Key priorities for the implementation of the 2023 ESC guidelines for the management of endocarditis in low-resource settings

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European Heart Journal - Quality of Care and Clinical Outcomes (2025) **11**, 691–697
https://doi.org/10.1093/ehjqcco/qcae106

ORIGINAL ARTICLE

Key priorities for the implementation of the 2023 ESC Guidelines for the management of endocarditis in low-resource settings

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Received 13 November 2024; accepted 13 December 2024; online publish-ahead-of-print 28 March 2025

European Society of Cardiology (ESC) Guidelines provide best practice, evidence-based recommendations for diagnosing and treating patients with cardiovascular diseases. It is not always possible for best practices to be followed, however, particularly in low-resource settings. To address this issue, a set of guideline-related documents were created to identify key priorities for users in these settings. The documents highlight the related recommendations and describe key strategies for clinicians to approach implementation of these recommendations or discuss alternatives which are in line with the intention of the recommendations, if not having all of the same advantages. The suggestions cannot be used as exact substitutes for the original recommendations in the guidelines, which have not been altered and continue to reflect best practice.

This document on key priorities for low-resource settings was developed by the task force chairs and other members of the task force who produced the 2023 ESC Guidelines for the management of endocarditis, which are freely available on the ESC website (https://www.escardio.org/Guidelines). This document also underwent external review including international experts from within and beyond Europe and ESC partner organizations, including the Interamerican Society of Cardiology (IASC), The Pan-African Society of Cardiology (PASCAR), the Asian Pacific Society of Cardiology and the ASEAN Federation of Cardiology.

Keywords Infective endocarditis • Low-resource settings • Recommendations • Antibiotic • Echocardiography • Cardiac implantable electronic device (CIED)

Introduction

Clinical practice guidelines aim to help health professionals with the management of complex clinical conditions via thorough, multidisciplinary evaluation of available medical literature, leading to the generation of recommendations and illustrative figures. However, members of guideline task forces frequently come from high-income countries with good access to modern and sometimes expensive diagnostic and therapeutic modalities, with little emphasis placed on the economic implications of these recommendations. The 2023 European Society of Cardiology

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(ESC) guidelines for the management of infective endocarditis (IE) summarized the evidence and made recommendations for the diagnosis and care of patients with IE,[1] a particularly challenging medical problem due to its uncommon and variable clinical presentations, as well as its high rates of accompanying morbidity and mortality.

It is recognized that the implementation of guideline recommendations varies based on local resource settings at centre, region, and country level.[2] Patients with IE may be particularly challenging to diagnose and treat in low- and middle-income countries (LMIC, as defined by the World Bank Atlas method).[3] Advanced imaging techniques are often required to confirm the diagnosis of IE, and complex cardiac surgical care is frequently indicated. Survey data obtained from national cardiology societies demonstrate that implementation of ESC Guideline recommendations is directly correlated with the gross national income of a country.[2] This is an important observation, since LMICs have a high burden of cardiovascular disease [particularly rheumatic heart disease (RHD)] and limited resources to successfully diagnose and treat IE.[4–7] It has also been demonstrated that quality of care for IE patients within LMICs is lower than in higher income countries.[8] IE patients in LMICs experience delayed diagnoses, increased complications, decreased cardiac surgery rates, and increased mortality rates compared to high income countries.[9] Additionally, wealth distribution within countries may also have an impact on therapeutic outcomes,[6] further exacerbating health inequalities within LMICs.[6] Finally, current guidelines are mostly based on clinical studies performed in high income countries, since LMICs frequently lack the resources to generate their own guideline documents and the evidence generated in those countries is scarce.[4,7]

For all of the above reasons, the current document summarizes key priorities for the management of patients with IE in LMICs based on the 2023 ESC Guidelines for the management of IE.[1] The current document aims to provide health care and allied professionals and patients from LMICs with ways to prioritize and implement some of the most important recommendations from the main document (*Figures 1* and *2*), which should be examined in detail to answer further questions and serve as an accompaniment to the current document. In particular, the topics of IE prevention, early IE diagnosis, and early implementation of adequate antibiotic therapy, as well as cardiac surgery if indicated, are focused on, as the cornerstones of effective and economically viable options to improve outcomes in LMICs.

PRIORITY 1. Increase awareness of the importance of IE prevention.

