The promise and challenges of oral step-down therapy for infective endocarditis in South Africa – Rethinking endocarditis treatment

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ABSTRACT

Infective endocarditis (IE) remains a complex clinical challenge globally and in South Africa, where it predominantly affects a younger population. Historically, it was managed with prolonged intravenous (IV) antibiotic therapy, an approach mainly based on expert opinion and low-level evidence. However, recent studies, including the landmark Partial Oral Treatment of Endocarditis (POET) trial, have demonstrated that oral step-down therapy is a safe and effective alternative in selected, clinically stable patients. Modern oral antibiotics now exhibit pharmacokinetic profiles comparable to their IV counterparts, and multiple randomised controlled trials (RCT) have confirmed their efficacy in clearing bacteraemia. While oral step-down therapy has been adopted in high-income settings and incorporated into international guidelines, its implementation in South Africa faces significant challenges. These include a high burden of blood culture-negative infective endocarditis (BCNIE), unique pathogens, such as *Bartonella* species (spp.) and *Mycobacterium tuberculosis* (TB), systemic healthcare constraints, limited access to cardiac surgery, and barriers to patient education and follow-up. In South Africa, locally feasible strategies are required to enable the safe and effective use of oral step-down therapy. Continued local research is needed to guide policy and adapt global evidence to the realities of the South African healthcare system.
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INTRODUCTION

IE continues to pose a clinical challenge globally, including in South Africa, where it predominantly affects a younger population.[1] Most IE complications, such as embolic events, heart failure, and uncontrolled infection, usually occur in the initial stages of the disease.[2] This highlights the importance of prompt diagnosis and intensive IV therapy during this period. Traditionally, IE was managed exclusively with prolonged courses of parenteral antibiotics, primarily based on historical data and expert opinion.

The longstanding practice of prolonged IV therapy has been increasingly questioned in recent years, particularly following the findings of the POET trial, which contributed to the incorporation of oral step-down therapy in the latest European Society of Cardiology (ESC) endocarditis guidelines.[3,4] This evidence-based strategy reduces hospitalisation costs, has fewer healthcare-associated complications, and enhances patient comfort without adversely affecting clinical outcomes.[5]

However, oral step-down treatment of IE is not yet widely implemented in South Africa. Given the high burden of prolonged hospital stays, constrained inpatient capacity, and barriers to accessing sustained IV therapy, particularly in rural and resource-limited settings, oral step-down therapy may offer a pragmatic, cost-effective, and clinically safe alternative to conventional IV regimens.

Background on infective endocarditis in South Africa

The high prevalence of rheumatic heart disease in South Africa has historically been a prominent predisposing factor, now compounded by rising rates of IV drug use and a growing number of patients with prosthetic valves and cardiac implantable electronic devices.[6-10] Previously, the viridans group streptococci were the predominant cause of blood culture-positive infective

endocarditis (BCPIE) in South Africa.[7,10] However, the pathogen profile has shifted to resemble those observed in high-income countries, where *Staphylococcus aureus* predominates.[1,11]

This trend was observed across multiple South African studies. De Villiers, et al.[12] reported that *S. aureus* was the most frequent pathogen in left-sided (19%) and right-sided (73%) IE at Groote Schuur Hospital between 2009 and 2016. Similarly, Meel, et al.[8] documented *S. aureus* dominance in a Gauteng cohort with a high prevalence of IV drug use, reflecting an epidemiologic shift linked to evolving risk factors. A retrospective analysis from the Western Cape (2017–2018) similarly found *S. aureus* in 43% of culture-positive cases, reflecting a move away from viridans streptococci toward staphylococcal predominance.[1] Consequently, empiric antibiotic regimens for IE now routinely include anti-staphylococcal coverage.[11]

Prosthetic valve endocarditis (PVE) accounts for approximately 13–16% of IE cases in South Africa and is associated with significantly higher morbidity and mortality than native valve endocarditis (NVE).[13] Mkoko, et al.[13] reported that 13.3% of cases were PVE, half of which occurred within 1 year of valve surgery in the Groote Schuur IE registry (2017–2019). Moreover, these patients had notably higher rates of septic shock (22.2% vs. 7%) and heart block (27.8% vs. 12%) compared with NVE. *Staphylococcus* (38.9%) and *Streptococcus* spp. (22.2%) were the most frequent pathogens, with 27.8% being culture negative. In-hospital mortality for PVE was high at 55.6%, compared with 31.6% for NVE. These distinctions highlight the unique microbiological patterns, clinical challenges, and management requirements for PVE in the South African setting.

