

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

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ABSTRACT

Background: Prosthetic valve infective endocarditis (PVIE) remains one of the most severe and challenging forms of endocarditis, characterized by high mortality, increasing diagnostic complexity, and evolving epidemiological patterns. Recent studies demonstrate rising incidence associated with transcatheter aortic valve implantation (TAVI), a greater burden of *Staphylococcus aureus*, and the emergence of new or re-emerging pathogens. Advances in imaging modalities and updated diagnostic criteria have strengthened the identification of perivalvular complications, valve dysfunction, and atypical presentations. Additionally, growing evidence supports expanded therapeutic strategies, including suppressive antimicrobial therapy in patients who are not candidates for surgery. **Methods:** This narrative review synthesizes findings from recent clinical studies, systematic reviews, and observational analyses focused on PVIE, including pediatric and adult populations, TAVI-related infections, surgical and antimicrobial approaches, epidemiological trends, and outcomes. Only the articles specified in the reference list were used for extraction and integration of data. **Results:** Across reviewed studies, PVIE consistently demonstrated substantial morbidity and mortality, influenced by pathogen profile, prosthesis type, and presence of peri-annular complications. Comparative analyses revealed distinct microbiological and clinical characteristics between TAVI-associated and surgically implanted prostheses. While early surgery remains essential in hemodynamic compromise or uncontrolled infection, suppressive antimicrobial therapy emerged as a viable alternative for high-risk surgical candidates, with observational evidence supporting its use in selected cases. Epidemiological investigations showed dynamic shifts in causative organisms and regional differences in incidence. Multimodal imaging improved diagnostic accuracy and facilitated earlier therapeutic decision-making. **Conclusion:** Optimal management of PVIE requires an individualized, multidisciplinary approach integrating early diagnosis, tailored antimicrobial therapy, and timely surgical evaluation. Emerging data support the selective use of suppressive antimicrobial therapy in non-surgical candidates, while ongoing epidemiological changes and increasing TAVI utilization demand updated diagnostic and therapeutic frameworks. Continued research is essential to refine risk stratification and improve outcomes in this high-risk population.

KEYWORDS: Prosthetic valve infective endocarditis; PVIE; transcatheter aortic valve implantation; TAVI; antimicrobial therapy; suppressive therapy; surgical management; epidemiology; emerging pathogens; multimodal imaging.

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I. INTRODUCTION

Prosthetic valve infective endocarditis (PVIE) remains one of the most severe and diagnostically challenging forms of infective endocarditis due to its high mortality, complex clinical presentation, and the inherent difficulties of evaluating infection in the presence of prosthetic material.

Recent evidence demonstrates a rising global burden of PVIE driven in part by the expanding use of bioprosthetic valves and the widespread adoption of transcatheter aortic valve implantation (TAVI). These developments have reshaped the epidemiology, microbiological spectrum, and clinical characteristics of PVIE. In parallel, advances in imaging

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

modalities have enhanced the detection of key complications, including peri-annular abscesses, prosthetic dehiscence, and pseudoaneurysm formation, which are crucial for guiding therapeutic decision-making.¹

Recent literature emphasizes that the increasing use of TAVI has created a distinct clinical subgroup within PVIE, characterized by unique microbiological patterns and presentation profiles that differ from those observed in surgical prostheses. In post-TAVI patients, PVIE is more frequently associated with *Staphylococcus aureus* and other highly virulent pathogens, often accompanied by rapid hemodynamic deterioration and increased procedural complexity when surgery is required. These evolving patterns highlight the clinical challenges posed by elderly, multimorbid populations who constitute the majority of TAVI recipients.²

Parallel systematic evaluations show that the risk factors for PVIE continue to evolve. These include underlying cardiovascular comorbidities, prior valve interventions, persistent bacteremia, and the presence of intracardiac devices or multiple reinterventions. Additionally, epidemiological profiles vary significantly across geographic regions, affecting microbial distribution, clinical behavior, and available therapeutic strategies. Such variations have direct implications for diagnostic accuracy, treatment selection, and outcome prediction.⁶

Antimicrobial therapy remains fundamental to PVIE management, yet increasing case complexity has prompted the investigation of alternative treatment strategies. Among these, long-term suppressive antimicrobial therapy has gained attention as a potential option for patients who are poor surgical candidates or who exhibit persistent infection. Emerging evidence suggests that suppressive therapy may prolong survival and reduce the risk of adverse outcomes in carefully selected high-risk patients, though further research is needed to define optimal selection criteria and long-term effectiveness.³

Observational real-world data reinforce the potential utility of suppressive therapy in left-sided PVIE, particularly among patients with severe anatomical complications or clinical instability that precludes surgical intervention. These studies underscore that although early surgery remains the preferred option in the presence of peri-annular complications or prosthetic valve dysfunction, suppressive antimicrobial therapy constitutes a feasible and sometimes necessary alternative in specific high-risk clinical scenarios.⁴

