

# The Association Between Clinical Obesity And Diabetes-related Foot Ulceration

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**Abstract:** Diabetes-related foot ulceration (DFU) remains one of the most multifactorial complications of diabetes mellitus, responsible for high rates of lower limb amputation (LLA), excess mortality and major health-system expenditure. Despite obesity and DFU growing exponentially worldwide and sharing many interconnected risk factors, peer-reviewed literature exploring the associations between these two conditions is limited. This review synthesizes epidemiological, genetic and mechanistic data to argue that obesity should be positioned centrally in DFU risk assessment and management. Establishing responsive and personalized treatments and management plans for individuals with obesity and DFUs is important for effective limb preservation

**Key words:** *diabetes mellitus, diabetes-related foot ulceration, risk factors, clinical obesity, lower limb amputation*

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Awareness of diabetes mellitus (DM) as a condition and comorbidity has grown significantly with technological breakthroughs and growing investment in research by governments across the world.<sup>1</sup> Despite obesity and diabetes-related foot ulceration (DFU) growing exponentially worldwide and sharing many interconnected risk factors, peer-reviewed literature exploring the associations between these two conditions is limited.<sup>2</sup> Further, DFU remains one of the most multifactorial complications of DM, responsible for high rates of lower limb amputation (LLA), excess mortality and major health-system expenditure. Despite advances in diabetes care, the global burden of DFU continues to rise.<sup>3</sup>

Obesity, with a prevalence nearing one billion people globally, is defined by the World Health Organization as “abnormal or excessive fat accumulation that poses a risk to health”.<sup>4</sup> A DFU is defined by the International Working Group on the Diabetic Foot (IWGDF) as a full thickness wound that penetrates the epidermis and at least part of the dermis, occurring on the foot of a person with DM.<sup>5</sup> Recent estimates suggest that \$231 billion US of intergovernmental funding is

targeted towards treatment of DFU worldwide.<sup>6</sup>

Various psychological, socio-economic and biobehavioural factors are commensurate with chronic complications associated with obesity and DFUs.<sup>7</sup> Limited infrastructure and clinical resources within health-care systems directly impact the effectiveness of treatments and reduce continuity of care for service users.<sup>8</sup> Moreover, with increasing demand for screenings and treatments from ageing global populations and stretched capacity across health services and independent providers, cases of obesity and DFUs are rising.<sup>9</sup> While hyperglycaemia, peripheral neuropathy (PN) and peripheral arterial disease (PAD) are well-recognised drivers, excess adiposity has emerged as an up-stream modifiable determinant of both DFU incidence and delayed healing.<sup>10</sup> This review synthesises epidemiological, genetics, and mechanistic data to argue that obesity should be positioned centrally in DFU risk-assessment and management. Establishing responsive and personalized treatments and management plans for individuals with obesity and DFUs is important for effective limb preservation.

## Obesity As An Upstream Driver Of DFU

Epidemiological and genetic evidence points to excess adiposity as an independent risk factor for developing DFU. In a cross-sectional study of 400 Sudanese patients, overweight individuals were more than twice as likely to have a DFU than those with a normal body mass index (BMI) (56 % vs 46 %;  $p = 0.04$ ).<sup>11</sup> Comparable associations have been reported in other low- and middle-income settings. A Somali multicentre survey identified an odds ratio of 4.63 (95% CI 2.08–10.30) for DFU among overweight or obese patients,<sup>12,13</sup> while a retrospective cohort in Ethiopia demonstrated a high adjusted odds ratio of 27.76 (95 % CI 13.96–55.23) for ulceration in obese participants.<sup>14</sup>

Evidence from high-income countries supports a more indirect role of obesity. In a large prospective cohort of US veterans with DM Boyko et al. identified peripheral neuropathy, peripheral arterial disease and foot deformity as the dominant predictors of incident DFU, while body weight contributed primarily through interactions with plantar pressure and biomechanical stress rather than an independent risk factor.<sup>15,16</sup> Similarly, Lavery et al., incorporated body weight into multivariable DFU risk models, demonstrating that excess weight amplified mechanical stress and callus formation in neuropathic feet, thereby increasing ulcer risk indirectly.<sup>17</sup>

