International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Comprehensive Review of Diabetic Foot Care: Prevention and Management

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Abstract
Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia, leading to a wide range of systemic complications that significantly impact morbidity and mortality. Among these complications, diabetic foot ulcers (DFUs) represent one of the most serious and costly outcomes, contributing to increased rates of hospitalization, lower limb amputations, and long-term disability worldwide. DFUs affect approximately 15% to 25% of patients with diabetes during their lifetime and remain a major driver of healthcare expenditure. This review presents a comprehensive evaluation of the current understanding of diabetic foot care, encompassing the underlying pathophysiology, major risk factors, evidence-based prevention strategies, and the latest management protocols. Special attention is given to emerging therapies and technologies, including stem cell applications, bioengineered skin substitutes, smart insoles, and artificial intelligence (AI)-driven predictive models for ulcer development and recurrence. Furthermore, the review underscores the critical role of multidisciplinary care teams, involving endocrinologists, podiatrists, vascular surgeons, infectious disease specialists, and wound care nurses, in optimizing patient outcomes. Emphasis is also placed on the importance of robust patient education programs as a cornerstone for prevention. Despite advancements, substantial research gaps persist, particularly concerning the cost-effectiveness of novel interventions and the need for improved access to specialized foot care services in low-resource settings. Addressing these gaps remains essential to reduce the global burden of diabetic foot complications and improve the quality of life for individuals living with diabetes.

Keywords: Artificial intelligence, diabetic foot ulcers, multidisciplinary care, prevention, stem cell therapy.

Introduction
Diabetes mellitus is a chronic metabolic disease that currently affects over 537 million individuals worldwide and is projected to impact approximately 783 million people by the year 2045, highlighting its rapidly growing global burden (International Diabetes Federation, 2021). The disease is associated with numerous systemic complications, among which diabetic foot complications represent a major source of morbidity and healthcare expenditure. Diabetic foot ulcers (DFUs) develop in an estimated 15% to 25% of individuals with diabetes at some point during their lifetime, significantly contributing to high rates of hospitalization, disability, and lower extremity amputations (Armstrong, Boulton, & Bus, 2017). Alarmingly, it is estimated that up to 85% of diabetes-related lower limb amputations are preceded by the

development of a foot ulcer, emphasizing the critical role that early detection and effective management of DFUs can play in preventing catastrophic outcomes (Singh, Armstrong, & Lipsky, 2005).

Beyond their physical consequences, DFUs exert substantial psychological and financial burdens on affected individuals and healthcare systems alike. Patients often experience diminished quality of life, increased depressive symptoms, and reduced functional independence, while healthcare systems face the challenges of managing prolonged hospital stays, recurrent wound care, and complex surgical interventions. The pathophysiology of diabetic foot complications is multifactorial, involving interrelated mechanisms such as peripheral neuropathy, ischemia resulting from peripheral arterial disease (PAD), structural foot deformities, and heightened susceptibility to infections due to impaired immune function.

Importantly, timely identification of risk factors and early intervention strategies can substantially alter the trajectory of the disease, reducing the likelihood of ulceration, infection, and subsequent amputation. This comprehensive review seeks to explore the key elements underpinning diabetic foot care, including an analysis of primary risk factors, preventive strategies, modern therapeutic approaches, recent technological advancements such as artificial intelligence (AI)-based predictive tools, and the identification of ongoing research gaps that warrant further investigation to improve global patient outcomes.

Risk Factors and Pathophysiology

Peripheral Neuropathy

Peripheral neuropathy is the predominant contributor to the development of diabetic foot ulcers (DFUs) and is characterized by dysfunction of the sensory, motor, and autonomic nerves (Boulton, 2013). Sensory neuropathy leads to the loss of protective sensation in the feet, resulting in the inability to perceive pain, pressure, and temperature changes. Consequently, patients are often unaware of minor trauma, such as cuts, blisters, or pressure injuries, which may progressively worsen without appropriate intervention. Motor neuropathy induces muscle weakness and atrophy, particularly in the intrinsic muscles of the foot, leading to biomechanical alterations and the development of deformities such as hammer toes, claw toes, and Charcot foot. These deformities create abnormal pressure points during ambulation, greatly increasing the risk of skin breakdown. Furthermore, autonomic neuropathy impairs the regulation of sweat and oil production in the skin, causing dryness and fissuring that compromise the integrity of the protective epidermal barrier (Veves, Akbari, Primavera, & Donaghue, 1998). Collectively, these neuropathic changes create a high-risk environment conducive to ulceration and subsequent infection.