The high incidence of BCNIE continues to be a problem. Despite this, the addition of routine serological and surgical specimen analysis has proven to increase the detection of a causative pathogen.[11] A recent study conducted in the Western Cape identified *Bartonella* spp. as a common cause of BCNIE, contrasting with developed countries where *Coxiella burnetii* is more common.[14,15] BCNIE is associated with worse outcomes, but more recent reports found similar mortality rates between BCPIE and BCNIE.[1]

ORAL STEP-DOWN ANTIBIOTIC THERAPY: GLOBAL EVIDENCE

Historical context: the rationale for intravenous treatment

Before the discovery of antimicrobial therapy, IE was considered almost universally fatal, with mortality rates approaching 99%.[5] The introduction of sulphonamides in the mid-1930s marked the beginning of oral antibiotic therapy, followed by the development of oral tetracyclines and macrolides in the late 1940s and early 1950s.[16] Despite initial promise, these early oral agents were ineffective in treating IE.[16] The discovery of IV penicillin in the 1940s was a major therapeutic breakthrough, significantly improving survival and achieving cure rates as high as 85%.[16] Although oral formulations of penicillin soon became available, they were considered unreliable for treating IE due to concerns regarding subtherapeutic blood and tissue concentrations, as well as the poor clinical outcomes associated with other oral antibiotics.[5] As a result, prolonged IV therapy became the standard of care for IE.

Re-emergence of interest in oral therapy

In retrospect, the limited efficacy observed with early oral regimens was likely attributable to the intrinsic limitations of the antimicrobial agents themselves, rather than the route of administration. Advances in pharmacokinetics have demonstrated

TABLE I: Summary of key clinical studies supporting oral step-down therapy in infective endocarditis.

Study	Design (*n*)	Population/ pathogens	Inclusion criteria for step-down	Oral regimens used	Key findings
Stamboulian, et al. (1991)	RCT (**n** = 30)	Left-sided streptococcal IE	Completed 2 weeks IV ceftriaxone	Oral amoxicillin × 2 weeks	100% cure in both arms at 3–6 months, reduced length of hospital stay.
Heldman, et al. (1996)	RCT (**n** = 85)	Right-sided ***S. aureus*** IE; IVDU	Febrile, IVDU	Oral ciprofloxacin + rifampicin	Comparable efficacy, reduced adverse drug reactions.
Mzabi, et al. (2016)	Observational (**n** = 426)	Mixed IE (left/ right); ***Streptococcus***, ***E. faecalis***, ***S. aureus***	Completed 7 days IV, stable clinical/lab parameters, negative blood cultures	Amoxicillin, clindamycin, fluoroquinolone, rifampicin	Similar mortality and relapse rate.
Tissot-Dupont, et al. (2019)	Observational (**n** = 341)	***S. aureus*** IE	Completed 7 days IV co-trimoxazole + clindamycin	High dose co-trimoxazole × 5 weeks	Reduced length of hospital stay and mortality rate.
POET trial (Iversen, et al., [2019])	RCT (**n** = 400)	Left-sided IE (***Streptococcus***, ***S. aureus***, ***E. faecalis***, CNS)	≥ 10 days IV, stable, afebrile ≥ 48 hours, CRP ↓, no surgical indication	Amoxicillin, moxifloxacin, fusidic acid, linezolid, rifampin, dicloxacillin (dual therapy)	Oral step-down non-inferior.

