International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	CURRENT DIAGNOSTIC AND THERAPEUTIC APPROACHES TO PERIPROSTHETIC JOINT INFECTION: A NARRATIVE REVIEW
DOI	https://doi.org/10.31435/ijitss.3(51).2026.6224
RECEIVED	26 May 2026
ACCEPTED	11 August 2026
PUBLISHED	20 August 2026
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CURRENT DIAGNOSTIC AND THERAPEUTIC APPROACHES TO PERIPROSTHETIC JOINT INFECTION: A NARRATIVE REVIEW

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ABSTRACT

Background: Periprosthetic joint infection (PJI) remains one of the most serious complications after total hip and knee arthroplasty. Although its incidence after primary arthroplasty is relatively low, PJI causes major morbidity, repeated surgery, prolonged antimicrobial treatment, impaired function, and substantial healthcare costs. Diagnosis is difficult because clinical findings may be nonspecific, particularly in chronic low-grade infection, and no single test reliably confirms or excludes infection in all clinical settings.
Objective: This narrative review summarizes contemporary diagnostic approaches to PJI and discusses current therapeutic strategies in relation to major definitions, guidelines, and recent evidence.
Methodology: PubMed, Google Scholar, and the Cochrane Library were searched for English-language publications on hip and knee PJI, with emphasis on consensus definitions, diagnostic criteria, synovial biomarkers, microbiological and molecular diagnostics, imaging, surgical treatment, antimicrobial therapy, and suppressive treatment. The search was updated through March 2026.
Results: Current diagnosis relies on multimodal assessment integrating clinical findings, serum inflammatory markers, synovial fluid analysis, microbiology, histopathology, and selected imaging studies. The 2018 ICM/MSIS criteria and the 2021 EBJIS definition remain the most influential frameworks. Treatment is primarily surgical and includes DAIR, one-stage revision, and two-stage revision supported by targeted antimicrobial therapy.
Conclusion: Effective PJI management requires individualized multidisciplinary decision-making. Emerging biomarkers, molecular methods, artificial intelligence, and antibacterial implant technologies are promising but require further validation before routine implementation.

KEYWORDS

Periprosthetic Joint Infection; Arthroplasty; Diagnosis; Synovial Biomarkers; DAIR; Revision Arthroplasty

CITATION

Krzysztof Bednarski, Natalia Kornacka, Bartosz Zawadzki, Jakub Zwardoń, Katarzyna Naja, Miłosz Rewekant, Zuzanna Walczak, Anna Świerczek, Aleksander Gajkowski, Tomasz Adam Szczepanowski. (2026) Current Diagnostic and Therapeutic Approaches to Periprosthetic Joint Infection: a Narrative Review. *International Journal of Innovative Technologies in Social Science*. 3(51). doi: 10.31435/ijitss.3(51).2026.6224

1. Introduction

Total hip and knee arthroplasty are among the most successful interventions in modern orthopaedic surgery. They provide durable pain relief, functional recovery, and quality-of-life improvement for patients with advanced degenerative, inflammatory, or post-traumatic joint disease (Learmonth et al., 2007). As populations age and the number of arthroplasty procedures continues to rise, implant-related complications have become increasingly important for orthopaedic practice, infectious diseases, rehabilitation medicine, and healthcare planning. Among these complications, periprosthetic joint infection (PJI) remains one of the most challenging because it threatens both implant survival and patient well-being (Kapadia et al., 2016; Tande & Patel, 2014).

PJI is commonly understood as infection involving a joint prosthesis and the surrounding periprosthetic tissues. It usually reflects microbial contamination of the implant environment, followed by bacterial adherence to prosthetic or host surfaces and, in many cases, biofilm formation (Sendi & Zimmerli, 2011; Zimmerli et al., 2004). Although reported incidence after primary hip or knee arthroplasty is often approximately 1% to 2%, and higher after revision arthroplasty, the clinical and economic consequences are disproportionally severe (Kapadia et al., 2016; Kurtz et al., 2012). Patients may require repeated operations, prolonged hospitalization, complex antimicrobial therapy, and extended rehabilitation. PJI is also associated with impaired mobility, reduced independence, psychological distress, and increased mortality risk in frail patients (Nelson et al., 2023).

A central feature of PJI pathogenesis is biofilm-mediated persistence. Within a biofilm, microorganisms become embedded in an extracellular matrix, show altered metabolic activity, and demonstrate reduced susceptibility to host immune mechanisms and antimicrobial agents (Zimmerli & Sendi, 2017). This biological

behavior explains why treatment frequently requires a combination of surgical intervention and antimicrobial therapy rather than antibiotics alone. It also explains why delayed diagnosis can compromise the success of implant-retaining strategies and increase the need for complex revision surgery (Osmon et al., 2013; Tande & Patel, 2014).