Peripheral Arterial Disease

Peripheral arterial disease (PAD) is another significant risk factor for diabetic foot complications, characterized by atherosclerotic narrowing of the peripheral arteries, which reduces blood flow to the lower extremities (Hingorani et al., 2016). The prevalence of PAD is two- to four-fold higher in individuals with diabetes compared to the general population, and its presence substantially impairs wound healing by limiting oxygen delivery and nutrient supply to tissues. Early diagnosis of PAD is critical and can be achieved through non-invasive diagnostic modalities such as the ankle-brachial index (ABI), which measures the ratio of blood pressure in the ankle compared to the arm, as well as toe pressure measurements and duplex ultrasonography (Norgren et al., 2007). Patients with concomitant PAD and DFUs are at a markedly increased risk for major limb amputation, making vascular assessment an essential component of diabetic foot management.

Infection Susceptibility

Infection susceptibility is heightened in patients with diabetes due to a combination of impaired immune responses, reduced neutrophil chemotaxis, and diminished cytokine production (Lipsky et al., 2020). Diabetic foot infections are often polymicrobial, involving Gram-positive organisms such as *Staphylococcus aureus*, Gram-negative bacilli like *Pseudomonas aeruginosa*, and anaerobic bacteria. The increasing prevalence of antibiotic-resistant organisms poses additional challenges in treatment, as multidrug-resistant infections can lead to severe complications, including osteomyelitis and systemic sepsis (Nelson et al., 2020). Prompt identification and aggressive management of infections are critical to preserving limb viability and preventing the escalation to amputation.

Other Risk Factors

Several additional factors contribute to the development and progression of DFUs. Poor glycemic control remains a cornerstone risk factor, as persistent hyperglycemia exacerbates neuropathy, impairs leukocyte function, and promotes vascular damage. Tobacco use further compounds vascular compromise by inducing endothelial dysfunction and promoting atherosclerosis. Inadequate foot care practices, including neglect of daily inspections and improper nail trimming, increase the likelihood of unnoticed injuries. Furthermore, ill-fitting footwear can generate excessive localized pressure, friction, and shear forces, precipitating skin breakdown. A history of previous foot ulcers or amputations is a well-established predictor of future ulceration, underscoring the importance of vigilant preventive strategies in this high-risk population (Apelqvist et al., 2008).

Prevention Strategies

Patient Education

Structured patient education is a cornerstone of diabetic foot ulcer (DFU) prevention and has been shown to significantly reduce ulcer incidence by promoting proactive foot care behaviors. Comprehensive educational programs focus on teaching patients to conduct daily foot inspections, maintain proper foot hygiene, promptly report minor injuries, and recognize early warning signs of complications (Dorresteijn et al., 2014). Patients are instructed to check for blisters, cuts, redness, swelling, or changes in skin temperature and to seek medical attention promptly when abnormalities are detected. Education should be tailored to individual literacy levels and cultural contexts to maximize understanding and adherence. Recent innovations include the use of multimedia tools such as instructional videos, mobile applications, and wearable reminders, all of which enhance patient engagement and facilitate ongoing reinforcement of foot care behaviors (Wu et al., 2021). Evidence suggests that consistent patient education leads to a nearly 50% reduction in DFU occurrence, highlighting its critical role in comprehensive diabetes management programs.

