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Colonoscopy Outcomes by Duration of NPO Status Prior to Colonoscopy with Moderate or Deep Sedation

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) clinicians, managers and policymakers as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout the VA, and some evidence syntheses inform the clinical guidelines of large professional organizations.

QUERI provides funding for four ESP Centers and each Center has an active university affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence;
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at Nicole.Floyd@va.gov.

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INTRODUCTION

Fourteen million colonoscopies are performed annually in the United States for screening, diagnosis, surveillance, and treatment of numerous colonic conditions. Colonoscopies require bowel preparation for cleansing to sufficiently visualize the colon lining and maximize quality and safety. However, inadequate preparation occurs in approximately 25% of colonoscopies, leading to cancellations, rescheduling, difficulty in detecting colonic polyps or other pathology,[1,2] poor patient adherence, as well as longer procedure time. Increased financial and opportunity costs and patient dissatisfaction result.[3]

To optimize colon lining visualization, patients are advised to divide the bowel preparation regimen over two sessions (known as "split-dose preparation"): 1) the evening prior to the colonoscopy (PM dose) and 2) the morning of the colonoscopy (AM dose); the latter taken ideally within 2-6 hours of the planned procedure.[4-7] In addition, some level of sedation (typically moderate or deep) is used in almost all colonoscopies to facilitate patient comfort and procedure quality.[8,9]

For both moderate and deep sedation there is significant variation among anesthesia providers as to the acceptable timing of NPO ("nothing by mouth") including how many hours prior to the planned procedure the last bowel preparation dose can be taken in order to minimize anesthesia risk (primarily aspiration). Practice guidelines from the American Society of Anesthesiologists Committee on Standards and Practice Parameters for preoperative fasting for healthy patients undergoing elective procedures suggest the following minimum fasting periods with the goal of minimizing anesthesia-related risks (primarily aspiration): 2 hours for clear liquids (*eg*, water, fruit juice without pulp, carbonated beverages, clear tea, and black coffee), 6 hours for non-human milk, and 6 hours for a light meal (*ie*, toast and clear liquids).[10] The guideline authors note that published clinical evidence is insufficient to clearly define a relationship between NPO status and risk of emesis/reflux or pulmonary aspiration. Furthermore, it is unclear how different bowel preparation agents would be classified (clear liquids or not), how the potential toxicity of bowel preparation agents might impact anesthesia-related risks, and how the volume of bowel preparation agent consumed might differ from the volume of liquids considered acceptable in the guidelines.

An optimal bowel preparation and NPO status seeks to balance the need for optimal colonic preparation, patient convenience, and scheduling efficiency (typically a shorter NPO window status) with anesthesia safety concerns for an elective procedure (typically a longer NPO status). Furthermore, performing procedures with moderate or deep sedation requires development of and adherence to local and/or national policy measures that cross multiple procedures and physician specialties. These policies include recommendations regarding NPO status. Failure to adhere to NPO status can result in cancellation or rescheduling of procedures or poor procedure preparation. This can lead to reduced procedure quality, resource efficiency, patient satisfaction, and adherence.

The purpose of this report was to review the evidence on the relationship between timing of NPO and the incidence of aspiration and other anesthesia-related harms during elective colonoscopy as

well as colonoscopy rescheduling. In addition, we also reviewed the evidence on the benefits and harms of variable timing of NPO status on colonoscopy outcomes including colonoscopy quality measures, rescheduling, resource use, and patient satisfaction. The review may be used to guide policy within the VA. With input from stakeholders and TEP members, we developed the following Key Questions:

Key Question 1. Does the incidence of aspiration and other anesthesia-related harms for colonoscopy vary by NPO status or bowel prep timing (*eg*, > 6 hours, 2-6 hours, < 4 hours, and < 2 hours)? Does the incidence of anesthesia-related harms by NPO status vary by: a) patient characteristics (age, race, sex, obesity, comorbidities) or b) sedation (moderate, deep)?

Key Question 2. What is the effect of variable timing of bowel prep and NPO status on the quality of the bowel preparation, diagnostic yield, and colonoscopy procedural quality indicators (*eg*, completion rates, adenoma detection rate, total procedure time, cecal intubation time and withdrawal time)?

Key Question 3. What is the effect of NPO status prior to colonoscopy on resource use (*eg*, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures)?

Key Question 4. What is the effect of bowel preparation and NPO status prior to colonoscopy on patient adherence to bowel preparation, colonoscopy, and/or rescheduled colonoscopy, and satisfaction with bowel preparation and/or colonoscopy?

We defined the following Population, Intervention, Comparator, Outcomes, Timing, and Setting (PICOTS) for the review:

Population: Adults undergoing bowel preparation and elective colonoscopy with moderate or deep sedation
Intervention(s): NPO status 2-4 hours (liquids and bowel preparation allowed up to 2 hours prior to procedure)
Comparator(s): Alternative timing of NPO
Outcome(s): (NOTE: limited to findings according to NPO status prior to colonoscopy)

Co-primary outcomes: aspiration, rescheduled colonoscopies
Secondary outcomes: adverse events (including bowel perforation and other anesthesia-related harms), diagnostic yield, completion rate, adenoma detection rate, false negative colonoscopies
Intermediate outcomes: quality of bowel preparation, hospitalizations, costs, total procedure time, cecal intubation time, withdrawal time, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time, patient adherence, patient satisfaction, volume of gastric contents, pH of gastric contents

Timing: Start of sedation for colonoscopy to completion of sedation for colonoscopy
Setting: Inpatient or outpatient clinics

METHODS

TOPIC DEVELOPMENT

This topic was nominated by Jason Dominitz, MD, MHS, National Program Director for Gastroenterology, Office of Patient Care Services. Additional stakeholders were identified to include both gastroenterology and anesthesiology: John Sum-Ping, MD, Chair, National Director, Anesthesia Service; Art Wallace, MD, PhD, Chief, Anesthesia Service, San Francisco VA Medical Center; and Deborah Fisher, MD, MHS, Chair, National VA Gastroenterology Field Advisory Committee. The key questions were formulated with input from a Technical Expert Panel (TEP) consisting of gastroenterologists and anesthesiologists.

SEARCH STRATEGY

We searched MEDLINE (OVID) for articles published from 1990 through October 2014. Our search was designed to identify studies of any design. We limited the search to studies involving human subjects published in the English language. Search terms included the following Medical Subject Headings (MeSH): Colonoscopy, Cathartics, Polyethylene Glycols, Phosphates, and Respiratory Aspiration of Gastric Contents. The full search strategy is presented in Appendix A. We also searched reference lists of guidelines, existing reviews, and included studies and we received reference suggestions from stakeholders and TEP members.

STUDY SELECTION

Abstracts of citations identified from the literature search were assessed for relevance by an investigator. We included studies of any design that reported outcomes following bowel preparation if at least one preparation was completed within 8 hours of the colonoscopy procedure. We also include population-based studies of adverse events during colonoscopy. Additional inclusion criteria were as follows:

- Study of adults
- Study of colonoscopy with moderate or deep sedation (studies related to colorectal surgery or involving general anesthesia were excluded)
- Reports outcomes of interest during colonoscopy or recovery from colonoscopy (*ie,* studies of aspiration during bowel preparation were excluded)

Full text reports of studies identified as potentially eligible (or indeterminate, *eg,* title only) were obtained for further review using the inclusion and exclusion criteria described above. Each article was independently reviewed by 2 investigators. Reasons for excluding a study at full text review were noted.

DATA ABSTRACTION

Eligible studies were reviewed for outcomes of interest by investigators. From studies of different preparation-to-procedure or NPO intervals, study characteristics (inclusion/exclusion criteria and details about the preparation interventions or NPO status), patient characteristics, and outcomes data were abstracted onto tables by one investigator and verified by a second. Our

focus was on outcomes from different preparation-to-procedure intervals and not different preparation substances.

RISK OF BIAS ASSESSMENT

We assessed the risk of bias of randomized controlled trials (RCTs) and controlled clinical trials (CCTs) based the following criteria: allocation sequence generation, allocation concealment, blinding, completeness of outcome reporting, and selectiveness of outcome reporting – a modification of the Cochrane approach to determining risk of bias.[11] For observational studies we identified the following criteria and evaluated risk of bias for each study:

1) Study design (prospective vs retrospective)
2) Population (consecutive or not)
3) Analysis of findings
   a. Was the method for handling missing data reported and appropriate?
   b. Were the characteristics the different NPO groups similar?

Individual studies were rated as low, moderate, or high risk of bias. Low risk of bias RCTs had adequate allocation sequence generation and allocation concealment, blinding, and few patients with incomplete data. Low risk of bias observational studies were prospective, enrolled consecutive patients, had appropriate methods for handling missing data (or no missing data), and characteristics of the NPO groups were similar.

DATA SYNTHESIS

We described and qualitatively compared the patient characteristics, study characteristics, intervention timing, and findings of included studies. Due to variation in the preparation-to-procedure interval and/or NPO status across studies and different systems used to report outcomes, we summarized most outcomes narratively.

