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ADVANCING PRECISION MEDICINE IN SURGICAL INFECTIONS THROUGH MOLECULAR DIAGNOSTICS, MICROBIOME ANALYSIS, AND ARTIFICIAL INTELLIGENCE: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Surgical infections remain important causes of postoperative morbidity, prolonged hospitalization, reoperation, implant failure, antimicrobial exposure, and increased healthcare expenditure. Conventional microbial culture remains central to diagnosis but may fail after antimicrobial exposure or in infections involving biofilms, low microbial burdens, anaerobes, fastidious organisms, or complex polymicrobial communities. Molecular diagnostics, microbiome analysis, and artificial intelligence provide complementary methods for improving pathogen detection, identifying endogenous sources of infection, predicting risk, and supporting postoperative surveillance.

Objective: This systematic review evaluated the clinical applications, diagnostic contributions, limitations, and future role of molecular diagnostics, microbiome analysis, and artificial intelligence in precision management of surgical infections.

Methods: MEDLINE/PubMed, Embase, Scopus, Web of Science, and the Cochrane Library were searched for studies published from January 2000 through February 2026. Search terms combined surgical-site infection, postoperative infection, implant infection, periprosthetic joint infection, molecular diagnosis, polymerase chain reaction, next-generation sequencing, metagenomics, microbial cell-free DNA, microbiome, machine learning, deep learning, and wound imaging. Primary clinical studies that evaluated these technologies for infection prediction, diagnosis, prevention, surveillance, or treatment guidance were included. Reviews, laboratory-only studies, case reports, non-surgical studies, and reports without clinically relevant outcomes were excluded. Eleven primary studies were included in the qualitative synthesis. Owing to heterogeneity in surgical settings, specimen types, diagnostic platforms, reference standards, and computational outcomes, statistical pooling was not undertaken.

Results: Four studies primarily evaluated molecular detection of established or suspected infection, three investigated perioperative or implant-associated microbial communities, three evaluated artificial-intelligence-assisted postoperative surveillance, and one evaluated sequencing-guided antimicrobial prophylaxis. Broad-range 16S ribosomal RNA polymerase chain reaction identified bacterial DNA in 53 of 97 conventionally culture-negative surgical-site infection specimens, producing an additional detection rate of 54.6%. Sequencing and microbial cell-free DNA increased pathogen identification in selected periprosthetic joint infections but generated uncertainty concerning contamination, organism viability, and clinical significance. In a prospective spinal-fusion cohort, 86% of surgical-site infections were attributable to strains carried by patients before surgery, supporting the importance of endogenous microbial reservoirs. Colorectal microbiome studies demonstrated differences in intraoperative microbial communities before clinical infection developed. Artificial-intelligence systems using wound images and patient-reported outcomes achieved clinically promising discrimination and substantially reduced simulated clinical-review workload. A multicentre wound-image model achieved 94% accuracy for incision recognition and an area under the receiver-operating-characteristic curve of 0.81 for infection detection.

Conclusions: Molecular diagnostics currently provide the clearest clinical contribution in culture-negative, antimicrobial-pretreated, polymicrobial, and implant-associated infections. Microbiome analysis has improved understanding of endogenous infection sources and may eventually support individualized prevention. Artificial intelligence can facilitate remote monitoring, risk stratification, and surveillance but requires external validation, calibration assessment, equitable datasets, and clinical governance. These technologies function best as additions to high-quality specimen collection, conventional culture, histopathology, surgical source control, and antimicrobial stewardship.

KEYWORDS: artificial intelligence; metagenomic sequencing; microbial cell-free DNA; microbiome; molecular diagnostics; precision medicine; surgical-site infection

1. INTRODUCTION

Surgical infections encompass superficial incisional infection, deep incisional infection, organ-space infection, postoperative intra-abdominal sepsis, mediastinitis, prosthetic-joint infection, vascular-graft infection, and other implant-associated infections. These complications may lead to wound breakdown, prolonged antimicrobial therapy, reoperation, removal of implanted material, functional impairment, readmission, and mortality.

Diagnosis has traditionally depended on clinical assessment, inflammatory markers, imaging, microscopy, histopathology, and microbial culture. Culture remains essential because it demonstrates organism viability and permits phenotypic antimicrobial-susceptibility testing. Nevertheless, its diagnostic yield may be reduced by antimicrobial administration before sampling, inadequate specimen quality, low microbial burden, anaerobic or fastidious organisms, biofilm formation, delayed transport, and failure to provide appropriate incubation conditions.

Culture-negative infection creates substantial uncertainty. Patients may receive prolonged empirical broad-spectrum treatment, undergo repeated procedures, or remain untreated for an unexpected pathogen. Conversely, highly sensitive molecular methods may detect microbial nucleic acid originating from contamination, colonization, or non-viable organisms rather than active infection.