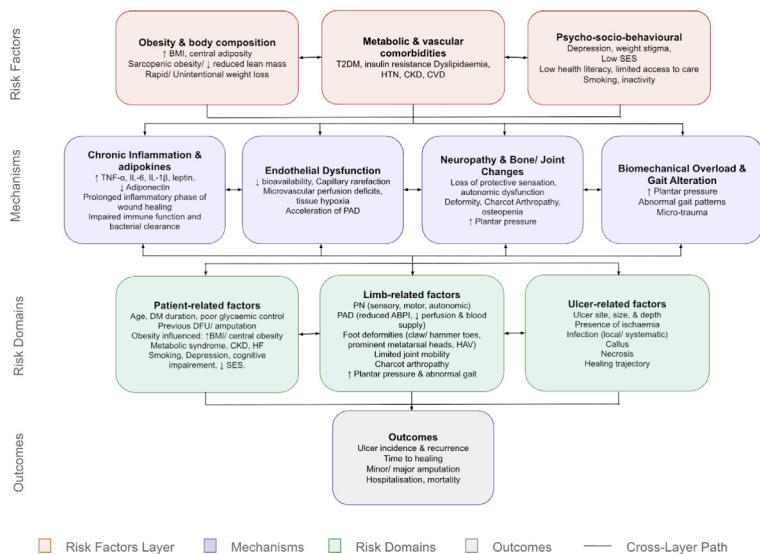
## Genetic And Biomechanistics

Mendelian-randomisation analyses of more than 85 phenotypes in the FinnGen and UK-Biobank cohorts identified BMI as a stronger causal inference for DFU, diabetic polyneuropathy and peripheral artery disease, independent of glycaemic traits.<sup>18</sup> Each standard deviation increases in genetically predicted BMI increased DFU risk by  $\approx 24$  % (OR 1.24; 95 % CI 1.09–1.42 per  $\text{kg}/\text{m}^2$ ), with a modestly stronger effect in men.<sup>18</sup> Parallel analyses using the U.S. NHANES (1999-2004) demonstrated that BMI and newer adiposity metrics,

weight-adjusted waist index (WWI) (OR=1.95), body roundness index (BRI) (OR=1.47) and relative fat mass (RFM) (OR=1.13), were positively associated with prevalent DFU after multivariable adjustment (BMI OR 1.07 per unit).<sup>19</sup> This suggests that indices capturing central adiposity and lean-mass deficits may be more informative for DFU risk stratification.

These epidemiological findings align with mechanistic evidence linking obesity-driven chronic inflammation, endothelial dysfunction and insulin resistance to impaired microvascular perfusion and delayed wound healing.<sup>20</sup> Biomechanical studies further demonstrate that increased body weight raises plantar pressure, particularly beneath the forefoot, providing a mechanical substrate upon which neuropathy and vascular disease act to precipitate ulceration via repetitive micro-trauma in insensate feet.<sup>9</sup> In patients with diabetic neuropathy, higher body weight has been shown to increase plantar stress, while modest weight reduction reduces plantar loading, supporting a causal biomechanical pathway linking obesity to DFU risk.<sup>21,22</sup>

These mechanisms act across the patient-, limb- and ulcer-related risk domains described by Monteiro-Soares and colleagues, ultimately shaping DFU incidence, healing trajectory, amputation risk and mortality.<sup>23</sup> (See Figure 1.)



**Figure 1:** Multifactorial pathways linking obesity to diabetic foot ulcer risk and outcomes, structured by patient-, limb- and ulcer-related factors adopted from Monteiro-Soares et al., 2020.

DFU and obesity represent a multifactorial nexus, each exerts independent pathogenic effects (inflammation, insulin resistance, endothelial dysfunction, altered biomechanics) that synergistically worsen ulcer risk. Therefore, a coordinated, multidisciplinary approach targeting metabolic, vascular, biomechanical and psychosocial factors is required.

### **Obesity And Ulcer Severity Or Healing Outcomes**

Among patients with established DFU, most prospective investigations report that a higher BMI was associated with delayed wound healing and increased amputation risk. In a Saudi Arabian cohort, individuals with normal BMI achieved complete ulcer healing within three months in 61% of cases, compared with 24% of obese patients. Participants with obesity also required longer treatment durations and experienced higher amputations rates.<sup>24</sup> A similar pattern was observed in a Pakistani cohort of 125 inpatients, where obesity correlated with larger ulcer size, prolonged duration and a 18.4 % amputation incidence.<sup>25</sup> An Indian prospective study of 102 patients with DFU concluded the obesity paradox was unsupported, as higher BMI and HbA1c were strongly associated with non-salvageable limbs.<sup>26</sup> These clinical findings may be explained by the biological impact of obesity on wound repair. The inflammatory, proliferative and remodelling phases of cutaneous repair are each vulnerable to the combined effects of systemic inflammation, hypoxia and mechanical stress. Consequently, obesity can prolong the inflammatory phase, blunt angiogenesis, impair fibroblast migration and reduce collagen maturation, hallmarks of the delayed healing observed clinically in obese DFU patients.

