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Review

Targeting the Perioperative Microbiome: Emerging Strategies to Reduce Post-Surgical Infections

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Abstract

Background: Despite major advances in aseptic techniques and antibiotic prophylaxis, surgical site infections (SSIs) remain a leading cause of postoperative morbidity and a significant contributor to global healthcare burden. Increasing evidence indicates that the perioperative microbiome encompassing gut, skin, and mucosal microbial communities play a critical role in immune regulation, wound healing, and host defense. Perioperative disruptions to microbial homeostasis can induce dysbiosis, impair epithelial barrier integrity, and amplify inflammatory responses, thereby increasing susceptibility to infection. Targeted modulation of this microbial interface represents an emerging frontier in precision surgical care. **Methods:** A systematic evidence-based review of peer-reviewed literature published between 2020 and 2025 was conducted using PubMed, Scopus, the Cochrane Library and Web of Science. Eligible studies included clinical trials, translational investigations, and *in vivo* models evaluating microbiome-targeted interventions, predictive microbial biomarkers, or artificial intelligence (AI)-based surgical site infection (SSI) risk modeling. Data extraction focused on intervention type, study design, microbiome outcomes, immune markers, and infection rates. **Results:** Microbiome-directed strategies including probiotics, prebiotics, synbiotics, and fecal microbiota transplantation (FMT) were associated with enhanced mucosal integrity, reduced pathogenic colonization, and modulation of inflammatory pathways. Adjunctive approaches such as photobiomodulation therapy and probiotic-coated dressings demonstrated synergistic benefits. AI-driven microbiome analytics enabled personalized SSI risk prediction through microbial profiling. **Conclusion:** Microbiome-informed perioperative care offers a paradigm shift toward personalized, antimicrobial-sparing SSI prevention. Future translation requires standardized protocols, validated predictive models, and integration of AI-assisted clinical decision-support systems.

Keywords

Perioperative microbiome modulation, Surgical site infection, Probiotics, Predictive biomarkers, Precision surgery

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1. Introduction

Surgical site infections (SSIs) remain a major postoperative complication despite advances in aseptic technique, surgical skill, and prophylactic antibiotic protocols [1,2]. Traditional paradigms of surgical site infection (SSI) prevention have focused on external contamination and operative sterility, yet mounting evidence implicates the patient's own microbiome as the primary reservoir for these infections [1,3]. The perioperative microbiome comprising diverse bacterial communities on the skin, nasal passages, gastrointestinal tract, and other mucosal surfaces often harbors strains resistant to conventional antibiotics, highlighting the need for interventions that extend beyond standard prophylaxis [4]. Endogenous bacteria introduced into the surgical field during incision or implantation can establish biofilms on tissues and foreign materials, complicating eradication and recovery, particularly in procedures involving prosthetics or implants [5,6].

Epidemiologic analyses indicate that the majority of SSIs originate from patient-resident flora rather than exogenous sources, with strain-level concordance between preoperative colonizing bacteria and postoperative infectious isolates frequently observed [1,4]. Such findings underscore the inadequacy of broad-spectrum prophylaxis alone and motivate strategies targeting modifiable microbial reservoirs. Preoperative screening for pathogens such as *Staphylococcus aureus*, coupled with tailored decolonization measures topical antiseptics, nasal mupirocin, and targeted skin preparation has demonstrated reductions in deep incisional and organ-space infections [7]. Implementation of these interventions in a facility-specific context, informed by local epidemiology and resistance patterns, allows for precision prevention while mitigating collateral impacts on commensal microbiota [8].

The challenge of rising antimicrobial resistance further complicates perioperative infection control. Widespread use of potent antibiotics, while temporarily reducing infection risk, can accelerate selection for multidrug-resistant organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β -lactamase-producing Enterobacterales, which undermine the efficacy of conventional prophylaxis and extend hospital stays [3,9]. Consequently, stewardship principles that integrate microbiome-informed approaches with judicious antibiotic use are critical. Multidisciplinary teams combining infectious disease specialists, microbiologists, and surgical practitioners are increasingly recommended to optimize prophylaxis, incorporating preoperative colonization data and resistance profiling to tailor interventions [10,11].

Emerging microbiome-targeted strategies offer promising alternatives or adjuncts to conventional antibiotic regimens. Phage therapy, for instance, exploits bacteriophages engineered to selectively lyse biofilm-forming pathogens without disrupting commensal communities, providing a precision approach particularly relevant in orthopedic or implant-heavy surgeries where biofilm-mediated SSIs are prevalent [12,13]. Early-phase clinical trials report substantial reductions in SSI incidence and biofilm burden with minimal impact on the broader microbiome, positioning phage therapy as a viable component of perioperative infection management [14]. Similarly, selective digestive decontamination protocols, which suppress pathogenic gram-negative populations while preserving host immunity, have demonstrated efficacy in high-risk colorectal and gastrointestinal procedures [15-17]. These approaches not only reduce SSI rates but also maintain mucosal defense against opportunistic overgrowth, highlighting the importance of microbiome preservation in infection prevention.

Comprehensive perioperative infection control now requires integration of traditional sterile technique with microbiome-informed interventions. Decolonization that balances effective SSI reduction with antibiotic stewardship [1,7,10]. In practice, these strategies demand facility-level adaptation, continual onization bundles, phage therapy, selective digestive decontamination, and robust surveillance systems collectively enable targeted prevention monitoring of microbial resistance patterns, and dynamic risk modeling that incorporates patient-specific vulnerabilities such as age, comorbidities, and immunological status [6,11,18]. By addressing the endogenous microbial reservoirs central to postoperative infections, these approaches represent a paradigm shift from reactive treatment toward proactive, precision-guided SSI prevention, promising improved patient outcomes across diverse surgical specialties.

This review synthesizes current and emerging evidence on microbiome-targeted perioperative strategies for SSI prevention. By integrating microbiology, immunology, and surgical practice, it highlights a paradigm shift toward microbial restoration and resilience as a foundation for personalised, sustainable, and effective perioperative care.

