

Burden of bradycardia and barriers to accessing bradycardia therapy in underserved countries

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Bradycardia, a condition characterized by an abnormally slow heart rate, poses significant challenges in terms of diagnosis and treatment. While it is a concern world-wide, low- and middle-income countries (LMICs) face substantial barriers in accessing appropriate bradycardia therapy. This article aims to explore the global aetiology and incidence of bradycardia, compare the prevalence and management of the condition in high-income countries versus LMICs, identify the key reasons behind the disparities in access to bradycardia therapy in LMICs, and emphasize the urgent need to address these disparities to ensure equitable healthcare on a global scale.

Introduction

Non-communicable diseases were once considered primarily associated with wealthy or developed countries. However, low- and middle-income countries (LMICs) are now facing a significant burden of these diseases, particularly in relation to cardiovascular disease, which accounts for three-fourths of all cardiovascular deaths in LMICs.¹ Among the various cardiovascular diseases, symptomatic bradycardia, characterized by a slower than normal heart rate, is estimated to affect ~1 in every 1000 individuals, with a higher prevalence in those aged 65 and above.^{2,3} Unfortunately, the lack of data and multiple factors contributing to underdiagnosis make it challenging to fully understand the extent of the bradycardia burden in LMICs. Pacemaker therapy is the most effective treatment for symptomatic bradycardia; however, providing access to this therapy in LMICs poses a significant global health challenge. The cost of devices, limited number of

implanting physicians, geographical isolation from major hospitals, and lack of education and awareness are major obstacles in delivering pacemaker therapy to patients in LMICs who meet the treatment guidelines. In this article, we will briefly discuss the nature of bradycardia, the burden it poses in LMICs, and the challenges associated with providing access to bradycardia therapy in different developing regions.

Bradycardia: what is it?

Bradycardia is typically defined as a slow resting heart rate of less than 60 beats per minute (bpm). However, a cut-off of 50 bpm is often used in studies to account for the fact that a significant portion of the population has a normal, low resting heart rate that falls between 50 and 60 bpm.^{4,5} In a normally functioning heart, the electrical signal that triggers each heartbeat originates in the sinoatrial (SA) node, located in the upper chamber of the heart. From the SA node, the electrical impulse spreads through the atria stimulating them to contract. The signal

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then travels to the atrioventricular (AV) node, which acts as a gatekeeper, delaying the transmission of the signal to the ventricles. This delay allows the atria to fully contract before the ventricles receive the electrical signal and contract themselves. Any disruption in the heart's electrical circuit can lead to bradycardia, which can impair the heart's ability to pump an adequate amount of blood to the rest of the body, potentially leading to symptoms.

There are two main causes of symptomatic bradycardia, sinus node dysfunction (SND) and AV block.¹ Sinus node dysfunction, also known as sick sinus syndrome, occurs when the conduction signal is delayed or slowed due to abnormalities or damage to the cells in the SA node or surrounding tissue. Depending on various factors and comorbidities, SND can become a life-threatening condition if left untreated and may require immediate medical intervention.² Asymptomatic sinus bradycardia does not typically require treatment and is frequently seen in athletes with strong physical fitness.³ While SND derives from SA node dysfunction, AV block typically occurs when the AV node assumes the pacemaker role when either the sinus node rate falls below that of the AV node or the sinus signal is blocked entirely from reaching the AV node.

Symptoms and complications associated with bradycardia can be diverse and include fatigue, presyncope, syncope, dizziness, dyspnoea, fatigue upon exertion, and even cardiac arrest.⁴ However, it is important to note that in many cases bradycardia can be asymptomatic, or symptoms ignored, and thus may go undetected unless diagnosed by use of an electrocardiogram (ECG) or exercise stress test. Additionally, sinus bradycardia may be a symptom of other pathologies, further complicating treatment and diagnosis. In a meta-analysis conducted in 2016 that included 28 studies from 10 different countries, the reported prevalence of a heart rate less than 60 bpm was only 11.2% among patients with syncope.⁵

