BMJ Best Practice

Diabetes-related foot disease

Straight to the point of care

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Summary

Diabetes-related foot disease, including ulcers and infections, is a common and costly complication of diabetes mellitus.

Most diabetic foot ulcers are caused by repetitive trauma sustained during activity on a structurally abnormal, insensate foot.

Ulcers act as a portal of entry for bacterial infections. Preventing and/or healing ulcers helps prevent infections and thereby minimises risk of limb loss.

Prevention and identification may be by primary care physicians; however, UK guidance recommends referring all patients with active foot problems to a multidisciplinary diabetic foot care clinic or inpatient unit.

Antibiotics are recommended for management of infection, with associated drainage/debridement of any ongoing deep soft-tissue infection. Amputation is typically reserved for gangrene, loss of limb function, and severe non-reconstructable peripheral arterial disease.

Definition

The term 'diabetes-related foot disease' means disease of the foot in a person with current or previously diagnosed diabetes mellitus, including one or more of the following: peripheral neuropathy, peripheral artery disease, ulcer (i.e., a break in the skin that includes as a minimum the epidermis and part of the dermis), infection (i.e., any soft-tissue or bone infection occurring in the diabetic foot, including osteomyelitis), neuro-osteoarthropathy, gangrene, or amputation.[1][2]

Epidemiology

Diabetes mellitus is one of the most common chronic diseases in the UK. In 2023, there were 4.3 million people in the UK living with a diagnosis of diabetes.[3] This issue is global: in 2021, there were estimated to be 529 million people living with diabetes, equivalent to 6.1% of the world's population.[4] The prevalence of diagnosed diabetes mellitus in adults in the US increased from 7.1% in 2001-2004 to 10.1% in 2017-2020.[5] During 2021, the number of people in the US with diagnosed or undiagnosed diabetes was estimated to be 38.4 million (11.6% of the US population).[6]

It is estimated that up to one in three people with diabetes will have a diabetic foot ulcer at some point in their lives.[7] In 2016, some 131 million people were estimated to be living with diabetes-related lower-extremity complications, equivalent to 1.8% of the global population, with males and people aged 50-69 years disproportionately affected.[8] Diabetes is the most common cause of non-traumatic limb amputation, with foot ulcers preceding more than 80% of amputations.[9]

Peripheral sensory neuropathy and peripheral arterial disease (PAD) in patients with diabetes have an important role in the development of diabetic foot ulcers and risk of limb loss.[10] The prevalence of sensory neuropathy in diabetic populations is between 40% and 60%.[10] The prevalence of PAD in people with diabetes is 20% to 28%, rising to 50% among those with established diabetic foot ulcers.[11]

In one prospective cohort study of patients with diabetes without ulceration at enrolment, the incident rate of diabetic foot ulcers was 5 per 100 person-years.[12] In England and Wales, 108,450 ulcer episodes in people with diabetes were registered with the National Diabetes Foot Care Audit between 2014 and 2021.[13] There was a steady increase in ulcer episodes each audit year, from approximately 5000 registered in 2014-2015 to approximately 25,000 in 2019-2020 (although there was a decrease in reported episodes in 2020-2021, coinciding with the COVID-19 pandemic).[13] Of those with severe ulcers, 2.7% underwent major amputation (above the ankle) within 6 months, an approximately four-fold higher proportion than those with less severe ulcers, and 15% died within 1 year.[13]

In the US, the incidence of lower-extremity amputation was 6.8 per 1000 people with diabetes in 2020.[6] Unfortunately, significant treatment variability has been identified both in Europe and the US.

Aetiology

Various factors increase the risk of developing a diabetic foot ulcer.[14] These factors fall into three main categories:

- Abnormal distribution of plantar pressures due to structural/biomechanical abnormalities (e.g., bunions, hammer or mallet toes, midfoot deformities as a result of Charcot neuro-osteoarthropathy), impaired joint mobility, gait abnormalities, and motor neuropathies
- Impaired protective mechanisms (e.g., dry skin, immune system abnormalities, peripheral artery disease)
- Impaired recognition due to sensory neuropathy and/or visual impairments.

In most patients, epithelial ulceration results from repetitive trauma from the shoe contacting various prominent skin surfaces of the foot during ambulation. This, in addition to various combinations of the above factors, leads to a portal of entry for bacterial inoculation into the foot. Moreover, puncture wounds, along with these various risk factors, may also lead to bacterial inoculation and subsequent infection.

Pathophysiology

A healthy, intact visco-elastic and supple epithelium is the most important protection against foot infection. When various combinations of risk factors are present, ulceration or puncture injuries occur. The longer the duration of a wound, the higher the risk of both soft-tissue and bone infection. Infection often spreads along anatomical planes in the foot and will often cause hyperglycaemia. Chronic hyperglycaemia may lead to sensory neuropathy and immune system dysfunction, but hyperglycaemia does not directly affect the development of foot infections.

Untreated macrovascular atherosclerotic disease (typically popliteal- and tibial-level) poses a higher risk for foot infections among those with unhealed foot ulcers and increases the risk for amputation.[15] [16] Although microvascular abnormalities (including abnormal arteriovenous shunting and basement membrane thickening) are often present in patients with diabetes mellitus, there has been no evidence that occlusive phenomena in the microvasculature of the foot (i.e., small-vessel disease) contributes significantly to ulcer development, infection, or poor healing. Indeed, it was pointed out decades ago that a belief in the concept of small-vessel disease often leads to inappropriate pessimism towards the treatment of diabetic foot infections.[17]

There is significant overlap between risk factors for macro- and microvascular disease in diabetes-related foot disease, but in general hypercholesterolaemia and hypertension are more often associated with macrovascular disease development, whereas hyperglycaemia is most often associated with microvascular disease.[18] Many cardiovascular risk factors, such as tobacco use, are strongly associated with worsening of both macro- and microvascular disease, and both processes contribute to non-healing of diabetic foot ulcers. Cellular dysfunction is also thought to play a significant role in delayed wound healing, in particular dysregulation of immune cells causing chronic inflammation, and damage to endothelial and smooth muscle cells which impairs angiogenesis.[18]

The pathophysiological factors contributing to diabetes-related foot disease can be further compounded by societal and ethnic health disparities: US studies have found higher amputation rates among communities with economic hardship and rural-dwelling populations, and among Black and African-American, Hispanic and Latino, and Native American populations.[18] In the UK, by contrast, studies have found lower amputation rates in African and Caribbean men and in people of South Asian origin, compared to other ethnic groups, suggesting these discrepancies are driven more by socio-economic and regional variations than genetic factors.[19] [20]

Case history

Case history #1

A 62-year-old man with diabetes mellitus presents with a 3-day history of progressive left foot swelling, redness, and malaise. He reports noticing a blister on his forefoot several months ago after he started wearing work boots for a new job. He has dressed the area daily with bandages; however, it has not healed. He also has a history of sensory neuropathy, chronic kidney disease (stage 2), and hypertension. He is a smoker (1 pack per day). Physical examination is notable for fever (38.1°C [100.6°F]) and mild tachycardia (pulse rate of 105 bpm). There is a malodorous left foot ulcer overlying the first metatarsophalangeal joint. Fluctuance and blanching erythema extends 4 cm beyond the ulcer border. The remaining areas of the foot and ankle are notable for moderate pitting oedema. The dorsalis pedis pulse is palpable.

Case history #2

A 70-year-old man presents with a 3-month history of a non-healing foot ulcer. He is unsure how it began. He reports seeing a podiatrist once in the past, but failed to return for follow-up care. His medical history is notable for diabetes mellitus, remote stroke without residual neurological deficit, laser photocoagulation for retinopathy, and two previous percutaneous coronary interventions following myocardial infarcts. He stopped smoking cigarettes 3 years ago. Physical examination is notable for a plantar forefoot ulcer beneath the second metatarsal head. There is no associated erythema, swelling, or foul odour. No pedal pulses are palpable.

Other presentations

Posterior heel ulcers occur less frequently in ambulatory patients; they are often due to decubitus pressure in non-ambulatory patients who are debilitated by reduced mobility (e.g., by previous stroke or due to increased bed rest). Leg/calf ulcers (occurring between the knee and the malleoli at the ankle) are generally due to chronic venous insufficiency. Occasionally, infections are initiated by a puncture wound rather than ulceration from repetitive trauma.

Approach

General practitioners and primary care nurses are generally on the front line of care for patients with diabetes. As such, they have a key role in preventing and identifying active diabetic foot problems.

Diabetologists, specialist podiatrists, and other medical specialists are key in the evaluation and management of these patients, both in multidisciplinary diabetic foot clinics and when patients with diabetes are admitted for other acute medical conditions.

In the UK, the National Institute for Health and Care Excellence (NICE) recommends that any patient with an active diabetic foot problem is seen by the multidisciplinary foot care team within 1 working day.[9] If the problem is limb-threatening or life-threatening, refer the patient immediately to acute services and follow your local protocol to inform the multidisciplinary foot care service.[9]

A structured assessment of the risk of foot problems must be done:[9] [36]

- When diabetes is diagnosed and at least annually thereafter in all patients with diabetes (more frequently for those assessed to be at moderate or high risk of foot complications). See Screening for more details.
- Whenever a patient with diabetes is admitted to hospital for any reason or if there is any change in their status during an admission
- Whenever a patient with diabetes presents with a foot problem of any kind.

The main goals of the initial evaluation include:

- Identifying the presence of any foot ulcers.
- Assessing for any clinical symptoms or signs of infection, inflammation, or gangrene.
- Assessing for the presence of sensory neuropathy, ideally using a 10-g monofilament, but if this is not available the Ipswich Touch Test is a suitable alternative (lightly touching the tips of the patient's toes with the tip of your index finger for 1-2 seconds).[9] [36]
- Assessing for the presence of impaired vibration perception, using a 128-Hz tuning fork.[36]
- Documenting pedal pulses.
- Assessing for any signs of deformity.

This should be done even when there is no suspicion of diabetes-related foot disease.

- Bear in mind that the absence of symptoms does not exclude foot disease. The patient may have asymptomatic neuropathy, peripheral arterial disease, pre-ulcerative signs, or even an ulcer.[9] [36]

An active ulcer immediately requires a greater sense of urgency and should be classified according to the degree of tissue loss, the presence/degree of ischaemia, and the presence/degree of infection. The key factors associated with occurrence or recurrence include the presence of sensory neuropathy (loss of protective sensation); the presence of vascular disease; and/or a past history of an ulcer, Charcot's neuro-osteoarthropathy, or amputation. These three factors can easily be screened without complex equipment.[23]

History

Strong risk factors for diabetes-related foot disease include: sensory neuropathy, peripheral arterial disease, previous history of foot ulcer, previous history of major amputation, foot deformities, and end-stage renal disease.[9] [12] [14] [21] [22] [23] [24]

A diabetic foot ulcer is defined as a break in the skin that includes as a minimum the epidermis and part of the dermis and which occurs below/distal to the malleoli in a person with diabetes.[1]

Most patients who develop foot ulcers have at least some degree of sensory neuropathy. Sensory neuropathy blunts or obviates the nociceptive feedback that usually signals an injury sustained during ambulation or via a puncture wound. Lack of protective sensation due to sensory neuropathy is most often due to diabetes but can occasionally be due to other causes (e.g., alcohol abuse).