RATING THE BODY OF EVIDENCE

We rated the overall strength of the body of evidence for our primary and secondary outcomes using the method reported by Owens et al.[12] Separate ratings were generated for RCTs/CCTs and observational studies.

PEER REVIEW

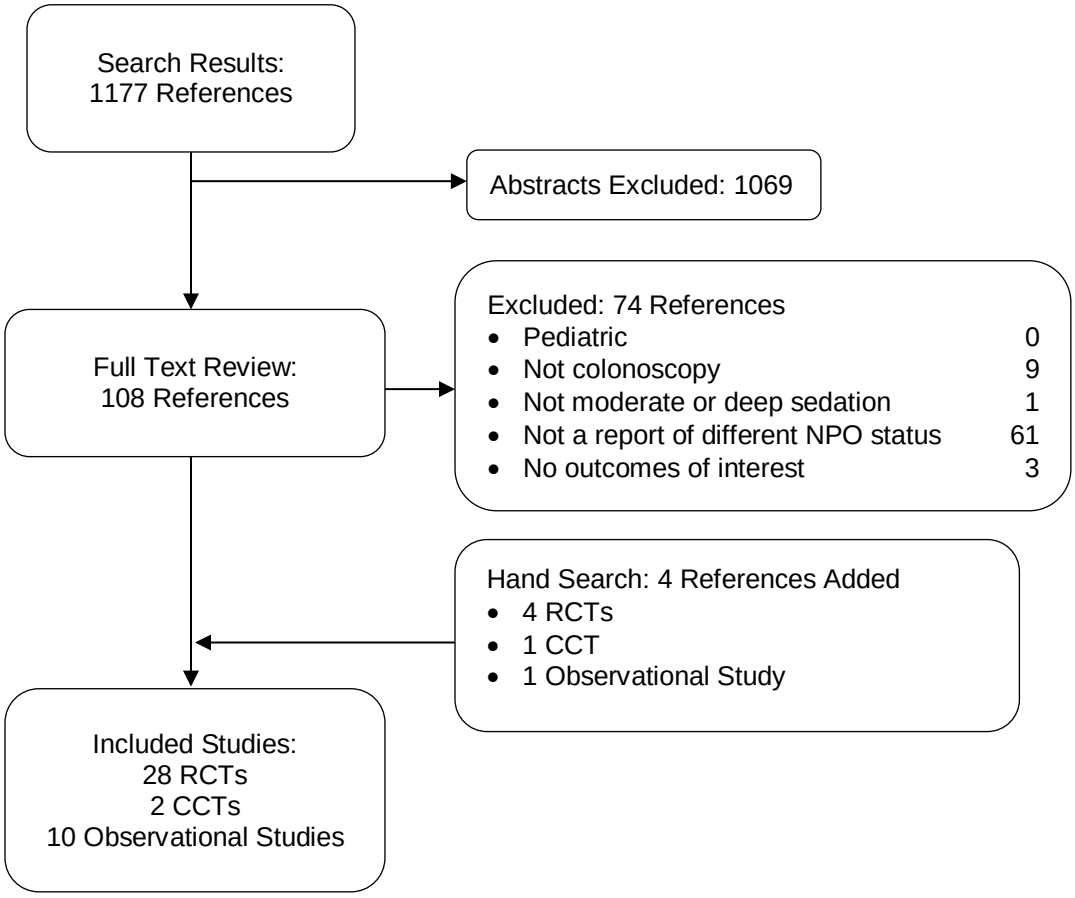
A draft version of this report was reviewed by clinical content experts and clinical leadership. Their comments and our responses are presented in Appendix B and the report has been modified as needed.

RESULTS

LITERATURE FLOW

Our literature search yielded 1177 abstracts or titles (Figure 1). After reviewing the abstracts we excluded 1069 and performed full text review of 108 articles. We excluded 74 articles and included 34. A hand-search of reference lists of guidelines, existing reviews, and included studies yielded another 6 articles for a total of 40 included studies of different bowel preparation or NPO status intervals (28 RCTs, 2 controlled CCTs, and 10 observational studies).

Figure 1: Literature Flow Chart



OVERVIEW

Baseline characteristics for the 40 RCTs, CCTs, and observational studies[13-53] reporting outcomes of interest are presented in Table 1. A total of 22,936 patients were evaluated; approximately one-half of the patients were from the United States or Canada. Mean age was 57 years in the 34 studies reporting. Sixty-one percent of colonoscopies were screening colonoscopies. Detailed study characteristics and risk of bias criteria are presented in Appendix C, Table 1.

From each included study, we identified a minimum time from the end of preparation until the procedure. Three studies[36,38,43] did not provide enough information to determine a minimum time. We also extracted information about timing of liquids allowed prior to the procedure from the 11 studies that reported that information. Figure 2 displays the minimum times based on bowel preparation time and the time before the procedure that clear liquids were allowed.

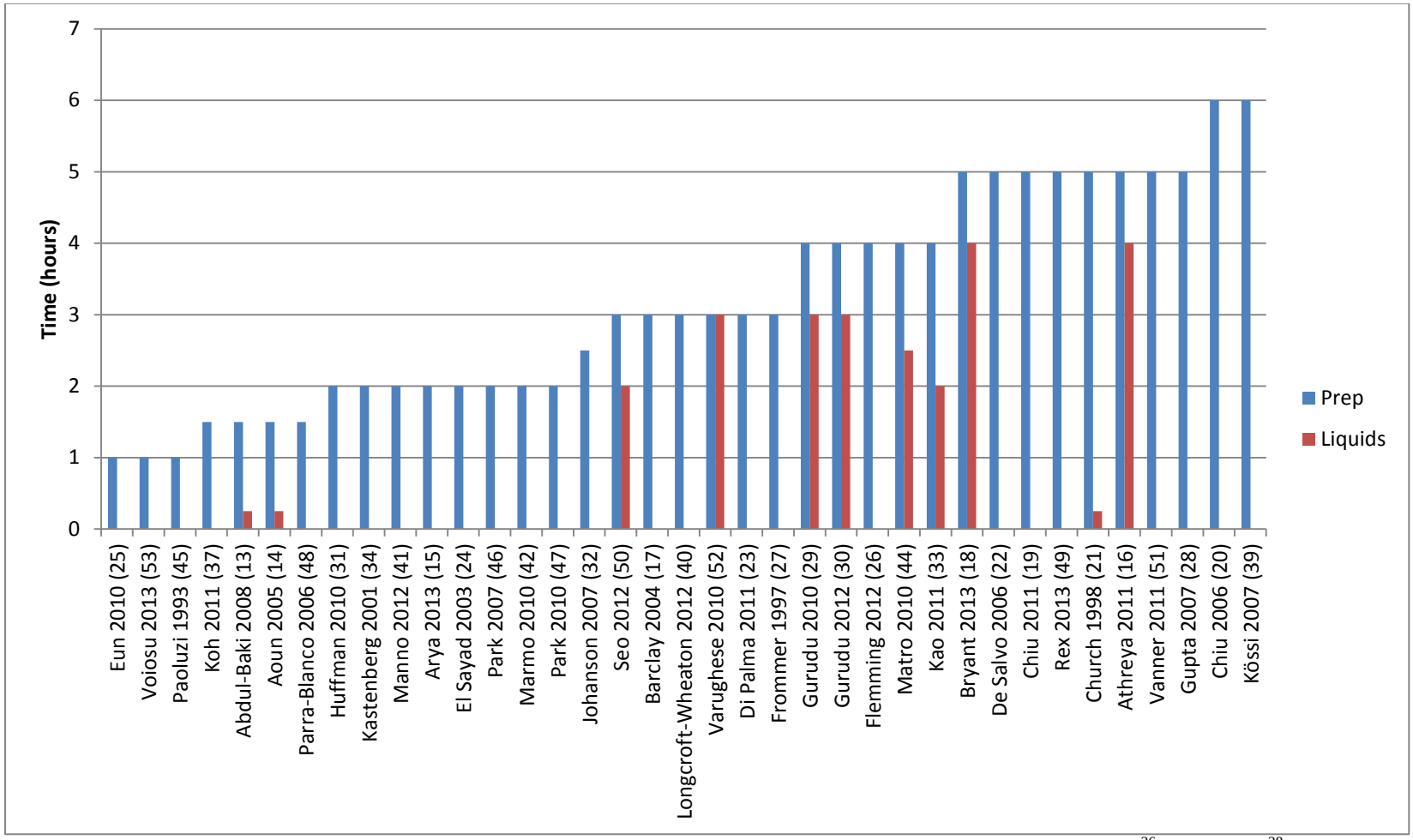
An overview of outcomes reported in each study is presented in Table 2. An NPO status of > 8 hours indicates that the bowel preparation was completed the night before colonoscopy but the exact time of completion and time of colonoscopy were not reported. Our predefined primary and secondary outcomes were rarely reported. Six studies reported our co-primary outcome of aspiration[29,31,41,43,44,52]; one reported rescheduled colonoscopies.[38] Of our secondary and intermediate outcomes, all but one study reported quality of the bowel preparation. Few studies reported other adverse events, diagnostic yield, completion rates, adenoma detection rate, total procedure time, cecal intubation time, withdrawal time, patient adherence, patient satisfaction, or volume of gastric contents. No studies reported false negative colonoscopies, hospitalizations, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time, or acidity of the gastric contents. Detailed outcome data are presented in Appendix C, Tables 2 through 6.

