International Journal of Medical Sciences And Clinical Research

VOLUME Vol.06 Issue03 2026
PAGE NO. 1-8

Multi-Omics–Enabled Diagnostic Pathways for Optimizing Clinical Management of Prosthetic Valve Infective Endocarditis

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Received: 09 January 2026; **Accepted:** 07 February 2026; **Published:** 01 March 2026

Abstract: Prosthetic valve infective endocarditis (PVIE) remains among the most clinically complex infectious syndromes because diagnosis is frequently time-sensitive, microbiology can be inconpletely informative, host responses are heterogeneous, and management decisions must balance antimicrobial efficacy, embolic and hemodynamic risk, and surgical timing. Contemporary “omics” technologies—genomics, transcriptomics, proteomics, metabolomics, and integrative multi-omics—offer a pathway to strengthen PVIE care by moving beyond single-marker diagnostics toward composite, mechanism-informed signatures of pathogen presence, virulence, host immune activation, tissue injury, and treatment response (Horgan & Kenny, 2011; D’Adamo et al., 2021; Chen et al., 2023). However, clinical translation is constrained by analytic complexity, interpretability, operational feasibility, and the risk of overpromising clinical utility without robust validation (Boyd et al., 2014; Subramanian et al., 2020; Wekesa & Kimwele, 2023). This study develops a publication-ready conceptual and methodological framework for integrating multi-omics diagnostics into PVIE clinical pathways, with the goal of improving diagnostic certainty, prognostic stratification, and treatment monitoring. Using a structured qualitative synthesis of the provided literature, we derive a PVIE-specific multi-omics logic model that maps clinical questions to omics layers, proposes integration strategies suited to heterogeneous clinical data, and anticipates implementation challenges in real-world endocarditis teams (Subramanian et al., 2020; Shahrajabian & Sun, 2023; Sibilio et al., 2025). Particular attention is given to PVIE due to Staphylococcus aureus, given its clinical severity and prognostic importance, and to emerging echocardiographic criteria and evolving clinical research directions in infective endocarditis (Diego-Yagüe et al., 2024; Poggio Pantte & Santa María, 2024; Editorial, 2023; Olmos et al., 2024). The resulting framework emphasizes clinical actionability, staged implementation (from targeted panels to integrative signatures), and governance of uncertainty to ensure that multi-omics strengthens rather than complicates patient care (Boyd et al., 2014; D’Adamo et al., 2021).

Keywords: Prosthetic valve endocarditis; multi-omics integration; transcriptomics; clinical proteomics; translational diagnostics; risk stratification; antimicrobial monitoring.

Introduction: Prosthetic valve infective endocarditis is a high-stakes clinical syndrome situated at the intersection of microbiology, cardiology, cardiac surgery, and immunopathology. Unlike many infectious conditions where diagnosis can be made with relatively direct microbiologic confirmation and imaging, PVIE is characterized by diagnostic ambiguity, heterogeneous presentations, and a narrow therapeutic window in which delays can translate to embolic events, structural valve failure, sepsis, or death. Contemporary clinical research continues to refine criteria and improve pathways, but persistent challenges remain, especially

where standard diagnostics are insensitive, slow, or discordant with the clinical picture (Editorial, 2023; Olmos et al., 2024; Poggio Pantte & Santa María, 2024). In this context, multi-omics diagnostics are attractive not as a replacement for clinical reasoning, but as a method to make clinical reasoning more evidence-dense: to capture biology that routine tests miss and to contextualize pathogen and host signals within interpretable models of disease (Horgan & Kenny, 2011; Chen et al., 2023; Sibilio et al., 2025).

The rationale for multi-omics in PVIE begins with a basic observation: endocarditis is not merely the presence of a pathogen in blood. It is an evolving interaction among microbial colonization or invasion of prosthetic material, local tissue injury, systemic inflammation, coagulation perturbation, immune activation or dysregulation, and organ-level consequences. A purely organism-centered approach can miss clinically decisive information—such as whether inflammation is escalating, whether embolic risk is increasing, or whether a patient is shifting into immune-paralysis or hyperinflammation—especially when cultures are negative, intermittent, or confounded by prior antibiotics. Multi-omics aims to integrate layers of biological measurement—genes, transcripts, proteins, and small molecules—each offering a different lens on the disease process (Horgan & Kenny, 2011; D'Adamo et al., 2021; Subramanian et al., 2020).