The clinical diagnosis of PJI is often uncertain. Acute postoperative or hematogenous infection may present with pain, erythema, wound drainage, fever, and local inflammatory signs. In contrast, chronic low-grade infection may manifest only as persistent pain, stiffness, instability, or progressive functional decline, thereby mimicking aseptic loosening, mechanical failure, or inflammatory arthropathy (Kapadia et al., 2016; Tande & Patel, 2014). No single laboratory, microbiological, histopathological, or imaging test is sufficiently accurate across all clinical scenarios. Consequently, modern diagnosis relies on integrated criteria that combine several findings within structured diagnostic frameworks, particularly the 2018 International Consensus Meeting/Musculoskeletal Infection Society (ICM/MSIS) criteria and the 2021 European Bone and Joint Infection Society (EBJIS) definition (McNally et al., 2021; Parvizi et al., 2018).

Management is equally complex. Debridement, antibiotics, and implant retention (DAIR), one-stage revision, and two-stage revision all have a role, but none is universally appropriate. The choice of strategy depends on symptom duration, infection chronicity, implant stability, soft-tissue quality, bone stock, pathogen profile, antimicrobial susceptibility, surgical risk, and patient expectations (Osmon et al., 2013). In selected patients who are not candidates for curative surgery, suppressive antimicrobial therapy may be considered, but this approach remains noncurative and must be balanced against toxicity, resistance, and long-term uncertainty (Aboltins et al., 2025; Harrabi et al., 2025).

The objective of this review article is to provide a clinically oriented overview of current diagnostic and therapeutic approaches to PJI after hip and knee arthroplasty. The review focuses on contemporary definitions, guideline-based diagnostic work-up, serum and synovial biomarkers, microbiological and molecular diagnostics, imaging, surgical strategies, antimicrobial treatment, suppressive therapy, and emerging directions relevant to future practice.

2. Methodology

This manuscript was designed as a narrative review. A narrative approach was selected because the aim was to synthesize clinically relevant evidence, definitions, and guideline recommendations rather than to answer a narrowly framed quantitative question suitable for meta-analysis. The review focused on PJI after total hip and knee arthroplasty, as these procedures account for the largest proportion of clinically relevant lower-limb arthroplasty infections and are the main focus of most diagnostic definitions and treatment algorithms. The intended audience includes clinicians involved in arthroplasty care and researchers interested in diagnostic standardization, treatment selection, and emerging technologies.

A literature search was conducted in PubMed, Google Scholar, and the Cochrane Library. The search was updated through March 2026. Search terms included: "periprosthetic joint infection," "prosthetic joint infection," "PJI diagnosis," "PJI treatment," "EBJIS definition," "ICM criteria," "MSIS criteria," "alpha-defensin," "calprotectin," "leukocyte esterase," "DAIR," "one-stage revision," "two-stage revision," "biofilm," "molecular diagnostics," "next-generation sequencing," and "suppressive antibiotic therapy." Boolean combinations of these terms were used when appropriate, and reference lists of key reviews, consensus documents, and guidelines were checked to identify additional relevant publications.

Priority was given to consensus definitions, clinical practice guidelines, systematic reviews, meta-analyses, randomized trials, prospective cohort studies, and large retrospective clinical series. Earlier landmark publications were retained when they remained foundational for understanding PJI pathogenesis, diagnostic criteria, biofilm biology, or antimicrobial treatment. Publications were considered eligible when they were written in English and addressed diagnosis, classification, microbiology, imaging, surgical management, antimicrobial therapy, or emerging technologies relevant to hip or knee PJI. Case reports, small case series with limited generalizability, papers focused exclusively on primary prophylaxis, and publications without sufficient methodological or clinical relevance were not prioritized.

The selected literature was reviewed qualitatively. Extracted information included diagnostic definitions, laboratory and synovial thresholds, clinical indications for surgical strategies, antimicrobial principles, limitations of emerging diagnostic tools, and areas of uncertainty. Because this is a narrative review, no formal PRISMA flow diagram, registration protocol, or structured risk-of-bias assessment was performed. The synthesis therefore emphasizes clinical interpretation, consistency with contemporary standards of care, and practical relevance for multidisciplinary decision-making. To improve transparency, the manuscript distinguishes established diagnostic and treatment standards from emerging or investigational approaches. This limitation is acknowledged in the Discussion.

3. Results

The literature supports a multimodal and individualized approach to PJI. Contemporary practice is shaped by standardized diagnostic definitions, increasing use of synovial biomarkers, improved microbiological techniques, cautious adoption of molecular methods, and a more nuanced view of surgical strategy. The following subsections summarize the main findings of the narrative synthesis.

3.1 Definition and classification of periprosthetic joint infection

A consistent definition of PJI is essential for clinical care, research comparability, and communication between specialists. Historically, variation in definitions made it difficult to compare treatment success, diagnostic accuracy, and epidemiological data across studies. Modern frameworks have improved this problem by defining major and minor diagnostic components and by recognizing that some cases are clinically equivocal rather than clearly infected or noninfected (McNally et al., 2021; Parvizi et al., 2018).