2. Methodology

2.1 Research Design

This study employed a systematic and integrative review design following the PRISMA 2020 guidelines. The review aimed to synthesize emerging evidence on the modulation of the perioperative microbiome and its clinical impact on postoperative SSIs. Four major electronic databases PubMed, Scopus, Web of Science, and Cochrane Library were systematically searched for articles published between 2020 and 2025. The review process followed the PRISMA framework through identification, screening, eligibility assessment, and inclusion of studies, ensuring transparency and reproducibility.

2.2 Search Strategy and Selection Criteria

A predetermined search protocol was used combining controlled vocabulary (MeSH) and free-text keywords to maximize retrieval of relevant studies. Search terms included *perioperative microbiome*, *probiotics*, *surgical site infection*, *gut–skin axis*, *microbial therapeutics*, and *microbial modulation*, applied both individually and in combination.

Studies were included if they met the following criteria:

Investigated perioperative modulation of the microbiome (gut, skin, or both).

Reported postoperative outcomes, specifically SSI incidence, as well as immune or microbial composition changes.

Included human participants or animal models.

Published in English between 2020 and 2025.

Studies were excluded if they were editorials, commentaries, conference abstracts, or did not report relevant microbiome or SSI data. This refined criterion explicitly ensured that included studies could provide evidence on the clinical impact of microbiome interventions on SSI rates.

2.3 Data Extraction and Synthesis

Data were independently extracted by two reviewers using a structured template. Extracted parameters included:

Author(s) and publication year.

Study design and population characteristics.

Intervention details (type and timing: pre-, intra-, or postoperative).

Primary clinical outcomes, including SSI incidence, microbial diversity indices, and biomarkers of inflammation.

The methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists for systematic reviews and experimental studies. Any discrepancies were resolved by consensus.

Due to heterogeneity in study designs, interventions, and outcome measures, a narrative synthesis approach was applied. Studies were thematically categorized based on the type of microbiome interventions and their observed clinical effects on SSI incidence, enabling a clear link between microbiome modulation and postoperative infection outcomes.

3. The Microbiome Landscape of Perioperative

The perioperative period is a critical window in which host–microbe interactions significantly shape surgical outcomes, as surgical stress, antibiotics, and other perioperative factors disrupt the gut and skin microbiomes altering immune responses and metabolic homeostasis which can compromise wound healing and increase vulnerability to SSI and other complications. For example, perioperative perturbations in the commensal microbiota have been linked to higher postoperative infectious risks, while microbiome stability is associated with improved recovery and reduced infection incidence, underscoring the importance of the gut and skin microbial ecosystems in optimal surgical recovery and SSI prevention [19].

3.1 Dynamics of Gut Microbiota During Surgery

The gut microbiota is a metabolically active ecosystem that regulates immune function, nutrient metabolism, and the integrity of the intestinal epithelial barrier. Perioperative interventions, including anesthesia, fasting, mechanical bowel preparation, and prophylactic antibiotics, can disrupt this ecosystem, resulting in significant dysbiosis [20].

3.1.1 Perioperative Dysbiosis Drivers

Although bowel preparation and fasting reduce intraoperative contamination, they deplete mucosal nutrients and beneficial commensals. Similarly, prophylactic antibiotics, while essential for infection prevention, further disrupt microbial balance by suppressing obligate anaerobes and promoting the growth of antibiotic-resistant taxa. Surgical stress responses exacerbate this imbalance by favoring facultative anaerobes, such as *Escherichia coli* and *Klebsiella* spp., over beneficial Firmicutes and Bacteroidota [20]. This “oxygen hypothesis” describes how oxygen leakage into the gut lumen selects for pathobionts capable of metabolizing reactive compounds, compromising gut integrity [21].

3.1.2 Temporal Microbial Perturbation

Microbial shifts occur within hours after incision. Proteobacteria rapidly increase, and intra-rectal lactate rises, reflecting metabolic stress and intestinal remodeling, as shown in intraoperative sampling studies of colorectal and pancreatic surgeries [21]. These transient dysbiotic states often go undetected in routine postoperative stool tests, highlighting the importance of real-time microbial monitoring to capture dynamic fluctuations [21].

3.1.3 Pathophysiological Consequences

Intestinal dysbiosis, marked by diminished populations of obligate anaerobes from Bacteroidota and Firmicutes alongside elevated Proteobacteria such as *E. coli* and *Klebsiella* spp., fosters both local and systemic inflammation as well as bacterial translocation, potentially precipitating infectious complications during visceral surgery. This microbial shift compromises intestinal barrier integrity, enabling pathogen translocation that manifests as SSIs, anastomotic leakage, and secondary infected pancreatic fistulas in procedures involving the pancreas, liver, or esophagus [22].

Mechanistically, the intraoperative expansion of Proteobacteria particularly Enterobacteriaceae like *E. coli* and *Klebsiella* spp. in rectal contents during rectal and duodenopancreatic resections serves as a predictor of septic complications [23]. This rapid dysbiosis, observable at the conclusion of surgery, correlates with the development of severe postoperative infections, underscoring the critical role of perioperative microbial dynamics in determining patient outcomes [23]. By compromising mucosal and systemic immune homeostasis, this dysbiotic shift not only promotes local tissue inflammation and impaired wound healing but also facilitates the translocation of pathogens that drive systemic inflammatory cascades and infectious complications [23].

3.1.4 Diversity and Functional Deterioration of the Microbes

Depletion of microbial diversity compromises the ecological stability and functional resilience of the gut microbiota. Postoperative dysbiosis is often characterized by the overgrowth of opportunistic and facultative pathogenic genera, accompanied by a marked reduction in specialized obligate anaerobic bacteria responsible for key metabolic functions. These metabolic specialists include butyrate-producing taxa such as *Faecalibacterium prausnitzii*, *Roseburia* spp., *Eubacterium* spp., and members of the Lachnospiraceae and Ruminococcaceae families, which play a central role in the fermentation of dietary fibers into short-chain fatty acids (SCFAs), particularly butyrate [23].

