




NARRATIVE REVIEW

Early intervention and care for Diabetic Foot Ulcers in Low and Middle Income Countries: Addressing challenges and exploring future strategies: A narrative review

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Abstract

Background and Aims: Diabetic Foot Ulcers (DFUs) are a significant health concern, particularly in Low- and Middle-Income Countries (LMICs). This review explores key strategies for managing DFUs in LMICs, including integrating podiatry, endocrinology, and wound care services, educating patients, promoting self-care, and preventive measures to reduce amputation rates.

Methods: A comprehensive literature review was conducted, focusing on studies conducted in Low and Middle Income Countries to facilitate a qualitative analysis. The review examined the aetiology and risk factors to developing DFUs, clinical presentation, multidisciplinary management and evidence based interventions, challenges to the provision of care and future directions, all pertaining to DFUs in low and middle income countries.

Results: The aetiology and risk factors contributing to the development of DFUs are complex and multifaceted. Factors such as limited access to health care, inadequate diabetes management, and socioeconomic disparities significantly influence the incidence of DFUs. Clinical presentation varies, with patients often presenting at advanced stages of the disease due to delayed or missed diagnoses. Multidisciplinary management, incorporating podiatry, endocrinology, and wound care services, has exhibited substantial promise in enhancing patient outcomes. Evidence-based interventions, including offloading techniques, wound debridement, and the use of advanced wound dressings, have proven effective in promoting ulcer healing.

Conclusion: The burden of DFUs in LMICs requires comprehensive strategies. Integrating podiatry, endocrinology, and wound care services, along with patient education and self-care practices, is essential for reducing amputations

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and improving patients' quality of life. Regular follow-up and early detection are vital for effective DFU management, emphasizing the need for ongoing research and investment in LMIC health care infrastructure. Embracing these multi-disciplinary, patient-centered approaches can effectively address the challenge of DFUs in LMICs, leading to better patient outcomes and improved quality of life.

KEYWORDS

diabetes, foot ulcers, lower and middle-income countries, wound care

1 | INTRODUCTION

Diabetic Foot Ulcers (DFUs) are chronic cutaneous lesions that develop on the feet of individuals afflicted with diabetes mellitus.¹ Early-stage DFUs signify the initial phases of ulcer formation and represent significant complications associated with diabetes, giving rise to considerable morbidity, disability, and mortality.² The aetiology of DFUs stems from a multifactorial interplay involving peripheral neuropathy, peripheral arterial disease, foot deformities, and traumatic events.¹ These ulcers predominantly manifest in weight-bearing regions of the foot and are susceptible to infection, exacerbating wound healing.^{1,2}

In Low and Middle-income Countries (LMICs), managing DFUs presents unique challenges due to resource constraints, inadequate health care infrastructure, and a higher prevalence of risk factors associated with foot ulcer development.^{3,4} LMICs often face a scarcity of health care professionals trained in diabetic foot care, limited availability of specialized wound care products, and financial constraints that limit access to comprehensive treatment.³⁻⁵ Consequently, DFUs in LMICs are often diagnosed at advanced stages, leading to more complex wounds and an elevated risk of amputation and mortality.^{4,6,7}

The management of early DFUs is crucial to preventing complications and improving patient outcomes. Early detection and intervention can significantly improve wound healing, reduce the need for amputation, and improve the quality of life for individuals with DFUs.^{4,6,7} However, the management strategies employed in LMICs for early DFUs may differ from those in high-income countries (HICs) due to resource constraints and other contextual factors.⁵

Moreover, the evaluation of early DFU management outcomes in LMICs holds paramount importance in appraising the efficacy of existing strategies and pinpointing areas necessitating enhancement. Patient-centric outcomes, encompassing wound healing rates, amputation incidence, quality of life, and health care resource utilization, offer invaluable insights into the effectiveness of management approaches.²⁻⁷

Furthermore, a comprehensive discussion of the economic ramifications of early DFU management assumes significance in

emphasizing potential cost savings linked to efficacious interventions and advocating for reasonable resource allocation.

2 | METHODOLOGY

This narrative review endeavors to establish a comprehensive framework for early intervention and care of DFUs in LMICs as categorized by the World Bank Income Groups. LMIC classification is based on Gross National Income (GNI) per capita, denominated in United States Dollars (USD), calculated using conversion factors derived from the Atlas method. The countries falling within these income groups are subject to annual updates. To ensure a rigorous and all-encompassing approach, specific inclusion and exclusion criteria were meticulously applied.

The inclusion criteria for this review encompassed full-text articles composed in English with no specific time frame of published studies. To ensure a comprehensive literature review, multiple databases, including PubMed, EMBASE, Google Scholar, the Cochrane Library, and Scopus, were utilized.

Key terms such as "Early Intervention," "DFUs," "Care," and "LMICs" were used in combination with additional terms relevant to the topic, such as "Challenges," "Strategies," "Intervention Programs," and "LMIC Health care." This approach ensured that relevant articles addressing early intervention, care, and future strategies for DFUs in LMICs were included in the review.

Consequently, the review incorporated descriptive studies, intervention studies, cohort studies, and observational studies, providing a holistic perspective on early intervention and care for DFUs in LMICs. The inclusion of investigations conducted in both clinical and community health care settings further contributed to the breadth of knowledge covered in this review. Standalone abstracts, case reports, posters, and unpublished or nonpeer-reviewed studies were excluded. By adopting these exclusion criteria, the review aimed to prioritize the inclusion of high-quality and reliable evidence.

A summary of the methodology employed is presented in Table 1.

TABLE 1 Summary of the methodology employed in the drafting of this review.

