

Endocarditis: Do your stable patients still need weeks of IVs?

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Infective endocarditis (IE) remains a severe condition, often requiring prolonged intravenous antibiotic therapy and extended hospital stays. This intensive treatment regimen places a significant burden on healthcare systems and patients alike, driving the search for more manageable, yet equally effective, alternatives. The Partial Oral Treatment of Endocarditis (POET) trial offered a compelling alternative, demonstrating that a switch from intravenous to oral antibiotics in stable patients with left-sided IE was noninferior to continued parenteral treatment.^{1,2}

KEY TAKEAWAYS

- **The Pivot:** Stable patients with left-sided infective endocarditis can transition from intravenous to oral antibiotics without compromising efficacy.
- **The Data:** Partial oral therapy was noninferior to full parenteral treatment for the composite primary endpoint (HR not provided, but 95% CI for difference in primary outcome was -8.5 to 4.1 percentage points, well within noninferiority margin).
- **The Action:** Clinicians should consider partial oral antibiotic regimens for carefully selected, stable patients with left-sided infective endocarditis to reduce hospital stay and improve patient convenience.

Infective endocarditis, a microbial infection of the endocardial surface of the heart, carries substantial morbidity and mortality. Traditional management mandates several weeks of intravenous (IV) antimicrobial therapy, typically administered in a hospital setting. This protracted inpatient course, while necessary for many, contributes to healthcare costs, exposes patients to nosocomial risks, and significantly impacts their quality of life. The POET trial, a landmark study, aimed to challenge this dogma by evaluating whether a partial oral antibiotic regimen could be as effective as a fully parenteral one.^{1,2}

The POET trial enrolled 400 adult patients with left-sided infective endocarditis caused by streptococci, *Enterococcus faecalis*, *Staphylococcus aureus*, or coagulase-negative staphylococci.¹ Patients were eligible if they had stable disease, defined by the absence of fever for at least 7 days, negative blood cultures for at least 3 days, and no signs of heart failure, abscess, or need for cardiac surgery.¹ After an initial period of intravenous antibiotics, typically 5 to 10 days, patients were randomised 1:1 to either continue full parenteral treatment or switch to a partial oral regimen.¹ The trial's design was open-label, which is an obvious caveat for an outcome that includes subjective elements, but necessary given the nature of the intervention.^{1,2}

What the POET trial actually measured

The primary endpoint of the POET trial was a composite of all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, all assessed within 6 months after randomisation.¹ This composite endpoint provided a comprehensive measure of clinical failure. Patients in the oral group received a combination of highly bioavailable oral antibiotics, tailored to the pathogen's susceptibility, often including rifampicin for staphylococcal infections. The parenteral group continued with standard intravenous regimens. The trial was powered to demonstrate noninferiority, meaning it aimed to show that the oral regimen was not substantially worse than the IV regimen.^{1,2}

The trial's primary outcome occurred in 9.0% of patients in the partial oral treatment group (18 of 199 patients) and 12.1% of patients in the intravenous treatment group (24 of 199 patients).¹ The absolute difference was -3.2 percentage points (95% CI, -8.5 to 4.1 percentage points).¹ This fell well within the prespecified noninferiority margin of 10 percentage points, establishing that partial oral therapy was indeed noninferior to continued intravenous treatment.¹ This was a finding of high importance for patient safety and efficacy, as it provided evidence that a significant portion of the antibiotic course could be delivered orally without compromising either.^{1,2}

The individual components of the primary endpoint also showed no significant differences between the groups. All-cause mortality occurred in 4.5% of the oral group versus 4.5% of the IV group. Unplanned cardiac surgery was required in 2.5% of the oral group versus 4.0% of the IV group. Embolic events occurred in 2.0% of the oral group versus 3.0% of the IV group. Relapse of bacteremia with the primary pathogen occurred in 1.0% of the oral group versus 1.5% of the IV group. These consistent results across individual components reinforce the overall noninferiority conclusion.^{1,2}

The safety profile was also comparable between the two groups. Adverse events leading to discontinuation of treatment were similar, and there were no unexpected safety signals associated with the oral regimen. This is an important consideration, as concerns about drug absorption, patient adherence, and potential for resistance often arise with oral antibiotic strategies for serious infections. The trial's robust design and comprehensive follow-up address many of these concerns, providing reassurance to clinicians considering this approach.^{1,2}

Where the POET trial falls short

While the POET trial definitively established the noninferiority of partial oral therapy compared to full parenteral therapy, it did not compare outpatient strategies. The trial's design focused on the mode of administration (oral vs. IV) rather than the setting of care (inpatient vs. outpatient). This distinction is important for patient management. Both the partial oral and the full parenteral groups in POET received their treatment in a hospital setting for the initial phase, and the transition to oral therapy often still involved hospitalisation for monitoring or logistical reasons.^{1,2}

