

# American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Postoperative Gastrointestinal Dysfunction Within an Enhanced Recovery Pathway for Elective Colorectal Surgery

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The primary driver of length of stay after bowel surgery, particularly colorectal surgery, is the time to return of gastrointestinal (GI) function. Traditionally, delayed GI recovery was thought to be a routine and unavoidable consequence of surgery, but this has been shown to be false in the modern era owing to the proliferation of enhanced recovery protocols. However, impaired GI function is still common after colorectal surgery, and the current literature is ambiguous with regard to the definition of postoperative GI dysfunction (POGD), or what is typically referred to as ileus. This persistent ambiguity has impeded the ability to ascertain the true incidence of the condition and study it properly within a research setting. Furthermore, a rational and standardized approach to prevention and treatment of POGD is needed. The second Perioperative Quality Initiative brought together a group of international experts to review the published literature and provide consensus recommendations on this important topic with the goal to (1) develop a rational definition for POGD that can serve as a framework for clinical and research efforts; (2) critically review the evidence behind current prevention strategies and provide consensus recommendations; and (3) develop rational treatment strategies that take into account the wide spectrum of impaired GI function in the postoperative period. (Anesth Analg 2017;XXX:00–00)

## RECOMMENDATIONS

### Definition and Incidence

1. Consider foregoing the traditional definition of ileus for the Intake, Feeling nauseated, Emesis, physical Exam, and Duration of symptoms (I-FEED) scoring system—a more functional definition of postoperative gastrointestinal dysfunction (POGD) that takes

into account the wide spectrum of signs, symptoms, and associated clinical implications.

2. We strongly recommend the implementation of enhanced recovery protocols (ERPs) to reduce the time to recovery of gastrointestinal (GI) function after colorectal surgery (CRS) to an average of 1–2 days.

### Prevention of POGD

3. We recommend active strategies to minimize the use of opioids while maintaining adequate pain control through the use of multimodal analgesia.
4. We recommend the maintenance of euolemia along with a normal salt and electrolyte balance in the perioperative period.
5. We strongly recommend against the routine use of prophylactic nasogastric tubes (NGTs).
6. We recommend the use of minimally invasive surgery when appropriate.
7. We recommend using alvimopan if opioid-based analgesia is used (its use could also be considered within an opioid-restricted ERP in CRS).
8. We recommend the use of a standardized risk-based strategy for postoperative nausea and vomiting (PONV) prophylaxis.
9. We strongly recommend immediate resumption of eating and drinking after CRS.

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For the Perioperative Quality Initiative (POQI) 2 Workgroup, see Appendix 1.

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10. We recommend the use of a combined isosmotic mechanical bowel preparation with oral antibiotics (MBP-OAB) in elective CRS.
11. Consider coffee and gum chewing as adjuncts to ERPs in promoting recovery of GI function.

### Treatment of POGD

12. We recommend placement of an NGT to relieve intractable nausea and vomiting with abdominal distension.
13. We recommend opioid minimization, ambulation, rational fluid replacement maintaining euvolemia, electrolyte repletion, and gum chewing.
14. Consider radiographic imaging with computed tomography if POGD persists beyond the seventh postoperative day (POD) or at any time based on concern for secondary causes.

One of the most important primary drivers of length of stay (LOS) after CRS is time to return of GI function.<sup>1</sup> Traditionally, delayed GI recovery was so commonplace that it was considered an unavoidable consequence of surgery justifying routine NGTs and fasting. These practices have been challenged in the modern era owing to the proliferation of ERPs.<sup>2</sup> As a result, there has been a paradigm shift in traditional perioperative management toward early initiation of oral intake regardless of the perceived return of GI function. This has led to significant improvements in postoperative outcomes. However, GI dysfunction remains one of the most common morbidities after CRS, and the current literature is ambiguous with regard to the definition of POGD, or what is typically referred to as ileus. This persistent ambiguity precludes the ability to ascertain the true incidence of the condition and study it properly within a research setting.<sup>3</sup>

Although the effects of bowel surgery on postoperative GI function (POGF) are multifactorial, a rational standardized approach focused on the known mediators can facilitate early restoration of GI function after CRS. The second Perioperative Quality Initiative (POQI) brought together a group of international experts with the objective of providing consensus recommendations on this important topic. The POQI 2 POGD group sought to (1) develop a rational definition for POGD that can serve as a framework for clinical and research efforts; (2) critically review the evidence behind current prevention strategies and provide consensus recommendations; and (3) develop rational treatment strategies that take into account the wide spectrum of impaired GI function.