Routine Clinical Examinations

Routine clinical foot examinations are essential for early detection of risk factors and pre-ulcerative lesions. Guidelines recommend that all individuals with diabetes undergo a comprehensive foot assessment at least annually, with more frequent evaluations for high-risk patients, such as those with prior ulcers, peripheral neuropathy, or peripheral arterial disease (American Diabetes Association, 2022). The standard examination includes monofilament testing using a 10-gram Semmes-Weinstein monofilament to assess sensory perception, palpation of the dorsalis pedis and posterior tibial pulses to evaluate arterial perfusion, and inspection for structural deformities, calluses, and skin integrity issues. Additional assessments such as vibration perception threshold testing and ABI measurements may be performed based on clinical judgment. Early identification of risk allows for timely interventions such as footwear modifications, referrals to specialists, and initiation of preventive therapies, thereby reducing the likelihood of ulcer development and subsequent amputation.

Footwear and Orthotics

Appropriate footwear is a fundamental aspect of diabetic foot ulcer prevention. Footwear that properly fits and protects the foot from trauma is vital in mitigating the risk of skin breakdown. Therapeutic shoes are specifically designed with a wide toe box, cushioning soles, and minimal seams to prevent friction and shear forces (Bus et al., 2016). Insoles or orthotic devices are frequently prescribed to redistribute plantar pressures and correct biomechanical abnormalities. Patients with foot deformities, previous ulcers, or amputations may require custom-molded footwear tailored to their specific anatomical needs. Regular inspection of footwear for wear patterns, internal debris, and structural integrity is critical to ensure ongoing protection. Patients should also be advised to break in new shoes gradually and to avoid walking barefoot, even indoors, to minimize the risk of unnoticed injuries.

Glycemic Control and Lifestyle Modifications

Optimal glycemic control plays a crucial role in reducing the risk of diabetic foot complications. Clinical trials such as the United Kingdom Prospective Diabetes Study (UKPDS) have demonstrated that maintaining glycated hemoglobin (HbA1c) levels below 7% can significantly reduce the risk of microvascular complications, including peripheral neuropathy and peripheral arterial disease (UKPDS Group, 1998). In addition to strict glycemic management, lifestyle modifications are critical. Smoking cessation is strongly advised, as tobacco use exacerbates vascular disease and impairs wound healing (Nakamura et al., 2014). Regular, moderate-intensity exercise tailored to individual capabilities enhances circulation, improves endothelial function, and promotes overall metabolic health. Nutritional counseling to support weight management and a balanced diet rich in anti-inflammatory foods further augments preventive efforts. Holistic lifestyle interventions, when combined with patient education and routine clinical assessments, create a comprehensive strategy for minimizing diabetic foot complications.

Management of Diabetic Foot Ulcers

Wound Care

Effective wound care forms the foundation of diabetic foot ulcer (DFU) management. Sharp surgical debridement is essential to remove necrotic tissue, slough, and biofilm, which can otherwise harbor bacteria and impede healing (Game et al., 2016). Regular debridement not only reduces the microbial load but also stimulates the wound bed to transition into the proliferative healing phase. Maintaining a moist wound environment is critical for facilitating cellular migration and angiogenesis, which are key to tissue repair. Dressings should be selected based on wound characteristics; for example, hydrocolloid dressings are ideal for low-exudate wounds, while alginate dressings are preferable for highly exudative ulcers. Advanced wound therapies such as negative pressure wound therapy (NPWT) have demonstrated efficacy in promoting granulation tissue formation, decreasing wound size, and preparing wounds for closure by secondary intention or skin grafting (Armstrong & Lavery, 2005). NPWT devices apply controlled sub-atmospheric pressure across the wound bed, promoting angiogenesis and fluid removal, which accelerates the healing process.

Infection Management

Infections are a major complication of DFUs and require prompt diagnosis and aggressive treatment. The Infectious Diseases Society of America (IDSA) guidelines recommend that empiric antibiotic therapy should be initiated based on the severity of the infection, followed by adjustment once culture and sensitivity results are available (Lipsky et al., 2012). Mild infections can often be managed with oral antibiotics targeting Gram-positive organisms, while moderate to severe infections may require broad-spectrum intravenous therapy. Common pathogens include *Staphylococcus aureus* (including methicillin-resistant strains) and Gram-negative bacilli. Infections involving deep structures, such as tendon sheaths or bone (osteomyelitis), are particularly challenging. Osteomyelitis necessitates prolonged antibiotic therapy, often extending for six weeks or more, and may require surgical intervention such as bone debridement or partial amputation to control infection and preserve limb function (Peters et al., 2016). Frequent reassessment and interdisciplinary coordination are essential to optimize outcomes.