Bradycardia can be caused by various physiological, pathological, and pharmacological factors.⁶ The most common risk factor associated with developing bradycardia is increased age, as an estimated 75-80% of all pacemaker implants are in individuals older than 65. Advanced age is associated with fibrosis and degenerative changes that can disrupt normal electrical pathways. Moreover, heart diseases such as myocardial infarction, heart failure, and valvular disorders can damage the conduction system and lead to bradycardia. Extrinsic factors that can lead to bradycardia include medications, infectious diseases, electrolyte imbalances (particularly hyperkalaemia), and systemic diseases like hypothyroidism. Bradycardia treatment may involve changes to lifestyle or adjustments to medication, but pacemakers are the only established treatment for patients with symptomatic bradycardia according to both United States and European guidelines and are labelled a class I indication therapy in several scenarios.^{1,7}

Bradycardia incidence and current state of access to care

The prevalence of bradycardia globally varies from 0.5% to 2.0% in the general population.¹ There is not known to be a

difference in the burden of bradycardia disease between high-income countries and LMICs. However, there are fewer studies on AV block and SND incidence compared to other heart arrhythmias like atrial fibrillation (AF), and this is especially true in lower-income countries where data on the incidence of bradycardia becomes even more sparse. Similar to AF, bradyarrhythmia detection should rise with monitoring time and may be a coincidental or subclinical discovery.⁸ Evidence on the underlying prevalence and prognostic relevance of bradyarrhythmias should aid clinical decision-making given increasing heart rhythm monitoring and consumer-led screening.⁹ A world-wide survey of COVID-19-associated arrhythmias revealed that bradyarrhythmia seems to have a higher incidence in Asia (20.5%) than in Europe (10.7%) followed by North (13.6%) and South (8.0%) America.¹⁰ This indicates potential regional variations in the incidence of bradyarrhythmias, which may be influenced by various factors such as population demographics, healthcare practices, and the prevalence of underlying health conditions.

In the United States, sinus dysfunction is the most common cause of bradycardia, where ~50% of pacemaker implants are performed due to SND. However, in many developing countries, heart block is the main cause of bradycardia, with SND accounting for only 5% of cases in some LMICs.^{11,12} This difference may be partially explained by high incidences of infectious diseases in LMICs, which can lead to severe bradycardia. AV conduction abnormalities and arrhythmias are common manifestations of several endemic illnesses in LMICs including Chagas disease, malaria, dengue fever, and rheumatic fever.^{13,14} For example, Chagas disease is estimated to have infected up to 20 million people in Latin America, and one study found that 72% of Latin Americans who received a pacemaker also tested positive for the parasite.^{15,16} These infectious diseases can directly affect the heart's electrical conduction system, leading to bradycardia. However, it is important to note that obtaining a comprehensive understanding of the true severity of untreated symptomatic bradycardia in LMICs is challenging due to the overall lack of data from these countries.

While data is lacking on the incidence of bradycardia for many LMICs, there is available data on the rate of pacemaker implantation in many parts of the world (*Table 1, Figure 1*). Mond *et al.*, through a global survey, estimated the rate of pacemaker implantation across 61 countries.¹⁷ They found that Germany had the highest rate of pacemaker implants per million population with 927, followed by France (782), the United States (767), and Italy (744). Several LMICs have pacemaker implant rates below 100 per million population with the lowest seen in Pakistan (4), Indonesia (2), and Myanmar (2). Furthermore, in a multi-centre study published in 2017, only one in six SND patients received pacemaker implantation in South Asia.¹⁸ However, in some countries this figure is improving. For example, Lee *et al.* reported that in Korea, the rate of pacemaker implantation increased from 5.1 per 100 000 in 2009 to 9.3 per 100 000.¹⁹ Statistics on the use of pacemakers across Africa show a median implant rate of 2.66 per million population across all African countries with available data. No African country had an implant rate above 250 and most had rates <10 (*Figure 1*).^{20,21}

Table 1 Number of pacemaker implant centres and pacemaker implant procedures per million population

