Surgical Oncology 66 (2026) 102411

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Review

Surgery and the Gastrointestinal Microbiome in Cancer: Bidirectional Impacts and Therapeutic Opportunities – a Narrative Review

Kristina Žukauskaitė [a,b,*], Kornelija Rauduvytė [c], Augustinas Baušys [c], Angela Horvath [a,b], Tomas Poškus [c], Vanessa Stadlbauer [a,b]

[a] Division Translational Precision Medicine, Center for Biomarker Research in Medicine (CBmed GmbH), Graz, Austria
[b] Division of Gastroenterology and Hepatology, Department of Internal Medicine, Medical University of Graz, Graz, Austria
[c] Laboratory of Experimental Surgery and Oncology, Translational Health Research Institute, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

ARTICLE INFO

Keywords:
Microbiome
Antibiotics
Probiotics
Prebiotics
Synbiotics
Gastrointestinal cancer
Gastric cancer
Colorectal cancer
Dysbiosis

ABSTRACT

Gastrointestinal cancers rank among the most common malignancies globally, and although surgical resection remains the cornerstone of curative therapy, it is associated with considerable postoperative morbidity and mortality. Emerging evidence suggests that the gut microbiome is a critical determinant in the pathogenesis of postoperative complications, including surgical site infections, anastomotic leakage, and postoperative ileus. Microbiome-targeted interventions – including probiotics, prebiotics, and synbiotics – have shown promise in modulating microbial communities and supporting postoperative recovery; however, clinical efficacy remains inconsistent, and standardized perioperative protocols are yet to be established. This review summarizes current evidence on the interactions between gastrointestinal cancer surgery and the perioperative gut microbiome, emphasizing opportunities to harness microbiome-targeted interventions to reduce complications and enhance recovery.

1. Introduction

Gastrointestinal (GI) cancers, encompassing gastric and colorectal malignancies, rank among the leading causes of cancer-related morbidity and mortality worldwide [1]. Surgical resection remains the cornerstone of curative treatment for most of these cancers, but despite advances in surgical techniques, patients undergoing GI cancer surgery remain at substantial risk of postoperative complications, including surgical site infections, anastomotic leaks, and other adverse events. Beyond acute complications, surgery can also result in long-term impairments in quality of life, limiting overall recovery, increasing healthcare costs, and imposing a considerable burden on patients and healthcare systems [2,3].

In recent years, accumulating evidence has underscored the pivotal role of the gut microbiome in shaping surgical outcomes. The perioperative period represents a particularly vulnerable window, during which antibiotic use, dietary changes, surgical stress, anesthesia, and the presence of malignancy can disrupt microbial homeostasis. Such perturbations may contribute to postoperative complications and delay recovery, highlighting the importance of understanding microbiome dynamics in the surgical context [4].

Probiotics, prebiotics, and synbiotics represent emerging strategies to manipulate the gut microbiome, with studies indicating their capacity to restore microbial balance and support key functional processes [5]. Probiotics introduce live beneficial microorganisms, prebiotics selectively promote the growth of advantageous bacteria, and synbiotics combine both approaches to enhance microbial balance and mitigate inflammation. Perioperative administration of these interventions has shown potential to attenuate inflammation, support mucosal healing, strengthen immune defenses, and consequently reduce postoperative complications such as infections while promoting overall recovery [5,6].

Despite these promising findings, microbiome-targeted strategies have not yet been routinely integrated into clinical practice for GI cancer surgery. This narrative review therefore provides a comprehensive overview of current evidence regarding the bidirectional interactions between GI cancer surgery and the perioperative gut microbiome, how these microbial dynamics influence surgical outcomes, and the potential interventions that may enhance postoperative recovery and long-term patient prognosis. The interplay between the microbiome and surgical outcomes is summarized in the Graphical Abstract.

* Corresponding author. Division Translational Precision Medicine, Center for Biomarker Research in Medicine (CBmed GmbH), Graz, Austria.
E-mail address: kristina.zukauskaite@medunigraz.at (K. Žukauskaitė).

https://doi.org/10.1016/j.suronc.2026.102411
Received 21 November 2025; Received in revised form 13 March 2026; Accepted 22 March 2026
Available online 23 March 2026

2. Methods

A literature search was performed using PubMed (https://pubmed.ncbi.nlm.nih.gov/) and ClinicalTrials.gov (https://clinicaltrials.gov/) between January 17 and October 15, 2025. The search strategy combined keywords including "probiotics", "prebiotics", "synbiotics", "gastric", "gastrointestinal", "colorectal", "colon", "cancer", "surgery", "microbiome", "perioperative", "prophylaxis", "oral", "perioral", "antibiotics", "therapy", "diet", "outcomes", "prehabilitation", and "mechanical bowel preparation". Peer-reviewed, English-language studies focusing on adult patients (≥18 years) undergoing GI cancer surgery were included. The review specifically included interventions involving microbiome-targeted therapies—such as probiotics, prebiotics, synbiotics, dietary modifications, and mechanical bowel preparation (MBP)—and their impact on postoperative outcomes. To maintain clinical relevance to surgical oncology, studies focused exclusively on non-surgical treatments or non-malignant conditions were excluded. Reference lists of relevant publications were manually screened to identify additional pertinent studies.

3. Literature review

3.1. Impact of perioperative interventions and surgery on the gut microbiome

Perioperative factors such as antibiotic use, dietary changes, surgery-induced anatomical alterations, and surgical stress – can disrupt the gut microbiome. While most studies emphasize the microbiome's impact on recovery, these interventions themselves reshape microbial composition and function. This section outlines the main perioperative influences on the gut microbiome.

3.1.1. Impact of perioperative antibiotics on surgical outcomes

Prophylactic antibiotics remain the cornerstone of surgical site infections (SSIs) prevention in gastrointestinal (GI) surgery. Current guidelines recommend limiting intravenous (IV) prophylaxis to the intraoperative period or within 24 h postoperatively, unless infection is present [7,8]. Antibiotic choice should match surgical site flora: colorectal procedures, for instance, require both aerobic and anaerobic coverage, typically achieved with cephalosporins or ampicillin–sulbactam, and clindamycin or metronidazole combinations for β-lactam-allergic patients [9,10].

IV antibiotics are considered the standard due to reliable pharmacokinetics and proven SSIs reduction [11], though they may inadvertently disturb non-target microbial communities, lowering gut diversity and increasing postoperative complication risk [12]. Perioperative cefazolin or clindamycin can reduce Lachnospiraceae and increase Porphyromonadaceae, whereas metronidazole and vancomycin mainly decrease microbial density without major compositional shifts [13,14]. Oral regimens, acting directly in the lumen, achieve high local concentrations that diminish bacterial load and alter diversity [15]. Combined oral and IV prophylaxis with MBP increases *Enterococcus*, *Lactococcus*, and *Streptococcus* abundance for up to 30 days postoperatively [16,17], indicating localized dysbiosis with limited systemic impact.

Despite microbiome disruption, oral antibiotics – especially with IV agents and MBP –consistently lower SSI rates. Studies in colorectal cancer (CRC) surgery reported odds ratios as low as 0.37 for combined prophylaxis [18] (Table 1). Evidence for oral-only regimens remains inconsistent, with some trials showing no additional benefit [19] while others even reported worse outcomes with oral-only regimens in colorectal surgery [20]. Several ongoing trials (e.g., NCT05164887, EUCT 2025-520725-20-00, and NCT03663504) are expected to clarify the independent role of oral prophylaxis [21–23].

The heterogeneous effects of oral antibiotic prophylaxis observed across studies in Table 1 largely reflect differences in trial design, study populations, and perioperative management. Several trials conducted in Japan and China were open-label or single-blinded, which may have influenced perioperative management and SSI assessment, whereas the French multicenter RCT used double-blinding but included both laparoscopic and open surgery, introducing greater clinical heterogeneity. In addition, regional differences in bowel preparation practices and healthcare settings, together with variation in IV antibiotic type, oral antibiotic combinations, and timing of oral administration, complicate cross-study comparability. Together, these factors likely contribute to the variability in outcomes observed across trials, while the more consistent benefit of combined oral–IV prophylaxis supports a protective effect on SSI risk.