Methodology steps	Description
Literature search	PubMed, EMBASE, Google Scholar, the Cochrane Library, SCOPUS
Inclusion criteria	Full-text articles published in English with no specific date limit. Various study designs, such as observational, case-control, cohort, cross-sectional, and randomized controlled trials. Studies conducted in countries defined as LMICs by the World Bank Income Group, based on Gross National Income (GNI) per capita, denominated in United States Dollars (USD). Studies addressing DFU
Exclusion criteria	Stand-alone abstracts and unpublished studies. Non English Studies Case Reports
Search terms	Key terms such as “Early Intervention,” “DFUs,” “Care,” and “LMICs” were used. Additional search terms included “Challenges,” “Strategies,” “Intervention Programs,” and “LMIC Health care.”
Additional search	A manual search was conducted to find references for recently published, procedure-specific reviews.
Sample size requirement	No strict sample size requirement

3 | DFUS IN LMICs: AETIOLOGY AND RISK FACTORS, PATHOPHYSIOLOGY AND CLINICAL PRESENTATION

3.1 | Aetiology and risk factors

While the pathophysiological markers of risk underlying the emergence of DFUs remain consistent across both LMICs and HICs, involving the development of diabetic peripheral neuropathy, peripheral arterial disease, and trauma, in addition to an array of contributory factors like diabetes duration, suboptimal glycemic control, diabetic retinopathy or nephropathy, noncompliance with medical directives, and negligent behavior, recent studies have shed light on the significance of LMIC-specific contextual risk factors.⁸ For instance, a multitude of investigations have established statistical associations between socioeconomic determinants, such as low socioeconomic status, poverty levels, reduced access to health care services, and lower educational attainment—factors more pertinent to LMICs—to be linked to a heightened prevalence of DFUs.^{9,10}

Delving further into the subject, the genesis of DFUs in LMICs emerges from a convergence of factors, including inadequate foot care practices, limited awareness of diabetes and foot care, and a confluence of other risk factors.^{8,11,12} Notably, inadequate adherence to appropriate foot care practices and a dearth of awareness regarding diabetes and foot care loom as central contributors to DFU prevalence in LMICs.^{8,11,13,14} For instance, research in India unveiled a disconcertingly low adherence rate, with a mere 16% of diabetic patients adhering to recommended foot care practices, including regular inspection, cleaning, and moisturization.¹¹ Similarly, a study in a rural population in Bangladesh highlighted the substantial influence of inadequate patient education, contributing to a high DFU prevalence rate of 45.5%.⁸ Additionally, investigations among the

Iranian population with type 2 diabetes mellitus underscored a significant knowledge deficit, with 60% unaware of the crucial importance of adequate foot care.¹⁵

Risk factors, including ill-fitting footwear, walking barefoot outdoors, infrequent foot washing, and limited access to suitable footwear, exacerbate the development of foot ulcers among individuals with diabetes in LMICs.^{8,11,15–18} These risk factors, coupled with a lack of awareness and inadequate foot care practices, significantly augment the susceptibility to foot ulcers in LMICs.

3.2 | Biopsychosocial analysis of DFUs and its relationship to LMICs

The pathophysiology of DFUs emanates from the presence of diabetes mellitus, a chronic metabolic disorder characterized by elevated blood sugar levels. Poorly controlled diabetes mellitus significantly contributes to the development of foot ulcers.^{19–21} Chronic hyperglycemia, the persistent elevation of blood glucose levels, instigates systemic changes in the body, including microvascular and macrovascular complications.^{20,21} Peripheral neuropathy, a prominent complication associated with chronic hyperglycemia, affects more than half of the diabetic population.²¹ It involves damage to the peripheral nerves, impacting sensory, motor, and autonomic functions. Notably, the loss of protective sensation in the feet, a characteristic feature of peripheral neuropathy, diminishes individuals' awareness of pain or discomfort.^{20,21} As a result, individuals may unknowingly subject their feet to trauma, repetitive injuries, or prolonged pressure, exacerbating existing damage. Prolonged trauma or pressure on the feet can eventually lead to skin breakdown, such as blisters, calluses, or abrasions, increasing the risk of developing foot ulcers.

