

# Hospital Microbiome and Infection Control

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**Abstract** - The hospital microbiome represents a complex and dynamic ecological network that significantly influences infection control and antimicrobial resistance within healthcare environments. Its composition is shaped by patient populations, healthcare workers, infrastructure, and environmental factors such as cleaning practices and ventilation systems. Advancements in culture-independent and metagenomic techniques have transformed our understanding of microbial diversity in hospital settings, revealing both protective and pathogenic roles of microbial communities. These insights highlight how the hospital microbiome can modulate pathogen persistence, antibiotic resistance gene transfer, and outbreak dynamics. Integrating microbiome data into infection prevention strategies—including surface decontamination, architectural design, and surveillance programs—offers innovative pathways for controlling healthcare-associated infections. However, translating microbiome findings into actionable policies remains challenging due to methodological, ethical, and regulatory constraints. This review discusses the composition, function, and control of hospital microbial ecosystems, with emphasis on emerging microbiome-informed interventions and the need for interdisciplinary collaboration to build resilient hospital environments.

**Key Words:** Hospital microbiome, infection control, antimicrobial resistance, metagenomics, healthcare-associated infections, environmental microbiology

## 1. INTRODUCTION

Hospitals have traditionally been perceived as sterile environments designed to promote healing and prevent disease transmission. However, contemporary microbiological research has redefined this notion by demonstrating that hospitals possess distinct and dynamic microbial ecosystems—collectively referred to as the hospital microbiome. This microbiome comprises a complex assemblage of bacteria, fungi, viruses, and other microorganisms inhabiting hospital surfaces, instruments, ventilation systems, and even the skin and mucosa of patients and healthcare workers. Far from being merely contaminants, these microbial communities coexist, compete, and exchange genetic material, influencing both health-promoting and pathogenic processes in the clinical setting.

The growing burden of healthcare-associated infections (HAIs) and the rapid spread of multidrug-resistant organisms (MDROs) have amplified interest in understanding the hospital microbiome. According to global surveillance data, HAIs affect millions of patients annually, imposing significant clinical, economic, and public health burdens. Traditional infection control strategies—centered on sterilization, antimicrobial use, and contact isolation—while effective to a degree, have not completely curtailed nosocomial pathogen transmission. This shortfall suggests that reducing infection risk requires a more comprehensive understanding of microbial ecology rather than merely targeting individual pathogens. The hospital microbiome, therefore, represents both a reservoir and a regulator of infectious agents and antimicrobial resistance genes.

Advancements in metagenomics, high-throughput sequencing, and bioinformatics have revolutionized the profiling of hospital-associated microbial communities. These approaches reveal extensive microbial diversity, uncovering not only pathogens but also numerous commensals that shape overall ecosystem stability through competitive exclusion, resource partitioning, and biofilm modulation. Factors such as ventilation design, surface materials, cleaning regimens, and human occupancy patterns further influence microbial dynamics. As evidence accumulates, it has become clear that sustaining a balanced hospital microbiome may be critical to reducing pathogen persistence, curbing resistance gene dissemination, and supporting long-term infection prevention.

Despite these insights, the integration of microbiome science into infection control policies remains limited. Barriers persist in standardizing sampling strategies, interpreting complex ecological data, and translating microbiome analytics into actionable hospital practices. There is also a pressing need to align microbiome research with public health frameworks, clinical epidemiology, and facility engineering to develop holistic infection prevention approaches that are both scientifically robust and operationally feasible.

The objective of this review is to synthesize current knowledge on the composition, dynamics, and influence of the hospital microbiome in infection control. It critically examines how microbial ecosystems in hospital environments contribute to pathogen reservoirs and antimicrobial resistance, discusses recent methodological advances enabling microbiome surveillance, and explores translational opportunities for microbiome-informed infection prevention strategies. By bridging microbiology, epidemiology, and environmental design, this review aims to highlight the transformative potential of microbiome research in shaping the next generation of infection control paradigms.[1–4]

## 2. COMPOSITION AND DYNAMICS OF THE HOSPITAL MICROBIOME

The hospital microbiome reflects the cumulative microbial load of patients, healthcare workers, equipment, air systems, and the built infrastructure, collectively forming a highly dynamic ecosystem. Microorganisms continuously colonize hospital environments through various sources, including patient skin, saliva, respiratory secretions, and fecal matter; the hands and garments of healthcare workers; and contaminated medical instruments or surfaces. Ventilation and air filtration systems further contribute by mediating airborne microbial dispersion, with studies demonstrating that room airflow, air exchange rates, and filtration quality strongly influence microbial load and diversity within different hospital compartments. The introduction of fresh microbes via daily human activity creates a constant flux, while cleaning practices and disinfection measures exert selective pressures that shape the composition of surviving microbial taxa.