The 2018 ICM/MSIS criteria use major criteria and a weighted minor-criteria scoring system. Major criteria include a sinus tract communicating with the prosthesis or two positive cultures with phenotypically identical organisms. Minor criteria incorporate serum markers, synovial leukocyte count, polymorphonuclear neutrophil percentage, synovial biomarkers, intraoperative findings, histopathology, and culture results. A cumulative score of 6 or more indicates infection, whereas intermediate scores may require further intraoperative evidence (Parvizi et al., 2018). The strength of this framework is its structured and reproducible format, which is useful for both research and clinical decision-making.

The EBJIS definition introduced a three-level model: infection unlikely, infection likely, and infection confirmed (McNally et al., 2021). This model reflects the reality that diagnosis is often probabilistic. It is particularly helpful in chronic low-grade infection, culture-negative cases, and patients with borderline synovial or serum findings. The EBJIS definition also supports clinical judgment by allowing clinicians to identify patients in whom infection cannot yet be confirmed but should remain a central diagnostic concern. Table 1 summarizes key differences between these two frameworks.

PJI may also be classified according to timing and clinical course. Traditional categories include early, delayed, and late infection. In practical decision-making, however, the distinction between acute postoperative infection, acute hematogenous infection, and chronic infection is often more informative because it directly influences eligibility for DAIR and the likelihood of successful implant retention (Osmon et al., 2013; Tande & Patel, 2014). Acute infections with a stable implant and short symptom duration may be managed with implant retention, whereas chronic infection usually requires component exchange.

Table 1. Key contemporary diagnostic frameworks for periprosthetic joint infection.

Framework	Diagnostic logic	Key strengths	Important limitations
2018 ICM/MSIS criteria	Major criteria plus a weighted minor-criteria score integrating serum, synovial, microbiological, histopathological, and intraoperative findings.	Structured scoring; widely used in research and clinical practice; supports reproducibility.	Borderline cases may remain difficult; performance varies with chronic low-grade infection, prior antibiotics, and local test availability.
2021 EBJIS definition	Three-level model: infection unlikely, infection likely, and infection confirmed.	Clinically pragmatic; useful for equivocal cases; avoids an overly binary interpretation.	Requires careful clinical interpretation and may be less straightforward for studies needing a single dichotomous endpoint.

Note. DAIR = debridement, antibiotics, and implant retention; EBJIS = European Bone and Joint Infection Society; ICM/MSIS = International Consensus Meeting/Musculoskeletal Infection Society; PJI = periprosthetic joint infection.

3.2 Etiopathogenesis and risk factors

The etiopathogenesis of PJI reflects interactions between microorganisms, implant surfaces, host immunity, soft tissues, and surgical factors. Most infections are believed to result from perioperative contamination, although hematogenous seeding can occur at any time after implantation. Less commonly, infection may spread from adjacent tissues (Kapadia et al., 2016; Tande & Patel, 2014). The implanted prosthesis provides a surface that facilitates microbial adherence, and once bacteria establish a biofilm, eradication becomes substantially more difficult (Sendi & Zimmerli, 2011; Zimmerli & Sendi, 2017).

Gram-positive organisms remain the most common pathogens. Staphylococcus aureus and coagulase-negative staphylococci, particularly Staphylococcus epidermidis, are especially important because of their capacity to adhere to biomaterials and form biofilm (Tande & Patel, 2014; Zimmerli et al., 2004). Streptococci, enterococci, Gram-negative bacilli, anaerobes, polymicrobial infections, and multidrug-resistant organisms also occur and may complicate treatment selection. Low-virulence organisms may produce subtle clinical symptoms but persistent implant-associated infection, while highly virulent organisms more commonly cause acute inflammatory presentations (Kapadia et al., 2016).

Risk factors can be grouped into host-related, surgical, and implant-related categories. Host-related risk factors include obesity, diabetes mellitus, inflammatory arthropathy, malnutrition, smoking, immunosuppression, renal disease, poor skin condition, previous surgery at the same site, and multiple comorbidities (Kapadia et al., 2016; Tande & Patel, 2014). Surgical risk factors include prolonged operative time, wound complications, hematoma, poor soft-tissue envelope, inadequate debridement, and revision surgery. These factors are clinically important because they influence both infection risk and treatment success. A patient with chronic infection, compromised soft tissues, and multiple comorbidities may require a different strategy than a medically fit patient with an acute postoperative infection and a stable implant.

3.3 Clinical presentation and diagnostic suspicion

Clinical presentation varies widely. Pain is the most common symptom and may be the only manifestation in chronic low-grade infection (Kapadia et al., 2016). Patients may also report stiffness, instability, reduced range of motion, declining walking tolerance, or difficulty bearing weight. These symptoms are nonspecific, which explains why chronic PJI may be misinterpreted as aseptic loosening, polyethylene wear, instability, fracture, or unexplained postoperative pain.