Surgical infection also reflects more than the presence of an isolated pathogen. Development of infection depends on the interaction among the patient's microbiota, immune status, comorbidities, antimicrobial exposure, operative technique, tissue perfusion, contamination level, foreign material, and postoperative wound environment.

Precision medicine integrates individual biological and clinical characteristics to guide prevention, diagnosis, and treatment. In surgical infection, this approach includes:

1. direct molecular detection of microbial pathogens;
2. identification of resistance determinants;
3. characterization of endogenous microbial reservoirs;
4. analysis of perioperative microbial communities;
5. integration of operative, clinical, laboratory, and imaging information;
6. computational prediction of infection risk; and
7. individualized antimicrobial and source-control strategies.

Broad-range polymerase chain reaction, multiplex assays, targeted sequencing, metagenomic next-generation sequencing, and microbial cell-free DNA can identify organisms without relying solely on growth in culture. Microbiome analysis evaluates entire microbial communities and may reveal ecological patterns that precede infection. Artificial intelligence can process complex perioperative datasets and support remote postoperative monitoring.

The three approaches address distinct weaknesses of conventional care. Molecular techniques improve pathogen detection, microbiome analysis clarifies infection origin and microbial ecology, and artificial intelligence assists integration of longitudinal multidimensional data. This review examined the evidence supporting their use in surgical infections and evaluated their potential roles within an integrated precision-medicine pathway.

2. METHODS

2.1 Review Design

The review followed the reporting principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement.

2.2 Review Question

The review addressed the following question:

Among patients undergoing surgery or being evaluated for postoperative, surgical-site, or implant-associated infection, how have molecular diagnostics, microbiome analysis, and artificial intelligence been used for infection prevention, prediction, diagnosis, surveillance, or management?

2.3 Eligibility Criteria

Population

Studies involving adults or children were eligible when participants:

- underwent an operative procedure;
- received a surgical implant;
- underwent revision or implant-removal surgery;
- had suspected or confirmed postoperative infection;
- had suspected or confirmed surgical-site infection; or
- participated in postoperative wound-surveillance programmes.

Technologies

Eligible technologies included:

- broad-range bacterial or fungal polymerase chain reaction;
- organism-specific or multiplex polymerase chain reaction;
- 16S or 18S ribosomal RNA sequencing;

- internal transcribed spacer sequencing;
- targeted next-generation sequencing;
- metagenomic next-generation sequencing;
- microbial cell-free DNA sequencing;
- whole-genome comparison of colonizing and infection isolates;
- skin, intestinal, wound, or implant microbiome profiling;
- machine learning;
- deep learning;
- natural-language processing;
- computer vision; and
- multimodal computational models.

Outcomes

Eligible studies reported one or more of the following:

- pathogen-detection yield;
- diagnostic sensitivity or specificity;
- culture–molecular concordance;
- organism detection in culture-negative infection;
- alteration of antimicrobial prophylaxis or treatment;
- association between microbial-community features and infection;
- postoperative infection incidence;
- predictive discrimination;
- external validation;
- remote-monitoring performance; or
- clinical-review workload.

Exclusion Criteria

The review excluded:

- laboratory-only studies without patient-level outcomes;
- animal studies;
- isolated case reports;
- conference abstracts without sufficient data;
- non-surgical infection studies;
- non-clinical algorithm-development reports;
- narrative commentaries; and
- reports without relevant diagnostic, preventive, predictive, or management outcomes.

2.4 Information Sources and Search Period

MEDLINE/PubMed, Embase, Scopus, Web of Science, and the Cochrane Library were searched for literature published from January 2000, through February 2026. Reference lists of eligible articles and relevant evidence reviews were also examined.

2.5 Search Strategy

The searches combined controlled terms and free-text keywords relating to surgery, infection, molecular testing, microbial communities, and computational methods.

The principal search structure was: (“surgical site infection” OR “postoperative infection” OR “surgical infection” OR “wound infection” OR “periprosthetic joint infection” OR “implant-associated infection” OR “organ-space infection”) AND (“molecular diagnosis” OR PCR OR “16S rRNA” OR “next-generation sequencing” OR metagenomics OR “microbial cell-free DNA” OR microbiome OR microbiota OR “artificial intelligence” OR “machine learning” OR “deep learning” OR “computer vision” OR “wound image”).

2.6 Study Selection

Titles and abstracts were screened for relevance to surgical infection and the technologies of interest. Potentially eligible reports underwent full-text assessment. Eligibility was determined according to the predefined population, technology, and outcome criteria.

Eleven primary studies formed the final qualitative evidence set. Systematic reviews and meta-analyses were used to contextualize the findings but were not counted among the primary included studies.