Table 1. Summary of Baseline Characteristics

Characteristic	Mean (range) *Unless Otherwise Noted*	Number of Studies Reporting
Total number of patients evaluated	22,936 (80 to 5175)	40
Randomized controlled trials, number of patients	9304 (80 to 895)	28
Controlled clinical trials, number of patients	740 (328 to 412)	2
Observational studies, number patients	12,892 (100 to 5175)	10
Age of subjects, years (range of means)	57 (44 to 63)	34
Age of subjects, range of median years	55 to 65	3
Gender, male, % of patients	46 (28 to 81)	38
Indication for colonoscopy-screening, % of patients	61 (0[a] to 100)	20
Location - USA/Canada, number of patients	12,208 (100 to 5175)	17
Location - Asia/Australia, number of patients	8045 (80 to 3079)	14
Location - Europe, number of patients	2683 (160 to 895)	9

[a] Two studies reported that screening was not an indication for colonoscopy. Chiu 2006[20] included participants who had colorectal neoplasms detected at a screening colonoscopy and were scheduled for a second colonoscopic examination for either elective polypectomy or endoscopic mucosectomy. Manno 2012[40] included participants with a positive fecal occult test or those in surveillance post-polypectomy.

Figure 2. Minimum Time from End of Bowel Preparation to Procedure (Blue Lines) or Time Before Procedure when Liquids were Stopped (Red Lines)[a,b,c]



[a] 3 studies did not provide sufficient information to determine a minimum time from end of preparation to procedure (Khan 2010,[36] Kolts 1993,[38] Mathus-Vliegen 2013[43])

[b] Studies where patients were allowed liquids until time of procedure are indicated by a time of 0.25 hours

[c] Citations are author, year (reference number)

Table 2. Overview of Outcomes Reported

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes														
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Abdul-Baki 2008[13] Group 1: ≥ 1.5 hours Group 2: > 8 hours											✓				✓	✓							
Aoun 2005[14] Group 1: ≥ 1.5 hours Group 2: > 8 hours											✓				✓	✓						✓	
Arya 2013[15] Group 1: ≥ 2 hours Group 2: > 8 hours											✓												
Athreya 2011[16] Group 1: 5-9 hours Group 2: > 8 hours											✓	✓	✓	✓									
Barclay 2004[17] Group 1: < 3 hours Group 2: ≥ 5 hours				✓							✓				✓	✓							
Bryant 2013[18] Group 1: 5-7.5 hours Group 2: > 8 hours											✓												
Chiu 2011[19] Group 1: 5-9 hours Group 2: >8 hours							✓				✓												
Chiu 2006[20] Group 1: 6-8 hours Group 2: > 8 hours					✓	✓					✓												
Church 1998[21] Group 1: 5-8 hours Group 2: > 8 hours				✓		✓					✓		✓	✓									

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes															
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
De Salvo 2006[22] Group 1: 5-8 hours Group 2: >8 hours						✓					✓													
Di Palma 2011[23] Group 1: 3-9 hours Group 2: > 8 hours											✓													
El Sayed 2003[24] Group 1: ≥ 2 hours Group 2: > 8 hours											✓													
Eun 2011[25] Group 1: ≥ 1 hour Group 2: > 7 hours											✓				✓									
Flemming 2012[26] Group 1: ≥ 4 hours Group 2: > 8 hours			✓	✓		✓					✓													
Frommer 1997[27] Group 1: 3-9 hours Group 2: > 8 hours											✓													
Gupta 2007[28] Group 1: ≥5 hours Group 2: > 8 hours											✓					✓								
Gurudu 2010[29] Group 1: ≥ 4 hours Group 2: > 8 hours	✓						✓				✓													
Gurudu 2012[30] Group 1: ≥ 4 hours Group 2: > 8 hours						✓	✓				✓			✓										
Huffman 2010[31] Group 1: ≥ 2 hours Group 2: > 8 hours	✓																					✓		

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes															
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Johanson 2007[32] Group 1: 2.5-4.5 hours Group 2: > 8 hours				✓							✓													
Kao 2011[33] Group 1: 4-8 hours Group 2: > 8 hours											✓													
Kastenberg 2001, 2007[34,35] Group 1: 2-4 hours Group 2: > 8 hours						✓					✓													
Khan 2010[36] Group 1: Split-dose[c] Group 2: > 8 hours											✓													
Koh 2011[37] Group 1: 1.5-3.5 hours Group 2: 6-8 hours											✓													
Kolts 1993[38] Group 1: Split-dose[c] Group 2: > 8 hours Group 3: > 8 hours		✓									✓													
Kössi, 2007[39] Group 1: ≤ 6 hours Group 2: 6-12 hours Group 3: ≥ 12 hours						✓					✓					✓								
Longcroft-Wheaton 2012[40] Group 1: > 3 hours Group 2: > 5 hours							✓				✓				✓	✓								
Manno 2012[41] Group 1: 2 hours Group 2: >8 hours	✓										✓				✓	✓								

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes															
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Marmo 2010[42] Group 1: ≤ 2 hours Group 2: >8 hours						✓					✓													
Mathus-Vliegen 2013[43] Group 1: Split-dose[c] Group 2: > 8 hours	✓			✓							✓													
Matro 2010[44] Group 1: 4 hours Group 2: 4 hours (split-dose)	✓				✓	✓	✓				✓	✓		✓	✓	✓								
Paoluzi 1993[45] Group 1: 1-2.5 hours Group 2: > 8 hours											✓													
Park 2007[46] Group 1: ≥ 2 hours Group 2: > 8 hours											✓		✓		✓	✓								
Park 2010[47] Group 1: 2-5 hours Group 2: > 8 hours											✓				✓	✓								
Parra-Blanco 2006[48] Group 1: 1.7-7 hours Group 2: > 8 hours					✓		✓				✓													
Rex 2013[49] Group 1: 5-9 hours Group 2: > 8 hours				✓		✓					✓				✓									
Seo 2012[50] Group 1: ≤ 3 hours Group 2: > 8 hours											✓													

Author, Year NPO Status Groups[a]	Primary Outcomes		Secondary Outcomes						Intermediate Outcomes														
	Aspiration (k=6)	Rescheduled Colonoscopies (k=1)	Bowel Perforation (k=1)	Other Adverse Events (k=7)	Diagnostic Yield (k=3)	Completion Rate (k=11)	Adenoma Detection Rate (k=7)	False Negative Colonoscopy	Hospitalizations	Costs	Quality of Bowel Preparation (k=39)	Total Procedure Time (k=3)	Cecal Intubation Time (k=4)	Withdrawal Time (k=5)	Patient Adherence (k=11)[b]	Patient Satisfaction (k=11)[b]	Unused Procedure Slots	Delays, Rescheduling	Delays, Diagnosis	Increased Volume, Procedures	Scheduler/Nurse Time	Volume of Gastric Contents (k=2)	pH of Gastric Contents
Vanner 2011[51] Group 1: > 5 hours Group 2: > 8 hours						✓					✓												
Varughese 2010[52] Group 1: ≥ 3 hours Group 2: > 8 hours	✓						✓				✓	✓	✓	✓	✓	✓							
Voiosu 2013[53] Group 1: 1-7 hours Group 2: > 8 hours				✓							✓												

[a] NPO status > 8 hours indicates bowel preparation completed the night before colonoscopy but exact time of completion and time of colonoscopy not reported
[b] Data on patient adherence and patient satisfaction extracted only from studies using same bowel preparation substance in the study groups (k=21)
[c] Time of morning dose or time of colonoscopy not reported

KEY QUESTION 1. Does the incidence of aspiration and other anesthesia-related harms for colonoscopy vary by NPO status or bowel prep timing (*eg*, > 6 hours, 2-6 hours, < 4 hours, and < 2 hours)?

Does the incidence of anesthesia-related harms by NPO status vary by:

A) Patient characteristics (age, race, sex, obesity, comorbidities)

B) Sedation (moderate, deep)?

Findings from Trials of Different Bowel Preparation Protocols

Aspiration Risk (Appendix C, Table 2)

Six studies reported on aspiration (sample sizes ranged from 136 to 1,345).[29,31,41,43,44,52] In 5 of these studies no aspirations occurred during colonoscopy[29,31] or during colonoscopy or within the 30 days post-colonoscopy,[43] or there were no complications related to sedation.[41,52]

One observational study (moderate risk of bias) reported no aspiration events in 1,345 patients.[29] Bowel preparation regimens were completed either the morning of the procedure (at least 4 hours prior to colonoscopy) or the evening before the colonoscopy. All patients were allowed to drink clear liquids up to 3 hours before the procedure.