Acute postoperative infection and acute hematogenous infection usually present more dramatically. Findings may include erythema, warmth, swelling, wound drainage, tenderness, fever, and elevated serum inflammatory markers. Acute hematogenous infection may occur after a symptom-free interval and may follow bacteremia from dental, urinary, skin, respiratory, or gastrointestinal sources, although the source is not always identified (Osmon et al., 2013; Tande & Patel, 2014). A sinus tract communicating with the prosthesis is highly specific and is recognized as a major diagnostic criterion in contemporary frameworks (McNally et al., 2021; Parvizi et al., 2018).

The distinction between acute and chronic infection is not merely descriptive. It guides treatment selection. DAIR is most appropriate when symptoms are short in duration, the implant is stable, modular components can be exchanged, the soft-tissue envelope is acceptable, and the pathogen is susceptible to effective antimicrobial therapy (Osmon et al., 2013). Chronic infection is less suitable for implant retention because mature biofilm, implant loosening, and prolonged microbial persistence decrease the probability of cure.

3.4 Diagnostic work-up

The diagnostic work-up should begin with clinical assessment, review of surgical history, symptom duration, wound status, risk factors, and previous antimicrobial exposure. Initial plain radiographs are useful to evaluate implant position, loosening, osteolysis, fracture, and bone loss, but radiographic findings are neither sensitive nor specific for infection (Hoveidaei et al., 2024). The AAOS guideline also supports a structured diagnostic approach using inflammatory markers, aspiration, and synovial analysis in suspected PJI (American Academy of Orthopaedic Surgeons, 2019). When PJI is suspected, serum inflammatory markers are commonly used as first-line screening tests. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) remain widely available and clinically useful, especially in acute infection, but both can be normal in chronic low-grade infection and elevated in noninfectious inflammatory states (Zmistowski et al., 2014).

Joint aspiration is a critical diagnostic step when suspicion persists. Ideally, synovial fluid should be obtained before antimicrobial therapy is started, provided the patient is clinically stable. Synovial leukocyte

count and polymorphonuclear neutrophil percentage are among the most informative preoperative tests and are incorporated into both ICM/MSIS and EBJIS-based approaches (McNally et al., 2021; Parvizi et al., 2018). Interpretation should account for the type of joint, timing after surgery, inflammatory disease, metallosis, fracture, recent surgery, and bloody aspirates.

Rapid synovial tests may improve clinical decision-making. Leukocyte esterase is inexpensive and quick, but blood contamination can interfere with interpretation (Wetters et al., 2012). Alpha-defensin has shown high diagnostic accuracy and may be less affected by prior antibiotic exposure than conventional culture, although cost and availability may limit routine use (Deirmengian et al., 2015). Calprotectin has emerged as another promising synovial biomarker, with recent meta-analytic evidence suggesting favorable diagnostic performance and potential point-of-care utility (Festa et al., 2024). However, thresholds, assay methods, and real-world implementation remain incompletely standardized.

D-dimer was incorporated into the 2018 ICM/MSIS criteria, but later studies have shown inconsistent diagnostic performance (Maritati et al., 2025; Parvizi et al., 2018). Therefore, it should not be interpreted in isolation. In general, serum and synovial biomarkers are best used as components of a broader diagnostic framework rather than as stand-alone tests. A negative biomarker result does not completely exclude infection in a high-risk clinical scenario, and a positive result may require confirmation through microbiology, histopathology, or intraoperative assessment.

3.5 Microbiological, histopathological, and molecular diagnostics

Microbiological confirmation is central because it enables targeted antimicrobial therapy. Preoperative aspiration cultures and intraoperative tissue cultures remain standard methods. At surgery, multiple tissue samples should be taken from representative periprosthetic sites using separate instruments to reduce contamination and increase diagnostic yield (Osmon et al., 2013; Zmistowski et al., 2014). Sampling after antibiotics have been given may reduce culture sensitivity, although antibiotics should not be delayed in unstable patients.

Conventional culture has important limitations. Biofilm-associated organisms may be present at low metabolic activity or low burden, and prior antimicrobial therapy can reduce recovery. Culture-negative PJI therefore remains a significant clinical problem (Tande & Patel, 2014). Sonication of removed implants can improve diagnostic yield by dislodging microorganisms from the prosthetic surface and is particularly useful in chronic infection or previously treated cases (Trampuz et al., 2007). Nevertheless, sonication requires appropriate laboratory infrastructure and standardized interpretation.

Histopathology provides complementary evidence, especially when cultures are negative or equivocal. Acute neutrophilic inflammation in periprosthetic tissue supports infection and is incorporated into diagnostic frameworks (Parvizi et al., 2018; Zmistowski et al., 2014). Histopathology can be particularly valuable during revision surgery when preoperative tests are borderline. However, frozen-section and permanent-section interpretation can vary according to sampling site, threshold definition, and local pathology expertise.