Awareness of preventative measures should be high amongst health care professionals providing care for and in patients at high and intermediate risk of IE. Prevention includes patient education (e.g. proper oral hygiene, skin hygiene, and early contact with medical services in case of fever without obvious reason) and general prevention measures (e.g. disinfection of wounds, strict infection control measures for any at-risk procedure, and curative antibiotics for any focus of bacterial infection). In addition, efforts should focus on reducing the most prevalent risk factor for IE in LMICs, namely rheumatic heart disease (RHD).[10] Antibiotic prophylaxis for orodental procedures is recommended in high-risk patients, with the most common being those with a history of previous IE and patients who have undergone a previous heart valve procedure. Even though the evidence of the efficacy of antibiotic prophylaxis to prevent IE has been developed mainly in high income countries, there is no reason to consider different recommendations for LMICs.

Relevant recommendations	Class	Level
General prevention measures are recommended in individuals at high and intermediate risk for infective endocarditis.	I	C
Antibiotic prophylaxis is recommended in dental extractions, oral surgery procedures, and procedures requiring manipulation of the gingival or periapical region of the teeth in individuals at high risk for infective endocarditis.	I	B
Periprocedural antibiotic prophylaxis is recommended in patients undergoing surgical or transcatheter implantation of a prosthetic valve, intravascular prosthetic material, or CIED.	I	B

Key strategy for implementation of this priority in low-resource settings

Continuous education, promotion, and advocacy efforts are important to make sure that preventive measures are widely available to the general population. Intermediate risk patients [including patients with RHD, non-rheumatic degenerative valve disease, cardiovascular implanted electronic devices, congenital valve abnormalities (e.g. bicuspid aortic valve), or hypertrophic cardiomyopathy] require preventative measures alone, while high risk patients (e.g. patients with unoperated cyanotic conditions, previous IE, or previous heart valve surgery or transcatheter valve implantation) require antibiotic prophylaxis in addition to preventative measures when exposed to high risk orodental interventions.

PRIORITY 2. Implementation of the endocarditis team and specialty centres.

Establishing multidisciplinary Endocarditis Teams results in earlier and more accurate diagnosis of the primary disease and its complications. Referring Centres should have a functioning Endocarditis Team consisting of at least one cardiologist with a special focus on imaging (i.e. echocardiography) and an infectious disease specialist. In contrast, core Endocarditis Team members in Heart Valve Centres consist of cardiologists, cardiac surgeons, cardiac imaging experts, as well as infectious disease specialists, and microbiologists with knowledge of local epidemiology. In cases with specific clinical questions, adjunct specialties including radiologists, neurologists, critical care specialists etc. should be consulted. Although not all of these listed specialties may be available in some low-resource settings, it is important to designate local clinics and local clinicians with a special interest in IE, since it is an uncommon disease with variable presenting symptoms and a high rate of morbidity and mortality. Such local experts in Referring Centres should be in regular contact with extra-regional Heart Valve Centres in order to obtain medical advice, and to enable rapid transfer of patients with IE who develop complications (e.g. severe valve insufficiency, heart failure, uncontrolled infection, recurrent embolization) which may require surgical intervention. The Heart Valve Centres may be organized at a more central or