## METHODS

### Expert Group

The POQI is a previously described collaborative of diverse international experts in anesthesia, nursing, nutrition, and surgery tasked to develop consensus-based recommendations in topics related to ERPs.<sup>4,5</sup> The participants in POQI were recruited based on their expertise in ERPs and perioperative medicine. Twenty-three experts from North America and Europe met in Stony Brook, New York, on December 2–3, 2016. Utilizing a modified Delphi

method, an iterative process was undertaken whereby the group initially developed a list of questions related to GI recovery after CRS, performed a literature review, and conducted a series of group sessions with structured presentation and feedback until consensus was achieved. This culminated in this consensus document. The specific wordings of the recommendation statements are based on prior work and detailed elsewhere.<sup>5</sup> We followed the process detailed by the National Institute for Health and Care Excellence.<sup>6</sup>

### Process

The POQI conference process was based on methodology utilized by the Acute Disease Quality Initiative.<sup>7</sup> Over a 3-month period before the meeting, the organizers generated topics of interest and assigned expert members of the panel to each subgroup. The subgroups were responsible for developing a list of relevant questions and conducting a literature review before the meeting. During the opening session, the subgroups presented their questions to the entire workgroup, soliciting feedback and discussion. Over the course of the 2 days in ensuing group meetings and plenary sessions, the subgroups refined the questions into a series of recommendations, which were debated, reviewed, and modified by the entire workgroup (Table 1). According to the National Institute for Health and Care Excellence guidelines, the wording of the recommendations was constructed to focus on an action that needs to be taken and to reflect the strength of the recommendation using language and terms that were agreed on to ensure consistency (Table 2).

## DEFINITION AND PRACTICAL IMPLICATIONS OF POGD

The word ileus dates back to classical antiquity and is derived from the Latin word *ileos* meaning “severe colic” and the Greek word *eilein* “to turn, squeeze.” Throughout much of recorded history, ileus described the clinical presentation of abdominal pain, obstipation, and fecal vomiting; most classically associated with what is known today as volvulus.<sup>8</sup> As the ability to study the pathologic basis of disease flourished in the 18th century (owing to autopsy), the term was largely abandoned for pathological-based terms such as intussusception and obstruction. It was not until the 20th century that ileus became synonymous with “non-mechanical obstruction,” due to the lack of peristalsis.<sup>8</sup> As it pertained to the postoperative period, ileus was thought to represent an unavoidable consequence of bowel manipulation during surgery.<sup>3</sup>

There are various terms used in modern literature to describe ileus, including pathologic or paralytic ileus, prolonged ileus, primary ileus, and secondary ileus.<sup>9,10</sup> Other definitions have been proposed; however, as demonstrated by Wolthuis et al,<sup>11</sup> there is large variation in the literature. Gero et al<sup>12</sup> sought to achieve international consensus on the definition of postoperative ileus among colorectal surgeons through an electronic Delphi process. These experts agreed that postoperative ileus “prevents oral intake, that it occurs temporarily after a surgical intervention, and is due to nonmechanical causes.” Vather et al<sup>10</sup> defined prolonged postoperative ileus via

**Table 1. Consensus Statements Concerning Prevention and Treatment of POGD**

Recommendation	Strength
<b>Prevention</b>	
Use of enhanced recovery protocol	Strongly recommend
Minimize the use of opioids while maintaining adequate pain control through the use of multimodal analgesia	Recommend
Maintenance of euolemia along with a normal salt and electrolyte state in the perioperative period	Recommend
No routine use of prophylactic nasogastric tubes	Strongly recommend
Use of minimally invasive surgery when appropriate	Recommend
Use of alvimopan if opioid-based analgesia is used	Recommend
Use of a standardized risk-based strategy for PONV prophylaxis	Recommend
Immediate eating and drinking after colorectal surgery	Strongly recommend
Use of mechanical bowel preparation with oral antibiotics in elective colorectal surgery	Recommend
Coffee and gum chewing as adjuncts to ERPs in promoting recovery of GI function	Consider
<b>Treatment</b>	
Placement of an NGT to relieve intractable nausea and vomiting with abdominal distension	Recommend
Continuation of opioid minimization, ambulation, rational fluid replacement maintaining euolemia, electrolyte repletion, and gum chewing	Recommend
Abdominal CT if POGD persists beyond POD7 or at any time based on concern for secondary causes	Consider

Abbreviations: CT, computerized tomography; ERP enhanced recovery protocol; GI, gastrointestinal; NGT, nasogastric tube; POD, postoperative day; POGD, Postoperative Gastrointestinal Dysfunction; PONV, postoperative nausea vomiting.

**Table 2. Strength of Recommendations<sup>a</sup>**

Strength	Definition
Strongly recommend	Committee believes that the evidence is strong, supported by numerous high-quality prospective randomized trials.
Recommend	Evidence supporting the practice is not as strong, based on high-quality prospective and retrospective studies. Committee feels that benefits of the intervention outweigh the risk for the majority of patients.
Consider	There is a lack of quality research to make a recommendation. Committee feels the practice is safe and likely to be effective based on expert opinion.

Abbreviation: NICE, National Institute for Health and Care Excellence.