The second study, also observational and moderate risk of bias, enrolled 301 patients.[31] One group completed bowel preparation at least 2 hours before the procedure (mean NPO time of 5.1 hours). The second group completed bowel preparation the evening before (mean NPO time of 13.5 hours). No patient had “clinical evidence” of aspiration. The volume of the gastric contents did not differ significantly.

One RCT used medical charts and a complications database to identify aspiration events during colonoscopy or in the 30 days following colonoscopy for 200 patients.[43] No events were reported.

The 2 studies reporting no complications related to sedation were both RCTs with enrollments of 136[52] and 336[41] respectively. In the first study, with moderate risk of bias, patients in one group completed preparation by 10 am for an afternoon colonoscopy (1 pm or later); the other group completed preparation the night before the procedure.[52] Both groups were allowed clear liquids until 10 am. In the second study, with low risk of bias, one group completed preparation 2 hours before the procedure and the other group completed preparation the day before.[41]

One small (n=125 randomized), low risk of bias RCT reported one aspiration event requiring hospitalization during colonoscopy under moderate sedation.[44] The patient was described as severely obese (BMI = 40 kg/m^2) but with no other obvious risk factors for aspiration. The patient was assigned to consume 1 L of a bowel preparation agent 7 hours before colonoscopy and an additional 1 L 4 hours before. Patients in this trial were allowed clear liquids until 2.5 hours before the procedure. The patient was hospitalized for 24 hours and treated with oral antibiotics for one week.

Other Harms (Appendix C, Table 5)

Seven studies (6 moderate risk of bias, 1 low risk of bias) reported on other harms. In 4 studies, there were no adverse events, specifically no complications of bowel perforation or bleeding up to the time of leaving the endoscopy office[26] or no serious adverse events.[17,21,53] One of these studies interviewed patients 2 days post-colonoscopy,[17] one recorded adverse events through approximately 2 hours post-colonoscopy,[53] and one did not provide a timeframe.[17]

Three studies reported adverse events with harms occurring in less than or equal to 1% of procedures. In 2 studies, there was one event in the longer NPO status group and no events in the shorter NPO status group.[32,43] One RCT with 402 patients reported lower gastrointestinal bleeding post-colonoscopy in one patient (0.5%) who completed bowel preparation more than 8 hours before colonoscopy.[32] Another RCT, with 200 patients, reported severe retrosternal pain in one patient (1%) 3 hours after the colonoscopy. Anteroseptal infarction was diagnosed. The patient was in the group that had morning colonoscopies following bowel preparation completed the evening before.[43] A third RCT, with 603 patients, reported acute pancreatitis in one patient (0.3%) who completed bowel preparation between 5-9 hours before colonoscopy and non-cardiac chest pain in one patient (0.3%) who completed bowel preparation more than 8 hours before colonoscopy.[49] It was unclear if these events occurred during bowel preparation, during colonoscopy, or post-colonoscopy. The study included follow-up visits at 24 to 48 hours, one week, and 4 weeks.

Gastric Volume and Acidity (Appendix C, Table 6)

Two studies reported no difference in volume of gastric contents. In one low risk of bias RCT,[14] 141 patients were assigned to complete bowel preparation the morning of and at least 1.5 hours prior to the procedure or the evening before the procedure. Both groups were allowed water until the time of the procedure. Approximately 25% of patients in each group underwent tandem esophagogastroduodenoscopy (EGD) and gastric volume was assessed. The second study was a moderate risk of bias observational study.[31] The split-dose preparation group completed preparation by 2 hours prior to the procedure. Findings were compared to a group that completed bowel preparation the day before the colonoscopy; additional clear fluids were allowed "as desired." EGD was performed immediately before colonoscopy for both groups. No study reported the acidity of the gastric contents.

Additional Studies of Aspiration during Colonoscopy

Several hospital- or population-based studies have also reported on aspiration during colonoscopy. However, none documented duration of NPO status prior to the colonoscopy. In a large database study, the incidence of aspiration requiring hospitalization during 165,527 outpatient diagnostic colonoscopies in 100,359 Medicare patients age 66 years and older (mean age = 76 years) was 0.14% for patients having colonoscopy under deep sedation requiring anesthesia assistance (as identified by a *CPT-4* code) and 0.10% for patients under moderate sedation without anesthesia assistance.[54] A study of 23,508 outpatient colonoscopies at 3 hospitals in Australia reported one case (0.004%) of aspiration requiring hospitalization in a patient undergoing colonoscopy with general anesthesia.[55] A study of 3,155 colonoscopies performed with sedation managed by an anesthesiologist in adults at a single hospital in Italy reported that 0.16% of patients undergoing colonoscopy had an aspiration requiring "some intervention by an anesthesiologist."[56] Aspirations requiring hospitalizations were not reported.

Patients were instructed to fast according to guidelines in place at the time – clear liquids up to 2 hours before the procedure and a light meal (toast and clear liquid) up to 6 hours before the procedure.

KEY QUESTION 2. What is the effect of variable timing of bowel prep and NPO status on the quality of the bowel preparation, diagnostic yield, and colonoscopy procedural quality indicators (*eg*, completion rates, adenoma detection rate, total procedure time, cecal intubation time and withdrawal time)?

Quality of the Bowel Preparation

Thirty-nine studies (28 RCTs, 2 CCTs, and 9 observational studies) reported on the effect of variable timing of bowel preparation on quality of the bowel preparation (Appendix C, Table 3).[13-30,32-53] Eleven of these studies (6 RCTs, 1 CCT, 4 observational) also reported the time prior to colonoscopy when water or other clear liquids were allowed, ranging from 4 hours until the time of the procedure.[13,14,16,18,21,29,30,33,44,50,52] Although different rating scales were used to rate the quality of the bowel preparation, quality of the bowel preparation was consistently rated higher for NPO intervals of 6 hours or less compared to intervals of more than 8 hours.

Of the 28 studies (n=11,698) that only reported timing of bowel preparation and compared shorter (1-6 hours) versus longer intervals (8-12 hours) between bowel preparation administration and colonoscopy, 21 reported significantly higher quality of bowel preparation with a shorter interval between preparation and colonoscopy and 7 reported no significant difference.

Limited data suggest that consumption of water or clear liquids, including preparation solutions, from 0 to 4 hours prior to colonoscopy does not affect quality of the bowel preparation. Of the 11 studies (n=10,931) reporting timing of liquid consumption, 3 allowed water or other clear liquids up to the time of the procedure and 2, 1, 3, and 2 studies allowed water intake up to 2 hours, 2.5 hours, 3 hours, and 4 hours prior to colonoscopy, respectively. Nine studies reported significantly higher quality rating of the preparation in the group completing bowel preparation less than 8 hours prior to colonoscopy (minimum NPO status based on bowel preparation of 1.5 to 6 hours) compared to the group completing bowel preparation more than 8 hours prior to colonoscopy. One study reported no significant difference in quality of preparation between groups completing bowel preparation the morning of the colonoscopy or in a split-dose (evening before/morning of colonoscopy). Both groups completed bowel preparation 4 hours prior to colonoscopy. The remaining study reported higher quality in the shorter NPO duration group but no statistical analysis was possible.

Other Secondary or Intermediate Outcomes

Few studies reported other secondary or intermediate outcomes.

Diagnostic yield (k=3) (Appendix C, Table 3; Figure 3)

One moderate risk of bias RCT (n=121) reported a significantly higher total number of lesions detected in patients with who completed bowel preparation 6 to 8 hours before colonoscopy compared to more than 8 hours (2.8 vs 1.9, P = .03).[20] No differences were noted for either

proximal lesions or advanced lesions. All patients in this study had colon neoplasms detected during a previous colonoscopy.

A second moderate risk of bias RCT (n=197) reported a significantly greater yield of flat lesions in patients who completed bowel preparation 1 to 7 hours before colonoscopy compared to those who completed preparation more than 8 hours before (22% vs 9%, P < .05); no difference were reported for "any polyp" (52% vs 45%) or "protruding polyps" (40% vs 42%).[48]

A low risk of bias RCT (n=125) reported significantly more "findings" (adenoma or cancer) per patient (0.70 vs 0.46, P = .047) in the group that completed bowel preparation in the morning compared to a group that used a split-dose protocol.[44] Both groups completed the preparation 4 hours prior to colonoscopy and were allowed clear liquids up to 2.5 hours before the procedure.