Even as omics approaches have matured in other disease domains, clinical deployment demands caution. The history of omics translation includes examples where technological capability outpaced interpretability and where enthusiasm risked bypassing rigorous clinical validation. A balanced view emphasizes both potential and limitations: clinical care improves when omics-derived results are reliable, actionable, and properly contextualized, and it may worsen if complex assays yield ambiguous information that clinicians cannot responsibly act upon (Boyd et al., 2014). This caution is particularly relevant in PVIE, where the stakes are immediate and decisions frequently involve surgery, prolonged antimicrobial courses, and resource-intensive monitoring.

The provided literature collectively supports three premises relevant to PVIE. First, omics technologies are increasingly "clinically real" rather than purely research tools, with translational pathways maturing and clinical use-cases expanding (D'Adamo et al., 2021; Chen et al., 2023). Second, multi-omics integration is the central challenge: individual layers can be informative, but integrated interpretation is necessary to realize clinical value in complex diseases (Subramanian et al., 2020; Shahrajabian & Sun, 2023; Sibilio et al., 2025). Third, PVIE is an area where incremental improvements in diagnostic certainty and prognostication can have outsized clinical benefit, especially in severe etiologies such as Staphylococcus aureus PVIE where prognosis is guarded and time to decisive management matters (Diego-Yagüe et al., 2024; Editorial, 2023).

PVIE also sits within an evolving diagnostic ecology. Echocardiographic criteria and imaging interpretations continue to develop, including proposed criteria such as isolated prosthetic aortic valvulitis described as a new criterion of infective endocarditis, reflecting how clinicians continue to seek more sensitive and specific markers of disease presence on prosthetic structures (Poggio Pantte & Santa María, 2024). Similarly, contemporary reviews highlight new directions in infective endocarditis clinical research, indicating that the field is actively searching for improved diagnostic and risk frameworks (Editorial, 2023; Olmos et al., 2024). Multi-omics must be positioned within this ecology: it should complement imaging and microbiology by improving interpretive confidence and by resolving borderline clinical states where existing criteria are insufficient.

A key justification for focusing multi-omics on PVIE is that prosthetic devices introduce unique biological contexts. Prosthetic surfaces may alter microbial adherence, immune interactions, and local tissue responses. Device-related infections can involve biofilm-associated states, and host responses may differ from native valve infections. While the provided sources do not focus on biofilm in PVIE specifically, they emphasize that multi-omics in human disease is often necessary precisely because complex diseases are not reducible to single variables and because their biology is multi-layered and context-dependent (Chen et al., 2023; Sibilio et al., 2025). In PVIE, the context of prosthetic material and postoperative anatomy adds layers of complexity that make integrative approaches especially compelling.

At the same time, a major barrier is the mismatch between omics workflows and urgent clinical decision-making. Omics assays can be slow, expensive, and dependent on specialized expertise. Integration approaches may require advanced computational models, which can be difficult to validate and harder to interpret at the bedside. Deep learning approaches for multi-omics integration are widely discussed as promising, yet their clinical adoption requires careful attention to bias, generalizability, and interpretability, particularly in high-stakes medical decisions (Wekesa & Kimwele, 2023). Thus, the central question is not "Can multi-omics be applied?" but "How can multi-omics be applied in a staged, clinically coherent manner that improves PVIE outcomes without introducing undue complexity or uncertainty?" (Boyd et al., 2014;

Subramanian et al., 2020; Sibilio et al., 2025).

This article addresses that question by developing a publication-ready framework for integrating multi-omics into PVIE diagnosis and management. The approach is intentionally clinical-pathway-oriented: it maps each omics layer to practical PVIE decisions (initial diagnosis, organism inference where microbiology is incomplete, risk stratification, monitoring response, detecting relapse), and it proposes integration strategies compatible with the realities of hospital care (Subramanian et al., 2020; Shahrajabian & Sun, 2023). It also explicitly addresses uncertainty governance—how clinicians should interpret and act on multi-omics outputs, and how to avoid the clinical hazards of overinterpretation (Boyd et al., 2014). Finally, it situates the framework in the context of recent PVIE evidence and evolving IE criteria, with special attention to S. aureus PVIE due to its prognostic relevance (Diego-Yagüe et al., 2024; Editorial, 2023; Poggio Pantte & Santa María, 2024).

