

Evidence-based Synthesis Program (ESP)

Outcomes by Duration of NPO Status Prior to Colonoscopy

A Systematic Review of the Evidence

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Disclosure

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Evidence-based Synthesis Program (ESP)

VA Evidence-based Synthesis (ESP) Program Overview

- **Sponsored by VA Office of R&D and Quality Enhancement Research Initiative (QUERI).**
- **Established to provide timely and accurate syntheses/reviews of healthcare topics identified by VA clinicians, managers and policy-makers, as they work to improve the health and healthcare of Veterans.**
- **Builds on staff and expertise already in place at the Evidence-based Practice Centers (EPC) designated by AHRQ. Four of these EPCs are also ESP Centers:**
 - Durham VA Medical Center; VA Greater Los Angeles Health Care System; Portland VA Medical Center; and Minneapolis VA Medical Center.

Evidence-based Synthesis Program (ESP)

- **Provides evidence syntheses on important clinical practice topics relevant to Veterans, and these reports help:**
 - develop clinical policies informed by evidence,
 - the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
 - guide the direction for future research to address gaps in clinical knowledge.
- **Broad topic nomination process – e.g. VACO, VISNs, field – facilitated by ESP Coordinating Center (Portland) through online process:**

<http://www.hsrd.research.va.gov/publications/esp/TopicNomination.cfm>

Evidence-based Synthesis Program (ESP)

- **Steering Committee** representing research and operations (PCS, OQP, ONS, and VISN) provides oversight and guides program direction.
- **Technical Expert Panel (TEP)**
 - Recruited for each topic to provide content expertise.
 - Guides topic development; refines the key questions.
 - Reviews data/draft report.
- **External Peer Reviewers & Policy Partners**
 - Reviews and comments on draft report
- **Final reports posted on VA HSR&D website and disseminated widely through the VA.**

<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

Evidence-based Synthesis Program (ESP)

Current Report

Colonoscopy Outcomes by Duration of NPO Status Prior to Colonoscopy with Moderate or Deep Sedation (August 2015)

Full-length report available on ESP website:

<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

Background

- 14 million colonoscopies performed in the US annually
- Colonoscopies require bowel preparation for cleansing to sufficiently visualize the colonic lining
- To maximize cleansing, bowel preparation is split into two sessions (split dose): evening prior to colonoscopy and morning of the colonoscopy
- Some level of sedation (typically moderate) is used

Background

- Goal set by US multi-society on colon cancer screening for adequate preparation: $\geq 85\%$ of cases
- Monitoring of preparation quality recommended by most recent VHA CRC Screening Directive (December 2014)
- Recent GI multi-society guidelines recommend using split preparation with 2-4 hours between last dose of purgative and colonoscopy

Rex DK et al. Quality indicators for GI Endoscopic procedures. AJG 2015;110-72-90

http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=3068

Johnson DA et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc. 2014;80(4):543-62

Background

- 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
 - 6 hours for a light meal (*ie*, toast and clear liquids)

Background

- An optimal bowel preparation and NPO status seeks to balance:
 - 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)

Study Aims

- To review the evidence on relationship between timing of NPO and incidence of aspiration, other anesthesia related harms, and colonoscopy outcomes

PICOTS

- 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

PICOTs (cont)

- *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

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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)?

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Key Questions

- **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?

Search Strategy

- MEDLINE (OVID) for articles published from 1990 through October 2014
- Any study design, with information on duration of NPO
- Limited to human subjects and published in the English language
- Also searched reference lists of guidelines, existing reviews, reference suggestions from stakeholders and TEP members