Completion rates (k=11) (Appendix C, Table 3; Figure 3; Figure 4)

Results from 5 RCTs providing sufficient information to permit pooling found no difference in completion rates between shorter and longer NPO status (RR 1.00 [95%CI 0.98, 1.01).[20-22,26,34]

One additional low risk of bias RCT (n=895) reported an overall completion rate of 95% but significantly fewer aborted procedures due to inadequate bowel preparation when the preparation was completed 2 hours or less before colonoscopy (93%) compared to more than 8 hours before colonoscopy (79%).[42]

A high risk of bias observational study (n=5,175) reported a significantly higher colonoscopy completion rate in patients completing bowel preparation 4 hours or more before colonoscopy (96%) compared to 8 hours or more (94%). Patients in both groups were allowed liquids until 3 hours before the procedure.[30]

Another study, a low risk of bias RCT not included in the figure because both groups completed bowel preparation 4 hours before colonoscopy, reported no significant difference in completion rate between the single dose (98%) or split-dose (100%) groups.[44]

Three studies provided completion rates but did not report separate results for the NPO status groups: a moderate sized RCT,[49] a moderate sized observational study,[39] and a small observational study.[51] The completion rates were 96%,[39] 99%,[49] and 95%.[51]

Adenoma detection rate (k=7) (Appendix C, Table 3; Figure 3; Figure 4)

One high risk of bias observational study (n=5,175) reported a significantly higher adenoma detection rate of in patients who completed bowel preparation 4 hours or more before colonoscopy compared to those completing preparation more than 8 hours before (32% vs 27%, P < .001).[30] All patients in this study were allowed liquids until 3 hours prior to the procedure. Another observational study (n=3,079, moderate risk of bias) found significantly higher detection of proximal adenomas in patients who completed bowel preparation 5 to 9 hours before colonoscopy compared to more than 8 hours (11% vs 9%, P = .04) although overall detection did not differ (17% vs 15%, P = .11).[19] Four studies (3 moderate risk of bias, 1 low risk of bias) reported no difference in detection rate between groups with shorter versus longer times between completion of bowel preparation and the procedure.[29,40,48,52] One of the studies allowed liquids until 3 hours prior to the procedure.[29]

In the study comparing single dose to split-dose preparation, both completing preparation 4 hours before colonoscopy with liquids allowed until 2.5 hours before, the overall detection rate was higher in the morning-only preparation group (37% vs 25%, P = .04).[44] For high-risk adenoma or cancer, the difference was not significantly different (13% vs 11%, P = .28).

Total procedural time (k=3) (Appendix C, Table 4)

Total procedure time, reported in 3 studies, did not differ between groups. In one high risk of bias CCT (n=325) completion of bowel preparation 5 to 9 hours before the procedure was compared to preparation the night before.[16] In the second study, a moderate risk of bias RCT (n=136), bowel preparation was completed 3 hours or more before the procedure compared to more than 8 hours.[52] The third study, a low risk of bias RCT (n=125), compared morning-only preparation to split-dose preparation.[44] One of these studies allowed patients to consume clear fluids up to 4 hours before the procedure[16] and another up to 2.5 hours before the procedure.[44] The other study required all patients to be NPO after 10 am for an afternoon colonoscopy.[52]

Cecal intubation time (k=4) (Appendix C, Table 4)

One low risk of bias RCT (n=303) reported shorter cecal intubation time (a measure of higher bowel preparation and colonoscopy quality) in patients who completed bowel preparation at least 2 hours before colonoscopy compared to more than 8 hours.[46] Times did not differ in the 2 other, moderate risk of bias, RCTs (n=453)[21,52] or the CCT (n=325)[16] reporting this outcome. In one of the RCTs finding no difference, patients were allowed water until the time of the procedure.[21] The other 2 studies (1 moderate risk of bias RCT, 1 high risk of bias CCT) allowed clear fluids until 4 hours before the procedure[16] or required patients to be NPO after 10 am prior to an afternoon colonoscopy.[52]

Withdrawal time (k=5) (Appendix C, Table 4)

One high risk of bias observational study (n=5,175) reported a shorter withdrawal time (a measure of higher bowel preparation and colonoscopy quality) in patients with a time from completion of bowel preparation of 4 hours or greater compared to more than 8 hours (12 minutes vs 15 minutes, P < .001).[30] Patients were allowed clear liquids until 3 hours before colonoscopy. Three other studies (1 low risk of bias RCT, 2 moderate risk of bias RCTs, and one high risk of bias CCT) reporting withdrawal time found no difference between shorter and longer NPO intervals[16,21,52] or between morning-only and split-dose preparation.[44] One RCT allowed water until the time of the procedure, one RCT allowed clear liquids up to 2.5 hours before the procedure, one RCT required patients to be NPO after 10 am for an afternoon procedure, and the CCT allowed clear fluids until 4 hours before colonoscopy.

Figure 3. Completion Rate, Adenoma Detection Rate, and Diagnostic Yield: Outcomes from Randomized Controlled Trials

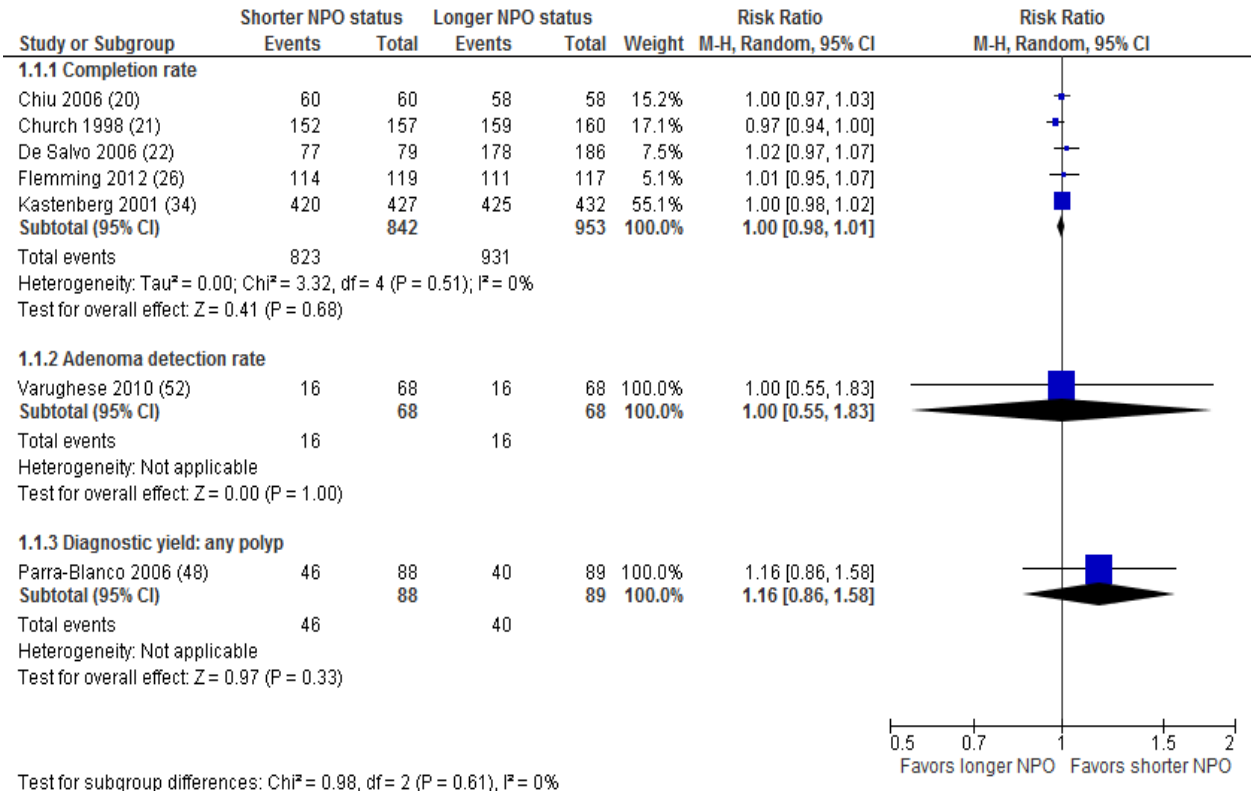
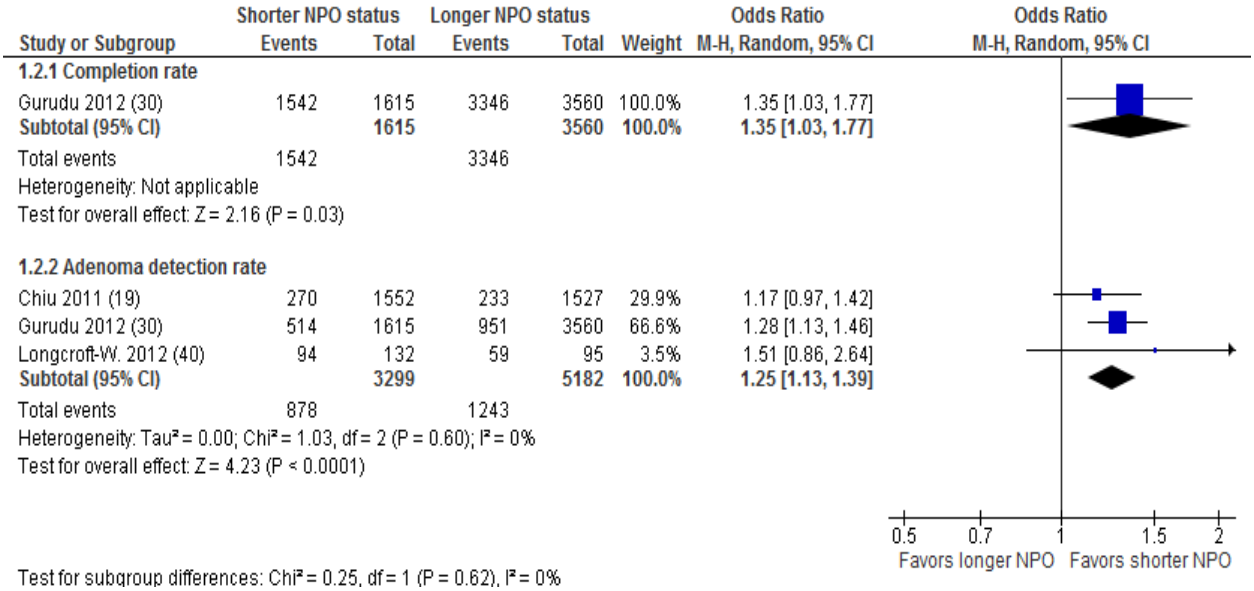