METHODOLOGY

This study uses a structured qualitative synthesis and framework-development methodology grounded strictly in the provided references. The objective is not to introduce external empirical datasets, but to construct a clinically coherent, evidence-consistent conceptual and operational model for multi-omics–enabled PVIE care. The methodology is designed to mirror how translational frameworks are responsibly built when primary clinical validation is outside scope: by systematically extracting claims, constraints, and opportunities from the literature; by organizing them into a clinical logic model; and by specifying testable, implementable pathway elements (Subramanian et al., 2020; Shahrajabian & Sun, 2023; Sibilio et al., 2025).

Corpus definition and inclusion criteria

All references provided by the user were treated as the complete corpus. They include: foundational descriptions of omics modalities (Horgan & Kenny, 2011), balanced ethical and clinical perspectives on genomic testing (Boyd et al., 2014), translational reviews of omics technologies (D'Adamo et al., 2021), surveys and methods reviews on multi-omics and integration strategies (Subramanian et al., 2020; Shahrajabian & Sun, 2023; Chen et al., 2023; Wekesa & Kimwele, 2023; Sibilio et al., 2025), and infective endocarditis–specific clinical research and updates, including PVIE due to S. aureus and evolving diagnostic thinking (Diego-Yagüe et al., 2024; Editorial, 2023; Olmos et al., 2024; Poggio Pantte & Santa María, 2024). References focused on cancer transcriptomics and proteomics were included as translational analogs demonstrating how omics modalities enter clinical practice and how diagnostic commercialization and clinical utility evolve (Sager et al., 2015; Latterich et al., 2008; López et al., 2012). A renal omics chapter was included as an additional translational analog emphasizing modality breadth and clinical utility across organ systems (Tagoe et al., 2026).

Analytic procedure: extraction, coding, and mapping

The synthesis proceeded in three stages:

1. Concept extraction. From each source, we extracted (a) claims about what omics modalities can measure; (b) claims about clinical utility, limitations, and translation requirements; and (c) methodological recommendations for integration and interpretation (Horgan & Kenny, 2011; Boyd et al., 2014; D'Adamo et al., 2021; Subramanian et al., 2020; Sibilio et al., 2025).

2. Thematic coding. Extracted concepts were coded into PVIE-relevant categories: diagnostic uncertainty, pathogen inference, host-response stratification, prognostic enrichment, therapeutic monitoring, relapse prediction, implementation feasibility, and governance/ethics (Boyd et al., 2014; Editorial, 2023; Olmos et al., 2024). Separate coding captured integration strategies: early integration versus late integration, network-based integration, model-based fusion, and deep learning approaches (Subramanian et al., 2020; Wekesa & Kimwele, 2023; Shahrajabian & Sun, 2023; Sibilio et al., 2025).

3. Clinical pathway mapping. We mapped the coded concepts to a staged PVIE pathway: presentation and suspicion; evidence gathering and differential diagnosis; confirmation and classification; risk stratification and surgical planning; antimicrobial selection and monitoring; and post-treatment surveillance. Each stage was linked to a set of omics outputs that could plausibly support decision-making, with explicit attention to constraints identified in the literature, such as interpretability needs, overdiagnosis risk, and translation barriers (Boyd et al., 2014; D'Adamo et al., 2021; Subramanian et al., 2020).

Framework validation logic

Because primary validation is outside scope, we used internal coherence checks based on the corpus. A proposed pathway element was retained only if it satisfied two conditions: (1) it aligned with modality capabilities and integration realities described in omics references (Horgan & Kenny, 2011; Chen et al., 2023; Sibilio et al., 2025), and (2) it mapped to a PVIE clinical need consistent with IE research directions and PVIE outcome concerns in the provided endocarditis literature (Diego-Yagüe et al., 2024; Editorial, 2023; Olmos et al., 2024). Where the corpus emphasized caution (e.g., balanced perspectives on genomic

testing), the framework incorporated explicit safeguards such as staged implementation, uncertainty grading, and clinician interpretive guidance (Boyd et al., 2014).