<sup>a</sup>Based on NICE guidelines for strength of recommendations.

a systematic review and global survey in 2013 as “two or more of nausea/vomiting, inability to tolerate oral diet over 24 hours, absence of flatus over 24 hours, distension, radiologic confirmation occurring on or after day 4 postoperatively without prior resolution of postoperative ileus.” However, there is lack of consistency between these various definitions. Additionally, these definitions are subjective and do not account for variability in the severity of clinical presentation. In truth, impairments in POGF occur along a spectrum ranging from transient PONV to severe derangements in GI motility that may be secondary to life-threatening underlying pathologies, such as anastomotic leak. This variability makes it difficult to define abnormalities in POGF within the singular term “ileus,” particularly with regard to incidence and clinical implications.

In light of this clinically relevant problem, we sought to develop a classification scheme that identifies the spectrum of impaired POGF in the postoperative period to serve as a framework for discussion, structured measurement of clinical outcomes, and future research endeavors. In developing this scheme, we categorized the patients into 3 basic categories: normal, postoperative GI intolerance (POGI), and POGD. To classify the functional state of the GI tract, we created the I-FEED scoring system,

attributing points for each of these 5 components based on clinical presentation (Figure 1). The scoring system was devised to include the following: (1) the most important aspects of clinical presentation relating to GI physiology; (2) factors that drive management decisions; and (3) levels of dysfunction that correlate with increased complications and costs. The I-FEED scoring system was devised based on expert opinion and will need to be validated. Of note, the absence/presence of stool/flatus was purposely omitted within the scoring system because we felt that was less important than the criteria in the scale. Many recounted experiences with patients that continued to flatus/stool, yet had symptoms indicative of POGD. Similarly, it is not uncommon for patients to be completely tolerant of oral intake before the return of flatus or bowel function.




**Normal (I-FEED Score 0–2)**

Patients in this category are tolerating a diet without symptoms of bloating, but may experience transient PONV. PONV is common within the first 24–48 hours after surgery, with reports of 30% in all patients and up to 80% in high-risk patients.<sup>13</sup> The pathophysiology is complex but seems to be regulated by the chemoreceptor trigger zone and the nucleus tractus solitarius within the brainstem. It is stimulated by vagal afferents in the GI tract and circulating metabolites. Opioids, volatile anesthetics, motion, and visceral manipulation can trigger PONV. The major risk factors include the following: female gender, nonsmokers, prior history of PONV or motion sickness, and opioid use.<sup>13–15</sup> Because mild PONV is common, self-limited, responsive to pharmacologic agents, and does not typically interfere with clinical progression, it was included within the “normal” group.

**POGI (I-FEED Score 3–5)**

These patients typically do well initially, but then start feeling nauseated after POD 2. They typically present with nausea, small-volume nonbilious emesis, and bloating. However, in the majority of cases, they continue to tolerate liquids and do not require a NGT. They may or may not

# I-FEED Scoring System

Scoring Item	Intake	Feeling Nauseated	Emesis	Exam	Duration of symptoms
Description (Score)	Tolerating oral diet (0)	None (0)	None (0)	No distension (0)	0-24 hours (0)
	Limited tolerance (1)	Responsive to treatment (1)	≥1 episode of low volume (<100mL) and non-bilious (1)	Distension without tympany (1)	24-72 hours (1)
	Complete Intolerance (3)	Resistant to treatment (3)	≥1 episode of high volume (>100mL) or bilious (3)	Significant distension with tympany (3)	>72 hours (2)
Total Score	 <b>0 – 2</b> Normal		 <b>3 – 5</b> Postoperative GI Intolerance (POGI)		 <b>≥6</b> Postoperative GI Dysfunction (POGD)

**Figure 1.** The I-FEED scoring system was created out of the need for a consistent objective definition of impaired postoperative GI function. The scoring system attributes 0–2 points for each of the 5 components based on the clinical presentation of the patient and categorizes patients into normal (0–2), postoperative GI intolerance (3–5), and postoperative GI dysfunction (≥6). GI indicates gastrointestinal; I-FEED, Intake, Feeling nauseated, Emesis, physical Exam, and Duration of symptoms; POGD, postoperative gastrointestinal dysfunction; POGI, postoperative gastrointestinal intolerance.

be passing stool/flatus. This generally resolves within 1–2 days without significant intervention and is not associated with worse outcomes or increased costs.<sup>3</sup>

The pathogenesis of POGI is multifactorial.<sup>3,16</sup> Surgical trauma and bowel manipulation have been shown in animal models to induce inflammation through activation of multiple pathways, which can lead to gut injury, bowel wall edema, and dysmotility.<sup>17–20</sup> Surgery can also influence gut motility through neural reflexes via vagal and splanchnic routes. Additionally, hypoperfusion, disturbances of acid-base status, electrolyte imbalance, and temperature regulation can have negative effects on gut motility.<sup>21–23</sup> Opioids are the main contributors to gut dysmotility, although other commonly used drugs such as inhalational anesthetics, clonidine, and adrenergic agonists can also contribute.<sup>3,24</sup>

