choice of screening modalities and adherence to guideline recommendations; (4) to understand how integrated systems achieve high levels of performance (e.g., electronic medical record decision support, performance incentives); and (5) to study how practices outside of integrated systems can create an infrastructure that promotes high performance.

Effective Strategies for Increasing Appropriate Use. The panel recommends research to (1) evaluate interventions aimed at patients, providers, systems of health care, and communities to increase rates of screening and appropriate follow-up; (2) eliminate racial/ethnic, socioeconomic, and geographic disparities in colorectal cancer screening; (3) assess sustainability of successful interventions that increase the rate of colorectal cancer screenings and disseminate evidence-based interventions; and (4) improve the acceptability and performance of screening techniques.

Current and Projected Colorectal Cancer Screening Capacity. The panel recommends (1) modeling and other research approaches to assess the demand and capacity for colorectal cancer screening across geographic areas; (2) research assessing various options for expanding the supply of providers, including additional specialists, and more widespread use of appropriately trained primary care physicians or non-physician providers conducting lower endoscopy; and (3) further research on what constitutes adequate training.

Effective Monitoring of Use and Quality of Colorectal Cancer Screening. In addition to the comprehensive monitoring infrastructure recommended above, the panel recommends research that (1) examines strategies for community and regional monitoring of colorectal cancer screening outcomes and the performance of methods used to screen; and (2) evaluates the performance of new colorectal cancer screening tests as they emerge.

Conclusion

The panel finds that despite substantial progress toward higher colorectal cancer screening rates nationally, screening rates fall short of desirable levels. Targeted initiatives to improve screening rates and reduce disparities in underscreened communities and population subgroups could further reduce colorectal cancer morbidity and mortality. This could be achieved by utilizing the full range of screening options and evidence-based interventions for increasing screening rates. With additional investments in quality monitoring, Americans could be assured that all screening achieves high rates of cancer prevention and early detection. To close the gap in screening, this report identifies the following priority areas for implementation and research to enhance the use and quality of colorectal cancer screening:

- Eliminate financial barriers to colorectal cancer screening and appropriate follow-up.

- Widely implement interventions that have proven effective at increasing colorectal cancer screening, including patient reminder systems and one-on-one interactions with providers, educators, or navigators.

- Conduct research to assess the effectiveness of tailoring programs to match the characteristics and preferences of target population groups to increase colorectal cancer screening.

- Implement systems to ensure appropriate follow-up of positive colorectal cancer screening results.

- Develop systems to assure high quality of colorectal cancer screening programs.

- Conduct studies to determine the comparative effectiveness of the various colorectal cancer screening methods in usual practice settings.

State-of-the-Science Panel

Donald Steinwachs, Ph.D.
Panel and Conference Chair
Professor and Interim Director
Johns Hopkins Institute for Policy Studies
Director
Health Services Research and Development Center
Bloomberg School of Public Health
The Johns Hopkins University
Baltimore, Maryland

Jennifer Dacey Allen, D.Sc., M.P.H., R.N.
Assistant Professor
Dana-Farber Cancer Institute
Harvard Medical School
Boston, Massachusetts

William Eric Barlow, Ph.D.
Senior Biostatistician
Cancer Research and Biostatistics
Research Professor
Department of Biostatistics
University of Washington
Seattle, Washington

R. Paul Duncan, Ph.D.
Professor and Chair
Department of Health Services Research, Management, and Policy
College of Public Health and Health Professions
University of Florida
Health Science Center
Gainesville, Florida

Leonard E. Egede, M.D., M.S.
Professor of Medicine
Department of Medicine
Director
Center for Health Disparities Research
Medical University of South Carolina
Charleston, South Carolina

Lawrence S. Friedman, M.D.
Professor of Medicine
Harvard Medical School
and Tufts University School of Medicine
Chair, Department of Medicine
Newton-Wellesley Hospital
Newton, Massachusetts

Nancy L. Keating, M.D., M.P.H.
Associate Professor of Medicine and Health Care Policy
Department of Health Care Policy
Harvard Medical School
Boston, Massachusetts

Paula Kim
Chief Executive Officer
Translating Research Across Communities
Green Cove Springs, Florida

Judith R. Lave, Ph.D.
Professor of Health Economics
Director
Pennsylvania Medicaid Policy Center
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, Pennsylvania

Thomas A. LaVeist, Ph.D.
William C. and Nancy F. Richardson Professor in Health Policy
Director, Hopkins Center for Health Disparities Solutions
Johns Hopkins Bloomberg School of Public Health
Baltimore, Maryland

Roberta B. Ness, M.D., M.P.H.
Dean and M. David Low Chair in Public Health
University of Texas
School of Public Health
Houston, Texas

Robert J. Optican, M.D.
Director of Cardiothoracic Imaging
Baptist Memorial Hospitals
Memphis, Tennessee

Beth A. Virnig, Ph.D., M.P.H.
Professor
University of Minnesota School of Public Health
Division of Health Policy and Management
Minneapolis, Minnesota