Butyrate serves as the primary energy source for colonocytes and is essential for maintaining epithelial barrier integrity, promoting mucosal repair, and regulating immune homeostasis through anti-inflammatory signaling pathways. The depletion of these metabolic specialists results in reduced short-chain fatty acid (SCFA) availability, leading to impaired epithelial healing, increased intestinal permeability, and heightened inflammatory responses. This metabolic insufficiency further predisposes the postoperative gut environment to mucosal injury and increases susceptibility to secondary infections by opportunistic pathogens.

Restorative strategies aimed at correcting postoperative dysbiosis increasingly focus on re-establishing these functional microbial groups. Interventions such as probiotics, synbiotics, and fecal microbiota transplantation (FMT) have demonstrated potential to restore microbial diversity, enhance SCFA production, and improve gut barrier function. Consequently, these microbiota-targeted therapies are gaining recognition as adjunctive approaches to support gastrointestinal recovery and reduce postoperative complications. This review examines the critical role of butyrate-producing microbiota in mitigating postoperative ileus through enhanced epithelial barrier function, anti-inflammatory effects, and modulation of intestinal motility [24-26].

3.2 Wound Colonisation and Microbiota of the Skin

The skin microbiome acts as the body's first ecological defense against environmental pathogens. Resident commensals contribute substantially to colonisation resistance, barrier maintenance, and immune modulation. Key members of the healthy skin microbiota include *Staphylococcus epidermidis*, *Cutibacterium acnes*, and *Corynebacterium* species, which occupy ecological niches on the skin and compete with opportunistic pathogens for nutrients and adherence sites. These organisms produce antimicrobial compounds and interact with keratinocytes and immune cells to sustain cutaneous homeostasis and limit pathogenic overgrowth [27].

3.2.1 Disruption During Surgical Preparation

Although preoperative antiseptics with agents such as chlorhexidine or povidone-iodine is fundamental for reducing SSIs, these antiseptics non-selectively reduce both commensal and pathogenic skin microbes. This temporary depletion of beneficial flora creates an ecological niche that may be exploited by opportunistic or hospital-acquired organisms, particularly in immunocompromised patients or those with impaired wound healing. Changes in microbial diversity and composition on the skin following antiseptic application have been documented, with potential implications for postoperative colonisation and SSI risk [28].

3.2.2 Beneficial Effects of Commensal Flora

Commensal strains exert protective effects through multiple mechanisms. *Staphylococcus epidermidis* secretes sphingomyelinases and antimicrobial peptides that strengthen the skin barrier, inhibit pathogen growth, and modulate immune signaling pathways, thereby promoting keratinocyte proliferation and wound repair. *Cutibacterium acnes* can produce short-chain fatty acids and bacteriocins that suppress the virulence and biofilm formation of *Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Corynebacterium* spp., enriched in healing wounds, may contribute to colonisation resistance and niche protection against more virulent bacteria. These host-microbe interactions reflect the beneficial role of resident microbes in regulating inflammation and supporting timely wound healing [29].

3.2.3 Surgical Wound Microbial Recolonization

After incision, the wound environment becomes a dynamic microbial niche influenced by residual skin commensals, ambient exposure, and host immunity. Early recolonisation by beneficial microbes correlates with more effective epithelialisation and reduced infection risk, while delayed or aberrant recolonisation may predispose to persistent inflammation, delayed healing, and SSI development. Innovative approaches such as probiotic-, prebiotic-, and postbiotic-coated dressings aim to modulate the wound microbiota by promoting desirable microbial communities that enhance barrier restoration, suppress pathogenic colonisation, and support re-epithelialisation. Preclinical and clinical studies indicate that such formulations can regulate inflammation, reduce bacterial load, and accelerate tissue repair, although more robust human trials are needed to translate these findings into standard clinical practice.

3.3 Interaction between Gut and Skin Microbiomes

New data indicates a gut-skin axis, in which gut dysbiosis affects skin immunity and wound healing via systemic immunometabolic mechanisms. This bidirectional communication is based on circulating microbial metabolites, cytokines and neuroendocrine mediators [30].

3.3.1 Gut-Skin Communication Mechanisms

Gut-derived metabolites like SCFAs, tryptophan derivatives and bile acids control cytokine secretion and epithelial remodeling of distal tissues, including the skin. On the other hand, cutaneous inflammation can initiate gut dysbiosis through neuroendocrine signaling through stress. This feedback loop of two directions highlights how microbial homeostasis should be maintained at various body sites to facilitate immune resistance and tissue repair in the perioperative environment [30].

3.3.2 Clinical Implications on SSI Prevention

Understanding the interplay between the gut and skin microbiomes has important clinical implications for SSI prevention. Increasing evidence indicates that the gut microbiome influences systemic immune responses and wound healing, which can affect susceptibility to postoperative infections. For example, disturbances in the intestinal microbiota have been linked to higher SSI risk even in the absence of direct intestinal barrier breach, suggesting mechanisms such as immune modulation and microbial “Trojan horse” translocation may contribute to infection at distant surgical sites [31]. Modulating the gut microbiome through preoperative nutritional optimization, prebiotics, probiotics, and other microbiota-targeted therapies has been proposed as an adjunct to conventional SSI prevention strategies to enhance barrier function and host defenses. A healthy gut microbial ecosystem supports systemic anti-inflammatory pathways and improves mucosal integrity, which may indirectly facilitate better cutaneous immune resistance and reduce postoperative infectious complications. These insights underscore the potential value of incorporating microbiome-focused interventions into comprehensive SSI prevention bundles in surgical care [32].

3.3.3 Future Perspectives

The development of multi-omics technologies and integrative analytics (including sequencing and predictive models) enables patient-specific microbiome profiling that can be correlated with postoperative outcomes, helping identify individuals at higher risk for dysbiosis-related complications and potentially guiding personalized interventions within enhanced recovery after surgery (ERAS) frameworks [33].