Spatial variation within hospital environments has been shown to exert a profound effect on microbial diversity. Distinct zones—such as operating rooms, intensive care units (ICUs), and patient wards—harbor unique microbiome signatures linked to their patient throughput, ventilation designs, and

degrees of environmental control. For example, microbial communities near patients' beds, sink drains, and equipment panels often display higher abundance of *Staphylococcus*, *Acinetobacter*, and *Pseudomonas*, reflecting their association with nosocomial reservoirs. Conversely, administrative or laboratory spaces exhibit greater microbial evenness due to limited patient contact and relatively stable microclimates. Temporal dynamics further modify these patterns; newly operational facilities show rapid microbial succession as environmental and human-associated microbes establish equilibrium, while routine cleaning and patient turnover continually reset microbial communities.

Environmental and architectural parameters play critical roles in shaping microbiome stability. Ventilation systems, humidity levels, and air exchange mechanisms determine airborne microbial dispersal and survival. A 2024 cross-sectional ICU study demonstrated that wards equipped with laminar airflow (LAF) ventilation exhibited increased microbial richness and more balanced community structure compared to non-LAF areas, suggesting that airflow design may promote ecological stability by reducing pathogen dominance. Similarly, surfaces exposed to high traffic—door handles, equipment switches, and railings—experience frequent microbial exchange, effectively forming microbial 'hubs' within the hospital. Conversely, areas subjected to excessive disinfection and low humidity often harbor reduced microbial diversity but favor biofilm-forming, stress-tolerant pathogens such as *Acinetobacter baumannii*.

Recent advances in metagenomic and high-throughput sequencing (HTS) technologies have revolutionized the characterization of hospital microbial communities. Studies employing 16S rRNA gene profiling and shotgun metagenomics have revealed that the hospital environment serves as an interface linking the patient and environmental microbiomes. Environmental metagenomics has identified both commensal and pathogenic species coexisting within microbial assemblages of sinks, air ducts, and medical surfaces, indicating that gene transfer events—particularly involving antibiotic resistance genes—occur across spatial and taxonomic boundaries. Such findings underscore the value of genome-resolved metagenomics for tracking resistance dissemination and identifying reservoirs of high clinical relevance.

The interactions between pathogenic and commensal microbial populations profoundly influence infection risk and ecosystem resilience. Commensal species can inhibit pathogen colonization through competition for nutrients, secretion of antimicrobial peptides, and modulation of surface biofilms, while pathogenic bacteria exploit ecological disturbances to proliferate. Disruption of microbial balance—caused by antibiotic overuse, extreme sterilization, or microclimatic alterations—often leads to opportunistic pathogen dominance, thereby increasing the likelihood of healthcare-associated infections. Understanding these interactions at the community level positions the hospital microbiome as a central mediator in infection ecology and provides a framework for rethinking infection prevention strategies through ecological and microbiological principles.[5–7]

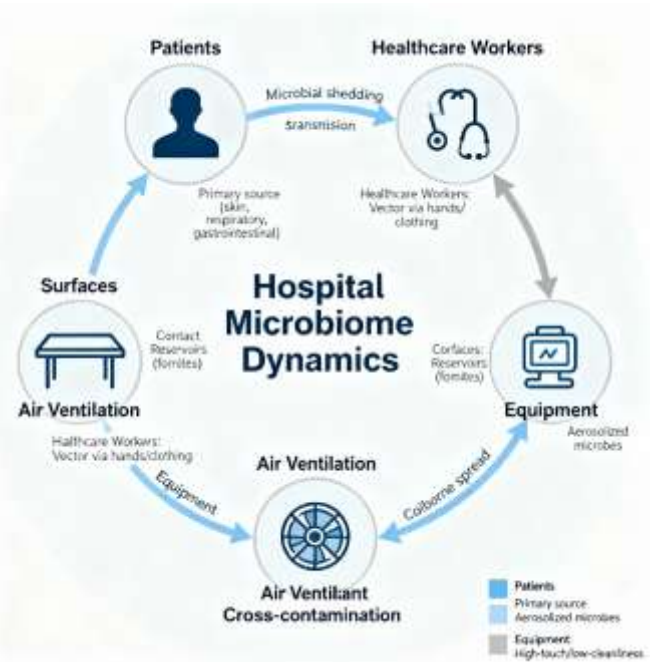


Figure 1 Hospital microbiome dynamics

### 3. MICROBIOME-DRIVEN PATHOGEN PERSISTENCE AND TRANSMISSION

The hospital microbiome exerts a significant influence on the persistence and dissemination of pathogens through intricate ecological, molecular, and structural mechanisms. Within this shared environment, commensal and pathogenic microorganisms coexist and interact dynamically, shaping pathogen survival, colonization, and virulence potential. The persistence of nosocomial pathogens is not merely a result of contamination but rather a consequence of selective adaptation to the unique microecological pressures within hospital systems—such as frequent disinfection, antibiotic exposure, and close human contact. These pressures select for microbial species capable of forming biofilms, resisting desiccation, and exchanging genetic material that drives antimicrobial resistance.

