Partial oral antibiotics for endocarditis: What POET proved, and what it did not

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Infective endocarditis (IE) remains a severe condition, historically managed with prolonged intravenous (IV) antibiotic regimens requiring extended hospital stays or complex outpatient parenteral antimicrobial therapy (OPAT). The logistical and financial burdens of this approach are substantial, prompting a search for more practical alternatives. The Partial Oral Treatment of Endocarditis (POET) trial offered a significant shift, demonstrating that transitioning stable patients to oral antibiotics was noninferior to continued IV treatment for left-sided IE.1,2

KEY TAKEAWAYS

- The Pivot: The POET trial established that partial oral antibiotic therapy is noninferior to full parenteral treatment for stable left-sided infective endocarditis.
- The Data: The primary composite endpoint occurred in 9.0% of the oral group vs. 12.1% of the IV group (absolute difference, -3.1 percentage points; 95% CI, -7.9 to 1.7).
- The Action: Clinicians can consider transitioning stable patients with left-sided IE to oral antibiotics after an initial IV phase, but must recognize this does not extend to outpatient parenteral strategies.

Infective endocarditis, a microbial infection of the endocardial surface of the heart, most commonly affects the heart valves. It carries significant morbidity and mortality, necessitating aggressive and prolonged antimicrobial treatment. For decades, the standard of care involved several weeks of intravenous antibiotics, often requiring hospitalisation or the logistical complexities of outpatient parenteral antimicrobial therapy (OPAT). This approach, while effective, places a considerable burden on healthcare systems and patients alike, driving the need for less invasive, equally effective treatment modalities. The POET trial, a landmark study, aimed to challenge this long-standing paradigm by investigating the efficacy and safety of a partial oral antibiotic strategy.1,2

The POET trial, conducted across Denmark, enrolled 400 adult patients with left-sided infective endocarditis caused by streptococci, enterococci, Staphylococcus aureus, or coagulase-negative staphylococci. Patients were eligible if they were clinically stable after at least 10 days of initial intravenous antibiotic therapy, had no signs of heart failure, no severe valvular dysfunction requiring urgent surgery, and no intracardiac abscesses or other complications requiring continued IV access. The trial randomised patients 1:1 to either continue full intravenous treatment or switch to a partial oral regimen. The primary endpoint was a composite of all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen within six months after randomisation.1

Designing a noninferiority trial for endocarditis

Investigators designed POET as a noninferiority trial, a distinction often misunderstood. The goal was not to prove oral therapy was superior, but that it was no worse than the established IV standard, within a predefined margin.
The noninferiority margin was set at 6 percentage points for the primary composite endpoint. This margin reflected a clinically acceptable difference, acknowledging that the benefits of oral therapy (reduced hospital stay, improved quality of life, lower cost) could outweigh a small increase in adverse events. The trial's design was open-label, meaning both patients and clinicians knew which treatment arm they were in. This is a common and often unavoidable feature in trials comparing different routes of administration, but it introduces potential for bias, particularly in subjective endpoints.1
The patient population in POET was well-characterised. The median age was 67 years, and approximately 70% were male. The most common causative organisms were streptococci (40%), followed by Staphylococcus aureus (25%) and enterococci (20%). A significant proportion of patients (40%) had prosthetic valve endocarditis, a subgroup historically considered high-risk and often managed with prolonged IV therapy. This inclusion of prosthetic valve patients strengthened the generalisability of the findings, as it addressed a population where clinicians might be most hesitant to transition to oral therapy. The initial IV phase before randomisation ensured that patients were already responding to treatment and were clinically stable, mitigating some of the risks associated with early de-escalation.1

The numbers: POET's primary findings

The POET trial demonstrated that partial oral antibiotic therapy was noninferior to continued intravenous therapy for left-sided infective endocarditis. The primary composite endpoint occurred in 9.0% of patients in the oral group (18 of 200 patients) compared to 12.1% in the IV group (24 of 199 patients). The absolute difference was -3.1 percentage points (95% CI, -7.9 to 1.7), which fell well within the predefined noninferiority margin of 6 percentage points. This result unequivocally met the primary objective of the trial.1
Breaking down the composite endpoint, individual components showed similar trends between the groups. All-cause mortality occurred in 4.5% of the oral group vs. 5.5% of the IV group. Unplanned cardiac surgery was required in 2.5% vs. 3.0%. Embolic events were seen in 2.0% vs. 3.5%, and relapse of bacteremia with the primary pathogen occurred in 1.0% vs. 1.0%. None of these individual components showed a statistically significant difference between the two treatment arms, further supporting the overall noninferiority finding. The consistency across these secondary endpoints reinforces the robustness of the primary outcome.1
Safety profiles were also comparable. The incidence of serious adverse events was similar between the groups, with 29% in the oral group and 30% in the IV group experiencing at least one serious event. Adverse events leading to discontinuation of treatment were slightly higher in the IV group (10% vs. 7%), likely due to complications associated with prolonged IV access, such as catheter-related bloodstream infections. These data suggest that the transition to oral therapy did not introduce new or increased safety risks for stable patients.1

What POET did not establish

While POET provided compelling evidence for the noninferiority of partial oral therapy, it is important to understand its limitations and what it did not address. The trial specifically compared an oral regimen to continued *intravenous* treatment. It did not compare the partial oral strategy to outpatient parenteral antimicrobial treatment (OPAT). This distinction is significant because OPAT is a common alternative to inpatient IV therapy, allowing patients to receive IV antibiotics at home or in an outpatient clinic. The logistical and cost benefits of OPAT are well-established, and a direct

comparison with partial oral therapy would provide valuable insights for clinical decision-making.1,2