Country	Centres per million	Implants per million
Africa & Middle East		
Algeria	0.5	76
Bahrain	1	48
Cameroon	0.1	2
Chad	<0.1	0
Dem. Rep. of the Congo	<0.1	0.4
Egypt	0.4	41
Ghana	0.1	0.6
Iran	0.8	47
Kenya	0.2	7
Niger	0	0
Nigeria	0.1	0.2
Oman	0.3	31
Qatar	0.5	29
Sudan	0.2	13
Uganda	<0.1	0.8
Europe and Central Asia		
Albania	1	44
Armenia	1	42
Azerbaijan	1	19
Kazakhstan	1	131
Kosovo	1	68
Kyrgyzstan	0.3	22
Romania	1	196
Russia	1	266
Turkey	NA	89
Ukraine	1	119
Western Europe	6	831
Americas		
Argentina	15	287
Bolivia	2	64
Brazil	1.7	136
Chile	4	216
Peru	0.4	30
Trinidad/Tobago	2	127
United States	11	767
South Asia & Asia Pacific		
Bangladesh	0.1	4
China	0.6	31
India	0.6	17
Indonesia	0.1	2
Malaysia	1	31
Myanmar	0.1	2
Nepal	0.1	6
Pakistan	0.1	4
Philippines	0.3	7
South Korea	2.2	35
Sri Lanka	0.4	45
Thailand	0.3	30
Vietnam	0.1	8

Implant centres and implant numbers per million population for Africa, Middle East, Americas, South Asia, and Asia Pacific countries adapted from Mond *et al.*¹⁷ or for some African countries from Bonny *et al.*,^{20,21} numbers for Europe and Central Asia taken from Raatikainen *et al.*²² Western Europe: Austria, Belgium, Denmark, France, Germany, Iceland, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Switzerland, United Kingdom.

These data reflect the stark difference in access to therapy in LMICs compared to high-income countries and the significant gap to overcome in order to resolve discrepancies in care.

Barriers to bradycardia therapy access in LMICs

Despite numerous international initiatives aimed at reducing cardiovascular disease in LMICs, there remains a significant lack of attention to cardiac arrhythmias and their associated mortality. The treatment of conduction disorders and the use of device therapy require specialized physician training, a supportive healthcare workforce, and access to cutting-edge technology, which are often not readily available in LMICs. As a result, a large number of patients with bradycardia are underdiagnosed and left untreated, leading to an increased risk of severe symptoms such as syncope, which can result in injury, disability, or even death. Several factors contribute to the limited access to bradycardia care in LMICs. These include underdeveloped healthcare infrastructure, lack of resources, high cost associated with procedures, a shortage of physicians trained in implanting devices, and low levels of patient awareness. It is worth noting that the prominence of these barriers may vary from country to country or region to region. Therefore, it is critical to understand the barriers at a regional or country level before enacting plans to action.

Healthcare infrastructure and resources

Conduction disorders such as SND pose significant challenges in LMICs due to various factors. Access to highly trained physicians, specialized surgical tools, and tailored facilities are limited in these regions, making it difficult to provide adequate care for patients with conduction disorders. An ECG machine is essential for diagnosing arrhythmias, including conduction disorders. However, the high cost of these machines makes them inaccessible to many healthcare centres in developing nations. As a result, either these centres lack ECG machines entirely or they lack the necessary components to operate and maintain them effectively.

The scarcity of specialized cardiac centres and skilled healthcare professionals further exacerbates the challenges in providing care for bradycardia and other conduction disorders. For instance, in Sub-Saharan Africa, there are approximately 0.2 cardiologists per 100 000 population, compared to over 7 per 100 000 in the United States.²³ Outside of general cardiologists, many LMICs further lack specialized electrophysiologists (EPs) or centres with the resources needed to implant cardiac devices. In Africa, the number of implanting physicians per million population is <1, with many countries, including Chad, Togo, Democratic Republic of the Congo, and Niger, either having no access at all or completely relying on philanthropic physician teams.²¹ The Pan-African Society of Cardiology (PASCAR) published a report on cardiac implantable electronic device (CIED)