4. New Microbiome-Regulating Interventions

The perioperative period represents a critical window for microbiome manipulation to mitigate SSIs and support recovery. Emerging evidence indicates that restoring microbial balance exerts an anti-dysbiosis effect against disturbances induced by surgical stress, anesthesia, and perioperative antibiotics [34-36]. Major surgical procedures expose the intestinal microbiota to inflammatory and antimicrobial stressors, leading to dysbiosis characterized by shifts in luminal and fecal microbial composition, which can precipitate complications such as infections and anastomotic leaks [23,37]. Proper restoration of commensal bacteria during this period may prevent such postoperative complications and improve recovery. This is especially crucial in gastrointestinal surgery, where preoperative interventions including fasting, mechanical bowel preparation, and prophylactic antibiotics further exacerbate microbial disruption [35].

4.1 Probiotic and Synbiotic Supplementation

Probiotics microorganisms administered in sufficient quantities to confer health benefits have garnered significant attention as perioperative adjuncts for SSI prevention and immune modulation [34,35]. When combined with complementary prebiotics as synbiotics, they offer enhanced colonization efficiency, metabolic synergy, and functional restoration of the intestinal microbiota.

Both animal and human studies demonstrate that perioperative administration of *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces boulardii* improves intestinal barrier integrity, modulates systemic inflammatory responses, and reduces the incidence of postoperative infections [35,36]. The timing of supplementation is critical: preoperative administration

(e.g., starting 3-7 days before surgery) primes mucosal immunity, while continued postoperative supplementation supports microbiome recovery and maintenance of barrier function. These findings highlight probiotics and synbiotics as safe, effective, and ecologically targeted interventions for enhancing host resiliency and reducing SSI risk during the perioperative period.

Some of the probiotic consortia increase the generation of butyrate, strengthening tight junctions in the epithelia and inhibiting translocation of pathogens (Figure 1) [2]. Newer synbiotic preparations that include *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* have demonstrated potential in the restoration of microbial diversity after antibiotic prophylaxis [8,24]. These new formulations could enable a shift toward precision microbiome therapeutics, customized to the microbial and immunological phenotype of each individual.

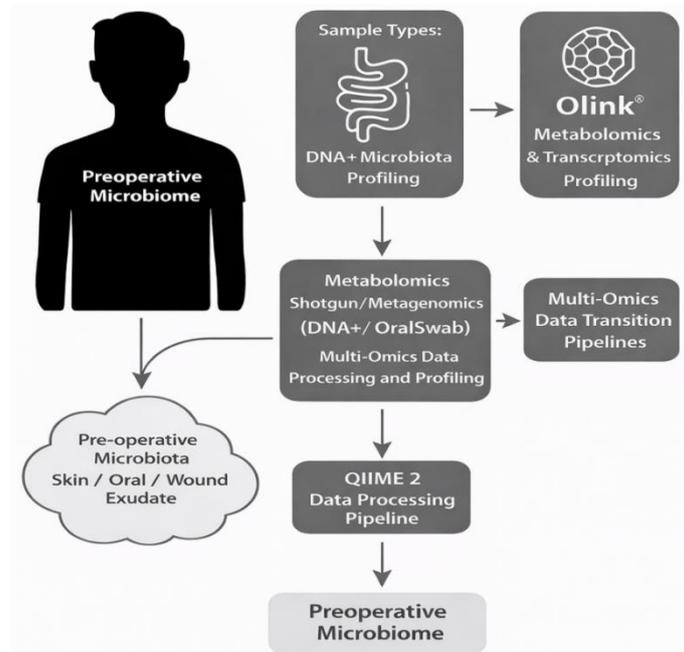


Figure 1. Predicting multi-OMIC with biomarker sampling framework.

The perioperative period is a kind of a window where host microbiome can be manipulated to achieve optimal immune resilience and surgical recovery. There is mounting clinical and translational evidence that microbiome modulation specifically tailored to address anaesthetic exposure, surgical stress, and antibiotic prophylaxis is beneficial in reducing dysbiosis, in turn, reducing postoperative complications including SSIs, ileus, and systemic inflammation [34].

This part summarises the recent developments in microbiome-based perioperative therapies and includes probiotic and synbiotic supplementation, prebiotic dietary interventions, antibiotic stewardship, microbiota restoration through FMT, and non-pharmacological treatments, such as photobiomodulation. Put together, these interventions constitute paradigm shift, i.e. the eradication of pathogens to ecological recovery and stability of the host microbial ecosystem.

4.2 Prebiotic Dietary Measures

Prebiotics, non-digestible fermentable fibers such as inulin, resistant starches, and oligosaccharides, selectively stimulate the growth of beneficial gut bacteria and promote the production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate. These microbial metabolites enhance mucosal immunity, maintain intestinal barrier integrity, and mitigate systemic inflammation, thereby supporting recovery from surgical interventions [35,38].

Among SCFAs, butyrate plays a particularly critical role: it serves as the primary energy source for colonocytes, upregulates tight junction protein expression, and suppresses pro-inflammatory signaling pathways. Butyrate-producing bacteria, such as *Roseburia* and *Eubacterium*, are often depleted during perioperative dysbiosis, providing a strong rationale for dietary interventions aimed at restoring their abundance [39,40]

Current studies further indicate that preoperative and postoperative prebiotic supplementation has extragastrointestinal effects, notably on the gut-brain axis. Increased SCFA levels have been associated with reduced postoperative cognitive dysfunction and delirium, which are increasingly recognized complications in older surgical patients [39,40]. Perioperative administration of prebiotics such as inulin and galactooligosaccharides enhances populations of butyrate-producing bacteria, improves colonic anastomotic healing, and strengthens gut barrier function in experimental models [35].

Integrating nutritional prehabilitation into perioperative care is therefore a low-risk, low-cost strategy to enhance microbial stability and systemic resilience, complementing other microbiome-targeted interventions for improved surgical outcomes.