CNS: coagulase-negative staphylococci, CRP: C-reactive protein, E. faecalis: Enterococcus faecalis, IE: infective endocarditis, IV: intravenous, IVDU: intravenous drug use, n: number, RCT: randomised controlled trial, S. aureus: Staphylococcus aureus.

that several modern oral antibiotics can achieve blood concentrations comparable to those attained with IV formulations.[17] In keeping with these findings, RCTs have proven that adequate dosing of oral antibiotics can effectively clear bacteraemia in patients with IE.[5] Oral step-down therapy involves initiating treatment with IV antibiotics until the patient reaches clinical stability, followed by a switch to appropriate oral antibiotics.[3]

Research supporting oral step-down therapy in infective endocarditis

Spellberg, et al.[5] identified 21 observational studies and 3 RCTs supporting the use of oral step-down therapy in selected patients with IE (Table I). These studies reported similar cure rates across IV-only and oral step-down regimens, and an overall lower mortality in the oral groups. However, limitations include heterogeneity in lead-in duration (ranging from 0 to 24 days), variations in antibiotic protocols, and underrepresentation of methicillin-resistant *S. aureus* (MRSA) cases and IV drug users.[5] Among these studies, the retrospective analysis by Mzabi, et al.[18] reviewed 426 IE patients (214 switched to oral vs. 212 managed with IV only). They found similar mortality and relapse rates in the oral step-down cohort.[18] However, as a non-randomised study, differences in baseline comorbidities and illness severity may have influenced their outcomes, and follow-up intervals were not standardised, challenging the reliability of relapse comparisons.

In 2019, Tissot-Dupont, et al.[19] evaluated the efficacy of a switch to oral antibiotics on day 7 in patients with *S. aureus* IE. The study implemented a pre–post design involving 341 consecutive patients with *S. aureus* IE; 170 received standard IV therapy, and a subsequent cohort of 171 were managed with a protocol switch (IV co-trimoxazole and clindamycin for 1 week, followed by 5 weeks of high-dose oral co-trimoxazole).[19] The oral group demonstrated reduced 30-day mortality (7% vs. 14%) and lower long-term mortality (19% vs. 30%). Limitations include its non-randomised design and a lack of MRSA-specific data.

The first RCT evaluating oral step-down therapy in IE was conducted in 1991 by Stamboulian, et al.[20] In their trial, 30 patients with penicillin-susceptible streptococcal endocarditis were randomised to receive either 4 weeks of IV ceftriaxone or 2 weeks of IV ceftriaxone followed by 2 weeks of oral amoxicillin. All patients were successfully treated for IE, and most were managed as outpatients, avoiding ~ 380 hospital days in total. Limitations include a small sample size and narrow inclusion criteria (only uncomplicated left-sided streptococcal IE).[20]

Heldman, et al.[21] were the first to evaluate exclusive oral antibiotic therapy for IE. In their randomised trial, 85 patients with right-sided *S. aureus* IE were assigned to receive either exclusive IV therapy or an entirely oral antibiotic regimen. Clinical cure rates and mortality were comparable between the two groups, with the oral treatment group experiencing fewer adverse drug reactions.[21] This trial had limited generalisability due to its exclusive focus on right-sided disease in IV drug users, lack of allocation concealment or blinding, and limited representation of MRSA or prosthetic valve infections.

The POET trial remains the largest and most influential RCT on oral step-down therapy in patients with IE. Iversen, et al.[3] enrolled 400 patients with left-sided endocarditis caused by *Streptococcus*, *Enterococcus faecalis*, *S. aureus*, or coagulase-negative staphylococci. After 10 days of IV therapy, patients who met clinical stability criteria and had no surgical indications after transoesophageal echocardiography were randomised to continue IV antibiotics or switch to oral treatment. The trial demonstrated the non-inferiority of oral step-down therapy in terms of a composite primary outcome including all-cause mortality, unplanned cardiac surgery, embolic events, or relapse bacteraemia, even in people requiring surgery or with PVE.[22] Furthermore, follow-up data at 3 and 5 years post-randomisation revealed no evidence of delayed treatment failure in the step-down therapy group.[23] Study limitations include a small percentage of MRSA cases and IV drug users, only left-sided IE caused by specific pathogens, need for therapeutic drug monitoring, use of combination, high-dose oral regimens, and intense follow-up that may not be feasible in all settings. This landmark trial has been pivotal in validating oral step-down therapy as a non-inferior alternative to prolonged IV treatment. It has paved the way for its adoption as a potential new standard of care in appropriately selected patients with IE.