RESULTS

The results of this synthesis are presented as a set of integrated findings: (1) a PVIE-specific multi-omics logic model; (2) a staged diagnostic pathway; (3) a monitoring and prognostic pathway; and (4) an implementation and governance architecture that anticipates clinical constraints. Rather than numerical outcomes, the "findings" are structured as descriptive, actionable components that can be operationalized and empirically tested in future PVIE cohorts, consistent with the translational stance recommended in the omics literature (D'Adamo et al., 2021; Subramanian et al., 2020; Sibilio et al., 2025).

1) PVIE-specific multi-omics logic model: from clinical questions to biological layers

A central finding is that multi-omics becomes clinically meaningful only when each omics layer is explicitly tied to a clinical question. The corpus repeatedly emphasizes that omics data are rich but not self-interpreting, and that integration must serve a diagnostic or therapeutic purpose (Boyd et al., 2014; Subramanian et al., 2020; Shahrajabian & Sun, 2023). Applying this to PVIE yields a logic model with four recurrent PVIE questions:

- Is active prosthetic valve infection present now? This question relates to diagnostic certainty and differential diagnosis when signs and imaging may be ambiguous (Editorial, 2023; Poggio Pantte & Santa María, 2024).
- What is driving the clinical syndrome—pathogen burden, host response, or both? This question addresses cases where blood cultures are negative or discordant with clinical severity and where host-response patterns may help interpret ongoing risk (Boyd et al., 2014; Chen et al., 2023).
- What is the patient's short-term risk trajectory (complications, deterioration, mortality)? PVIE outcomes can deteriorate rapidly, particularly in severe etiologies such as S. aureus PVIE described with clinical features and prognosis in recent work (Diego-Yagüe et al., 2024).
- Is therapy working, and when is it safe to de-escalate or to delay surgery? This question relates to monitoring and actionable thresholds, where multi-omics could contribute if structured as longitudinal signatures rather than single timepoints (D'Adamo et al., 2021; Sibilio et al., 2025).

In this logic model, each omics layer contributes distinct but complementary evidence:

- Genomics contributes stable information about host predisposition and, where pathogen genomic information is available, organism characterization and potential resistance inference. The literature stresses both the promise and the need for a balanced, cautious approach in clinical genomics—highlighting that genomic signals can be powerful but also ethically and interpretively complex (Boyd et al., 2014; Horgan & Kenny, 2011).
- Transcriptomics offers a dynamic lens on biological activity—immune activation, inflammation, and cellular responses. While the corpus includes transcriptomics examples in cancer diagnostics, the translational lesson is that transcript signatures become clinically useful when linked to clear decisions, validated across contexts, and operationalized through reproducible workflows (Sager et al., 2015; Subramanian et al., 2020).
- Proteomics captures effectors and functional processes closer to phenotype. Clinical proteomics literature emphasizes technology maturation and clinical application potential, while also underlining translation barriers and the need for robust clinical interpretation (Latterich et al., 2008; López et al., 2012).
- Metabolomics and related "small-molecule" profiles offer rapid, physiology-proximal signals that can reflect systemic stress, organ dysfunction, and inflammatory states. The broader omics overview emphasizes metabolomics as a core modality within the omics family, often valuable for capturing current physiological state (Horgan & Kenny, 2011; Shahrajabian & Sun, 2023).
- Integrated multi-omics becomes the mechanism to reconcile discordant signals and derive composite clinical signatures, but only if integration strategies are fit-for-purpose and interpretable (Subramanian et al., 2020; Wekesa & Kimwele, 2023; Sibilio et al., 2025).

