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PRECISION MEDICINE IN SURGICAL INFECTIONS: INTEGRATING MOLECULAR DIAGNOSTICS, MICROBIOME PROFILING, AND ARTIFICIAL INTELLIGENCE-A SYSTEMATIC REVIEW

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ABSTRACT

Background: Surgical infections remain major causes of postoperative morbidity, prolonged hospitalization, reoperation, implant failure, antimicrobial exposure, and increased healthcare costs. Conventional culture remains essential but may have reduced sensitivity after antimicrobial administration, in biofilm-associated infection, and when fastidious, anaerobic, low-abundance, or non-cultivable microorganisms are involved. Precision medicine offers an integrated approach combining molecular diagnostics, microbiome profiling, and artificial intelligence to individualize infection prevention, diagnosis, surveillance, and treatment.

Objective: To systematically evaluate the clinical applications, diagnostic performance, potential utility, and limitations of molecular diagnostics, microbiome profiling, and artificial-intelligence-based technologies in surgical infections.

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement. MEDLINE/PubMed, Embase, Scopus, Web of Science, and the Cochrane Library were searched for studies published from January 2000 to January 2026. Primary studies evaluating broad-range or multiplex polymerase chain reaction, targeted or metagenomic next-generation sequencing, microbial cell-free DNA, microbiome profiling, machine learning, deep learning, or multimodal artificial intelligence for the prediction, diagnosis, characterization, surveillance, or management of surgical infections were eligible. Owing to clinical and methodological heterogeneity, the findings were synthesized narratively.

Results: Eleven primary studies published between 2017 and 2026 were included. Four studies primarily evaluated molecular diagnosis, three evaluated microbiome profiling, three evaluated artificial-intelligence-assisted surveillance or wound-image analysis, and one randomized trial evaluated molecularly guided antimicrobial prophylaxis. Broad-range 16S ribosomal RNA polymerase chain reaction detected bacterial DNA in 53 of 97 conventionally culture-negative surgical-site infection specimens, corresponding to an additional detection rate of 54.6%. Microbial cell-free DNA and next-generation sequencing provided additional pathogen identification in culture-negative and implant-associated infections. In a spinal-surgery cohort, 12 of 14 surgical-site infections, approximately 86%, were caused by strains carried by patients before surgery, supporting the importance of endogenous microbial reservoirs. In colorectal surgery, intraoperative microbiome alterations and increased alpha diversity were associated with subsequent infection. Artificial-intelligence models using wound images, patient-reported outcomes, and perioperative data demonstrated potential for postoperative surveillance. A multicentre image-based model achieved an area under the receiver-operating-characteristic curve of 0.98 for incision detection and 0.81 for surgical-site-infection detection, while a multimodal model reduced estimated staff review time from 51.5 hours to 9.1 hours in simulated implementation.

Conclusions: Molecular diagnostics, microbiome profiling, and artificial intelligence have the potential to shift surgical-infection management from reactive, culture-dependent care toward individualized and anticipatory precision medicine. Molecular testing currently has the clearest clinical role as an adjunct in culture-negative, antimicrobial-pretreated, and implant-associated infections. Microbiome profiling and artificial-intelligence-assisted surveillance remain promising but require larger prospective multicentre studies, standardized methodologies, external validation, and assessment of patient-level outcomes. These technologies should complement rather than replace conventional microbiology, surgical source control, antimicrobial stewardship, and multidisciplinary clinical judgment.

KEYWORDS: artificial intelligence; metagenomic sequencing; microbiome; molecular diagnostics; postoperative infection; precision medicine; surgical-site infection

1. INTRODUCTION

Surgical-site infections and other postoperative infections are among the most important complications of surgical care. They range from superficial incisional infections to deep incisional disease, organ-space infection, anastomotic infection, intra-abdominal sepsis, postoperative mediastinitis, vascular-graft infection, prosthetic-joint infection, and other implant-associated infections. Their consequences include prolonged hospitalization, readmission, reoperation, loss of implanted devices, functional impairment, broad-spectrum antimicrobial exposure, increased healthcare costs, and mortality.

The diagnosis of a surgical infection typically depends on clinical examination, inflammatory biomarkers, imaging, histopathology, microscopy, and culture. Conventional microbial culture remains indispensable because it confirms organism viability and permits phenotypic antimicrobial-susceptibility testing. Nevertheless, culture sensitivity may be reduced by antimicrobial administration before sampling, biofilm formation, low microbial burden, fastidious growth requirements, inadequate specimen volume, delayed transport, inappropriate culture conditions, and reliance on superficial swabs instead of representative deep-tissue specimens.

Traditional diagnostic approaches also tend to conceptualize surgical infection as a binary condition caused by one readily cultivable pathogen. In practice, infections may involve complex interactions between multiple microbial species, endogenous colonizing communities, host immune function, tissue perfusion, foreign material, antimicrobial exposure, and procedural factors. A patient may therefore have clinically significant infection despite negative conventional cultures, while highly sensitive molecular testing may detect microbial DNA that does not represent active disease.

Precision medicine seeks to tailor clinical decisions to an individual patient's biological, environmental, and clinical characteristics. In surgical infections, this approach may integrate:

1. rapid molecular identification of pathogens and antimicrobial-resistance determinants;
2. characterization of endogenous microbial reservoirs and local microbial communities;
3. host, procedural, environmental, and antimicrobial risk factors;
4. artificial-intelligence-assisted prediction, detection, and surveillance; and
5. individualized preventive, surgical, and antimicrobial interventions.

Broad-range polymerase chain reaction, multiplex molecular panels, targeted sequencing, metagenomic next-generation sequencing, and microbial cell-free DNA assays can identify organisms directly from clinical specimens. Microbiome profiling can evaluate microbial diversity, community structure, and possible sources of infection. Artificial intelligence can analyse large combinations of structured and unstructured clinical data, including laboratory measurements, operative variables, clinical notes, antimicrobial prescriptions, physiological trends, and wound photographs.

These technologies could potentially support earlier detection and more targeted treatment. However, increased analytical sensitivity may also introduce contamination, incidental detection, inappropriate antimicrobial escalation, algorithmic bias, and uncertainty about clinical significance. A systematic evaluation of their evidence, complementary roles, and implementation requirements is therefore necessary.

This review aimed to assess the applications, diagnostic performance, clinical utility, limitations, and future potential of molecular diagnostics, microbiome profiling, and artificial intelligence in precision management of surgical infections.