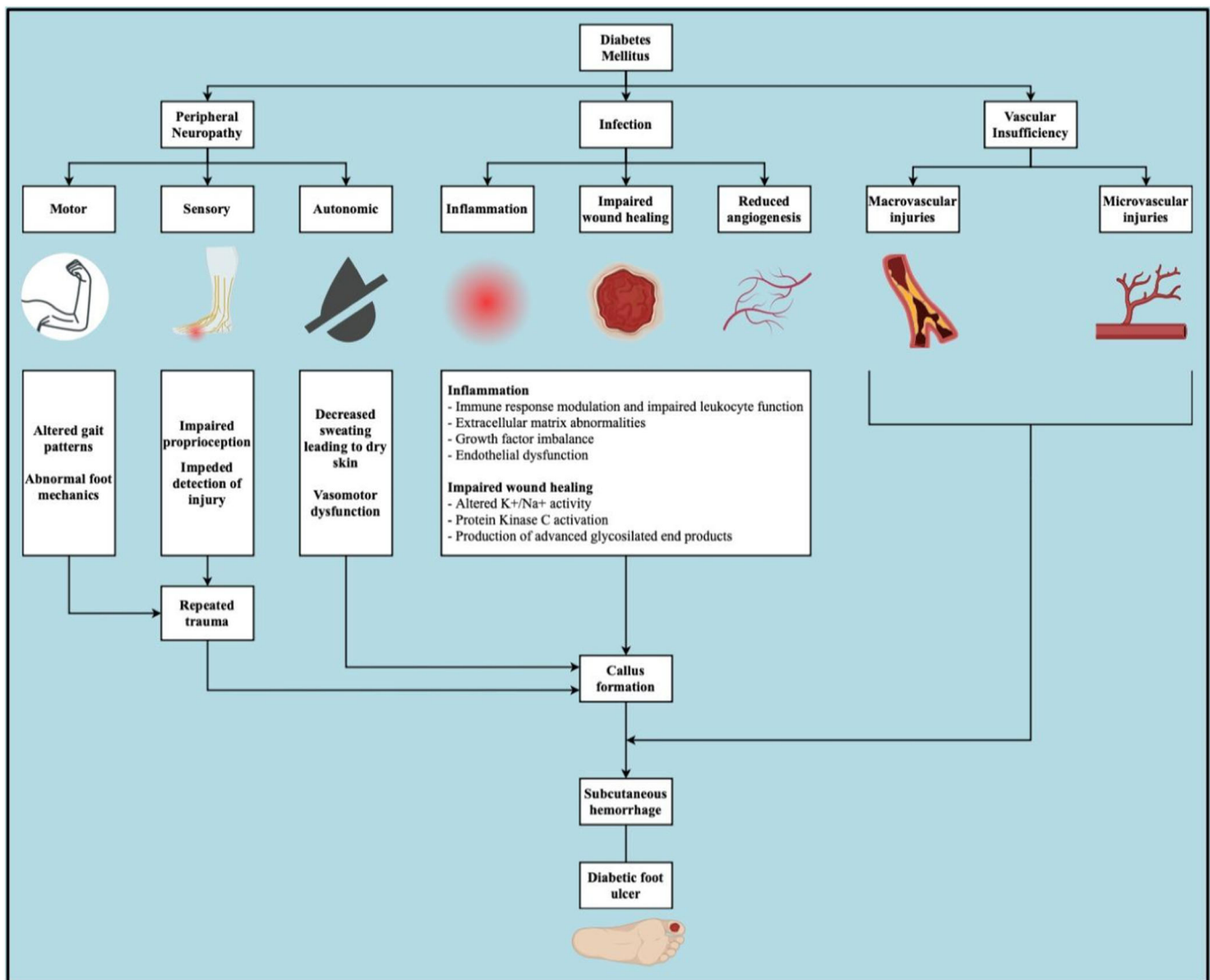


FIGURE 1 Pathophysiology of DFUs. (Created with [Biorender.com](https://www.biorender.com)). DFU, Diabetic Foot Ulcer.

Furthermore, once a breach in the skin occurs, it becomes vulnerable to bacterial infection, further hindering wound healing and potentially promoting the spread of infection.²² Impaired wound healing is a defining characteristic of DFUs, primarily attributed to reduced blood flow, impaired angiogenesis, and dysfunctional inflammatory responses in individuals with diabetes mellitus.²³ These factors allow foot ulcers to progress and become chronic, nonhealing wounds. The inadequate management of underlying factors, such as uncontrolled diabetes and peripheral neuropathy, perpetuates this cycle, resulting in recurrent foot ulcers and an elevated risk of complications.^{24,25}

From a biopsychosocial perspective, various contextual factors unique to LMICs appear to significantly exacerbate and accelerate the progression of DFUs among individuals with diabetes. Extensive research consistently demonstrates that social deprivation, notably prevalent in LMICs, exhibits a robust association with suboptimal glycemic control and heightened cardiovascular-diabetic morbidities. Social deprivation, in turn, contributes to an elevated incidence of

DFUs in such settings.²⁶ Inadequate hygiene practices encompass ill-fitting footwear, walking barefoot outdoors, infrequent foot washing, and limited access to appropriate footwear within these regions. Such practices increase the risk of hardening and skin scraping, leading to an increased predisposition to infections.^{8,11,16} In addition, challenges to the access of hypoglycemic medications and barriers to accessing cardiovascular care compound the further progression of diabetic complications, such as DFUs, in such environments.²⁷ A pictographical analysis of the pathophysiology of DFUs has been provided in Figure 1.

3.3 | Clinical presentation and complications of DFUs in LMICs

A profound comprehension of the clinical manifestation and concomitant complexities of DFUs stands as an imperative prerequisite for their efficacious management, particularly in LMICs. In

LMICs, DFUs typically manifest as a composite of peripheral neuropathy, vascular insufficiency, and concurrent infections.²⁸ Further studies have also revealed a predominant presentation of nonhealing ulcers accompanied by indications of infection, pain, and a history of prior ulcers among most patients in this context.²⁹ These patterns have consistently emerged across multiple LMICs.^{4,7,30} Multi-faceted factors, including limited access to health care resources, inadequate diabetes management, socioeconomic disparities, and suboptimal health care infrastructure contribute to the acute presentation of DFUs in LMICs.³¹ The complications stemming from DFUs in LMICs are notably multifaceted, with infections such as cellulitis, osteomyelitis, and gangrene frequently encountered. Significantly, these complications tend to progress swiftly due to delayed diagnosis and treatment.^{4,7,30}

Furthermore, it is noteworthy that patients afflicted with DFUs in LMICs often delay seeking medical attention until the disease has progressed to advanced stages.^{4,7} This delay exacerbates the clinical presentation and leads to worse outcomes. Understanding the unique clinical characteristics of DFUs in LMICs is paramount for health care providers and policymakers, as it necessitates the development of tailored interventions to alleviate the burden of diabetic foot complications in these regions.

4 | IMPORTANCE OF EARLY INTERVENTION AND ADEQUATE CARE OF DFU; EVIDENCE FROM VARIOUS LMICS

4.1 | Early identification and diagnosis

Early identification and diagnosis of DFUs constitute critical measures for preventing complications and enhancing patient outcomes. A body of research has underscored the adverse consequences associated with delayed diagnosis, including an elevated risk of infection, amputation, and mortality.^{4-7,32-34} Within LMICs, investigations have consistently demonstrated that early identification of DFUs confers numerous advantages, encompassing higher healing rates, reduced amputation frequencies, decreased health care expenditures, and enhanced overall quality of life for affected individuals.⁴⁻⁷

The contrast in mortality rates between LMICs and HICs further underscores the significance of early identification. Mortality rates are markedly lower in HICs, where DFUs are diagnosed promptly, and mortality rates are markedly lower; for instance, research conducted in Manchester, England, and the USA reports mortality rates of 4% and 2%, respectively.^{35,36} In contrast, LMICs, where DFUs have historically been diagnosed at later stages, exhibit higher mortality rates, such as 14% in Benin (Southern Nigeria) and 10.7% in Indonesia.^{32,37} In light of these findings, health care professionals should accord paramount importance to timely diagnosis and institute systematic screening programs targeting at-risk individuals. Timely diagnosis not only serves to avert severe complications and reduce health care burdens but also substantiates its role as a

crucial determinant of mortality disparities observed between LMICs and HICs.