#### Mechanisms of Pathogen Survival and Colonization

Hospital-associated pathogens endure by exploiting ecological niches created by environmental stressors and host interactions. High-touch surfaces, plumbing systems, and medical devices serve as persistent reservoirs. Pathogens such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis* exhibit remarkable desiccation tolerance and can persist for months on inanimate surfaces. The surrounding microbial community often enhances this persistence through cooperative metabolic interactions, including nutrient sharing and metabolic cross-feeding. Moreover, commensal members of the hospital microbiome can inadvertently promote pathogen survival by occupying similar niches, creating competition-driven selection pressure that favors resistant or stress-tolerant microbes.

#### Biofilm Formation as a Pathogen Reservoir

Biofilm formation represents a defining mechanism through which hospital pathogens achieve persistence and resistance. Biofilms—structured microbial aggregates encased in an extracellular polymeric matrix—form on a variety of medical devices and abiotic surfaces, including catheters, ventilators, and sink drains. Within these biofilms, pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* exhibit up to a thousand-fold higher resistance to antibiotics compared to planktonic cells. Studies

have shown that approximately 60–70% of healthcare-associated infections (HAIs) involve biofilm-producing organisms. Mechanistically, biofilms restrict antimicrobial penetration, promote efflux pump expression, and induce phenotypic heterogeneity that enhances survival under antimicrobial stress. Furthermore, biofilms frequently harbor multiple microbial species, facilitating interspecies communication through quorum sensing and promoting the horizontal transfer of antibiotic resistance genes.

#### **Microbial Community Shifts and Outbreaks**

Disruption of the balanced hospital microbial community (“microbial dysbiosis”) often precedes or accompanies outbreaks of notorious nosocomial pathogens. Environmental microbiome analyses have linked community disturbances to outbreaks involving *Clostridioides difficile*, *Acinetobacter baumannii*, and methicillin-resistant *Staphylococcus aureus* (MRSA). For instance, widespread use of broad-spectrum disinfectants and antiseptics can selectively eliminate commensal bacteria, thereby reducing ecological competition and providing open niches for opportunistic pathogens. *C. difficile* outbreaks in intensive care units have been associated with decreased microbial diversity on surfaces and in air systems, emphasizing the link between diversity loss and pathogen dominance. Similarly, *A. baumannii* thrives in post-cleaning microenvironments that favor desiccation-resistant species, while MRSA proliferation correlates with repeated antibiotic exposure and high-frequency patient turnover.

#### **Horizontal Gene Transfer and Mobile Genetic Elements**

Horizontal gene transfer (HGT) represents one of the most critical processes driving hospital pathogen evolution. The hospital environment serves as a highly favorable milieu for genetic exchange due to close microbial proximity and the selective pressure imposed by antibiotics. Antibiotic resistance genes are frequently located on mobile genetic elements (MGEs), including plasmids, integrons, and transposons, that can traverse species and genus boundaries. Genome-resolved metagenomic analyses have uncovered extensive HGT events among environmental isolates of *Enterobacter hormaechei*, *Escherichia coli*, and *Klebsiella pneumoniae*. Such genetic fluidity allows for the rapid dissemination of carbapenemase (e.g., blaVIM, blaKPC) and extended-spectrum  $\beta$ -lactamase (ESBL) determinants, significantly amplifying the threat of untreatable infections in healthcare settings. Sink drains, ventilation ducts, and hospital plumbing have been identified as microhabitats facilitating MGE transfer and potential pathogenic recombination events.

#### **Microbiome-Altering Interventions**

Emerging strategies targeting the hospital microbiome aim to suppress pathogen persistence while maintaining beneficial microbial balance. Ultraviolet-C (UV-C) disinfection systems have been shown to reduce surface pathogen load effectively, though repeated use may also suppress nonpathogenic environmental taxa, potentially creating ecological vacuums for recontamination. Probiotic cleaning systems, which use nonpathogenic *Bacillus* species to competitively exclude pathogens, have shown promise in reducing multidrug-resistant bacterial contamination while preserving overall microbial diversity. Other biocontrol approaches involve environmentally sustainable decontamination agents that minimize selective pressure for resistance. Integrating these interventions with real-time metagenomic surveillance can provide an adaptive infection control strategy grounded in microbial ecology rather than sterilization alone.

