**Perioperative care – decoding postoperative ileus**

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## Introduction

Postoperative ileus is a temporary cessation of coordinated intestinal motility after surgery. It is characterised clinically as a disruption of normal bowel function in the absence of a mechanical obstruction. It becomes clinically apparent several days after surgery, comprising symptoms of abdominal distension, vomiting, and constipation, often necessitating the placement of a nasogastric tube (1). Postoperative ileus is a common complication, occurring in 10-20% of patients undergoing major abdominal surgery (2). Patients at greater risk tend to be male, undergoing longer procedures with a higher degree of surgical stress, and receiving large quantities of opioid-based analgesia after surgery (1). This has a profound impact on recovery after surgery, increasing the risk of venous thromboembolism and hospital acquired infections. It is also burdensome for healthcare systems, reducing bed capacity and increasing healthcare costs by up to 70% (3). Accordingly, the prediction, diagnosis, and treatment of ileus is now considered to be amongst the highest research priorities in surgery (4).

## Pathogenesis and mechanisms

The physiological and pathological mechanisms leading to postoperative ileus have perplexed healthcare professionals for decades and are still incompletely understood (5). Broadly, the onset of ileus is considered to comprise two distinct phases: an early neurogenic phase and a later inflammatory phase. During the early phase, stimuli from the initial incision stimulate spinal afferent nerve fibres, activating an inhibitory feedback pathway in the spinal cord which transiently abolishes motility across the intestinal tract. During the inflammatory phase, intestinal handling leads to the release of peritoneal mast cells, increasing intestinal permeability to luminal bacteria and activating intestinal macrophages. Large numbers of nitric oxide- and prostaglandin-releasing leucocytes

are then recruited, whose actions impair the contractility of intestinal smooth muscle. Ultimately, this inflammatory cascade leads to the generalised pattern of intestinal dysmotility, characterised clinically as postoperative ileus (6). The use of opioid analgesia augments these mechanisms by inhibiting propulsive intestinal motility, as do fluctuations in fluid balance, hormonal homeostasis, and electrolyte concentrations (7).

**Perspectives around postoperative ileus**

Traditionally, postoperative ileus was considered to be a normal effect of surgery until it was later recognised as a preventable event (5). Previous research tended to focus on complications considered to be more dangerous for patients and burdensome to health systems, such as anastomotic dehiscence, venous thrombo-embolism, and surgical site infection. With far greater focus on the patient voice over the last 10 years, however, the true impact of ileus has emerged, illustrated by qualitative studies exploring patients' and health professionals' experiences. Notably, these have highlighted the deleterious effects of ileus on patients, driven physically by its disabling symptoms and psychologically through uncertainty. As well, the disruption to health systems and professionals, largely due to a lack of proven interventions to reduce ileus and mitigate its effects (8).

**Interventions for postoperative ileus – old, new, and future**

Recent advances in perioperative care have generated a range of strategies aimed at reducing the impact and incidence of postoperative ileus (Table 1). Broad evidence supports pathway-based approaches that combine minimally invasive surgery, enhanced recovery after surgery protocols and multimodal analgesia. Evidence for other specific interventions is mixed and often contradictory.

*Chewing gum*

Chewing gum is inexpensive and generally well tolerated by patients. Enhanced recovery after surgery guidelines provide a moderate recommendation for its use (9). Its therapeutic potential has been attributed to an efferent cephalic-vagal response and increase in promotility hormones in response to mastication. Numerous studies have explored the clinical effectiveness of chewing gum, with highly variable results. One of the largest studies comprising 1000 patients across 12 hospitals in the Netherlands found that chewing gum did not reduce length of stay or time to intestinal recovery (10).

*Probiotics*

Probiotics are beneficial bacteria that help to maintain intestinal homeostasis. They exert their effects through various mechanisms, including competitive inhibition of bacterial adherence and translocation, production of bacteriocins and defensins, and enhancement of barrier function through increased mucus production. Enhanced recovery after surgery guidelines provide a moderate recommendation for its use (9). Whilst high quality data are lacking, in a meta-analysis of clinical studies (n=21), probiotic supplementation was associated with improved intestinal recovery after surgery, identifying it as a potentially promising intervention to reduce ileus (11).