2.7 Data Extraction

The following information was extracted:

- first author;
- publication year;

- country;
- study design;
- surgical specialty;
- clinical population;
- sample size;
- biological specimen or digital data source;
- index technology;
- comparator or reference standard;
- principal result;
- clinical implication; and
- reported limitation.

2.8 Quality Appraisal

Diagnostic studies were appraised according to the QUADAS-2 domains of patient selection, index-test conduct and interpretation, reference-standard validity, and participant flow.

Prediction-model studies were assessed according to PROBAST principles, including:

- participant selection;
- predictor definition;
- outcome determination;
- number of infection events;
- missing-data management;
- class imbalance;
- overfitting;
- data leakage;
- calibration;
- internal validation; and
- external validation.

Randomized evidence was assessed according to randomization, intervention adherence, outcome measurement, missing data, and selective reporting.

2.9 Data Synthesis

The evidence was synthesized narratively because the studies differed substantially in surgical specialty, infection definition, specimen type, molecular target, sequencing method, microbiome pipeline, artificial-intelligence architecture, comparator, and outcome.

The synthesis was organized into:

1. molecular diagnosis of surgical infection;
2. perioperative microbial ecology;
3. artificial-intelligence-assisted prediction and surveillance; and
4. integrated precision-medicine applications.

3. RESULTS

3.1 Study Profile

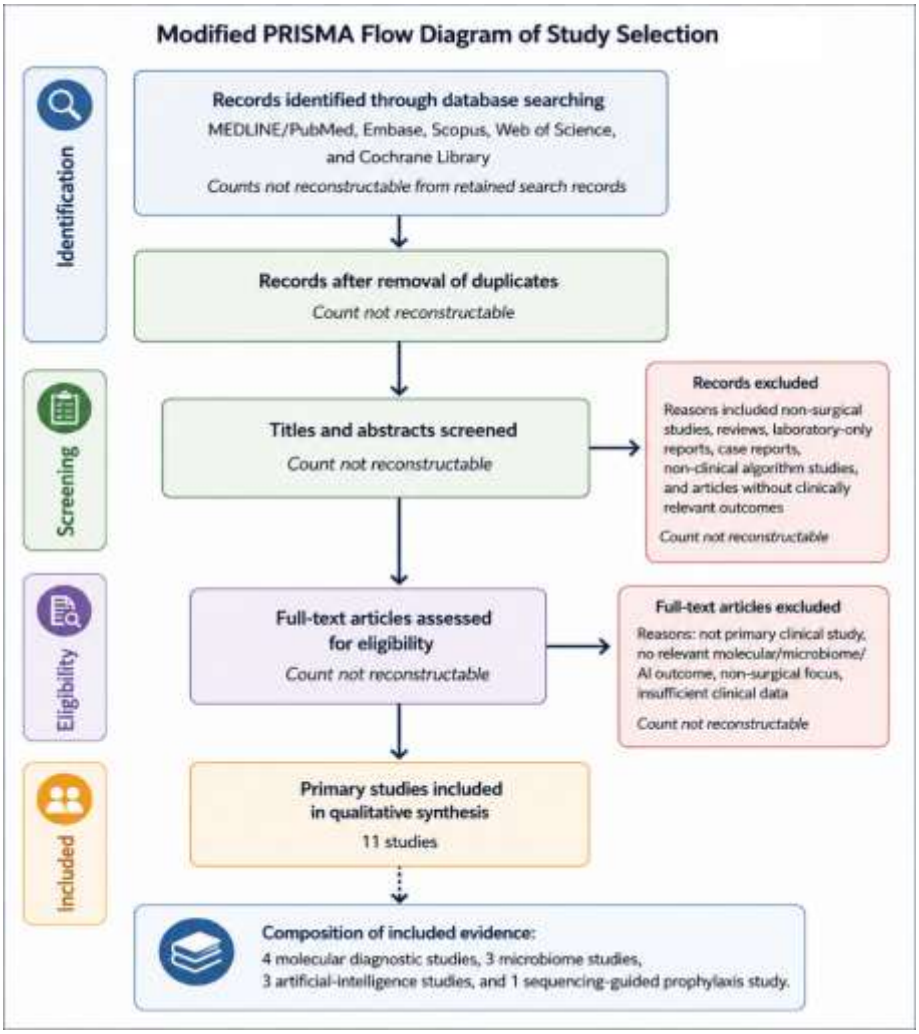
Eleven primary studies published between 2017 and 2026 were included.

The evidence comprised:

- 4 molecular diagnostic studies;
- 3 microbiome studies;
- 3 artificial-intelligence studies; and
- 1 randomized sequencing-guided prophylaxis study.

The surgical settings included:

- periprosthetic and implant-associated infection;
- instrumented spinal surgery;
- colorectal and gastrointestinal surgery;
- urinary-stone surgery;
- implant-based breast reconstruction;
- general postoperative surgical-site infection; and
- remote postoperative wound monitoring.