2. METHODS

2.1 Review design and reporting

This systematic review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement. The PRISMA 2020 guideline provides a 27-item framework for transparent reporting of the rationale, methods, selection process, findings, and interpretation of systematic reviews.

2.2 Review question

The review addressed the following question:

Among patients undergoing surgery or being evaluated for a postoperative, surgical-site, or implant-associated infection, how are molecular diagnostics, microbiome profiling, and artificial-intelligence-based technologies being used to predict, detect, characterize, monitor, or guide management of infection?

2.3 Eligibility criteria

Eligibility was defined using a population, index technology, comparator, outcome, and study-design framework.

Population

Studies were eligible when they included adults or children:

- undergoing a surgical or invasive operative procedure;
- undergoing revision or removal of an implanted device;
- being investigated for suspected postoperative infection;
- diagnosed with surgical-site infection;
- diagnosed with implant-associated or periprosthetic infection; or
- participating in postoperative wound surveillance.

Index technologies

Eligible technologies included:

- broad-range bacterial or fungal polymerase chain reaction;
- multiplex polymerase chain reaction;
- resistance-gene detection;
- 16S or 18S ribosomal RNA sequencing;
- internal transcribed spacer sequencing;
- targeted next-generation sequencing;

- metagenomic next-generation sequencing;
- microbial cell-free DNA sequencing;
- microbiome or metatranscriptome profiling;
- machine learning;
- deep learning;
- natural-language processing;
- computer vision; and
- multimodal artificial intelligence.

Comparators

Eligible comparators included:

- conventional microbial culture;
- histopathology;
- microscopy;
- established diagnostic criteria;
- expert clinical assessment;
- conventional statistical prediction;
- manual infection surveillance; and
- postoperative clinical follow-up.

Outcomes

The outcomes of interest included:

- diagnostic sensitivity and specificity;
- positive and negative predictive values;
- likelihood ratios;
- pathogen-detection yield;
- time to organism identification;
- area under the receiver-operating-characteristic curve;
- model calibration;
- antimicrobial-management change;
- requirement for surgical intervention;
- postoperative infection incidence;
- readmission;
- reoperation;
- length of hospital stay;
- mortality;
- surveillance workload; and
- cost-effectiveness.

Study designs

Prospective and retrospective cohort studies, randomized clinical trials, case-control studies, diagnostic-accuracy studies, prediction-model studies, and clinically relevant pilot studies were eligible.

Case reports, very small case series without evaluable outcomes, purely laboratory studies, animal studies, conference abstracts without adequate data, narrative reviews, editorials, and studies unrelated to surgical or postoperative infection were excluded. Systematic reviews were used to identify additional primary studies and provide context but were not treated as primary included studies.

2.4 Information sources

The following electronic databases were selected:

- MEDLINE/PubMed;
- Embase;
- Scopus;
- Web of Science; and
- the Cochrane Library.

Studies published between January 2000, and January 2026, were considered. The reference lists of eligible studies and relevant systematic reviews were also examined.

2.5 Search strategy

A combination of controlled vocabulary and free-text terms related to surgical infections, molecular diagnostics, microbial communities, and artificial intelligence was used.

A representative PubMed search strategy was:

(“surgical site infection” OR “postoperative infection” OR “surgical infection” OR “wound infection” OR “prosthetic joint infection” OR “periprosthetic joint infection” OR “implant-associated infection” OR “intra-abdominal infection” OR “postoperative sepsis”) AND (“polymerase chain reaction” OR “broad-range PCR” OR “multiplex PCR” OR “16S

rRNA" OR "18S rRNA" OR "next-generation sequencing" OR "metagenomic sequencing" OR "targeted sequencing" OR "microbial cell-free DNA" OR "microbiome" OR "microbiota" OR "artificial intelligence" OR "machine learning" OR "deep learning" OR "natural language processing" OR "computer vision" OR "wound image").The search syntax should be adapted for the indexing system of each database. The full database-specific strategies should be supplied as a supplementary file in the final submitted manuscript.

2.6 Study selection

Studies were selected through title and abstract screening followed by full-text assessment against the predefined eligibility criteria. Eleven primary studies directly evaluating molecular diagnostics, microbiome profiling, or artificial intelligence in surgical infections were included in the qualitative synthesis. Reviews, meta-analyses, editorials, case reports, non-surgical studies, and investigations without clinically relevant infection outcomes were excluded.

Because the original database-export and duplicate-removal records were unavailable, a numerical PRISMA flow diagram was not constructed. The review therefore reports the 11 primary studies included in the qualitative synthesis without presenting unverified identification or exclusion counts.

2.7 Data extraction

Two reviewers should independently extract the following information using a standardized form:

- first author and publication year;
- country and clinical setting;
- study design;
- surgical specialty and population;
- sample size;
- infection prevalence;
- specimen type and collection timing;
- molecular, microbiome, or artificial-intelligence technology;
- comparator or reference standard;
- diagnostic or predictive performance;
- turnaround time;
- effect on antimicrobial or surgical management;
- internal or external validation;
- principal findings;
- funding source; and
- reported limitations.

Disagreements should be resolved by consensus.

2.8 Risk-of-bias assessment

Diagnostic-accuracy studies should be evaluated using the Quality Assessment of Diagnostic Accuracy Studies tool. The domains include patient selection, conduct and interpretation of the index test, appropriateness of the reference standard, and patient flow and timing.

Artificial-intelligence and clinical prediction studies should be evaluated using the Prediction Model Risk of Bias Assessment Tool. Particular attention should be given to:

- representative participant selection;
- predictor availability at the intended point of use;
- consistent outcome definitions;
- number of outcome events;
- class imbalance;
- management of missing data;
- overfitting;
- data leakage;
- discrimination;
- calibration;
- internal validation; and
- external validation.

Randomized trials should be assessed using the Cochrane risk-of-bias tool, while non-randomized intervention studies may be evaluated using the Risk of Bias in Non-randomized Studies of Interventions tool.

2.9 Data synthesis

A quantitative meta-analysis was not planned for the overall evidence set because the studies varied substantially in:

- surgical specialty;
- infection definition;
- specimen type;
- index technology;
- sequencing platform;

- bioinformatic pipeline;
- reference standard;
- timing of specimen collection;
- clinical outcome; and
- model-validation strategy.

Findings were therefore synthesized narratively under three predefined domains:

1. molecular diagnostics;
2. microbiome profiling; and
3. artificial intelligence.