4.3 Antibiotic Stewardship and Microbiota-Sparing Methodologies

Antibiotic prophylaxis remains an essential component of modern surgical practice due to its proven effectiveness in reducing the incidence of SSIs. However, inappropriate antibiotic selection, prolonged exposure, or excessive dosing can disrupt commensal microbial communities and contribute to antimicrobial resistance, thereby posing risks to long-term patient health. To mitigate these challenges, antimicrobial stewardship programs in surgical settings increasingly emphasize evidence-based, single-dose prophylaxis strategies that minimize unnecessary antibiotic exposure while maintaining effective protection against bacterial contamination during surgical procedures [41].

This stewardship-driven approach aligns with contemporary clinical guidelines that advocate for careful agent selection, narrow antimicrobial spectra, and precise timing to achieve adequate bactericidal concentrations against anticipated wound pathogens. Such measures optimize SSI prevention while limiting collateral damage to beneficial microbiota [42]. Institutional-level optimization further strengthens these efforts through structured antimicrobial stewardship programs that actively engage perioperative teams, promote adherence to standardized protocols, and ensure accurate timing of prophylactic antibiotic administration [43].

Collectively, these strategies support a shift toward microbiota-sparing prophylaxis, integrating precision-based antibiotic use with stewardship principles to balance effective infection control and microbiome preservation in surgical care.

4.4 FMT and Microbiota Therapeutics

FMT is an effective approach to restore microbial balance in the gut by moving the stool based microbial communities of healthy donors into patients with dysbiosis. Although it has been traditionally used to treat recurrent *Clostridioides difficile* infection, its possible use in perioperative settings is increasingly becoming popular.

Preclinical studies have shown that preoperative FMT has the potential to prevent post-operative infections, reestablish SCFA-producing taxa as well as controlling systemic inflammation [12]. In animal models, young donor transplantation recovered gut barrier integrity and alleviated neuroinflammation in aged recipients, and decreased postoperative cognitive dysfunction [25].

In order to address the issue of donor variability and scalability, research has focused on synthetic microbiota formulations - defined consortia of cultured, beneficial microbes intended to capture the effect of FMT and achieve safety and scalability [8]. The next-generation probiotics will hope to uncouple microbiota restoration and dependence on donors, and allow regulator-compliant prophylaxis.

New biological therapeutics also increase the microbiota-based perioperative toolkit. Adjunctive therapies to facilitate immune modulation and wound healing include engineered strains of bacteria that can express anti-inflammatory peptides, antibiotic-resistant pathogen targeted bacteriophages and postbiotic metabolites (e.g., butyrate analogues) [23,35].

4.5 Non-Antibiotic Microbiota Regulation and Photobiomodulation

In addition to biological and nutritional interventions, photobiomodulation (PBM) has become an innovative, non-invasive method of human microbiome regulation and recovery promotion. PBM entails using low-level red or near-infrared light to specific tissues, which affect the mitochondrial activity, immune signaling, and ecology of the microbes [23].

Recent research indicates that PBM has the potential to raise the proportions of good bacterial genera like *Akkermansia* and *Roseburia* that are known to promote the integrity of the mucosa and metabolic homeostasis [35]. The intervention seems to lower the levels of the inflammatory cytokines, enhance the oxygenation of tissues, and speed up the process of wound healing. These results place PBM as a microbiota-friendly substitute to chemical sterilisation which facilitates microbial resilience and inhibits risk of infection. PBM represents the future of eco-surgical procedures that combine biophysics and microbial ecology as the next generation by improving the microbiome diversity without any antibiotic or foreign micro.

4.6 Future Perspectives

The incorporation of microbiome science in surgical medicine is a major breakthrough in the field of perioperative care. Microbiota modulation as a component of multimodal prehabilitation and Enhanced Recovery After Surgery (ERAS) could enhance the prevention of infection, immune regulation, and tissue repair. Moreover, the potential impacts include patient-specific microbiome profiling with antimicrobial resistance dynamics that will redefine the help of preventing SSI with consideration of microbiological, metabolic, immunological, and socioecological determinants that are external to traditional pathogen acquisition frameworks [44].

The next direction of study should be focused on a number of areas that are interrelated. To begin with, integration of multi-omics will be necessary, especially the simultaneous use of metagenomics, metabolomics, and transcriptomics to describe the composition, functional activity, and dynamics of the microbiome in high resolution during the

perioperative period. Second, personalized intervention programs should be developed, such as individualized probiotic, prebiotic, synbiotic, or antibiotic treatment, based on initial microbial composition, functional markers, and host genome data.

Also, systems biology modelling provides an exciting way to build mechanistic models of microbial ecology, host immune responses, and surgical stress interactions to predict patient-specific recovery patterns and postoperative risks. In addition to these methods, artificial intelligence-based digital twin technologies can help monitor changes in the microbiome in real time and dynamically optimize therapeutic interventions in the process of perioperative care.

By combining the principles of ecological microbiome with the tools of precision medicine, it is possible to make microbiome modulation a quantifiable, non-targeted, and therapeutic intervention of perioperative care, eventually enhancing patient outcomes of surgery and decreasing postoperative morbidity.

5. Translational and Clinical Implications

The perioperative microbiome represents a new plane of risk management in the operation room, cutting across molecular biology and clinical practice. The clue to the accuracy of perioperative medicine (PPM) is the translation of the mechanistic knowledge into a practical clinical guideline. Three key areas of translation are presented in this section, namely: (1) SSI-risk biomarkers using microbiome; (2) microbiome modulation to integrate into the existing surgical workflow; and (3) barriers to clinical adoption caused by regulatory and standardization concerns [23,44].

5.1 Predictive Microbiome Biomarkers

Biomarkers derived from the microbiome are being recognized as highly effective predictors of surgical site infections (SSIs) and perioperative complications. Both taxonomic and functional microbial signatures are real-time biological indicators of the host-microbe interface and could be better predictors of risk than more traditional risk predictors (e.g., wound classification or surgery length) [44]. It is emerging that a great number of SSIs are endogenous and not caused by contamination of the environment by the patient. As an example, nasal carriage of *Staphylococcus aureus* has been reported as a significant risk factor of deep postoperative infection following colorectal surgery, and intestinal isolates of *Enterococcus* and *Klebsiella* have been reported to cause postoperative wound infections.