Figure 4. Completion Rate and Adenoma Detection Rate: Outcomes from Observational Studies



KEY QUESTION 3. What is the effect of NPO status prior to colonoscopy on resource use (*eg*, costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures)?

One moderate risk of bias RCT reported rescheduled colonoscopies.[38] The percentage of rescheduled colonoscopies was significantly lower (P = .011) in the group that completed bowel preparation on the morning of the procedure (3%) taking a split-dose of a sodium phosphate regimen than in groups consuming a polyethylene glycol solution (8%) or a castor oil solution (24%) the evening before the procedure. Differences in the bowel preparation solutions between groups limit our ability to draw firm conclusions about the role of NPO status on rescheduling.

No other study reported resource use. Although some studies reported inadequate bowel preparation quality, they did not report whether the colonoscopy was repeated.

KEY QUESTION 4. What is the effect of bowel preparation and NPO status prior to colonoscopy on patient adherence to bowel preparation, colonoscopy, and/or rescheduled colonoscopy and satisfaction with bowel preparation and/or colonoscopy?

Data are limited on the effect of bowel preparation and NPO status on patient adherence, colonoscopy rescheduling, and satisfaction. We extracted data on adherence and satisfaction from studies where the same bowel preparation substance (*eg*, polyethylene glycol) was used for all patients (Appendix C, Table 4). Compared to a same-day regimen (completed the day before colonoscopy), a split-dose regimen was associated with greater adherence to bowel preparation in 4 studies[13,14,41,46] with a significantly greater adherence in 2 of those studies, both low risk of bias RCTs.[13,14] Two studies, one low risk of bias observational study and one moderate risk of bias RCT, that included a dose on the day of the procedure for all patients reported better completion of the preparation in patients who finished the preparation closer to the time of the procedure (approximately 3 hours vs 5 hours or more in both studies).[17,40] A third study, a low risk of bias observational study, reported no difference between groups completing bowel preparation less than 4 versus more than 4 hours prior to colonoscopy.[25] Three studies, high, moderate, and low risk of bias RCTs, reported no difference in compliance with a split-dose regimen compared to a same day regimen.[44,47,52] One low risk of bias RCT reported treatment-emergent adverse events leading to discontinuation of the preparation in 2 of 603 patients (0.3%) with no difference between the split-dose or same-day groups.[49]

We extracted elements of satisfaction that would be impacted by different schedules for bowel preparation (Appendix C, Table 4). Five studies reported on work or school time lost. Two low risk of bias RCTs found no difference in the percentage of patients reporting work or school time missed between split-dose and same-day groups.[13,14] Another low risk of bias RCT reported that 85% of the morning-only preparation group compared to 55% of the split-dose group (P = .019) reported no interference with work on the day before the procedure. One moderate risk of bias RCT reported significantly fewer hours lost form work with a split-dose regimen.[28] The fourth study, a low risk of bias observational study, reported that completion of the bowel preparation

regimen closer to the time of the procedure (3 hours or more compared to 5 hours or more) caused less interruption of sleep.[40]

Eight studies reported on sleep disturbance. Two moderate risk of bias RCTs found less sleep disruption in patients on a split-dose protocol[28,52] and a third low risk of bias observational study found less sleep disruption with a protocol that required completion of the preparation regimen closer to the procedure time (3 hours or more compared to 5 hours or more).[40] Five RCTs, 3 low and 1 high risk of bias, found no difference in sleep disruption between split-dose and same-day regimens.[13,14,44,45,47] One low risk of bias observational study reported no differences in difficulty traveling to the colonoscopy among patients who completed the preparation fewer than 6 hours (3.8%), 6 to 12 hours (5.6%), or more than 12 hours (4.9%) before the procedure.[39]

SUMMARY AND DISCUSSION

KEY FINDINGS AND STRENGTH OF EVIDENCE

Key Findings and Strength of Evidence

- Hospital- or population-based studies have reported that the risk of aspiration serious enough to require hospitalization during colonoscopy is very low (1 in 1000 or less). However, these studies have not documented NPO status and it is possible that the low rates are driven by more individuals having longer rather than shorter NPO status.

- In 3 RCTs and 2 observational studies (total n=2,318) comparing shorter NPO status to NPO status of at least 8 hours, no aspiration events were reported. Bowel preparation was completed at least 2 hours prior to colonoscopy in 2 studies and at least 3 hours prior to colonoscopy in one study. Another study allowed clear liquids up to 3 hours prior to colonoscopy and the remaining study only reported that bowel preparation was completed in the morning for an afternoon colonoscopy.

- One small RCT (n=113) reported a significantly lower percentage of rescheduled colonoscopies in the split-dose group compared to 2 groups that completed preparation the evening before the colonoscopy, although different preparation agents were used in the 3 groups. No studies reported on other resource use outcomes including unused procedure slots or increased volume of procedures by NPO status.

- Few studies assessing NPO status specified adverse events associated with colonoscopy as an outcome of interest and therefore adverse events may be underreported.

- Time from completion of colonic preparation to colonoscopy of 1 to 6 hours is associated with greater bowel preparation quality than time intervals of greater than 8 hours. Of 24 studies comparing split-dose versus non-split-dose preparation, 20 reported higher quality of bowel preparation with split-dose.

- Completion rate was not significantly different between NPO status groups in 5 RCTs; one large observational study reported a greater completion rate with shorter NPO status. Results were mixed for diagnostic yield and adenoma detection rate with no consistent findings based on NPO status. One study reported no documented complications of bowel perforation; no study reported on false negative colonoscopy.

- Among studies reporting adherence to the bowel preparation regimen, time lost from work, or sleep disruption, results were mixed with no clear benefit of split-dose regimens over same day regimens.

- Studies of NPO status typically excluded patients with serious comorbidities.

- For our co-primary outcomes, strength of evidence was low for aspiration and insufficient for rescheduled colonoscopies. For secondary outcomes, strength of evidence was moderate for completion rate based on pooled results from 5 RCTs, low for adenoma

detection rate based on pooled results from 3 observational studies, and insufficient for diagnostic yield, bowel perforation, and false-negative colonoscopy (Appendix D).

DISCUSSION

Colonoscopy is now the most frequently performed procedure in the US.[57] The indications for colonoscopy include diagnostic evaluation of symptoms, screening, and surveillance. The goals of a successful colonoscopy program are safe and high-quality colonoscopic exams. Challenges to these goals include limited colonoscopy capacity, complexity of patient scheduling, and adequate bowel cleansing to ensure a high-quality exam. Quality of bowel preparation may be improved by administering the purgative agent closer to the time of colonoscopy, a practice widely adopted by the gastroenterology community in the form of split-dose preparation. However, optimizing bowel preparation quality needs to be balanced against potential increased risk of adverse events related to shorter duration of NPO status prior to colonoscopy.

This systematic review was conducted to review the evidence on the relationship between timing of NPO and the incidence of aspiration and colonoscopy rescheduling. Other outcomes included other anesthesia-related harms, bowel preparation quality, colonoscopy quality measures, resource use, and patient satisfaction.

NPO Status and Aspiration Requiring Hospitalization

The most important potential risk of a shorter NPO duration is aspiration requiring hospitalization. The overall reported risk of aspiration events serious enough to require hospitalization during colonoscopy is extremely low. A population-based study in the US reported that between 0.1% and 0.14% of adults age 66 and older (mean = 75 years) had an aspiration requiring hospitalization during colonoscopy. Aspiration requiring hospitalization reported in adults of younger age was much lower. Although aspiration risk appears to be related to deep sedation, it is unknown if other factors, such as patient comorbidities, may be confounding that relationship. We found 5 studies (n=2,318) reporting no episodes of aspiration or sedation-related complications with NPO durations as low as 2 to 4 hours. One additional RCT (n=125) reported a single aspiration event but NPO status was 4 hours or less in both study groups. The “tolerable” rate of aspiration threshold for individuals undergoing an elective procedure that could potentially be modified by NPO status is not known. However, as with all procedures, adverse events will not be zero and the reported percents of aspirations requiring hospitalization events are of similar magnitude to other commonly accepted adverse effects of similar severity encountered in other procedures. Although the studies enrolled a total of 2,443 patients, the numbers may be still too small to assess for a rare outcome such as aspiration. We found 7 studies assessing other harms related to colonoscopy but none of the harms were related to timing of NPO prior to colonoscopy.