Molecular diagnostics, including broad-range polymerase chain reaction and next-generation sequencing, are increasingly studied. These tools may improve pathogen detection in culture-negative infection, polymicrobial infection, or infection with fastidious organisms (Tarabichi et al., 2018). They may also be useful after prior antibiotics. However, limitations are substantial: contamination can produce false-positive results, DNA from nonviable organisms may be detected, and clinically irrelevant signals can be difficult to interpret (Maritati et al., 2025). At present, molecular techniques should be viewed as adjunctive tools rather than replacements for culture, histopathology, and clinical assessment.

3.6 Imaging

Imaging has a supportive role in PJI diagnosis. Plain radiographs should usually be obtained first because they are accessible and helpful for assessing loosening, osteolysis, periosteal reaction, component migration, fracture, and bone loss. However, radiographic abnormalities are often late and nonspecific, and normal radiographs do not exclude infection (Hoveidaei et al., 2024).

Ultrasonography may identify joint effusion, superficial collections, sinus tracts, or soft-tissue abnormalities and can guide aspiration. Computed tomography can assist in evaluating bone loss, abscesses, and complex anatomy, although metal artifacts may limit interpretation. Magnetic resonance imaging with metal artifact reduction sequences has improved evaluation of soft tissues, collections, sinus tracts, and marrow changes in selected cases (Hoveidaei et al., 2024).

Nuclear medicine techniques are most relevant when conventional evaluation remains inconclusive. Labeled leukocyte scintigraphy, especially when combined with bone marrow imaging and interpreted in experienced centers, can help distinguish infection from aseptic loosening (Signore et al., 2019). FDG-PET/CT and SPECT/CT are also studied, but specificity may be reduced by sterile inflammation, recent surgery, foreign-body reaction, and postoperative remodeling (Hoveidaei et al., 2024; Signore et al., 2019). Therefore, imaging results should be integrated with clinical, laboratory, synovial, microbiological, and histological findings.

3.7 Standards of surgical treatment

Surgery remains the cornerstone of curative PJI management. Antimicrobial therapy is essential but usually cannot eradicate established biofilm infection without appropriate surgical source control (Osmon et al., 2013; Zimmerli & Sendi, 2017). The main surgical strategies are DAIR, one-stage revision, and two-stage revision. The optimal approach should be individualized and ideally discussed by a multidisciplinary team including orthopaedic surgeons, infectious disease specialists, microbiologists, radiologists, and pathologists.

DAIR is generally considered for acute postoperative or acute hematogenous infection when the implant is stable, soft tissues are acceptable, symptoms are short in duration, and the pathogen is susceptible to effective antimicrobial therapy (Osmon et al., 2013). Thorough debridement, irrigation, exchange of modular components, and adequate sampling are important technical elements. DAIR success depends on early intervention, organism virulence, biofilm maturity, host factors, and surgical quality. Staphylococcus aureus infection, delayed debridement, poor soft tissues, sinus tract, and retained modular components are commonly associated with worse outcomes.

One-stage revision involves removal of all components, extensive debridement, and immediate reimplantation during the same operation. Potential advantages include fewer operations, reduced hospitalization, faster functional recovery, lower overall burden, and potentially lower cost in selected patients (Gehrke et al., 2013). Evidence increasingly supports one-stage revision in carefully selected cases, particularly when the pathogen is known, soft tissues are adequate, bone loss is manageable, and effective antimicrobial therapy is available. The INFORM trial found that single-stage revision was not superior to two-stage revision for patient-reported outcomes at 18 months in hip PJI, but it had advantages in cost effectiveness and some early outcomes (INFORM Trial Group et al., 2022). These findings support patient selection rather than universal adoption.

Two-stage revision remains widely used, especially for chronic infection, uncertain microbiology, resistant or difficult-to-treat organisms, extensive bone or soft-tissue compromise, and failed previous treatment (Osmon et al., 2013). The first stage includes implant removal, extensive debridement, and commonly placement of an antibiotic-loaded spacer, followed by systemic antimicrobial therapy and delayed reimplantation. Two-stage revision can be effective, but it imposes substantial morbidity, repeated hospitalization, prolonged rehabilitation, and risk of spacer-related complications. Recent systematic review evidence suggests that single-stage and two-stage revision can achieve comparable results in selected populations, although heterogeneity and selection bias remain important limitations (Zhao et al., 2024). Contemporary evidence therefore supports moving away from a rigid hierarchy in which two-stage revision is considered the only standard for chronic PJI. Instead, surgical strategy should be matched to infection characteristics, host risk, local expertise, and patient goals. Table 2 summarizes the principal treatment strategies.

Table 2. Main surgical and antimicrobial strategies in periprosthetic joint infection.