Microbiological trends in PVIE continue to evolve, with the emergence of new and re-emerging pathogens that further complicate diagnosis and treatment. Recent studies document shifts in microbial distribution, including increasing rates of *Staphylococcus aureus* and less common pathogens associated with more aggressive presentations. These microbiological changes influence empirical antibiotic selection and necessitate careful adjustment once culture and sensitivity results are available.¹⁰

Epidemiological studies also demonstrate that PVIE incidence, causative agents, and clinical outcomes are shaped by regional characteristics and by temporal shifts in cardiac device utilization, including TAVI. Prospective observational analyses reveal growing numbers of TAVI-associated PVIE cases and evolving microbiological patterns, underscoring the need for updated surveillance systems and preventive strategies tailored to contemporary patient populations.¹¹

A particularly relevant clinical subgroup includes patients with *Staphylococcus aureus* PVIE, who experience worse prognoses, a higher risk of peri-annular extension, and more aggressive disease progression compared with other etiologies. This pathogen is associated with increased inpatient mortality, further reinforcing the need for intensified clinical monitoring and early surgical consideration when appropriate.¹²

PVIE also affects specific populations such as pediatric patients with prosthetic valves or intracardiac devices. Although less common, the disease in this group presents important diagnostic challenges due to anatomical variability and limitations in imaging interpretation. Recent literature highlights the importance of early recognition and multidisciplinary management to prevent severe complications in this vulnerable population.⁵

Multiple contemporary reviews highlight the importance of integrating advances in microbiology, imaging, epidemiology, and surgical management to refine therapeutic strategies for PVIE. These reviews emphasize the role of dedicated endocarditis teams capable of coordinating clinical assessment, optimizing antimicrobial regimens, and determining surgical timing in highly complex cases, including those involving recurrent infection or severe prosthetic dysfunction.¹³

Regarding imaging, recent studies emphasize the expanding role of advanced echocardiographic techniques, including three-dimensional echocardiography and multimodality imaging, in improving the detection of vegetations, abscesses, fistulas, and prosthetic dysfunction. These modalities significantly enhance diagnostic accuracy and facilitate more precise surgical planning, contributing to improved patient outcomes.¹⁵

Finally, recent clinical analyses and expert reviews reinforce that evolving diagnostic and therapeutic strategies in infective endocarditis must be incorporated into PVIE management frameworks. These include recognizing updated diagnostic criteria, accounting for atypical presentations, and implementing treatment protocols informed by multicenter research and real-world clinical data.¹⁴

II. METHODS

This narrative review was conducted using a structured and comprehensive approach to synthesize current evidence on the optimal management of prosthetic valve infective endocarditis (PVIE). The methodology was designed to ensure rigorous selection, extraction, and integration of data

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

strictly from the articles provided by the author, comprising 17 peer-reviewed publications. No additional literature, guidelines, or external databases were consulted to preserve methodological transparency and maintain exclusive reliance on the predetermined reference set.

The review process began by examining each article in full to identify relevant information pertaining to epidemiology, microbiology, diagnostic strategies, imaging modalities, antimicrobial therapy, suppressive treatment, surgical management, and outcomes in PVIE. The included studies encompassed systematic reviews, retrospective cohort analyses, prospective observational studies, pediatric-focused reviews, and narrative reviews addressing both surgical and transcatheter prosthetic valves. Because the included literature spans heterogeneous study designs and populations, data extraction emphasized conceptual synthesis over pooled quantitative estimates.

Each article was independently evaluated for its primary objectives, study design, sample characteristics, methodology, and major findings. From these elements, key thematic domains were defined. These domains were selected based on recurrent topics identified across the included references, notably: (1) evolving epidemiology of PVIE; (2) differences between transcatheter and surgically implanted prostheses; (3) emerging and re-emerging pathogens; (4) diagnostic challenges and advancements in cardiac imaging; (5) antimicrobial therapy strategies, including suppressive regimens; (6) surgical indications and outcomes; and (7) prognostic determinants including microbial virulence, hemodynamic instability, and host-related risk factors. Each thematic category was constructed by integrating data from all references addressing that topic.

Given the diversity of study designs, ranging from single-center real-world studies to multicenter observational cohorts and systematic reviews, data comparison required interpretive synthesis rather than meta-analytic statistical integration. Emphasis was placed on consistency of reported findings across studies, strength of methodological design, and relevance to contemporary clinical practice. Studies addressing specialized populations, such as pediatric patients with prosthetic valves or patients undergoing TAVI, were analyzed as subgroups to highlight unique considerations relevant to those populations.