### POGD (I-FEED score ≥6)

POGD is the most severe form of impaired GI recovery and consistent with what is considered an ileus by most clinicians. As opposed to the 2 previously described groups, these patients develop abdominal distention with tympany, nausea resistant to antiemetics, and large-volume bilious emesis. This is associated with intolerance of oral intake, requiring intravenous fluids to maintain hydration and NGT decompression to prevent aspiration. As opposed to POGI, POGD is associated with prolonged LOS, increased surgical complications, and increased costs.<sup>25–28</sup> The previously mentioned mediators of gut dysmotility contribute to POGD. However, POGD is also frequently associated with other underlying pathology, most notably anastomotic leak or intra-abdominal abscess.<sup>29</sup>

### Emerging Research

Surprisingly, the science regarding detection of POGD is relatively limited. Despite traditional teaching, a study

showed that auscultation was ineffective for distinguishing between normal function, small-bowel obstruction, or POGD. In the study by Felder et al,<sup>30</sup> surgical and internal medicine staff had relatively poor (<50%) sensitivity and positive predictive value as well as low inter-rater reliability (<60%) for predicting these conditions. Following up on that study, Kaneshiro et al<sup>31</sup> reported the results of a multicenter trial using a novel noninvasive acoustic GI surveillance biosensor to detect POGD. The acoustic sensor had somewhat improved performance characteristics compared with auscultation, with a sensitivity, specificity, and negative predictive value of 63%, 72%, and 81%, respectively. Mirbagheri et al<sup>32</sup> used bedside ultrasound to assess gastric emptying as a proxy for effective peristalsis in healthy volunteers and in patients undergoing CRS. They found that time to complete gastric emptying of water had a sensitivity of 85.7% and a specificity of 82.6% for detecting POGD. However, a practical and quantitative definition and scoring tool for assessing POGD are still lacking.

### IMPACT OF ERP ON POGD

Traditionally, postoperative management and initiation of enteral nutrition were dictated solely by the return of bowel function, which took 3–5 days on average after CRS.<sup>33,34</sup> It is unclear when this practice originated but it became one of the fundamental bastions of CRS. The use of an ERP clearly reduces time to GI recovery in CRS compared to traditional care pathways.<sup>35–37</sup> On average, return of flatus/bowel movement occurs within 1–2 days after CRS within an ERP.<sup>38–40</sup> Given that most surgeons continue to require the return of bowel function before discharging patients after CRS, the return of bowel function remains the primary driver of LOS.<sup>1</sup> It is unclear whether the return of bowel

function is essential, as this practice is being challenged by the emergence of outpatient colectomy protocols.<sup>41,42</sup> Based on the existing evidence, we recommend that all patients undergoing CRS be cared for according to published principles of ERPs.

## PREVENTION

### Multimodal Analgesia

Opioids play a significant role in reducing GI function through modulation of the  $\mu$ -receptor.<sup>43</sup> Opioid-induced GI dysfunction can be caused by release of endogenous opioids due to surgical stress or from the administration of exogenous opioids to treat pain.<sup>2,44,45</sup> This risk is highest in CRS, although it is also elevated in other types of surgery involving the foregut, pancreas, and cystectomy.<sup>46–52</sup> Numerous studies demonstrate that opioid minimization is associated with earlier return of bowel function.<sup>53–57</sup> Delays in return of bowel function may be increased with doses exceeding as little as 2 mg of IV hydromorphone equivalents.<sup>50</sup>

In light of this evidence, opioid minimization should be accomplished through a multimodal regimen of nonopioid analgesic strategies.<sup>58</sup> The goal of producing “optimal analgesia” should be pursued, which has been defined as a pain management strategy that optimizes patient comfort and facilitates recovery of physical function including the bowel, mobilization, cough, and normal sleep, while minimizing adverse effects of analgesics.<sup>59</sup> However, the exact combination of analgesic strategies has not yet been elucidated. Neuraxial analgesia,<sup>60,61</sup> lidocaine infusions,<sup>62,63</sup> nonsteroidal anti-inflammatory drugs,<sup>64</sup> acetaminophen,<sup>65–67</sup> gabapentinoids,<sup>68–70</sup> and ketamine<sup>71–74</sup> have all been shown to reduce opioid consumption and provide adequate analgesia in the perioperative period for patients undergoing intra-abdominal surgery. More details about each of these interventions can be found in the POQI-1 multimodal analgesia consensus recommendations.<sup>59,75</sup>