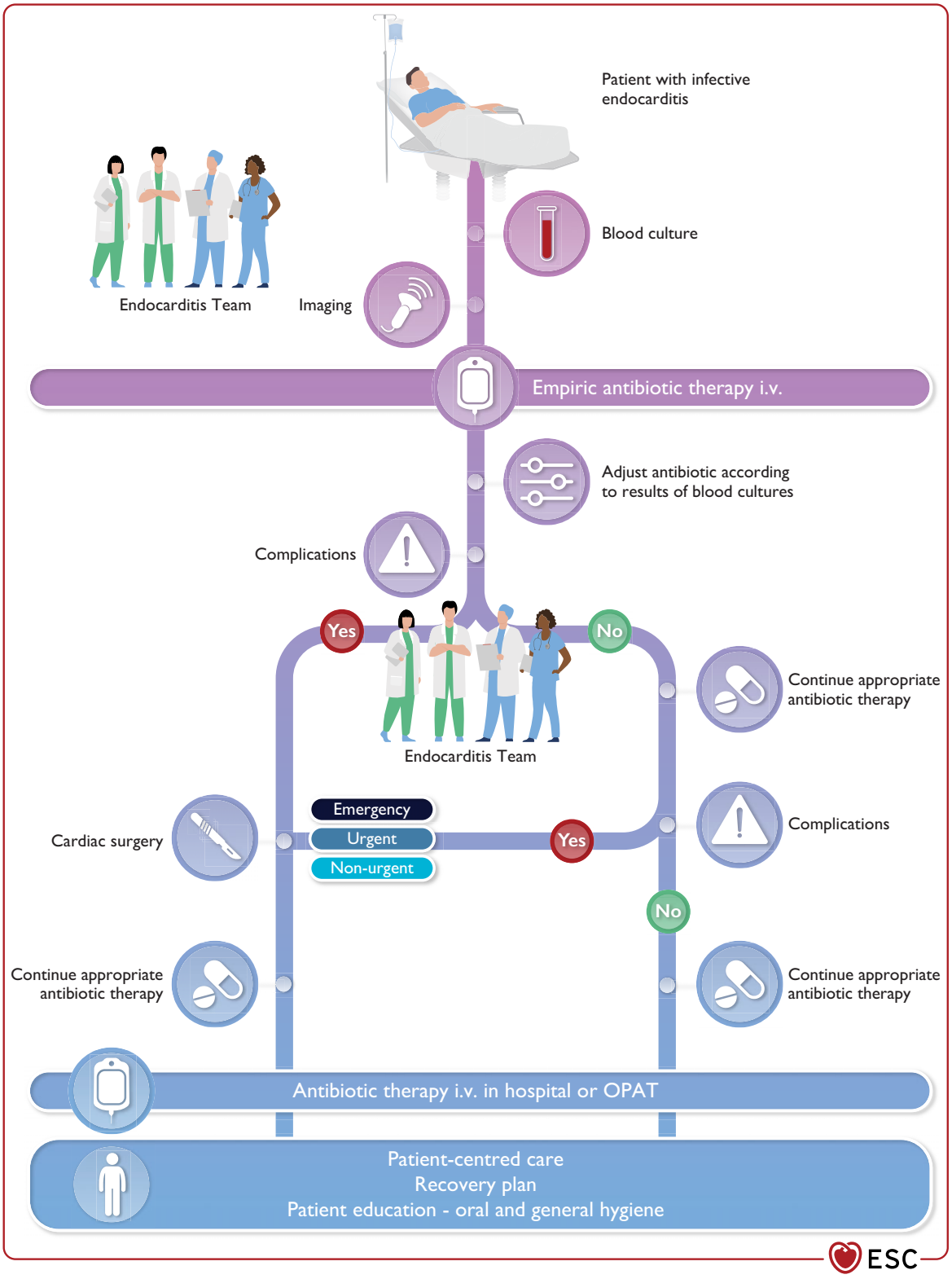

Figure 1 Management of patients with infective endocarditis. i.v., intravenous; OPAT, outpatient parenteral antibiotic therapy. Credit line: Delgado, V. et al. 2023 ESC Guidelines for the management of endocarditis Eur Heart J, Volume 44, Issue 39, Pages 3948–4042, by permission of the European Society of Cardiology.