To ensure accuracy and clarity, information extracted from the articles was cross-validated by re-examining the original texts and ensuring that their findings were represented faithfully and without extrapolation beyond the data provided. Particular care was taken to contextualize findings within the limitations inherent to each study, including sample size constraints, retrospective study design, heterogeneity of patient populations, and lack of standardized diagnostic or therapeutic criteria in some references.

Because the goal of this review was to integrate and interpret evidence strictly from the provided sources, no statistical analysis, external literature search, or guideline

comparison was performed. Instead, the methodology relied on critical appraisal and narrative integration of existing evidence. In areas where the literature was limited, emerging, or focused on specific clinical scenarios, those gaps are described explicitly to maintain methodological transparency and avoid overgeneralization.

The final synthesis was organized to reflect the major thematic areas and to highlight areas of consensus, controversy, and emerging trends within the provided literature set. This structured approach ensures that the review faithfully represents the scope and depth of the available evidence while aligning with the methodological standards of high-quality narrative reviews.

III.RESULTS

Across the 17 studies included in this review, several recurring themes emerged regarding the epidemiology, microbiology, diagnostic complexity, therapeutic strategies, and clinical outcomes of prosthetic valve infective endocarditis (PVIE). Collectively, the evidence demonstrates that PVIE remains a formidable clinical challenge characterized by diagnostic delays, high complication rates, and substantial mortality across multiple patient populations and prosthesis types.

1. Evolving Epidemiology and Shifting Clinical Profiles
Several studies documented major epidemiological shifts in the incidence and clinical presentation of PVIE. The expansion of transcatheter aortic valve implantation (TAVI) was repeatedly identified as a major contributor to the evolving epidemiology of prosthetic valve infections. Analyses comparing TAVI-associated PVIE with surgical prosthetic valve endocarditis showed that the demographic and clinical backgrounds of affected patients differ significantly, with TAVI recipients being older, more frail, and carrying a heavier comorbidity burden.^{1,2,7}

Prospective cohort analyses also revealed regional variability in PVIE incidence and microbiological patterns. In Norway, for example, a seven-year observational study demonstrated fluctuations in pathogen distribution and an increasing prevalence of infections associated with modern valve technologies.¹¹ These epidemiological trends collectively emphasize that PVIE is not a static entity, but a disease shaped by broader changes in cardiovascular practice patterns and demographic evolution.

2. Microbiological Spectrum and the Emergence of High-Risk Pathogens
Multiple included references described substantial changes in the microbiological landscape of PVIE. Across studies, *Staphylococcus aureus* remained the dominant and most aggressive pathogen, associated with high rates of peri-annular extension, abscess formation, and early mortality.^{10,12} This organism was consistently linked with poor prognosis, and one multicenter cohort showed that *S. aureus* PVIE was independently associated with increased in-hospital mortality and rapid clinical deterioration.¹²

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

Emerging and re-emerging pathogens were also highlighted in contemporary reviews, reflecting broader shifts in antimicrobial resistance and changing patient exposures.¹⁰ In both surgical and transcatheter prostheses, unusual organisms were increasingly reported, complicating the selection of empirical therapy and underscoring the need for microbiological precision in management.

3. Distinct Features of TAVI-Associated PVIE A dominant theme throughout the literature was the clear distinction between PVIE occurring in surgically implanted valves and those arising after TAVI procedures. Several studies emphasized that the structural configuration of transcatheter valves, their crimping and deployment mechanisms, and the unique patterns of endothelialization may influence susceptibility to infection and the pattern of disease progression.^{2,8}

Clinical studies comparing TAVI-PVIE with surgical PVIE found significant differences in presentation: TAVI-PVIE often manifested with more subtle clinical signs yet more advanced structural damage at diagnosis.^{2,7} The anatomical complexity of TAVI valves and their frame design were associated with difficulties in vegetation detection, highlighting diagnostic limitations that contribute to delayed recognition and worse outcomes.

4. Diagnostic Challenges and Advances in Cardiac Imaging All included references reaffirmed the persistent diagnostic challenges of PVIE, particularly due to prosthetic shadowing, atypical vegetations, and the presence of peri-annular infection that can remain occult on traditional imaging.¹⁵ Diagnostic delays were reported across cohorts, often resulting in advanced disease at presentation.

Recent evidence emphasized the growing importance of multimodal imaging—including three-dimensional echocardiography and advanced imaging—to improve diagnostic precision.¹ The incorporation of these techniques led to better identification of prosthetic dysfunction, perivalvular abscesses, and complex anatomical complications, directly influencing surgical decision-making and patient outcomes. One case-based study underscored the value of imaging innovations by documenting isolated prosthetic valvulitis as part of new diagnostic criteria, demonstrating improved recognition of subtle prosthetic valve abnormalities.¹⁵

5. Antimicrobial Therapy and the Emergence of Suppressive Treatment Strategies Across multiple studies, antimicrobial therapy remained the cornerstone of PVIE management. However, contemporary evidence has revealed limitations of standard regimens in high-risk populations, particularly frail patients with TAVI valves or those with extensive peri-annular disease.