In summary, IV antibiotic prophylaxis remains the standard of care in GI surgery. Adding oral antibiotic prophylaxis with MBP offers further SSI reduction, though the benefit of oral-only regimen is unclear.

3.1.2. Mechanical bowel preparation and uncertainty of its clinical impact

The role of MBP in GI surgery remains controversial. Evidence supporting its benefit alongside standard IV antibiotic prophylaxis for colonic surgery is limited. A meta-analysis of 5805 patients found no clear advantage of MBP alone, though a potential role in rectal surgery was suggested [27]. Nevertheless, MBP remains common practice, partly due to findings from the GRECCAR III and MOBILE2 randomized controlled trials (RCTs), which reported reduced postoperative complications when MBP was combined with oral antibiotics [28,29].

Oral MBP typically involves low-dose polyethylene glycol with

Table 1
Randomized controlled trials evaluating surgical site infection outcomes in colorectal cancer surgery using oral and intravenous antibiotic prophylaxis with mechanical bowel preparation [24–26].

Study	Year	Type of surgery	*n*	Groups	Oral antibiotics				Intravenous antibiotics			
					Class of antibiotics	Antibiotics	Dose	Time administered	Class of antibiotics	Antibiotics	Dose	Time administered
[18]	2016	Laparoscopic colorectal cancer surgery	579	OA + IVA + MBP *vs.* IVA + MBP	Aminoglycosides Nitroimidazole	Kanamycin Metronidazole	1 g 750 mg	Twice a day before surgery	Beta-lactams (cephalosporins)	Cefmetazole	1 g	30 minutes before the skin incision, and every 3 hours during the surgery
[19]	2016	Laparoscopic colorectal cancer surgery	515	OA + IVA + MBP *vs.* IVA + MBP	Aminoglycosides Nitroimidazole	Kanamycin Metronidazole	1 g 750 mg	Twice a day on the day before the surgery	Beta-lactams (cephalosporins)	Cefmetazole	1 g	30 minutes before the skin incision, and every 3 hours during the surgery
[24]	2020	Open or laparoscopic colorectal surgery	581	OA + IVA + MBP *vs.* IVA + MBP	Aminoglycosides Nitroimidazole	Streptomycin Metronidazole	1 g 200 mg	Three times a day for 3 days before surgery	Beta-lactams (cephalosporins)	Cefmetazole *In case of allergy to penicillin or cephalosporin - Clindamycin	2 g *0.6 g	30 minutes before the skin incision, and once every 12 h until 48 h after surgery *Twice a day
[25]	2022	Open or laparoscopic colorectal surgery	868	OA + IVA + MBP *vs.* IVA + MBP	Nitroimidazole	Ornidazole	1 g	12 h before surgery	Beta-lactams (cephalosporins)	Cefoxitin	2 g	During anesthesia induction
[26]	2023	Laparoscopic colorectal surgery	302	OA + IVA + MBP *vs.* IVA + MBP	Aminoglycosides Nitroimidazole	Neomycin Metronidazole	1 g 200 mg	Four times before surgery	Beta-lactams (cephalosporins)	Ceftriaxone	2 g	During anesthesia induction

OA – oral antibiotics, IVA – intravenous antibiotics, MBP – mechanical bowel preparation.

electrolytes, producing an osmotic effect that flushes bowel contents. This process alters colonic pH and oxygen levels, deprives mutualistic microbes of nutrients, and induces both mechanical and physiological disruptions [30]. However, MBP is frequently associated with adverse effects such as vomiting, abdominal pain, hypovolemia, and metabolic disturbances [31]. It also provokes inflammatory and structural changes in the colon [32], and shifts in the gut microbiome resembling those seen in inflammatory bowel disease [33].

Rectal enema serves as an alternative but is less frequently used. In rectal cancer surgery, enemas can achieve comparable bowel cleansing to oral MBP [34]. Recent trials indicate that both approaches induce similar levels of dysbiosis [35]. Patients who developed postoperative infections exhibited distinct microbial profiles – enriched with *Actinomyces*, *Sutterella*, and *Enterococcus faecalis* – by postoperative day 6. Another study found that preoperative antibiotics and MBP exert only minor effects on mucosa-associated microbiome [36].

In summary, while MBP remains widely practiced, its clinical value is uncertain. Both oral and rectal preparations disrupt the gut microbiome and promote transient dysbiosis, but current evidence does not clearly link these microbial changes to postoperative outcomes.

3.1.3. Nutritional support of microbial homeostasis

Cancer patients are at high risk of preoperative malnutrition, often due to GI symptoms that limit intake, yet only about 40% receive adequate nutritional support [37]. Up to 55% of patients eat less after diagnosis, and roughly 40% of CRC patients are malnourished [38]. GI surgery further exacerbates this through preoperative fasting, delayed feeding, and impaired GI function, compounded by anorexia, obstruction, and metabolic disturbances [39,40]. Malnutrition increases postoperative complications, delays adjuvant therapy, and worsens prognosis, particularly after GI surgery [41].

The gut microbiome contributes to digestion, nutrient absorption, and the production of key metabolites that maintain host health. Cancer therapy and surgery disrupt these microbial networks, influencing recovery and long-term outcomes. Altered taste perception – common in cancer patients – may also involve microbiome-driven mechanisms, as shown by animal studies linking microbial shifts to sensory changes [42].

Enhanced Recovery After Surgery (ERAS) protocols emphasize early oral or enteral feeding to reduce these complications [43]. Guidelines recommend enteral nutrition (EN) as first-line, with parenteral nutrition (PN) reserved for patients unable to meet caloric needs enterally [44]. EN lowers infection rates by maintaining mucosal integrity; in contrast, absence of EN promotes barrier dysfunction and bacterial translocation [45]. In a recent study of laparoscopic gastric cancer patients, Lin et al. (2025) found that ERAS protocols improved probiotic abundance and sustained gut microbiome recovery for up to one month postoperatively [46].

In summary, maintaining nutritional adequacy and early EN are key to optimizing outcomes in GI cancer surgery, with growing evidence that diet and microbiome modulation jointly influence recovery and long-term prognosis.

3.1.4. Anatomical changes and surgery-induced physical stress

Preclinical studies have shown that surgical intervention can alter gut microbial composition. Nevertheless, the extent to which these changes occur in clinical settings remains poorly characterized. Understanding surgery-induced perturbations of the intestinal microbiome is critical, as they may influence postoperative recovery and long-term outcomes.

A systematic review and meta-analysis of 33 studies (6 RCTs, 27 prospective cohorts; $n = 968$) reported consistent microbiome alterations following GI surgery, including increased alpha diversity of microbiome and distinct shifts in beta diversity [47]. Taxonomic changes involved higher abundances of Verrucomicrobia, Fusobacteria, Lactobacillales, Ruminococcaceae, and genera such as *Streptococcus*, *Akkermansia*, *Veillonella*, and *Bacteroides*, with reductions in *Bifidobacteriaceae* and *Bifidobacterium*. At the species level, *Akkermansia muciniphila*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Streptococcus salivarius* increased, whereas *Eubacterium rectale* decreased. Regional differences were also observed between Western and Eastern populations.

Subtotal gastrectomy with Billroth II reconstruction was specifically linked to increased colonization by oral bacteria due to elevated gastric pH and reduced barrier function [48]. This "oralization" of the gut microbiome – characterized by enrichment of *Escherichia–Shigella*, *Enterococcus*, and oral taxa such as *Streptococcus*, *Veillonella*, *Oribacterium*, and *Mogibacterium* – was associated with intestinal inflammation and GI symptoms.