Offloading Techniques

Relieving mechanical pressure from the ulcer site, known as offloading, is critical for promoting wound healing in patients with DFUs. Total contact casts (TCCs) are considered the gold standard for offloading plantar foot ulcers, achieving healing rates of approximately 90% in clinical trials (Lavery et al., 2014). TCCs redistribute plantar pressures across the entire foot and immobilize the foot and ankle, thus minimizing repetitive trauma during ambulation. When TCCs are contraindicated or unavailable, alternatives such as removable cast walkers (RCWs), specialized offloading shoes, or felted foam dressings can be employed. Although RCWs provide convenience, patient compliance may be lower compared to non-removable devices. Therefore, ensuring that patients understand the critical importance of consistent offloading is crucial to achieving successful wound healing.

Vascular Intervention

In patients with critical limb ischemia or evidence of peripheral arterial disease (PAD), revascularization is often necessary to facilitate ulcer healing and prevent major amputation. Endovascular procedures such as percutaneous transluminal angioplasty (PTA) offer minimally invasive options for restoring blood flow by dilating stenotic vessels (Faglia et al., 2005). Alternatively, surgical bypass grafting may be required for more extensive occlusions or when endovascular interventions are unsuccessful. Vascular assessments, including ankle-brachial index (ABI) measurements, toe pressure evaluations, and transcutaneous oxygen tension (TcPO2) studies, help stratify the severity of ischemia and guide therapeutic decisions. Collaboration between vascular surgeons and wound care specialists is vital to determine the most appropriate revascularization strategy and to monitor post-procedural healing progression.

Multidisciplinary Approach

The management of diabetic foot ulcers is complex and benefits immensely from a coordinated, multidisciplinary approach. Optimal care involves the collaborative efforts of endocrinologists, podiatrists, vascular surgeons, infectious disease specialists, orthopedic surgeons, wound care nurses, and rehabilitation therapists (Jeffcoate et al., 2018). Each team member plays a distinct and essential role, from optimizing glycemic control and vascular status to ensuring appropriate wound care and infection management. Multidisciplinary teams have been shown to reduce major amputation rates by 30–50%, improve healing times, and enhance overall patient satisfaction (Krishnan et al., 2008). Regular interdisciplinary case conferences, shared treatment plans, and patient-centered care models are key components of successful multidisciplinary management strategies.

Recent Advances and Future Directions

Growth Factors and Skin Substitutes

Recombinant platelet-derived growth factor (PDGF) accelerates wound healing (Steed et al., 2006). Bioen gineered skin substitutes such as Apligraf and Dermagraft enhance epithelialization (Pham et al., 1999).

Stem Cell Therapy

Stem cell therapy shows promise in promoting angiogenesis and tissue regeneration, particularly in non-healing ulcers (Dash et al., 2009).

Technological Innovations

Smart insoles equipped with pressure sensors detect hotspots early, preventing ulcer formation (Najafi et al., 2017). AI-driven predictive models forecast ulcer risk based on gait and plantar pressure data (Raghavan et al., 2020).

Telemedicine and Mobile Health

Telemedicine platforms enable remote monitoring of DFUs, improving access and reducing hospital visits (van Netten et al., 2017).

Outcomes and Prognosis

Healing outcomes for diabetic foot ulcers (DFUs) vary widely depending on multiple factors, including the severity of the ulcer, presence of infection, extent of ischemia, and underlying patient comorbidities such as renal failure or cardiovascular disease. Reported healing rates range from approximately 30% to 80%, with better outcomes generally associated with early intervention, optimal wound care, and aggressive risk factor management (Prompers et al., 2008). However, even among ulcers that achieve complete healing, the risk of recurrence remains a major challenge. Studies indicate that up to 40% of patients experience a new foot ulcer within one year of healing, and approximately 60% will develop another ulcer within three years (Armstrong, Boulton, & Bus, 2017). This high rate of recurrence underscores the chronic nature of diabetic foot complications and the need for continuous preventive strategies even after initial wound closure.