If an infection is present, it is common for patients to note the onset of foot pain in a previously insensate area. The presence of fever, chills, malaise, or anorexia is suggestive of an infection.[9]

Ask the patient whether they have had any history of micro- or macrovascular complications, claudication, or issues with glucose control.

Physical examination

Always examine the skin integrity of the foot and any muscular deformities in a well-lit room. When the feet are examined in a patient with diabetes, shoes, socks, bandages, and dressings should be removed, and both feet should be examined for evidence of:[9]

- Neuropathy: NICE recommends using a 10-g monofilament; the International Working Group on the Diabetic Foot suggests the Ipswich Touch Test or a 128-Hz tuning fork can be used as an alternative[24]
- Limb ischaemia (by palpation of pedal pulses, with absence of both pulses indicating peripheral arterial disease)
- Ulceration
- Callus formation
- Infection and/or inflammation
- Deformity
- Gangrene
- Charcot's neuro-osteoarthropathy

When examining the feet, pay special attention to weight-bearing areas, as the majority of non-healing foot ulcers and infections occur in these areas, resulting from repetitive trauma during ambulation on an insensate, sometimes structurally abnormal foot.

Patients with Charcot's neuro-osteoarthropathy leading to midfoot collapse may develop ulcers and infections in the midfoot that are associated with the structural abnormalities there.

Heel ulcers can develop due to pressure in non-ambulatory patients debilitated by other comorbidities or medical events (e.g., a history of stroke). They occur less frequently in ambulatory patients.

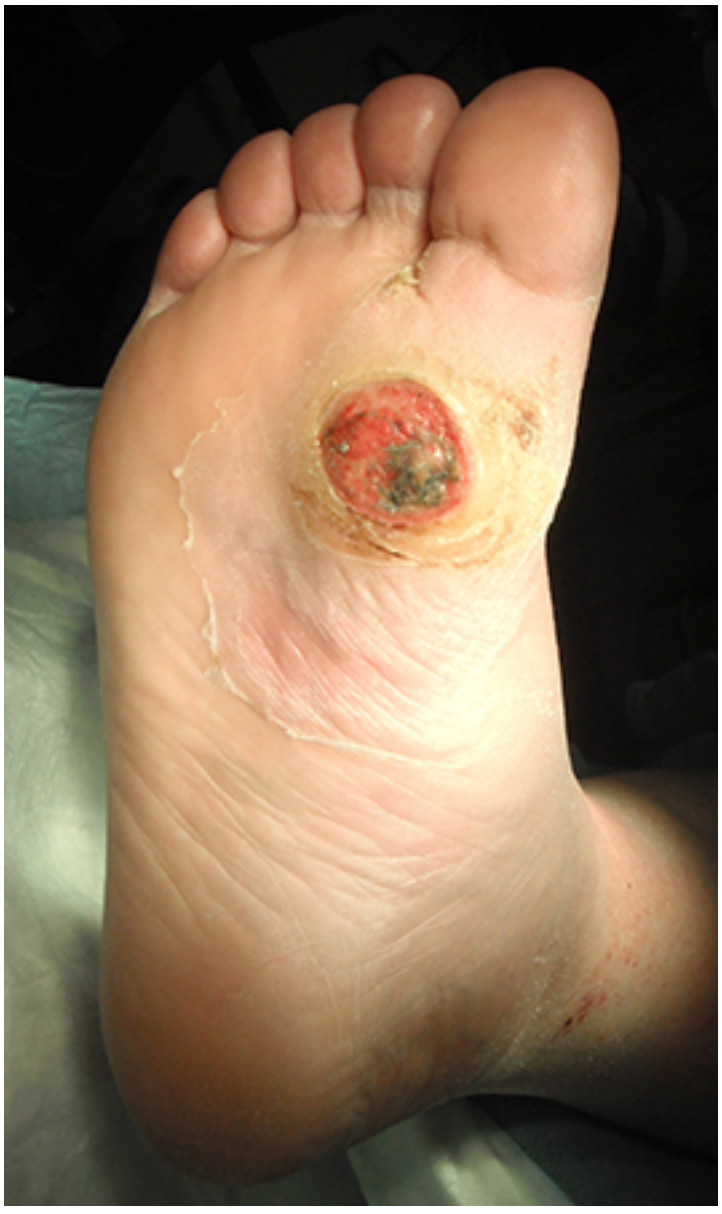
Whenever an ulcer is identified, document its size, depth, and position and classify it using a standardised system (for further details, see Diagnostic criteria). In the UK, NICE recommends use of the SINBAD system (Site, Ischaemia, Neuropathy, Bacterial Infection, Area, and Depth) to record the severity of the ulcer.[9] The result should be submitted to the NHS National Diabetes Foot Care Audit. [NHS National Diabetes Foot Care Audit] (https://digital.nhs.uk/data-and-information/clinical-audits-and-registries/national-diabetes-foot-care-audit)

Oedema and localised warmth of the foot, ankle, or calf is suggestive of infection. Erythema is suggestive of cellulitis, with or without a deep soft-tissue infection (i.e., abscess). Fluctuance is also suggestive of an abscess. Occasionally, infections are initiated by a puncture wound rather than ulceration from repetitive trauma. According to NICE and the IWGDF/Infectious Diseases Society of America (IDSA), a diabetic foot infection is defined by the presence of at least two of the following:[9] [40]

- Local swelling or induration
- Erythema (>0.5 cm around the wound)
- Local tenderness or pain
- Local warmth
- Purulent discharge

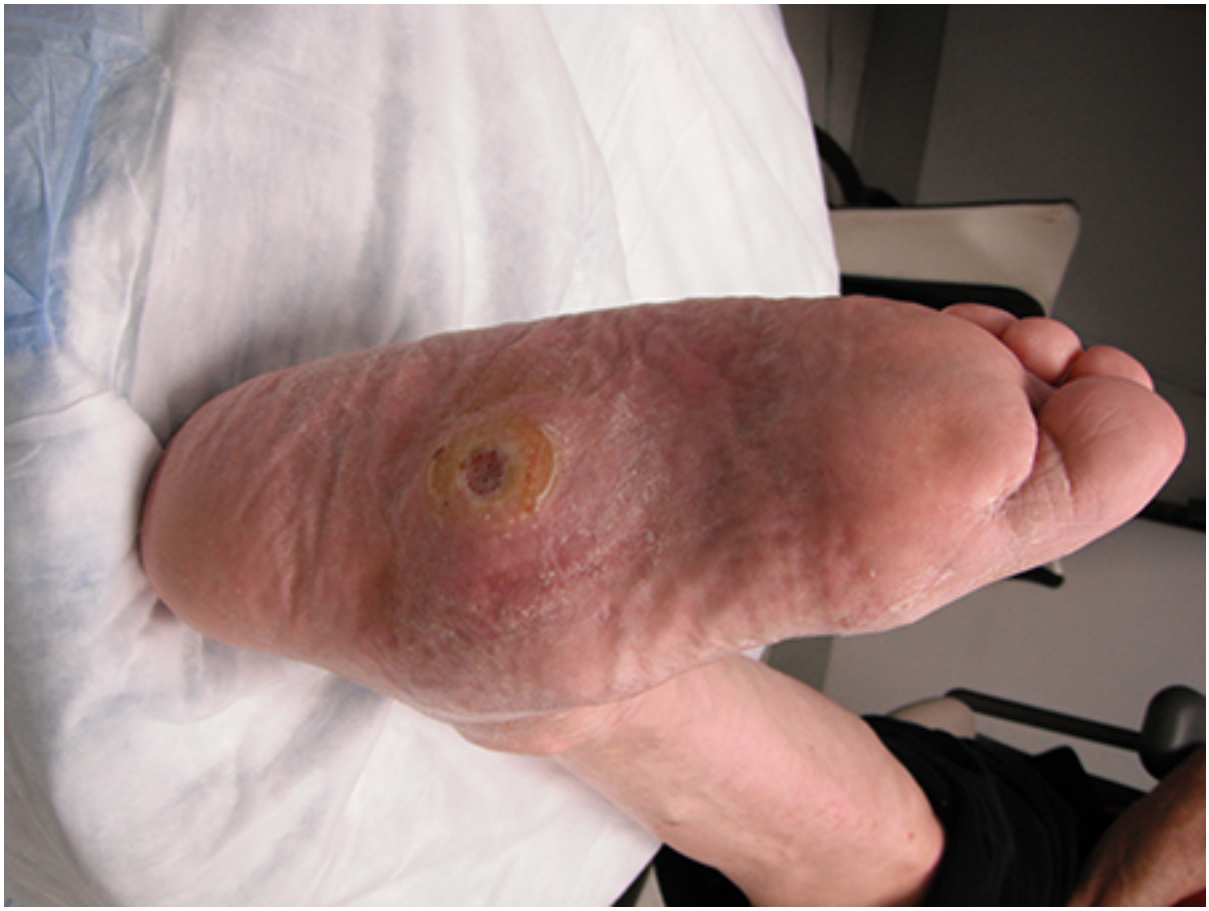
Classify and document the severity of any infection as mild, moderate or severe using the IWGDF/ Infectious Diseases Society of America (IDSA) system.[40]

It is worth noting that because of the impaired immune response and abnormal arteriovenous shunting present in the neuropathic foot, clinical signs of infection in patients with diabetes may be more subtle than in non-diabetic patients.



Uninfected foot ulcer overlying the plantar aspect of the first metatarsophalangeal joint. Note the hyperkeratotic skin (callus) surrounding the wound edge

From the collection of Dr Neal R. Barshes; used with permission



Midfoot ulcer in a patient with Charcot arthropathy (midfoot collapse)