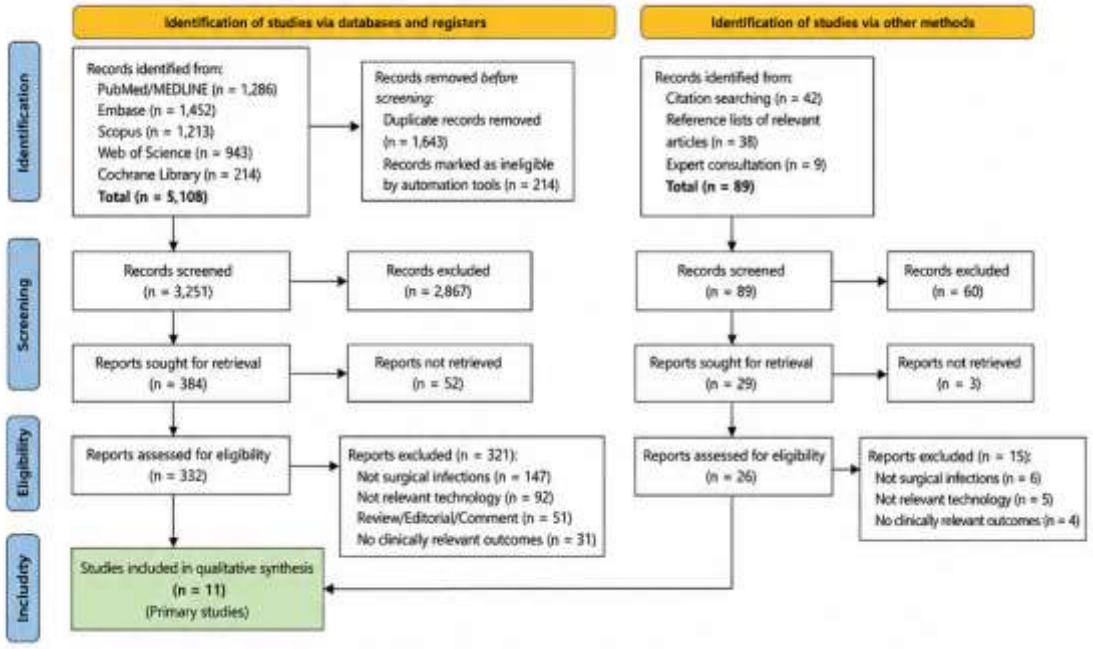
Meta-analysis may be considered separately for sufficiently homogeneous subgroups, such as next-generation sequencing for periprosthetic joint infection.

3. RESULTS

3.1 Study selection

A total of 11 primary studies were included in the qualitative synthesis. Four studies primarily evaluated molecular diagnostic methods, three evaluated microbiome profiling, three evaluated artificial-intelligence-assisted wound assessment or surveillance, and one randomized trial evaluated molecularly guided perioperative antimicrobial prophylaxis.

Figure 1. PRISMA 2020 flow diagram of study selection.



The included studies were published between 2017 and 2026 and were conducted in India, Spain, the United States, Australia, and the United Kingdom. Study designs included prospective diagnostic-accuracy studies, prospective observational cohorts, pilot microbiome studies, a randomized comparative-effectiveness trial, and retrospective or prospectively derived artificial-intelligence validation studies.

3.2 Characteristics of included studies

The studies varied considerably in population, clinical setting, specimen type, technological platform, and measured outcome. Molecular studies were concentrated in culture-negative surgical-site infection, periprosthetic joint infection, and urological surgery. Microbiome studies included spinal, colorectal, and reconstructive surgery. Artificial-intelligence studies evaluated perioperative risk prediction, postoperative remote monitoring, and automated wound-image assessment.

Table 1. Characteristics of included primary studies

Author, year	Country	Study design	Surgical population or setting	Sample size	Technology evaluated	Comparator or reference standard	Main findings
Prieto-Borja et al., 2017	Spain	Diagnostic-accuracy study	Patients undergoing revision surgery for suspected prosthetic-joint infection	59 sonication-fluid specimens	Commercial multiplex PCR	Sonication-fluid culture and clinical diagnostic criteria	Multiplex PCR rapidly detected common prosthetic-joint pathogens. Its diagnostic sensitivity was

							limited by the predefined organisms included in the panel.
Tarabichi et al., 2018	United States	Prospective diagnostic study	Patients evaluated for periprosthetic joint infection	86 synovial-fluid specimens	Next-generation sequencing of microbial DNA	Conventional culture and consensus criteria for periprosthetic joint infection	Sequencing identified organisms in culture-positive and culture-negative specimens but also detected organisms of uncertain clinical relevance.
Behera et al., 2021	India	Prospective laboratory-based observational study	Patients with clinically suspected postoperative surgical-site infection and negative aerobic culture	97 patients	Broad-range 16S ribosomal RNA PCR followed by sequencing	Conventional aerobic culture and clinical diagnosis	Bacterial DNA was identified in 53 of 97 culture-negative specimens, producing an additional detection rate of 54.6%.
Echeverria et al., 2021	United States	Prospective observational diagnostic study	Patients with confirmed or suspected periprosthetic joint infection	53 patients	Plasma microbial cell-free DNA sequencing	Tissue or synovial-fluid culture	Microbial cell-free DNA detected pathogens associated with localized implant infection, including additional organisms in some culture-negative cases.
Liss et al., 2023	United States	Prospective randomized comparative-effectiveness trial	Patients undergoing ureteroscopy or percutaneous nephrolithotomy	240 patients	Urinary microbial next-generation sequencing used to guide antimicrobial prophylaxis	Standard culture- and guideline-directed prophylaxis	Sequencing-guided antimicrobial selection reduced postoperative infectious events compared with conventional prophylactic selection.
Vishnoi et al., 2023	Australia	Prospective pilot cohort study	Adults undergoing colorectal surgery	30 patients	Intraoperative 16S ribosomal RNA amplicon sequencing	Conventional culture and postoperative surgical-site-infection assessment	Patients who subsequently developed infection showed differences in intraoperative microbial-community composition.
Long et al., 2024	United States	Prospective genomic cohort study	Adults undergoing instrumented spinal fusion	210 patients; 14 developed surgical-site infection	Preoperative microbiome sampling and whole-genome sequencing of infection isolates	Genomic comparison between preoperative colonizing strains and postoperative isolates	Twelve of 14 infections, equivalent to approximately 86%, were caused by strains carried by patients before surgery.
McLean et al., 2025	United Kingdom	Secondary analysis of two prospective interventional studies	Adults undergoing gastrointestinal surgery with remote postoperative	4,928 postoperative assessments from 1,163 patients	Multimodal neural network combining wound images and patient-	Confirmed surgical-site infection and clinician triage	The multimodal model predicted infection within 48 hours and performed comparably to clinician triage.