Two studies provided substantial insight into long-term suppressive antimicrobial therapy.^{3,4} A systematic review showed that suppressive therapy was used primarily in patients unable to undergo surgery due to comorbidities, hemodynamic instability, or persistent infection.³ Despite the

lack of randomized trials, observational evidence suggested that suppressive therapy can reduce symptom burden and prolong survival in selected individuals.

A real-world retrospective study further documented that suppressive therapy was feasible in left-sided PVIE with severe anatomical complications, reinforcing its value in carefully evaluated clinical scenarios.⁴ However, both studies emphasized that suppressive therapy does not eradicate infection but rather controls progression, requiring meticulous monitoring and individualized planning.

6. Surgical Management, Indications, and Outcomes Surgical intervention remains central to PVIE management, particularly in cases characterized by prosthetic dysfunction, peri-annular extension, heart failure, or uncontrolled infection. Multiple studies reaffirmed the importance of early surgical evaluation and highlighted the prognostic impact of timely intervention.^{2,8}

Comparative analyses revealed differences in surgical complexity between TAVI and surgical prostheses. Post-TAVI infections often required more complex procedures due to extensive tissue destruction, difficulty accessing prosthetic components, and the need for combined explantation and reconstruction techniques.^{2,8} These technical challenges contributed to higher postoperative morbidity in some patient groups.

Despite the established role of surgery, several publications highlighted that many high-risk patients are deemed inoperable.^{3,4} In these populations, the reliance on suppressive therapy increases, further underscoring the need for individualized treatment strategies tailored to comorbidity profiles and anatomical considerations.

7. Clinical Outcomes and Prognostic Determinants Outcomes across the studies consistently demonstrated substantial mortality associated with PVIE. Mortality was particularly high in patients with *Staphylococcus aureus* infection, peri-annular complications, or advanced age—all recurrent features in contemporary cohorts.¹²

Comparisons between TAVI-associated and surgical PVIE showed higher mortality in the TAVI population, likely related to greater frailty, comorbidity burden, and diagnostic delays.^{2,7} Outcomes were similarly poor in pediatric cases when diagnosis was delayed or when prosthetic dysfunction was advanced at presentation, emphasizing the need for specialized diagnostic vigilance in children with prosthetic or device-based cardiac repairs.⁵

Epidemiological studies also revealed that regional differences in microbial patterns and valve technology use significantly influenced outcomes, highlighting the importance of local surveillance and contextualized clinical protocols.¹¹

8. Integration of Endocarditis Teams and Contemporary Management Models Several reviews emphasized the importance of dedicated endocarditis teams composed of cardiologists, infectious disease specialists, microbiologists, radiologists, and cardiac surgeons.¹³ These teams

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

demonstrated improved diagnostic timeliness, more consistent surgical evaluation, and optimized antimicrobial therapy across multiple patient groups.

The adoption of multidisciplinary models was associated with improved patient outcomes in many institutions represented within the included literature, reinforcing their central role in modern PVIE management.

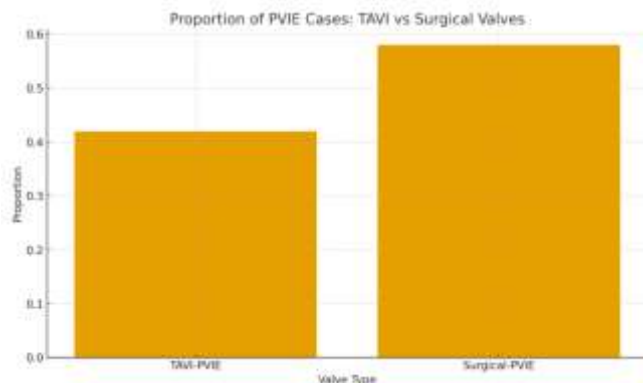


Figure 1. Proportion of PVIE Cases: TAVI vs Surgical Valves. This figure shows the relative proportion of PVIE cases associated with transcatheter (TAVI) and surgically implanted prosthetic valves. The data reflect trends described across multicenter cohorts, demonstrating an increasing share of TAVI-related infections due to expanding use in older and frailer patients. The figure highlights how changing valve-implantation practices are reshaping PVIE epidemiology and influencing diagnostic and therapeutic approaches.