4.2 | Multidisciplinary approach to DFU management

DFUs are a common and severe complication of diabetes, particularly in LMICs, where access to adequate care may be limited. Implementing a multidisciplinary approach to DFU management is crucial for improving patient outcomes and reducing the burden of lower extremity amputations (LEAs). Collaborative efforts between different specialties and health care professionals are essential for providing comprehensive care and addressing the complex needs of patients with DFUs.

4.2.1 | Role of various health care professionals

A collaborative and multidisciplinary approach involving various health care professionals is crucial in the management of DFUs in LMICs. By working together, these professionals can provide comprehensive care, address the complex needs of patients, and improve patient outcomes.

Integrated foot care programs that bring together podiatrists, endocrinologists, and wound care specialists have shown effectiveness in LMICs. These programs have included regular foot examinations, patient education on foot hygiene and self-care, comprehensive wound care, and coordinated management of diabetes-related factors.^{38,39} By integrating these different specialties, patients received holistic care that targeted both the underlying diabetes management and the specific needs of their foot ulcers.

To support the implementation of integrated foot care programs, it is essential to focus on training and capacity-building for health care professionals. Providing specialized training to primary care physicians, nurses, and other health care providers in DFU management has been shown to improve their knowledge and skills in wound care, reducing the burden on specialized care.⁴⁰ LMICs can develop a strong workforce capable of addressing the growing DFU burden by improving the skills and expertise of health care professionals.

Community engagement and patient empowerment are crucial aspects of DFU management, as demonstrated by studies. It has been shown that a significant number of DFUs occur among the rural population due to a lack of awareness and insufficient patient education.^{8,11} These findings emphasize the importance of education and awareness in preventing and managing DFUs. Community-based programs that raise awareness about foot care, diabetes management, and the early signs of DFUs have demonstrated positive outcomes in LMICs. Empowering patients through education on self-care, regular foot examinations, and prompt reporting of abnormalities can contribute to early detection and timely intervention, thus reducing the risk of complications.³⁹ By involving the community and

empowering patients, health care professionals can work with patients as active partners in their care.

Therefore, a collaborative and multidisciplinary approach involving podiatrists, endocrinologists, wound care specialists, primary care physicians, nurses, and other health care professionals is essential for effective DFU management in LMICs. By integrating these specialties, providing training and capacity building, engaging the community, and empowering patients, health care systems can improve patient outcomes, reduce the burden of amputations, and promote better overall care for individuals with DFUs.

4.2.2 | Integration of podiatry, endocrinology, and wound care

Integrating podiatry, endocrinology, and wound care services has shown promising results in LMICs. Studies conducted have revealed that this integrated approach resulted in improved patient outcomes in terms of reduced amputation rates and an increase in limb salvage by enabling early risk factor identification, timely interventions, and comprehensive management of DFUs.⁴¹

Health care professionals in podiatry, endocrinology, and wound care play vital roles in managing DFUs. Podiatrists provide comprehensive foot care services, including assessment, prevention, and treatment. Their involvement has consistently shown significant contributions to DFU management. Studies in LMIC settings have demonstrated that involving podiatrists in DFU care significantly reduces amputation rates, promotes faster wound healing, and reduces hospitalization rates.^{4,7,42} Furthermore, the inclusion of podiatrists in multidisciplinary foot care teams has led to a 56–85% reduction in major amputations.⁴³ Their responsibilities include assessing foot complications, conducting regular foot examinations, providing appropriate footwear, and educating patients on foot care practices.

Endocrinologists specialize in managing diabetes, a critical factor in the development and progression of DFUs. Their expertise in glycemic control and diabetes-related complications is invaluable in DFU management. Studies conducted in LMIC contexts have shown that patients receiving care from endocrinologists have better glycemic control, lower DFU recurrence rates, and a reduced risk of foot ulcers.⁴⁴ Endocrinologists contribute by optimizing blood glucose control, managing comorbidities, and providing medication guidance to promote wound healing. Wound care specialists, such as wound care nurses, also play a critical role in managing DFUs. They assess wound severity, implement evidence-based wound care protocols, and monitor wound healing progress. Their early assessment and appropriate wound care significantly reduced the risk of infection and amputation.⁴³

4.3 | Evidence-based interventions for DFUs

Early intervention and adequate care are crucial to preventing DFUs from progressing to severe infections, gangrene, and amputations.

Several evidence-based interventions have shown effectiveness in LMICs and involve a multidisciplinary approach with health care professionals from different specialties. The following key interventions have been shown to be beneficial.

4.3.1 | Wound dressings

Wound dressings are essential for promoting a healthy wound environment, enhancing healing, and providing antimicrobial properties in the management of DFUs. In cases where DFUs are infected, timely initiation of appropriate antibiotic therapy is crucial to controlling and eradicating the infection. A study conducted in a tertiary hospital in Pakistan demonstrated that oral antibiotics, when administered promptly, improved wound healing, reduced infection rates, and minimized the need for amputation.⁴⁵

Research conducted in LMICs has delved into the efficacy of various wound dressings for treating DFUs. These investigations have shed light on the advantages of honey-based dressings over conventional alternatives in promoting wound healing and reducing infection rates. This has provided compelling evidence to support using honey-based dressings for DFUs; unprocessed honey emerged as a particularly effective treatment, demonstrating remarkable improvements in healing nonhealing wounds and ulcers. It has also further reinforced the benefits of honey-based or normal saline dressings over iodine or hydrogen peroxide alternatives. Within the studies, honey-based or saline dressings reduced healing time, lower hospital costs, decreased amputation rates, and mitigated dressing-related irritation, signifying their superiority in DFU management.⁴⁶