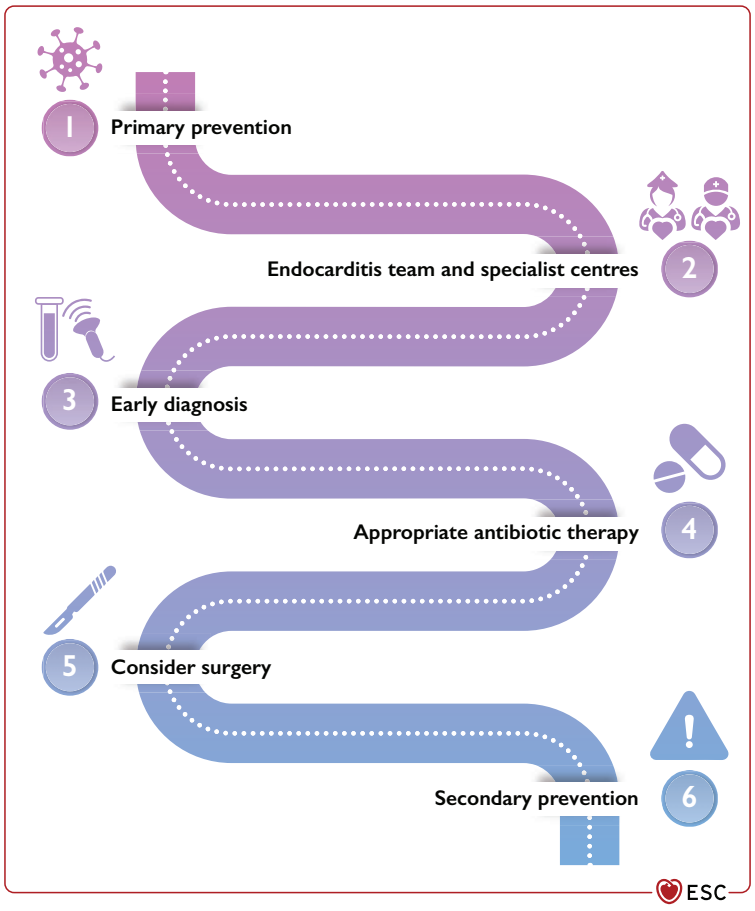

Figure 2 The six key priorities for the implementation of the 2023 ESC Guidelines for the management of endocarditis in low-resource settings.

extra-regional level in LMICs with limited specialist capabilities. However, health care organizers should be encouraged and empowered to develop such Referring and Heart Valve Centres in order to develop local and national expertise and improve patient outcomes.

Relevant recommendation	Class	Level
Diagnosis and management of patients with complicated IE are recommended to be performed at an early stage in a Heart Valve Centre, with immediate surgical facilities and an 'Endocarditis Team' to improve the outcomes.	I	B

Key strategy for implementation of this priority in low-resource settings

Local Endocarditis Teams should be established and IE should be treated using a multidisciplinary approach including all specialists with direct involvement in the diagnostic and therapeutic processes. Heart Valve Centres with advanced cardiac imaging and cardiac surgery capabilities should be implemented within a nationwide strategy for treating patients with complex IE. Digital tools that help to share information between referring and Heart Valve Centres are valuable to further facilitate the communication and earlier transfer of patients to receive appropriate diagnostic tests and treatment, if required.

PRIORITY 3. Early diagnosis of infective endocarditis.

Initial clinical assessment should include evaluation of cardiac and non-cardiac risk factors, supportive clinical context, and physical examination findings including potential bacterial portals of entry. In patients with suspected IE, multiple blood cultures need to be drawn prior to initiation of antibiotic therapy and echocardiography performed. Transthoracic and, when available, transoesophageal echocardiography (TOE) are the

first-line imaging techniques used to diagnose IE. In patients with suspected IE and limited access to advanced cardiac imaging, empirical antibiotic treatment can be commenced without waiting to establish a diagnosis of definite IE.

Relevant recommendations	Class	Level
TTE is recommended as the first-line imaging modality in suspected IE.	I	B
TOE is recommended in all patients with clinical suspicion of IE and negative or non-diagnostic TTE, or when a prosthetic heart valve or an intracardiac device is present.	I	B
Repeating TTE and/or TOE is recommended as soon as a new complication of IE is suspected (new murmur, embolism, persisting fever and bacteraemia, heart failure, abscess, atrioventricular block).	I	B

Key strategy for implementation of this priority in low-resource settings

Patients presenting with symptoms suggestive of IE should be treated at facilities with both microbiological expertise as well as echocardiographic imaging capabilities. Where this is not available, patients should be referred to centres with corresponding capabilities.

PRIORITY 4. Early initiation of appropriate antibiotic therapy.

Identification of the pathogenic microorganisms is crucial for appropriate antibiotic therapy and improves prognosis of patients with IE. The 2023 ESC Guideline on IE management lists several antibiotic options for most common microorganisms and should be consulted for more details.[1] Empirical antibiotic regimens should be implemented prior to identification of the pathogenic microorganism and need to be adapted according to the local microbiological reports, antibiotic response and resistance, and the availability of antibiotics. Local data on the most common microorganisms and antibiotic resistance should also be used to inform antibiotic treatment decisions. Where these antibiotics are not available, local microbiology advice should be sought whilst the recommended antibiotics are sourced. During the early critical phase, patients should be treated with intravenous rapid bactericidal antibiotic combinations and cardiac surgery performed when indicated with the aim of eliminating infected material. After 10 days of appropriate intravenous antibiotic treatment initiation and/or 7 days post-surgery, the antibiotic treatment should be continued to complete 4–6 weeks to eliminate the resting bacteria. During this phase, switching to outpatient parenteral antibiotic treatment or partial oral treatment can be performed in patients with left-sided IE caused by specific microorganisms and if clinical stability is ascertained, which includes the performance of a TOE to exclude new indications for surgery. This shift in antibiotic treatment paradigm was based on the results of the POET trial which was performed in Denmark.[11] Whether the results are reproducible in LMICs needs to be demonstrated.