Inclusion Criteria

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

Risk of Bias Assessment

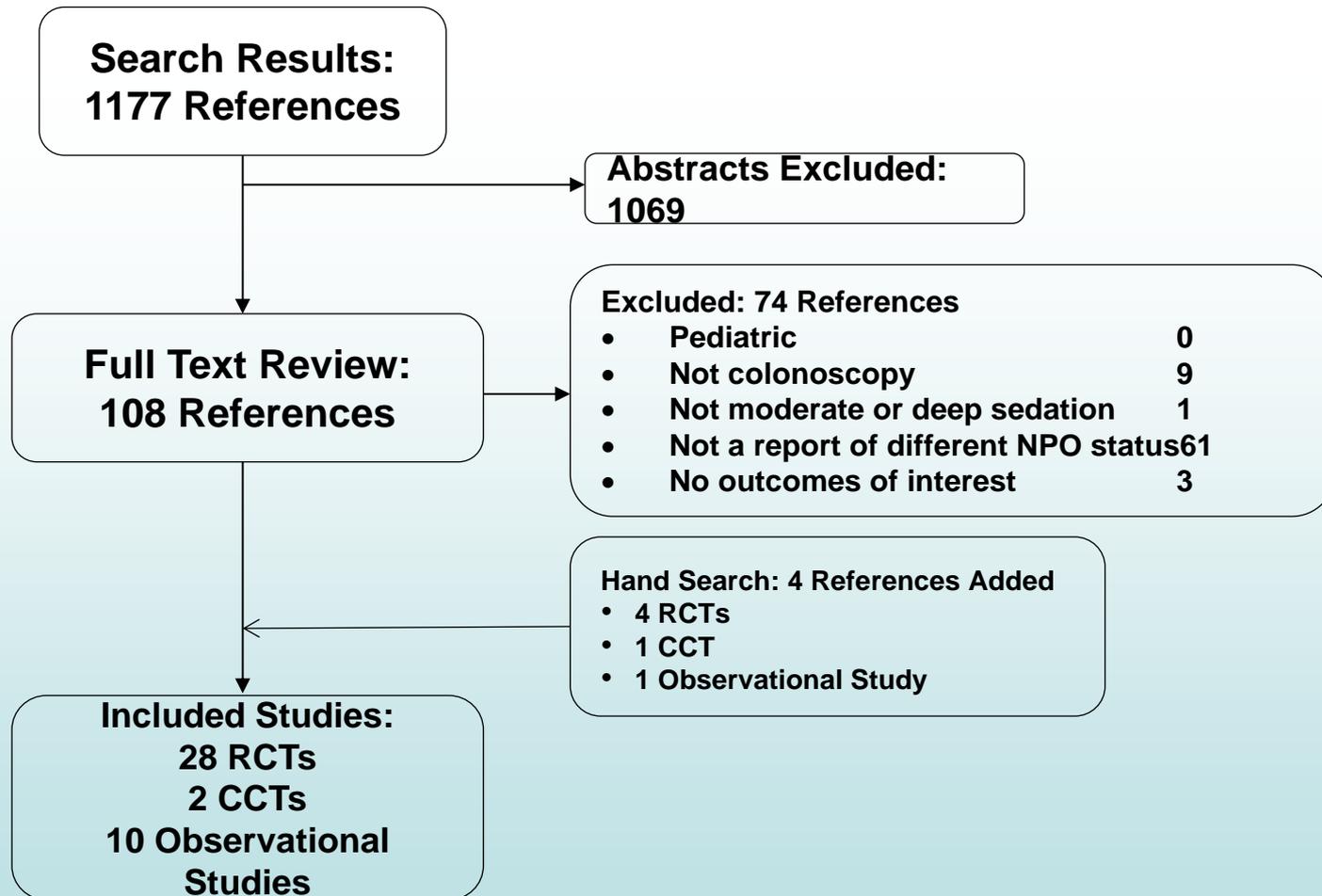
- For randomized controlled trials (RCTs) and controlled clinical trials (CCTs): allocation sequence generation, allocation concealment, blinding, completeness of outcome reporting, and selectiveness of outcome reporting
- For observational studies: population (consecutive or not), analysis of findings (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

Rating the Body of Evidence

- Overall strength of evidence for *primary* and *secondary* outcomes rated: insufficient, low, moderate, or high
- Rating considers: risk of bias, consistency, directness, and precision*
- Separate ratings for RCTs and observational studies

*Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions--Agency for Healthcare Research and Quality and the Effective Health-Care Program. *J Clin Epidemiol.* 2010;63(5):513-23.