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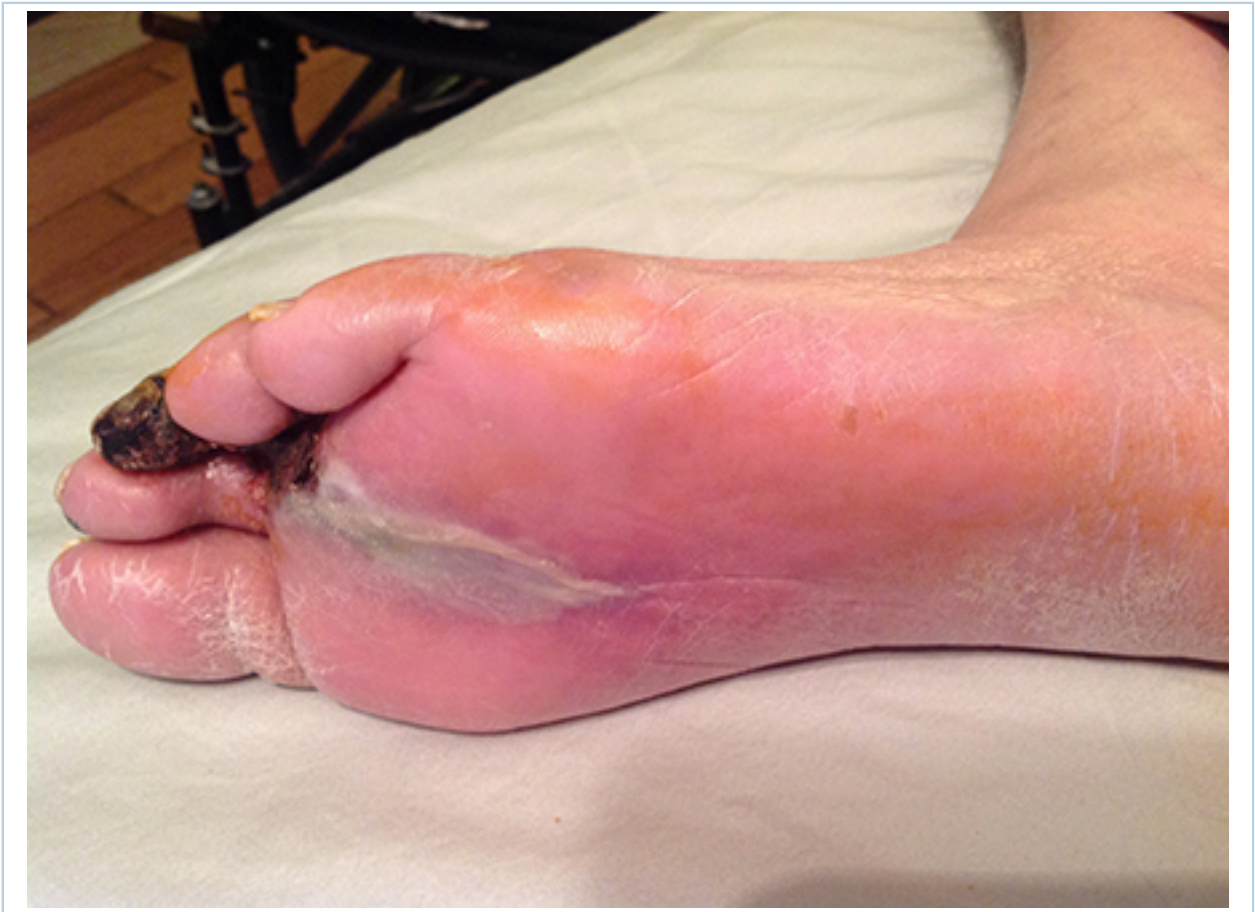

A foot infection originating from a gangrenous third toe. Note the erythema and fluctuance in the midfoot. An abscess cavity was found tracking under the longitudinal section of macerated skin

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When examining any infected foot ulcer, it is essential to consider whether there is underlying osteomyelitis, as its presence greatly increases the risk of amputation.[40] Osteomyelitis is particularly likely in wounds that are wide, deep, have been present for many weeks, are located over a bony prominence, show visible bone, or are accompanied by an erythematous, swollen ('sausage') toe.[40]

To assess for osteomyelitis, perform a probe-to-bone test as part of the physical examination, by gently inserting a sterile blunt metal probe into the wound. The test is defined as positive if the user feels a hard, gritty structure (i.e., bone) against the end of the probe. Although its reliability varies by users' technique and experience, overall the probe-to-bone test is the most useful examination technique for diagnosing osteomyelitis in diabetic foot infections (in conjunction with imaging and serum biomarkers), according to the IWGDF and IDSA. Its sensitivity and specificity are 0.87 and 0.83, respectively, suggesting that a positive result in a high-risk patient supports the diagnosis, whereas a negative result in a low-risk patient helps rule it out.[40]

For more information, see Assessing severity of infection and Diagnostic criteria .

Pedal pulse examination

Pulse examination is the most accessible modality for evaluating arterial blood flow to the foot; however, even when performed by an experienced physician such as a vascular surgeon, inter-observer agreement is modest.

The examination can be further impaired by the foot and ankle oedema that is common in a patient with a foot infection.

Nevertheless, the ability to palpate normal pedal pulses usually indicates adequate arterial perfusion to the foot. Absent or weak pulses in the presence of an active ulcer should prompt referral for evaluation and non-invasive testing.

Augmenting the examination with a handheld continuous-wave Doppler probe provides additional information when properly performed and interpreted. This is a non-invasive test.[41]

While monophasic signals do suggest significant peripheral arterial disease, biphasic signals do not exclude it.

In addition to pedal pulse examination, the American Diabetes Association recommends assessing capillary refill time, rubor on dependency, pallor on elevation, and venous filling time as other potential markers of peripheral arterial disease.[37]

Investigations

The diagnosis of foot complications in a person with diabetes is fundamentally a clinical diagnosis based on thorough history and examination: no blood tests are universally recommended, beyond those which form part of routine diabetes care. However in all patients with a suspected foot infection, initial investigations should include a full blood count (to assess for leucocytosis), blood glucose level, and inflammatory biomarkers such as C-reactive protein, erythrocyte sedimentation rate, or procalcitonin.[40] Renal function tests may provide prognostic information; presence of chronic kidney disease increases risk of amputation and all-cause mortality.[42] [43] Renal function tests can also be helpful in determining the feasibility of giving iodinated contrast for arterial imaging (if necessary). See Acute kidney injury (Prevention) .

Consider x-rays to determine the extent of diabetes-related foot problems if the clinical examination is suggestive of any bone or joint deformities, in particular if suspecting osteomyelitis or acute Charcot's neuro-osteoarthropathy (ideally a weight-bearing view).[9]

Characteristic radiographic features of osteomyelitis include loss of bone cortex, focal loss of trabecular pattern, periosteal reaction, bone sclerosis, and abnormal soft tissue density in the subcutaneous fat suggesting a deep ulcer or sinus tract.[40] Plain x-rays are less sensitive during the acute phase of osteomyelitis, and should be repeated in 2-3 weeks if suspicion is still high after a normal initial x-ray.[40] Although x-ray remains first line for diagnosing osteomyelitis due to its low cost and widespread availability, further imaging may be required, particularly to differentiate from non-infectious structural changes related to Charcot's neuro-osteoarthropathy. Magnetic resonance imaging of the foot is considered the best imaging test for this purpose and is recommended by NICE and the IWGDF when the initial x-ray is normal and the clinical suspicion of osteomyelitis remains.[9] [40] 18F-fluorodeoxyglucose positron emission tomography (FDG-PET/CT), 99mTc-exametazime Hexa Methyl Propylene Amine Oxime (HMPAO)-labelled white blood cell scintigraphy, or 99mTc-labeled Ubiquicidin (UBI) SPECT/CT single photon emission computed tomography (SPECT/CT) can be considered as alternatives to MRI for diagnosing osteomyelitis.[40]

If a diabetic foot infection is suspected and a wound is present, NICE recommends sending a soft-tissue or bone sample from the base of the debrided wound for microbiological examination.[9] Tissue

specimens collected via curettage or biopsy provide culture results with higher specificity and sensitivity than superficial swabs, although are more burdensome to collect.[40]

- If this cannot be obtained, then a deep-tissue swab should be taken to help guide choice of antibiotic.[9]
- In low-resource settings, a Gram-stain smear may be used as an alternative to culture to visualise the class of causative pathogen.[40]

Peripheral arterial disease (PAD)

If physical examination of a patient with a diabetic foot ulcer finds anything other than clearly palpable pulses (e.g., weak pulses, examination limited by oedema), order non-invasive vascular testing (ankle/toe pressures or arterial waveforms) for the assessment of PAD.[11]

- In the UK, NICE recommends calculating resting ankle-brachial pressure index (ABI) in patients with suspected peripheral arterial disease.[9] Results may be falsely elevated in patients with diabetes because of calcified arteries. Therefore, never rule out a diagnosis of PAD in a patient with diabetes solely based on a normal or raised ABI.[41]
- The IWGDF notes that no one test has been found to reliably exclude PAD in patients with a diabetic foot ulcer. Its 2023 guidelines, joint with the European Society for Vascular Surgery and Society for Vascular Surgery, recommend evaluation of pedal Doppler waveforms in combination with ankle systolic pressure, ABI, toe systolic pressure, and toe brachial index (TBI). PAD is less likely if ABI is 0.9 to 1.3, TBI is ≥0.70, and triphasic or biphasic pedal Doppler waveforms are present.[11]
- The American Diabetes Association (ADA) recommends performing Doppler ultrasound with pulse volume recordings and ankle/toe pressures in any patient with a history and examination suggestive of PAD. ABIs should be calculated but interpreted carefully, as results can be inaccurate in people with diabetes due to arterial calcification. Toe systolic blood pressure is preferred, as this is more accurate than ABI alone: toe pressures <30 mmHg are suggestive of PAD and poor ulcer healing. Individuals with abnormal pulse volume tracings and toe pressures <30 mmHg with foot ulcers should be referred for immediate vascular evaluation.[37]
- Guidelines from the American College of Cardiology Foundation and the American Heart Association state that a resting ABI is indicated in patients who have non-healing foot ulcers, as well as patients with exertional leg symptoms, patients aged 50 years or older with diabetes or a history of smoking, and all other patients aged 65 years and older, in order to establish a diagnosis of lower extremity peripheral arterial disease.[44]

When considering a revascularisation procedure in a patient with PAD and a diabetic foot ulcer, arterial imaging should be performed to provide detailed anatomical information of the lower limb vasculature including the presence, severity, and distribution of arterial stenoses.[11] Arterial imaging should extend all the way from the aorta to the foot, with detailed imaging of the tibial and pedal vessels in particular.

Arterial duplex ultrasound is non-invasive and is recommended by NICE as first-line imaging for all people with PAD for whom revascularisation is being considered.[41] Visualisation is, however, hampered by multi-segment disease and extensive arterial calcification. Angiography is often preferred to duplex ultrasound for this purpose: modalities include computed tomographic angiography, magnetic resonance angiography, and catheter digital subtraction angiography.[11] Of these, catheter digital subtraction angiography is considered the gold standard, according to the joint guidelines from the IWGDF, the European Society for Vascular Surgery and the Society for Vascular Surgery.[11] However, the guidelines

note that each technique has its advantages and disadvantages, and the choice depends on local availability and expertise.

For more information, see Peripheral arterial disease .

Classification of diabetic foot ulcers

A diabetic foot ulcer is a break in the skin that includes as a minimum the epidermis and part of the dermis and which occurs below/distal to the malleoli in a person with diabetes.[1] By history and clinical examination, diabetic foot ulcers can be classified as neuropathic, neuro-ischaemic (a combination of neuropathy and ischaemia), or ischaemic.[36] The majority of foot ulcers are purely neuropathic or neuro-ischaemic. Only a small percentage are purely ischaemic: these tend to be painful and follow from minor trauma.[36]

The SINBAD (Site, Ischaemia, Neuropathy, Bacterial Infection, Area, and Depth) scoring system is recommended by the IWGDF for assessing and classifying diabetic foot ulcers, as well as for audit, benchmarking, and communication between healthcare professionals.[7] [45] It is well validated and simple to use, and contains the majority of prognostic clinical features that predict outcome including likelihood of amputation. SINBAD is also recommended by NICE and is the system used by the UK National Diabetes Foot Care Audit.[9] [46] SINBAD uses a scoring system with a maximum of 6 points. A score of 3 or more is associated with an increased time to healing and greater risk of eventual failure to heal.[45] When using the SINBAD system for communication between healthcare professionals, clinicians should describe the individual variables rather than a total score.[7]

The WIfI (Wound, Ischaemia, Foot Infection) scoring system is also widely used for classifying and describing diabetic ulcers, and is recommended for this purpose by the American Heart Association on the grounds that it also helps determine amputation risk and aids clinical decision-making.[18] The IWGDF also endorses the WIfI system as a valid alternative to SINBAD for classifying and describing diabetic ulcers, provided there is sufficient expertise and resources to use it.[7] As with SINBAD, it is recommended that clinicians report the individual variables that make up the WIfI system, rather than giving a total score, when communicating between healthcare professionals.