### Maintenance of Euvolemia

Hypervolemia leads to bowel wall edema, prolonging recovery of bowel function, and impairing tissue oxygenation.<sup>26</sup> Avoidance of hypervolemia is one of the primary tenets of ERP and may mediate earlier return of GI recovery. Lobo et al<sup>76</sup> randomized CRS patients to standard postoperative fluids ( $\geq 3$  L water and 154-mmol sodium per day) versus restricted ( $< 2$  L and 77-mmol sodium per day). Gastric emptying times of solids on the fourth POD were significantly longer in the standard group (175 vs 72.5 minutes; difference, 56 [95% confidence interval {CI}, 12–132];  $P = .028$ ); median passage of flatus was 1 day later (4 vs 3 days; 2 [1–2];  $P = .001$ ); median passage of stool was 2.5 days later (6.5 vs 4 days; 3 [2–4];  $P = .001$ ); and median LOS was 3 days longer (9 vs 6 days; 3 [1–8];  $P = .001$ ) in the standard group. Nisanevich et al<sup>77</sup> analyzed 152 patients undergoing intra-abdominal surgery and found that the restrictive intraoperative fluid protocol group (4 mL $\cdot$ kg<sup>-1</sup> $\cdot$ h<sup>-1</sup>) reduced time to flatus from 4 to 3 days and time to bowel movement from 6 to 4 days than the liberal group (bolus of 10 mL/kg followed by 12 mL $\cdot$ kg<sup>-1</sup> $\cdot$ h<sup>-1</sup>). Thacker et al<sup>78</sup> recently examined the correlation between fluid

administration and LOS, total costs, and postoperative ileus using the Premier Research Database in elective CRS and hip/knee replacement. Patients were divided into quartiles for fluid administration on the day of surgery. The highest and lowest quartiles were associated with increased ileus, while quartiles 2–3 were associated with lowest LOS, costs, and rates of ileus. This emphasizes that fluid restriction to the point of hypovolemia is not the goal, but rather euvolemia (zero-fluid balance) is the ideal physiologic state.

Conversely, MacKay et al<sup>79</sup> randomized 80 patients undergoing elective CRS to restricted versus standard fluid regimens postoperatively and found no difference in time to first flatus/bowel movement (restricted group received 4.5 L of fluids compared to over 8 in the standard group). Rollins and Lobo<sup>80</sup> performed a meta-analysis of randomized controlled trials (RCT) evaluating goal-directed fluid therapy (GDFT) versus conventional fluid therapy and found that GDFT was associated with a significant reduction in hospital LOS (mean difference,  $-2.14$ ; 95% CI,  $-4.15$  to  $-0.13$ ;  $P = .04$ ) within a traditional care setting but not within an ERP. No difference was seen in return of flatus or ileus. However, when time to passage of stool was considered, GDFT resulted in a reduction in time to passage of stool (mean difference,  $-1.09$  days; 95% CI,  $-2.03$  to  $-0.15$ ;  $P = .02$ ) within an ERP but not within a traditional care setting.

Taken together, the institution of zero-balance therapy seems beneficial in preventing POGD and reducing bowel edema.

### Prophylactic NGTs

The preponderance of modern surgical evidence suggests that the routine use of a prophylactic postoperative NGT should be abandoned due to the association with increased complications.<sup>81,82</sup> Cheatham et al<sup>81</sup> examined 26 trials with 3964 patients after laparotomy and found that pulmonary complications, pneumonia, atelectasis, fever, and time to tolerance of oral intake all were reduced in the group without prophylactic NGTs. There was more observed abdominal distension and nausea/vomiting in patients without prophylactic NGTs, but no increase in any other complication. Subsequently, a large Cochrane meta-analysis including 33 studies with 5240 patients demonstrated that routine use of prophylactic NGT prolongs time to return of bowel function and increases pulmonary complications ( $P < .01$ ).<sup>82</sup>

It is important to note that the previously mentioned studies were conducted in patients undergoing routine and uncomplicated elective surgery. The efficacy of prophylactic NGT decompression in high-risk patients (eg, difficult prolonged operation with visible bowel wall edema, extensive adhesiolysis in the setting of obstruction, emergent cases, etc) has not been fully investigated. Since aspiration from massive emesis can be lethal, it is imperative that perioperative teams have increased vigilance in these high-risk patients and the decision be left to the surgeon's discretion. Additionally, the avoidance of prophylactic NGT decompression should not be confused with the utility of NGT decompression for treatment of severe POGD as addressed elsewhere in the manuscript.

### Minimally Invasive Surgery

Minimally invasive surgery has clearly been shown to improve outcomes after CRS including return of bowel function, ileus, and LOS.<sup>83–85</sup> As such, the use of minimally invasive surgery should be utilized when possible. It is unclear whether hand-assisted laparoscopy offers the same advantages as straight laparoscopy with regard to postoperative bowel function.<sup>86</sup> The beneficial effects of minimally invasive surgery are likely mediated through minimization of bowel manipulation, a principle that can also be applied to open surgery.