2) Staged diagnostic pathway: from single-layer triage to integrative confirmation

A second major finding is that a practical PVIE pathway should be staged. The omics corpus warns against jumping directly into maximal complexity; instead, it implicitly supports progression from targeted testing toward integrated testing as clinical need increases and as infrastructure matures (Boyd et al., 2014; D'Adamo et al., 2021). For PVIE, the staged pathway includes:

- Stage A: Clinical suspicion with minimal-delay omics augmentation. At this stage, omics should not be an exhaustive multi-omics stack. Instead, it should be a

limited set of assays designed to rapidly improve the probability of active infection versus mimics. This staging aligns with the translational emphasis on feasibility and interpretability (D'Adamo et al., 2021).

- Stage B: Diagnostic refinement when conventional evidence is incomplete. If imaging findings are borderline or if emerging criteria (e.g., proposed valvulitis criteria) raise suspicion without definitive confirmation, transcriptomic/proteomic signatures of infection-related host response may strengthen or weaken the case for PVIE, thereby guiding further invasive evaluation or surgical consultation (Poggio Pantte & Santa María, 2024; Subramanian et al., 2020).
- Stage C: Integrated confirmation and classification. In high-stakes cases—particularly with severe clinical trajectories such as S. aureus PVIE—multi-omics integration can be used to classify phenotype: predominant bacterial burden signal, predominant hyperinflammatory response, mixed pattern, or immune-exhaustion pattern. This classification is conceptually consistent with multi-omics methods aimed at complex disease phenotyping (Chen et al., 2023; Sibilio et al., 2025).
- Stage D: Longitudinal monitoring and relapse risk. Once therapy is initiated, repeated measurements at clinically meaningful intervals can determine whether the patient's biological trajectory is improving, plateauing, or worsening, improving the timing of decisions such as escalation of care or surgery (D'Adamo et al., 2021; Sibilio et al., 2025).

This staged model directly incorporates the cautionary principle from clinical genomics: more data do not necessarily mean better decisions unless interpretation and validation are rigorous (Boyd et al., 2014).

3) Prognostic enrichment: integrating PVIE clinical prognosis with host-response signatures

PVIE prognosis depends on multiple factors: pathogen type, complications, and timing of intervention. The inclusion of S. aureus PVIE prognosis in the corpus underscores the clinical need for better stratification tools because S. aureus PVIE is associated with severe outcomes and urgent management decisions (Diego-Yagüe et al., 2024). The multi-omics literature suggests that complex disease prognosis can be strengthened by integrated signatures rather than single biomarkers, particularly when those signatures capture multiple biological axes (Subramanian et al., 2020; Chen et al., 2023).

Therefore, an important result is the identification of a prognostic enrichment approach: integrate host transcriptomic activity (immune activation intensity), proteomic indicators of tissue injury and inflammation, and metabolomic signals of systemic stress. The goal is not to replace clinical risk assessment but to reduce uncertainty in borderline cases and to identify discordant trajectories early—such as a patient who appears clinically stable but whose biological signature suggests escalation risk, or a patient whose symptoms persist but whose biological trajectory indicates recovery (Sibilio et al., 2025; D'Adamo et al., 2021). Because PVIE management often involves balancing medical therapy and surgical timing, improved prognostic resolution can have immediate clinical impact (Editorial, 2023; Olmos et al., 2024).

4) Implementation architecture: integration strategies and interpretability constraints

A final result is that the integration method must be chosen based on the clinical question and institutional capacity. The integration literature describes multiple approaches, including early integration (combining features across modalities), late integration (separate models combined at decision level), and deep learning approaches capable of capturing nonlinear relationships (Subramanian et al., 2020; Wekesa & Kimwele, 2023; Sibilio et al., 2025). For PVIE, the key interpretability constraint is that clinicians must understand what an output means in terms of action. A black-box prediction that "PVIE risk is high" is less clinically useful if it does not indicate whether the risk derives from pathogen burden, host hyperinflammation, tissue injury, or confounding comorbidities—especially when management choices diverge (Boyd et al., 2014; Wekesa & Kimwele, 2023).

Thus, the framework prioritizes interpretable integration: rule-based or model-based integration that can present clinicians with layered evidence statements (e.g., "host inflammatory signature consistent with active infection," "proteomic injury markers elevated," "trajectory improving") rather than a single opaque score. This emphasis aligns with the balanced perspective on clinical genomic testing and with the integration literature's recognition that interpretability is central to clinical translation (Boyd et al., 2014; Subramanian et al., 2020; Shahrajabian & Sun, 2023).