Evidence limitations and remaining gaps

The real-world application of the findings above was evaluated in a nationwide Danish observational study, which confirmed that the use of oral step-down therapy was associated with shorter hospital stays and reduced 6-month mortality, thereby supporting the extrapolation of the POET trial results to routine clinical practice in high-income settings.[24] However, despite the growing body of evidence supporting oral step-down therapy in high-income countries, a paucity of data exists from low- to middle-income countries, where resource constraints, differing epidemiological patterns, educational barriers, and health system challenges may influence the feasibility and safety of this approach.[1,11,25-28]

While the clinical rationale and emerging data supporting oral step-down therapy in IE are promising, it is important to recognise the current limitations of the evidence to avoid overstating its generalisability. The POET trial, the key RCT supporting this approach, enrolled a highly selected group of stable patients with left-sided IE who had received at least 10 days of IV therapy, had undergone transoesophageal echocardiography, and were infected with a limited range of pathogens. Patients with right-sided IE, polymicrobial infections, persistent bacteraemia, or complications requiring surgery were excluded. Thus, while the POET trial demonstrated non-inferiority in this narrow group, it does not establish equivalence across all IE cases. Given these gaps, especially in the South African context where pathogen diversity and healthcare resources differ, further local research is essential to confirm the safety and efficacy of oral step-down therapy before widespread implementation.

CURRENT GUIDELINES AND PRACTICES IN SOUTH AFRICA

Due to limited local data on IE, South African healthcare practitioners often rely on guidelines developed in high-income countries for clinical decision-making, even within resource-constrained settings.[29] The South African Heart Association (SA Heart®) is an affiliated member of the ESC and endorses the ESC clinical practice guidelines, with adaptations to accommodate local healthcare circumstances.[30] However, to date, no South African adaptation of the most recent ESC endocarditis guideline has been developed to support the integration of oral step-down therapy in stable patients. Consequently, patients are often still admitted for 4–6 weeks to complete their IV antibiotic regimens.

IE diagnosis in South Africa is often hampered by limited access to advanced diagnostics, delayed microbiological confirmation, and a high burden of BCNIE.[11] These limitations reduce the sensitivity and specificity of the modified Duke criteria, which form the diagnostic cornerstone in many settings.[31] In response, the International Society for Cardiovascular Infectious Diseases (ISCVID) proposed a revision of these criteria to enhance diagnostic accuracy.[32] Among the key changes is the reclassification of positive *Bartonella* spp. serology as a major microbiological criterion, reflecting its increasingly recognised role in BCNIE. In contrast, the most recent ESC guidelines still classify positive *Bartonella* spp. serology as a minor diagnostic criterion.[4] This discrepancy may contribute to the underdiagnosis of definitive IE in South Africa, where *Bartonella* spp. are recognised as a significant cause of BCNIE.[15] Their identification is further complicated by limited access to serological and molecular diagnostic tools.[33]

Notably, the management of *Bartonella* endocarditis already incorporates an oral step-down component as patients typically receive an initial 2 weeks' IV gentamicin in combination with oral doxycycline, followed by prolonged doxycycline monotherapy.[4,15] More broadly, the use of oral antibiotics in IE is not a new concept in South Africa. As early as 1988, a small prospective study of 15 patients with uncomplicated NVE reported an 87% cure rate using high-dose oral amoxicillin alone, highlighting local precedent for alternative treatment strategies in carefully selected cases.[34]

Potential relevance of oral step-down therapy in South Africa

Oral step-down therapy presents a potentially valuable treatment strategy in the South African context, where prolonged hospitalisation for IV antibiotic therapy places substantial strain on healthcare infrastructure. This approach offers several advantages, including shorter inpatient stays, improved bed availability, reduced healthcare costs, and greater patient autonomy and comfort.[5,35] In resource-limited settings with high inpatient demand and workforce constraints, transitioning the appropriate patients to oral therapy could help alleviate systemic pressures without compromising clinical outcomes.