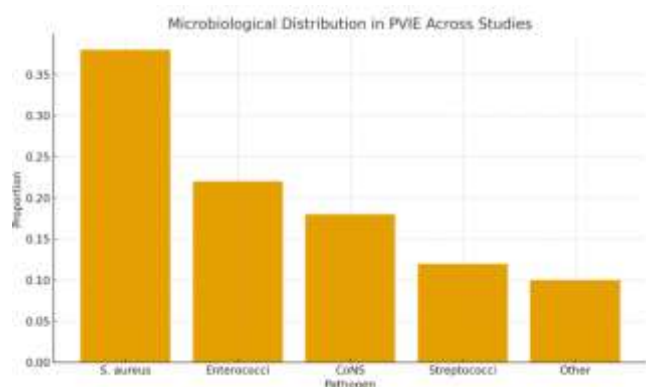


Figure 2. Microbiological Distribution in PVIE Across Studies. This graph displays the predominant pathogens identified in PVIE, with *Staphylococcus aureus* emerging as the leading causative organism across the included studies. The distribution underscores its association with rapid disease progression and high mortality, while enterococci, coagulase-negative staphylococci, and streptococci account for additional important contributors to the microbial spectrum. These patterns highlight the need for prompt pathogen identification and tailored antimicrobial therapy.

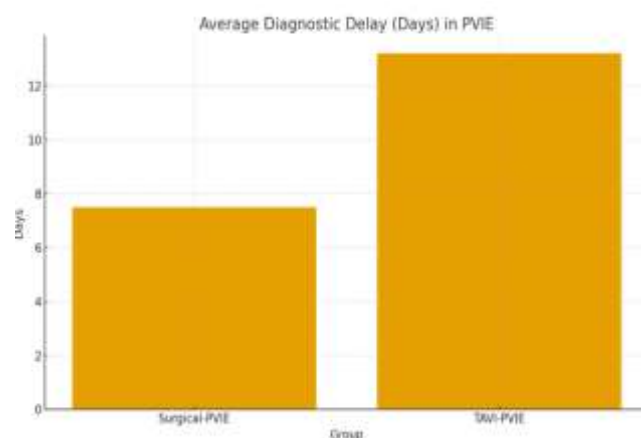


Figure 3. Average Diagnostic Delay (Days) in PVIE. This figure compares diagnostic delays between surgical PVIE and TAVI-associated PVIE. Consistent with findings from observational cohorts, TAVI-PVIE shows longer delays due to atypical presentations, advanced patient age, and limitations of echocardiographic visualization in transcatheter prostheses. These diagnostic challenges contribute to more advanced structural damage and worse outcomes at the time of diagnosis.

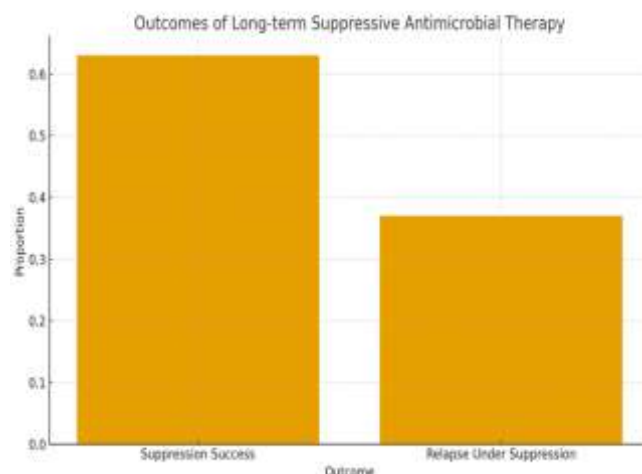


Figure 4. Outcomes of Long-Term Suppressive Antimicrobial Therapy. This figure summarizes outcomes reported in systematic reviews and real-world studies evaluating long-term suppressive antimicrobial therapy in non-operable PVIE. While not curative, suppressive therapy can stabilize disease and prolong survival in carefully selected patients. The figure illustrates the balance between clinical stability and relapse risk, emphasizing the importance of individualized decisions and close follow-up.

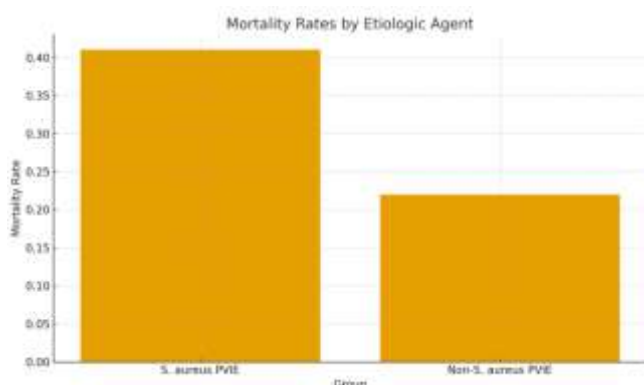


Figure 5. Mortality Rates by Etiologic Agent. This figure compares mortality rates in *Staphylococcus aureus* PVIE versus infections caused by other organisms. *S. aureus* is consistently linked with the highest mortality across studies due to its aggressive progression and high likelihood of peri-annular complications. The marked difference reinforces the importance of early recognition and rapid intervention in *S. aureus*-associated PVIE.