In summary, pathogen persistence in hospital environments is a multifactorial process governed by ecological interactions,

genetic exchange, and biofilm-mediated resilience. Understanding these complex processes within the context of the hospital microbiome is crucial for designing next-generation infection control measures that not only eradicate pathogens but also preserve microbial equilibrium and environmental resilience.[8–11]

### **4. MICROBIOME SURVEILLANCE AND DIAGNOSTIC ADVANCES**

Advancements in molecular and computational technologies have redefined hospital microbiome surveillance, allowing for a far more precise understanding of microbial community structure, dynamics, and function than was previously possible through culture-based methods. Traditional microbiological assays—while valuable for identifying culturable pathogens—capture only a small fraction of microbial diversity. In contrast, culture-independent, high-throughput sequencing techniques now provide comprehensive taxonomic and functional insights that underpin modern infection prevention and control strategies.

#### **Contemporary Approaches to Microbiome Assessment**

Among molecular tools, 16S rRNA gene amplicon sequencing remains the most widely used method for assessing bacterial diversity in hospital environments. By targeting conserved and hypervariable regions of the 16S rRNA gene, this approach enables taxonomic identification down to the genus level and quantitative estimation of microbial composition. Recent studies have employed 16S sequencing to characterize hospital surface microbiota, highlighting considerable variation in bacterial profiles across wards and cleaning cycles. Complementing this, shotgun metagenomic sequencing provides a more holistic representation by capturing all microbial DNA present, including bacteria, fungi, viruses, and archaea. It allows the simultaneous identification of resistance genes, virulence factors, and mobile genetic elements, thereby directly linking environmental microbiomes to nosocomial infection risk. Compared to amplicon-based methods, metagenomics offers higher resolution and functional annotation capacity, albeit at greater computational and financial cost.

These genomic approaches have largely supplanted traditional enrichment cultures, revealing previously uncultivable taxa and hidden reservoirs of antimicrobial resistance. The integration of semi-selective culture enrichment with metagenomic sequencing further enhances the detection of low-abundance or slow-growing organisms from critical hospital sites such as wastewater and sink drains. Collectively, the combination of metagenomics and culture-independent surveillance represents a paradigm shift toward comprehensive microbial risk profiling in healthcare environments.

#### **Integration with Infection Control Monitoring Systems**

The translation of microbiome data into actionable infection control strategies requires integration with conventional surveillance systems. Modern hospital infection control departments increasingly interface bioinformatics pipelines with epidemiological monitoring, patient microbiota sampling, and environmental screening programs. Data derived from metagenomic sequencing can be correlated with clinical pathogen isolates, antimicrobial consumption records, and outbreak timelines, allowing spatiotemporal modeling of pathogen persistence and transmission. For instance, correlating microbial community shifts with sanitation logs has elucidated the microbial consequences of over-disinfection, prompting policy revisions toward balanced, evidence-based hygiene practices.

### Artificial Intelligence and Predictive Bioinformatics Modeling

The vast datasets generated by next-generation sequencing (NGS) necessitate the use of artificial intelligence (AI) and advanced bioinformatics for meaningful interpretation. Machine learning algorithms are now being deployed to predict antimicrobial resistance (AMR) emergence and identify potential outbreak precursors. AI tools such as DeepARG, ResFinder, and PointFinder leverage deep neural networks to detect resistance determinants from genomic data with high precision, even for genes lacking prior annotation. Further, AI-driven anomaly detection models can identify unusual microbial patterns in real time, permitting earlier intervention during infection outbreaks. When integrated with hospital information systems, predictive analytics can model microbial community trajectories and forecast infection risks at ward-level granularity, offering a proactive rather than reactive approach to infection prevention.

### Metatranscriptomics and Metabolomics for Functional Profiling

While metagenomics reveals taxonomic and genetic potential, metatranscriptomics and metabolomics uncover active metabolic functions and interspecies interactions within microbial communities. Metatranscriptomics captures RNA transcripts to identify actively expressed genes, elucidating which microbial populations are functionally dominant under specific environmental pressures. Such analyses enable researchers to distinguish between dormant and metabolically active pathogens in hospital settings, improving risk assessment accuracy. In tandem, metabolomics characterizes the biochemical outputs of microbiomes—such as short-chain fatty acids, biofilm-mediated metabolites, and antimicrobial compounds—which may modulate surface colonization and resistance transfer. The integration of multi-omics data thus offers a comprehensive understanding of both the structure and functional dynamics of hospital microbiota.

### Real-Time Microbial Surveillance and Outbreak Prevention

The ultimate goal of microbiome surveillance is dynamic, continuous risk monitoring. Real-time metagenomic analysis platforms now enable near-instantaneous detection of resistance genes and emerging pathogens, dramatically improving outbreak management capability. Portable sequencers combined with AI-assisted analytics provide on-site diagnostics that can identify microbial clusters and track source contamination within hours, minimizing transmission risks. When linked to hospital IoT-based monitoring systems, such platforms facilitate automated alerts for infection control units upon detecting deviations in microbial composition. These digital microbiome surveillance frameworks represent the future of predictive infection prevention—empowering healthcare institutions to transition from reactive containment toward anticipatory ecological management of the hospital microbiome.