Literature Flow Chart



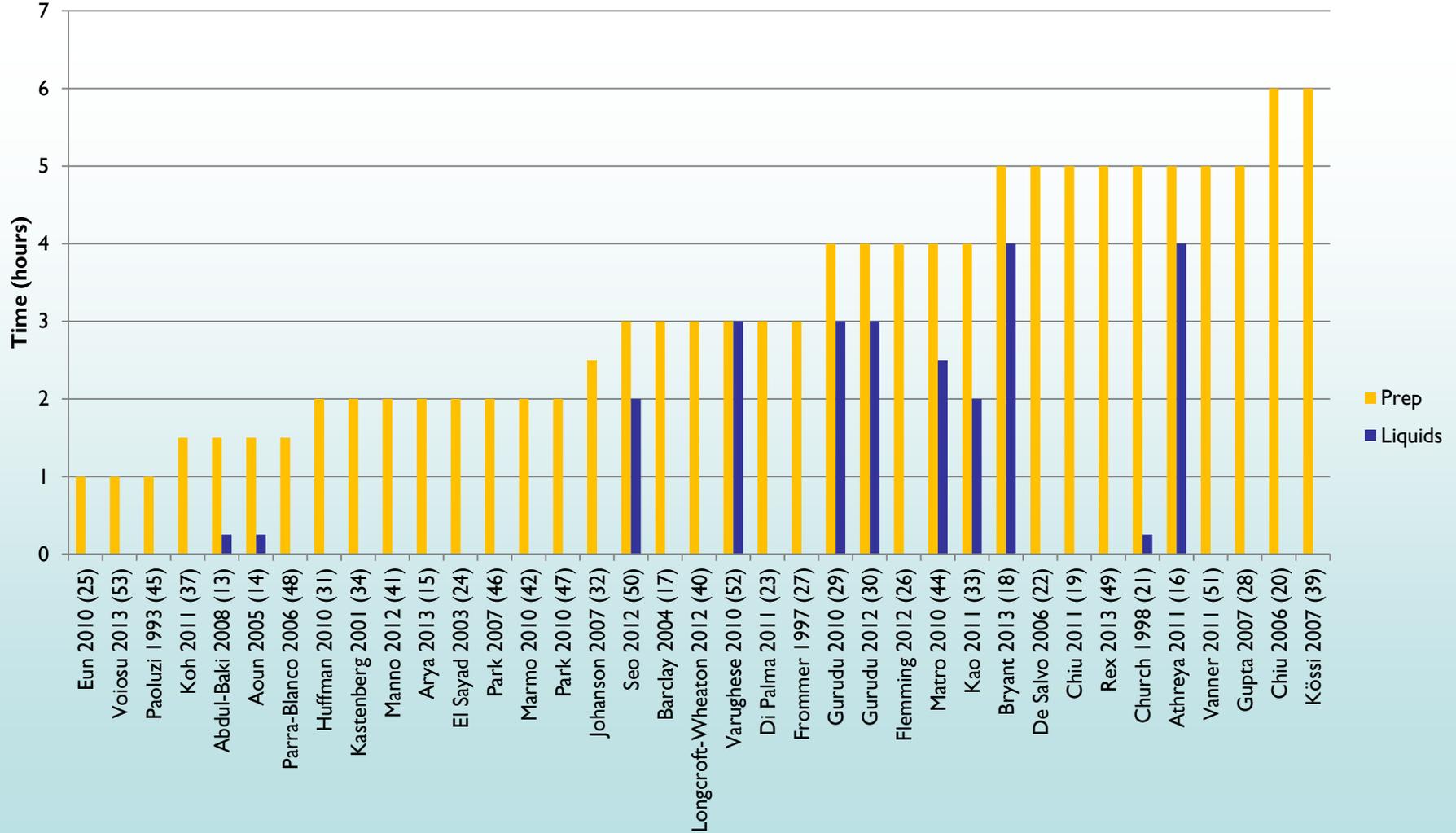
Results

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 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

Results

- For each study we identified a minimum time from the end of preparation until the procedure
- We also extracted information about timing of liquids allowed prior to the procedure from the 11 studies that reported that information

Results



Results KQ1: Aspiration Risk

- Six studies reported on aspiration (N=136 to 1,345);
2 low risk of bias, 4 moderate risk of bias
- 5 of 6 reported no aspiration events
- One low risk of bias RCT (n=125) reported 1 aspiration event requiring hospitalization during colonoscopy under moderate sedation. The patient was obese (BMI = 40 kg/m²) and assigned to consume half of the preparation agent 4 hours before.
- **Overall low strength evidence that shorter duration of NPO is not associated with higher incidence rate of aspiration.**

Results KQ1: Rescheduled Colonoscopies

- One moderate risk of bias RCT (n=113)
- Completed prep in AM: 3%
- Completed prep night before: 8% (PEG) and 24% (Caster oil solution)
- **Overall strength of evidence was insufficient that duration of NPO is associated with rescheduled colonoscopies**