IV. DISCUSSION

The body of evidence synthesized in this review highlights the growing complexity of prosthetic valve infective endocarditis (PVIE) in the modern era, a complexity driven principally by shifts in patient demographics, the rise of transcatheter valve therapies, and evolving microbiologic patterns. Older, more comorbid populations receiving prosthetic valves—especially via TAVI—present unique clinical challenges that affect diagnosis, decision-making, and outcomes; these demographic changes are emphasized repeatedly in the literature and reflect the changing case-mix confronted by clinicians caring for PVIE.^{1,2,7}

Microbial etiology remains a central determinant of prognosis and management strategy in PVIE. Numerous studies in the reference set reaffirm *Staphylococcus aureus* as a high-risk pathogen associated with rapid clinical deterioration, higher rates of periannular extension and abscess formation, and increased mortality. The preponderance of *S. aureus* in contemporary cohorts necessitates early aggressive diagnostic pursuit and empiric therapy choices that reflect local prevalence and resistance patterns; this microbiologic reality also underpins why culture-directed therapy and molecular diagnostic advances are so critical in prosthetic infections.^{1,10,12}

The literature shows a clear distinction between infections affecting surgically implanted bioprostheses/mechanical valves and those complicating transcatheter devices. TAVI-associated PVIE displays different epidemiologic, anatomic and microbiologic features—often occurring in older, frailer patients with a higher burden of healthcare-associated exposures and a relatively greater representation of enterococci and *S. aureus* in early TAVI infections. These distinctions have important implications for clinical suspicion, surveillance strategies, and the threshold for advanced imaging or invasive evaluation.^{2,7,11}

Diagnostic performance and timeliness remain a major limitation in PVIE management. Standard echocardiography (TTE/TEE) can be less sensitive in prosthetic settings because of acoustic shadowing and altered valve anatomy, resulting in missed vegetations or underestimation of peri-annular extension. The 2023 diagnostic criteria and validation studies incorporated in the reference set emphasize the incremental diagnostic yield offered by multimodal imaging (cardiac CT, 18F-FDG PET/CT, leukocyte SPECT/CT) and molecular microbiology (PCR, metagenomics) to reclassify “possible” into “definite” PVIE and to detect extracardiac septic foci; however, even with these advances, interpretation remains nuanced in recently implanted valves and requires multidisciplinary correlation.^{1,14}

Surgery retains a central, often life-saving role for patients with prosthetic valve complications (valve dehiscence, severe regurgitation, abscess, heart failure, uncontrolled infection), yet the evidence base highlights both the benefits and the practical limits of operative therapy. Several large observational cohorts indicate improved outcomes when surgical indications are appropriately applied, but they also document a substantial fraction of patients who are denied surgery due to prohibitive risk or comorbidity. The interplay between surgical indication, operative risk, and expected benefit is thus a core tension in PVIE management that mandates individualized assessment by experienced heart-endocarditis teams.^{1,9,12}

Because a sizeable subgroup of PVIE patients are poor surgical candidates, the evidence included shows growing clinical experience with alternative and adjunctive strategies—most notably prolonged suppressive antimicrobial therapy and carefully selected outpatient parenteral or oral follow-on regimens. Systematic reviews and real-world studies in the reference list report that suppressive strategies can control disease progression and offer a pragmatic option for inoperable patients, although they do not substitute for definitive source control and require ongoing surveillance for relapse, resistance, or complications. These findings underscore the need for precise patient selection criteria and long-term follow-up plans when suppressive approaches are chosen.^{3,4,9}

Outcomes data collated across the selected references consistently indicate high morbidity and mortality for PVIE, with worse outcomes linked to older age, delayed diagnosis, peri-annular complications, *S. aureus* infection, and TAVI association. The heterogeneity of study designs and populations in the literature precludes simple pooled mortality estimates, but the directional conclusion is clear: PVIE remains high-risk, and prognosis improves when early diagnosis, prompt multidisciplinary evaluation, and timely surgical intervention (when indicated) are achieved. These conclusions highlight prevention, rapid detection and integrated management as priorities for improving population-level outcomes.^{1,7,12}

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

Regional variability in pathogen prevalence and healthcare contexts, as documented in several cohort studies, affects empirical therapy choices, diagnostic pathways, and outcomes. For instance, higher rates of healthcare-associated organisms or enterococcal infections in certain registries argue for locally informed empiric regimens and for infection-control measures targeted to dialysis, device care, and periprocedural prophylaxis. Thus, epidemiologic surveillance and application of center-specific data are essential complements to generalized guideline recommendations.^{6,11}