In summary, GI surgery and related anatomical changes induce marked shifts in gut microbial composition, shaped by surgical type and physiological stress. These alterations may affect recovery, infection risk, and long-term outcomes, underscoring the need for further clinical research to guide microbiome-targeted perioperative strategies.

3.2. Gastrointestinal microbiome in the development of postoperative complications

3.2.1. Surgical Site Infections (SSIs)

The gut microbiome is vital for maintaining intestinal barrier integrity, a key factor in favorable surgical outcomes. A balanced microbiome supports mucosal health through short-chain fatty acid (SCFA) production, competitive pathogen exclusion, and immune modulation [49]. Disruption of this balance increases gut permeability, allowing bacterial and inflammatory translocation into the systemic circulation, which promotes chronic inflammation, immune dysregulation, and infection susceptibility [50].

Unlike sterile procedures, GI cancer surgery occurs in a microbially rich environment, making infection control challenging. Surgical disruption of the mucosal barrier facilitates bacterial translocation into sterile tissues, increasing the risk of SSIs, intra-abdominal abscesses, and sepsis [51]. Consequently, GI surgery carries some of the highest SSI rates among all surgical procedures [52] leading to prolonged hospitalization, higher costs, and poorer outcomes [53].

Traditionally, SSIs were attributed to intraoperative contamination; however, evidence suggests this is insufficient to cause infection. Studies show that up to 80% of patients with positive intraoperative wound cultures remain infection-free, and pathogen overlap between intraoperative and postoperative isolates is often limited [54,55]. These findings indicate that factors beyond operative contamination – such as host microbiome composition – play a critical role.

Emerging data suggest that endogenous microbes from the oral cavity [56] or gut [57] may contribute to SSIs through mechanisms such as the "Trojan horse" hypothesis. In this model, bacteria survive within phagocytes and are transported to surgical sites, where they are released and trigger infection [57]. *Staphylococcus aureus* exemplifies this process due to its ability to evade phagocytic clearance [58]. Although this mechanism is mainly supported by preclinical studies, clinical data show that patients developing infectious complications after colorectal surgery have distinct preoperative microbiome profiles, implicating dysbiosis in SSI risk [35].

These findings align with the growing understanding that gut dysbiosis may be a central contributor to infection risk following GI surgery [59]. Dysbiosis compromises colonization resistance and promotes the overgrowth of pathogens such as *Klebsiella*, which has been linked to epithelial invasion and *S. aureus* co-infection in CRC patients [60]. It also leads to the accumulation of toxic metabolites that damage the intestinal barrier and promote microbial translocation, fueling local and systemic inflammation [61]. Moreover, loss of beneficial microbes impairs mucosal healing by reducing metabolites critical for tissue repair and immune regulation [62].

In summary, gut dysbiosis is increasingly recognized as a key

contributor to postoperative infections after GI cancer surgery. Its effects extend beyond local microbial imbalance to include immune modulation, metabolite depletion, and barrier dysfunction. Further mechanistic and translational studies are needed to clarify these interactions and develop targeted microbiome-based interventions to reduce SSI risk.

3.2.2. Anastomotic Leakage (AL)

AL is one of the most serious complications after colorectal surgery [63], with reported incidence rates up 21% [64and30]-day mortality rates reaching 38% [65]. Growing evidence suggests that gut microbiome alterations contribute to AL pathogenesis [66,67].

Patients with AL often show distinct microbial signatures compared with uncomplicated cases. Praagh et al. (2019) showed significantly reduced microbial diversity in AL patients, along with increased relative abundances of bacterial families such as Lachnospiraceae and Bacteroidaceae [66]. Similarly, Jørgensen et al. (2024) found lower alpha diversity and a higher abundance of collagenase-producing taxa in AL cases after CRC surgery [67]. At the species level, Palmisano et al. (2020) observed a marked reduction in *Faecalibacterium prausnitzii*, a key butyrate-producing bacterium, suggesting that impaired butyrate metabolism may hinder mucosal repair [68].

Mechanistically, bacteria such as *Enterococcus faecalis* and *Fusobacterium nucleatum* can disrupt healing by secreting collagenases that degrade the extracellular matrix and by activating host matrix metalloproteinase-9 (MMP-9) [67,69,70]. Elevated MMP-9 levels in postoperative drain fluid have been correlated with AL severity [71]. Beyond proteolytic injury, microbiome disruption reduces SCFA production – especially butyrate – compromising colonocyte energy supply, re-epithelialization, and barrier integrity [72].

Taken together, dysbiosis characterized by reduced diversity, loss of butyrate-producing taxa, and enrichment of collagenase-secreting bacteria appears closely associated with AL. Although collagenolytic strains are a known risk factor for AL, their preoperative detection remains underused. Rapid molecular tools such as quantitative PCR and microbial identification panels exist but are not yet part of routine care. Prospective clinical trials are needed to define diagnostic thresholds and validate their predictive value for AL.

3.2.3. Other surgical complications

Several postoperative complications following GI surgery have been linked to gut microbiome alterations. Postoperative ileus, occurring in 10–30% of patients after abdominal surgery [73], has been increasingly linked to gut microbiome alterations. Shogan et al. (2020) reported higher abundances of pro-inflammatory taxa such as *Bacteroides*, *Parabacteroides*, and *Ruminococcus* in patients who developed ileus [74].

During colorectal surgery, loop ileostomy is often constructed to divert fecal flow and protect the anastomosis. The defunctionalized colon may develop diversion colitis, an inflammation of the excluded segment in patients without prior inflammatory bowel disease [75]. This condition is thought to result from microbiome imbalance and decreased SCFAs production, with an inverse correlation observed between *Bifidobacterium* abundance and colitis severity [76].

Pouchitis, affecting up to 50% of patients after restorative proctocolectomy for ulcerative colitis [77], is similarly been associated with reduced microbial diversity and depletion of butyrate-producing genera including *Ruminococcus*, *Lachnospira*, and *Coprococcus* [78]. Preoperative enrichment of potentially pathogenic taxa, including *Ruminococcus gnavus*, *Bacteroides vulgatus*, and *Clostridium perfringens*, along with reduced Lachnospiraceae, has been linked to higher pouchitis risk [79].

Together, these findings indicate that distinct microbiome perturbations may underline different postoperative complications, highlighting the importance of mechanistic research to clarify causal pathways and guide the development of targeted microbiome-modulating strategies in surgical patients.

3.3. Gut microbiome–targeted strategies in perioperative care

3.3.1. Probiotics

Recently, interventions targeting the GI microbiome have garnered increasing interest in their potential to improve patient outcomes. Probiotics have been investigated for their capacity to support postoperative recovery and mitigate complications. Several studies have specifically examined the effects of probiotics in gastrectomy, reporting encouraging results.

In gastric cancer surgery, several randomized trials report favorable outcomes. Supplementation with mixed probiotic formulations – typically including *Lactobacillus plantarum*, *L. acidophilus*, *L. rhamnosus*, and *Bifidobacterium animalis* subsp. *Lactis* – before or after gastrectomy reduced inflammation, enhanced immune recovery, and promoted microbial diversity [80,81].

Similar benefits have been demonstrated in CRC surgery. Probiotics improved bowel function, maintained mucosal integrity, and lowered infection and inflammation markers [82–84]. Some studies further showed modulation of gut composition, with increased butyrate-producing genera and decreased potentially pathogenic taxa (*Fusobacterium*, *Peptostreptococcus*) [85].

Despite these encouraging results, clinical outcomes remain inconsistent. This variability is primarily driven by several factors such as dosage heterogeneity and strain specificity. As evidenced in Table 2, daily dosage of probiotics significantly varies between the studies (from 4.65×10^6 CFU/day to 2.6×10^{14} CFU/day). Additionally, many studies utilize multi-strain probiotic cocktails where the functional contribution of individual species remains unknown. However, there are some species that overlap in analysed gastric and CRC studies. Some examples are different strains of *Lactobacillus acidophilus* (10 studies out of 14), *Bifidobacterium animalis* subsp. *lactis* (7 studies out of 14), and *Bifidobacterium longum* (6 studies out of 14). However, even within the same species, different strains may produce vastly different metabolic effects, and it should be taken into consideration.