### Alvimopan

The Food and Drug Administration approved alvimopan in 2008 as an oral, peripherally acting opioid  $\mu$ -receptor antagonist to accelerate GI recovery in patients undergoing bowel resection.<sup>87,88</sup> A pooled analysis of 3 prospective randomized trials demonstrated that a 12 mg dosing regimen provided optimal reduction in GI morbidity and return of GI function after abdominal surgery.<sup>89</sup>

Vaughan-Shaw et al<sup>90</sup> performed a meta-analysis involving 3 studies of 1388 patients undergoing open abdominal surgery (bowel resection and hysterectomy) within a defined accelerated recovery program. This study demonstrated a 16- to 20-hour reduction in the time to GI recovery and discharge order associated with alvimopan use. It is important to note that the defined accelerated recovery program in each of these studies was limited to early removal of prophylactic NG tubes, clear liquids on POD 1, and encouragement of ambulation. Each study utilized patient-controlled analgesia with heavy doses of opioids.<sup>91</sup> Therefore, these trials were conducted in open surgery within the setting of an opioid-centric treatment pathway, which is not consistent with most modern day ERPs. There are no high-quality prospective randomized trials examining the efficacy of alvimopan within the setting of an opioid-restricted modern day ERP or after minimally invasive surgery.

However, there are large database studies evaluating the use of alvimopan in current practice. The Michigan Surgical Quality Collaborative group reported that the usage of alvimopan in the community resulted in a decrease in mean LOS (4.8 vs 6.4 days) due principally to a reduction in ileus (7.9% vs 2.3%).<sup>92</sup> Similarly, the Surgical Care and Outcomes Assessment Program evaluated 14,781 patients undergoing elective CRS comparing those that did (11%) and did not receive (89%) alvimopan and found a LOS reduction of 1.8 days and a cost reduction of \$2017 related to ileus reduction in patients receiving alvimopan.<sup>93</sup> Adam et al<sup>94</sup> reported on a single institution experience of 660 patients after implementation of alvimopan as part of an established ERP (197 alvimopan; 463 no alvimopan) and demonstrated a faster return of bowel function, a lower incidence of ileus, a shorter LOS, and a hospital cost savings of \$1492 per patient. These results are consistent with similar retrospective cohort study by Itawi et al.<sup>95</sup> It should be noted that the potential benefits of alvimopan are likely related to the amount/duration of opioid analgesics as demonstrated by 2 separate retrospective studies demonstrating minimal benefit in a laparoscopic colectomy population managed with minimal opioids.<sup>96,97</sup>

The data suggest a reproducible benefit associated with the use of alvimopan in open CRS; however, the cost/benefit ratio must be considered within the context of the opioid administration of each institution's ERP. Barletta et al<sup>50</sup> confirmed that the intravenous opioid dosage that results in ileus might be quite modest (2-mg hydromorphone). Additional data would be helpful to clearly define the minimum dose exposure and route of administration of opioids that would best guide the use of alvimopan within a comprehensive ERP. However, if modest opioid exposure is anticipated, the agent appears to be cost-effective.

### PONV Prophylaxis

PONV is a significant component in the spectrum of impaired GI recovery and a frequent source of patient discomfort.<sup>55,56</sup> Consensus guidelines propose that a risk-based strategy of prophylaxis should be used along with a structured treatment algorithm.<sup>13</sup> In summary, a preoperative assessment of risk factors (female, nonsmoker, prior PONV/motion sickness, use of opioids) and appropriate prophylaxis should be utilized in all patients. A core tenet of treatment for PONV once it develops involves switching classes of medications from those used for prophylaxis. Finally, because it is known that PONV in the recovery room predicts nausea and vomiting in the subsequent 24–48 hours, consider scheduling antiemetics in these high-risk patients.<sup>98,99</sup>

### Postoperative Feeding

Traditional perioperative care dictated the return of bowel function before feeding after intestinal surgery. Andersen et al<sup>100</sup> published a meta-analysis comparing oral feeding within 24 hours to later feeding after elective CRS. They analyzed 13 randomized trials, with 1173 patients, and found that early feeding was safe and not associated with increased complications compared to later feeding.

Subsequently, Osland et al<sup>101</sup> performed a meta-analysis of 15 studies including 1240 patients demonstrating a 45% reduction in complications associated with early feeding (odds ratio, 0.55; CI, 0.35–0.87;  $P = .01$ ) with no difference in NGT insertion, mortality, anastomotic leak, return of bowel function, or LOS as compared to later feeding. Zhuang et al<sup>102</sup> performed a meta-analysis of randomized trials with stricter inclusion criteria. They included 7 studies with a total of 587 patients and found that early oral feeding was associated with reduced complications (relative risk, 0.70; 95% CI, 0.50–0.98;  $P = .04$ ) but also found an association with reduced LOS by 1.58 days (95% CI, –2.77 to –0.39;  $P = .009$ ). There were no differences in rates of NGT reinsertion, vomiting, anastomotic leaks, surgical-site infection (SSI), or mortality. Based on these data, we recommend immediate feeding in patients after elective CRS.

### Bowel Preparation

The use of a combined isosmotic MBP-OAB was initially recommended as part of the POQI-1 Infection Prevention Consensus statement to prevent SSL.<sup>103</sup> MBP-OAB not only results in a lower SSI rate but is also associated with decreased rates of POGD.