3.2 Characteristics of Included Studies

Table 1. Characteristics of the 11 included primary studies

Study	Country	Design	Clinical setting	Sample or data volume	Technology	Principal finding
Prieto-Borja et al., 2017	Spain	Diagnostic-accuracy study	Revision surgery for suspected prosthetic-joint infection	Sonication-fluid specimens	Multiplex PCR	Rapidly detected common implant-associated pathogens but could not identify organisms absent from the panel.
Tarabichi et al., 2018	United States	Prospective diagnostic study	Suspected periprosthetic joint infection	86 synovial-fluid specimens	Next-generation sequencing	Identified organisms in culture-positive and selected culture-negative specimens; some detections had uncertain clinical significance.
Behera et al., 2021	India	Prospective observational study	Culture-negative surgical-site infection	97 specimens	Broad-range 16S rRNA PCR and sequencing	Detected bacterial DNA in 53 specimens, corresponding to 54.6%.
Echeverria et al., 2021	United States	Prospective diagnostic study	Periprosthetic joint infection	53 patients	Plasma microbial cell-free DNA sequencing	Demonstrated that DNA from localized implant infection could be detected in peripheral blood.
Vishnoi et al., 2023	Australia	Prospective pilot study	Colorectal surgery	Pilot surgical cohort	Intraoperative 16S rRNA sequencing	Identified differences in microbial-community patterns between patients who developed infection and those who did not.
Liss et al., 2023	United States	Randomized comparative-effectiveness trial	Ureteroscopy and percutaneous stone surgery	Clinical trial cohort	Microbial sequencing-guided prophylaxis	Individualized antimicrobial selection reduced postoperative infectious events.

Long et al., 2024	United States	Prospective genomic cohort	Instrumented spinal fusion	210 patients; 14 developed SSI	Preoperative microbiome sampling and genomic matching	Twelve of 14 infections were caused by strains carried by patients before surgery.
McLean et al., 2025	United Kingdom	Secondary analysis and external validation	Gastrointestinal postoperative monitoring	Patient-generated images and symptom assessments from two studies	Multimodal neural network	Predicted SSI within 48 hours and reduced simulated staff-review time by approximately 80%.
Barnes et al., 2025	United States	Prospective pilot study	Implant-based breast reconstruction	10 patients	Peri-expander 16S rRNA sequencing	Detected microbial DNA around breast implants but did not establish whether all detections represented active infection.
Muaddi et al., 2025	United States	Multicentre development and validation study	Postoperative wound surveillance	More than 20,000 images from more than 6,000 patients	Deep-learning image pipeline	Achieved 94% accuracy for incision recognition and an area under the curve of 0.81 for SSI identification.
Vishnoi et al., 2026	Australia	Prospective cohort	Elective bowel resection	123 patients; 16 developed SSI	Intraoperative 16S rRNA microbiome analysis	Patients who developed SSI had greater intraoperative alpha diversity.

Abbreviations: PCR, polymerase chain reaction; rRNA, ribosomal RNA; SSI, surgical-site infection.

3.3 Molecular Diagnosis of Surgical Infection

3.3.1 Broad-Range Polymerase Chain Reaction

Broad-range bacterial PCR amplified conserved bacterial genomic regions without requiring organism-specific primers. It was particularly useful when conventional culture remained negative despite clinical evidence of infection.

Behera et al. examined 97 culture-negative surgical-site specimens and identified bacterial DNA in 53, representing 54.6% of the study population. The molecular method detected anaerobic, viable-but-nonculturable, and difficult-to-grow organisms that had not been recovered by routine aerobic culture.

The findings demonstrated that culture negativity did not necessarily represent microbiological sterility. However, broad-range PCR could not independently distinguish among active infection, residual DNA from non-viable organisms, environmental contamination, or low-level colonization.

Clinical interpretation depended on:

- specimen depth and sterility;
- adequacy of collection;
- previous antimicrobial treatment;
- organism abundance;
- findings in negative controls;
- histopathological evidence;
- operative findings; and
- clinical response.

3.3.2 Multiplex Polymerase Chain Reaction

Multiplex PCR simultaneously detected a predetermined group of organisms and selected resistance markers. Its main advantages were rapid turnaround and standardized interpretation.

In implant-associated infection, sonication fluid provided a useful specimen because ultrasound released biofilm-associated organisms from removed hardware. Multiplex PCR improved rapid identification when the causal organism was represented on the assay panel. Its major limitation was restricted organism coverage. Off-panel pathogens remained undetected, and a negative panel did not exclude infection. Multiplex PCR therefore functioned as a rapid adjunct rather than an alternative to conventional culture.

3.3.3 Next-Generation Sequencing

Targeted sequencing amplified selected microbial genes, whereas metagenomic sequencing recovered microbial nucleic acid without restricting analysis to predefined organisms.