In summary, integrating genomic, transcriptomic, and computational innovations into infection surveillance systems enhances the precision, timeliness, and comprehensiveness of pathogen monitoring. As these technologies become more accessible and standardized, microbiome-informed diagnostic and surveillance strategies will form the backbone of next-generation hospital infection control. [12–14]

## 5. INTEGRATING MICROBIOME KNOWLEDGE INTO INFECTION CONTROL POLICY

The integration of microbiome science into hospital design and infection management heralds a paradigm shift from pathogen-centric disinfection to ecosystem-based infection control. Incorporating microbial ecological principles within healthcare infrastructure, cleaning strategies, and training frameworks enables a balance between minimizing pathogenic risks and preserving microbial diversity critical for environmental resilience.

### Microbiome-Informed Hospital Design and Ventilation Systems

Hospital infrastructure profoundly influences the spatial behavior of microbial communities. Ventilation and air-handling systems, in particular, shape the distribution and persistence of airborne microorganisms. Studies emphasize that ventilation rate alone does not ensure pathogen control; airflow patterns, diffuser placement, and temperature gradients critically determine microbial dispersion and sedimentation. Temperature-controlled Airflow (TAF) and Laminar Air Flow (LAF) designs have shown superior efficiency in reducing airborne particulate matter compared to turbulent mixing systems. In parallel, hybrid mechanical–natural ventilation (MV–NV) frameworks have achieved enhanced dilution of airborne pathogens in wards and isolation rooms by optimizing exhaust location and air change per hour (ACH) values.

From a microbiome perspective, hospital architecture should promote microbial balance, not sterility. Incorporating non-pathogenic bioactive surface coatings, humidity control, and microbially neutral materials can help sustain microbial equilibrium and reduce dominance by desiccation-tolerant pathogens.

### Implications for Cleaning Protocols and Antimicrobial Stewardship Programs

Traditional disinfection practices relying on broad-spectrum biocides often induce ecological collapse, inadvertently favoring antimicrobial resistance. Recent interventions utilizing probiotic-based sanitation systems (PBS) address this limitation by competitively excluding nosocomial pathogens. Agents such as *Bacillus subtilis*, *Priestia megaterium*, and *Bacillus pumilus* have been deployed in biocleaning solutions (e.g., PCHS, SYN BIO) across European hospitals, demonstrating up to 90% reduction in *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* while lowering antibiotic resistance gene prevalence.

These microbial-based cleaning systems enhance environmental microbiota resilience by establishing stable, nonpathogenic communities that resist recolonization by harmful species. Integration of such ecological cleaning solutions complements antimicrobial stewardship programs (ASPs), which aim to rationalize antibiotic use and mitigate selective pressures for resistance. Together, these strategies exemplify a dual ecological-antimicrobial framework for infection control.

### Training and Professional Development in Microbiome Awareness

Effective application of microbiome-informed infection control requires interdisciplinary literacy among healthcare professionals. Training modules should incorporate fundamentals of microbial ecology, biofilm dynamics, and genomic monitoring into existing clinical microbiology and infection control curricula. Programs inspired by emerging National Action Plans on Antimicrobial Resistance (AMR)

now advocate cross-disciplinary education—linking infection control officers, environmental engineers, and genomic scientists—to interpret metagenomic data and translate findings into practice. Building such competency ensures that microbiome-based interventions are applied contextually, safely, and sustainably across healthcare facilities.

#### Case Studies of Microbiome-Guided Interventions

Successful microbiome-guided implementations have underscored tangible benefits in real healthcare environments.

- In Berlin hospitals, the use of microbial-based cleaners led to statistically significant reductions in resistant gene prevalence on sink and surface microbiota over 30 days.
- Hybrid probiotic disinfection trials in Italy and Slovenia demonstrated sustainable declines in *Acinetobacter baumannii* and MRSA contamination across ICU environments.

Ventilation modification projects using targeted exhaust positioning and HEPA filtration achieved improved microbial air quality and decreased infection incidence, illustrating the potential of microbial-ecological ventilation design.

Collectively, these implementations highlight the feasibility of ecological engineering combined with targeted sanitation in reducing pathogen reservoirs without sterilizing beneficial microbiota.

#### Economic and Policy Considerations

Integrating microbiome-based measures into infection control policy carries initial cost implications due to the need for metagenomic equipment, bioinformatics capacity, and environmental redesign. However, cost-benefit analyses consistently support these investments, demonstrating long-term savings through reduced HAI rates, shortened patient stays, and decreased antimicrobial expenditures. Probiotic cleaning systems, for instance, have lower operational costs over time owing to reduced chemical consumption and decreased resistance-driven outbreaks. Health-economic modeling indicates that microbiome-informed infection control could yield up to a 25–40% reduction in HAI-related costs in tertiary care centers by balancing ecological stability with disinfection efficacy.