### **Weight Reduction, Bariatric Surgery And The Diabetic Foot**

The clinical impact of intentional weight reduction on diabetic foot outcomes remains unclear. A case report described a woman with class III obesity (BMI 54.5 kg/m<sup>2</sup>) who achieved substantial weight

loss following bariatric surgery and improved glycemic control, yet continued to experience neuropathy and foot deformity.

Increased physical activity combined with unmodified footwear preceded the development of a new ulcer and Charcot neuroarthropathy.<sup>27</sup> A recent scoping review identified only two relevant publications, both case-based, suggesting that rapid weight loss may alter foot biomechanics and increase susceptibility to Charcot changes.<sup>28</sup>

In more recent years, modern pharmacological weight loss therapies, such as GLP-1 receptor agonists, have proven to suppress the appetite.<sup>29</sup> A narrative review concluded that from the ten studies they reviewed, these medications can reduce caloric intake by 16-39%.<sup>30</sup> Meanwhile, patients with DFU typically require higher amounts of protein and energy in their diet to support healing (approx. 30-35 kcal/kg/day and 1.25-1.5 g/kg/day of protein).<sup>31</sup> As identified in a recent scoping review, the substantial reduction in caloric intake inadvertently limits the amount of protein and key micronutrients required for collagen synthesis and delays the progression through inflammatory and proliferative phases of wound healing.<sup>32</sup>

While these therapies offer clear benefits in improving glycemic control, their use in patients at risk of diabetic foot complications should be accompanied by a MDT to monitor potential nutritional and biomechanical risks.

In contrast, a randomized nutrition intervention trial in overweight and obese DFU patients (mean baseline BMI = 33.5 kg/m<sup>2</sup>) demonstrated that tailored dietary education and supplementation accelerated ulcer healing by approximately thirteenfold without worsening glycaemic control, indicating that nutritional optimization rather than weight loss alone may drive improved outcomes.<sup>33</sup>

Earlier studies similarly reported that poor nutritional status predicts delayed healing and adverse outcomes independently of BMI, reinforcing that nutritional adequacy is not reliably captured by body weight alone.<sup>34</sup>

## The ‘Obesity Paradox’ In DFU

The concept of an ‘obesity paradox’ originates largely from cardiovascular and DM mortality studies, where overweight status has been associated with lower mortality, a pattern widely attributed to residual confounding, reverse causation and survival bias.<sup>35</sup> In the UK CPRD and Scottish Diabetes Research Network cohort, overweight and obese individuals demonstrated lower DFU incidence after extensive adjustment. The authors described these findings as novel and noted the potential influence of residual confounding and survival bias.<sup>36</sup> In contrast, systematic reviews of diabetic foot cohorts consistently associate underweight status with higher amputation and mortality, while higher BMI is linked to increased ulcer incidence and delayed healing.<sup>37</sup> However, these associations diminish after accounting for reverse-causation (weight loss due to chronic illness), survivor bias and incomplete adjustment for comorbidities. In contrast, among patients with established DFU, higher BMI consistently predicts larger ulcers, slower healing and more amputations, arguing that the paradox is a statistical artifact rather than a true protective effect. However, there is a gap in the literature addressing this, which requires studies with larger sample sizes to form generalizable data. Overall, current evidence therefore favours viewing obesity as a modifiable risk factor rather than a protective factor in the context of DFU.

**Table 1:** Links between Obesity & DFUs

Links between Obesity and DFUs	
Body Mass Index	Biomechanical loading, genetics, increased risk of neuropathy and PAD.
Chronic Inflammation	Endothelial dysfunction, impaired microvasculature, delayed wound healing.
Poor nutritional status	Appetite suppression, rapid weight reduction, inadequate protein and micronutrient consumption.

## Psycho-Socioeconomic Biobehavioural Factors

Intertwined with the pathological process of obesity are further intrinsic and extrinsic factors which contribute to a compromised wound healing environment and poor adherence to DFU management plans. The Psycho-Socioeconomic Biobehavioural (PSB) Framework categorizes these areas into key constituent parts.<sup>38</sup> (See Figure 2.)

Firstly, psychological barriers to adherence in patients with obesity and DFUs may include mental health conditions such as depression and anxiety or ambivalence to self-care plans.<sup>39</sup> Existing systematic reviews have included studies which suggest that patients aged between 33-79 are more likely to display symptoms of major depression following admission in an acute hospital setting.<sup>40</sup> This places a unique spotlight on acute multi-disciplinary foot care and the importance of addressing a patient’s psychological state alongside the treatment of a DFU. Moreover, patients referred to community podiatry clinics following discharge from the hospital may experience a continuation of these symptoms. This emphasizes the need for patient notes to highlight depression as a key indicator of adherence in a patient’s health-care records.