4.3.2 | Negative pressure wound therapy (NPWT)

NPWT involves the application of subatmospheric pressure to the wound site, representing a promising intervention for managing DFUs. This innovative technique can potentially expedite wound healing by mitigating oedema, augmenting blood flow, and facilitating the removal of infectious materials. Within the context of LMICs, studies conducted have consistently illustrated the manifold advantages of NPWT compared to conventional wound dressings. Notably, research conducted in Nigeria and India has contributed to the body of evidence supporting the adoption of NPWT for DFUs. These studies have consistently highlighted the tangible benefits of NPWT, which encompass accelerated wound healing, diminished amputation rates, and an overall enhancement in the quality of life for patients undergoing this advanced therapy.^{47,48} These compelling findings underscore the imperative of making NPWT accessible and readily available within LMICs, as this advanced therapeutic approach has the potential to significantly augment treatment outcomes for individuals grappling with the challenging complexities of DFUs. Consequently, expanding the utilization of NPWT in LMICs represents a vital step towards improving the management and prognosis

of DFUs, ultimately alleviating the burden of this diabetic complication on affected individuals and health care systems.^{47,48}

4.3.3 | Offloading devices

Offloading devices, encompassing total contact casts and removable walkers, play a pivotal role in managing DFUs by effectively reducing pressure on ulcers and facilitating the wound healing process. Within the context of LMICs, pertinent research studies substantiate the significance of offloading devices in enhancing the prognosis of DFUs.

A study on the topic in LMICs represents a seminal contribution; this study unequivocally demonstrated that applying total contact casts significantly reduced the healing time and the incidence of major amputations among Indian patients grappling with DFUs.⁴⁹

Furthermore, another noteworthy study conducted in resource-limited settings within India investigated the cost-effectiveness of offloading DFUs through the use of removable cast walkers. The findings of this study substantiated the merits of this approach, revealing remarkable enhancements in healing rates and a reduction in amputation rates among patients who availed themselves of removable cast walkers in comparison to those relying on traditional footwear or no offloading devices.⁵⁰ These compelling findings underscore the importance of incorporating cost-effective offloading devices into the treatment strategies employed within LMICs. Such devices have the potential to considerably improve treatment outcomes for DFUs, thus mitigating the adverse impact of this debilitating complication in resource-constrained settings.^{49,50} By emphasizing the integration of accessible and efficacious offloading techniques, health care systems in LMICs can enhance the management of DFUs and alleviate the associated burden on patients and health care infrastructure.

4.3.4 | Hyperbaric oxygen therapy (HBOT)

HBOT involves exposing patients to pure oxygen within a pressurized chamber, thereby increasing the oxygen supply to the wound area. A study conducted in Egypt investigated the efficacy of HBOT for DFUs and reported significantly improved healing rates and reduced amputation rates in patients who received HBOT compared to those who received standard care alone.⁵¹

Similarly, a systematic review and meta-analysis indicated that HBOT yielded significant benefits for treating DFUs. The HBOT group exhibited a higher rate of complete healing of DFUs (62%) and lower major amputation rates (24%).⁵² The study concluded that a regimen of 40 HBOT sessions is necessary to reduce major and minor amputation rates.⁵² These findings collectively suggest that HBOT could represent a valuable intervention for managing DFUs within the context of LMICs. The demonstrated improvements in healing rates and reduced amputation rates underscore the potential of HBOT to enhance the outcomes of DFU treatment in

resource-constrained settings. As such, incorporating HBOT into the armamentarium of interventions for DFUs in LMICs merits consideration as a means to alleviate the burden of this condition on affected individuals and health care systems.

4.3.5 | Growth factors and bioengineered skin substitutes

Studies have investigated the use of growth factors and bioengineered skin substitutes to promote healing in DFUs. A multicenter trial conducted in a limited resource setting demonstrated that intralesional infiltration of recombinant epidermal growth factor (EGF) significantly improved the healing of Wagner's grade 3 or 4 DFUs. Specifically, dose-specific EGF treatment resulted in a higher rate of granulation tissue coverage, faster wound healing, and increased wound closure compared to placebo. The study reported minimal adverse events.⁵³ These findings suggest that growth factors and bioengineered skin substitutes have the potential to serve as valuable adjuncts to DFU management in LMICs.

4.3.6 | Vascular intervention

Addressing underlying vascular complications is essential to managing DFUs. Revascularization procedures, including angioplasty or bypass surgery, can improve blood flow to the affected foot, promote wound healing, and reduce the risk of amputation. The Asia-Pacific consensus meeting demonstrated that vascular interventions resulted in improved outcomes and reduced rates of major amputation in patients with DFUs.⁵⁴

4.4 | Patient education and self-care practices

Effective patient education and self-care practices are pivotal components in the comprehensive management of DFUs, particularly in the challenging context of LMICs. These practices empower individuals with diabetes to actively prevent and manage DFUs. Key aspects encompass.

4.4.1 | Foot care education

In LMICs, where limited educational resources pose significant challenges, foot care knowledge and foot-health practices among diabetic patients are evidenced to be poor. Studies have revealed a significant association between illiteracy and inadequate foot care knowledge and practices. Educational interventions utilizing visual aids and graphics assisted in promoting literacy and adequate foot care practices. These interventions prove to be highly effective in improving understanding and engagement, particularly among illiterate individuals. Consequently, these initiatives have significantly

reduced DFU incidence and subsequent amputations, underscoring the vital role of patient education in preventing complications.⁵⁵

4.4.2 | Footwear and pressure redistribution

Appropriate footwear and pressure redistribution techniques are essential for preventing DFU formation and reducing the risk of recurrence. In 2015, D-foot International initiated a low-cost, long-lasting, fit-for-purpose footwear project across Pakistan, manufacturing and distributing 20,000 pairs of such shoes.⁵⁶ This noteworthy initiative demonstrated exceptional results, with only a small proportion of at-risk patients developing first or recurrent ulcers during the project's 3-year duration. Moreover, patients at very high risk reported no new amputations, thus illustrating a significant reduction in the incidence of DFUs and foot-related complications. These outcomes highlight the tangible clinical impact of the project and the substantial potential of customized footwear in preventing diabetes-related foot complications in at-risk individuals.⁵⁶