To classify the severity of an infected diabetic foot ulcer, the IWGDF recommends use of the IWGDF/InfectiousDiseases Society of America system as the first-choice option to determine whether the infection is mild, moderate, or severe. This system is also recommended by NICE in the UK.[9]

No scoring systems are currently recommended by the IWGDF for predicting the outcome of an ulcer in a specific individual.[7]

For more details on these severity classification systems, see Diagnostic criteria .

Assessing severity of infection

In a person with diabetes and an infected foot ulcer, the IWGDF recommends the IWGDF/IDSA system to classify the severity of infection and guide infection management.[7] This system is also recommended by NICE in the UK.[9]

Infection severity

- 1: Uninfected
    - No systemic or local symptoms or signs of infection

- 2: Mild
    - IWGDF/IDSA: presence of ≥2 of the following: local swelling or induration, erythema 0.5 to <2.0 cm around the wound, local tenderness or pain, local increased warmth, or purulent discharge (exclude other causes of inflammatory response, such as trauma, gout, acute Charcot's neuro-osteoarthropathy, fracture, thrombosis, and venous stasis).[40]
- 3: Moderate
    - IWGDF/IDSA: infection (as for mild severity above) with no systemic manifestations and involving erythema extending ≥2 cm from the wound margin, and/or tissue deeper than skin and subcutaneous tissues (e.g., tendon, muscle, joint, and bone). Add 'O' for any infection involving bone (osteomyelitis).[40]
- 4: Severe
    - IWGDF/IDSA: any foot infection with associated manifestations of systemic inflammatory response syndrome, as manifested by ≥2 of the following: temperature >38°C or <36°C, heart rate >90 beats/min, respiratory rate >20 breaths/min or $PaCO_2$ < 4.3 kPa (32 mmHg), WBC count >12 × 10^9 cells/L (12,000/microlitre) (leukocytosis) or <4 × 10^9 cells/L (4000/microlitre) (leukopenia); or a normal WBC count with >10% immature (band) forms. Add 'O' for any infection involving bone (osteomyelitis).[40]

Making an accurate diagnosis of osteomyelitis in a diabetic foot can be difficult as there is no universally accepted definition or criteria, and low levels of agreement between commonly used diagnostic tests. Nevertheless, based on current evidence, the IWGDF and IDSA recommend a combination of probe-to-bone test, plain x-ray (and/or further imaging such as MRI), and serum inflammatory markers to support the diagnosis.[40] Bone biopsy is potentially definitive but not widely available, and lacks data demonstrating clear benefits to its use.[40]

History and exam

Key diagnostic factors

history of diabetes mellitus (common)

- Present in the majority of patients presenting with a foot ulcer or foot infection, and in all patients with diabetes-related foot disease.

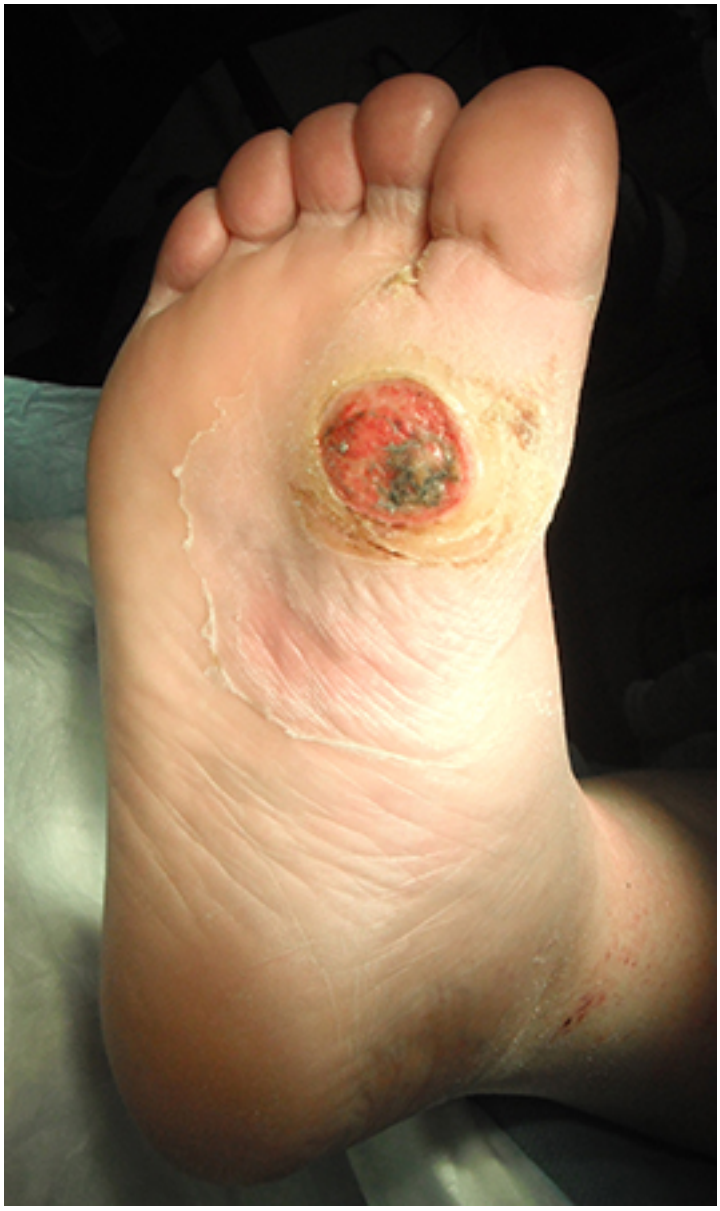
presence of risk factors (common)

- Key risk factors include sensory neuropathy, peripheral arterial disease, previous history of foot ulcer, foot deformity, limited foot and/or ankle joint mobility, previous history of major amputation, and end-stage renal disease requiring renal replacement therapy.

foot ulcer (common)

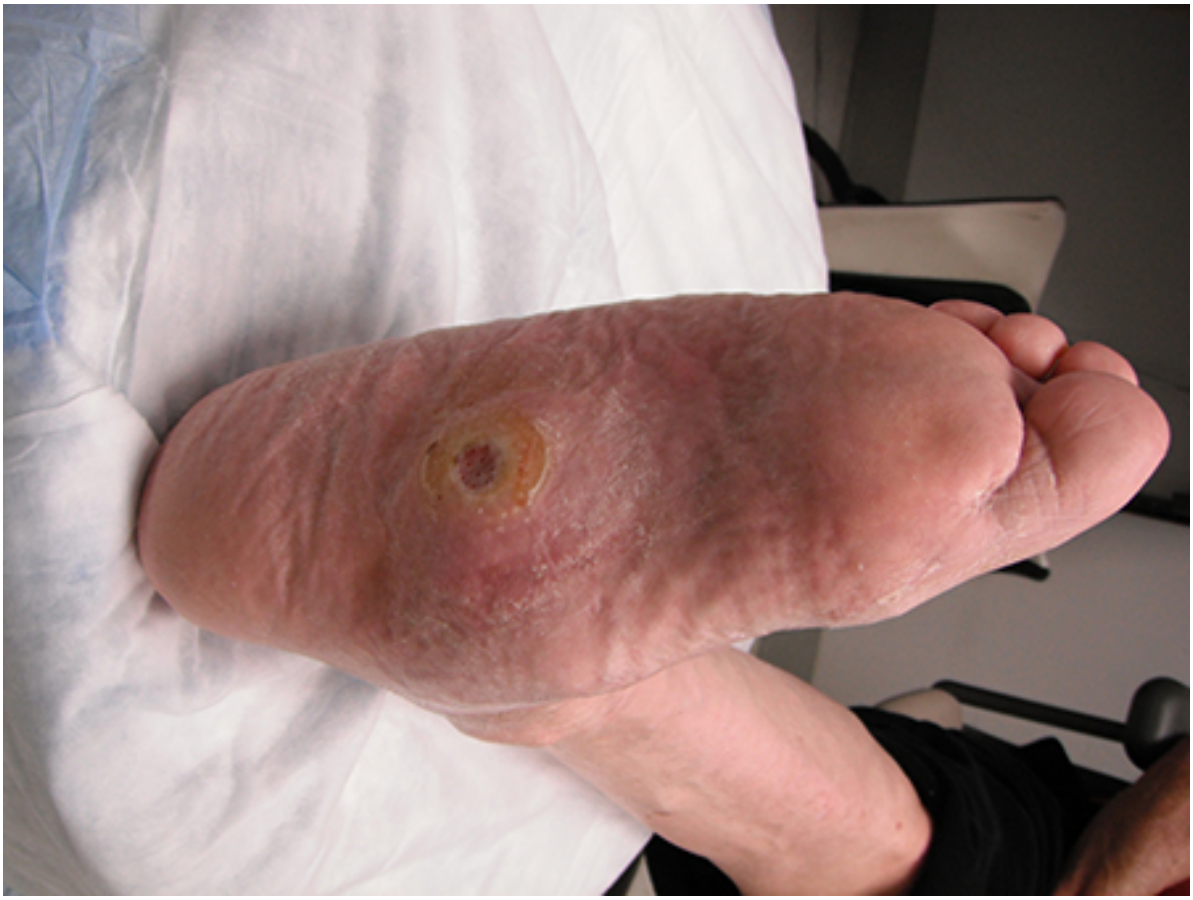
- A diabetic foot ulcer is defined as a break in the skin of the foot in a person with diabetes that includes as a minimum the epidermis and part of the dermis.[1] The majority of non-healing foot ulcers and

foot infections occur in weight-bearing areas of the foot, and result from repetitive trauma during ambulation on an insensate, sometimes structurally abnormal foot.

- Patients with Charcot's neuro-osteoarthropathy leading to midfoot collapse may develop ulcers and infections in the midfoot that are associated with structural abnormalities there. Heel ulcers may be due to pressure on the heels in non-ambulatory patients debilitated by other comorbidities or medical events; they occur less frequently in ambulatory patients.
- 

Uninfected foot ulcer overlying the plantar aspect of the first metatarsophalangeal joint. Note the hyperkeratotic skin (callus) surrounding the wound edge

From the collection of Dr Neal R. Barshes; used with permission



Midfoot ulcer in a patient with Charcot arthropathy (midfoot collapse)

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foot pain (common)

- Most patients who develop foot ulcers have at least some degree of sensory neuropathy. Sensory neuropathy blunts or obviates the nociceptive feedback that usually signals an injury sustained during ambulation or via a puncture wound. However, it is common for patients to note the onset of foot pain in a previously insensate area when an infection is present.

loss of protective sensation (common)

- A sign of peripheral neuropathy, characterised by an inability to sense light pressure. Assessed using a 10-g monofilament.[9]

foot deformity (common)

- Foot deformities can cause alteration in pressure distribution, predisposing the skin to traumatic ulceration.

fever or chills (uncommon)

- Suggests infection.