Results

Study NPO Status (Intervention/ Control)	Aspiration, n/N (%)		Rescheduled colonoscopies, n/N (%)	
	NPO group 1	NPO group 2	NPO group 1	NPO group 2
Gurudu 2010 ²⁹ NPO status 1: ≥ 4 hours NPO status 2: > 8 hours	No episodes of bronchoaspiration were recorded, including in the procedures performed in patients taking same-day bowel preparation		NR	NR
Huffman 2010 ³¹ NPO status 1: ≥ 2 hours NPO status 2: > 8 hours	None of the patients in any group had clinical evidence of aspiration during their procedures		NR	NR
Kolts 1993 ³⁸ NPO status 1: Hours unclear (last dose 6 am) NPO status 2: > 8 hours NPO status 3: > 8 hours	NR		1/34 (3%)	Group 2: 3/38 (8%) Group 3: 10/41 (24%) (P = .011)
Manno 2012 ⁴¹ NPO status 1: 2 hours NPO status 2: > 8 hours	No major complications related to sedation		NR	NR
Mathus-Vliegen 2013 ⁴³ NPO status 1: Hours unclear (Split-dose, PM exam) NPO status 2: > 8 hours	No events during 30-day period (from charts of patients and a complication database)		NR	NR
Matro 2010 ⁴⁴ NPO status 1: 4 hours (am prep only) NPO status 2: 4 hours (pm/am prep)	1.6 (1/62) Aspirated during procedure	0/54	NR	NR
Varughese 2010 ⁵² NPO status 1: ≥ 3 hours NPO status 2: > 8 hours	No sedation complications		NR	NR

Results KQ1: Other Harms

- Seven studies (6 moderate risk of bias, 1 low risk of bias) reported on other harms.
- 4 studies reported no adverse events
- Three studies reported adverse events ($\leq 1\%$ of procedures):
 - LGI bleeding in NPO >8 hours
 - MI (NPO >8 hours)
 - Pancreatitis (NPO 5-9 hours)
 - Non cardiac chest pain (NPO >8 hours)

NPO Status and Gastric Volume

- Two studies (n=141 and 712; one low risk of bias, one moderate risk of bias) tandem EGD
- 1.5 hours vs. overnight NPO: Similar gastric volume
- 2 hours before vs. day before NPO: Similar gastric volume

NPO Status and Gastric Volume

	N	Gastric volume
EGD only (NPO P MN)	411	14.6 ml
Evening before dosing	47	20.2 ml
Split dose (2 hour before COL)	254	19.7 ml

Huffman et al. GIE 2010;72:516-22

Hospital or Population Based Studies on Aspiration during Colonoscopy

Study	N	Rate of aspiration for COL	Notes
Cooper GS et al. JAMA Int Med 2013;22:551-6	165,527 (CMS pts)	0.10% for moderate sedation 0.14% for deep sedation	Duration of NPO not reported
Viiala CH et al. Intern Med J2003;33:355-9	23,508 (3 hospitals in Australia)	0.004% with GA	Duration of NPO not reported
Agostoni M et al GIE 2011;74:266-75	3,155 (Italy)	0.16% (moderate and deep sedation)	Aspirations requiring hospitalizations not reported. Allowed clear liquids up to 2 hours before the procedure

Results KQ2: Colonoscopy Outcomes

- Thirty-nine studies (28 RCTs, 2 CCTs, and 9 observational studies)
- Different rating scales were used
- 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
- Our study focus was secondary outcomes: completion rates, diagnostic yield, ADR, total procedure time, and withdrawal time

Results KQ2: Diagnostic Yield (n=3)

	NPO group 1 % (n/N) or mean (SD)	NPO group 2 % (n/N) or mean (SD)
<p>Chiu 2006 NPO status 1: 6-8 hours NPO status 2: > 8 hours Note: lesions detected in first and second colonoscopies</p>	<p>Total lesions 2.78 (0.29) Proximal 1.52 (0.22) Advanced 0.87 (0.13)</p>	<p>Total lesions 1.90 (0.27) P = .028 Proximal 0.97 (0.24) P = .094 Advanced 0.55 (0.10) P = .056</p>
<p>Matro 2010 NPO status 1: 4 hours (am prep only) NPO status 2: 4 hours (pm/am prep)</p>	<p>"Findings" per patient 0.70 (1.3)</p>	<p>"Findings" per patient 0.46 (1.0) P = .047</p>
<p>Parra-Blanco 2006 NPO status 1: 1.5-7 hours (PEG) NPO status 2: 1.5-7 hours (NaP) NPO status 3: > 8 hours (PEG) NPO status 4: > 8 hours (NaP)</p>	<p>Groups 1 & 2 Any polyp 52 (46/88) Flat lesions 22 (19/88) Protruding polyps 40 (35/88)</p>	<p>Groups 3 & 4 Any polyp 45 (40/89) Flat lesions 9 (8/89) P = .02 Protruding polyps 42 (37/89)</p>