Strategy	Typical role	Potential advantages	Main limitations
DAIR	Selected acute postoperative or acute hematogenous infection with stable implant and short symptom duration.	Implant preservation; lower surgical burden; faster recovery when successful.	Lower success in chronic infection, mature biofilm, delayed presentation, unstable implants, poor soft tissues, or difficult pathogens.
One-stage revision	Selected chronic infections with known pathogen, good soft tissue, manageable bone loss, and available effective antibiotics.	Single operation; faster rehabilitation; lower treatment burden and potential cost advantages.	Requires strict selection and experienced teams; not suitable for uncontrolled sepsis, severe soft-tissue compromise, or uncertain microbiology.
Two-stage revision	Complex chronic infection, uncertain pathogen, resistant organisms, major bone or soft-tissue compromise, or failed prior treatment.	Established option for difficult cases; allows interval therapy and delayed reconstruction.	High morbidity; repeated operations; long rehabilitation; spacer complications; not always feasible in frail patients.
Suppressive antimicrobial therapy	Noncurative option when surgery is not possible, declined, or unlikely to succeed.	May reduce symptoms and delay progression in selected patients.	Does not eradicate infection; long-term toxicity, resistance, adherence issues, and uncertain optimal duration.

Note. Treatment selection should be individualized according to infection chronicity, implant stability, host status, pathogen profile, soft-tissue condition, bone loss, and local expertise.

3.8 Targeted antimicrobial therapy and suppressive treatment

Antimicrobial therapy should be guided by microbiological diagnosis whenever possible. Cultures should be obtained before antibiotics are started in clinically stable patients, because premature antimicrobial exposure may reduce diagnostic yield (Osmon et al., 2013). Empirical therapy may be necessary in patients with systemic illness, sepsis, or rapidly progressive infection, but treatment should be narrowed once culture and susceptibility data are available.

Drug selection should consider pathogen susceptibility, oral bioavailability, bone and joint penetration, interaction profile, toxicity, renal and hepatic function, and biofilm activity. Rifampicin-containing combinations are often considered in staphylococcal implant-retaining strategies because rifampicin has activity against biofilm-associated staphylococci, although it should not be used as monotherapy because of rapid resistance development (Zimmerli & Sendi, 2017). Gram-negative infections require pathogen-specific therapy based on susceptibility and host factors. The duration of therapy depends on surgical strategy, pathogen, host risk, and clinical response.

The route of antimicrobial therapy has evolved. Historically, prolonged intravenous therapy was common, but evidence from complex bone and joint infection supports early transition to highly bioavailable oral therapy in appropriately selected patients (Li et al., 2019). This does not mean that all PJI patients should receive short or oral-only treatment. Rather, it supports individualized treatment plans that consider stability, source control, organism susceptibility, absorption, adherence, and follow-up capacity.

Suppressive antimicrobial therapy may be considered when curative surgery is not feasible, declined by the patient, or unlikely to succeed because of severe comorbidity, limited reconstruction options, poor soft tissues, or high surgical risk (Aboltins et al., 2025; Harrabi et al., 2025). It is generally a noncurative strategy aimed at symptom control, prevention of progression, and preservation of function. Contemporary literature highlights potential benefit in carefully selected patients, but uncertainties remain regarding patient selection, drug choice, dose, monitoring, duration, resistance, and endpoint definitions. SAT should therefore be presented as a pragmatic option for selected noncurative scenarios rather than a substitute for surgical source control.

3.9 Emerging directions

Research in PJI increasingly focuses on earlier diagnosis, improved pathogen detection, individualized risk stratification, and prevention of biofilm persistence. Synovial biomarkers remain a major area of development. Alpha-defensin, leukocyte esterase, and calprotectin can increase diagnostic confidence, particularly when standard tests are borderline (Deirmengian et al., 2015; Festa et al., 2024; Wetters et al., 2012). Wider implementation will require standardized cut-off values, cost-effectiveness data, and clearer pathways for interpretation in inflammatory disease, early postoperative settings, metallosis, and culture-negative cases.

Molecular diagnostics may become increasingly important in culture-negative and polymicrobial infection. Next-generation sequencing can detect organisms missed by standard culture, but it also generates interpretive challenges, especially when microbial DNA is present at low levels or when contamination is possible (Maritati et al., 2025; Tarabichi et al., 2018). Future studies should clarify how molecular results should influence antimicrobial selection, surgical decision-making, and outcome prediction.

Artificial intelligence and machine learning are being explored for PJI risk prediction, diagnostic integration, and pathology interpretation. Early studies suggest that AI tools may help integrate clinical, laboratory, imaging, and histopathological data, and AI-assisted pathology has shown promising performance in experimental and early translational settings (Tao et al., 2024; Vulpe et al., 2025). At present, these approaches remain investigational. Before routine adoption, they require external validation, transparency, integration into clinical workflows, and evidence that they improve outcomes beyond expert multidisciplinary assessment.