Second, socioeconomic barriers to adherence in patients with obesity and DFUs may include unemployment, lack of mobility and urbanization. The 2024 Darzi Report investigating the NHS in England highlighted that “health inequalities are headed in the wrong direction” with the poor housing, low income and insecure employment contributing to increased demand from a “society in distress”, including a rapid increase in rates of obesity. This is an important backdrop to the challenges clinicians face in addressing complex socioeconomic barriers alongside foot health inequity.<sup>41</sup>

Third, biobehavioural barriers to adherence in patients with obesity and DFUs may include iatrogenic weight loss from GLP-1 receptor agonists, Vitamin D deficiency, sleep apnea and self-neglect.<sup>42</sup> A recent multicentre cross-sectional study suggests this is particularly prevalent in developing countries such as Ethiopia.<sup>43</sup>

However, further primary studies are required to better understand the association between these conditions and specific behaviours in individuals with obesity and DFUs to advance health, disease risk and recovery globally.

By incorporating motivational interviewing techniques (engaging, focusing, evoking and planning) into the provision of education, ascertaining barriers earlier in a patient's care can be addressed.<sup>44</sup> With the SINBAD classification system for DFUs validated internationally as a communicative tool between clinicians,<sup>45</sup> a validated system is required for communication between a clinician and patient to address barriers to adherence. Primary studies investigating the validity and reliability of the PSB framework are required to provide clarity on its efficacy in clinical practice.

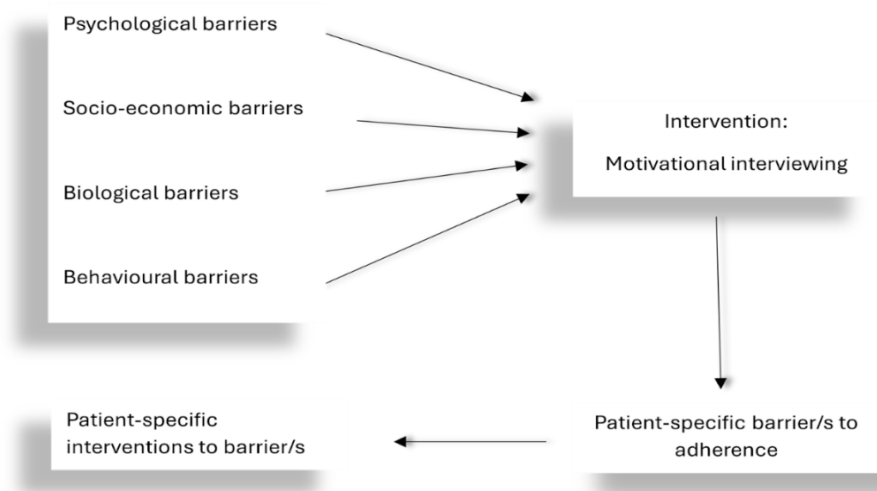
Conclusively, the complexity of the solution to poor adherence in patients with obesity and DFUs is commensurate with the conglomerate of barriers which a patient may reveal.<sup>36</sup> By integrating elements of motivational interviewing techniques into patient communication, clinicians are better placed to elicit vital information pertaining to barriers to adherence in patients with obesity and DFUs.

## Conclusion

The rise in global cases of obesity and DFUs suggests urgent action is needed across health-care sectors to manage commensurate increases in demand for wound care.

Current literature reveals several key gaps in evidence. First, longitudinal studies tracking changes in BMI, central adiposity indices such as WWI, BRI and ABSI and sarcopenic obesity in relation to incident DFU are needed to define dose response relationships and sex specific effects. Second, prospective trials examining the effects of intentional weight loss, through surgical or lifestyle interventions, on plantar pressure, bone density, neuropathy progression and ulcer recurrence are required to inform clinical guidance. Third, integrated intervention studies combining weight management, nutritional optimization, glycemic control and structured foot protection strategies, including custom orthoses and multidisciplinary foot care, should evaluate whether a comprehensive approach improves long-term outcomes. Until such evidence is available, excess adiposity should be considered a modifiable upstream determinant of DFU, alongside established vascular, neurological, metabolic and biomechanical contributors to ulcer development and healing.

With an increase in ageing populations and non-communicable diseases worldwide, eliminating ritualistic practice with better communication channels between podiatrists and multi-disciplinary teams can improve visibility of outcomes and coordination of bariatric care and DFU care. By developing clear clinical pathways between podiatry and nutrition services, wound balance can be achieved, alongside better performance frameworks and surveillance initiatives to advance limb preservation outcomes.



**Figure 2:** Psycho-socioeconomic Biobehavioural Framework for addressing barriers to adherence in patients with obesity & DFUs

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