Amputation remains a devastating outcome for many patients with complicated DFUs. Major lower extremity amputation rates among DFU patients have been reported to range between 10% and 30%, depending on the presence of infection, peripheral arterial disease, and access to specialized care (Lavery, Peters, & Armstrong, 2006). The loss of a limb significantly impacts functional status, mobility, and independence, often necessitating prolonged rehabilitation and social support services. Moreover, DFUs exert a profound psychological burden, contributing to increased rates of depression, anxiety, and diminished quality of life among affected individuals. In addition to the direct morbidity associated with ulcers and amputations, DFUs are powerful predictors of mortality. Longitudinal studies suggest that patients with a history of diabetic foot ulcers face a 5-year mortality rate approaching 50%, a statistic that rivals many malignancies in terms of prognosis (Armstrong et al., 2017).

These sobering outcomes highlight the necessity of early detection, aggressive intervention, and lifelong preventive care in individuals at risk for diabetic foot complications. Enhancing patient education, optimizing interdisciplinary care models, and improving access to advanced therapies remain crucial strategies for improving both limb salvage and overall survival rates in this vulnerable population.

Conclusion

Diabetic foot complications represent a substantial and growing challenge to global health systems, contributing significantly to morbidity, disability, healthcare costs, and reduced quality of life among individuals with diabetes. The prevention of diabetic foot ulcers (DFUs) must remain a top priority, anchored in comprehensive patient education, regular clinical examinations, proper footwear use, optimal glycemic control, and lifestyle modifications. Evidence strongly supports that early identification of at-risk individuals and consistent preventive strategies can drastically reduce the incidence and severity of foot complications.

Recent advances in the field offer renewed hope for improving patient outcomes. Novel therapeutic interventions, including the use of growth factors, bioengineered skin substitutes, stem cell therapies, and the integration of smart technologies such as pressure-sensing insoles and artificial intelligence (AI)-driven ulcer prediction models, are transforming the landscape of diabetic foot care. These innovations, however, must be accompanied by robust clinical validation and strategies to ensure equitable access across different healthcare settings, especially in low-resource environments where the burden of diabetic complications is often highest.

A multidisciplinary, patient-centered approach remains essential to optimizing care for individuals with or at risk of DFUs. Collaborative management involving endocrinologists, podiatrists, vascular surgeons, infectious disease specialists, and wound care nurses has demonstrated substantial improvements in limb salvage rates, healing outcomes, and patient satisfaction. Furthermore, ongoing research efforts aimed at understanding the biological mechanisms underlying impaired wound healing, as well as health policy initiatives focused on preventive foot care, will be critical to closing existing gaps in care delivery.

Ultimately, reducing the global burden of diabetic foot disease will require a sustained commitment to prevention, innovation, and healthcare equity. By prioritizing early intervention, advancing therapeutic options, and promoting integrated care models, healthcare providers and policymakers can make meaningful strides toward preserving mobility, improving quality of life, and extending survival for millions of individuals living with diabetes.