In addition to operational benefits, partial oral therapy may align with patient preferences, particularly for individuals from rural or underserved areas who face geographic and financial challenges due to prolonged hospitalisation. Reduced hospitalisation may also lower the risk of nosocomial infections and improve quality of life for stable patients.[36] Identifying potential candidates for oral step-down therapy through local implementation research could enable South Africa to safely adopt oral step-down therapy, drawing from international evidence while addressing local health system realities.

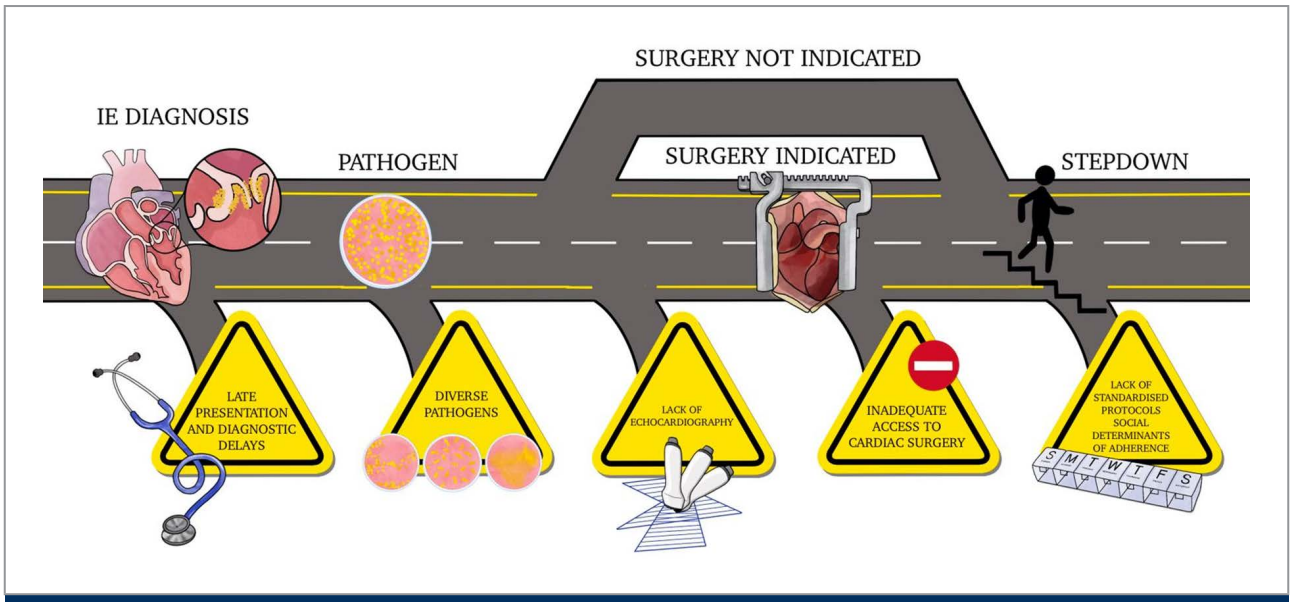

FIGURE 1: Barriers on the road to oral step-down therapy in resource-limited settings (see text for implementation strategies.)
IE: infective endocarditis.

CHALLENGES IN THE SOUTH AFRICAN CONTEXT

Implementing oral step-down therapy in South Africa presents various challenges (Figure 1). The local microbiological landscape is distinct, with a notably high burden of BCNIE, reported to range between 40% and 60% of all IE cases in some South African cohorts.[8,11] As mentioned, *Bartonella* spp. are among the leading causes of BCNIE in this setting.[14] Although TB is highly prevalent in South Africa, TB endocarditis remains rare.[37] Most reported cases are anecdotal or limited to isolated case reports. While TB may occasionally be identified as a cause of BCNIE, it contributes minimally to the overall IE burden in clinical practice. Also, it does not typically fall within the scope of patients considered for oral step-down therapy.