Other diagnostic factors

malaise (common)

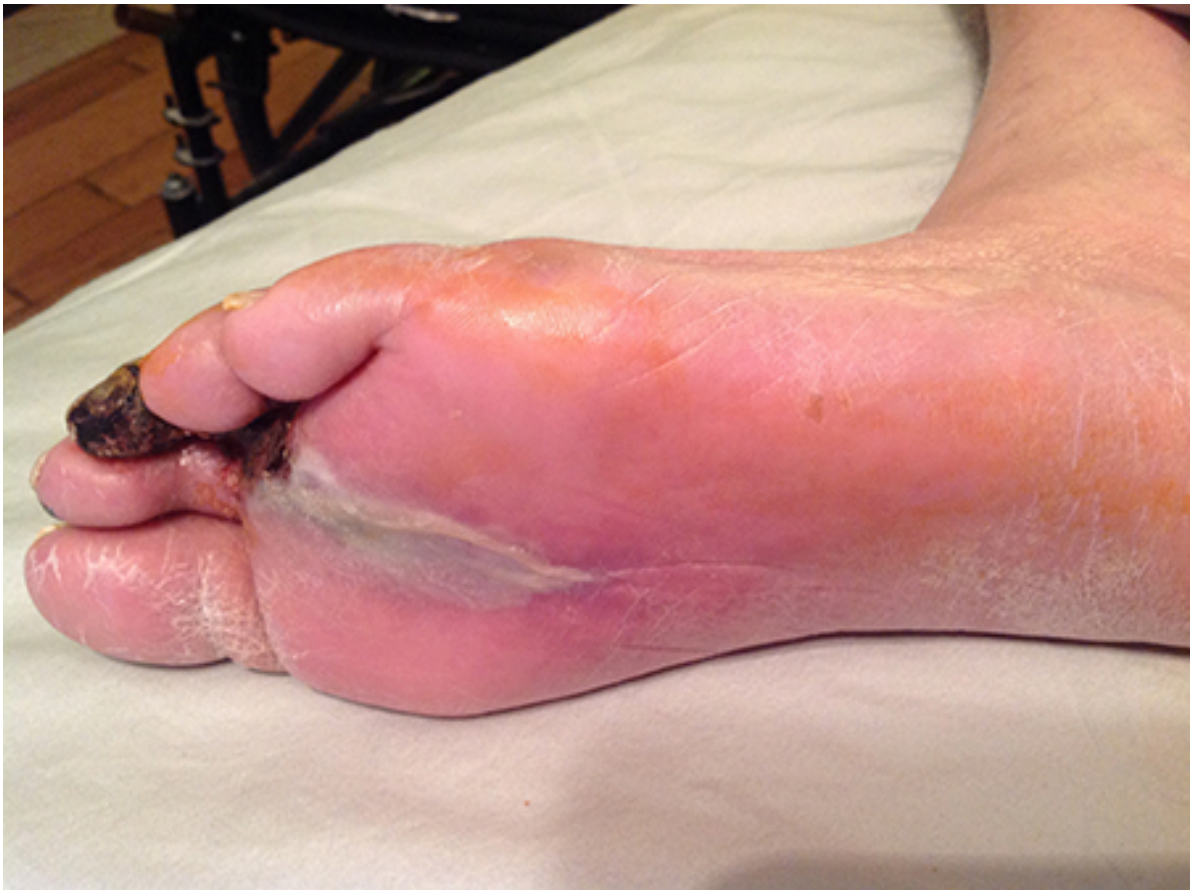
- Suggests infection.

anorexia (common)

- Suggests infection.

foot erythema (common)

- Suggests cellulitis, with or without deep soft-tissue infection (i.e., abscess).



A foot infection originating from a gangrenous third toe. Note the erythema and fluctuance in the midfoot. An abscess cavity was found tracking under the longitudinal section of macerated skin

From the collection of Dr Neal R. Barshes; used with permission

- However, in the absence of an open ulcer the diagnosis of acute Charcot's neuro-osteoarthropathy of the foot in a patient with peripheral sensory neuropathy should also be considered.

oedema of foot, ankle, or calf (common)

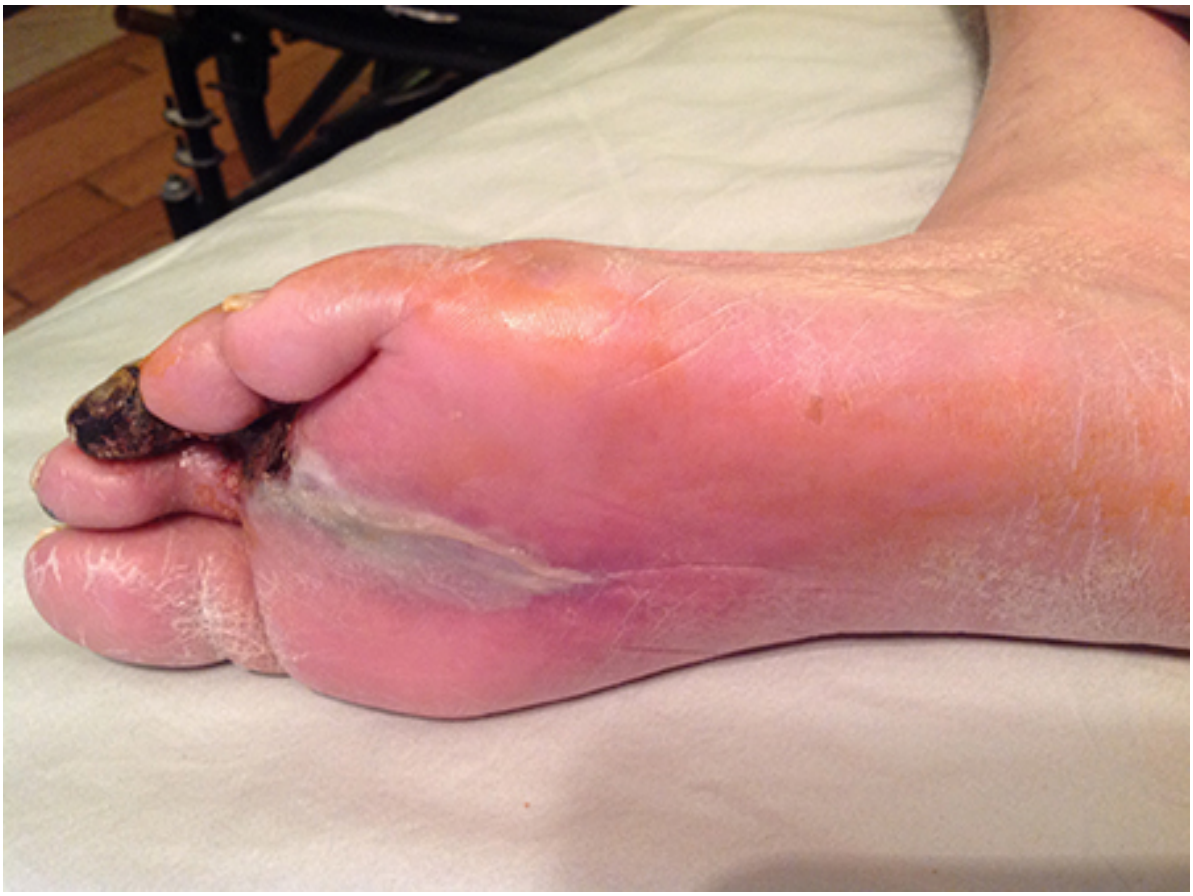
- Suggests infection.
- However, in the absence of an open ulcer the diagnosis of acute Charcot's neuro-osteoarthropathy of the foot in a patient with peripheral sensory neuropathy should also be considered.

absent pedal pulses (common)

- Consistent with the presence of peripheral artery disease.
- Ability to palpate normal pedal pulses usually indicates adequate arterial perfusion to the foot. Absent pulses in the presence of a diabetic foot ulcer should prompt referral for evaluation and non-invasive testing. In the UK, the National Institute for Health and Care Excellence recommends that the patient should be referred to the multidisciplinary foot care team within 1 working day.[9]

fluctuance (uncommon)

- The presence of pus suggests a deep soft-tissue infection (i.e., abscess).



A foot infection originating from a gangrenous third toe. Note the erythema and fluctuance in the midfoot. An abscess cavity was found tracking under the longitudinal section of macerated skin

From the collection of Dr Neal R. Barshes; used with permission

Risk factors

Strong

previous history of foot ulcer

- Approximately 40% of patients with a previous foot ulcer have a recurrence within 1 year of ulcer healing, with almost 60% experiencing a recurrence within 3 years and 65% within 5 years.[21]

previous history of amputation

- Leg amputation elevates the risk of ulceration in the contralateral foot through gait abnormalities and increased plantar pressures.[14] [22]

sensory neuropathy

- Aside from a previous history of ulcer or amputation, sensory neuropathy is the single most influential factor associated with the risk of foot ulcers (and subsequent infection or limb loss).[12] [23] It blunts or obviates the nociceptive feedback that usually signals an injury sustained during ambulation or via a puncture wound. Every patient with diabetes should have a foot assessment at least annually that includes a sensory examination: NICE recommends using a 10-g monofilament for this purpose; the International Working Group on the Diabetic Foot suggests the Ipswich Touch Test or a 128-Hz tuning fork can be used as alternatives.[9] [24]

peripheral arterial disease

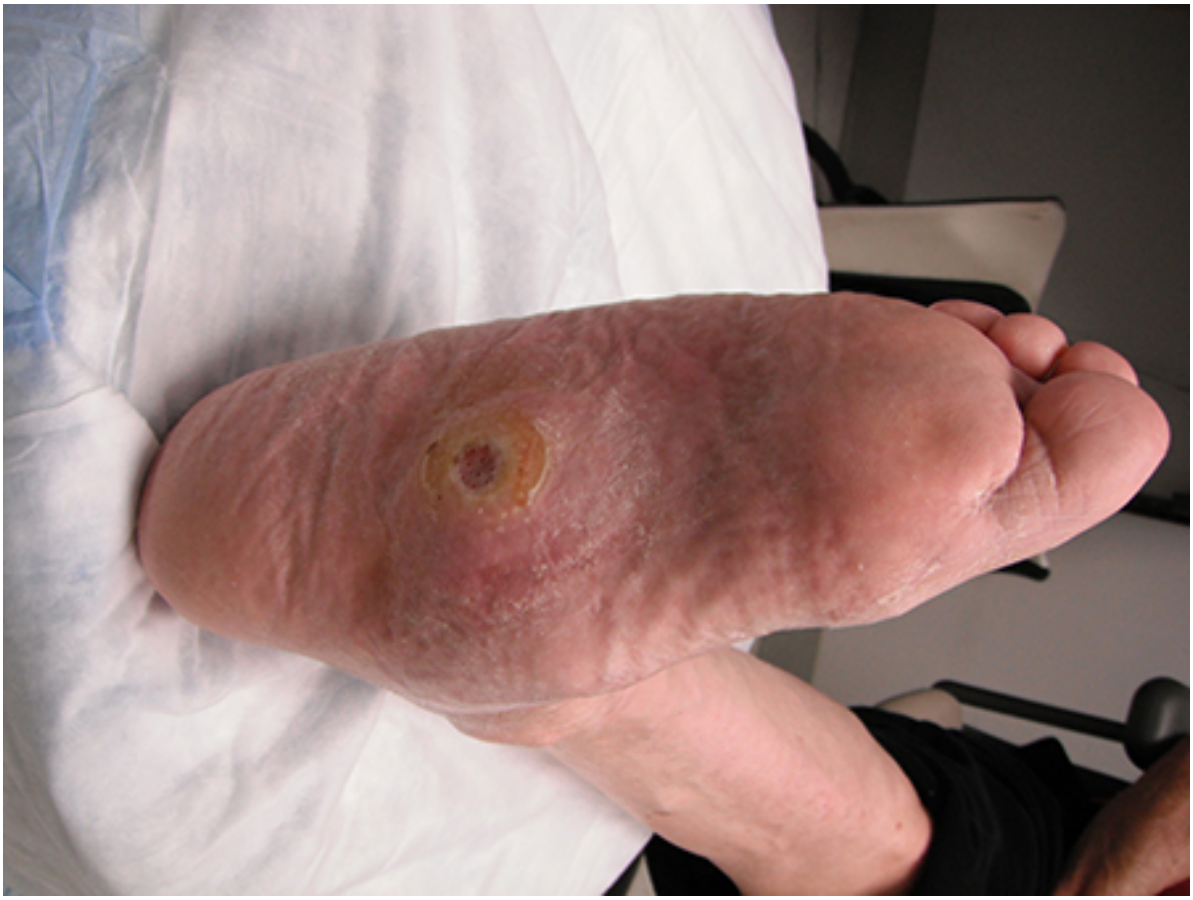
- Diabetes increases the risk of developing peripheral artery disease (PAD), and the presence of PAD increases the risk of foot ulcer development.[11] The prevalence of PAD in people with diabetes is 20% to 28%, rising to 50% among those with established diabetic foot ulcers.[11] Every patient with diabetes should be checked for PAD at least annually, by palpation of peripheral pulses.[9] [24] Further investigations for PAD are indicated if the physical examination finds anything other than clearly palpable pulses.