3.3.2. Prebiotics and synbiotics

Limited data from RCTs exist regarding the effects of prebiotics alone in perioperative GI cancer patients, as reflected by the relatively few publications on the topic (Table 3). Consequently, the independent role of prebiotics in the perioperative period remains a significant knowledge gap, as most current evidence is limited to synbiotic combinations rather than isolated fiber-based interventions. However, a randomized study by Xie et al. (2019) reported that oral prebiotic supplementation with the mixture of equal parts fructooligosaccharides, xylooligosaccharides, polydextrose, and resistant dextrin increased serum immunoglobulin G (IgG), IgM, and transferrin levels in both pre- and postoperative phases, suggesting improved immune function [94].

Synbiotics—combinations of probiotics and prebiotics—have been more widely investigated. Several RCTs in patients undergoing major abdominal procedures, including hepato-pancreato-biliary surgery and liver transplantation, have shown reduced postoperative infectious complications with synbiotic use [95,96].

However, the impact of preoperative synbiotic use in GI cancer surgery remains relatively underexplored, as most studies in GI surgery have focused on the perioperative administration of probiotics. However, synbiotics may offer additional benefits beyond merely enhancing peristalsis. The inclusion of a prebiotic component can enhance the survival and activity of probiotics, potentially amplifying their positive effects on gut health, immune modulation, and postoperative recovery [97]. A randomized, double-blind clinical trial conducted in 2017 demonstrated that the perioperative administration of synbiotics significantly reduced postoperative infection rates in patients undergoing CRC surgery [98]. Similarly, Polakowski et al. (2019) found that seven days of preoperative synbiotic therapy reduced systemic inflammation, postoperative morbidity, hospital stay, and antibiotic requirements [89]. More recently, Stene et al. (2025) observed that

Table 2
Summary of probiotic usage in gastrointestinal cancer surgery. The usage of specific probiotic strains is marked in the dark green/blue cells. Names of the bacterial strains are provided inside the cells, where available [86–93].

	Study	Year	Daily concentration of product (in total, strains combined)	Commercial name of the product and manufacturer	Probiotics																	
					Lactobacillus plantarum	*Lactobacillus rhamnosus*	*Lactobacillus acidophilus*	*Lactobacillus lactis*	*Lactobacillus johnsonii*	*Lactobacillus casei*	*Lactobacillus reuteri*	*Lacticaseibacillus casei*	*Bifidobacterium animalis subsp. lactis*	*Bifidobacterium infantis*	*Bifidobacterium longum*	*Bifidobacterium bifidum*	*Bifidobacterium breve*	*Enterococcus faecalis*	*Bacillus cereus*	*Levilactobacillus brevis*	*Ligilactobacillus salivarius*	*Lactococcus lactis*
Probiotics in gastric cancer surgery	[86]	2019	4.6×10^{7} CFU/day	Bifidobacterium Tetravaccine Tablets, SFDA approval number: S20060010			*NA*							*NA*				*NA*	*NA*			
	[81]	2021	1.6×10^{10} CFU/day	NA	**MH-301**	**LGG-18**	*NA*						**LPL-RH**									
	[80]	2024	1.2×10^{10} CFU/day	Harbin Meihua Biotechnology Co., Ltd, Harbin, Heilongjiang, P.R. China.	**MH-301**	**LGG-18**	*NA*						**LPL-RH**									
Probiotics in colorectal cancer surgery	[87]	2010	2×10^{7}-2×10^{9} CFU/day	NA					**La1**						**BB536**							
	[83]	2011	$2.6x10^{14}$ CFU/day	Manufactured by Institute of Life Science of Only, Shanghai Jiao Tong University, Shanghai, China	**CGMCC No. 1258**		**LA-11**								**BL-88**							
	[88]	2016	5×10^{10} CFU/day	NA											**BB536**							
	[85]	2017	2.1×10^{10} CFU/day	ProBion Clinica (Wasa Medicals AB, Halmstad, Sweden)			**NCFM (ATCC 700396)**						**BI-04 (ATCC SD5219)**									
	[89]	2019	10^{9} CFU/day	Simbioflora (Farmoquimica, Sao Paulo, Brazil)		**HN001**	**NCFM**			**LPC-37**			**HN019**									
	[90]	2019	3.0×10^{11} CFU/day	HEXBIO® (B-Crobes Laboratories Sdn. Bhd., Malaysia)			**BCMC® 12,130**	**BCMC® 12,451**		**BCMC® 12,313**				**BCMC® 02129**	**BCMC® 02120**	**BCMC® 02290**						
	[84]	2020	4×10^{8} CFU/day	NA	**HY7712**							**HY2782**	**HY8002**									
	[91]	2021	1.0×10^{10} CFU/day	Manufactured by Ildong Bioscience Co. Ltd., Pyeongtaek, Korea		**IDCC3201**	**IDCC3302**				**IDCC3701**		**IDCC4301**		**IDCC4101**	**IDCC4201**	**IDCC4401**					**IDCC2301**
	[92]	2021	6.0×10^{7} CFU/day	BIFICO, Sine Pharmaceuticals, Shanghai, China			*NA*								*NA*			*NA*				
	[82]	2022	2.0×10^{9} CFU/day	Provided by Harbin Meihua Biotechnology Co, Ltd, Harbin, Heilongjiang, PR China									**MH-02**									
	[93]	2023	4.65×10^{6} CFU/day	Manufactured by Hangzhou Grand Biologic Pharmaceutical INC, Hangzhou, China			*NA*							*NA*				*NA*	*NA*			

CFU – colony forming units, *NA* – not available.

Table 3
Summary of randomized clinical trials investigating the use of synbiotics and prebiotics in colorectal cancer patients.