Gastric volume and acidity are regarded as markers of potential aspiration risk and severity. We found 2 studies that showed no difference in gastric volume with shorter (less than 2 hours before colonoscopy) versus overnight duration of NPO status prior to colonoscopy.[14,31] Other studies of NPO status and gastric volume/pH before endoscopy or surgery also reported no differences. A 1996 study measured volume and pH of gastric aspirate in 88 patients undergoing endoscopy.[58] Patients were randomly assigned to an overnight fast (both food and fluids) or consumption of 330 ml water at 7:30 am on the day of the procedure (with no food after

midnight). The mean time from the fluid intake until endoscopy was 117 minutes. There was no significant difference between the 2 study groups in gastric volume (12.5 ml in the fluid intake group, 10.0 ml in the fasting group) or pH (2.0 in both groups). A subsequent study found no difference in gastric volume or pH between groups of patients assigned to drink 200 ml of water or full fat milk 90 minutes before endoscopy.[59] Similarly, a study of 126 patients scheduled for elective surgery with general anesthesia found no difference in gastric fluid volume or pH between groups of patients who drank 300 mL of clear liquid of their choice 2 hours before the procedure and those who continued to fast after midnight.[60] These results suggest that gastric volume and acidity do not differ whether water or other liquids are consumed 2 hours prior to a procedure compared to longer NPO durations.

It is important to note that not all aspirations are clinically significant pulmonary aspirations and many authors may include passive regurgitation. Warner et al[61] outlined the diagnostic criteria for pulmonary aspirations as follows: 1) the presence of bilious secretions or particulate matter within the tracheo-bronchial tree by direct suctioning or by fiberoptic bronchoscopy, or 2) after the episode of passive regurgitation, postoperative chest radiograph demonstrated a new infiltrate that did not exist in the preoperative chest radiograph or on physical examination and that developed postoperatively within 24 hours. Using these criteria, a large population-based study reported a 4 year retrospective analysis (2001-2004) of perioperative pulmonary aspiration events.[62] Of 99,441 surgical cases in adults performed with anesthesia, 14 had aspiration events for a rate of 1 in 7,103 or 0.014%. Ten of the 14 cases (70%) were the result of improper anesthesia technique. This suggests that the true risk of pulmonary aspiration may be lower than 1 in 1000. Studies of a US Medicare population,[54] outpatients from 3 hospitals in Australia,[55]and a single hospital in Italy[56] provide supporting evidence. For aspiration events serious enough to require hospitalization, the risk may be as low as 0.01%. These risks need to be weighed against the benefit of shorter NPO.

The concern shared by anesthesia providers is the risk of aspiration due to short duration between administration of purgative and the procedure. This concern is addressed by the American Society of Anesthesiology (ASA) guideline that recommends 2 hours of NPO prior to moderate sedation.[10] Adherence to this guideline would permit use of split-dose regimens and reduce procedure cancellations due to patient oral ingestion at intervals greater than 2 hours prior to a procedure. However, based on responses from 55 VA chiefs of anesthesiology in March 2014, anesthesiologists across VHA appear to have differing policies and practices regarding NPO for elective procedures. For example 38% stated they require NPO after midnight, 15% require NPO for 6 hours, 11% require NPO for 6 hours for food and 4 hours for clear liquids (including 1 liter of bowel preparation solution), 32% require NPO for 6 hours for food and 2 hours for clear liquids (including 1 liter of bowel preparation solution), 2% require NPO for 6 hours for food and one hour for clear liquids (including 1 liter of bowel preparation solution), and 4% don't have a rule for NPO status for gastrointestinal procedures.(Personal Communication, Art Wallace, March 2014)

Possible reasons for not adhering to the ASA guidelines are concerns that laxatives may not be treated similar to ingestion of clear liquids and that the volume of laxative may be larger than that of other clear liquids. Studies that evaluated ingestion of clear liquids up to 2 hours prior to anesthesia administration suggest that this ingestion does not affect stomach volume or pH compared to earlier ingestion.[14,31,58-60] Other reasons for non-adherence of anesthesia providers to the ASA guidelines need to be explored.

NPO Status and Adequacy of Bowel Cleansing

For an effective and safe colonoscopy program, the adequacy of bowel cleansing is paramount. We found 39 studies (n=22,629) that reported the association of duration of NPO and quality of preparation comparing shorter (1 to 6 hours) versus longer duration (8 to 12 hours) between bowel preparation and colonoscopy. Thirty-one reported higher quality of bowel preparation with a shorter interval between preparation and colonoscopy and 8 reported no significant difference.

We were most interested in studies that reported NPO of < 4 hours compared to longer durations of NPO, as this is likely the most commonly used duration of NPO with the newer split-dose bowel preparations. We found 23 studies (RCTs or observational) that compared or included duration of NPO of < 4 hours to longer durations (usually > 8 hours). Nineteen reported a higher quality preparation with shorter duration (< 4) of NPO, 3 showed no difference, and 1 did not report on prep quality.

Multiple gastroenterology societies in the US and Europe have established guidelines in response to the recognized importance of adequate bowel preparation quality. The US Multi-Society Task Force on Colorectal Cancer, the European Society of Gastrointestinal Endoscopy and others[5,7,63] now recommend using split-dose regimens for bowel preparation, such that the second dose of laxative is administered 4 to 6 hours before the colonoscopy with completion at least 2 hours before the exam.

Inadequate bowel preparation has multiple adverse consequences, both direct and downstream, that can broadly be categorized as the following:

1) Efficacy: Inadequate bowel preparation is associated with lower adenoma detection rates and lower cecal intubation rates which are risk factors for missed lesions, thus reducing the effectiveness of colonoscopy.[64,65]

2) Safety: Inadequate bowel preparation is associated with increased risk of electrocautery, longer procedure time, and reduced patient comfort, which can reduce the safety of colonoscopy.[66]

3) Capacity: Demand for colonoscopy is high given both screening and diagnostic indications, and the current capacity is inadequate to meet this demand. The VHA devotes a large amount of resources to improve the colonoscopic capacity and many VA facilities rely heavily on fee-basis and non-VA care to meet the colonoscopic capacity. Hence, maximizing capacity is of key importance in the VHA. Inadequate bowel preparation may reduce the colonoscopic capacity through cancelled procedures and resources required for rescheduling. Additionally, this may lead to poor patient satisfaction and delays in care. One study reported that for every 1% increase in inadequate bowel preparation, the cost of colonoscopy delivery increased by 1%.[3]

4) Effectiveness: Inadequate bowel preparation impairs a thorough inspection of the colonic mucosa and results in incomplete exams. Patients with incomplete exams may never reschedule, or at the very least, have delayed diagnostic evaluation due to rescheduling. Delays in diagnostic or screening exams may reduce the effectiveness of a colonoscopy

> program. The current VHA directive requires a colonoscopy within 60 days of a positive FOBT. Inadequate bowel preparation resulting in rescheduling colonoscopy may contribute to delays in colonoscopy. Unsatisfactory quality of cleansing also results in physicians recommending a repeat colonoscopy exam at a shorter interval compared to intervals recommended by multi-society guidelines. In one study, bowel preparations of fair quality were associated with more aggressive follow-up intervals in 60% of average risk asymptomatic individuals undergoing screening colonoscopy.[67]

Furthermore, quality of bowel preparation, adenoma detection rate, and cecal intubation rate are proposed quality measures for colonoscopy programs, at the facility and individual level. These have been adopted by the Centers for Medicare & Medicaid Services (CMS) as metrics in the physician quality reporting system (PQRS), associated with financial incentives, and starting in 2015, financial penalties to eligible practices.[68]

There are multiple bowel preparation agents available in the US, all with a single goal of achieving high quality of colon cleansing. Recent studies have focused on the different regimens of administration of the purgative and clearly demonstrate that, for better cleansing, splitting the dose, in which the laxative is split into two doses taken the day before and the day of colonoscopy, is superior to administering the entire laxative the night before the colonoscopy.[4] A recent meta-analysis of 29 studies comparing split-dose regimens to night-before regimens reported a rate difference of 22% (95%CI 16%, 27%) in achieving better cleansing with split-dose prep.[69] The study also found that the time interval between last administration of laxative and colonoscopy was the main factor driving the effect. The risk difference between split and non-split preparation was maintained when colonoscopy was performed within 3 hours from the end of laxative intake, but decreased after 4 to 5 hours (risk difference 18%), and was not statistically significant when the time interval was >5 hours. The authors also found higher compliance with the split-dose regimen (risk difference 9.4%; 95%CI 0.06, 0.13) regardless of type of laxative.