end-stage renal disease

- Although the precise mechanism is not known, end-stage renal disease has a significant impact on both the risk of developing, and the ability to heal foot ulcers. Patients with end-stage renal disease, including anyone on renal replacement therapy, are at high risk of developing foot ulcers.[9] [24] Renal insufficiency is also associated with the development of PAD and peripheral neuropathy.[25] [26]

foot deformities

- Structural foot deformities pose an ulceration risk by leading to improper distribution of pressure across the foot during ambulation. The presence of any foot deformity, in combination with sensory neuropathy or peripheral arterial disease, is considered a moderate risk factor for ulceration in the 2023 IWGDF risk stratification system. A foot deformity is defined as alterations or deviations from the normal shape or size of the foot, such as hammer toes, mallet toes, claw toes, hallux valgus, prominent metatarsal heads, pes cavus, pes planus, pes equinus, or results of Charcot's neuro-osteoarthropathy, trauma, amputations, other foot surgery or other causes.[24]
- Midfoot deformity as a result of Charcot's neuro-osteoarthropathy (i.e., midfoot collapse) is uncommon, but when present it can represent a significant challenge. Midfoot ulcers associated with deformity resulting from Charcot's neuro-osteoarthropathy are difficult to offload and heal. Osteomyelitis in the midfoot is more difficult to address with surgery without jeopardising the foot stability.



Midfoot ulcer in a patient with Charcot arthropathy (midfoot collapse)

From the collection of Dr Neal R. Barshes; used with permission

Weak

limited foot and/or ankle joint mobility

- Joint immobility in patients with diabetes mellitus is thought to be the result of deposition of advanced glycation end-products.
- Stiffness of the Achilles' tendon and/or gastrocnemius muscle may reduce ankle dorsiflexion, thereby increasing pressure in the forefoot during the push-off phase of gait. An inability to passively dorsiflex the ankle past neutral (i.e., to passively achieve an angle of <90° between the plantar foot and the calf) is considered abnormal.[27]
- There is some evidence that addressing ankle equinus via orthopaedic/podiatric lengthening procedures may help the healing of forefoot ulcers and may reduce their recurrence.[28]

visual impairment

- In addition to hindering the ability to visually inspect one’s feet, visual impairment in the setting of diabetes mellitus is often a marker of microvascular complications.

poor glycaemic control

- There is a very clear causal relationship between poor glucose control and the development of sensory neuropathy (among other microvascular complications). However, after adjusting for the presence or absence of sensory neuropathy, glucose control itself has a weaker association with the development of foot ulcers.[12]

Charcot's neuro-osteoarthropathy

- The presence of Charcot's neuro-osteoarthropathy predisposes to bone and joint deformities, which are themselves risk factors for development of foot ulceration and infection. However, there is currently insufficient evidence to support the inclusion of Charcot's neuro-osteoarthropathy as an independent risk factor for these outcomes by itself, according to the IWGDF.[24] [29]

obesity

- Obesity has been associated with increased prevalence of foot ulcers in those with diabetes.[30] [31] It is not known whether weight reduction in those with obesity may reduce the risk; there are currently no intervention studies.

obstructive sleep apnoea

- There is a suggested association between presence of obstructive sleep apnoea (OSA) and development of foot ulcers in those with diabetes.[32] [33] [34] OSA may also affect wound healing; but current data are inconsistent and more studies are needed.[35]

Investigations

1st test to order

Test	Result
clinical diagnosis • The diagnosis of diabetes-related foot disease is based primarily on a thorough, structured clinical examination, which should be performed in all patients with newly diagnosed diabetes. Examination should be repeated lifelong at regular intervals, as determined by risk stratification systems, guidelines, and local screening protocols.[36]	**may show ulcers or pre-ulcerative skin lesions, bone or joint deformities, impaired sensation or proprioception, weak or absent pulses, and/or signs of infection, inflammation or ischaemia**

Other tests to consider

Test	Result
FBC • Ordered in all patients with suspected diabetic foot infection as part of IWGDF/IDSA system for classifying infection severity. WBC count correlates poorly with infection severity.[40]	**may show leucocytosis**
blood glucose level • Ordered in all patients with suspected diabetic foot infection. Often elevated in the presence of infection.	**may be elevated**
microbiological culture • If a diabetic foot infection is suspected and a wound is present, send soft-tissue or bone samples from the base of the wound for microbiological evaluation.[9] This should ideally be a tissue specimen aseptically collected by curettage or biopsy: although more burdensome to collect, tissue specimens provide culture results with higher specificity and sensitivity than superficial swabs.[40] If this is not possible, NICE recommends that a deep swab be taken as it may provide useful information on the choice of antibiotic treatment.[9] • In low-resource settings, a Gram-stain smear may be used as an alternative to culture to visualise the class of causative pathogen.[40]	**positive for causative organism in infection; sensitivities may guide antibiotic treatment**
erythrocyte sedimentation rate • May suggest the presence of an infection, especially if highly elevated (≥ 70 mm/h). But accuracy can be affected by comorbidities such as anaemia, and tends to rise slowly so may not be elevated in early acute infections.[40]	**elevated**
C-reactive protein • May suggest the presence of an infection; however, has medium sensitivity/specificity.[47] • Levels rise quickly with acute infection, and correlate well with severity of infection.[40]	**elevated**
renal function • May provide prognostic information; presence of chronic kidney disease increases risk of amputation and all-cause mortality.[42] [43] Can also be helpful in determining the feasibility of giving certain antibiotics and iodinated contrast for arterial imaging (if necessary).	**variable**
ankle/toe pressures • If physical examination of a patient with a diabetic foot ulcer finds anything other than clearly palpable pulses (e.g., weak pulses, examination limited by oedema), order non-invasive testing of ankle/toe pressures.[11] • The UK National Institute for Health and Care Excellence recommends calculating resting ankle-brachial index (ABI) in patients with suspected peripheral arterial disease (PAD) but warns that a diagnosis of PAD cannot be excluded based solely on a normal or raised ABI result.[9] [41] • The International Working Group on the Diabetic Foot notes that no one test has been found to reliably exclude PAD in patients with a diabetic foot ulcer. Its guidelines recommend evaluation of pedal Doppler waveforms in combination with ankle systolic pressure, ABI, toe systolic pressure, and toe brachial index (TBI).[11]	**ABI reduced if PAD present; PAD is less likely if ABI is 0.9 to 1.3, TBI is ≥0.70, and triphasic or biphasic pedal Doppler waveforms are present[11]**

Test	Result
x-ray foot • To be considered in all patients, to determine the extent of diabetes-related foot complications, and particularly in any patients with suspected osteomyelitis or Charcot's neuro-osteoarthropathy. Weight-bearing films should be considered whenever feasible, especially in patients with Charcot's neuro-osteoarthropathy.[9] [40]	**may show hypolucencies, cortical destruction/ osteolysis, and/or joint subluxation**
angiography • Considered to be the best test for diagnosing peripheral artery disease. • May also provide the opportunity for endovascular intervention. • Imaging should extend all the way from the aorta to the foot, with detailed imaging of the tibial and pedal vessels in particular.[11]	**haemodynamically significant (i.e., >50%) stenosis or occlusions between the aorta and the foot (if peripheral artery disease present)**
MR angiography • Can be used to obtain anatomical information when considering revascularising a patient's lower extremity, but does not define the extent of calcification within arteries.[11]	**depiction of the foot arterial tree and accurate detection of arterial stenosis**
CT angiography • Diagnostic accuracy is affected by the presence of severe arterial calcification.[11]	**depiction of the foot arterial tree and accurate detection of arterial stenosis**
intra-arterial digital subtraction angiography • Gold standard imaging technique, especially for arteries below the knee and foot, but not as widely available as other modalities. Often used when CT or MR angiography are unavailable, fail to clearly define the anatomy, or when endovascular intervention is planned.[11]	**depiction of the foot arterial tree and accurate detection of arterial stenosis**
MRI foot • Considered the best imaging test for diagnosing osteomyelitis.	**hypo-intense areas of bone on T1 sequences; hyper-intense areas of bone on T2 sequences (if osteomyelitis present)**
arterial duplex ultrasound • Can provide anatomical details and physiological assessment of blood flow at specific arterial sites from the abdominal to the tibial arteries. • It requires specialist equipment and technical expertise to perform. • The UK National Institute for Health and Care Excellence suggests that duplex ultrasound should be offered as first-line imaging to all people with peripheral arterial disease for whom revascularisation is being considered.[41]	**assessment of the peripheral arterial circulation helps determine whether peripheral arterial disease is present**

Emerging tests

Test	Result
serum procalcitonin • May be elevated in infected diabetic foot ulcers but little correlation with infection severity. Expensive and not available in many laboratories.[40]	**may be elevated**
18F-fluorodeoxyglucose (FDG)-PET/CT • Can be considered as an alternative to MRI for diagnosing diabetes-related osteomyelitis of the foot, if MRI is contraindicated.[40]	**may support a diagnosis of osteomyelitis**
99mTc-exametazime Hexa Methyl Propylene Amine Oxime (HMPAO)-labeled white blood cell scintigraphy • Can be considered as an alternative to MRI for diagnosing diabetes-related osteomyelitis of the foot, if MRI is contraindicated.[40]	**may support a diagnosis of osteomyelitis**
99mTc-labeled Ubiquicidin (UBI) SPECT/CT single photon emission computed tomography (SPECT/CT) • Can be considered as an alternative to MRI for diagnosing diabetes-related osteomyelitis of the foot, if MRI is contraindicated.[40]	**may support a diagnosis of osteomyelitis**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Venous leg ulcer	• Generally occurs in the gaiter area of the leg (i.e., below the knee, above the malleoli), and rarely occurs on the dorsum of the foot. • May have surrounding lipodermatosclerosis (i.e., skin thickening and discoloration due to inflammation, scarring, and haemosiderin deposition).	• Ultrasound or venous plethysmography: can confirm venous incompetence, which makes this diagnosis more likely; however, venous leg ulcers can occasionally occur in the setting of a competent superficial venous system.
Gout	• May be associated with pain, swelling, and erythema in the forefoot, but is not generally adjacent to a foot ulcer. May occur in the setting of previous history of gout or secondary to open gout.	• Plain x-ray of foot: shows radiographic signs of gout (i.e., joint space narrowing, periarticular erosions, tophaceous arthritis).
Acute Charcot's neuro-osteoarthropathy	• May cause pain, erythema, and swelling. • May not be associated with a foot ulcer.	• Plain x-ray: may show cortical destruction, bony fragmentation, fractures, dislocation, and structural abnormalities of the foot. A normal x-ray does not rule out Charcot's neuro-osteoarthropathy. • MRI of foot: shows structural abnormalities of bone fracture and dislocation and, in active Charcot, bone marrow oedema.