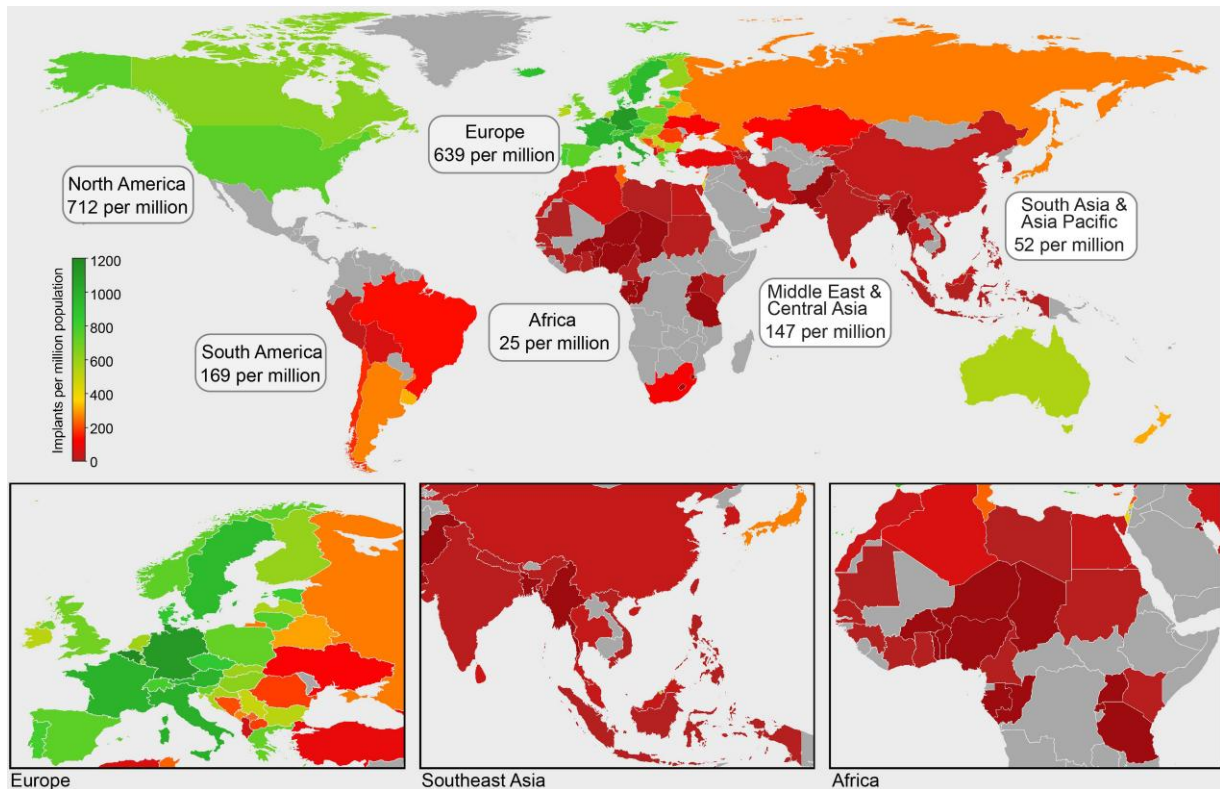


Figure 1 Number of pacemaker implants per million population world-wide. Numbers were derived from either Mond *et al.*,¹⁷ Raatikainen *et al.*,²² or Bonny *et al.*²¹ Countries in grey did not have available data on pacemaker implant rates. Below, from left to right, are zoomed-in images for delineation of countries in Europe, Southeast Asia, and Africa/Middle East, respectively.

and EP procedures in 31 African countries, it revealed that 20% of sub-Saharan Africa lacked the facilities needed for pacemaker implant procedures.²⁰ As a result, humanitarian missions were needed to treat AV block or ensure patients received necessary pacemaker implantations in other countries. Due to these constraints, which are most prominent in African countries, it was found that 50% of patients in the Africa-Pace programme who were recommended for a pacemaker died while waiting for humanitarian missions to arrive.²⁴ The burden of bradycardia can therefore be significantly higher in underserved countries with unnecessary loss of life, highlighting the need for greater investment in healthcare resources to address this issue.