4.4.3 | Regular follow-up and early detection

Consistent follow-up and early detection play pivotal roles in the comprehensive management of DFUs. Recent studies have investigated the significance of early screening for all individuals with diabetes, introducing a comprehensive screening protocol encompassing routine foot examinations, utilization of a state-of-the-art 3D thermal camera-assisted system, and patient education on recognizing the initial signs and symptoms of DFUs. The outcomes of these efforts have yielded compelling results, showcasing a substantial reduction in LEA rates. This underscores the profound positive influence of maintaining regular follow-up appointments and achieving early detection as essential components in addressing the challenge of DFUs within LMICs.³³

5 | CHALLENGES IN DFU MANAGEMENT IN LMICS

5.1 | Lack of awareness and delayed detection

In LMICs, the lack of awareness and delayed detection of DFUs presents substantial challenges in their management. A comprehensive understanding of diabetes and its complications is essential for timely DFU identification. Early detection plays a pivotal role in initiating timely interventions and treatment plans, thereby preventing the exacerbation of ulcers into more severe wounds. Delayed detection, however, leads to an elevated risk of infection, tissue damage, and the necessity for amputation. This situation significantly burdens already strained health care systems, necessitating more extensive and costly interventions.³⁰ The study revealed a consistent pattern of neglect and delayed presentation of DFUs among newly

diagnosed patients with type 2 diabetes mellitus, with DFUs present in 4.54% of newly diagnosed diabetic patients. Comparable patterns of neglect have also been observed in other LMIC populations, including Nigeria and Indonesia.^{32,37,57} This lack of awareness is further evident in studies conducted in northeast India, where knowledge about DFUs was found to be low, resulting in higher incidences of complications.⁵⁸

Multiple factors contribute to this lack of awareness. Firstly, limited access to information, low health literacy, and the high cost of appropriate footwear hinder early detection of DFUs and contribute to delayed presentations. Additionally, the absence of formal education and insufficient health education initiatives in LMICs play a significant role in perpetuating this issue.⁵⁸ Resource constraints and inadequate infrastructure further impede the implementation of educational programs and comprehensive public health campaigns to raise awareness about diabetes, its complications, and preventive measures.

Consequently, an overall lower level of health literacy among individuals hinders their understanding of diabetes-related complications. In some LMICs, limited access to information due to poor English literacy and the absence of culturally appropriate educational materials are additional barriers to raising awareness about DFUs. Financial constraints and the prioritization of immediate needs over preventive health care contribute to delayed health care-seeking behavior and hinder early detection and treatment of DFUs. Furthermore, cultural and social factors, such as a preference for traditional remedies or self-medication, significantly influence health-seeking behaviors and perceptions of illnesses. These factors further contribute to delayed presentations of DFUs in LMICs.^{58,59}

5.2 | Inadequate referral systems

A robust and well-established referral system is essential for the comprehensive and timely management of DFUs, given their multifactorial nature involving vascular, neurological, and metabolic factors. These complexities necessitate the involvement of a multidisciplinary team (MDT) of health care professionals to devise tailored treatment plans, deliver holistic care, and initiate timely interventions, ultimately leading to improved outcomes. Global guidelines have underscored the importance of MDTs in DFU management, as they significantly reduce amputation rates.^{1,60,61}

However, in the context of LMICs, the referral system faces several barriers and unmet needs. Challenges encompass inadequate post-referral management in tertiary facilities, poor patient compliance following referrals, and the reluctance of primary care workers to refer cases.^{62,63} The involvement of community health care workers in the referral process has received limited attention in LMICs. Additionally, establishing efficient reporting mechanisms and feedback systems has encountered difficulties, thereby diminishing the effectiveness of the referral system.⁶²⁻⁶⁴ Improving management at the primary care level offers better opportunities for preserving limbs in tertiary care settings, thereby leading to improved patient outcomes.

5.3 | Inadequate care and further preventative measures at the first presentation

The International Working Group on the Diabetic Foot (IWGDF) recommends standard wound cleansing with normal saline and cost-effective dressings like gauze in low-resource settings.⁶⁵ However, some LMIC hospital settings often resort to herbal remedies as first-line treatments, despite their lack of endorsement. Cultural boundaries and traditional beliefs influence the reluctance to embrace recent advances in DFU care, hindering the utilization of trained health care professionals.⁶⁶

Studies have also underscored knowledge and practice gaps in foot care among diabetes patients in Nigeria, with only 30.1% demonstrating good knowledge and 10.2% exhibiting good practice.⁶⁷ Poor foot care is significantly associated with illiteracy, low socioeconomic status, and a lack of awareness regarding appropriate actions and footwear inspection. The study also highlights the scarcity of health care professionals experienced in diabetic foot care in such regions. Common practices and a reliance on traditional and alternative remedies before seeking professional health care delay presentations of DFUs in LMICs.⁶⁸ These findings underscore the need for targeted educational programs to reduce diabetic foot complications, particularly in resource-limited settings and LMICs.

5.4 | Economic burden in LMICs

The economic burden of DFUs is substantial in LMICs, primarily due to limited government health care funding and financial constraints individuals face. Costs associated with wound dressings, medications, surgical procedures, and hospitalizations impose a significant financial burden on individuals, health care systems, and governments. For instance, while the United States annually spends \$176 billion on diabetic-related expenditures, one-third of this is attributed to lower-extremity conditions.⁶⁹ Comparatively, LMICs like Brazil and Trinidad and Tobago, which bear a higher disease burden, face estimated direct medical costs of \$70 million and \$85 million, respectively.^{70,71} LMICs generally have lower health expenditures per capita, presenting challenges in accessing adequate care.⁷² The increasing prevalence of diabetes and its complications further exacerbates the economic burden, underscoring the urgent need to prioritize effective management and prevention strategies in LMICs.