Criteria

A diabetic foot ulcer is a break in the skin that includes as a minimum the epidermis and part of the dermis and which occurs below/distal to the malleoli in a person with diabetes.[1] By history and clinical examination, diabetic foot ulcers can be classified as neuropathic, neuro-ischaemic (a combination of neuropathy and ischaemia), or ischaemic.[36] The majority of foot ulcers are purely neuropathic or neuro-ischaemic. Only a small percentage are purely ischaemic: these tend to be painful and follow from minor trauma.[36]

SINBAD system for classification of diabetic foot ulcers

The SINBAD (Site, Ischaemia, Neuropathy, Bacterial Infection, Area, and Depth) scoring system is recommended by the IWGDF for assessing and classifying diabetic foot ulcers, as well as for audit, benchmarking, and communication between healthcare professionals.[7] [45] It is well validated and simple to use, and contains the majority of prognostic clinical features that predict outcome including likelihood of

amputation. SINBAD is also recommended by NICE and is the system used by the UK National Diabetes Foot Care Audit.[9] [46]

SINBAD uses a scoring system with a maximum of 6 points. A score of 3 or more is associated with an increased time to healing and greater risk of eventual failure to heal.[45] When using the SINBAD system, for communication between healthcare professionals, clinicians should describe the individual variables rather than a total score.[7]

Site

- Forefoot (0 points)
- Midfoot and hindfoot (1 point)

Ischaemia

- Pedal blood flow intact: at least one palpable pulse (0 points)
- Clinical evidence of reduced pedal flow (1 point)

Neuropathy

- Protective sensation intact (0 points)
- Protective sensation lost (1 point)

Bacterial infection

- None (0 points)
- Present (1 point)

Area

- Ulcer <1 cm^2 (0 points)
- Ulcer ≥1 cm^2 (1 point)

Depth

- Ulcer confined to skin and subcutaneous tissue (0 points)
- Ulcer reaching muscle, tendon, or deeper (1 point)

WIfI scoring

The WIfI (Wound, Ischaemia, Foot Infection) scoring system is also widely used for classifying and describing diabetic ulcers, and it is recommended for this purpose by the American Heart Association on the grounds that it also helps determine amputation risk and aids clinical decision-making.[18] The IWGDF also endorses the WIfI system as a valid alternative to SINBAD for classifying and describing diabetic ulcers, provided there is sufficient expertise and resources to use it.[7] As with SINBAD, it is recommended that clinicians report the individual variables that make up the WIfI system, rather than giving a total score.

The WIfI system can also be used in two other clinical situations: to stratify the likelihood of healing and amputation risk in patients with diabetes, peripheral arterial disease, and a foot ulcer or gangrene; and to describe infected ulcers (although the IWGDF/Infectious Diseases Society of America [IDSA] classification is recommended as first-choice for the latter scenario).[7]

Wound (W):

- 0: no ulcer or gangrene
- 1: mild - small, shallow ulcer(s) on distal leg or foot; no exposed bone (unless limited to distal phalanx); no gangrene
- 2: moderate - deeper ulcer with exposed bone, joint, or tendon; generally not involving the heel; shallow heel ulcer without calcaneal involvement; gangrenous changes limited to digits

- 3: severe - extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer and/or calcaneal involvement; extensive gangrene involving forefoot and/or midfoot; full thickness heel necrosis and/or calcaneal involvement

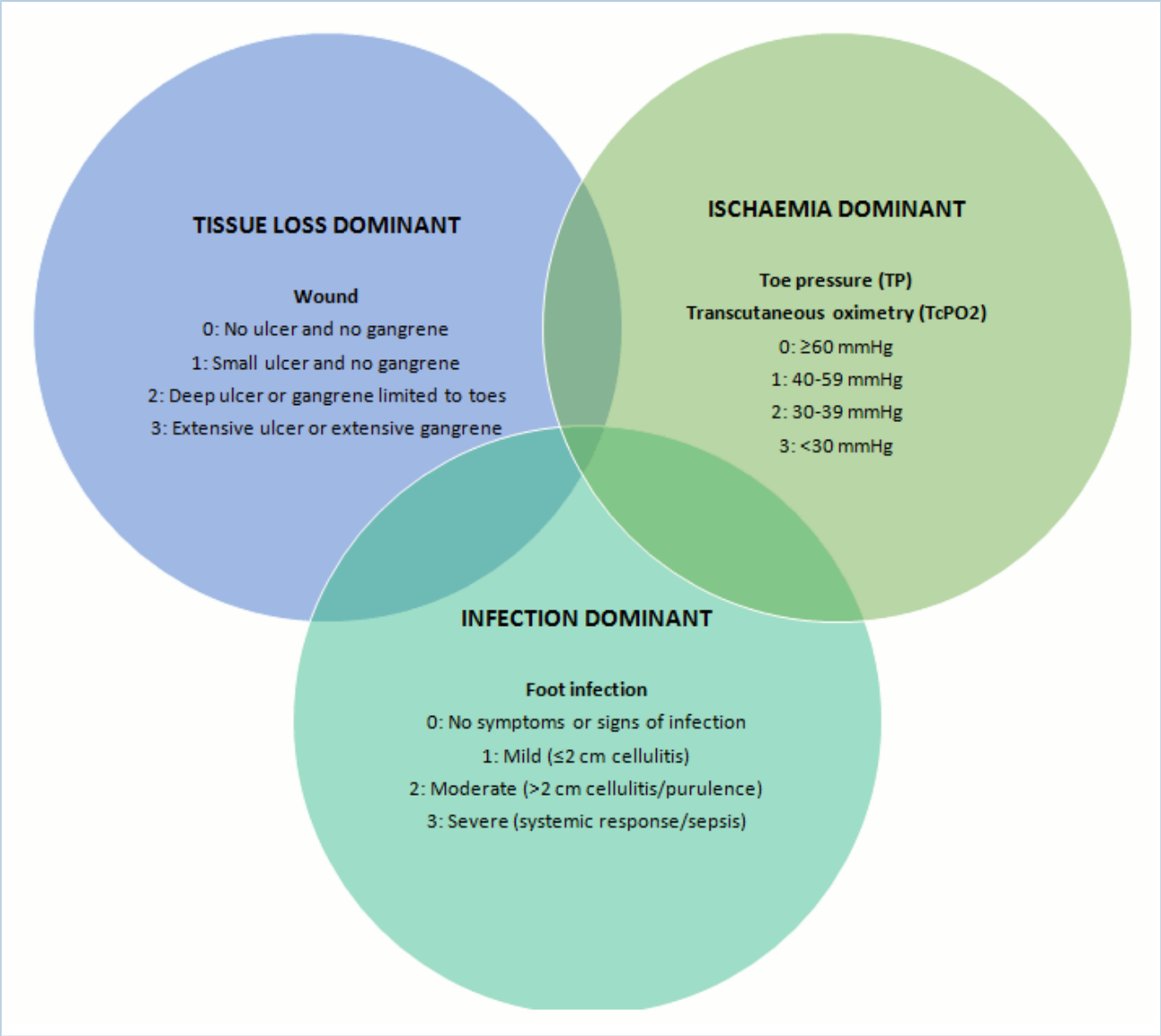
Ischaemia (I):

- 0: ankle-brachial index (ABI) ≥0.80; ankle systolic pressure >100 mmHg; toe pressure (TP)/transcutaneous oximetry ($TcPO_2$) ≥60 mmHg
- 1: mild - ABI 0.6 to 0.79; ankle systolic pressure 70-100 mmHg; TP/$TcPO_2$ 40-59 mmHg
- 2: moderate - ABI 0.4 to 0.59; ankle systolic pressure 50-70 mmHg; TP/$TcPO_2$ 30-39 mmHg
- 3: severe - ABI ≤0.39; ankle systolic pressure <50 mmHg; TP/$TcPO_2$ <30 mmHg

Foot infection (fI):

- 0: no symptoms or signs of infection
- 1: mild - infection present, as defined by the presence of at least two of the following:
    - Local swelling or induration
    - Erythema >0.5 cm to ≤2 cm around ulcer
    - Local tenderness or pain
    - Local warmth
    - Purulent discharge
- 2: moderate - local infection (as described above) with erythema >2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis); no systemic inflammatory response signs
- 3: severe (limb and/or life-threatening) - local infection (as described above) with signs of systemic inflammatory response syndrome as manifested by at least two of the following:
    - Temperature >38°C (>100.4°F) or <36°C (<96.8°F)
    - Heart rate >90 bpm
    - Respiratory rate >20 breaths/minute or $PaCO_2$ <32 mmHg
    - WBC count >12 × 10^9 cells/L (12,000/microlitre) (leukocytosis) or <4 × 10^9 cells/L (4000/microlitre) (leukopenia); or a normal WBC count with >10% immature (band) forms

A simple Venn diagram has been designed to assist clinicians in using the WIfI system, to determine which of the three factors (wound, ischaemia, or infection) is dominant.



Diabetic foot problems can be related to the presence of a wound, ischaemia, or infection (WIfI). Which of these parameters is dominant can vary, and a flexible long-term management approach is needed. The Venn diagram shows intersecting rings of dominance for these three parameters, with gradings listed for each. The shaded areas represent combinations of these parameters of dominance
From the collection of Dr David G. Armstrong and Dr Joseph L. Mills Sr; used with permission

Foot infections

According to NICE and the IWGDF/IDSA, a diabetic foot infection is defined by the presence of at least two of the following:[9] [40]

- Local swelling or induration
- Erythema (>0.5 cm around the wound)
- Local tenderness or pain
- Local warmth
- Purulent discharge

IWGDF/IDSA infection classification

In a person with diabetes and an infected foot ulcer, the IWGDF and NICE recommend the IWGDF/IDSA infection classification as the first choice to characterise the infection and guide management.[9] [40] The WIfI system, described above, can be used as an alternative for this purpose.