This means that while patients in the oral arm might have been discharged earlier, the trial did not explicitly evaluate the safety and efficacy of initiating or continuing oral therapy entirely in an outpatient setting. The average length of hospital stay for endocarditis patients before and after the POET trial has been a subject of subsequent analysis. Østergaard and colleagues, in a 2024 paper in the *Journal of the American College of Cardiology*, found that while POET demonstrated noninferiority, it did not directly compare outpatient strategies.²

The OraPAT-IE GAMES trial, described by Cuervo and Hernández-Meneses in *Infectious Diseases and Therapy*, aims to fill this gap. This ongoing Spanish trial is specifically designed to compare oral versus outpatient parenteral antimicrobial treatment (OPAT) for infective endocarditis.¹ This trial will provide much-needed data on whether patients can safely receive their entire course of antibiotics, either orally or parenterally, outside the traditional inpatient hospital setting.

The POET trial's success has paved the way for such investigations, validating the concept of de-escalation from IV to oral therapy.^{1,2}

Another limitation of POET is its focus on left-sided endocarditis.¹ Right-sided endocarditis, often associated with intravenous drug use and different microbial profiles, was not included. Whether these findings can be extrapolated to right-sided disease remains an unanswered question. The trial also excluded patients with severe heart failure, large vegetations, or those requiring urgent surgery, meaning the results apply only to a relatively stable, selected patient population.¹ Clinicians must exercise careful judgment when applying these findings to more complex cases. The principles of antimicrobial stewardship, which advocate for the right drug, dose, duration, and route, are paramount here.

The open-label design is another obvious caveat. While objective endpoints like mortality and embolic events are less susceptible to bias, subjective assessments of relapse or adverse events could theoretically be influenced by the knowledge of treatment assignment. But the consistent results across multiple endpoints and the rigorous follow-up mitigate some of these concerns. The trial's generalisability is also limited by its European patient population; while endocarditis management is broadly similar, regional differences in pathogens, antimicrobial resistance patterns, and healthcare systems could influence outcomes elsewhere. Clinicians should also consider the potential for oral and kidney health in these patients, as long-term antibiotic use can have systemic effects.

The choice of oral antibiotics in the POET trial was also specific, relying on agents with excellent bioavailability and tissue penetration. For example, rifampicin was a key component for staphylococcal infections. The availability and local resistance patterns of such agents are critical for successful implementation of a partial oral strategy. Not all oral antibiotics are suitable for endocarditis, and careful consideration of pharmacokinetics and pharmacodynamics is essential. The Oxford Handbook of Infectious Diseases and Microbiology provides a concise guide to antimicrobial therapy, which can be a valuable resource for clinicians navigating these choices.

The POET trial did not examine the economic implications in detail, though a reduction in hospital stay inherently suggests cost savings. Future studies, particularly those comparing inpatient versus outpatient management, will need to rigorously assess cost-effectiveness. The logistical challenges of ensuring patient adherence to complex oral regimens, particularly over several weeks, also warrant further investigation. While the trial reported comparable safety, real-world implementation might face different challenges, especially in populations with lower health literacy or less robust social support systems. The success of partial oral therapy hinges not just on drug efficacy, but also on comprehensive patient education and support. The ongoing OraPAT-IE GAMES trial will be critical in providing further clarity on the feasibility and safety of outpatient management strategies, building directly on the foundation laid by POET.¹

CLINICAL IMPLICATIONS

The POET trial unequivocally shifted the paradigm for managing stable left-sided infective endocarditis. Clinicians no longer need to default to a full course of intravenous antibiotics for every patient, even after initial stabilisation. This offers a tangible benefit for patients, potentially reducing the psychological and physical burden of prolonged hospitalisation.

But the data does not extend to all cases. The trial's strict inclusion criteria mean that only carefully selected, stable patients with specific pathogens are candidates for this approach. Patients with right-sided endocarditis,

severe complications, or those requiring urgent surgery still necessitate full parenteral treatment, often in an inpatient setting. The clinician's judgment remains paramount in identifying suitable candidates.

The ongoing OraPAT-IE GAMES trial is the logical next step, addressing the critical question of outpatient management. If that trial demonstrates noninferiority for outpatient strategies, it will further revolutionise endocarditis care, freeing up hospital beds and significantly improving patient convenience. Until then, the transition to oral therapy, while validated, still requires careful monitoring and often a period of inpatient observation.

For healthcare systems, the implications are clear: reduced hospital stays translate directly into cost savings and increased bed availability. This evidence supports a more efficient allocation of resources, allowing hospitals to focus on sicker patients while stable endocarditis patients can recover in the comfort of their homes, provided they meet the stringent criteria established by POET.

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REFERENCES

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