In conclusion, embedding microbiome science into infection control policy necessitates a shift toward ecological resilience, sustainable sanitation, and predictive air management. Future frameworks must fuse microbiome monitoring, evidence-based building design, and ecological stewardship to transform hospitals into dynamic, health-supportive microbial environments rather than sterile battlegrounds against microbes.[15–18]

## 6. CHALLENGES AND FUTURE PERSPECTIVES

Although hospital microbiome research has achieved remarkable progress in recent years, translating this knowledge into practical infection control frameworks remains complex due to technological constraints, regulatory ambiguities, and ethical considerations. Simultaneously, emerging opportunities in systems biology and synthetic microbiome engineering hold promise for revolutionizing environmental infection management.

#### Technological Limitations in Sampling and Sequencing Standardization

One of the foremost barriers to advancing hospital microbiome science lies in the lack of standardization across sampling, sequencing, and data processing methodologies. Current microbiome studies employ diverse protocols for surface

swabbing, air sampling, and fluid collection, leading to substantial variability in microbial recovery rates and community composition. For example, differences in swab material, elution buffers, and DNA extraction methods can alter microbial yield and bias results towards more resilient taxa. Similarly, the choice between 16S rRNA gene amplicon sequencing and shotgun metagenomics introduces variability in taxonomic resolution and functional annotation. Short-read sequencing platforms often fail to discriminate between closely related species, while host DNA contamination remains a major impediment, particularly in low-biomass hospital samples. Moreover, the absence of unified bioinformatics pipelines and threshold criteria for microbial detection undermines cross-study comparability. Establishing validated, multicenter reference standards—encompassing sample handling, sequencing depth, and data curation—is thus essential for reproducibility and meaningful epidemiological inference.

#### Translational Barriers: From Data to Actionable Infection Control

Despite the surge in microbiome-related data, converting sequencing outputs into operational infection prevention strategies remains challenging. Metagenomic datasets are inherently complex, requiring advanced computational capacity and interdisciplinary interpretation to extract clinically relevant signals. Variability in environmental microbiome signatures across wards and hospitals limits generalizability, while the dynamic nature of microbial communities complicates identification of “baseline” healthy microbiota for hospital environments. Infection control professionals often lack the interpretive training necessary to integrate microbiome insights into routine surveillance or cleaning schedules. Furthermore, there is a disconnect between genomic data acquisition and real-time hospital decision-making. Linking microbial trends with infection incidence through adaptive dashboards and spatiotemporal analytics remains underdeveloped, underscoring the need for translational infrastructures that bridge molecular analytics with epidemiological practice.

#### Regulatory, Ethical, and Data-Sharing Challenges

The rapid acceleration of microbiome research has outpaced existing regulatory and ethical frameworks. The European Union’s new Substances of Human Origin (SoHO) regulation, extended in 2025 to include microbiome-derived interventions, now classifies many research entities as “SoHO establishments” with mandatory authorization for storage, processing, and dissemination of microbial materials. This represents progress toward oversight but introduces compliance burdens, particularly for exploratory hospital studies. Moreover, microbiome data, often containing human genetic material, pose privacy concerns analogous to those in genomics research, raising questions of data ownership and re-identification risk. Ethical frameworks must ensure that microbial surveillance in hospitals is both transparent and voluntary, with clear boundaries between environmental monitoring and patient genomic data collection. Furthermore, equitable data-sharing mechanisms are essential to prevent research monopolization and promote collaborative standardization globally.

#### Synthetic Biology and Precision Microbiome Engineering

Future developments in synthetic biology and precision microbiome engineering hold transformative potential for infection control. Synthetic biology enables the rational design of beneficial microbial strains that can modulate hospital microbiomes to suppress pathogen colonization. CRISPR/Cas-driven systems are being explored for targeted degradation of

antimicrobial resistance genes and virulence factors within microbial populations. Engineered microbial consortia—comprising biofilm-resistant and antimicrobial-producing strains—are being tested as probiotic coatings on hospital surfaces and within plumbing systems to inhibit colonization by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. Furthermore, synthetic biosensors capable of detecting volatile metabolites related to infection outbreaks could supplement real-time surveillance. However, these technologies necessitate environmental risk assessment for genetic stability, containment, and ecological safety before deployment.

### Interdisciplinary Collaboration and Future Directions

The complexity of hospital microbial ecosystems demands close collaboration among microbiologists, epidemiologists, clinicians, architects, and bioengineers. Microbiologists provide fundamental ecological understanding, while architects and environmental engineers contribute expertise in spatial design and ventilation control to promote balanced microbial dispersion. Epidemiologists and bioinformaticians, on the other hand, are integral in quantifying links between microbial community dynamics and infection outcomes. Establishing cross-disciplinary consortia and translational research hubs—similar to those in systems medicine—would facilitate harmonized study designs, data interoperability, and innovation pipeline development.