Another but unnoticed cause of infection is zoonotic transmission. Some of the animal-related endogenous microorganisms may be contracted by bite, scratching, or direct contact with the colonized animals; thus, there is a need to consider the interactions between hosts and the environment and the animals when evaluating the risk of infections [45].

The development of high-throughput sequencing and microbial signature profiling methods has enhanced the potential to identify pathogenic organisms, detect antimicrobial resistance determinants, and define previously unculturable microbes in complex microbial groups. They are considered to offer improved diagnostic accuracy and aid more correct perioperative risk stratification in clinical microbiology [30,33].

Simultaneously, predictive modelling, which has been enhanced by artificial intelligence, is reshaping risk evaluation through incorporation of the microbiome data with patient-specific clinical factors, including their nutritional status, surgical time, and comorbidities. Predictive models based on machine learning and nomograms can be used to justify personalized prophylaxis, such as tailored decolonization procedures or tailored probiotic therapy [10,33,36]. Regional calibration of these models is, however, necessary because microbiome composition in different populations is very different as a result of dietary, environmental, and antibiotic exposure variations. The absence of validated population-specific predictive instruments still constrains the fair application of resource-constrained environments [29]. The latest advancements in regionally adapted AI models, including local prevalence and antimicrobial resistance patterns, are welcome information on context-sensitive precision medicine [30].

In the future, data streams on perioperative microbiome tracking can be incorporated into AI-based surgical interfaces to provide real-time infection monitoring and respond to microbial reactions by adjusting antimicrobial/probiotic treatment. These strategies may enable precision surgery through adaptation and enhance patient outcomes as well as minimize after-surgery complications and antimicrobial abuse.

5.2 Surgical Protocols Integration

The incorporation of microbiome management into the operating room practice is an attempt to reduce a shift from the traditional model of infection control to a more comprehensive approach of microbial optimization. Conventional perioperative measures such as asepsis, antibiotic prophylaxis, and wound management are also vital but can be enhanced with microbiome-preserving measures that shield beneficial microbial communities whilst increasing pathogen proliferation [1].

Notably, microbiome modulation cannot be considered an alternative to aseptic and antibiotic practices but a complement. Probiotics used as preoperative supplements have been demonstrated to enhance mucosal tentorial activity, minimize bacterial translocation, and restrict postoperative endotoxemia. Likewise, maintenance of a protective microbiome using antiseptics that avoid altering the microbiome could be beneficial in the inhibition of the colonization

of *S. aureus* in ecological environments, including *Staphylococcus epidermidis*, which is a competitor to microorganisms like *S. aureus* [21,27].

Personalized prophylaxis in regard to the microbial risk profile of an individual is also likely to be part of the future of perioperative infection control. The moderated and low-risk microbial communities of patients can both be exposed to less or more advantageous exposure to antibiotics, thus dispensing with dysbiosis and antibiotic resistance. On the other hand, patients who have high-risk microbiota or colonization of multidrug-resistant organisms might need special measures like preoperative probiotics, synbiotics, or, in some particular situations, fecal microbiota transplantation to decrease colonization pressure. Additional microbial recovery, immune regulation, and wound healing after surgical stress can be enhanced by postoperative restorative interventions such as supplementation with short-chain fatty acids or novel modalities such as photobiomodulation [24,36].

Numerous studies are evidence-based in favor of multimodal integration as a part of a perioperational care model based on the microbiome. The microbiome-built perioperative care model (MiPCM) suggests a balanced intervention that includes nutritional prehabilitation, microbiota-sparing antibiotic stewardship, and postoperative microbial restoration to maintain the microbial diversity and enhance surgical outcomes. Clinical trials indicate that perioperative gut microbiome modulation with probiotics or synbiotics is linked to a considerably lower incidence of postoperative infection and enhanced recovery in adults undergoing elective abdominal surgery relative to standard care and that microbiome-specific preoperative and postoperative interventions can have a substantial effect on healing and complication risk [31,46].

Table 1. Integration of microbiome modulation into perioperative protocols.

Phase	Standard Practice	Microbiome-Integrated Add-on	Expected Outcome	Reference
Preoperative	Antibiotic prophylaxis	Targeted probiotics/synbiotics	Reduced dysbiosis, enhanced immunity	[47]
Intraoperative	Aseptic technique	Microbiota-sparing antisepsis	Preserved skin commensals	[48]
Postoperative	Wound care	SCFA supplements or FMT	Improved recovery, reduced SSI recurrence	[49]

5.3 Implementation Challenges

Although perioperative microbiome modulation is a potential area of infection prevention and surgical optimisation, uncertainty in regulation, technical variability, and socioeconomic barriers to its clinical implementation exist. These complex issues should be methodically tackled to introduce microbiome-based intervention into the routine of perioperative care.

5.3.1 Regulatory and Safety Issues

The natural biological complexity and diversity of microbiome-based therapeutics create enormous regulatory issues. Even though FMT has been approved by the United States Food and Drug Administration (FDA) as a recurrent case of *Clostridioides difficile* infection, it will be used as a perioperative prophylaxis is off-label, and requires strict safety validation [2].

One of the key issues relates to the risk of the pathogenic transmission and unintended immunologic reactions as the allergen sensitisation or unforeseen changes in microbial balance after transplantation. All these risks demonstrate the necessity of high-quality donor screening, control of microbial composition, and longitudinal follow-up of patients undergoing microbiome-based treatment [5].

New regulatory frameworks are being investigated by regulatory bodies like the FDA, the European Medicines Agency (EMA) and the World Health Organization (WHO) to adopt Live Biotherapeutic Products (LBPs), which include synthetic microbiota consortia, engineered probiotics and postbiotic preparations. Nevertheless, the lack of harmonised international standards of manufacturing, characterisation, and reporting of such therapies is an obstacle to scaling and reproducibility of such therapies at present. Microbiome-based protocols will thus need standardisation by introducing good microbiome practise (GMP), which are similar to pharmacological GMP, to guarantee uniform quality, safety, and traceability of studies and locations.