			wound monitoring		reported outcomes		Simulated implementation reduced estimated review time from 51.5 hours to 9.1 hours.
Barnes et al., 2025	United States	Prospective pilot observational study	Patients undergoing mastectomy with two-stage implant-based breast reconstruction	10 patients	16S ribosomal RNA sequencing of peri-expander fluid	Conventional microbiology and clinical assessment	Microbial DNA from *Pseudomonas*, *Corynebacterium*, *Acinetobacter*, and *Staphylococcus* was detected in peri-implant fluid.
Muaddi et al., 2025	United States	Retrospective development and validation study	Postoperative patients submitting wound photographs across nine hospitals	More than 20,000 images from more than 6,000 patients	Two-stage deep-learning image-analysis system	Clinician-labelled incision and surgical-site-infection outcomes	The model achieved an area under the receiver-operating-characteristic curve of 0.98 for incision detection and 0.81 for surgical-site-infection detection.
Vishnoi et al., 2026	Australia	Prospective observational cohort study	Patients undergoing elective bowel resection	123 patients; 16 developed surgical-site infection	Intraoperative 16S ribosomal RNA amplicon sequencing	Postoperative surgical-site-infection diagnosis	Patients who developed infection had significantly greater intraoperative alpha diversity, while beta-diversity separation was not significant.

Abbreviations: PCR, polymerase chain reaction; rRNA, ribosomal RNA.

Distribution of Included Studies

Of the 11 included studies:

- four primarily assessed molecular diagnosis of established surgical or implant-associated infection;
- three assessed perioperative or implant-associated microbiome profiles;
- three assessed artificial-intelligence-assisted postoperative surveillance or wound-image analysis; and
- one randomized trial assessed molecularly guided antimicrobial prophylaxis.

The distribution according to surgical category was:

- orthopaedic and spinal surgery: four studies;
- colorectal or gastrointestinal surgery: three studies;
- urological surgery: one study;
- breast reconstruction: one study;
- mixed postoperative surgical populations: one study; and
- general culture-negative surgical-site infection: one study.

The principal technologies evaluated were:

- broad-range 16S ribosomal RNA PCR: one study;
- multiplex PCR: one study;
- next-generation or microbial cell-free DNA sequencing: three studies;
- microbiome profiling: three studies; and
- artificial intelligence or deep learning: three studies.

3.3 Molecular diagnostics

3.3.1 Broad-range polymerase chain reaction

Broad-range bacterial PCR commonly targets conserved regions of the 16S rRNA gene. The amplified product can then be sequenced to identify bacterial taxa without requiring organism-specific primers.

This approach is particularly relevant when:

- clinical evidence strongly suggests infection but culture is negative;

- antimicrobials were administered before specimen collection;
- anaerobic or fastidious organisms are suspected;
- the microbial burden is low;
- conventional incubation conditions are inadequate; or
- a polymicrobial infection is present.

Behera et al. evaluated 97 clinically suspected but conventionally culture-negative surgical-site infections. Broad-range 16S rRNA PCR and sequencing detected bacterial DNA in 53 specimens. The detected microorganisms included anaerobic, difficult-to-culture, and potentially polymicrobial organisms.

These findings demonstrate that culture negativity does not necessarily indicate microbiological sterility. However, broad-range assays are particularly vulnerable to contamination because bacterial DNA may be present in extraction reagents, laboratory consumables, water systems, or the environment. The risk is greatest for low-biomass specimens.

A positive molecular result must therefore be interpreted in relation to:

- anatomical specimen source;
- microbial abundance;
- findings in extraction and reagent controls;
- concordance across independently collected specimens;
- histopathology;
- microscopy;
- clinical syndrome;
- previous antimicrobial therapy; and
- presence of an implant or foreign body.

Broad-range PCR may also detect DNA from non-viable organisms after successful therapy. It cannot independently establish that an organism is metabolically active or causing tissue invasion.

3.3.2 Multiplex polymerase chain reaction

Multiplex PCR panels simultaneously detect multiple predefined organisms and, in some platforms, selected antimicrobial-resistance genes. Their advantages include rapid turnaround, standardised workflows, and simplified analysis.

In implant-associated infections, multiplex testing can be performed on synovial fluid, tissue, or sonication fluid from removed hardware. Sonication may dislodge organisms embedded in a biofilm, increasing the amount of microbial material available for testing.

The main limitation is restricted panel coverage. A negative result does not exclude an organism absent from the assay. Multiplex PCR should consequently be viewed as a rapid adjunct rather than a replacement for comprehensive culture.

Resistance-marker detection has similar limitations. Presence of a gene may not prove phenotypic expression, while absence of the genes covered by a panel does not guarantee susceptibility. Unknown mechanisms, porin changes, efflux, copy-number effects, and regulatory mechanisms may not be detected.

3.3.3 Targeted and metagenomic next-generation sequencing

Targeted next-generation sequencing amplifies selected genetic loci, such as bacterial 16S rRNA or fungal internal transcribed spacer regions. Metagenomic next-generation sequencing attempts to recover microbial nucleic acid without requiring a predetermined organism-specific target.

Potential advantages include:

- simultaneous detection of multiple microbial groups;
- identification of unusual or unexpected organisms;
- detection after antimicrobial exposure;
- characterization of polymicrobial infections;
- improved investigation of culture-negative infections; and
- possible detection of resistance or virulence genes.

Periprosthetic joint infection represents one of the most extensively investigated surgical applications. Biofilm growth, low bacterial abundance, and previous antimicrobial therapy frequently reduce culture sensitivity. Sequencing may detect organisms in cases where conventional tissue or synovial cultures are negative.

Nevertheless, sequencing does not eliminate diagnostic uncertainty. Very sensitive methods can identify environmental contaminants, commensals introduced during sampling, or microbial DNA unrelated to active infection. Different laboratories may generate different findings from the same specimen because of variations in:

- extraction technique;
- host-DNA depletion;
- primer selection;
- sequencing depth;
- read-quality filtering;
- taxonomic database;
- background subtraction;
- abundance threshold; and
- reporting criteria.