DISCUSSION

The synthesis indicates that multi-omics can meaningfully strengthen PVIE management only if it is implemented as a clinically governed diagnostic pathway rather than as a purely technological add-on. The discussion below interprets the results through five themes: (1) why PVIE is especially suited to multi-omics; (2) how omics layers should be used to reduce diagnostic ambiguity; (3) how integration should be

constrained by clinical interpretability; (4) how PVIE research directions and evolving criteria create an opportunity for omics; and (5) limitations and future work for clinical translation.

PVIE as a "high-value" target for multi-omics translation

Multi-omics translation is most justified when clinical stakes are high, uncertainty is common, and existing tools leave a meaningful residual risk of error. PVIE matches these conditions. The infective endocarditis literature emphasizes ongoing innovation and "what is new" in clinical research, which implicitly acknowledges that the field is not yet satisfied with diagnostic precision and outcome optimization (Editorial, 2023). The emergence of proposed new criteria, such as isolated prosthetic aortic valvulitis as a criterion for IE, reflects efforts to detect disease earlier and more reliably, particularly in the prosthetic context where classic signs may be subtle or confounded (Poggio Pantte & Santa María, 2024). Multi-omics aligns with these efforts by providing additional biological evidence streams that can raise or lower suspicion.

However, the balanced genomics perspective is essential: PVIE is not the place for unvalidated novelty. Because decisions may involve major surgery and prolonged antimicrobial therapy, the tolerable rate of false positives and false negatives is low (Boyd et al., 2014). For that reason, the staged approach matters: early use should be conservative, supportive, and interpretable, while deeper integration should be reserved for cases where uncertainty remains and where the marginal benefit of added information is plausibly high (D'Adamo et al., 2021; Subramanian et al., 2020).

Reducing diagnostic ambiguity: layered evidence rather than single "omics answers"

A frequent misconception in omics translation is that a single "omics test" will replace clinical reasoning. The corpus argues against this by emphasizing complexity and integration challenges (Subramanian et al., 2020; Shahrajabian & Sun, 2023). PVIE diagnosis requires synthesis of symptoms, microbiology, imaging, and clinical evolution. Multi-omics should be conceptualized as additional layers of evidence. For example, if blood cultures are negative, an integrated host-response signature consistent with infection could support continued investigation or escalation, whereas a signature inconsistent with infection could push the clinician to reconsider alternative diagnoses or to interpret borderline imaging findings more cautiously (D'Adamo et al., 2021; Chen et al., 2023).

The transcriptomics literature in cancer diagnostics illustrates a key translational principle: transcript signatures are powerful when they are standardized, validated, and clinically linked to outcomes, but they can mislead when applied outside validated contexts (Sager et al., 2015). PVIE translation must therefore avoid simplistic cross-domain borrowing. The appropriate lesson is methodological: develop PVIE-specific signatures and validate them within PVIE populations, including diverse etiologies and varying timing relative to antibiotic exposure (Subramanian et al., 2020; Sibilio et al., 2025).

Proteomics offers similar lessons. The clinical proteomics literature demonstrates that proteomics can provide functional insight closer to phenotype and can support translational medicine, but it also implies that technical variation and interpretation difficulties can undermine clinical use if not managed (López et al., 2012; Latterich et al., 2008). For PVIE, proteomics should not be positioned as an all-purpose screen but rather as a targeted contributor to defined questions: evidence of ongoing inflammation, tissue injury, or immune activation consistent with persistent infection versus resolving disease (D'Adamo et al., 2021; Chen et al., 2023).

Integration strategies: why interpretability is not optional

Multi-omics integration methods range from relatively transparent statistical fusion to complex deep learning models (Subramanian et al., 2020; Wekesa & Kimwele, 2023; Sibilio et al., 2025). Deep learning integration can capture nonlinear relationships and complex interactions, which is attractive in a syndrome as complex as PVIE. Yet clinical reality demands interpretability. The balanced perspective on genomic testing highlights the ethical and practical risks of deploying tests whose implications are not clear to patients or clinicians, and whose results could lead to overdiagnosis or misdirected treatment (Boyd et al., 2014). In PVIE, the action consequences are significant, so interpretability becomes a core safety requirement.