The technology was most applicable to:

- culture-negative infection;
- previous antimicrobial exposure;
- polymicrobial infection;
- fastidious or unexpected organisms;
- recurrent infection; and

- implant-associated biofilm.

Next-generation sequencing studies in periprosthetic joint infection identified organisms missed by conventional culture. Meta-analytic evidence also indicated high diagnostic performance, although estimates varied according to specimen type, sequencing strategy, contamination control, and reference definition.

Sequencing created interpretive challenges because highly sensitive analysis frequently identified multiple microbial signals. A detected organism was considered more clinically plausible when it was present at substantial abundance, appeared in more than one specimen, was absent from negative controls, and corresponded with clinical, histological, or operative evidence.

3.3.4 Microbial Cell-Free DNA

Microbial cell-free DNA testing identified short fragments of microbial DNA circulating in plasma.

Echeverria et al. demonstrated that pathogen-derived DNA from localized periprosthetic joint infection could be detected in peripheral blood. The approach provided a minimally invasive option when direct sampling was difficult or unsafe.

Potential applications included:

- spinal infection;
- vascular-graft infection;
- deep postoperative collections;
- infection near critical anatomical structures; and
- patients unable to undergo invasive sampling.

The method did not independently establish the anatomical source of infection. A positive plasma result could also reflect microbial translocation or an infection at another site.

3.3.5 Sequencing-Guided Antimicrobial Prophylaxis

Liss et al. evaluated microbial sequencing to guide antimicrobial prophylaxis before urinary-stone procedures. Individualized selection was associated with fewer postoperative infectious events than conventional prophylaxis.

This finding demonstrated that molecular information could influence prevention rather than only diagnosis. The strategy was most relevant when patients had recurrent colonization, previous resistant organisms, repeated healthcare exposure, or recent antimicrobial use.

Molecularly guided prophylaxis remained dependent on careful interpretation. Detection of microbial DNA alone did not justify broader antimicrobial treatment without evidence that the organism was clinically relevant.

3.4 Microbiome Analysis

3.4.1 Endogenous Sources of Infection

The traditional model of surgical-site infection emphasized contamination from instruments, staff, or the operating environment. The included genomic evidence demonstrated that endogenous patient microorganisms accounted for a substantial proportion of infections.

Long et al. prospectively evaluated 210 patients undergoing instrumented spinal fusion. Fourteen developed SSI, and 12 of those infections were linked to strains already carried by the patient before surgery. Overall, 86% of infections originated from endogenous preoperative strains.

The findings shifted attention toward individual microbial reservoirs, including:

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

Endogenous origin did not diminish the importance of operating-room infection prevention. Instead, it demonstrated that universal preventive measures addressed only part of the infection pathway.

3.4.2 Perioperative Microbial-Community Patterns

Microbiome analysis assessed microbial communities rather than isolated pathogens. Relevant features included:

- alpha diversity within a specimen;
- beta diversity between patient groups;
- abundance of opportunistic organisms;
- depletion of protective commensals;
- presence of resistance genes; and
- ecological instability.

In colorectal surgery, intraoperative microbial profiles differed between patients who subsequently developed SSI and those who remained uninfected.

The 2026 bowel-resection cohort included 123 patients, of whom 16 developed SSI. Greater intraoperative alpha diversity was associated with subsequent infection, although overall community separation was less pronounced.

These findings indicated that progression to infection may depend on microbial-community structure and interactions rather than on the presence of one organism alone.

3.4.3 Implant-Associated Microbiomes

Surgical implants provided surfaces for bacterial attachment and biofilm formation. Organisms within biofilms demonstrated altered metabolism, reduced antimicrobial susceptibility, and increased tolerance of immune clearance.

Peri-implant sequencing detected microbial DNA even when conventional culture remained negative. Barnes et al. identified bacterial genera including *Pseudomonas*, *Corynebacterium*, *Acinetobacter*, and *Staphylococcus* in peri-expander fluid after breast reconstruction.

The principal interpretive problem was differentiation among:

- contamination;
- transient colonization;
- clinically silent biofilm;
- active implant infection; and
- residual microbial DNA.

Microbiome findings were most informative when combined with multiple deep specimens, histopathology, imaging, inflammatory evidence, implant stability, and operative findings.

3.5 Artificial Intelligence

3.5.1 Risk Prediction

Machine-learning models incorporated demographic, clinical, laboratory, and operative variables to estimate postoperative infection risk.

Commonly evaluated predictors included:

- age;
- body mass index;
- diabetes;
- smoking;
- anaemia;
- malnutrition;
- immune suppression;
- wound classification;
- emergency surgery;
- operative duration;
- blood loss;
- transfusion;
- implant placement; and
- previous antimicrobial exposure.