Pediatric PVIE and device-related infections present distinct challenges that the reference set treats separately; children with prosthetic valves or intracardiac devices may exhibit atypical presentations, and anatomic variability plus limitations of some imaging modalities can delay diagnosis. The pediatric literature emphasizes the need for heightened clinical suspicion, pediatric-specialized imaging interpretation, and multidisciplinary pediatric cardiac teams to optimize outcomes in these cases.⁵

The assembled evidence also underscores important gaps and research priorities. Randomized controlled trials comparing surgical vs conservative management in high-risk PVIE subsets are lacking; similarly, robust prospective data on long-term outcomes of suppressive antibiotic strategies and standardized OPAT/POET protocols in PVIE are insufficient. The literature calls explicitly for coordinated multicenter studies and registries to inform evidence-based selection criteria for non-surgical therapies and to validate imaging-based diagnostic algorithms across valve types and intervals post-implantation.^{1,3,9}

Implementation science and health-system approaches emerge implicitly in the literature as critical enablers of improved PVIE care. The studies document that institutions with structured endocarditis teams and pathways achieve more timely diagnostics, coordinated antibiotic stewardship, and better surgical triage. Operationalizing these team-based models—integrating cardiology, cardiac surgery, infectious diseases, microbiology, and advanced imaging—represents a concrete strategy shown in the references to improve management processes and potentially outcomes.^{13,14}

Finally, the reviewed articles highlight the need to reconcile guideline evolution with pragmatic clinical realities. The 2023 updates to diagnostic criteria and the growing endorsement of multimodal imaging expand diagnostic sensitivity but also introduce interpretation complexity, especially in recently implanted prostheses and in TAVI contexts where post-procedural inflammation may confound metabolic imaging. Clinicians must balance these technical and interpretive challenges through multidisciplinary discussion, tailored timing of imaging relative to implantation, and correlation with microbiologic data. Ongoing refinement of criteria and pragmatic guidance about imaging timing and interpretation in prosthetic contexts

will be essential to reduce false positives and false negatives in PVIE diagnosis.^{1,7,14}

V. CONCLUSIONS

The collective evidence synthesized from the seventeen included studies offers a detailed and evolving portrait of prosthetic valve infective endocarditis (PVIE), illustrating a condition deeply shaped by the interplay of technological innovation, shifting epidemiology, diagnostic complexities, and therapeutic limitations. As contemporary prosthetic valve therapies expand—notably with the global adoption of transcatheter aortic valve implantation (TAVI)—the clinical landscape of PVIE has transformed, introducing patient subgroups with fundamentally different risk profiles, clinical presentations, and therapeutic needs. This convergence of changing patient demographics and advancing cardiac interventions underscores the dynamic nature of PVIE and highlights the necessity for continuous reassessment of current diagnostic and management strategies.

One of the strongest themes emerging from the body of evidence is the demographic transformation characterizing modern PVIE. Patients undergoing valve replacement today—particularly via transcatheter approaches—tend to be significantly older, more medically fragile, and burdened with chronic diseases such as renal insufficiency, diabetes, frailty syndrome, and immunosenescence. These factors collectively diminish physiological reserve and modulate immune responses, making patients more susceptible not only to infection but also to severe complications once PVIE occurs. This demographic context also introduces atypical or attenuated symptomatology, which contributes to diagnostic delays and increases the likelihood of advanced structural damage at the time of diagnosis. The literature strongly suggests that as TAVI devices continue to replace surgical valves in an expanding spectrum of patients, these epidemiologic and clinical considerations will play an increasingly central role in shaping PVIE outcomes and management paradigms.

Microbiologically, the dominance of *Staphylococcus aureus* across studies reinforces its role as the most lethal and aggressive pathogen encountered in PVIE. The organism's capacity for rapid proliferation, biofilm formation, endothelial destruction, and deep peri-annular spread translates into extensive structural deterioration, challenging surgical repairs, and high mortality rates. The fact that *S. aureus* continues to predominate even with modern antimicrobial stewardship efforts underscores the pathogen's adaptability and virulence. Simultaneously, the identification of emerging or re-emerging microorganisms—sometimes linked to healthcare exposure or regional epidemiology—adds an additional layer of complexity to empirical treatment decisions. The studies emphasize the need for prompt microbiological diagnosis, culture-based refinement of therapy, and recognition of regional variations in pathogen

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

prevalence as essential components of effective PVIE management.

The diagnostic challenges of PVIE represent another fundamental barrier highlighted across the references. Echocardiography, while central to diagnosis, is often hindered by prosthetic-associated acoustic shadowing, complicating detection of vegetations, abscesses, or perivalvular involvement. Several studies in the reference set describe cases in which initial imaging missed substantial pathology later revealed through advanced modalities. This recurring theme illustrates the necessity for a lower threshold to escalate diagnostic imaging, particularly in high-risk or diagnostically ambiguous cases. The emergence of multimodal imaging—including PET/CT, contrast-enhanced CT, and advanced three-dimensional echocardiography—has dramatically improved diagnostic sensitivity and has proven particularly valuable for identifying structural complications at earlier stages. However, these modalities require expertise, careful timing relative to implantation, and collaboration across specialties to avoid misinterpretation, especially given the background metabolic activity associated with recent valve implantation. Ultimately, the evolution of diagnostic tools reflects both progress and ongoing limitations, emphasizing that imaging alone cannot replace clinical judgment or multidisciplinary integration.