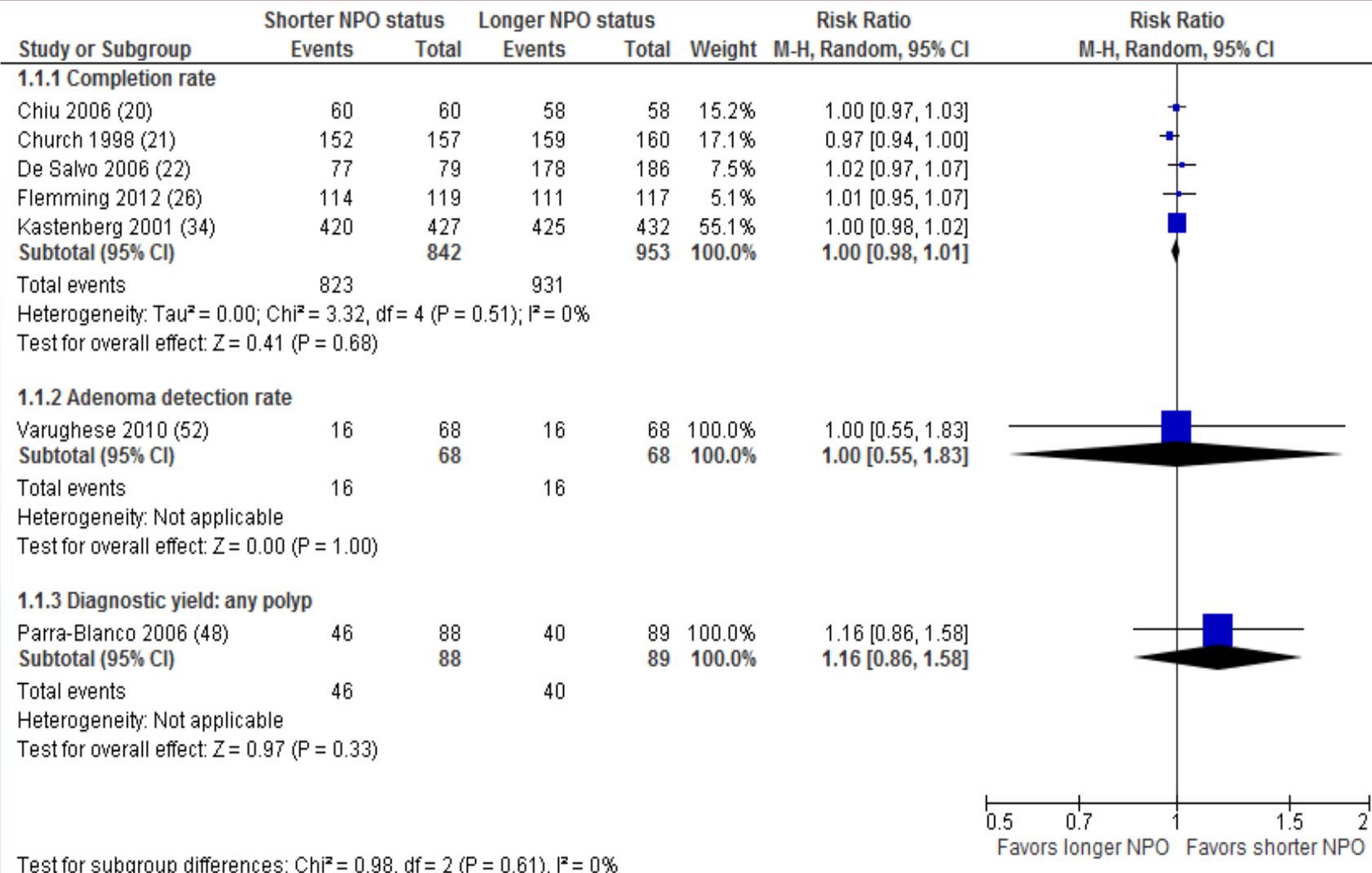
KQ2: Completion Rates

- 11 studies
- Results from 5 RCTs providing sufficient information to permit pooling found similar completion rates between shorter and longer NPO status (RR 1.00 [95%CI 0.98, 1.01])
- One RCT (n=895) reported an overall completion rate of 95%
- An 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%)
- One RCT, where both groups completed bowel preparation 4 hours before colonoscopy, reported a similar completion rate for the single dose (98%) or split-dose (100%) groups