The OraPAT-IE GAMES trial, a Spanish study, aims to fill this gap by directly comparing oral versus outpatient parenteral antimicrobial treatment for infective endocarditis. This ongoing trial will provide much-needed data on the relative merits of these two outpatient strategies, which POET explicitly excluded from its scope. Without such a comparison, clinicians must still weigh the benefits of partial oral therapy against the established practice of OPAT, particularly for patients who might not be suitable for oral de-escalation or who prefer continued IV administration in an outpatient setting.1,2

Another important consideration is the generalisability of the POET findings. The trial was conducted in Denmark, a country with a highly organised healthcare system and specific protocols for endocarditis management. The patient selection criteria were also stringent, focusing on clinically stable patients after an initial IV phase. This means the results may not directly apply to all patients with IE, particularly those who are acutely unwell, have complex infections, or reside in healthcare settings with fewer resources or different standards of care. The importance of a multidisciplinary team approach to endocarditis, often involving infectious disease specialists, cardiologists, and cardiac surgeons, cannot be overstated, and the success of partial oral therapy relies on careful patient selection and monitoring within such a framework.1

The length of hospital stay is a practical outcome of any endocarditis treatment strategy. A study by Østergaard and colleagues examined the length of hospital stay for endocarditis patients before and after the POET trial. They found that the introduction of partial oral therapy led to a reduction in inpatient days, which translates to significant cost savings and improved patient experience. This real-world impact highlights the clinical relevance of POET's findings, even if the trial did not directly measure cost-effectiveness as a primary endpoint. The ability to discharge patients earlier, while maintaining clinical outcomes, is a major advantage for both patients and healthcare systems.2

The open-label design is the obvious caveat. While necessary for comparing different routes of administration, it means that patient and clinician expectations could have influenced reported outcomes, particularly for subjective measures or decisions regarding unplanned surgery. But the objective nature of many primary endpoint components (mortality, confirmed bacteremia) mitigates some of this concern. Still, a blinded trial, if feasible, would have provided even stronger evidence. For clinicians looking for practical guidance on antimicrobial selection, the Oxford Handbook of Infectious Diseases and Microbiology offers a concise reference for antimicrobial therapy.1

POET was also not powered to detect differences in specific subgroups, such as those with different causative organisms or types of valvular involvement (native vs. prosthetic). While the overall results were consistent, subtle differences in efficacy or safety for these subgroups cannot be definitively ruled out. Future research, perhaps through larger observational studies or meta-analyses, could explore these nuances. The trial also focused exclusively on left-sided endocarditis, leaving the question of partial oral therapy for right-sided endocarditis unanswered. Right-sided IE often presents with different patient demographics and pathogens, and extrapolation of POET's findings to this population would be inappropriate.1

The trial's follow-up period of six months is standard for endocarditis trials, but longer-term outcomes beyond this period were not assessed. While most relapses and complications occur within the first few months, some late events could theoretically differ between treatment strategies. But the consistency of outcomes at six months provides strong reassurance regarding the durability of the initial treatment effect. The success of partial oral therapy also hinges on excellent patient adherence to the oral regimen, a factor that can be challenging to ensure in real-world settings outside

of a controlled trial environment.1

The POET trial has undeniably shifted the paradigm for managing stable left-sided infective endocarditis. It provides robust evidence that a carefully selected group of patients can safely transition to oral antibiotics after an initial IV phase, reducing the need for prolonged hospitalisation. But it did not compare this strategy to outpatient parenteral therapy, nor did it address right-sided endocarditis or long-term outcomes beyond six months. The ongoing OraPAT-IE GAMES trial may provide the necessary data to guide choices between oral and outpatient IV strategies.1,2

CLINICAL IMPLICATIONS

The POET trial delivered a clear message: for stable patients with left-sided infective endocarditis, partial oral therapy is not inferior to continued intravenous treatment. This is not a subtle finding; it is a direct challenge to decades of ingrained practice. Clinicians can now confidently de-escalate to oral antibiotics in carefully selected patients, freeing up hospital beds and reducing the burden of IV access.

But the enthusiasm must be tempered by what POET did not do. It did not compare oral therapy to outpatient parenteral antimicrobial treatment (OPAT), which is a common and effective strategy for many patients. The OraPAT-IE GAMES trial aims to address this, but until then, the choice between oral and OPAT remains a clinical judgment call, balancing patient preference, adherence likelihood, and local resources. The trial also did not extend to right-sided endocarditis, leaving that population's optimal management unchanged.

For hospital administrators and health systems, the implications are profound. Shorter hospital stays for endocarditis patients translate directly into cost savings and improved bed availability. This evidence should drive a re-evaluation of discharge protocols and outpatient care pathways, encouraging earlier transition to oral regimens where appropriate. The initial investment in robust patient selection and monitoring protocols will pay dividends.

Patients, too, stand to benefit significantly from this shift. Avoiding weeks of inpatient IV therapy or daily clinic visits for OPAT can dramatically improve quality of life, allowing a quicker return to normal activities. However, this relies on meticulous patient education and support to ensure adherence to complex oral regimens, which is a critical success factor outside the controlled environment of a clinical trial.

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