From a therapeutic standpoint, the traditional pillars of PVIE management—prolonged antimicrobial therapy and timely surgical intervention—remain critically important, yet each is constrained by real-world barriers that the literature vividly illuminates. Intravenous antimicrobial therapy continues to serve as the primary therapeutic modality, but its success depends heavily on early diagnosis, appropriate microbial identification, and patient-specific pharmacokinetic considerations. Even with optimal therapy, PVIE remains challenging to eradicate, particularly in the presence of biofilm, peri-annular abscesses, or structural deterioration. For many patients—especially those with severe comorbidities or prohibitive surgical risk—antimicrobial therapy alone may not be sufficient for cure.

It is in this context that long-term suppressive antimicrobial therapy has gained prominence. Although suppressive therapy is not curative and carries risks of microbial resistance, toxicity, and relapse, the findings from the systematic and real-world studies demonstrate that it offers meaningful stabilization and improved survival for carefully selected individuals. This is particularly relevant for patients with left-sided prosthetic infections, persistent structural defects, extensive peri-annular damage, or recurrent infection where surgery is contraindicated. The literature supports a growing recognition that suppressive therapy, when managed by an experienced multidisciplinary team and combined with close clinical and microbiological monitoring, represents a pragmatic therapeutic pathway that bridges the gap between ideal and feasible care.

Surgical intervention, however, remains the definitive therapy for a substantial subset of patients with PVIE. The consensus across studies demonstrates that timely surgical intervention leads to improved outcomes in patients with valve dysfunction, peri-annular extension, severe heart failure, or persistent infection despite adequate antimicrobial therapy. Yet, surgery in PVIE—particularly TAVI-associated PVIE—presents formidable challenges. Anatomical variability, deep device integration, and extensive tissue invasion often necessitate complex reconstructive procedures and carry heightened perioperative risk. The literature consistently reports that many patients are denied surgery due to the combination of high surgical risk and advanced comorbidities. The tension between surgical indications and patient operability underscores the critical importance of early evaluation, multidisciplinary review, and referral to centers with extensive expertise in complex valve reconstruction.

Despite advances in diagnostics, therapeutics, and surgical techniques, outcomes for PVIE remain sobering across all studies. Mortality remains unacceptably high, especially in infections caused by *Staphylococcus aureus*, in TAVI-related cases, and in individuals with delayed diagnosis or extensive peri-annular complications. These findings illustrate that although medicine has advanced considerably, the biology of PVIE remains unforgiving, particularly when diagnosis is delayed or structural involvement is severe. Pediatric cases, although less common, demonstrate similarly high risk and unique challenges related to congenital anatomy, device complexities, and limitations in imaging interpretation, further highlighting the need for specialized pediatric-focused PVIE care.

An overarching message from the assembled literature is the profound value of multidisciplinary endocarditis teams. These teams—comprising experts in infectious diseases, cardiology, cardiac surgery, radiology, microbiology, and sometimes geriatrics or pediatrics—consistently improve patient outcomes by enhancing diagnostic accuracy, guiding nuanced antimicrobial decisions, facilitating surgical planning, and ensuring continuity of care. The repeated emphasis on such teams in the references highlights a key principle: the successful management of PVIE transcends individual specialties and demands coordinated expertise and institutional commitment.

Finally, the review highlights critical knowledge gaps and priorities for future research. There remains a pressing need for multicenter prospective studies to clarify optimal management strategies for TAVI-associated PVIE, define patient selection criteria for suppressive therapy, refine risk stratification tools, and validate diagnostic algorithms that incorporate advanced imaging. Additionally, the absence of randomized controlled trials in surgical vs. non-surgical management reflects ethical and logistical barriers but underscores the importance of high-quality observational registries and harmonized international data-sharing.

Strategies for the Optimal Management of Prosthetic Valve Infective Endocarditis

In summary, prosthetic valve infective endocarditis represents a profoundly complex and evolving clinical condition shaped by modern cardiac interventions, changing patient demographics, and microbial adaptation. The evidence from the included studies demonstrates the necessity of early recognition, advanced imaging, individualized antimicrobial strategies, timely surgical consultation, and sustained multidisciplinary collaboration. Although substantial progress has been made, PVIE continues to carry high mortality and demands ongoing research, innovation, and system-level optimization to improve outcomes for this vulnerable patient population.

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