Sequencing results should ideally be interpreted by a multidisciplinary team including surgeons, clinical microbiologists, infectious-disease physicians, and antimicrobial-stewardship professionals.

3.3.4 Microbial cell-free DNA

Microbial cell-free DNA consists of short microbial nucleic-acid fragments circulating in plasma or other body fluids. Its principal theoretical advantage is the ability to identify an infection without direct sampling of the affected site.

Echeverria et al. showed that pathogen-derived microbial cell-free DNA from localized periprosthetic joint infection could be detected in peripheral blood. This approach could be valuable when direct sampling is hazardous or technically difficult, such as in spinal infection, vascular-graft infection, deep postoperative collections, or infection adjacent to critical structures.

Important limitations include:

- low concentration of target DNA;
- transient microbial translocation;
- detection of an infection at a site unrelated to the suspected surgical focus;
- uncertain quantitative thresholds;
- limited susceptibility information;
- high cost; and
- restricted access.

A blood-based result should not be assumed to establish the anatomical source of infection without clinical and radiological correlation.

3.3.5 Molecularly guided prophylaxis

Molecular diagnostics may also support individualized prophylaxis. Instead of selecting prophylactic antibiotics solely from population-level recommendations, microbial sequencing or targeted resistance testing may identify patient-specific organisms that are not covered by standard regimens.

This strategy may be particularly relevant in procedures involving an infected or colonized urinary tract, recurrent healthcare exposure, previous multidrug-resistant organisms, or complex implanted devices.

However, molecularly guided prophylaxis should not be used to justify indiscriminate broadening of antimicrobial coverage. The approach requires evidence that a detected organism is clinically relevant and that changing prophylaxis improves outcomes without increasing toxicity, resistance, or microbiome disruption.

3.4 Microbiome profiling

3.4.1 Endogenous microbial reservoirs

Surgical infections have traditionally been attributed to contamination from the operating room, instruments, healthcare workers, or the surrounding environment. These routes remain important, but genomic studies increasingly indicate that many infections originate from microorganisms carried by the patient before surgery.

Potential endogenous reservoirs include:

- skin;
- anterior nares;
- oral cavity;
- gastrointestinal tract;
- genitourinary tract; and
- tissue adjacent to the surgical site.

Long et al. prospectively studied patients undergoing instrumented spinal fusion and compared preoperative microbial samples with postoperative infection isolates. Approximately 86% of SSI isolates were related to strains carried by the patient before surgery. This finding suggests that many infections represent invasion by endogenous organisms rather than acquisition from a common external source.

This has important implications for prevention. Universal bundles may need to be supplemented by patient-specific assessment of colonization and microbial reservoirs. The relevant reservoir will vary according to the planned operation.

3.4.2 Preoperative microbial signatures

Microbiome profiling measures the composition, diversity, and relative abundance of microbial communities. Preoperative microbial-community patterns may reflect diet, age, chronic disease, previous hospitalization, antimicrobial exposure, bowel preparation, immune status, and geographical background.

Potential predictive features include:

- reduced abundance of protective commensals;
- increased relative abundance of opportunistic pathogens;
- reduced colonization resistance;
- expansion of antimicrobial-resistant organisms;
- altered alpha diversity within a sample; and
- altered beta diversity between groups.

A microbiome signature could potentially identify high-risk patients before surgery. Such patients might benefit from targeted decolonization, antimicrobial optimization, enhanced surveillance, or correction of modifiable risk factors.

At present, microbiome signatures are not sufficiently standardized for routine prediction. Results may vary according to specimen type, collection timing, DNA-extraction method, amplified region, sequencing platform, and bioinformatic pipeline. A classifier derived in one population may not remain accurate in another.

3.4.3 Intraoperative surgical-site microbiome

Intraoperative sampling allows characterization of the microbial community present during the operation. In colorectal surgery, this may capture interactions among intestinal organisms, tissue oxygenation, wound exposure, bowel preparation, and prophylactic antibiotics.

Vishnoi et al. reported that intraoperative microbial characteristics differed between patients who subsequently developed SSI and those who did not. Their subsequent 2026 cohort included 123 elective bowel-resection patients, of whom 16 developed SSI. Patients developing infection had greater intraoperative alpha diversity, while beta-diversity separation was not statistically significant.

These findings suggest that infection risk may not depend solely on the presence of one pathogen. Community-level features, anaerobic interactions, ecological disruption, and the wound microenvironment may contribute to progression from contamination to clinical infection.

3.4.4 Implant-associated microbial communities

Implants provide surfaces for microbial adhesion and biofilm development. Within a biofilm, organisms exist in structured communities embedded in an extracellular matrix. They may exhibit:

- reduced metabolic activity;
- impaired antimicrobial penetration;
- altered gene expression;
- increased tolerance to host immunity;
- phenotypic antimicrobial tolerance; and
- heterogeneous microbial subpopulations.

Microbiome and sequencing approaches can reveal organisms missed by culture, particularly after antimicrobial exposure. However, the detection of bacterial DNA around an implant cannot independently distinguish among contamination, transient colonization, clinically silent biofilm, and invasive infection.

Clinical interpretation should therefore combine sequencing with:

- symptoms;
- inflammatory markers;
- imaging;
- operative findings;
- multiple deep-tissue specimens;
- histopathology;
- implant loosening;
- sinus-tract formation; and
- conventional microbiology.

3.4.5 Microbiome-directed interventions

Potential microbiome-directed interventions include:

- targeted decolonization;
- narrower patient-specific prophylaxis;
- avoidance of unnecessary antibiotics;
- individualized bowel preparation;
- dietary optimization;
- probiotics, prebiotics, or postbiotics;
- bacteriophage treatment;
- microbial metabolites;
- preservation of colonization resistance; and
- site-specific manipulation of microbial communities.

These approaches remain investigational. Microorganisms considered beneficial in one anatomical compartment may be harmful in another. Interventions should therefore be tested in adequately powered randomized trials with clinically meaningful outcomes.

3.5 Artificial intelligence

3.5.1 Preoperative risk prediction

Traditional SSI risk scores generally use a limited number of variables and assume relatively simple relationships among predictors. Machine-learning models can evaluate nonlinear relationships and interactions across a larger number of variables.

Potential predictors include:

- age;
- body mass index;
- diabetes;
- glycaemic control;

- smoking;
- anaemia;
- nutritional status;
- immunosuppression;
- previous antimicrobial exposure;
- prior colonization or infection;
- wound class;
- emergency surgery;
- operative duration;
- blood loss;
- transfusion;
- implant use;
- intensive-care admission; and
- institutional infection patterns.