Therapeutic innovation also includes improved local antimicrobial delivery, antibacterial implant coatings, surface modifications that reduce bacterial adhesion, and materials designed to interfere with biofilm formation (Kapadia et al., 2016). These technologies are promising, but they should be described cautiously. Demonstrating antimicrobial activity in vitro or in early translational studies does not necessarily prove clinical benefit in complex revision arthroplasty. High-quality prospective trials and registry-based evaluations are needed to determine whether these innovations reduce infection recurrence, improve implant survival, or lower treatment burden.

3.10 Practical diagnostic and management pathway

In routine practice, the diagnostic pathway should be staged rather than fragmented. A patient with a painful arthroplasty should first undergo careful history taking, examination, review of operative records, and plain radiography. Particular attention should be paid to the timing of symptoms, history of wound problems, prior antibiotic exposure, comorbidities, dental or urinary infections, bacteremia, and previous revision procedures. If clinical suspicion persists, serum CRP and ESR are useful screening tests, but normal values should not end the investigation when symptoms, risk factors, or radiographic changes remain concerning (Osmon et al., 2013; Zmistowski et al., 2014).

The next step is usually aspiration for synovial leukocyte count, neutrophil percentage, culture, and selected biomarkers. Synovial tests should be interpreted according to the clinical context. For example, early postoperative inflammation, inflammatory arthropathy, fracture, metallosis, and blood contamination may complicate interpretation. If aspiration is dry or inconclusive, repeat aspiration, image-guided aspiration, or intraoperative sampling may be necessary. When revision surgery is performed, multiple tissue cultures, histopathology, and, where appropriate, sonication of removed components can increase diagnostic confidence (Trampuz et al., 2007).

Therapeutic planning should begin at the time infection is suspected, but definitive antimicrobial treatment should ideally follow appropriate sampling. The first clinical decision is whether the goal is curative or suppressive. In a medically fit patient with reconstructable bone and soft tissues, curative treatment is usually pursued. In a frail patient with severe comorbidity, unacceptable surgical risk, or limited reconstructive options, suppressive therapy or palliative symptom control may be more appropriate. This distinction should be discussed openly with the patient because the expected outcomes, burdens, and risks differ substantially.

For curative strategies, the key surgical question is whether implant retention is realistic. Acute infection with short symptom duration, a stable prosthesis, acceptable soft tissues, and an available biofilm-active antimicrobial regimen may justify DAIR. Chronic infection, loosening, sinus tract, severe soft-tissue compromise, or failed previous DAIR usually shifts the balance toward component exchange. One-stage revision should be considered when pathogen identification, susceptibility profile, soft-tissue quality, and

surgical expertise support immediate reimplantation. Two-stage revision remains important when infection is complex, microbiology is uncertain, or local reconstruction is difficult.

Follow-up should assess both infection control and patient-centered recovery. Traditional outcomes such as recurrence, reoperation, reimplantation success, and culture results remain important, but they do not fully describe the burden of PJI. Functional recovery, pain, mobility, adverse drug effects, psychological stress, and ability to return to daily activities should also be monitored. Follow-up schedules should be individualized but should include clinical assessment, inflammatory markers when clinically indicated, adverse-effect monitoring during antimicrobial therapy, and reassessment of function, particularly after revision surgery. Future research should use standardized definitions of treatment success that combine infection eradication with meaningful patient outcomes.

Patient communication is also an essential part of the pathway. Individuals with PJI often face several difficult choices, including implant retention versus revision, one-stage versus two-stage exchange, curative surgery versus suppression, and the risk of complications against the possibility of improved function. Shared decision-making should therefore include a clear explanation of expected treatment duration, probability of recurrence, need for further operations, antimicrobial adverse effects, rehabilitation burden, and realistic functional goals. This is especially important for older patients, patients with multiple comorbidities, and those whose social circumstances may limit adherence to prolonged therapy or follow-up. Clear documentation of these discussions may also improve continuity between surgical, infectious disease, rehabilitation, and primary care teams, particularly when care is delivered across several institutions or outpatient settings, after discharge and during long-term follow-up.

4. Discussion

This review highlights that PJI remains a diagnostic and therapeutic challenge because it is rarely defined by a single finding. Diagnosis is best understood as a structured probability assessment based on clinical presentation, serum inflammation, synovial analysis, microbiology, histopathology, and imaging. The 2018 ICM/MSIS criteria and the 2021 EBJIS definition have improved consistency, but neither eliminates the need for expert interpretation (McNally et al., 2021; Parvizi et al., 2018). The ICM/MSIS score is especially useful when a binary research definition is needed, whereas the EBJIS framework is clinically attractive because it recognizes intermediate probability states.

Synovial fluid analysis remains one of the most valuable parts of the diagnostic pathway. Leukocyte count and neutrophil percentage retain a central role, and rapid biomarkers may improve diagnostic confidence in selected situations (Deirmengian et al., 2015; Festa et al., 2024; Zmistowski et al., 2014). However, the enthusiasm for biomarkers must be balanced against real-world constraints. Thresholds may differ between acute and chronic infection, hip and knee arthroplasty, early and late postoperative periods, and patients with inflammatory or crystal arthropathy. A biomarker should therefore support, rather than replace, clinical reasoning.