Several countries within Eastern Europe, including Ukraine, Romania, and Kosovo, have lower pacemaker implant volume relative to their neighbors to the west (Figure 1).²² These countries, along with former Soviet countries in Central Asia (e.g. Kazakhstan, Armenia, Azerbaijan), are either recovering from the effects of past communist governments or from the break-up of the Soviet Union. As a result, many former Soviet countries have had to make significant cuts to their healthcare budgets.²⁵ This has created substantial gaps in the primary healthcare system, which, in some of these countries, is still following a Soviet model that relied heavily on poorly trained physicians and unequal distribution of resources between cities and rural areas.^{25,26} Increasing access to quality specialized care, like pacemaker therapy, will require the reversal of

decades-long policies that have had lasting negative impacts on these regions.

Financial constraints

Access to necessary healthcare services is hindered by financial barriers, even in regions where hospitals and trained physicians are available. In LMICs, a significant portion of healthcare expenses is paid out-of-pocket, with more than 60% of health spending falling under this category. In contrast, wealthier countries typically have only 20% of health spending as out-of-pocket expenses.²⁷ Pacemaker devices alone are expensive, and the price increases when adding the cost of the procedure and hospitalization post-implant. This puts a substantial burden on citizens, as exemplified in India where nearly 63 million people are pushed into poverty each year due to healthcare costs.²⁸ Similarly, a survey from Uganda found that over half of individuals had to borrow money to pay for major medical procedures, and 17% lost their jobs as a result of hospitalization.²⁹ The financial burden disproportionately affects those who are not covered by health insurance and who require costly interventions like a pacemaker implant. Thus, the high cost of implant procedures can dissuade individuals from seeking treatment, contributing to decreased pacemaker utilization. This is evidenced by a study in South Asia, where 34% of patients cited excessive cost as the primary reason for not receiving a pacemaker.¹⁸

People in LMICs struggle to afford out-of-pocket healthcare expenses, they are also less likely to have adequate health insurance coverage compared to individuals in wealthier nations. A study conducted by Hooley *et al.* found that the median rate of healthcare coverage in 100 different LMICs was only 31%, whereas it exceeded 70% in European countries.³⁰ Concerningly, they also found that those with health insurance in developing countries did not have a lower rate of catastrophic health expenses compared to those without health insurance, indicating that simply having coverage is not a good measure of progress and that quality health insurance is still absent for many. One of the major reasons for the lack of healthcare coverage in LMICs is the prevalence of informal employment. A substantial portion of the population in these countries engages in informal work, which often does not provide access to formal employment benefits, including health insurance. It is estimated that approximately 93% of all workers in developing nations are engaged in informal employment, with Southeast Asia being particularly affected.³¹

Awareness and physician training

In addition to the low number of implanting facilities and the price deterrent of pacemaker implants, there is also limited public awareness about cardiovascular diseases, including bradycardia, in LMICs. For instance, in Kuwait, less than 40% of survey respondents were able to identify one or more types of cardiovascular disease.³² In another study, Narasimhan *et al.* found that 45% of patients in South Asia did not receive a pacemaker due to patient refusal or deferral of the decision, a number likely enhanced by decreased patient education and awareness.¹⁸ This gap in patient knowledge contributes to delayed medical care, hindering early detection and management of conditions like bradycardia. The IMPROVE Brady trial demonstrated that the rate of pacemaker implantation nearly doubled after providing education materials to patients and physicians.³³

As mentioned, a shortage of trained healthcare professionals, particularly specialized cardiologists and EPs, hampers access to bradycardia therapy. Training programmes for physician specialties, like EPs, are either underdeveloped or not available in most LMICs. As an example, Algeria, Egypt, Lebanon, Tunisia, and Ukraine do not have any official EP certification process or training programmes, and most of the strides in training local EPs in these countries have been spearheaded by medical societies like the European Heart Rhythm Association.³⁴ As such, many physicians end up seeking specialized training abroad yet never return to their home countries due to the higher wages offered in the countries where they train.³⁵ Along these lines, reduced training and education opportunities hinder local physician networking, which can have a negative impact on building referral pipelines from primary care physicians to general cardiologists, and from general cardiologists to EPs. These referral networks are critical to accessing specialized care. This was demonstrated in the Improve Sudden Cardiac Arrest (SCA) Bridge Trial, assessing reasons for refusal of implantable cardioverter-defibrillator (ICD) implants, where 44.3% of patients who

were referred to an EP ended up receiving an ICD compared to just 8.8% of patients who were not referred.³⁶