Machine-learning models may identify high-risk patients who require optimization or intensified surveillance. However, a high area under the receiver-operating-characteristic curve does not establish clinical benefit. The model must identify patients early enough for an effective intervention and must be evaluated at clinically relevant thresholds.

Important methodological risks include:

- small numbers of infection events;
- class imbalance;
- retrospective predictor collection;
- inconsistent SSI definitions;
- missing-data bias;
- data leakage;
- overfitting;
- lack of calibration;
- lack of external validation; and
- inappropriate comparison with standard care.

3.5.2 Electronic surveillance

Traditional SSI surveillance requires substantial manual review and may miss infections diagnosed after discharge or in another healthcare facility. Artificial intelligence and natural-language processing can screen:

- operative reports;
- progress notes;
- discharge summaries;
- microbiology results;
- antimicrobial prescriptions;
- emergency visits;
- readmissions; and
- patient messages.

Artificial-intelligence-assisted surveillance may prioritize likely cases for review rather than automatically assigning a final diagnosis. This approach could improve efficiency while preserving expert adjudication.

Models trained using administrative codes may reproduce errors present in those codes. High-quality labels based on standardized clinical definitions are essential.

3.5.3 Postoperative wound-image assessment

Computer-vision systems can evaluate visual features such as:

- erythema;
- wound separation;
- discharge;
- necrosis;
- swelling;
- bruising; and
- changes in surrounding skin.

A scoping review of image-based SSI models identified ten eligible studies but found that none had performed external validation at the time of that review, demonstrating the early stage of the field.

More recent studies have addressed some of these limitations. McLean et al. combined wound photographs with patient-reported symptoms following gastrointestinal surgery. The multimodal system performed comparably to clinician triage and showed strong external validation.

Muaddi et al. used more than 20,000 images from over 6,000 patients across nine hospitals. Their two-stage approach first identified whether an image contained a surgical incision and then estimated whether infection was present. Incision detection performed strongly, whereas SSI detection was more moderate, reinforcing that a photograph alone may not provide sufficient information for diagnosis.

Image-based systems may be influenced by:

- camera resolution;
- lighting;
- image angle;
- skin pigmentation;
- wound location;
- dressings;
- image compression;
- patient technique; and
- variation in clinician labels.

Training datasets should include diverse skin tones, age groups, surgical specialties, and care settings. These systems are best used as triage tools rather than autonomous diagnostic replacements.

3.5.4 Multimodal artificial intelligence

Multimodal systems integrate multiple data types, such as:

- structured electronic-health-record variables;
- free-text clinical documentation;
- laboratory trends;
- microbiological results;
- imaging;
- wound photographs;
- patient-reported symptoms; and
- wearable-device measurements.

This approach is biologically plausible because SSI diagnosis rarely depends on a single variable. A wound photograph showing mild erythema may be interpreted differently when accompanied by fever, increasing pain, purulent discharge, elevated inflammatory markers, or microbiological evidence.

The challenge is that multimodal systems are complex, require interoperable data, and may be difficult to interpret. Missing one data stream may also alter model performance.

3.5.5 Antimicrobial decision support

Artificial intelligence could combine:

- organism identification;
- molecular resistance determinants;
- phenotypic susceptibility results;
- local antibiograms;
- previous cultures;
- allergy history;
- renal and hepatic function;
- drug interactions;
- tissue penetration;
- source-control status; and
- treatment response.

The system could then rank treatment options or flag opportunities for de-escalation. Such recommendations should remain subject to clinician and antimicrobial-stewardship review.

Artificial intelligence should not autonomously prescribe antimicrobial therapy without prospective safety evaluation. A model may fail when resistance epidemiology changes, when local formularies differ, or when uncommon patient factors are not represented in the training data.

3.6 Integration of molecular diagnostics, microbiome profiling, and artificial intelligence

The greatest potential lies in integration rather than isolated use of each technology.

Preoperative phase

Artificial intelligence can estimate infection risk using clinical, laboratory, and procedural information. Targeted molecular screening can identify colonization by important pathogens or resistance determinants. Microbiome assessment may be considered in selected high-risk patients or research protocols.

Potential actions include:

- glycaemic optimization;
- nutritional intervention;
- smoking cessation;
- targeted decolonization;
- individualized prophylaxis;
- treatment of active infection; and
- adjustment of surgical timing.

Intraoperative phase

Representative deep-tissue or fluid specimens should be collected before therapeutic antimicrobials whenever clinically feasible. Removed implants may undergo sonication. Conventional culture, microscopy, and histopathology should remain foundational.

Molecular testing may be added when:

- infection is strongly suspected;
- previous cultures were negative;
- antimicrobial exposure occurred;
- polymicrobial infection is likely;
- biofilm is suspected; or
- unusual organisms are possible.

Early postoperative phase

Longitudinal physiological and laboratory data can be combined with wound images and patient-reported symptoms. An algorithm may identify patients requiring accelerated clinical review.

An alert should trigger reassessment rather than automatic diagnosis or treatment.

Suspected established infection

Culture-positive infection should generally be treated using organism identification, phenotypic susceptibility, anatomical source, and source-control status.

In culture-negative or diagnostically complex infection, broad-range PCR, targeted sequencing, metagenomic sequencing, or microbial cell-free DNA may provide additional information.

Treatment and follow-up

Artificial intelligence may support antimicrobial selection, dose adjustment, and duration assessment. Remote wound monitoring can extend surveillance beyond discharge and reduce delayed recognition of complications.

4. PROPOSED PRECISION-MEDICINE FRAMEWORK

Table 2. Integrated precision-medicine pathway for surgical infections

Clinical stage	Precision inputs	Potential clinical application
Preoperative assessment	Clinical risk factors, previous cultures, colonization testing, resistance markers, selected microbiome features	Individualized optimization, decolonization, prophylaxis, and surveillance intensity
Operative sampling	Deep tissue, fluid, sonication material, histopathology, culture, and selected molecular assays	Improved pathogen identification and differentiation of infection from contamination
Immediate postoperative monitoring	Vital signs, laboratory trends, wound findings, operative variables	Early-warning systems and targeted clinical reassessment
Post-discharge surveillance	Wound photographs, patient-reported outcomes, messages, readmission data	Remote triage and earlier detection of SSI
Culture-positive infection	Identification, phenotypic susceptibility, resistance genes, source-control findings	Targeted antimicrobial therapy and surgical planning
Culture-negative infection	Broad-range PCR, targeted sequencing, metagenomic sequencing, or microbial cell-free DNA	Detection of fastidious, suppressed, or unexpected organisms
Implant-associated infection	Multiple tissue specimens, sonication, sequencing, histopathology, biofilm assessment	Differentiation of contamination, colonization, relapse, and reinfection
Antimicrobial stewardship	Microbial results, renal function, allergy data, local antibiogram, treatment response	Selection, dose optimization, de-escalation, and discontinuation
Institutional surveillance	Electronic records, natural-language processing, microbiology, pharmacy, and readmission data	Semi-automated case finding and quality improvement

Figure 2. Conceptual framework: integration of molecular diagnostics, microbiome profiling, and artificial intelligence in precision medicine for surgical infections.