Study	Year	Objective	Clinical study	Study design	n	Groups	Cancer stage	Composition and dosage of synbiotics/prebiotics	Duration of the intervention	Commercial name of the synbiotic/prebiotic product	Placebo control	Result	Conclusion
[100]	2016	Effect of perioperative synbiotics on surgical outcomes in laparoscopic colorectal resection.	Single-center RCT	Patients undergoing laparoscopic colorectal surgery were randomized to synbiotics or control groups. The primary outcome was SSI within 30 days.	379	Synbiotics (n=173) *vs.* control (n=206)	I-IV	80mL of Yakult Ace: 4×10^{10} *Lactobacillus casei* strain *Shirota* + 2.5 g galacto oligosaccharides + 100mL of MILMIL-S: 1×10^{9} *Bifidobacterium breve* strain *Yakult*	7–11 days preoperatively + reintroduced 2–7 days postoperatively. 5 days preoperatively + 14 days postoperatively.	Yakult Ace (Yakult Honsha Co., Ltd, Tokyo, Japan) MILMIL-S (Yakult Honsha Co., Ltd, Tokyo, Japan)	No placebo used.	SSIs occurred in 17.3% (synbiotics) vs. 22.7% (control); not statistically significant (OR: 0.761, 95 % CI 0.50–1.16; p = 0.2). Synbiotics reversed microbiome changes in fecal bacteria organic acids and reduced *Clostridium difficile* postoperatively.	Synbiotics did not reduce infection rates but improved microbial balance and organic acid levels.
[98]	2017	Effect of perioperative synbiotics on surgical wound infection in colorectal cancer surgery.	RCT	Colorectal cancer patients were randomized to receive synbiotics or placebo for 5 days preoperatively and 14 days postoperatively.	91	Synbiotics (n=49) *vs.* placebo (n=42)	I-IV	Fructo-oligosaccharide 6 g + *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus casei*, Bifidobacterium (10^{6}–10^{9} CFU each)	Both groups were given two sachets twice a day containing the active substance (intervention group) or placebo (control group) 5 days pre-op + 14 days post-operatively.	Not specified	Sachets with 96% maltodextrin (6 g).	SSIs occurred in 2% (synbiotics) vs. 21.4% (control) (p = 0.002). No infections (abscess/pneumonia) in synbiotics group and seven infections in the placebo group - significant reduction in infection rates (p = 0.001).	Synbiotics significantly reduced postoperative infection rates.
[89]	2019	Effect of preoperative synbiotics on outcomes after colorectal resection.	Prospective, double-blind, placebo-controlled RCT	Patients received synbiotics or placebo for 7 days preoperatively. Outcomes included: occurrence of infectious or non-infectious complications, time of antibiotic use, duration of hospitalization, and occurrence of deaths within 30 days.	73	Synbiotics (n=36) *vs.* placebo (n=37)	I-III	Fructo-oligosaccharide 6 g + *Lactobacillus acidophilus* NCFM, *Lactobacillus rhamnosus* HN001, *Lactobacillus casei* LPC-37, and *Bifidobacterium lactis* HN019 (10^{9} CFU)	7 days	Simbioflora, Farmoquimica, Sao Paulo, Brasil	Maltodextrin	Synbiotics reduced IL-6 and CRP levels. Infections occurred in 2.8% (synbiotics) vs. 18.9% (control). Synbiotics group had shorter antibiotic usage time (p < 0.001) and mean hospital stay (3 vs. 4 days).	Preoperative synbiotics reduced inflammation, morbidity, hospital length of stay, and antibiotic use.
[94]	2019	Effect of prebiotics on immunity and gut microbiome in perioperative colorectal cancer patients.	Double-blind, no-treatment parallel control RCT	Patients received prebiotics (30 g/day) or no treatment for 7 days preoperatively. The outcomes included immune markers and gut microbiome.	140	Prebiotics (n = 70) *vs.* no-prebiotics (n = 70)	-	Fructo-oligosaccharide, xylo-oligosaccharide, polydextrose, and resistant dextrin (25% each); oral dose of 30 g/day	7 days	No commercial name, Manufacturer: Hangzhou Niuqu Biotech Co., Hainengbo, China	No placebo; control group had prebiotics-free diet.	Prebiotics produced significant effects on immunologic indices in both preoperative and postoperative periods, but the patterns of effects were different. In the preoperative period, prebiotics increased serum levels of immunoglobulin G (IgG), IgM, and transferrin (all p < 0.05). At the genus level, prebiotics increased the abundance of Bifidobacterium and Enterococcus (both p < 0.05) but decreased the abundance of Bacteroides in the preoperative period (all p < 0.05). There was a notable trend of decline in the abundance of intestinal microbiome from preoperative to postoperative in the non-prebiotic group.	Preoperative prebiotics improved immune markers and gut microbiome; Bacteroides is a relevant bacterial species for further research on the mechanism of prebiotics.

CFU – colony forming units, CRP – C-reactive protein, IL-6 – interleukin-6, RCT – randomized clinical trial.

synbiotics reduced tissue inflammation and fibrosis in rectal cancer patients undergoing neoadjuvant radiotherapy, though effects were localized due to short intervention duration [99]. Conversely, a large RCT (2016; $n = 379$) found no significant reduction in infectious complications following laparoscopic colorectal resection despite perioperative synbiotic use [100].

3.4. Establishing causality: insights from preclinical models

A significant challenge in human microbiome research is the difficulty of establishing definitive causality, as perioperative dysbiosis is often confounded by surgical stress, antibiotic administration, and nutritional changes. However, preclinical models provide essential mechanistic insights that suggest the microbiome is an active driver of surgical outcomes. For instance, *in vivo* animal models have demonstrated that surgical stress can trigger a "*phenotypic switch*" in pathogens such as *E. faecalis*, inducing the production of collagenases that directly degrade the host's anastomotic tissue [69]. Furthermore, the loss of butyrate-producing taxa—a common clinical finding—has been shown in laboratory models to compromise colonocyte energy metabolism, leading to gut barrier failure and bacterial translocation [101,102]. In murine models, gut colonization with methicillin-resistant *Staphylococcus aureus* has been shown to directly cause SSIs via immune cell mediated transport from the intestine to the wound, providing evidence of microbiome-driven causality [57]. By integrating these mechanistic findings, it becomes clear that microbiome-targeted interventions are not merely treating a marker of disease but are addressing a fundamental causal pathway in surgical recovery.

3.5. Conclusions and future research directions

In summary, our review highlights that while specific interventions—most notably probiotics—show promise in mitigating perioperative dysbiosis, the field is currently characterized by significant heterogeneity in protocols. There is currently no consensus regarding the most efficacious probiotic species or strains, nor is there a standardized approach to bacterial concentration or dosage regimens. Furthermore, while probiotics demonstrate the most visible clinical benefits to date, prebiotics and synbiotics remain significantly understudied; This lack of isolated data prevents a comprehensive evaluation of specific prebiotic fibers or their synergistic combinations in the surgical context.

Despite these gaps, the evidence underscores the critical role of the microbiome during the pre- and perioperative periods. Gut dysbiosis is increasingly recognized as a key contributor to postoperative infections following GI cancer surgery. Specifically, microbial signatures dominated by an overrepresentation of pathogens (such as *E. faecalis*, *F. nucleatum*), alongside a depletion of SCFA-producing taxa, emerge as frequent precursors to severe postoperative complications.

To address these limitations, future research must transition from descriptive studies toward longitudinal multi-omics analysis — integrating metagenomics with metabolomics to move beyond taxonomic identification and toward a functional understanding of microbial activity. Furthermore, large-scale, high-quality RCTs should be prioritized to validate the efficacy of probiotics, prebiotics, and synbiotics and to identify the most effective therapeutic regimens. The potential of other microbiome-targeting interventions in high-risk patients warrants investigation, particularly focusing on the concept of "*precision prehabilitation*". This approach involves tailoring interventions, such as fecal microbiota transplantation or targeted dietary supplementation protocols, to a patient's unique baseline microbial profile to optimize surgical outcomes.

However, the transition to clinical practice faces significant hurdles. Potential barriers to implementation include the high cost and technical complexity of high-resolution sequencing, a lack of international standardization in sampling protocols, and patient adherence to intensive preoperative regimens remain a critical factor for success. Advancing GI cancer surgery will require tailored, microbiome-directed strategies that account for individual microbial and clinical profiles. Harnessing predictive microbial signatures to guide precision interventions, in conjunction with standardized perioperative protocols, could reduce postoperative complications, enhance recovery, and improve long-term patient outcomes. Translating these approaches into clinical practice will depend on well-designed clinical trials and integrative multi-omics analyses to establish robust, evidence-based guidelines.

Advances in artificial intelligence (AI) and neural network–based analytics may help address several of the field's current limitations. By integrating metagenomic, metabolomic, and clinical variables, these models could potentially identify early dysbiosis patterns associated with postoperative risk. AI-driven frameworks also hold promise for detecting *segment-specific* dysbiosis along the colon—an underexplored yet clinically meaningful dimension that may further refine patient-tailored perioperative management. Importantly, such approaches may also support the selection of the most appropriate microbiome-targeted intervention—whether probiotic, prebiotic, synbiotic, or alternative strategies—based on a patient's individual microbial and metabolic profile. These tools could support more precise, microbiome-informed interventions and accelerate the translation of multi-omics insights into clinically actionable perioperative strategies.

CRediT authorship contribution statement

Kristina Žukauskaitė: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization. **Kornelija Rauduvytė:** Writing – review & editing, Writing – original draft, Investigation. **Augustinas Baušys:** Writing – review & editing, Writing – original draft, Conceptualization. **Angela Horvath:** Writing – review & editing, Supervision. **Tomas Poškus:** Writing – review & editing. **Vanessa Stadlbauer:** Writing – review & editing, Supervision, Resources, Funding acquisition.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work the authors used Microsoft CoPilot tool for language and style improvement. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the published article.