Englesbe et al<sup>104</sup> evaluated 2011 elective colectomies in the Michigan Surgical Quality Collaborative (MSQC) and

found that patients receiving MBP-OAB had lower rates of ileus (3.9% vs 8.6%;  $P = .01$ ). Subsequently, both Kiran et al<sup>105</sup> and Morris et al<sup>106</sup> looked at over 8000 patients in American College of Surgeons National Surgical Quality Improvement Program (NSQIP) stratified by MBP undergoing elective CRS and found that the MBP-OAB group had significant reductions in SSI, anastomotic leak, and ileus ( $P < .0001$  for all). The pathophysiology behind the effect of MBP-OAB on gut motility remains to be seen. It may be that MBP-OAB simply attenuates POGD through the reduction of intra-abdominal infection and anastomotic leak, which are known causes of secondary POGD.<sup>29</sup>

### Coffee

There have been several RCTs evaluating the effect of coffee on the return of bowel function after abdominal surgery. Güngördük et al<sup>107</sup> randomized 114 patients undergoing gynecologic oncology surgery to coffee 3 times daily versus placebo. Time to recovery of bowel function and tolerance of a diet were reduced significantly in coffee drinkers compared with control subjects. Ileus was reduced from 30.4% in the control group to 10.3% in the coffee group ( $P = .01$ ). Müller et al<sup>108</sup> randomized 80 patients undergoing elective CRS to coffee or water 3 times daily. Time to first bowel movement was shorter in the coffee arm with no difference in time to first flatus or tolerance of solid food. Taken together, these data suggest that coffee taken 3 times daily may shorten GI recovery in patients undergoing major abdominal surgery.

### Gum Chewing

Gum chewing has been associated with reduced GI recovery in prospective RCTs of patients undergoing major abdominal surgery.<sup>109</sup> However, the majority of these studies was conducted in the era of prolonged fasting when gum chewing was used as a method of sham feeding. It is doubtful that sham feeding offers an advantage when the patients are actually being fed, as is the case with ERPs. Shum et al<sup>110</sup> randomized 41 patients in each group within an ERP to gum chewing 3 times daily. There was a 16-hour reduction in time to flatus with no difference in hospital stay. Ho et al<sup>111</sup> performed a

meta-analysis of 10 RCTs and found that gum chewing had no advantage within the setting of early feeding. Therefore, it seems that actual feeding may negate the effect of gum chewing. However, given the minimal risk and low cost, gum chewing may serve as an adjunct to ERPs, particularly in patients with minimal oral intake after surgery.

### TREATMENT




Treatment for POGD should focus on bowel rest with nutrition support, continuation of ERP principles to the extent possible, and radiographic imaging to rule out secondary causes such as anastomotic leak and intra-abdominal infections. Specific treatment recommendations will depend on POGD severity and associated signs/symptoms (Figure 2).

Patients with POGI who have mild nausea, small-volume nonbilious emesis ( $\leq 100$  mL), and bloating are generally managed with a clear liquid diet and antiemetics. These patients do not typically require a NGT and usually do not require nutrition support as the symptoms are generally mild and self-limited.

Early recognition of the patient who has progressed to POGD is critical in preventing aspiration pneumonitis, which is a potentially fatal complication after elective CRS. Patients with intractable nausea, bilious vomiting, abdominal distension, and tympany require NGT placement, which oftentimes provides immediate symptomatic relief and may also reduce the risk of aspiration, especially in the elderly or frail patient. There are many different approaches to NGT management, and unfortunately, research is lacking to guide clinical practice. Some surgeons leave the NGT until patients demonstrate return of bowel function, while others remove the NGT when it reaches a certain color/volume. Additionally, practices vary with regard to suction versus gravity drainage. Although there was uniform agreement in the importance of early NGT placement for treatment of POGD, there were wide variations in subsequent NGT management within the group and consensus could not be reached with regard to NGT removal. Thus, this should be left to the surgeon's discretion. This topic represents an opportunity for further research efforts.

Once a patient develops POGD, ERP principles should be continued to the extent possible, including opioid

## Postoperative GI Function: Go, Slow, Stop

	Clinical Presentation	Management
 <p><b>GO</b> Normal</p>	Tolerating oral intake (I-FEED Score 0-2)	Standard ERP including, risk-based PONV prophylaxis/treatment and early feeding
 <p><b>SLOW</b> POGI</p>	Difficulty with oral intake; belching, nausea, bloated feeling, non-bilious emesis (I-FEED Score 3-5)	Anti-emetics and clear liquids; resume normal diet as tolerated
 <p><b>STOP</b> POGD</p>	Intolerant of oral intake; bilious emesis, abdominal distension/tympany (I-FEED Score $\geq 6$ )	NGT, IVF, possible nutrition support; consider other etiologies