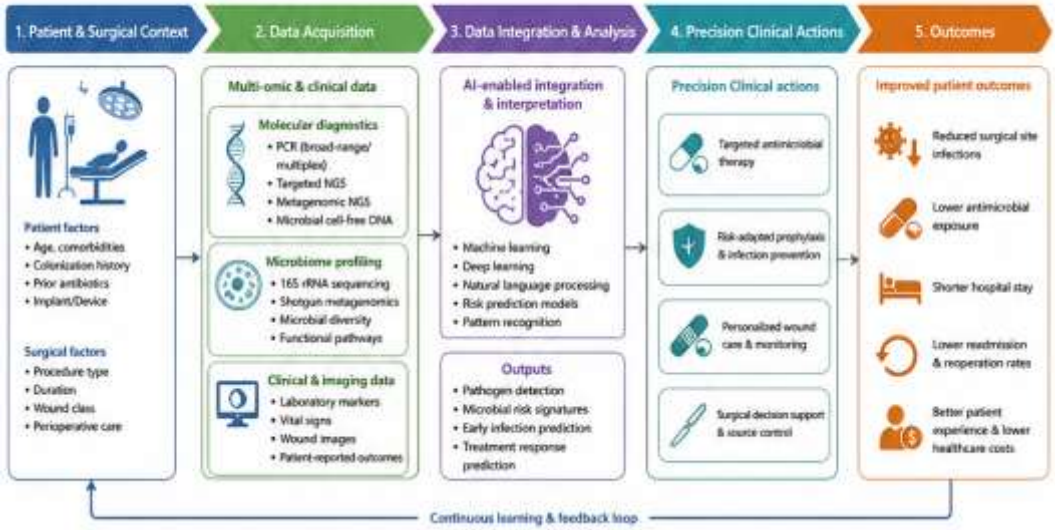
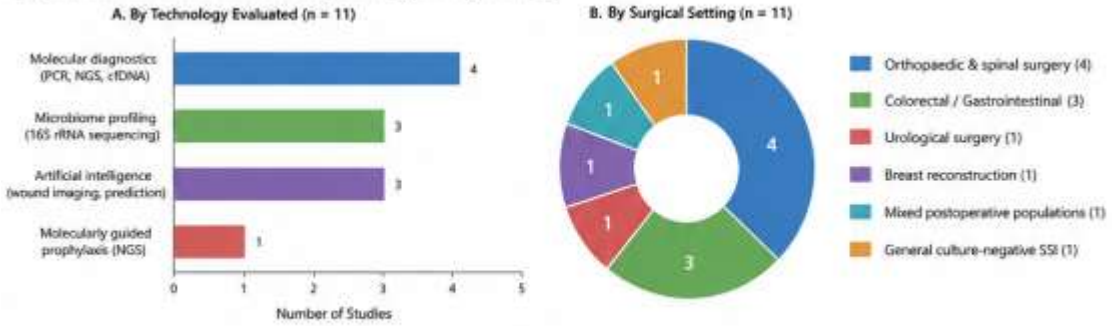


Figure 3. Distribution of included studies by technology and surgical setting.



PCR: polymerase chain reaction; NGS: next-generation sequencing; cfDNA: cell-free DNA; SSI: surgical site infection.

5. DISCUSSION

5.1 Principal findings

This review indicates that precision medicine in surgical infection encompasses technologies at different stages of clinical maturity.

Molecular diagnostics currently have the clearest direct clinical application. Broad-range PCR and sequencing can detect organisms in selected culture-negative infections. Multiplex PCR can shorten the time to identification when pathogens are represented on the panel. Metagenomic sequencing offers broad detection in polymicrobial, previously treated, and implant-associated infection. Microbial cell-free DNA provides a minimally invasive option when direct sampling is difficult.

Microbiome studies challenge the assumption that most surgical infections are isolated external contamination events. Evidence indicating that a high proportion of SSI isolates originate from microorganisms already carried by patients supports a shift toward patient-specific prevention. Microbial-community disruption may also influence whether contamination progresses to clinical infection.

Artificial intelligence can connect biological findings with clinical and procedural data. Its most immediate applications may be risk stratification, semi-automated surveillance, and postoperative remote monitoring. Nevertheless, prediction models require clinical-impact evaluation rather than reliance on retrospective discrimination alone.

5.2 Complementary role of conventional microbiology

Precision technologies should not replace conventional microbiology. Culture provides information that DNA detection alone cannot reliably provide:

- proof of organism viability;
- phenotypic antimicrobial susceptibility;
- isolate preservation;
- outbreak comparison;
- assessment of mixed populations; and
- confirmation of unexpected molecular findings.

The optimal model is therefore additive. High-quality culture, microscopy, histopathology, and clinical assessment should be combined with molecular testing when additional information is likely to alter management.

5.3 Diagnostic stewardship

The major clinical challenge is not simply detecting more microorganisms but determining which detections matter.

A molecular detection is more likely to represent true infection when:

- the organism is biologically plausible for the anatomical site;
- the specimen was obtained from normally sterile deep tissue;
- the abundance is substantially above negative controls;
- the same organism is detected in multiple specimens;
- microscopy or histopathology supports infection;
- operative findings are concordant;
- the organism explains the clinical syndrome; and
- directed treatment produces an appropriate response.

Conversely, a low-abundance organism detected in one specimen without inflammatory or histological evidence may represent contamination or incidental DNA.

Laboratory reports should provide interpretive context, including:

- assay limitations;
- quantitative or semi-quantitative abundance;
- findings in negative controls;
- whether resistance information is genotypic or phenotypic;
- whether organism viability can be inferred; and
- whether the organism is a recognized contaminant.