Machine-learning models frequently reported promising discrimination. However, earlier image-based SSI studies generally lacked external validation and had substantial risk of bias. A 2024 scoping review identified 10 eligible image-model studies among 715 unique screened records; none had performed external validation, and 9 were considered at high overall risk of bias.

3.5.2 Wound-Image Analysis

Computer-vision systems assessed postoperative photographs for:

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

Muaddi et al. evaluated more than 20,000 patient-submitted images from more than 6,000 patients across nine hospitals. Their two-stage system first recognized the presence of a surgical incision and then estimated infection probability.

The model achieved approximately 94% accuracy for incision recognition and an area under the receiver-operating-characteristic curve of 0.81 for SSI detection.

The lower performance for infection detection reflected the fact that a photograph alone could not capture fever, increasing pain, inflammatory markers, wound depth, or systemic deterioration.

3.5.3 Multimodal Postoperative Surveillance

McLean et al. combined patient-generated wound images with postoperative patient-reported outcomes. The model predicted confirmed SSI within 48 hours with performance comparable to clinician triage.

The multimodal model achieved a performance estimate of 0.762 compared with 0.777 for clinician triage and retained strong performance during external validation. Simulated implementation reduced estimated clinical-review time from 51.5 hours to 9.1 hours, representing an approximate 80% reduction.

The results supported the use of artificial intelligence for triage rather than autonomous diagnosis. The model identified patients requiring prompt review while reducing routine assessment of low-risk submissions.

3.5.4 Automated Surveillance

Artificial-intelligence-assisted surveillance integrated:

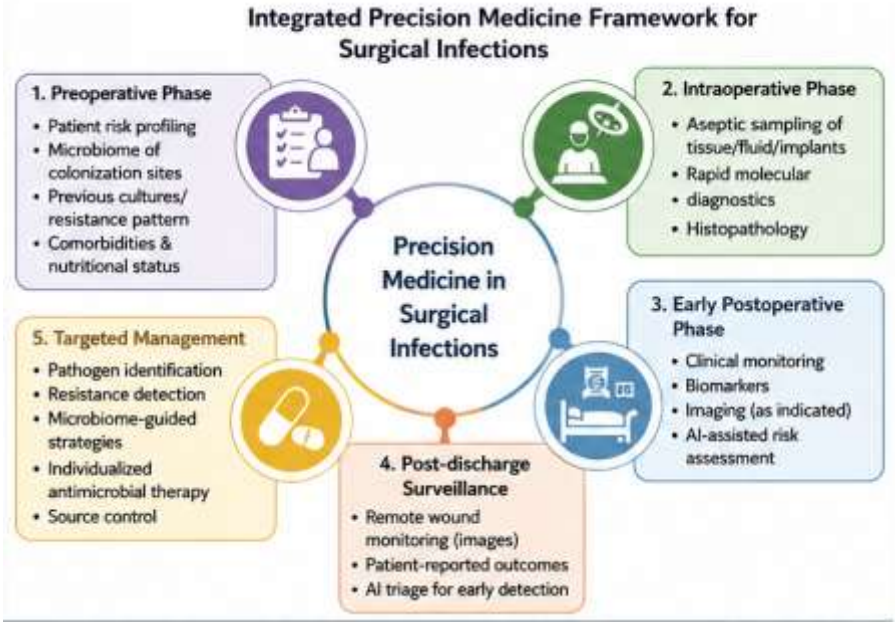
- clinical notes;
- microbiology results;
- antibiotic prescriptions;
- operative reports;
- emergency visits;
- hospital readmissions;
- wound photographs; and
- patient-reported symptoms.

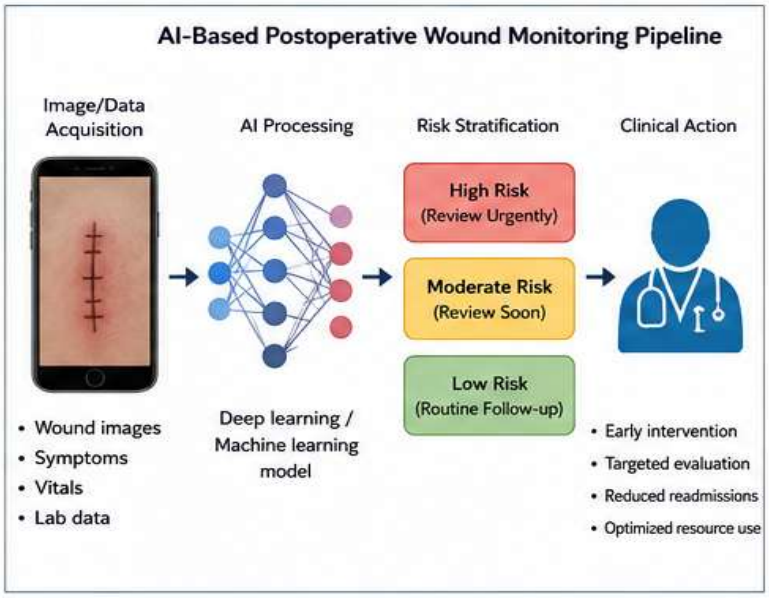
Automated systems improved scalability by prioritizing likely infection cases for expert adjudication. Their validity depended on the quality of the outcome labels used during training. Models trained on inaccurate administrative codes reproduced those inaccuracies.