- Three studies provided completion rates but did not report separate results for the NPO status groups: completion rates were 96%, 99% and 95%

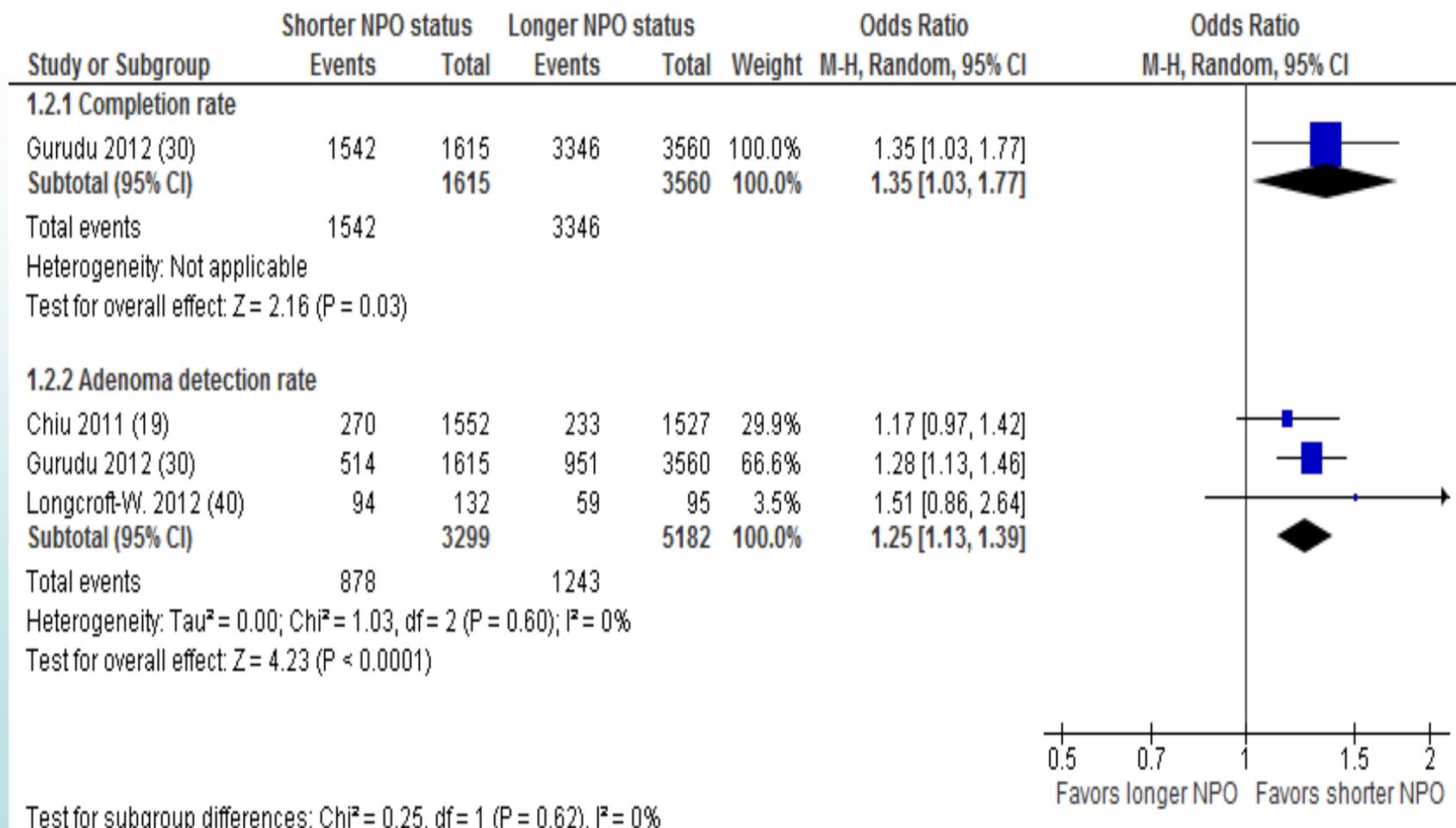
KQ2: Adenoma Detection Rate

- 7 studies:
 - 4 reported similar ADR
 - 2 reported higher ADR with shorter NPO (4 hours and 5-9 hours NPO compared to evening prior, respectively)
 - 1 (NPO of 4 hours in both groups) found higher ADR in morning-only preparation group