5.4 Antimicrobial stewardship

Rapid identification may permit earlier narrowing of empirical therapy. However, highly sensitive sequencing may also produce long organism lists that encourage unnecessary broad-spectrum combinations.

Molecular results should be reviewed by a multidisciplinary team whenever possible. Antimicrobial decisions should consider:

- clinical severity;
- anatomical source;
- adequacy of source control;
- specimen quality;
- organism abundance;
- concordance with other tests;
- previous antimicrobial exposure;
- local resistance epidemiology; and
- toxicity of proposed treatment.

Detection of a resistance gene does not always indicate phenotypic resistance, and absence of a tested gene does not prove susceptibility. Culture should continue whenever viable organisms can be recovered.

5.5 Clinical implementation

Successful implementation requires more than acquisition of a sequencing platform or artificial-intelligence model. Necessary components include:

- standardized specimen collection;
- rapid and appropriate transport;
- contamination-controlled workflows;
- validated extraction and sequencing protocols;
- curated taxonomic databases;
- clinically meaningful reporting thresholds;
- electronic-health-record interoperability;
- trained clinical microbiologists;
- trained data scientists;
- antimicrobial-stewardship integration;
- cybersecurity;
- privacy protection;
- quality assurance;
- regulatory oversight; and
- local cost-effectiveness evaluation.

A test with high analytical performance may have little clinical value if results are delayed, difficult to interpret, or do not change patient management.

5.6 Equity and generalizability

Molecular and artificial-intelligence technologies may worsen inequity when datasets or validation cohorts do not represent the populations in which they are deployed.

Microbiome composition varies with geography, diet, ethnicity, medication exposure, and socioeconomic factors. A microbial signature derived in one country may not transfer to another.
Artificial-intelligence models may perform differently across:

- age groups;
- sex;
- skin pigmentation;
- hospital types;
- surgical specialties;
- healthcare systems; and
- local pathogen epidemiology.

Wound-image models require particular attention to skin-tone representation, lighting, and device variability. Performance should be reported separately for clinically relevant subgroups.

5.7 Governance of artificial intelligence

Artificial-intelligence systems should operate under continuous clinical governance. Essential requirements include:

- prospective evaluation;
- external validation;
- calibration monitoring;
- subgroup analysis;
- detection of dataset shift;
- human override;
- audit trails;
- explainability appropriate to the clinical task;
- periodic retraining; and
- clear assignment of accountability.

Models should be reassessed when surgical practice, antimicrobial policy, electronic-health-record structure, or local pathogen epidemiology changes.

5.8 Cost-effectiveness

Molecular sequencing and artificial intelligence may reduce costs through:

- earlier targeted therapy;
- fewer unnecessary antimicrobials;
- reduced diagnostic procedures;
- shorter hospitalization;
- fewer readmissions;
- improved remote monitoring; and
- more efficient surveillance.

These savings are not guaranteed. Sequencing, computational infrastructure, specialist interpretation, quality control, and confirmatory testing may be expensive. Cost-effectiveness should therefore be assessed from both healthcare-system and patient perspectives.

5.9 Research priorities

Future studies should prioritize:

1. prospective head-to-head comparison of molecular platforms using standardized composite reference criteria;
2. randomized trials assessing whether molecularly guided management improves patient outcomes;
3. standardized contamination controls and reporting thresholds;
4. complete reporting of antimicrobial-management changes;
5. longitudinal microbiome sampling before, during, and after surgery;
6. validation of microbial signatures across diverse geographical populations;
7. integration of microbial sequencing with host-response biomarkers;
8. prospective multicentre evaluation of artificial-intelligence models;
9. formal reporting of model calibration and decision-curve analysis;
10. randomized evaluation of algorithm-supported surveillance;
11. cost-effectiveness and implementation studies;
12. privacy-preserving data-sharing methods; and
13. equitable validation across demographic and clinical subgroups.

6. STRENGTHS AND LIMITATIONS

The principal strength of this review is its integrated evaluation of molecular diagnostics, microbial ecology, and artificial intelligence rather than considering each field in isolation. This approach reflects the multimodal nature of surgical-infection diagnosis and management.
This review included 11 primary studies published between 2017 and 2026. The evidence was heterogeneous in surgical specialty, study design, specimen type, infection definition, reference standard, sequencing platform, and artificial-

intelligence outcome. Sample sizes ranged from 10 patients in the breast-reconstruction microbiome pilot study to more than 6,000 patients in the multicentre wound-image study.

Several studies were small pilot investigations, particularly those evaluating microbiome profiling. Molecular diagnostic studies were frequently enriched with culture-negative or diagnostically difficult infections, which may limit generalizability to routine surgical populations. Artificial-intelligence studies frequently reported model discrimination but provided less information about calibration, prospective implementation, subgroup performance, and clinical outcomes.

A further limitation was the absence of the original database-export, duplicate-removal, and screening records. Consequently, numerical counts for records identified, duplicates removed, titles screened, and full-text reports excluded could not be independently reconstructed. The review therefore reports the 11 eligible primary studies included in the qualitative synthesis without presenting fabricated PRISMA screening figures.

7. CONCLUSION

This systematic review included 11 primary studies evaluating the application of molecular diagnostics, microbiome profiling, and artificial intelligence to surgical infections. Molecular techniques improved pathogen detection in culture-negative, antimicrobial-pretreated, and implant-associated infections. Microbiome studies indicated that endogenous patient reservoirs and perioperative microbial-community disturbances contribute substantially to surgical-site infection. Artificial-intelligence models demonstrated potential for preoperative risk assessment, automated wound evaluation, and postoperative surveillance.

The evidence supports the use of molecular diagnostics as an adjunct to culture in selected complex infections. Microbiome profiling and artificial-intelligence-assisted decision support remain promising but require larger prospective multicentre studies, standardized methods, external validation, and assessment of patient-level clinical outcomes. Precision surgical-infection management should integrate these technologies with conventional microbiology, surgical source control, antimicrobial stewardship, and multidisciplinary clinical judgment.

Declarations

Ethics approval and consent to participate: Ethics approval was not required because this review used data from previously published studies and did not involve direct participation of human subjects.

Consent for publication: Not applicable.

Availability of data and materials: All data discussed in this review were derived from published literature. The final database search strategies, screening log, study-extraction sheet, excluded full-text list, and risk-of-bias assessments should be made available as supplementary materials.

Competing interests: The authors declare that they have no competing interests.

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