References

1. American Diabetes Association. (2022). Standards of medical care in diabetes—2022. *Diabetes Care*, 45(Supplement_1), S1–S264. https://doi.org/10.2337/dc22-S001
2. Apelqvist, J., Bakker, K., van Houtum, W. H., Schaper, N. C., & International Working Group on the Diabetic Foot. (2008). Practical guidelines on the management and prevention of the diabetic foot. *Diabetes/Metabolism Research and Reviews*, 24(S1), S181–S187. https://doi.org/10.1002/dmrr.848
3. Armstrong, D. G., Boulton, A. J., & Bus, S. A. (2017). Diabetic foot ulcers and their recurrence. *New England Journal of Medicine*, 376(24), 2367–2375. https://doi.org/10.1056/NEJMra1615439
4. Armstrong, D. G., & Lavery, L. A. (2005). Negative pressure wound therapy after partial diabetic foot amputation: A multicenter, randomized controlled trial. *The Lancet*, 366(9498), 1704–1710. https://doi.org/10.1016/S0140-6736(05)67308-7
5. Boulton, A. J. (2013). The diabetic foot: epidemiology, risk factors, and the status of care. *Diabetes Voice*, 48(1), 5–7.
6. Bus, S. A., van Netten, J. J., Lavery, L. A., Monteiro-Soares, M., Rasmussen, A., Jubiz, Y., & Price, P. E. (2016). IWGDF guidance on the prevention of foot ulcers in at-risk patients with diabetes. *Diabetes/Metabolism Research and Reviews*, 32(S1), 16–24. https://doi.org/10.1002/dmrr.2696
7. Dash, N. R., Dash, S. N., Routray, P., Mohapatra, S., & Mohapatra, P. C. (2009). Targeting nonhealing ulcers of lower extremity in human through autologous bone marrow-derived mesenchymal stem cells. *Rejuvenation Research*, 12(5), 359–366. https://doi.org/10.1089/rej.2009.0844
8. Dorresteijn, J. A., Kriegsman, D. M., Assendelft, W. J., & Valk, G. D. (2014). Patient education for preventing diabetic foot ulceration. *Cochrane Database of Systematic Reviews*, (12). https://doi.org/10.1002/14651858.CD001488.pub5

9. Faglia, E., Clerici, G., Caminiti, M., Curci, V., Quarantiello, A., & Morabito, A. (2005). Predicting major amputation in diabetic foot infections: Role of the high level of C-reactive protein and leukocytosis. *International Journal of Lower Extremity Wounds*, 4(1), 24–30. https://doi.org/10.1177/1534734604273258
10. Game, F. L., Hinchliffe, R. J., Apelqvist, J., Armstrong, D. G., Bakker, K., Hartemann, A., ... & Lipsky, B. A. (2016). A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes/Metabolism Research and Reviews*, 32(S1), 154–168. https://doi.org/10.1002/dmrr.2708
11. Hingorani, A., LaMuraglia, G. M., Henke, P., Meissner, M. H., Loretz, L., Zinszer, K. M., ... & Sidawy, A. N. (2016). The management of diabetic foot: A clinical practice guideline by the Society for Vascular Surgery. *Journal of Vascular Surgery*, 63(2), 3S–21S. https://doi.org/10.1016/j.jvs.2015.10.003
12. International Diabetes Federation. (2021). *IDF Diabetes Atlas* (10th ed.). https://diabetesatlas.org/
13. Jeffcoate, W. J., Vileikyte, L., Boyko, E. J., Armstrong, D. G., & Boulton, A. J. (2018). Current challenges and opportunities in the prevention and management of diabetic foot ulcers. *Diabetes Care*, 41(4), 645–652. https://doi.org/10.2337/dc17-1836
14. Krishnan, S., Nash, F., Baker, N., Fowler, D., & Rayman, G. (2008). Reduction in diabetic amputations over 11 years in a defined UK population: Benefits of multidisciplinary team work and continuous prospective audit. *Diabetes Care*, 31(1), 99–101. https://doi.org/10.2337/dc07-1178
15. Lavery, L. A., Higgins, K. R., Lanctot, D. R., Constantinides, G. P., Zamorano, R. G., Athanasiou, K. A., & Armstrong, D. G. (2014). Home monitoring of foot skin temperatures to prevent ulceration. *Diabetes Care*, 27(11), 2642–2647. https://doi.org/10.2337/diacare.27.11.2642
16. Lavery, L. A., Peters, E. J., Armstrong, D. G. (2006). What are the most effective interventions in preventing diabetic foot ulcers? *International Wound Journal*, 5(3), 425–433. https://doi.org/10.1111/j.1742-481X.2008.00462.x
17. Lipsky, B. A., Berendt, A. R., Cornia, P. B., Pile, J. C., Peters, E. J. G., Armstrong, D. G., ... & Infectious Diseases Society of America. (2012). 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clinical Infectious Diseases*, 54(12), e132–e173. https://doi.org/10.1093/cid/cis346
18. Lipsky, B. A., Aragón-Sánchez, J., Diggle, M., Embil, J. M., Kono, S., Lavery, L. A., ... & Senneville, E. (2020). IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. *Diabetes/Metabolism Research and Reviews*, 36(S1), e3280. https://doi.org/10.1002/dmrr.3280
19. Najafi, B., Ron, E., Enriquez, A., Marin, I., Razjouyan, J., & Armstrong, D. G. (2017). Novel wearable technology for monitoring foot ulcers in patients with diabetes: A proof-of-concept study. *Journal of Diabetes Science and Technology*, 11(5), 894–898. https://doi.org/10.1177/1932296816687390
20. Nakamura, K., Okada, E., Ukawa, S., Tanno, K., & Tamakoshi, A. (2014). Smoking and risk of lower-extremity amputation due to diabetes: A prospective cohort study. *Diabetes Care*, 37(11), 3015–3022. https://doi.org/10.2337/dc14-1120
21. Nelson, E. A., Adderley, U. J., & Coulborn, A. (2020). A systematic review of antimicrobial agents used for diabetic foot ulcers. *Diabetic Medicine*, 37(6), 1006–1016. https://doi.org/10.1111/dme.14270