Relevant recommendation	Class	Level
Outpatient parenteral or oral antibiotic treatment should be considered in patients with left-sided IE caused by *Streptococcus* spp., E. faecalis , *S. aureus*, or CoNS who were receiving appropriate i.v. antibiotic treatment for at least 10 days (or at least 7 days after cardiac surgery), are clinically stable, and who do not show signs of abscess formation or valve abnormalities requiring surgery on TOE.	IIa	A

CoNS, coagulase-negative staphylococci; IE, infective endocarditis; and TOE, transoesophageal echocardiography.

Key strategy for implementation of this priority in low-resource settings

Identification of the pathogenic microorganism should be sought in all patients with suspected or known IE with blood cultures drawn prior to antibiotic initiation. TOE is mandatory to ensure clinical stability prior to switching to outpatient parenteral antibiotic treatment or partial oral treatment.

PRIORITY 5. Consider surgical treatment.

Cardiac surgery is a key component in the management of patients with IE and is indicated in approximately half of those patients, although surgical resources may be sparse in LMICs.[9,12] Cardiac surgery is an integral part of the Endocarditis Team in Heart Valve Centres, and failure to perform surgery in IE patients with a surgical indication is associated with markedly worse survival rates in high and low income settings.[1,13] The main indications for surgery in IE patients include heart failure, local or systemic uncontrolled infection (including resistant or aggressive microorganisms such as *S. aureus*), and prevention of recurrent embolism. Right-sided IE may also require surgical therapy, although the prognosis is generally better than for left-sided IE. Surgical valve repair can be performed in select cases, however, the majority of patients require tissue debridement and heart valve replacement. For patients with CIED-associated endocarditis, complete CIED removal is recommended as conservative treatment is associated with increased mortality. In patients with uninfected left-sided prosthetic heart valves and CIED infection, complete CIED removal combined with prolonged antibiotic therapy may prevent left-sided valve infection.

Timing of surgery for different surgical indications can be found within the main document,[1] with emergent surgery performed within 24 h (regardless of the duration of antibiotic therapy), urgent surgery performed within 3–5 days of diagnosis, and non-urgent surgery performed later than 5 days but within the same hospitalization.

Relevant recommendations	Class	Level
Emergency surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary oedema or cardiogenic shock.	I	B
Urgent surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation or obstruction causing symptoms of heart failure or echocardiographic signs of poor haemodynamic tolerance.	I	B
Urgent surgery is recommended in locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation, prosthetic dehiscence, new atrioventricular block).	I	B
Urgent surgery is recommended in aortic or mitral NVE or PVE with persistent vegetation ≥10 mm after one or more embolic episodes despite appropriate antibiotic therapy.	I	B
Complete system extraction without delay is recommended in patients with definite CIED-related IE under initial empirical antibiotic therapy.	I	B

Key strategy for implementation of this priority in low-resource settings

Establishing cardiac surgery programs and Heart Valve Centres is of utmost importance to improve outcomes in IE patients. Establishing regional centres should be strongly encouraged and capacity development is critical, as all patients will ultimately benefit from this expertise. IE patients with indications for surgery should be treated in a timely fashion.

PRIORITY 6. Reduce recurrences of infective endocarditis.

Patients with previous IE should remain under surveillance for potential long-term complications. The patients should be educated about preventative measures and antibiotic prophylaxis, as well as the importance of immediate medical evaluation if fever, chills, or other signs of infection occur. Good oral health maintenance and advice about skin hygiene are mandatory. All bacterial infections should be treated with timely and curative antibiotic therapy.

Relevant recommendation	Class	Level
Patient education on the risk of recurrence and preventive measures, with emphasis on dental health, and based on the individual risk profile, is recommended during follow-up.	I	C

Key strategy for implementation of this priority in low-resource settings

Patients and their caregivers should be properly informed of their risk of IE recurrence and educated on preventive measures and self-monitoring.

Acknowledgements

Members of the Task Force for the 2023 ESC Guidelines for the management of endocarditis: Haran Burri, Stefano Caselli, Torsten Doenst, Stephane Ederhy, Paola Anna Erba, Dan Foldager, Jan Kovac, Owen I. Miller, Jose M. Miro, Michal Pazdernik, Eduard Quintana, Trine Bernholdt Rasmussen, Arsen D. Ristić, and Josep Rodés-Cabau.

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