KQ2: Completion Rates, ADR, and Diagnostic Yield - Outcomes from RCTs



KQ2: Completion Rates, ADR and Diagnostic Yield - Outcomes from Observational Studies



KQ2: Procedure Time, Withdrawal Time and Cecal Intubation Time

- Total procedure time:
 - 3 studies (2 RCTs, 1 CCT)
 - Similar results for shorter and longer NPO
- Cecal intubation time:
 - 4 studies (2 RCTs, 2 CCTs)
 - 1 reported shorter cecal intubation time with shorter NPO, 3 did not
- Withdrawal time:
 - 5 Studies (3 RCTs, 2 CCTs)
 - 1 reported shorter withdrawal time with shorter NPO, similar results in 4

KQ3: NPO Status on Resource Use

- No studies reported resource use (costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures)
- Although some studies reported inadequate bowel preparation quality, they did not report whether the colonoscopy was repeated

KQ4: Patient Adherence

- No consistent findings for adherence:
 - Better adherence to bowel preparation with split dose vs day before (4 RCTs)
 - Similar adherence - split dose vs same day (3 RCTs)
 - Better adherence if last dose completed closer to time of colonoscopy (1 RCT, 1 Obs. study)
 - Similar adherence (< 4 hours vs > 4 hours) (1 Obs. Study)

KQ4 Patient Satisfaction

- Extracted information on elements of satisfaction that would be impacted by different schedules for bowel preparation
- Work or school time lost (5 RCTs):
 - 3 reported fewer hours of work lost with split vs. day before preparation
 - 2 reported groups were similar
- Sleep disturbance (7 RCTs, 1 Obs. Study):
 - 3 found less disturbance with split preparation
 - 5 found groups were similar

Summary

- Hospital- or population-based studies have reported the risk of aspiration requiring hospitalization during colonoscopy is very low (1 in 1000 or less)
- Duration of NPO in these studies is unknown
- 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 completed at least 2 hours prior in 2 studies and at least 3 hours prior to colonoscopy in 1 study
 - Clear liquids allowed up to 3 hours prior to colonoscopy in 1 study
 - Final study only reported that bowel preparation completed in the morning for an afternoon colonoscopy

Summary

- One small RCT (n=113) reported a significantly lower percentage of rescheduled colonoscopies in the split-dose group compared to the evening before
- No studies reported on other resource use outcomes including unused procedure slots or increased volume of procedures by NPO status
- 20 of 24 studies reported that 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

Summary

- Completion rate was similar 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
- 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

Summary

Outcome	Strength of Evidence
Shorter NPO is not associated with higher risk of aspiration	Low (3 RCTs) Insufficient (2 Obs. Studies)
Shorter NPO is not associated with higher rescheduled COL	Insufficient
Shorter NPO is not associated with higher completion rate	Moderate (6 RCTs) Insufficient (1 Obs. Study)
Shorter NPO is associated with higher ADR	Insufficient (1 RCT) Low (3 Obs. Studies)
Shorter NPO is associated with higher diagnostic yield	Insufficient (2 RCTs)

Gaps and Future Directions

- Systematically assess duration of NPO status in relation to timing of colonoscopy and record serious adverse events, such as aspiration requiring hospitalization
- Special populations at higher risk of aspiration and other anesthesia related outcomes would be of particular interest, such as elderly patients, high comorbidities, disabilities that limit ability to follow instructions and complete preparation
- Evidence-based multi-society consensus guidelines are needed that bring together patient representatives and members from anesthesia, gastroenterology, and general medicine

Evidence-based Synthesis Program (ESP)

Questions?

**If you have further questions,
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The full report and cyberseminar presentation is available on the ESP website:

<http://www.hsrd.research.va.gov/publications/esp/>