5.3.2 Technical and Logistical Barriers

Inter-study technical heterogeneity is a major barrier to generating reproducible clinical evidence on microbiomes. Variations in sample collection timing, sequencing platforms, bioinformatics pipelines, and data normalization impede effective cross-study comparisons and meta-analyses [36,33].

Integrating multi-omics datasets (metagenomics, transcriptomics, metabolomics) with clinical metadata requires advanced computational infrastructure and interdisciplinary expertise spanning microbiology, systems biology, and data science. In many low-resource settings, these analytical capabilities are limited, slowing the pace of translational progress [36,30].

Ethical and consent considerations are also critical when using biological materials, including donor-derived microbiota or living microbial therapeutics. Patients must be fully informed of potential risks, such as microbial transmission, hereditary transfer, or unforeseen ecological consequences. Regulatory frameworks will need updates to include dynamic consent models that support ongoing data generation and microbiome monitoring [2,5].

A further logistical challenge is the preservation and transport of microbial formulations. Maintaining viability and compositional fidelity of live microbial consortia under varying conditions remains technically difficult, necessitating advanced methods such as lyophilization or encapsulation during storage and administration [36,24].

5.3.3 Economic and Accessibility Limitation

Another serious bottleneck is the economic viability of precision microbiome therapeutics. The high-cost advanced sequencing metagenomic profiling, and computational modelling are costly and not accessible in the resource-limited health system. In order to have fair translation, affordable locally customizable diagnostic platforms are necessary. Indicatively, reduced microbial risk panels, which rely on a limited number of predictive taxa or metabolites, may be utilised as screening measures of SSI risk in low-resource surgical units [28,29].

Equally, the realisation of locally fermented probiotic communities based on native microorganisms can provide a scalable strategy of sustaining ecological compatibility and cost-effectiveness. Such context-specific solutions play a crucial role in avoiding a global divide in the microbiome, with high income nations developing high precision microbiome treatments and the rest of the world left on trial and error with antibacterial treatments.

5.4 Future Outlook

The potential of microbiome science to transform perioperative medicine implies that surgical care will evolve from reactive management to predictive, adaptive, and personalized approaches [33,36]. The future may involve AI-enhanced decision support systems that continuously analyze microbial and immunological data to guide dynamic prophylactic or therapeutic interventions [10,33].

Using multi-omics datasets trained by machine learning algorithms, clinicians could predict dysbiosis trends in real time and prescribe targeted interventions, such as specific probiotic preparations or tailored antibiotic adjustments. Similarly, digital twin systems computerized models of patient-specific microbiome responses may allow testing of interventions virtually before clinical application [33,36].

Achieving this vision will require a collaborative ecosystem involving surgeons, microbiologists, computational biologists, and regulatory authorities. Multicenter clinical trials leveraging standardized data and interoperable AI platforms will be essential to validate efficacy, safety, and scalability [1,44].

Microbiome-informed perioperative care has the potential to redefine surgical recovery by focusing not solely on pathogen eradication but on restoring microbial ecology and resilience. This paradigm aligns with global health priorities emphasizing sustainable, precision-based, and antibiotic-sparing medicine [36,24].

The moral integrity, fair use, and cross-industry regulation of emerging technologies are critical considerations as these interventions evolve. Personalized microbiome modulation is poised to become a cornerstone of next-generation surgical practice, enabling surgeons to protect patients from postoperative infections through responsible and evidence-based implementation (Figure 2).

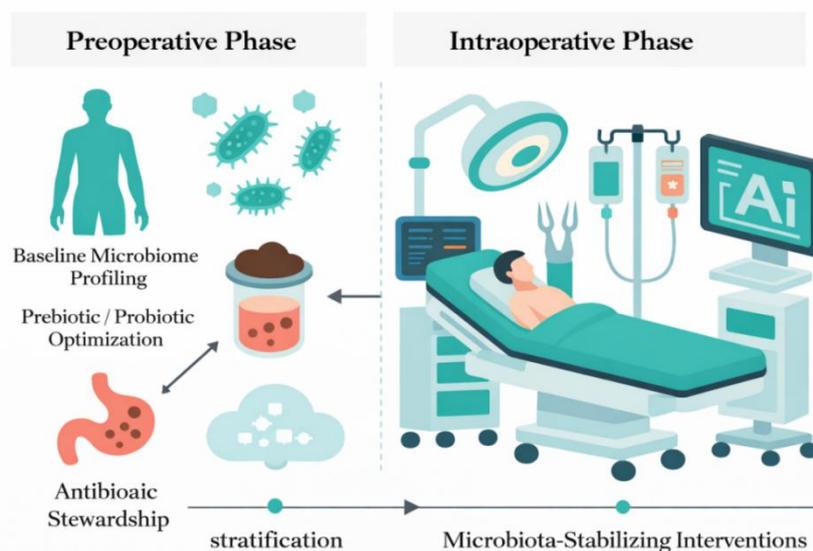


Figure 2. Conceptual framework for personalized perioperative microbiome management.

The convergence of microbiome science, AI and surgical innovation is tracing out a change in the future of perioperative care. Given the accumulating evidence that certain microbial communities in the host promote improved postoperative outcomes, future studies should switch the focus to precision-based and personalised and microbiota-specific interventions. Coupled with the high-resolution metagenomic, metabolomic, and transcriptomic data with the perioperative clinical parameters, predictive models can be built to rank patients in terms of their susceptibility to SSI and to offer customised microbiome-modulating measures [32-34].

It is possible to predict dysbiosis patterns and SSI risk using AI-based systems, and it only takes microbial signatures and intraoperative stress indicators, antibiotic therapy, nutritional conditions and immunologic indicators. These models have the potential to provide dynamic decision support, or triggers to prompt a specific intervention, including preoperative synbiotics, selective antibiotic de-escalation, or intraoperative microbial stabilisation, when included in electronic health records (EHRs) to protect microbial resilience proactively [35-37]. AI pipelines will become the key players in converting the information about the microbiomes into actionable perioperative protocols, as they become more mature and develop increased explainability.