3.6 Integrated Precision-Medicine Pathway

Table 2. Integrated pathway for precision management of surgical infections

Phase	Information used	Precision-medicine function	Clinical application
Preoperative evaluation	Comorbidities, previous microbiology, colonization, resistance history, procedure type	Individual risk characterization	Optimization, decolonization, and individualized prophylaxis
Intraoperative diagnosis	Deep tissue, fluid, implant sonication, histopathology, culture	Identification of pathogen and anatomical source	Early targeted therapy and source-control planning
Early postoperative period	Vital signs, laboratory trends, wound appearance, operative factors	Recognition of abnormal recovery patterns	Focused reassessment and diagnostic testing
Post-discharge monitoring	Wound images, symptoms, patient-reported recovery	Remote risk stratification	Early clinical review for high-risk patients
Culture-negative infection	Broad-range PCR, targeted sequencing, metagenomics, cell-free DNA	Detection of suppressed or unexpected organisms	Refinement of antimicrobial treatment
Implant-associated infection	Multiple tissue specimens, sonication, sequencing, histopathology	Assessment of biofilm-associated disease	Debridement, revision, retention, or removal planning
Antimicrobial management	Molecular findings, culture, resistance phenotype, organ function, source control	Individualized treatment selection	Spectrum adjustment, dosing, de-escalation, and discontinuation





4. DISCUSSION

4.1 Principal Findings

This review demonstrated that precision surgical-infection care developed through three complementary technological domains.

Molecular diagnostics improved organism detection when conventional culture was negative or incomplete. Microbiome analysis showed that many surgical infections originated from endogenous patient microorganisms and that community-level differences were present before infection became clinically apparent. Artificial intelligence supported postoperative risk assessment, wound surveillance, and remote triage.

The technologies addressed different clinical problems:

- molecular diagnostics addressed failure of pathogen recovery;
- microbiome analysis addressed incomplete understanding of microbial origin and ecology; and
- artificial intelligence addressed the challenge of interpreting large and changing clinical datasets.

4.2 Clinical Position of Molecular Diagnostics

Molecular testing provided the greatest value in selected high-complexity cases rather than as a universal replacement for culture.

The strongest indications included:

- convincing clinical evidence of infection with negative culture;
- previous antimicrobial administration;
- suspected implant-associated biofilm;
- polymicrobial infection;
- recurrent infection;
- suspected fastidious organisms; and
- discordance among clinical, histological, and culture findings.

Broad use in low-risk cases could increase cost and produce clinically irrelevant detections. The clinical benefit depended on whether the result changed antimicrobial or surgical management.

4.3 Interpretation of Highly Sensitive Tests

Increasing analytical sensitivity did not automatically improve diagnostic certainty.

Detection of microbial nucleic acid answered the question of whether microbial material was present. It did not necessarily establish whether the organism was alive, invasive, or responsible for the patient's symptoms.

Interpretation incorporated:

- anatomical plausibility;
- specimen sterility;
- organism abundance;
- concordance across specimens;
- negative-control results;
- histological inflammation;
- operative findings;
- antimicrobial exposure; and
- clinical response.

Reports containing long lists of low-abundance organisms risked encouraging unnecessary broad-spectrum therapy.

4.4 Implications of Endogenous Infection Sources

The finding that 86% of spinal surgical-site infections originated from preoperative patient strains challenged a purely environmental model of infection.

Operating-room precautions, hand hygiene, skin preparation, and sterile technique remained essential. However, these measures did not eliminate infection risk arising from the patient's skin, intestinal tract, or other endogenous reservoirs.

A precision-prevention model incorporated:

- previous microbiological results;
- colonization by resistant organisms;
- procedure-specific microbial reservoirs;
- patient-specific resistance profiles; and
- targeted decolonization or prophylaxis.

Routine whole-microbiome screening remained premature because reproducible clinical thresholds had not been established.

4.5 Role of Artificial Intelligence

Artificial intelligence was most useful as a support and prioritization system.

Remote wound monitoring generated large volumes of images and symptom reports. Manual review of every submission imposed a substantial workload. Multimodal algorithms reduced that burden by identifying high-risk patients for clinician assessment.

The technology did not replace direct examination. Image interpretation remained sensitive to:

- lighting;
- camera quality;
- viewing angle;
- wound location;
- dressings;
- skin pigmentation;
- image compression; and
- variation in clinical labels.