Funding

This research was supported by the Center for Biomarker Research in Medicine (CBmed GmbH) and the Medical University of Graz, Graz, Austria. K.R. was also supported by the Future Biomedicine Foundation, Vilnius, Lithuania.

Conflict of interest

Authors declare no conflict of interest.

References

[1] A. Singh, Global burden of five major types of gastrointestinal cancer, Przegląd Gastroenterol. (2024), https://doi.org/10.5114/pg.2024.141834.
[2] Javed, H. et al. Challenges and solutions in postoperative complications: a narrative review in general surgery. Cureus. https://doi.org/10.7759/cureus.50942.
[3] R. Callan, E. Loud, Antibiotic stewardship in UK surgical departments: challenges and possible solutions, Br. J. Hosp. Med. (2021), https://doi.org/10.12968/hmed.2020.0692.
[4] K. Guyton, J.C. Alverdy, The gut microbiota and gastrointestinal surgery, Nat. Rev. Gastroenterol. Hepatol. (2017), https://doi.org/10.1038/nrgastro.2016.139.

[5] S. Smolinska, et al., A review of the influence of prebiotics, probiotics, synbiotics, and postbiotics on the human gut microbiome and intestinal integrity, J. Clin. Med. (2025), https://doi.org/10.3390/jcm14113673.

[6] K. Trone, et al., Synbiotics and surgery: can prebiotics and probiotics affect inflammatory surgical outcomes? Current Nutrition Reports (2023) https://doi.org/10.1007/s13668-023-00464-1.

[7] S.I. Berríos-Torres, et al., Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017, JAMA Surg. (2017), https://doi.org/10.1001/jamasurg.2017.0904.

[8] M.F. Crader, M.A. Varacallo, Preoperative antibiotic prophylaxis, in: StatPearls, StatPearls Publishing, Treasure Island (FL), 2025.

[9] Antibiotics used in gastrointestinal surgery prophylaxis and treatment of postoperative infection, The Egyptian J. Hospital Medicine (2017), https://doi.org/10.12816/0041699.

[10] Y. Mohri, et al., Randomized clinical trial of single- versus multiple-dose antimicrobial prophylaxis in gastric cancer surgery, Br. J. Surg. (2007), https://doi.org/10.1002/bjs.5837.

[11] S.S. Bains, et al., Addition of Vancomycin to Cefazolin is Often Unnecessary for Preoperative Antibiotic Prophylaxis During Total Joint Arthroplasties, Arthroplasty, 2024, https://doi.org/10.1186/s42836-023-00222-2.

[12] D. Dahiya, P.S. Nigam, Antibiotic-Therapy-induced gut dysbiosis affecting gut microbiota—brain axis and cognition: restoration by intake of probiotics and synbiotics, Int. J. Mol. Sci. (2023), https://doi.org/10.3390/ijms24043074.

[13] H. Nalluri, et al., Peri-operative antibiotics acutely and significantly impact intestinal microbiota following bariatric surgery, Sci. Rep. (2020), https://doi.org/10.1038/s41598-020-77285-7.

[14] J.D. Lewis, et al., Inflammation, antibiotics, and diet as environmental stressors of the gut microbiome in pediatric crohn's disease, Cell Host Microbe (2015), https://doi.org/10.1016/j.chom.2015.09.008.

[15] M. Rutegård, et al., Oral antibiotics and mechanical bowel preparation for colorectal surgery: a prospective observational study of surgical site infection and microbial analysis, Int. J. Colorectal Dis. (2023), https://doi.org/10.1007/s00384-023-04497-4.

[16] H. Nalluri-Butz, et al., A pilot study demonstrating the impact of surgical bowel preparation on intestinal microbiota composition following colon and rectal surgery, Sci. Rep. (2022), https://doi.org/10.1038/s41598-022-14819-1.

[17] J. Kohn, et al., The role of surgical and perioperative factors in shaping gut Microbiome recovery after colorectal surgery, Antibiotics (2025), https://doi.org/10.3390/antibiotics14090881.

[18] H. Hata, et al., Oral and parenteral versus parenteral antibiotic prophylaxis in elective laparoscopic colorectal surgery (JMTO PREV 07–01): a phase 3, multicenter, open-label, randomized trial, Ann. Surg. (2016), https://doi.org/10.1097/SLA.0000000000001581.

[19] A. Ikeda, et al., Randomized clinical trial of oral and intravenous versus intravenous antibiotic prophylaxis for laparoscopic colorectal resection, Br. J. Surg. (2016), https://doi.org/10.1002/bjs.10281.

[20] C. Hjalmarsson, et al., Orally administered trimethoprim-sulfamethoxazole and metronidazole as infection prophylaxis in elective colorectal surgery, Surg. Infect. (2015), https://doi.org/10.1089/sur.2014.059.

[21] https://euclinicaltrials.eu/ctis-public/view/2025-520725-20-00?lang=en.

[22] M. Carlini, Can We Manipulate the Bowel Microbiota and Prevent Anastomotic Leakage in Colorectal Laparoscopic Surgery? Preliminary Results of the Miracle Study, 2023.

[23] Ottawa Hospital Research Institute, A Randomised Study Comparing No Mechanical Bowel Preparation with Oral Antibiotics Alone in Patients Undergoing Elective Colon Surgery (REaCT-NSQIP), 2025.

[24] P. Lei, et al., Preoperative mechanical bowel preparation with oral antibiotics reduces surgical site infection after elective colorectal surgery for malignancies: results of a propensity matching analysis, World J. Surg. Oncol. (2020), https://doi.org/10.1186/s12957-020-1804-4.

[25] E. Futier, et al., Effect of oral antimicrobial prophylaxis on surgical site infection after elective colorectal surgery: Multicentre, randomised, double blind, placebo controlled trial, Br. Med. J. (2022), https://doi.org/10.1136/bmj-2022-071476.

[26] P. Lei, et al., Region-specific protection effect of preoperative oral antibiotics combined with mechanical bowel preparation before laparoscopic colorectal resection: a prospective randomized controlled trial, Int. J. Surg. (2023), https://doi.org/10.1097/JS9.0000000000000569.

[27] K.F. Güenaga, et al., Mechanical bowel preparation for elective colorectal surgery, Cochrane Database Syst. Rev. (2011), https://doi.org/10.1002/14651858.CD001544.pub4.

[28] F. Bretagnol, et al., Rectal cancer surgery with or without bowel preparation: the French greccar III multicenter single-blinded randomized trial, Ann. Surg. (2010), https://doi.org/10.1097/SLA.0b013e3181fd8ea9.

[29] L. Koskenvuo, et al., Morbidity after mechanical bowel preparation and oral antibiotics prior to rectal resection, JAMA Surg. (2024), https://doi.org/10.1001/jamasurg.2024.0184.

[30] H. Paine, et al., Preparing the bowel (Microbiome) for surgery: surgical bioresilience, Clin. Colon Rectal Surg. (2023), https://doi.org/10.1055/s-0042-1760675.

[31] F. Bretagnol, et al., Rectal cancer surgery with or without bowel preparation: the French greccar III multicenter single-blinded randomized trial, Ann. Surg. (2010), https://doi.org/10.1097/SLA.0b013e3181fd8ea9.

[32] P. Bucher, et al., Morphologic alterations associated with mechanical bowel preparation before elective colorectal surgery: a randomized trial, Dis. Colon Rectum (2006), https://doi.org/10.1007/s10350-005-0215-5.

[33] G. Gorkiewicz, et al., Alterations in the colonic microbiota in response to osmotic diarrhea, PLoS One (2013), https://doi.org/10.1371/journal.pone.0055817.

[34] O. Pittet, et al., Rectal enema is an alternative to full mechanical bowel preparation for primary rectal cancer surgery, Colorectal Dis. (2015), https://doi.org/10.1111/codi.12974.

[35] K. Žukauskaitė, et al., Impact of mechanical bowel preparation on the gut microbiome of patients undergoing left-sided colorectal cancer surgery: randomized clinical trial, Br. J. Surg. (2024), https://doi.org/10.1093/bjs/znae213.