In future hospital ecosystems, infection control policy will increasingly combine high-resolution microbiome surveillance, synthetic biology innovations, and ecological design principles. Despite technological and ethical hurdles, this integrated approach offers an unprecedented opportunity to transition hospital infection control from reactive containment to proactive management of microbial health.[19–21]

## 7. CONCLUSIONS

The hospital microbiome has emerged as a critical determinant in the complex interplay between healthcare environments, human hosts, and infectious disease dynamics. Once perceived solely as a vector for contamination, it is now recognized as both a risk factor and an opportunity in infection control. The microbiome that pervades hospital surfaces, air systems, and medical equipment plays a dual role—facilitating pathogen persistence and antimicrobial resistance on one hand, yet offering an ecological buffer capable of suppressing opportunistic colonization through competitive interactions on the other. The concept of the hospital environment as a living ecosystem reframes infection prevention from a process of eradication toward ecological balance and resilience.

Integrating microbiome insights into evidence-based infection control policy is therefore paramount. Infection control frameworks must evolve beyond conventional sterilization and antimicrobial regimens to adopt data-driven microbial management practices grounded in environmental and genomic surveillance. The application of culture-independent sequencing—particularly metagenomic and metatranscriptomic analyses—enables a systems-level understanding of microbial community composition, functional dynamics, and the conditions that favor pathogen proliferation. Incorporating such diagnostics into hospital routine surveillance can enable predictive risk modeling, rapid outbreak detection, and personalized intervention strategies.

Importantly, the paradigm of “ecological infection control”—which emphasizes maintaining microbial equilibrium rather than indiscriminate sterilization—offers a sustainable approach to reducing healthcare-associated infections (HAIs). This approach aligns with principles of antimicrobial stewardship by

curbing selective pressure for resistance while preserving environmental commensals that provide natural colonization resistance. Interventions like probiotic cleaning systems, microbiome-informed ventilation design, and microbial biofilm mapping exemplify this integration of ecology with applied infection science. When combined with precision environmental monitoring and staff training, ecological infection control can significantly curtail HAI transmission and improve long-term hospital safety outcomes.

Moving forward, the convergence of microbiology, bioinformatics, synthetic biology, and hospital architecture must guide next-generation infection control. To bridge the gap between laboratory research and practical implementation, multidisciplinary collaborations are needed to standardize methodologies, develop ethical guidelines for microbiome surveillance, and engineer microbial consortia that can stably inhabit hospital ecosystems without pathogenic risk. Ultimately, continued investment in hospital microbiome research will be essential to transforming infection control from a reactive discipline into a proactive, ecologically sustainable science—one that not only prevents infections but also fosters microbial harmony within the healthcare environment

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The heading should be treated as a 3<sup>rd</sup> level heading and should not be assigned a number.

## REFERENCES

1. Cason, C., Caselli, E., D’Accolti, M., Mazzacane, S., Soffritti, I., Comar, M.: Next-generation sequencing and PCR technologies in monitoring the hospital microbiome and its drug resistance. *Front Microbiol.* 13, (2022). <https://doi.org/10.3389/fmicb.2022.969863>.
2. D’Accolti, M., Soffritti, I., Mazzacane, S., Caselli, E.: Fighting AMR in the Healthcare Environment: Microbiome-Based Sanitation Approaches and Monitoring Tools. *Int J Mol Sci.* 20, 1535 (2019). <https://doi.org/10.3390/ijms20071535>.
3. Valzano, F., Coda, A.R.D., Liso, A., Arena, F.: Multidrug-Resistant Bacteria Contaminating Plumbing Components and Sanitary Installations of Hospital Restrooms. *Microorganisms.* 12, 136 (2024). <https://doi.org/10.3390/microorganisms12010136>.
4. Caselli, E., Tarricone, R., Rognoni, C., Soffritti, I., D’Accolti, M., Bisi, M., Brusaferrero, S., Arnoldo, L., Mazzacane, S., Lanzoni, L., Volta, A.: Impact of a probiotic-based hospital sanitation on antimicrobial resistance and HAI-associated antimicrobial consumption and costs: a multicenter study. *Infect Drug Resist.* 12, 501–510 (2019). <https://doi.org/10.2147/idr.s194670>.
5. Ruuskanen, M.O., Havulinna, A.S., Sommeria-Klein, G., Lahti, L., Niiranen, T.J.: Modelling spatial patterns in host-associated microbial communities. *Environ Microbiol.* 23, 2374–2388 (2021). <https://doi.org/10.1111/1462-2920.15462>.
6. Mousa, W.K., Chehadeh, F., Husband, S.: Recent Advances in Understanding the Structure and Function of the Human Microbiome. *Front Microbiol.* 13, (2022). <https://doi.org/10.3389/fmicb.2022.825338>.
7. Cao, X., Hamilton, J.J., Venturelli, O.S.: Understanding and Engineering Distributed Biochemical Pathways in