Algorithms required prospective testing in the clinical environments where they were deployed.

4.6 Preservation of Conventional Microbiology

Culture remained indispensable despite advances in molecular detection.

It provided:

- evidence of organism viability;
- phenotypic antimicrobial susceptibility;
- preserved isolates for further analysis;
- outbreak-comparison material;
- confirmation of unexpected molecular results; and
- information about mixed microbial populations.

The strongest diagnostic approach combined conventional culture, histopathology, molecular testing, and clinical assessment rather than treating these methods as competitors.

4.7 Antimicrobial Stewardship

Precision diagnostics created opportunities for earlier targeted treatment and de-escalation. They also created a risk of overtreatment when multiple organisms or resistance genes were detected.

A molecular detection did not automatically justify antimicrobial therapy. Decisions incorporated:

- severity of illness;
- specimen quality;
- anatomical source;
- source-control adequacy;
- organism abundance;
- culture findings;
- phenotype–genotype concordance; and
- expected treatment toxicity.

Genotypic resistance results remained incomplete. Presence of a resistance gene did not always establish phenotypic expression, and absence of a tested gene did not prove susceptibility.

4.8 Implementation and Governance

Implementation required coordinated laboratory, clinical, and computational infrastructure.

Essential components included:

- standardized specimen collection;

- rapid transport;
- contamination-controlled laboratory workflows;
- validated sequencing methods;
- curated databases;
- transparent bioinformatic pipelines;
- clinically meaningful reporting thresholds;
- electronic-health-record integration;
- quality assurance;
- cybersecurity;
- privacy protection;
- antimicrobial-stewardship participation; and
- continuous performance review.

A technically accurate test had limited value when turnaround was slow, interpretation was unclear, or results did not influence management.

4.9 Equity and Generalizability

Microbiome composition varied with geography, diet, antimicrobial exposure, disease burden, and socioeconomic conditions. A microbial signature developed in one population did not necessarily generalize to another.

Artificial-intelligence models also risked unequal performance across:

- skin tones;
- age groups;
- sexes;
- surgical specialties;
- healthcare systems;
- camera devices; and
- geographic populations.

External validation and subgroup reporting were central to equitable implementation.

4.10 Research Priorities

The evidence identified several priorities:

1. prospective multicentre comparisons of molecular platforms;
2. standardized composite diagnostic reference criteria;
3. randomized studies of molecularly guided treatment;
4. standardized contamination-control reporting;
5. clinically interpretable abundance thresholds;
6. longitudinal microbiome sampling before and after surgery;
7. validation of microbiome signatures across populations;
8. prospective testing of artificial-intelligence systems;
9. calibration and decision-curve analysis;
10. comparison with clinician performance;
11. evaluation of antimicrobial-use outcomes;
12. cost-effectiveness studies;
13. patient-centred outcome assessment; and
14. implementation studies in resource-constrained settings.

5. STRENGTHS AND LIMITATIONS

This review integrated molecular diagnostics, microbial ecology, and artificial intelligence within one clinical framework. The approach reflected the multidimensional nature of surgical infection and demonstrated how the technologies addressed different diagnostic and preventive challenges.

The evidence remained heterogeneous. The studies involved different surgical specialties, infection definitions, specimen types, diagnostic platforms, bioinformatic methods, reference standards, and outcomes.

Several microbiome studies were exploratory and involved small cohorts. Molecular studies often included diagnostically difficult or culture-negative cases, limiting generalizability to unselected surgical populations. Artificial-intelligence studies varied in image quality, outcome labelling, external validation, and calibration reporting.

6. CONCLUSION

Precision medicine expanded surgical-infection management beyond conventional culture-based diagnosis.

Molecular methods improved pathogen detection in culture-negative, antimicrobial-pretreated, polymicrobial, and biofilm-associated infections. Microbiome analysis demonstrated that many surgical infections arose from organisms carried by patients before surgery and suggested that microbial-community characteristics may influence postoperative risk. Artificial intelligence supported remote wound monitoring, infection prediction, and surveillance prioritization.

The technologies were complementary rather than interchangeable. Their greatest clinical value emerged when they were integrated with:

- representative specimen collection;
- conventional culture;
- histopathology;
- surgical source control;
- antimicrobial stewardship; and
- multidisciplinary clinical judgment.

Molecular diagnostics had the strongest immediate application in complex and culture-negative infections. Microbiome-based prevention and artificial-intelligence-assisted surveillance remained promising but required standardized methods, prospective validation, equitable datasets, cost-effectiveness evidence, and continuous governance.

An effective precision-care model did not replace clinicians or conventional microbiology. It combined microbial, ecological, clinical, operative, and digital information to deliver more timely and individualized infection care.

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