Therefore, an important clinical implication is the need for decision-layer transparency even when underlying models are complex. One plausible compromise consistent with the corpus is to use deep learning or advanced integration as a "feature discovery" tool during research and validation, while deploying clinically digestible outputs in practice—e.g., structured interpretations or categorical risk states with explanations of contributing layers (Wekesa & Kimwele, 2023; Subramanian et al., 2020). This approach aligns with the broader integration literature's recognition that translation depends on trust, reproducibility, and clinician acceptance (Sibilio

et al., 2025; Shahrajabian & Sun, 2023).

PVIE due to Staphylococcus aureus: using severity to justify enhanced stratification

The PVIE-specific study on Staphylococcus aureus provides a direct justification for why enhanced diagnostic and prognostic tools matter. S. aureus PVIE is clinically severe, and outcomes depend on timely recognition and management strategy (Diego-Yagüe et al., 2024). Multi-omics could contribute in two ways consistent with the corpus:

1. Early identification of high-risk host-response trajectories—patients whose immune and injury signatures suggest likely deterioration even before overt clinical decline.

2. Therapy monitoring—distinguishing persistent biological activity (suggesting ongoing infection or uncontrolled inflammation) from post-infectious recovery states, potentially informing antimicrobial strategies and surgical timing (D'Adamo et al., 2021; Sibilio et al., 2025).

The endocarditis special issue editorial underscores that clinical research is actively seeking such improvements (Editorial, 2023). Meanwhile, broader clinical updates emphasize ongoing changes in IE management and diagnostics (Olmos et al., 2024). Multi-omics integration should be framed as part of this evolving research agenda, not as a standalone revolution.

Limitations and future scope

This article is constrained by its strict reliance on the provided references and therefore does not introduce new PVIE-specific omics datasets or external validation studies. As a result, the framework should be understood as an implementation-oriented conceptual model rather than as a validated clinical guideline. This limitation is consistent with the omics translation literature, which emphasizes that methods must be validated within target populations before clinical adoption (Boyd et al., 2014; Subramanian et al., 2020; Sibilio et al., 2025).

Future work implied by the corpus includes:

- PVIE cohort studies collecting longitudinal multi-omics with linked clinical outcomes to validate diagnostic and prognostic signatures (D'Adamo et al., 2021; Chen et al., 2023).
- Integration method benchmarking in PVIE settings, including interpretability comparisons between transparent and deep-learning approaches (Wekesa & Kimwele, 2023; Subramanian et al., 2020).
- Clinical workflow trials evaluating staged implementation, feasibility, turnaround times, clinician understanding, and downstream decision impacts (Boyd et al., 2014; Sibilio et al., 2025).
- Alignment with evolving diagnostic criteria such as new echocardiographic or imaging criteria proposals, ensuring omics complements rather than conflicts with emerging standards (Poggio Pantte & Santa María, 2024; Editorial, 2023).

CONCLUSION

Multi-omics diagnostics offer a credible pathway to strengthen prosthetic valve infective endocarditis care by providing layered evidence of pathogen–host interaction, functional injury, and disease trajectory. The provided literature supports both optimism and caution: omics technologies are increasingly translatable (Horgan & Kenny, 2011; D'Adamo et al., 2021; Chen et al., 2023), but clinical value depends on fit-for-purpose integration, interpretability, and governance of uncertainty (Boyd et al., 2014; Subramanian et al., 2020; Wekesa & Kimwele, 2023; Sibilio et al., 2025). By mapping omics layers to PVIE clinical questions, adopting a staged pathway approach, and prioritizing actionable interpretations—especially in severe contexts such as Staphylococcus aureus PVIE—multi-omics can evolve from exploratory research to a clinically responsible decision support infrastructure (Diego-Yagüe et al., 2024; Editorial, 2023; Olmos et al., 2024; Poggio Pantte & Santa María, 2024). The framework presented here is designed to be empirically testable and operationally feasible, laying a foundation for future PVIE multi-omics cohorts and implementation trials that can establish robust clinical utility and safety.

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