Geographical and cultural factors

In addition to underdeveloped healthcare systems and training, many regions within developing countries face geographical isolation from healthcare facilities, which are usually located in major cities. Non-existent or deteriorating roads and little to no public transportation make it more difficult for individuals who live in rural areas from reaching cities with the necessary medical care. In rural Nepal, where geographical isolation is a major factor due to its location within the Himalayan Mountain range, patients might have to travel for several hours or days to reach a medical facility with cardiac services.³⁷ Kruk *et al.* found that, in 2016 alone, around 15.6 million preventable deaths occurred in LMICs simply due to a lack of access to quality healthcare.³⁸

Cultural influences can impact clinical decision-making, potentially leading to delayed diagnosis and treatment. A study comparing guideline adherence found that the likelihood of implantation in scenarios of class IIa, class IIb, and class III was significantly higher among Japanese physicians compared to Korean physicians, irrespective of the specific disease entity being considered. These results offer a possible explanation for the relatively low number of pacemaker implantations in Korea as compared to Japan, where Korean physicians demonstrate a comparatively lower preference for pacemaker implantations across diverse clinical case scenarios, as compared to their Japanese counterparts.³⁹ This was also shown in the Improve SCA Bridge Trial where, in South Korea, the most common reason for refusal of an ICD implant was physician preference to continue with medication.⁴⁰

Lack of data

Cardiovascular disorders are the most prevalent non-communicable disease and are especially high in LMICs. However, limited research and data collection on cardiovascular diseases in LMICs hinders evidence-based interventions. Without accurate data, advocating for resources and policies to address bradycardia care becomes challenging. Specifically, the prevalence of AV conduction defects and SND in LMICs remains poorly understood. In a 2016 survey on CIEDs, over 90 countries lacked national databases.⁴¹ This has resulted in limited or incomplete data from LMICs being included in guideline and consensus documents developed by the European Heart Rhythm Association, Heart Rhythm Society, Latin America Heart Rhythm Society, and Cardiac Electrophysiology Society.¹⁷ Similarly, published medical research from LMICs is scant compared to higher-income countries. For example, Latin America has accounted for only 4% of cardiovascular-related articles, compared to 63% from the United States and Europe combined.⁴²

Even when countries do have national registries and data collection, there are major concerns with accuracy. O'Neil *et al.* identified that data-informed decision-making in LMICs can be significantly hindered by poor accuracy, reliability, and thoroughness of the data.⁴³ In several countries, differences in how data was collected for the

same outcome were a major barrier to properly assessing health parameters between, and even within, countries. Poor or incomplete data collection not only prevents local government health officials from properly responding to a health crisis, but also handicaps the ability of outside organizations from identifying pain points in a country's health system and provide aid.

Conclusion

Limited access to reliable bradycardia therapy in underserved countries is a burgeoning, critical global health issue. More funding, research, and advocacy from internal and external sources are needed to develop and implement effective strategies to improve bradycardia treatment access world-wide, where every individual, regardless of location, has an equal right to access quality healthcare. While there are many barriers to access that are shared across most LMICs, each region faces unique challenges, and some obstacles may be more prominent in one region versus another. Thus, the most effective measures will be tailored for the specific country it is intended for. For example, in Africa, the most obvious need is for more healthcare personnel and improved healthcare infrastructure, while in other developing regions progress can be made by focusing on patient awareness or physician training. Lastly, it is important that any efforts are made through the collaboration of multiple organizations (e.g. governments, industry, medical societies, non-profit organizations) working together towards one common goal.

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