*Non-steroidal anti-inflammatory drugs (NSAIDs)*

Non-steroidal anti-inflammatory drugs when used as part of multi-modal analgesia strategies may reduce the incidence of ileus. This is likely related to a relative reduction in opioid consumption and the attendant impact on intestinal motility. A meta-analysis of six RCTs involving 563 participants previously showed that NSAIDs reduce the time taken for patients to achieve return of bowel function and tolerate an oral diet (12). The

use of NSAIDs after colorectal surgery, however, is controversial. Conflicting studies have proposed associations between the use of NSAIDs and anastomotic leak, particularly with non-selective NSAIDs. Enhanced recovery guidelines recommend the use of selective NSAIDs for postoperative analgesia (9).

*Intravenous Lidocaine*

Local anaesthetic agents are commonly used for epidural analgesia, but recent studies have explored the role of intravenous preparations to reduce ileus. Intravenous lidocaine is thought to attenuate the inflammatory cascade, reduce pain, and decrease postoperative opioid requirements (1). Whilst several studies have explored its efficacy, most recently the ALLEGRO study showed that perioperative administration of 2% intravenous lidocaine did not improve the return of gut function after minimally invasive colonic resection (13). Furthermore, the safety of intravenous lidocaine was recently scrutinised, necessitating a consensus statement which recommended a maximum dose, duration, and monitoring precautions when used in the perioperative period (13).

*Mu-opioid antagonists (Alvimopam)*

Alvimopam is a solution to the adverse effects of opioids on intestinal motility. As a peripherally acting mu-opioid receptor antagonist, Alvimopam does not cross the blood-brain barrier and so is considered to mitigate the intestinal effects of opioid without compromising central analgesia. Several high-quality randomised trials have proven the clinical effectiveness of Alvimopam for improving intestinal recovery after colorectal surgery (14; 15). To date, however, the drug is only available in North America.

*Vagus nerve stimulation*

Vagus nerve simulation is a novel therapeutic which may reduce ileus through non-invasive stimulation of the cervical or auricular branches of the vagus nerve. Pre-clinical studies have shown that stimulation of the vagus nerve activates a cholinergic anti-inflammatory pathway which suppresses intestinal inflammation and prevents smooth muscle dysfunction. Early clinical studies have demonstrated early signals of efficacy, as well as the feasibility of delivering the intervention in clinical practice (8; 16). Future work is required to explore the clinical- and cost-effectiveness of this therapeutic.

**Challenges and future directions**

Developing and evaluating interventions to reduce ileus is challenging. Specific challenges include community-wide disagreement on the definition of ileus applied to outcome assessment, as well as persisting uncertainty around the mechanism of ileus. This restricts the development of new, evidence-based interventions that have a reasonable chance of patient benefit. Recent methodological developments, however, may improve our ability to undertake high quality evaluations. Notable examples include a core outcome set for ileus, providing a standard series of patient- and clinician-defined clinical outcomes, as well as a patient-reported outcome measure (17; 18). Platform trial designs may provide an opportunity to harness this improved methodological framework to facilitate efficient and definitive evaluations of multiple interventions. Before this, however, we must ensure that pipeline early-phase interventions for ileus (such as vagus nerve stimulation) are developed robustly with clear signals of potential efficacy.