- Microbial Communities. *Biochemistry*. 58, 94–107 (2018). <https://doi.org/10.1021/acs.biochem.8b01006>.
8. Smith, D.R.M., Temime, L., Opatowski, L.: Microbiome-pathogen interactions drive epidemiological dynamics of antibiotic resistance: A modeling study applied to nosocomial pathogen control. *Elife*. 10, e68764 (2021). <https://doi.org/10.7554/eLife.68764>.
9. Lax, S., Sangwan, N., Smith, D., Larsen, P., Handley, K.M., Richardson, M., Guyton, K., Krezalek, M., Shogan, B.D., Defazio, J., Flemming, I., Shakhsheer, B., Weber, S., Landon, E., Garcia-Houchins, S., Siegel, J., Alverdy, J., Knight, R., Stephens, B., Gilbert, J.A.: Bacterial colonization and succession in a newly opened hospital. *Sci Transl Med*. 9, eaah6500 (2017). <https://doi.org/10.1126/scitranslmed.aah6500>.
10. Carrie, A.: Rethinking Sterile: The Hospital Microbiome. *Environ Health Perspect*. 122, A182–A187 (2014). <https://doi.org/10.1289/ehp.122-A182>.
11. Kaseba, C., Sathyavathi, S., Lin, Z., Clement, T., Patrick, T., Fangqiong, L.: Intra-hospital microbiome variability is driven by accessibility and clinical activities. *Microbiol Spectr*. 12, e00296-24 (2024). <https://doi.org/10.1128/spectrum.00296-24>.
12. Silvester, R., Perry, W.B., Webster, G., Rushton, L., Baldwin, A., Pass, D.A., Byrnes, N.A., Farkas, K., Heginbotham, M., Craine, N., Cross, G., Kille, P., Kasprzyk-Hordern, B., Weightman, A.J., Jones, D.L.: Metagenomic profiling of hospital wastewater: A comprehensive national scale analysis of antimicrobial resistance genes and opportunistic pathogens. *Journal of Infection*. 90, 106503 (2025). <https://doi.org/https://doi.org/10.1016/j.jinf.2025.106503>.
13. Thomas, S., Bittinger, K., Livornese Jr, L.L.: Utilizing the biosimulator to analyze the environmental microbiome within the intensive care units of a hospital. *Biotechniques*. 77, 66–75 (2025). <https://doi.org/10.1080/07366205.2025.2467550>.
14. Adeoye, I.A., Keenum, I.: How does the sewer microbiome impact wastewater surveillance for antibiotic resistance? *Water Res X*. 28, 100378 (2025). <https://doi.org/https://doi.org/10.1016/j.wroa.2025.100378>.
15. Gorlach, J., Gazda, D., Trusz, A., Walaszczyk, J., Szczęśniak, S., Piekarska, K.: Ventilation and air conditioning systems are a source of antibiotic-resistant bacteria - A review. *Build Environ*. 271, 112583 (2025). <https://doi.org/https://doi.org/10.1016/j.buildenv.2025.112583>.
16. Brown, G.Z., Kline, J., Mhuireach, G., Northcutt, D., Stenson, J.: Making microbiology of the built environment relevant to design. *Microbiome*. 4, 6 (2016). <https://doi.org/10.1186/s40168-016-0152-7>.
17. Joseph, T.M., Abdulkasoud, S., Mortula, Md.M., Beheiry, S., Zareen, N.: Microbiomes of the built environment: a systematic literature review. *Front Built Environ*. Volume 11-2025, (2025).
18. Kaseba, C., Sathyavathi, S., Lin, Z., Clement, T., Patrick, T., Fangqiong, L.: Intra-hospital microbiome variability is driven by accessibility and clinical activities. *Microbiol Spectr*. 12, e00296-24 (2024). <https://doi.org/10.1128/spectrum.00296-24>.
19. Arif, S.J., Graham, S.P., Abdill, R.J., Blekhman, R.: Analyzing human gut microbiome data from global populations: challenges and resources. *Trends Microbiol*. (2025). <https://doi.org/10.1016/j.tim.2025.05.008>.
20. Drago, L.: Navigating microbiome variability: implications for research, diagnostics, and direct-to-consumer testing. *Front Microbiol*. Volume 16-2025, (2025).
21. Li, Y., Ma, A., Johnson, E., Eng, C., De, S., Jiang, S., Li, Z., Spakowicz, D., Ma, Q.: The new microbiome on the block: challenges and opportunities of using human tumor sequencing data to study microbes. *Nat Methods*. 22, 1788–1799 (2025). <https://doi.org/10.1038/s41592-025-02807-y>.