Speakers

John Z. Ayanian, M.D., M.P.P.
Professor, Medicine and Health Care Policy
Harvard Medical School
Professor, Health Policy and Management
Harvard School of Public Health
Boston, Massachusetts

Mary Barton, M.D., M.P.P.
Scientific Director, U.S. Preventive Services Task Force
Center for Primary Care, Prevention, and Clinical Partnerships
Agency for Healthcare Research and Quality (AHRQ)
Rockville, Maryland

Roshan Bastani, Ph.D.
Professor of Health Services
Associate Dean for Research
UCLA School of Public Health
Los Angeles, California

Allen J. Dietrich, M.D.
Associate Director of Population Sciences
Norris Cotton Cancer Center
Professor, Departments of Community and Family Medicine
Dartmouth Medical School
Lebanon, New Hampshire

Russell Harris, M.D., M.P.H.
Professor of Medicine
University of North Carolina School of Medicine
Cecil G. Sheps Center for Health Services Research
Chapel Hill, North Carolina

Debra J. Holden, Ph.D.
Community Health Psychologist
Senior Director, Community Health Promotion Research
RTI International
Research Triangle Park, North Carolina

C. Daniel Johnson, M.D.
Professor of Radiology
Mayo Clinic Arizona
Scottsdale, Arizona

Carrie N. Klabunde, Ph.D.
Epidemiologist
Health Services and Economics Branch
Applied Research Program
Division of Cancer Control and Population Sciences
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Jennifer Elston Lafata, Ph.D.
Department of Social and Behavioral Health, School of Medicine
Virginia Commonwealth University
Richmond, Virginia

Theodore R. Levin, M.D.
Research Scientist
Director of Colorectal Cancer Screening
Kaiser Permanente Northern California
Oakland, California

David A. Lieberman, M.D., FACG
Professor of Medicine and Chief
Division of Gastroenterology
Department of Medicine
Oregon Health and Science University/Veterans Affairs Medical Center
Portland, Oregon

Megan C. McHugh, Ph.D.
Director of Research
Health Research & Educational Trust
American Hospital Association
Washington, DC

Electra D. Paskett, Ph.D., M.P.H.
Marion N. Rowley Professor of Cancer Research
College of Public Health
The Ohio State University
Columbus, Ohio

Julietta Patnick, C.B.E., B.A. (Hons.)
Director
United Kingdom National Health Service Cancer Screening Programmes
Fulwood House
Sheffield S10 3TH
United Kingdom

David F. Ransohoff, M.D.
Professor of Medicine
Clinical Professor of Epidemiology
Schools of Medicine and Public Health
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina

Eric C. Schneider, M.D., M.Sc.
Senior Scientist and Director
RAND Boston
Associate Professor
Department of Health Policy and Management
Harvard School of Public Health
Boston, Massachusetts

Laura C. Seeff, M.D.
Acting Chief
Comprehensive Cancer Control Branch
Division of Cancer Prevention and Control
Centers for Disease Control and Prevention
Atlanta, Georgia

Steven H. Woolf, M.D., M.P.H.
Professor of Medicine
Departments of Family Medicine, Epidemiology, and Community Health
Director, VCU Center for Human Needs
Virginia Commonwealth University
Richmond, Virginia

Elizabeth M. Yano, Ph.D., M.S.P.H.
Adjunct Professor of Health Services
UCLA School of Public Health
Senior Social Scientist and Co-Director
VA Center for the Study of Healthcare Provider Behavior
VA Greater Los Angeles Healthcare System
Sepulveda, California

Ann G. Zauber, Ph.D.
Associate Attending Biostatistician
Department of Epidemiology and Biostatistics
Memorial Sloan-Kettering Cancer Center
New York, New York

Planning Committee

Carrie Klabunde, Ph.D.
Chairperson
Health Services and Economics Branch
Applied Research Program
Division of Cancer Control and Population Sciences
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Lisa Ahramjian, M.S.
Communications Specialist
Office of Medical Applications of Research
Office of the Director
National Institutes of Health
Bethesda, Maryland

John Z. Ayanian, M.D., M.P.P.
Professor
Medicine and Health Care Policy
Harvard Medical School
Health Policy and Management
Harvard School of Public Health
Boston, Massachusetts

Martin L. Brown, Ph.D.
Chief
Health Services and Economics Branch
Applied Research Program
Division of Cancer Control and Population Sciences
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Stephanie Chang, M.D., M.P.H.
Medical Officer
Evidence-Based Practice Centers Program
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality
Rockville, Maryland

Joseph Chin, M.D., M.S.
Medical Officer
Division of Medical and Surgical Services
Centers for Medicare and Medicaid Services
Baltimore, Maryland

Jennifer Miller Croswell, M.D.
Senior Advisor for the Consensus Development Program
Office of Medical Applications of Research
Office of the Director
National Institutes of Health
Bethesda, Maryland