Table 1. Interventions to prevent / treat postoperative ileus

| Intervention | Putative mechanism | Typical regimen / practical notes | Evidence / ERAS position & effect |
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| **Enhanced Recovery bundle (ERAS core elements: early feeding, multimodal analgesia, minimal drains, early mobilisation, fluid optimisation)** | Multimodal reduction of surgical stress response, earlier gut stimulation and less opioid use | Implement as standard perioperative package (pre → intra → post). Early oral intake as tolerated; multimodal analgesia to minimise opioids; discourage routine NG tubes/drains. | Central recommendation of ERAS 2025 — consistently associated with reduced POI incidence and shorter time to bowel function. |
| **Chewing gum (sham feeding)** | Stimulates salivary/gastrointestinal reflexes and vagal tone → promotes bowel motility | 10–20 minutes chew, 3× daily, starting early postoperative day 0–1 until first flatus/bowel motion in many trials | Multiple RCTs & meta-analyses show shorter time to flatus/BM and shorter LOS; inexpensive and low-risk — commonly recommended as adjunct. |
| **Early oral/enteral nutrition** | Restores luminal stimulation and mucosal integrity; promotes motility | Encourage oral intake as tolerated within 24 h after uncomplicated colorectal surgery | Part of ERAS core; associated with faster return of bowel function and reduced POI. |
| **Opioid-sparing / multimodal analgesia (including regional techniques)** | Reduces opioid-induced gut hypomotility | Use paracetamol, NSAIDs, gabapentinoids where appropriate, and regional/locoregional blocks to minimise systemic opioids | Strong ERAS recommendation — opioid minimisation reduces POI risk. |
| **Mu-opioid receptor antagonists (peripheral) — e.g., alvimopan** | Blocks peripheral μ-opioid receptors in gut without reversing central analgesia | Licensed protocol varies by region (preop dose then postoperative dosing for | RCTs and meta-analyses show reduced time to GI recovery and |

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| | | specified days) — availability and cost limit use in some centres | LOS after bowel resection; recommended as an option in settings where available. |
| **Intravenous lidocaine (systemic)** | Anti-inflammatory, anti-nociceptive and pro-motility effects when given perioperatively | IV infusion intra-op and early postop in selected patients (monitoring required) | Several trials/meta-analyses report faster return of bowel function and pain/opioid reduction; recommended as consideration in appropriate patients. |
| **Probiotics / synbiotics** | Modulation of gut microbiome and local inflammation → may aid motility recovery | Specific strains/doses vary across studies; usually started peri-/post-op | Emerging evidence (some RCTs/meta-analyses) suggests benefit for time to bowel function; evidence heterogenous — adjunctive option. |
| **Minimally invasive surgery (laparoscopic / robotic)** | Less surgical trauma and inflammatory response → faster GI recovery | Prefer MIS approaches when appropriate for patient and procedure complexity | Consistently associated with reduced POI and shorter LOS; core ERAS-compatible strategy. |
| **Avoid routine nasogastric tubes & routine intra-abdominal drains** | Prevents iatrogenic delay of enteral intake and reduces discomfort | Use selectively rather than routinely | ERAS advises against routine use after colorectal surgery — reduces factors predisposing |

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| | | | to delayed gut recovery. |
| **Vagus nerve stimulation / acupuncture / other neuromodulation (experimental)** | Augments vagal anti-inflammatory pathway and gut motility | Mostly investigational; some trials use transcutaneous stimulation or acupuncture points | Promising pilot data and biologic plausibility but still experimental — not standard; more high-quality RCTs required. |
| **Adjuncts with some supporting data (coffee, dexamethasone, selected herbal formulas, acetylcholinesterase-stimulants in select contexts)** | Various — pro-motility, anti-inflammatory, neurohormonal stimulation | Low-cost/low-risk options that have been tested in RCTs/meta-analyses (varied protocols) | Some positive trials for coffee and periop dexamethasone; evidence heterogenous and generally adjunctive — consider locally and as part of ERAS. |

**Table 1:** Summary of interventions to prevent or treat postoperative ileus. Interventions include multimodal perioperative strategies, pharmacological therapies, and adjuncts aimed at reducing surgical stress, opioid-induced gut hypomotility, and inflammation. **ERAS® Society Guidelines for Perioperative Care in Elective Colorectal Surgery, 2025** and supporting systematic reviews and meta-analyses. Evidence levels reflect reported outcomes in randomized trials and guideline recommendations.

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