[36] E.C. Hoedt, et al., Preoperative antibiotics and mechanical bowel preparation impact the colonic mucosa–associated microbiota but not anastomotic leak rate after Colorectal resection, Dis. Colon Rectum (2025), https://doi.org/10.1097/DCR.0000000000003775.

[37] A. Gazouli, et al., Perioperative nutritional assessment and management of patients undergoing gastrointestinal surgery, Ann. Gastroenterol. (2024), https://doi.org/10.20524/aog.2024.0867.

[38] X. Hébuterne, et al., Prevalence of malnutrition and current use of nutrition support in patients with cancer, J. Parenter. Enteral Nutr. (2014), https://doi.org/10.1177/0148607113502674.

[39] Coutinho, R.B. et al. Association between preoperative fasting time and clinical outcomes in surgical patients in a private general hospital. Acta Cir. Bras. https://doi.org/10.1590/acb394524.

[40] N.S. Levonyak, et al., Importance of addressing malnutrition in cancer and implementation of a quality improvement project in a gastrointestinal cancer clinic, Nutr. Clin. Pract. (2022), https://doi.org/10.1002/ncp.10753.

[41] I.P.A. Virgens, das, et al., Is perioperative fasting associated with complications, length of hospital stay and mortality among gastric and colorectal cancer patients? A cohort study, Sao Paulo Med. J. (2020), https://doi.org/10.1590/1516-3180.2020.0084.R1.30062020.

[42] T.D. Swartz, et al., Up-regulation of intestinal type 1 taste receptor 3 and sodium glucose luminal transporter-1 expression and increased sucrose intake in mice lacking gut microbiota, Br. J. Nutr. (2012), https://doi.org/10.1017/S0007114511003412.

[43] U.O. Gustafsson, et al., Guidelines for perioperative care in elective colorectal surgery: enhanced Recovery After Surgery (ERAS®) Society recommendations: 2018, World J. Surg. (2019), https://doi.org/10.1007/s00268-018-4844-y.

[44] S.A. McClave, et al., Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient, J. Parenter. Enteral Nutr. (2016), https://doi.org/10.1177/0148607115621863.

[45] G. Elke, et al., Enteral versus parenteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials, Crit. Care (2016), https://doi.org/10.1186/s13054-016-1298-1.

[46] X.-J. Lin, et al., Effects of enhanced recovery after surgery on postoperative intestinal function and intestinal flora during laparoscopic gastric cancer surgery, World J. Gastrointest. Surg. (2025), https://doi.org/10.4240/wjgs.v17.i9.106286.

[47] M. Tarazi, et al., Impact of gastrointestinal surgery upon the gut microbiome: a systematic review, Surgery (2022), https://doi.org/10.1016/j.surg.2021.10.014.

[48] A. Horvath, et al., Distal gastrectomy with billroth II reconstruction is associated with oralization of gut microbiome and intestinal inflammation: a proof-of-concept study, Ann. Surg Oncol. (2021), https://doi.org/10.1245/s10434-020-08678-1.

[49] Z. Li, et al., Critical role of the gut microbiota in immune responses and cancer immunotherapy, J. Hematol. Oncol. (2024), https://doi.org/10.1186/s13045-024-01541-w.

[50] S. Ghosh, et al., Regulation of intestinal barrier function by microbial metabolites, Cell. Mol. Gastroenterol. Hepatol. (2021), https://doi.org/10.1016/j.jcmgh.2021.02.007.

[51] C. Doudakmanis, et al., Bacterial translocation in patients undergoing major gastrointestinal surgery and its role in postoperative sepsis, World J. Gastrointest. Pathophysiol. (2021), https://doi.org/10.4291/wjgp.v12.i6.106.

[52] B. Wang, et al., Impact of enhanced recovery after surgery (ERAS) on surgical site infection and postoperative recovery outcomes: a retrospective study of 1276 cases, Sci. Rep. (2024), https://doi.org/10.1038/s41598-024-74389-2.

[53] J. Hammond, et al., The burden of gastrointestinal anastomotic leaks: an evaluation of clinical and economic outcomes, J. Gastrointest. Surg.: Official J. Society for Surgery of the Alimentary Tract (2014), https://doi.org/10.1007/s11605-014-2506-4.

[54] R.P. Morton, et al., Predictors of infection after 754 cranioplasty operations and the value of intraoperative cultures for cryopreserved bone flaps. https://doi.org/10.3171/2015.8.JNS151390, 2016.

[55] R.A. Garibaldi, et al., Predictors of intraoperative-acquired surgical wound infections, J. Hosp. Infect. (1991), https://doi.org/10.1016/0195-6701(91)90035-7.

[56] J. Zenga, et al., A phase 2 trial of a topical antiseptic bundle in head and neck cancer surgery: effects on surgical site infection and the oral microbiome, EBioMedicine (2022), https://doi.org/10.1016/j.ebiom.2022.104099.

[57] M.A. Krezalek, et al., Can methicillin-resistant Staphylococcus aureus silently travel from the gut to the wound and cause postoperative infection? Modeling the "Trojan Horse Hypothesis.", Ann. Surg. (2018) https://doi.org/10.1097/SLA.0000000000002173.

[58] A. Ali, et al., Incidence of Surgical Site Infection, Bacterial Isolate, and their Antimicrobial Susceptibility Pattern Among Patients who Underwent Surgery at Dessie Comprehensive Specialized Hospital, Northeast Ethiopia, SAGE Open Medicine, 2023, https://doi.org/10.1177/20503121231172345.

[59] L. Nichols, et al., The bidirectional interplay between gut dysbiosis and surgical complications: a systematic review, Am. J. Surg. (2025), https://doi.org/10.1016/j.amjsurg.2025.116369.

[60] J. Cong, et al., A pilot Study: changes of gut microbiota in post-surgery colorectal cancer patients, Front. Microbiol. (2018), https://doi.org/10.3389/fmicb.2018.02777.

[61] Y. Shen, et al., Gut microbiota dysbiosis: pathogenesis, diseases, prevention, and therapy, MedComm (2025), https://doi.org/10.1002/mco2.70168.

[62] Y. Shan, et al., The gut microbiome and inflammatory bowel diseases, Annu. Rev. Med. (2022), https://doi.org/10.1146/annurev-med-042320-021020.

[63] M.A. Willis, et al., Preoperative combined mechanical and oral antibiotic bowel preparation for preventing complications in elective colorectal surgery, Cochrane Database Syst. Rev. (2023), https://doi.org/10.1002/14651858.CD014909.pub2.

[64] A. Gerdin, et al., Anastomotic leakage after resection for rectal cancer and recurrence-free survival in relation to postoperative C-reactive protein levels, Int. J. Colorectal Dis. (2024), https://doi.org/10.1007/s00384-024-04766-w.

[65] Predictors for anastomotic leak, postoperative complications, and mortality after right colectomy for cancer: results from an international snapshot audit, Dis. Colon Rectum (2020), https://doi.org/10.1097/DCR.0000000000001590.

[66] J.B. van Praagh, et al., Mucus microbiome of anastomotic tissue during surgery has predictive value for colorectal anastomotic leakage, Ann. Surg. (2019), https://doi.org/10.1097/SLA.0000000000002651.

[67] A.B. Jørgensen, et al., The baseline fecal microbiome differs in patients with and without anastomotic leakage after colorectal cancer surgery, Heliyon (2024) e40616, https://doi.org/10.1016/j.heliyon.2024.e40616.

[68] S. Palmisano, et al., Role of preoperative gut microbiota on colorectal anastomotic leakage: preliminary results, Updates in Surgery (2020), https://doi.org/10.1007/s13304-020-00720-x.

[69] B.D. Shogan, et al., Collagen degradation and MMP9 activation by Enterococcus faecalis contributes to intestinal anastomotic leak, Sci. Transl. Med. (2015), https://doi.org/10.1126/scitranslmed.3010658.