NPO Status and Other Outcomes

We also examined the effect of variable timing of NPO on resource use, such as no-shows, cancellation, rescheduling, and other missed opportunities. Hypothetically, a shorter duration of NPO could improve capacity, if it reduced cancellations or aborted procedures due to poor preparation. On the contrary, a shorter duration of prep could be more difficult to adhere to, or to tolerate, resulting in missed appointments that would need to be rescheduled. We found one study (insufficient evidence) that reported fewer rescheduled colonoscopies in the shorter NPO status group and no studies reporting on other resource use outcomes.

Eleven studies reported on adherence to preparation or colonoscopy. Of these, 2 reported significantly higher adherence to preparation regimens with NPO of $\geq$ 1.5 hours versus > 8 hours and NPO of < 3 hours versus > 8 hours respectively.[13,21] The other 9 studies reported no difference in adherence to colonoscopy or to the preparation with variable duration of NPO. Patient satisfaction and willingness to repeat the preparation was higher with shorter duration of NPO, while less sleep loss was reported in 2 studies with NPO durations of $\geq$ 5 hours versus > 8 hours and $\geq$ 3 hours versus > 8 hours respectively. Of note, most studies had broad time ranges for duration of NPO status, and we were unable to derive a mean or median estimate.

Summary of Evidence

In summary, we found low-strength evidence that procedure-related harms, such as risk of aspiration or other anesthesia-related harms from colonoscopy are not related to duration of NPO status prior to colonoscopy (Appendix D). Aspiration requiring hospitalizations among individuals undergoing colonoscopy is very low (1 in 1000 or less) and consistent in magnitude with complications of similar severity occurring during elective procedures. It is important to acknowledge that in the US there are no systematic tracking methods to track complications from colonoscopy, especially related to NPO status, and there is the possibility of under- or mis-reporting. We found evidence that shorter duration of NPO status prior to colonoscopy (< 4 hours) is associated with higher-quality bowel cleansing compared to longer duration of NPO prior to colonoscopy (> 8 hours). We found moderate strength evidence that shorter duration of NPO is not associated with higher rates of completion, and insufficient or low-strength evidence that shorter duration of NPO affects adenoma detection rates, diagnostic yield, or false negative colonoscopy (Appendix D). While there are many studies evaluating the association of bowel preparation quality and colonoscopy yield and quality indicators, there is limited evidence showing the direct relationship between duration of NPO and these outcomes. Only one study reported the effect of NPO status prior to colonoscopy on resource use. Results were mixed for patient adherence and patient satisfaction.

LIMITATIONS AND APPLICABILITY

Our findings are limited by the relative paucity of information directly addressing the key questions. None of the studies were directly designed to address the key questions. Instead we used studies that primarily evaluated the effect of different regimens on bowel preparation to assess the effect of varying NPO status on the outcomes of interest for this report. Except for bowel preparation quality, few studies reported our outcomes of interest. In fact, only 5 studies reported on aspiration according to NPO status and one reported on rescheduling (our co-primary outcomes). Most studies examining different bowel preparation and NPO status were not adequately powered to detect aspirations requiring hospitalizations or designed to assess rescheduling due to NPO status.

Hospital- or population-based studies that reported on aspiration for individuals undergoing colonoscopy with sedation did not report NPO status. The largest study, and the only one conducted in the US, reported on patients age 66 and older (mean age 75 years). The applicability of results to younger individuals is uncertain, though the reported percentage may overestimate aspiration risk. Participants likely had wide ranges of NPO status timing, especially time from NPO to colonoscopy longer than 2 to 4 hours. Thus it is difficult to determine from these studies if and by how much aspiration risk may be effected by varying NPO status.

Definitions of aspiration methods for diagnosing aspiration varied. We were limited to reporting what was provided in published articles.

Many studies excluded patients with serious comorbidities. Few studies recorded mean or range of NPO status timing (including time of last ingestion of water, clear liquids, or bowel preparation substance). Furthermore, only 26 of 40 included studies reported on use of sedation during colonoscopy.

Populations enrolled in eligible studies were broadly applicable to many individuals undergoing elective colonoscopy in the United States. Eligible studies typically included patients 45 to 65 years with approximately 50% of patients enrolled in studies done in the US. Nearly one-half of patients were male and two-thirds of colonoscopies were performed for cancer screening. The largest study reporting on aspirations requiring hospitalization was completed in a US Medicare population. However, aspiration by NPO status was not provided in this study and few other studies were adequately designed to directly assess the role of NPO status on aspirations requiring hospitalizations or colonoscopy rescheduling.

RESEARCH GAPS/FUTURE RESEARCH

Our findings indicate important gaps including: 1) accurate assessment of aspiration requiring hospitalization and other serious anesthesia-related adverse events according to NPO status, 2) extent of and reasons for variation in anesthesia NPO status practice and policy, 3) effect of NPO status on procedure rescheduling and patient adherence and satisfaction, and 4) reasons for reduced patient adherence to recommendations for NPO status and bowel preparation.

Future studies to close these knowledge gaps could improve care quality. Studies are needed that systematically assess duration of NPO status in relation to timing of colonoscopy and record serious adverse events, such as aspiration requiring hospitalization, with standardized diagnostic criteria. This can be done through setting up prospective registries of Veterans undergoing colonoscopy to record timing of preparation, duration of NPO, and sedation procedures, and then tracking adverse events over the next 48 to 72 hours. Reporting of anesthesia-related complications is required per VHA and Joint Commission policy, and most VA medical centers have electronic reporting systems in place. Future efforts could be directed towards developing standard methods to collate this information and initiate analyses to assess the association of duration of NPO and colonoscopy outcome. In this regard, special populations at higher risk of aspiration and other anesthesia-related outcomes would be of particular interest, such as elderly patients, patients with high comorbidities, and those with disabilities that limit ability to follow and complete the bowel preparation instructions.

Future studies are also needed to determine and understand variability in NPO duration policies and practices across VA (especially practices that may not adhere to national society guidance statements) and to implement interventions to reduce variation. There is also a need to evaluate the effect of variable durations of NPO status prior to colonoscopy on patient satisfaction, adherence to colonoscopy, and impact on endoscopy scheduling processes, including delays in timely receipt of colonoscopy. A better understanding of why some patients do not adhere to NPO status recommendations and methods to improve communication and adherence are needed. Alternative scheduling methods, including later but same day colonoscopy, could also be evaluated to reduce “cancellations” due to NPO non-adherence. Colonoscopy without moderate or deep sedation, commonly used in other developed countries, could be offered to some patients, though concerns exist regarding patient comfort and colonoscopy quality.

National and international multi-society (gastroenterology, gastrointestinal endoscopy, colon and rectal surgery, and gastrointestinal and endoscopic surgery) guidelines[5,7,63] now recommend using split-dose regimens for bowel preparation, such that the second dose of laxative is administered 4 to 6 hours before the colonoscopy, with completion at least 2 hours before the exam. Additionally, the ASA guidelines support NPO of 2 hours after clear liquids.[10] However,

there is a need for larger studies comparing shorter durations of NPO prior to colonoscopy (such as 2 to 4 hours) to longer intervals of NPO prior to colonoscopy (such as ≥ 6 hours) that directly assess for colonoscopy effectiveness (such as detection rate of adenoma and neoplasia, completion rate) and safety outcomes (including aspiration). We also need studies evaluating the effect of variable duration of NPO status prior to colonoscopy on patient satisfaction, adherence to colonoscopy, and impact on endoscopy scheduling processes, including delays in timely receipt of colonoscopy.

Finally, evidence-based multi-society consensus guidelines are needed that bring together patient representatives and members from anesthesia, gastroenterology, and general medicine. Recommendations for NPO status also affect other gastroenterology procedures as well as procedures performed by other specialties (*eg,* pulmonary and cardiology). Therefore, including representatives across a wide range of disciplines and procedures would be helpful in developing evidence-based recommendations targeted to specific procedures and likely benefits and harms. Important items in guideline development include determining the "clinically important" balance between critical outcomes to anesthesiologists, gastroenterologists (and other specialty groups performing procedures), and patients, including aspiration rates due to NPO status, colonoscopy quality measures, resource use, and patient satisfaction and adherence.

CONCLUSIONS

Aspiration incidence requiring hospitalization during colonoscopy with moderate or deep sedation is very low and on the order of magnitude commonly accepted for adverse effects of similar clinical importance due to other elective procedures. Participants in hospital- and population-based studies likely had wide ranges of timing from NPO to colonoscopy and many were likely longer than 2 to 4 hours. No study documenting NPO status found that shorter NPO status prior to colonoscopy increased aspiration risk. We did not find direct evidence of the effect of NPO status on colonoscopy rescheduling. Shorter time from completion of colonic preparation to colonoscopy is associated with greater bowel preparation quality than longer time intervals.

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