Culture-negative infection remains a major problem. Sonication and molecular diagnostics can increase microbiological yield, but both require careful interpretation (Trampuz et al., 2007). Molecular methods are particularly attractive because they may identify pathogens after prior antibiotic exposure or in fastidious infection. Nevertheless, the detection of microbial DNA is not equivalent to proof of viable infection, and contamination can lead to overtreatment (Maritati et al., 2025). Future diagnostic pathways should define when molecular tests are indicated, how results should be weighted within existing criteria, and how they should influence antimicrobial choice.

Surgical decision-making has become more individualized. DAIR remains appropriate in selected acute cases, but success depends on early recognition, adequate debridement, modular component exchange, stable implants, and effective antimicrobial therapy. One-stage revision is increasingly recognized as a valid option in selected chronic infections, particularly in experienced centers with strong microbiological and reconstructive support (Gehrke et al., 2013; INFORM Trial Group et al., 2022). Two-stage revision remains important for complex cases, but it should not be presented as the only acceptable treatment for all chronic PJI. This shift reflects a broader movement from fixed algorithms toward patient-centered, risk-adapted management.

Antimicrobial management should also be individualized. The OVIVA trial supports early oral therapy in selected bone and joint infections, but translating this finding to PJI requires careful consideration of surgical strategy, pathogen susceptibility, biofilm activity, drug interactions, and adherence (Li et al., 2019). Suppressive therapy has a growing role in frail or surgically unsuitable patients, but it should be framed as a

noncurative approach with uncertain optimal parameters (Aboltins et al., 2025; Harrabi et al., 2025). Stewardship is essential because prolonged antimicrobial exposure may cause toxicity, select resistance, and complicate future treatment.

The main implication for clinical practice is that PJI should be managed by multidisciplinary teams. Orthopaedic surgeons provide source control and reconstruction, infectious disease specialists guide antimicrobial therapy, microbiologists optimize organism detection, pathologists support histological diagnosis, and radiologists assist in selected complex cases. Such collaboration is especially important in culture-negative infection, recurrent PJI, resistant organisms, and frail hosts. Multidisciplinary decision-making also improves communication with patients, who must understand the trade-offs between eradication, function, surgical burden, and long-term risk.

This review has limitations. It is a narrative review rather than a systematic review, and no formal risk-of-bias assessment, meta-analysis, or PRISMA-based selection process was performed. The synthesis may therefore be influenced by publication selection and author interpretation. However, the review emphasizes major guidelines, consensus definitions, landmark studies, randomized evidence where available, and recent reviews relevant to clinical practice. Future research should prioritize prospective comparative studies, standardized outcome definitions, better reporting of host and pathogen factors, and long-term patient-centered outcomes.

5. Conclusions

Periprosthetic joint infection remains one of the most difficult complications of hip and knee arthroplasty. Diagnosis should not rely on a single test but on a multimodal assessment integrating clinical findings, serum inflammatory markers, synovial analysis, microbiology, histopathology, and selected imaging modalities. The 2018 ICM/MSIS criteria and the 2021 EBJIS definition provide the principal contemporary diagnostic frameworks and should be used alongside clinical judgment.

Treatment requires individualized planning. DAIR, one-stage revision, and two-stage revision each have a role, and the optimal choice depends on infection chronicity, implant stability, soft-tissue status, bone loss, pathogen profile, host factors, and patient goals. Targeted antimicrobial therapy is essential, particularly in biofilm-associated infection, and suppressive therapy may be reasonable in selected noncurative scenarios. Emerging biomarkers, molecular diagnostics, artificial intelligence, and antibacterial implant technologies may improve future care, but broader implementation should be guided by high-quality prospective evidence and multidisciplinary expertise.

Funding: This research received no external funding.

Ethics approval: Not applicable. This narrative review did not involve human participants, human data, animals, or biological material requiring ethics committee approval.

Conflicts of interest: No conflicts of interest to declare.

Author contributions:

Conceptualization: Krzysztof Bednarski and Natalia Kornacka. Methodology: Krzysztof Bednarski, Validation: Bartosz Zawadzki, Jakub Zwardoń. Formal analysis: Katarzyna Naja, Tomasz Adam Szczepanowski. Investigation: Miłosz Rewekant and Zuzanna Walczak. Resources: Bartosz Zawadzki. Data curation: Krzysztof Bednarski, Writing - original draft preparation: Natalia Kornacka. Writing - review and editing: Krzysztof Bednarski and Anna Świerczek. Supervision: Natalia Kornacka and Aleksander Gajkowski. Project administration: Krzysztof Bednarski. All authors have read and approved the final manuscript.

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