A summary of the challenges encountered in DFU management in LMICs is provided in Figure 2.

6 | FUTURE STRATEGIES FOR REDUCING DFU-RELATED AMPUTATIONS IN LMICS

6.1 | Improving primary care and emergency department practices

To effectively reduce LEAs in LMICs, initiating improvements in primary care and emergency department practices is imperative.

A study conducted in Sudan identified several risk factors for amputation among patients with DFUs, including hypertension, retinopathy, nephropathy, large ulcer sizes (>2.5 cm), and neuropathy.⁷³ The development of an updated risk stratification system utilizing these risk factors to inform management and treatment protocols is therefore essential to preventing LEAs.

Additionally, health care nurses at the community level play a pivotal role in assessing patient needs and developing tailored education programs for patients and their families. These programs facilitate active participation in care, ultimately reducing foot-related complications associated with diabetes.⁷⁴

Strengthening the primary health care system and investing in diabetes management are essential to reducing complications and amputations, especially in rural areas. As the initial point of contact, primary care physicians can significantly contribute to diabetes management through active participation and cost-effective innovations such as telemedicine, effectively mitigating the risk of amputation in DFUs.

6.2 | Strengthening orthopaedic and diabetic foot clinics

In LMICs, limited access to specialized foot health services, such as podiatry, in primary health care facilities leads to inadequate risk assessment, suboptimal foot care practices, and DFU development. Establishing foot health services at the primary health care level can provide high-quality, cost-effective, and accessible care, addressing the needs of individuals with diabetes.

A study in Ghana highlighted the significance of diabetic clinics as the primary source of education and understanding about DFUs to reduce diabetes-related foot complications.²⁴ Categorizing patients based on risk factors at the primary health care level, particularly by nurses, is crucial for identifying those at risk for ulceration. This approach ensures accessibility to a broader population and is the initial entry point for individuals seeking foot health services.⁷⁴

6.3 | Referral criteria and timing of escalation in the management of DFUs

Developing standardized referral criteria and timely escalation pathways is vital for mitigating the risk of limb loss in DFUs. The International Diabetic Foot Care Group and the International Working Group on Diabetic Foot have proposed referral systems based on severity and care requirements, facilitating appropriate and timely referrals for DFU management. This approach is crucial for preventing complications and reducing amputations.

An observational study in Nigeria revealed an intra-hospital mortality rate of 21.4%, higher than studies in other LMICs such

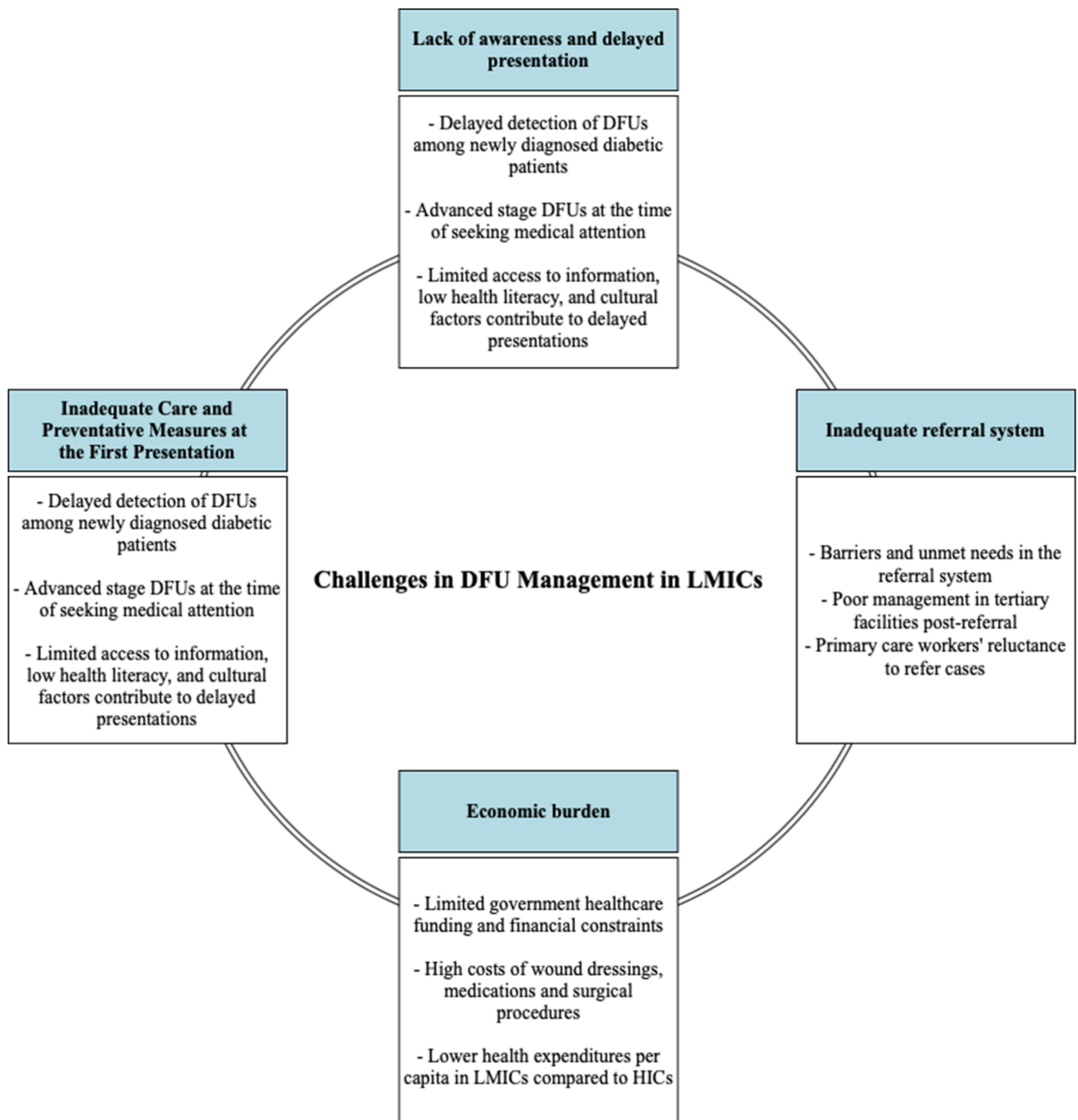


FIGURE 2 Challenges in DFU management in Low and Middle-Income Countries. DFU, Diabetic Foot Ulcer.