The most important possible way forward in the future is to develop specialised pre- and intraoperative microbial optimization programmes. Instead of a generalised model of probiotics, the goal is to individualise interventions according to the microbiome, resistome, and functional metabolome of the patient on the baseline. This can include personalised probiotics/prebiotics, nutritional adjustments to supplement production of short-chain fatty acids (SCFA), and gut barrier reintegration approaches including customised microbial consortia or non-natural postbiotics [38-40]. The introduction of such customised regimens days before surgery would potentially improve immune priming, reduce perioperative inflammation, wound healing, and reduce the risk of SSI.

The other interface is the development of bioengineered microbiome-aware surgical materials, such as probiotic-coated dressings and implants capable of releasing beneficial microbes or microbial metabolites (e.g. antimicrobial peptides) to the wound site. There are preliminary preclinical studies indicating that such functional biomaterials can prevent the colonisation of pathogens; they can promote tissue regeneration, and the translational potential of these biomaterials can transform postoperative care and infection management [41].

Nevertheless, the process of translation of concept to clinical use requires strict procedures. Further studies ought to include massive human clinical trials of microbiome-targeted therapies, in which product formulation, stability, storage, and delivery modalities have been adequately standardised. Regulations need to be changed to allow the acceptance of microbiome therapeutics, and multidisciplinary teams (surgeons, microbiologists, data scientists, regulatory experts) need to work together in order to create safe, scalable, and globally available usage.

6. Perioperative Microbiome Interventions

6.1 Preoperative Microbiome Modulation

Preoperative strategies focus on optimizing the gut and skin microbiome prior to surgery, primarily through probiotics, synbiotics, and dietary interventions. Several studies demonstrated that probiotics can stabilize the gut microbial ecosystem and reduce postoperative complications [20,23]. For instance, Nalluri et al. [20] reported significant reductions in dysbiosis and improved postoperative recovery following targeted probiotic supplementation in bariatric surgery patients, whereas Spari et al. [23] observed that synbiotics combinations of prebiotics and probiotics provided superior outcomes in reducing septic complications after peritoneal surgery.

Comparative evidence suggests that while probiotics alone confer benefits, synbiotics may offer enhanced immune modulation and infection prevention due to the synergistic effects of prebiotics supporting probiotic growth [46,47]. However, Nichols et al. [22] noted variability in effectiveness depending on baseline microbiota composition and surgical type, indicating that patient-specific factors can modulate response to preoperative interventions. Collectively, these findings highlight the importance of tailoring preoperative microbiome interventions to patient characteristics and surgical context.

6.2 Intraoperative Microbiota-Sparing Strategies

During surgery, aseptic technique remains fundamental, but microbiota-sparing approaches aim to minimize disruption of protective commensal communities. SanMiguel et al. [46] demonstrated that antiseptic agents, while reducing pathogen load, can differentially affect skin commensals in a body-site and patient-specific manner, suggesting the need for selective antisepsis. Comparative evidence indicates that standard antisepsis may inadvertently disrupt protective flora such as *Staphylococcus epidermidis*, whereas microbiota-sparing antiseptic regimens preserve commensals that competitively inhibit pathogenic colonization.

Moreover, antibiotic stewardship integrated into intraoperative protocols can reduce unnecessary broad-spectrum antibiotic exposure, thus minimizing dysbiosis and the emergence of multidrug-resistant organisms [3,6]. While evidence supports microbiota-sparing techniques as beneficial for reducing infection risk, the magnitude of effect varies across studies, highlighting a gap in standardized protocols for different surgical procedures.

6.3 Postoperative Microbiome Restoration

Postoperative interventions aim to restore microbial balance and improve recovery using FMT, SCFAs, or other targeted microbial therapies. Xu et al. [48] demonstrated that SCFA supplementation in murine models partially reversed surgery-induced microbial dysbiosis and improved behavioral outcomes, while Ma et al. [25] observed that microbial metabolites positively influenced intestinal motility and postoperative recovery in humans. These interventions contrast with traditional wound care alone, which may not address underlying microbial imbalance.

Comparative analysis indicates that FMT can produce more robust restoration of microbial diversity compared to SCFAs alone, particularly in patients with severe perioperative dysbiosis [1,25]. However, FMT carries logistical and safety considerations, such as donor screening and administration protocols, which may limit widespread application [1]. The evidence suggests a graduated approach, where SCFAs or targeted probiotics may be used in moderate cases of dysbiosis, whereas FMT may be reserved for high-risk or severe cases.

7. Conclusion

This study highlights that targeted perioperative microbiome modulation has clear clinical potential to reduce postoperative SSIs and improve patient recovery. In practical terms, interventions such as probiotics, prebiotics, synbiotics, and other microbiome-supportive strategies, when applied before or after surgery, may help strengthen host immunity, stabilize microbial balance, and lower infection risk, complementing existing aseptic measures and antibiotic prophylaxis rather than replacing them outright.

Evidence synthesized in this review indicates that maintaining a healthy gut and skin microbiome can positively influence wound healing, inflammatory response, and resistance to pathogenic colonization, all of which are critical determinants of SSI occurrence. From a clinical perspective, microbiome-based interventions are low-cost, generally safe, and feasible to integrate into perioperative care pathways, particularly for high-risk surgical patients.

The findings further suggest that individualized perioperative strategies, supported by microbiome profiling and emerging AI-assisted risk prediction models, could enable clinicians to identify patients at greater risk of SSIs and tailor preventive interventions accordingly. However, translation into routine clinical practice requires standardized intervention protocols, clearer regulatory guidance, and robust multicenter randomized controlled trials to validate efficacy, timing, and dosage. Recognizing the microbiome as a modifiable clinical factor introduces a practical and patient-centered approach to infection prevention. Integrating microbiome modulation into perioperative care represents a promising step toward precision-based, biologically informed surgical practice, with the potential to sustainably reduce SSIs and improve postoperative outcomes.

Conflict of Interest

The author declares no conflict of interest.

Generative AI statement

The author declares that no Gen AI was used in the creation of this manuscript.

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