There are currently no reported outbreaks of *Mycoplasma* IE in South Africa. However, the country has experienced significant levels of *Mycoplasma pneumoniae* respiratory infections, particularly among children and individuals living with human immunodeficiency virus (HIV).[38] A cluster of IE cases caused by non-toxigenic *Corynebacterium diphtheriae* was recently reported in the West Coast District of the Western Cape Province.[39] Moreover, outbreaks of brucellosis (*Brucella* spp.) have been reported, particularly affecting livestock in the KwaZulu-Natal Province.[40] While these outbreaks are primarily animal-focused, brucellosis is a recognised cause of IE, particularly in individuals with predisposing factors, such as prosthetic heart valves.[41] These outbreaks highlight the need for heightened awareness and surveillance of these isolates as a potential aetiology of IE, especially in endemic areas and among high-risk populations. The presence of these unique pathogens requires individualised antibiotic regimens, making it difficult to standardise oral step-down therapy protocols.

Access to healthcare services remains a significant barrier to optimal patient management in South Africa, particularly in rural and underserved areas.[28] Patients often struggle to attend follow-up appointments at referral facilities due to long distances, insufficient transportation, and financial limitations.[28,42,43] A study conducted at George Regional Hospital in the Western Cape found that non-attendance rates for outpatient appointments were as high as 40%.[44] In rural communities, the situation is often more pronounced. A study examining travel burdens for children admitted to hospitals in the Western Cape revealed significant disparities in travel distances to healthcare facilities.[45] Some communities had to travel up to 4 times the distance compared with others, highlighting the unequal access to healthcare.[45]

Early surgical intervention for IE patients with a surgical indication significantly reduces mortality and the incidence of cerebral embolism, without increasing the risk of peri-operative complications or infection relapse.[46,47] Despite evidence supporting early surgery, timely access to cardiac surgery remains a significant challenge in South Africa's public healthcare sector, which services more than 80% of the population.[25,48] This is driven by limited operating theatre availability, a shortage of theatre staff, and inadequate intensive care unit (ICU) capacity.[48] These systemic limitations often delay necessary surgeries, making it challenging to adhere to international guidelines.[47]

During these delays, patients are often kept in the hospital on prolonged IV antibiotic therapy. It is important to note that oral step-down therapy is only recommended for clinically stable patients with no surgical indications.[3] As such, patients awaiting cardiac surgery are generally excluded from oral step-down therapy, even if they are otherwise stable. While oral antibiotics can technically be administered in a hospital setting, their use in patients with persistent infection or structural complications requiring surgery is not supported by the current evidence. Consequently, delayed surgical access not only prolongs inpatient IV treatment but also limits the feasibility of implementing oral step-down therapy in a significant proportion of patients in the South African context.

In addition to structural barriers, long-term adherence to oral antibiotic regimens requires attention to multiple factors. While educational attainment can influence a patient's ability to understand treatment instructions, adherence is shaped more broadly by socio-economic status, health literacy, trust in the healthcare system, medication access, and the quality of patient–provider communication. In South Africa, 10.5% of adults aged 25–64 have only completed primary education without formal education, and only one-third have completed Grade 12.[27] Patient support strategies must extend beyond the educational level. Patients in rural settings may also face frequent medicine stockouts and poor access to follow-up care, both of which undermine adherence, regardless of literacy.[26]

These multifactorial challenges emphasise the urgent need for locally feasible and evidence-based strategies to implement oral step-down therapy for IE in South Africa. Interventions must go beyond clinical decision-making and address systemic barriers, such as inadequate access to surgical care, limited outpatient follow-up infrastructure, and the social determinants of adherence. Potential strategies include simplified and standardised oral treatment protocols, enhanced patient education through community health workers, integration of follow-up care into existing chronic disease platforms, and the use of digital tools to support care continuity.

In this regard, local research is critical to guide these adaptations, particularly to define appropriate patient selection criteria, measure outcomes, and evaluate the safety, cost-effectiveness, and acceptability of oral step-down regimens in the diverse South African settings. Investing in local data generation will be essential to inform national guidelines and ensure that this promising strategy can be implemented safely and equitably within the realities of South Africa's healthcare system.