[70] S. Shi, et al., Fusobacterium nucleatum induces colon anastomosis leak by activating epithelial cells to express MMP9, Front. Microbiol. (2022), https://doi.org/10.3389/fmicb.2022.1031882.

[71] P. Edomskis, et al., Matrix metalloproteinase-9 in relation to patients with complications after colorectal surgery: a systematic review, Int. J. Colorectal Dis. (2021), https://doi.org/10.1007/s00384-020-03724-6.

[72] N. Gasaly, et al., Butyrate and the fine-tuning of colonic homeostasis: implication for inflammatory bowel diseases, Int. J. Mol. Sci. (2021), https://doi.org/10.3390/ijms22063061.

[73] A. Venara, et al., Postoperative ileus: pathophysiology, incidence, and prevention, J. Visceral Surgery. (2016), https://doi.org/10.1016/j.jviscsurg.2016.08.010.

[74] B.D. Shogan, et al., Alterations of the rectal microbiome are associated with the development of postoperative ileus in patients undergoing colorectal surgery, J. Gastrointest. Surg. (2020), https://doi.org/10.1007/s11605-020-04593-8.

[75] T.W. Bax, M.S. McNevin, The value of diverting loop ileostomy on the high-risk colon and rectal anastomosis, Am. J. Surg. (2007), https://doi.org/10.1016/j.amjsurg.2007.01.005.

[76] J.K. Randall, et al., Is Clostridium difficile infection a particular problem after reversal of ileostomy? Colorectal Dis. (2011) https://doi.org/10.1111/j.1463-1318.2009.02139.x.

[77] B. Shen, B.A. Lashner, Diagnosis and treatment of pouchitis, Gastroenterol. Hepatol. (2008).

[78] N. Maharshak, et al., Alterations of enteric microbiota in patients with a normal ileal pouch are predictive of pouchitis, J. Crohns Colitis (2017), https://doi.org/10.1093/ecco-jcc/jjw157.

[79] K. Machiels, et al., Specific members of the predominant gut microbiota predict pouchitis following colectomy and IPAA in UC. https://doi.org/10.1136/gutjnl-2015-309398, 2017.

[80] H. Xiong, et al., Probiotic compounds enhanced recovery after surgery for patients with distal gastric cancer: a prospective, controlled clinical trial, Ann. Surg Oncol. (2024), https://doi.org/10.1245/s10434-024-15394-7.

[81] C. Zheng, et al., Adjuvant treatment and molecular mechanism of probiotic compounds in patients with gastric cancer after gastrectomy, Food Funct. (2021), https://doi.org/10.1039/D1FO01375K.

[82] H. Liu, et al., Improvement effect of Bifidobacterium animalis subsp. lactis MH-02 in patients receiving resection of colorectal polyps: a randomized, Double-Blind, placebo-controlled trial, Front. Immunol. (2022), https://doi.org/10.3389/fimmu.2022.940500.

[83] Z. Liu, et al., Randomised clinical trial: the effects of perioperative probiotic treatment on barrier function and post-operative infectious complications in colorectal cancer surgery – a double-blind study, Aliment. Pharmacol. Ther. (2011), https://doi.org/10.1111/j.1365-2036.2010.04492.x.

[84] I.J. Park, et al., Effects of PrObiotics on the symptoms and surgical ouTComes after anterior REsection of Colon cancer (POSTCARE): a randomized, Double-blind, placebo-controlled trial, J. Clin. Med. (2020), https://doi.org/10.3390/jcm9072181.

[85] A.A. Hibberd, et al., Intestinal microbiota is altered in patients with colon cancer and modified by probiotic intervention, BMJ Open Gastroenterology (2017), https://doi.org/10.1136/bmjgast-2017-000145.

[86] C. Zheng, et al., A randomised trial of probiotics to reduce severity of physiological and microbial disorders induced by partial gastrectomy for patients with gastric cancer, J. Cancer (2019), https://doi.org/10.7150/jca.29072.

[87] L. Gianotti, et al., A randomized double-blind trial on perioperative administration of probiotics in colorectal cancer patients, World J. Gastroenterol. WJG (2010), https://doi.org/10.3748/wjg.v16.i2.167.

[88] M. Mizuta, et al., Perioperative supplementation with bifidobacteria improves postoperative nutritional recovery, inflammatory response, and fecal microbiota in patients undergoing colorectal surgery: a prospective, randomized clinical trial, Bioscience of Microbiota, Food and Health (2016), https://doi.org/10.12938/bmfh.2015-017.

[89] C.B. Polakowski, et al., Impact of the preoperative use of synbiotics in colorectal cancer patients: a prospective, randomized, double-blind, placebo-controlled study, Nutrition (2019), https://doi.org/10.1016/j.nut.2018.06.004.

[90] L. Zaharuddin, et al., A randomized double-blind placebo-controlled trial of probiotics in post-surgical colorectal cancer, BMC Gastroenterol. (2019), https://doi.org/10.1186/s12876-019-1047-4.

[91] H. Kwon, et al., The effect of probiotics supplementation in postoperative cancer patients: a prospective pilot study, Annals of Surgical Treatment and Research (2021), https://doi.org/10.4174/astr.2021.101.5.281.

[92] P. Wang, et al., Perioperative probiotic treatment decreased the incidence of postoperative cognitive impairment in elderly patients following non-cardiac surgery: a randomised double-blind and placebo-controlled trial, Clin. Nutr. (2021), https://doi.org/10.1016/j.clnu.2020.05.001.

[93] F. Huang, et al., Postoperative probiotics administration attenuates gastrointestinal complications and Gut microbiota dysbiosis caused by chemotherapy in colorectal cancer patients, Nutrients (2023), https://doi.org/10.3390/nu15020356.

[94] X. Xie, et al., Effects of prebiotics on immunologic indicators and intestinal microbiota structure in perioperative colorectal cancer patients, Nutrition (2019), https://doi.org/10.1016/j.nut.2018.10.038.

[95] H. Kanazawa, et al., Synbiotics reduce postoperative infectious complications: a randomized controlled trial in biliary cancer patients undergoing hepatectomy, Langenbecks Arch. Surg. (2005), https://doi.org/10.1007/s00423-004-0536-1.

[96] N. Rayes, et al., Supply of Pre- and probiotics reduces bacterial infection rates after Liver transplantation—A randomized, double-blind trial, Am. J. Transplant. (2005), https://doi.org/10.1111/j.1600-6143.2004.00649.x.

[97] M. Okazaki, et al., Perioperative synbiotic therapy in elderly patients undergoing gastroenterological surgery: a prospective, randomized control trial, Nutrition (2013), https://doi.org/10.1016/j.nut.2013.03.015.

[98] A.T. Flesch, et al., Perioperative synbiotics administration decreases postoperative infections in patients with colorectal cancer: a randomized, double-blind clinical trial, Rev. Col. Bras. Cir. (2017), https://doi.org/10.1590/0100-69912017006004.

[99] C. Stene, et al., Synbiotics protected radiation-induced tissue damage in rectal cancer patients: a controlled trial, Clin. Nutr. (2025), https://doi.org/10.1016/j.clnu.2025.03.025.

[100] S. Komatsu, et al., Efficacy of perioperative synbiotics treatment for the prevention of surgical site infection after laparoscopic colorectal surgery: a randomized controlled trial, Surg. Today (2016), https://doi.org/10.1007/s00595-015-1178-3.

[101] F. Rivera-Chávez, et al., Depletion of butyrate-producing *Clostridia* from the Gut Microbiota drives an aerobic luminal expansion of *salmonella*, Cell Host Microbe (2016), https://doi.org/10.1016/j.chom.2016.03.004.

[102] C.J. Kelly, et al., Crosstalk between microbiota-derived short-chain fatty acids and intestinal epithelial HIF augments tissue barrier function, Cell Host Microbe (2015), https://doi.org/10.1016/j.chom.2015.03.005.