James Everhart, M.D., M.P.H.
Director
Epidemiology and Data Systems Program
Division of Digestive Diseases and Nutrition
Digestive Diseases Programs Branch
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland

Alaina K. Fournier, Ph.D.
Health Scientist Administrator
Evidence-Based Practice Centers Program
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality
Rockville, Maryland

Karen Huss, Ph.D., R.N., APRN–BC, FAAN, FAAAAI
Program Director
Cardiopulmonary and Critical Care Science
National Institute of Nursing Research
Training Coordinator
Division of Extramural Activities
National Institute of Nursing Research
National Institutes of Health
Bethesda, Maryland

Planning Committee members provided their input at a meeting held July 23–25, 2008. The information provided here was accurate at the time of that meeting.

C. Carl Jaffe, M.D.
Chief
Diagnostic Imaging
Cancer Imaging Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Supriya Janakiraman, M.D., M.P.H.
Staff Fellow
Evidence-Based Practice Centers Program
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality
Rockville, Maryland

Kathleen Jett, Ph.D., R.N., GNP–BC
Program Director
HIV/AIDS and Oncology
Office of Extramural Programs
National Institute of Nursing Research
National Institutes of Health
Bethesda, Maryland

David Kim, M.D.
Assistant Professor
Abdominal Imaging
Department of Radiology
University of Wisconsin School of Medicine and Public Health, Madison
Madison, Wisconsin

Barnett S. Kramer, M.D., M.P.H.
Associate Director for Disease Prevention
Director
Office of Medical Applications of Research
Office of the Director
National Institutes of Health
Bethesda, Maryland

David Lieberman, M.D., FACG
Professor of Medicine and Chief
Division of Gastroenterology
Department of Medicine
Oregon Health and Science University
Veterans Affairs Medical Center
Portland, Oregon

Robert Madoff, M.D.
Professor of Surgery
Chief
Division of Colon and Rectal Surgery
Stanley M. Goldberg, M.D. Chair in Colon and Rectal Surgery
University of Minnesota
Minneapolis, Minnesota

Kelli K. Marciel, M.A.
Communications Director
Office of Medical Applications of Research
Office of the Director
National Institutes of Health
Bethesda, Maryland

Helen Meissner, Ph.D., Sc.M.
Health Science Administrator
Office of Behavioral and Social Sciences Research
Office of the Director
National Institutes of Health
Bethesda, Maryland

Marion R. Nadel, Ph.D., M.P.H.
Epidemiologist
Epidemiology and Applied Research Branch
Division of Cancer Prevention and Control
Centers for Disease Control and Prevention
Atlanta, Georgia

Paul Pinsky, Ph.D.
Early Detection Research Group
Division of Cancer Prevention
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Susan C. Rossi, Ph.D., M.P.H.
Deputy Director
Office of Medical Applications of Research
Office of the Director
National Institutes of Health
Bethesda, Maryland

Planning Committee members provided their input at a meeting held July 23–25, 2008.
The information provided here was accurate at the time of that meeting.

Beth Collins Sharp, Ph.D., R.N.
Director
Evidence-Based Practice Centers Program
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality
Rockville, Maryland

Donald M. Steinwachs, Ph.D.
Panel and Conference Chairperson
Professor and Director
Health Services Research and Development Center
Department of Health Policy and Management
Bloomberg School of Public Health
The Johns Hopkins University
Baltimore, Maryland

Sally W. Vernon, Ph.D.
Director
Division of Health Promotion and Behavioral Sciences
Blair Justice, Ph.D. Professorship in Mind-Body Medicine and Public Health
Professor of Epidemiology and Behavioral Sciences
University of Texas–Houston
School of Public Health
Houston, Texas

Jane G. Zapka, Sc.D.
Professor
Biostatistics, Bioinformatics and Epidemiology
Medical University of South Carolina
Charleston, South Carolina

Planning Committee members provided their input at a meeting held July 23–25, 2008. The information provided here was accurate at the time of that meeting.

Conference Sponsors

National Cancer Institute
John E. Niederhuber, M.D.
Director

Office of Medical Applications of Research
Jennifer M. Croswell, M.D., M.P.H.
Acting Director

Conference Cosponsors

National Institute on Aging
Richard Hodes, M.D.
Director

National Institute of Nursing Research
Patricia A. Grady, Ph.D., R.N., F.A.A.N.
Director

National Institute of Diabetes and Digestive and Kidney Diseases
Griffin P. Rodgers, M.D., M.A.C.P.
Director

Office of Behavioral and Social Sciences Research
Christine A. Bachrach, Ph.D.
Acting Director

Conference Partners

Centers for Medicare & Medicaid Services
Charlene M. Frizzera
Acting Director

Health Resources & Services Administration
Mary Wakefield, Ph.D., R.N.
Administrator

Centers for Disease Control and Prevention
Thomas R. Frieden, M.D., M.P.H.
Director