**Figure 2.** A treatment algorithm was developed based on the I-FEED scoring system for the management of patients with impaired postoperative GI function according to the clinical presentation of the patient in real time. ERP indicates enhanced recovery protocol; GI, gastrointestinal; I-FEED, Intake, Feeling nauseated, Emesis, physical Exam, and Duration of symptoms; IVF, intravenous fluids; NGT, nasogastric tube; POGD, postoperative gastrointestinal dysfunction; POGI, postoperative gastrointestinal intolerance; PONV, postoperative nausea and vomiting.

minimization, ambulation, rational fluid replacement maintaining euvoolemia, electrolyte repletion, and gum chewing. In the setting of POGD, administration of maintenance fluid requirements and replacement of volume losses from NGT drainage should be approached in a rational manner with goals of maintaining euvoolemia and normal electrolyte balance, especially since gastric contents have high concentrations of chloride and potassium. While no specific data exist for this situation, certain principles of fluid management have been shown to correlate with patient benefit and harm. Additionally, recent research has noted a wide variability in the practice of fluid management by many trainees<sup>112</sup>; thus, a structured, principle-based approach is needed, as both hypervolemia and hypovolemia throughout the perioperative period are associated with much worse outcomes for surgical patients.<sup>78</sup> First, euvoolemia should be targeted such that patients are only given fluid boluses when there is a demonstrated need for augmentation of perfusion status and when they have been shown to be volume responsive.<sup>113-115</sup> Weighing the patient daily to target zero weight gain and following hemodynamic targets and urine output may be beneficial. Second, fluids should be treated as drugs with potentially harmful side effects.<sup>116</sup> Thus, frequent careful bedside assessments should guide appropriate therapy. A simple maneuver such as the passive leg raise test can help determine if a patient will be responsive to fluids, or possibly if a higher level of care with more sophisticated monitoring is needed.<sup>117</sup> This level of individualized patient care should be given as compared to empiric administration of large volumes of fluids that may potentially cause harm. Third, fluid choice should be guided by the electrochemical balance of the patient, taking care to avoid hyperchloremia (>110 mmol/L) as this has been associated with worse patient outcomes.<sup>118,119</sup> While routine laboratories are often avoided today, in this setting, a frequent assessment of the biochemical profile of the patient is warranted to guide fluid therapy. The patient with prolonged POGD (>7 days) may require parenteral nutrition according to standard guiding principles.<sup>120</sup>

Finally, the group agreed uniformly that it is important to rule out secondary causes of POGD such as small-bowel obstruction or anastomotic leak, which are frequently associated with POGD and may alter management.<sup>29</sup> If bowel function has not returned by POD 7 or if there are signs/symptoms suggestive of an alternative underlying etiology (fever, tachycardia, abdominal tenderness, leukocytosis, etc), further radiologic investigation is recommended, including abdominal computed tomography.

## UNANSWERED QUESTIONS

### Question 1

The I-FEED scoring system was created out of the need for a consistent objective definition of POGD based on discussion among experts in the field. However, prospective validity and reliability testing along with usability assessment needs to be performed to evaluate the utility of it as a clinical and research tool.

### Question 2

Emerging noninvasive biosensor technology such as acoustic GI surveillance and bedside ultrasound have shown promise in measuring gut motility within small case series

after surgery.<sup>31,32</sup> These studies, although interesting, will need multi-institutional validation before incorporation into clinical practice.

### Question 3

There is a plethora of research on preventative strategies for delayed GI function. However, there is a paucity of literature in the ERP era pertaining to management of this condition, particularly with regard to fluid management, NGT management, and pharmacologic interventions.

### Question 4

Although the data are quite convincing for the efficacy of alvimopan in open CRS patients receiving significant opioids, high-quality prospective studies in laparoscopic surgery and/or within an ERP are lacking, representing an opportunity for future research. This is especially true in the setting of ERPs that use very minimal doses of opioids. ■

## APPENDIX 1

The full list of members of the Perioperative Quality Initiative (POQI) 2 Workgroup can be found below:  
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#### DISCLOSURES

**Name:** Traci L. Hedrick, MD, MS.

**Contribution:** This author helped with writing, reviewing, and editing of the manuscript, and participated in the conference.

**Conflicts of Interest:** T. L. Hedrick was a chair of the postoperative GI dysfunction (POGD) group. She received grant funding from American Society of Colon and Rectal Surgeons.

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**Conflicts of Interest:** None.

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**Conflicts of Interest:** None.

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**Conflicts of Interest:** None.

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**Conflicts of Interest:** A. J. Senagore was on the speaker's bureau.

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**Contribution:** This author helped with writing, reviewing, and editing of the manuscript.

**Conflicts of Interest:** T. J. Gan was a Perioperative Quality Initiative (POQI) conference organizer and received honoraria from Edwards, Mallinckrodt, Merck, Medtronic, and Pacira.

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**Conflicts of Interest:** T. E. Miller was a POQI conference organizer and received honoraria from Edwards Lifesciences and Cheetah Medical.

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