OPPORTUNITIES AND FUTURE DIRECTIONS

While current guidelines recommend a treatment duration of 4–6 weeks for IE, this recommendation is based mainly on

historical practice, with supporting evidence drawn from consensus documents, retrospective studies, and case records.[49] Similarly, the recommendation to treat PVE for 6 weeks is based predominantly on expert opinion.[4] A retrospective review by Morris, et al.[50] investigated the outcome of patients with IE following valve surgery concerning the duration of antibiotic treatment. They found no difference in the relapse rate, regardless of whether patients were treated for 2 or 4 weeks post-surgery, suggesting that shorter antibiotic courses may be sufficient in selected cases.[50] This hypothesis is being tested in ongoing RCTs, such as POET II and SATIE (Shortened Antibiotic Treatment duration for Infective Endocarditis), which aim to evaluate the safety and efficacy of shortened antibiotic regimens in patients with IE.[51]

In keeping with the design of the POET trial, current ESC guidelines recommend combination oral antibiotic regimens for step-down therapy, consisting of 2 antibiotics with different mechanisms of action to ensure adequate concentrations of at least 1 antibiotic.[4] However, there is no evidence that combination oral antibiotic therapy is superior to monotherapy. On the contrary, it may be associated with increased adverse events and cost, and reduced patient adherence.[52] Monotherapy is effective in multiple real-world studies, raising questions about the necessity and long-term role of combination oral antibiotic regimens in step-down therapy.[18,52-55]

Several antibiotics, including linezolid, amoxicillin, rifampicin, moxifloxacin, and fusidic acid, all possess excellent oral bioavailability and tissue penetration, making them well-suited for oral step-down monotherapy in appropriate clinical settings.[52] In addition to its potential for drug–drug interactions, rifampicin should be used with caution in TB-endemic areas, where it remains a cornerstone of first-line TB therapy. Its use outside of standard TB regimens should be reserved for situations where no suitable alternatives exist, to mitigate the risk of selecting for rifampicin-resistant TB strains.[56]

Current ESC guidelines recommend step-down therapy exclusively in cases of left-sided IE caused by select Gram-positive organisms.[4] There is also evidence from small-scale studies supporting oral step-down therapy for uncomplicated right-sided methicillin-sensitive *S. aureus* IE.[57] However, if one accepts the underlying principle that certain oral antibiotics achieve bioavailability comparable to their IV counterparts, oral step-down therapy could theoretically be considered for IE caused by any pathogen, provided the chosen oral agent achieves adequate blood and tissue concentrations, and the patient meets clinical stability criteria.

To evaluate the safety, feasibility, and clinical outcomes of oral step-down therapy in the South African context, local prospective studies are essential. The Tygerberg Oral Antibiotic Step-down Therapy in Infective Endocarditis (TOAST-IE) study, currently underway, is an important first step in this direction. However, multicentre prospective cohorts across provinces will be critical to capture real-world heterogeneity, including patients with BCNIE, varying healthcare access, and comorbid conditions, such as HIV and TB.

There is currently no South African guideline on oral step-down therapy for IE. Developing locally relevant consensus statements or position papers, endorsed by national bodies such as SA Heart® or the National Department of Health, would provide a much-needed framework to support clinicians. These guidelines should incorporate patient selection criteria, antibiotic choices, monitoring protocols, and follow-up pathways, informed by local epidemiology and healthcare realities.

Effective implementation will require healthcare provider training, particularly at district and regional hospitals, in the selection, initiation, and monitoring of oral step-down regimens. In parallel, laboratories must be equipped to perform antibiotic susceptibility testing, therapeutic drug monitoring, and pathogen-specific diagnostics (e.g. *Bartonella* spp. serology). Task-sharing with nurses and community health workers, integration into chronic disease follow-up systems, and the use of mobile health platforms could improve care continuity in patients discharged on oral therapy.

CONCLUSION

This review reveals that many aspects of IE management are based on historical practices and outdated evidence. However, a growing body of high-quality pharmacokinetic, observational, and RCT data now support the efficacy of oral step-down therapy. In the South African context, the implementation of oral step-down therapy necessitates developing locally feasible strategies that account for the unique healthcare challenges and resource constraints. These strategies should include simplified step-down protocols, improved access to healthcare and surgical services, enhanced patient education, and better follow-up systems. Further local research is essential to guide policy and practice in this setting.

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