as Indonesia. The primary contributing factor to this increased mortality rate is inadequate referral from primary and secondary health facilities, which often lack the necessary expertise and facilities.^{4,32}

Coordinated care between institutions and education for healed ulcer patients are also critical to reducing the high recurrence rates of DFUs.⁷⁵ Establishing care networks, education, and training programs can address these challenges and improve outcomes.^{76–78}

6.4 | Implementing guidelines and protocols for DFU management

Global consensus guidelines on DFU referral are essential for establishing a standardized framework for health care professionals worldwide. Clinical practice guidelines (CPGs) have been developed in countries like Malaysia to ensure consistent and uniform care practices, irrespective of geographical location or health care setting. Establishing standardized guidelines is a foundation for education and

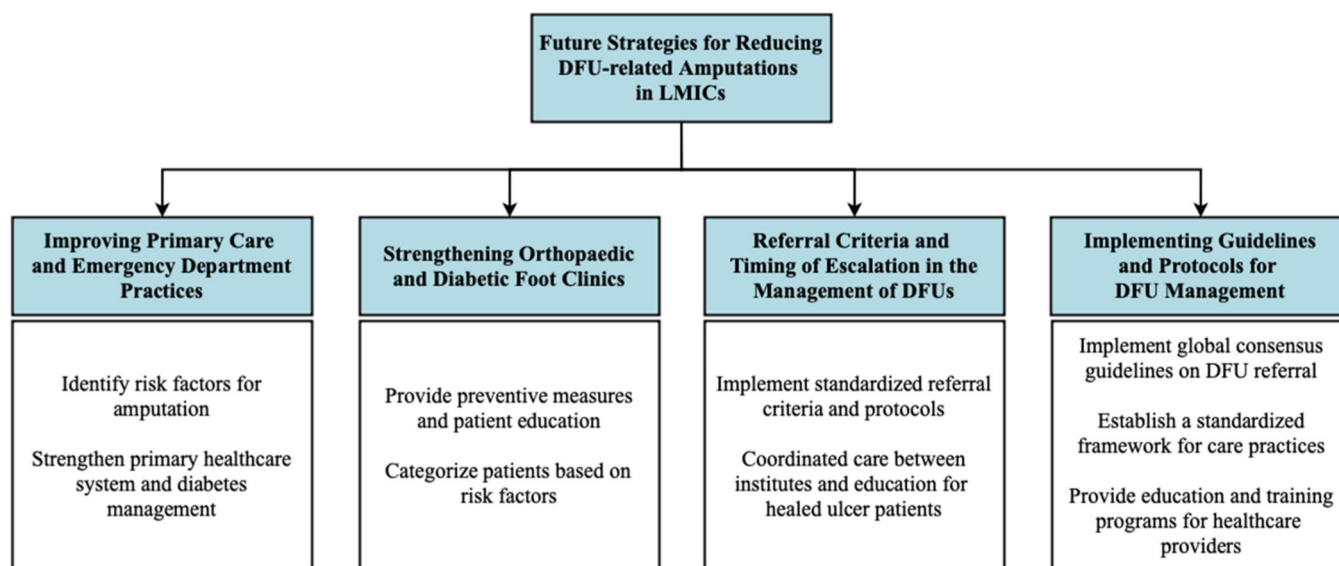


FIGURE 3 Future prospects for reducing DFU-related amputations in Low and Middle-Income Countries. DFU, Diabetic Foot Ulcer.

training programs, equipping health care providers with the necessary knowledge and skills for appropriate referrals. However, successful implementation of CPGs requires a strong commitment, including regular training programs and adequate funding.⁷⁹

A summary of the future prospects for reducing DFU-related amputations in LMICs is provided in Figure 3.

7 | CONCLUSION

DFUs represent a substantial challenge for LMICs. Nevertheless, integrating podiatry, endocrinology, and wound care services presents a promising opportunity to enhance DFU management and improve patient outcomes. Implementing key interventions and emphasizing patient education and self-care practices makes it possible to reduce amputation rates and enhance the overall quality of life for individuals affected by DFUs in LMICs.

To effectively address these challenges, targeted education initiatives, improved health care access, and proactive preventive strategies must be prioritized. Implementing integrated and multidisciplinary approaches is essential for successfully addressing the burden of DFUs in LMICs. By embracing a holistic and collaborative approach, health care systems and policymakers can make significant strides toward alleviating the impact of DFUs on patients and health care infrastructure in resource-constrained settings.

AUTHOR CONTRIBUTIONS

The study was conceptualized by Niranjna Swaminathan. Material preparation, data collection, and writing of first draft were completed by Niranjna Swaminathan, Wireko Andrew Awuah, Hareesha Rishab Bharadwaj, Sakshi Roy, Tomas Ferreira, Favour Tope Adebuseye, Isma Farah Nurlisa binti Ismail, Saleha Azeem, Toufik Abdul-Rahman,

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All authors have read and approved the final version of the manuscript, and Favour Tope Adebuseye had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis. Favour Tope Adebuseye affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study planned have been explained. Mentioned both here and in the manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data availability is not applicable to this article as no new data were created or analyzed in this study.

TRANSPARENCY STATEMENT

The lead author Favour Tope Adebuseye affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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