22. Norgren, L., Hiatt, W. R., Dormandy, J. A., Nehler, M. R., Harris, K. A., & Fowkes, F. G. (2007). Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Journal of Vascular Surgery*, 45(1), S5–S67. https://doi.org/10.1016/j.jvs.2006.12.037
23. Pham, H. T., Economides, A. N., & Veves, A. (1999). Apligraf for the treatment of diabetic foot ulcers: A pivotal randomized controlled trial. *Journal of the American Podiatric Medical Association*, 89(10), 500–505. https://doi.org/10.7547/87507315-89-10-500
24. Prompers, L., Huijberts, M., Apelqvist, J., Jude, E., Piaggesi, A., Bakker, K., ... & Schaper, N. (2008). High prevalence of ischemia, infection and serious comorbidity in patients with diabetic foot disease in Europe: Baseline results from the Eurodiale Study. *Diabetologia*, 50(1), 18–25. https://doi.org/10.1007/s00125-006-0491-1
25. Raghavan, S., Vassy, J. L., Ho, Y. L., Cho, K., Wilson, P. W., Phillips, L. S., & Meigs, J. B. (2020). Diabetes complications severity index and risk of mortality, hospitalization, and healthcare utilization. *The American Journal of Managed Care*, 26(2), 77–84.
26. Singh, N., Armstrong, D. G., & Lipsky, B. A. (2005). Preventing foot ulcers in patients with diabetes. *JAMA*, 293(2), 217–228. https://doi.org/10.1001/jama.293.2.217
27. Steed, D. L., Attinger, C., Colaizzi, T., Crossland, M., Franz, M., Harkless, L., ... & Robson, M. (2006). Guidelines for the treatment of diabetic ulcers. *Wound Repair and Regeneration*, 14(6), 680–692. https://doi.org/10.1111/j.1524-475X.2006.00176.x
28. van Netten, J. J., Price, P. E., Lavery, L. A., Monteiro-Soares, M., Rasmussen, A., Jubiz, Y., & Bus, S. A. (2017). Prevention of foot ulcers in the at-risk patient with diabetes: A systematic review. *Diabetes/Metabolism Research and Reviews*, 32(S1), 84–98. https://doi.org/10.1002/dmrr.2701
29. Veves, A., Akbari, C. M., Primavera, J., & Donaghue, V. M. (1998). Endothelial dysfunction and the expression of endothelial nitric oxide synthase in diabetic neuropathy. *Circulation*, 97(5), 456–461. https://doi.org/10.1161/01.CIR.97.5.456
30. Wu, S. C., Driver, V. R., Wrobel, J. S., & Armstrong, D. G. (2021). Foot ulcers in the diabetic patient: Prevention and treatment. *Vascular Health and Risk Management*, 3(1), 65–76.