IWGDF/ISDA classification consists of three grades of severity for diabetic foot infection. It was originally developed as part of the PEDIS classification for research purposes and is used as a guideline for management, in particular to identify which patients require hospital admission for intravenous antibiotics. It is a strong predictor of the need for hospitalisation.[48] It has also been validated for risk of both major and minor amputation.[49] [50]

Infection severity[40]

- 1: Uninfected
    - No systemic or local symptoms or signs of infection
- 2: Mild
    - Presence of ≥2 of the following: local swelling or induration, erythema 0.5 to <2.0 cm around the wound, local tenderness or pain, local increased warmth, or purulent discharge (exclude other causes of inflammatory response, such as trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, and venous stasis).
- 3: Moderate: Add 'O' for any infection involving bone (osteomyelitis)
    - Infection (as for mild severity above) with no systemic manifestations and involving erythema extending ≥2 cm from the wound margin, and/or tissue deeper than skin and subcutaneous tissues (e.g., tendon, muscle, joint, and bone). Add 'O' for any infection involving bone (osteomyelitis).
- 4: Severe: Add 'O' for any infection involving bone (osteomyelitis)
    - Any foot infection with associated manifestations of systemic inflammatory response syndrome, as manifested by ≥2 of the following: temperature >38°C or <36°C, heart rate >90 beats/minute, respiratory rate >20 breaths/minute or $PaCO_2$ < 4.3 kPa (32 mmHg), WBC count >12 × 10^9 cells/L (12,000/microlitre) (leukocytosis) or <4 × 10^9 cells/L (4000/microlitre) (leukopenia); or a normal WBC count with >10% immature (band) forms.

Screening

Screening for foot complications in people with diabetes over the age of 12 should be done at least once yearly.[9] [24] [37] The screening examination identifies risk factors and may help reduce the risk of limb loss. The importance of foot care must be emphasised to the patient as part of the annual assessment.[9]

See Diagnosis approach (Physical examination) for more information on how to perform a foot examination in a person with diabetes.

In the UK, the National Institute for Health and Care Excellence (NICE) recommends assessing the risk of foot problems in adults with diabetes:[9]

- At the time of diagnosis of diabetes, and then at least annually
- When any foot problems arise
- On any admission to hospital, and if there is any change in the patient's status when in hospital

Patients aged 12-17 years with diabetes should have their feet assessed annually by an appropriately skilled team (in the UK, this should be the paediatric care or transitional care team).[9]

NICE recommends stratifying the person's risk of developing a diabetic foot problem using the following classification.[9]

- Low risk: no risk factors present except callus alone.
- Moderate risk: one or more of deformity, neuropathy, or peripheral arterial disease.
- High risk: one or more of previous ulceration; previous amputation; on renal replacement therapy; neuropathy and non-critical limb ischaemia together; neuropathy in combination with callus and/or deformity; or non-critical limb ischaemia in combination with callus and/or deformity.
- Active diabetic foot problem: one or more of ulceration; infection; chronic limb-threatening ischaemia; gangrene; or suspicion of an acute Charcot neuro-osteoarthropathy, or an unexplained hot, swollen foot with a change in colour, with or without pain.

Refer any patient who is at moderate or high risk to a specialist foot protection service; in the UK, NICE recommends that any patient at high risk must be seen within 2-4 weeks and any patient at moderate risk must be seen within 6-8 weeks.[9] Foot reassessments should be carried out annually for those at low risk, every 3-6 months for those at moderate risk, and at least every 1-2 months for those at high risk.[9]

See Management approach (Prevention) for more information on the recommended frequency of foot checks following risk stratification.

The American Diabetes Association (ADA) also recommends screening for foot complications in patients with diabetes at least once yearly.[37] [51] At-risk individuals should be assessed at each visit and should be referred to foot care specialists for ongoing preventive care and surveillance.

The IWGDF has developed a risk stratification system for assessing a patient's risk of developing foot ulcers, which is also recommended by the ADA.[24] [37] [51] The frequency of foot checks can be determined based on this system, which groups people into risk categories from 0 to 4:

Category 0 (very low risk):

- No loss of protective sensation (LOPS) and no peripheral arterial disease (PAD):

Annual foot screening and examination

Category 1 (low risk):

- LOPS or PAD

Foot screening and examination once every 6-12 months

Category 2 (moderate risk):

- LOPS + PAD, or
- LOPS + foot deformity, or
- PAD + foot deformity

Foot screening and examination once every 3-6 months

Category 3 (high risk):

- LOPS or PAD, and one or more of the following:
  - History of a foot ulcer
  - A lower extremity amputation (minor or major)
  - End-stage renal disease

Foot screening and examination once every 1-3 months

LOPS is defined as a reduction in sensation or proprioception, as assessed using a 10-g monofilament, the Ipswich Touch Test, tuning fork or biothesiometer/neurothesiometer.

The IWGDF definition of 'foot deformity' includes any limitation in foot or ankle movement. See History and exam for the full list of deformities.

Patients with diabetic foot ulcers are at especially high risk of malnutrition. It is recommended that healthcare providers develop and implement a formalised nutrition screening and assessment protocol to help identify patients with or at risk of malnutrition. A number of validated screening tools are available; for example, Nutritional Risk Index (NRI), Malnutrition Universal Screening Tool (MUST), and Mini Nutritional Assessment (MNA).[52] Choice of screening tool depends on the population and available resources. If initial screening suggests an increased risk for malnutrition, the next step should be a thorough nutrition assessment; for example, Patient-Centered Subjective Global Assessment (PC-SGA) or Nutrition Focused Physical Assessment (NFPA).[52]

Approach

General practitioners and primary care nurses are generally on the front line of care for patients with diabetes. As such, they have a key role in preventing and identifying active diabetic foot problems. Diabetologists, specialist podiatrists, and other medical specialists may also be involved in the evaluation and management of these patients, particularly when people with diabetes are admitted for other acute medical conditions.

As well as multidisciplinary care, there are five key principles which form the mainstay of management of diabetic foot ulcers:[9] [36]

- Wound debridement
- Wound dressing
- Pressure offloading
- Treatment of infection
- Treatment of ischaemia and restoration of tissue perfusion

The majority of foot ulcers will heal provided treatment is based on these principles, according to the International Working Group on the Diabetic Foot (IWGDF).[36] They also emphasise the importance of holistic, person-centred care that goes beyond the feet, to include optimising glycaemic control and cardiovascular risk factors, treating oedema, malnutrition, and depression, and addressing other psycho-social difficulties.[36]

It is important to remember the need for proper management of the diabetes itself (e.g., regular check-ups, maintenance of target blood glucose levels, blood pressure, and lipid management) according to current guidelines. These goals do not change in the presence or absence of diabetes-related foot disease. There is some evidence that intensive glucose control is associated with a long-term reduction in risk of developing diabetic foot ulcers in patients with type 1 diabetes.[53]

Sodium-glucose cotransporter-2 (SGLT2) inhibitors should not be started in drug-naïve people with a diabetes-related foot ulcer or gangrene, and temporary discontinuation should be considered in people who develop a foot ulcer or gangrene while already using them, until the foot is healed, according to joint guidelines from the IWGDF, European Society for Vascular Surgery and Society for Vascular Surgery.[11] This is due to a rare but serious side effect of diabetic ketoacidosis (DKA) with SGLT2 inhibitors, which is made more likely during acute illness and peri-operative periods. As patients with peripheral arterial disease, foot ulcers or gangrene are vulnerable to infections and may need to undergo urgent surgery, it is therefore pragmatic to avoid these medications to reduce DKA risk. Moreover, canagliflozin was associated with an increased risk of amputation in one randomised controlled trial.[54] Although this finding has not been borne out by other studies, the guidelines note that people with foot ulcers were frequently excluded from clinical trials of SGLT2 inhibitors so their safety in these patients remains uncertain.[11]

For more information on the medical management of diabetes in general, see Type 2 diabetes in adults and Type 1 diabetes .

Referral for multidisciplinary care in hospital and community settings

Make an immediate referral to acute services for any patient who has a limb-threatening or life-threatening diabetic foot problem.[9]

In the UK, the National Institute for Health and Care Excellence (NICE) recommends informing the multidisciplinary foot care service so the patient can be assessed and an individualised treatment plan can be put in place.

If the patient is already in hospital when the foot complication is identified, ensure the multidisciplinary foot care team is alerted and involved in their care.[9]

Examples of limb-threatening and life-threatening diabetic foot problems include:

- Ulceration with fever or any signs of sepsis
- Ulceration with limb ischaemia
- Clinical concern that there is a deep-seated soft-tissue or bone infection (with or without ulceration)
- Gangrene (with or without ulceration)

For any other patient with an active diabetic foot problem, refer within 1 working day to the multidisciplinary foot care/foot protection service (according to local protocols).[9]

- The foot care service should triage the patient within 1 further working day.

It is worth noting that because of the impaired immune response and abnormal arteriovenous shunting present in the neuropathic foot, clinical signs of infection in people with diabetes may be more subtle than in people who do not have diabetes.

Always consider the possibility of other diagnoses, with a particular emphasis on more serious conditions such as sepsis, necrotising fasciitis, limb ischaemia, or osteomyelitis.[9]

See Sepsis in adults , Sepsis in children , and Osteomyelitis .

The multidisciplinary foot care team should be led by a named healthcare professional, and consist of specialists with skills in podiatry, wound care nursing, diabetology, diabetes specialist nursing, vascular surgery, orthopaedic surgery, infectious disease, biomechanics and orthoses, interventional radiology, and casting, as well as other allied health professionals who work together to optimise patient care.[9]

The American Diabetes Association (ADA) also advocates an interprofessional approach for all patients with foot ulcers and high-risk feet, ideally facilitated by a podiatrist.[37]

Wound debridement

Debridement of slough, necrotic tissue, and surrounding callus of the ulcer is recommended, after taking account of relative contraindications such as pain or severe ischaemia.[55] The goal of debridement is to create a clean wound bed and promote wound healing.

- Sharp debridement of ulcers using surgical instruments remains the standard of care, despite a lack of high-quality clinical trials to support its use.
- Neuropathic ulcers can usually be debrided without the need for local anaesthesia.[36]
- Numerous alternative debridement techniques exist, including using enzymes, larvae, hydrogels, lasers, and ultrasound; however, there is currently insufficient evidence to support the routine use of any of these over sharp debridement, according to the International Working Group on the Diabetic Foot (IWGDF).[55]
- Debridement of diabetic foot ulcers in a hospital setting should only be done by members of the multidisciplinary foot care team, using the technique that best matches their specialist expertise and clinical experience, the site of the diabetic foot ulcer, and the patient's

preference.[9] Community-based debridement should only be done by healthcare professionals with the relevant skills and training.[9]

- There is reasonable-quality evidence that negative pressure wound therapy after surgical debridement may decrease the time to healing and both NICE and the IWGDF recommend its use in this circumstance.[9][55]

See Emerging treatments for discussion of adjunctive therapies to promote wound healing in diabetic foot ulcers, including hyperbaric and topical oxygen therapy. Topical medications, vitamins, physical therapies, and gasses other than oxygen are not currently recommended for this purpose.[55]

Wound dressing

The choice of wound dressing when treating diabetic foot ulcers should depend on the clinical assessment of the wound.[9]

Evidence is sparse to inform decisions about the best choice of wound dressing for diabetic foot ulcers. Dressings that maintain a moist environment, including non-adherent dressings covered with a layer of gauze or other absorptive material, are commonly used.[56]

NICE and the IWGDF have concluded that evidence supports the use of a sucrose octasulfate-impregnated wound dressing on diabetic foot wounds after other modifiable factors such as infection have been treated.[55] [57] [58]

See Emerging treatments for discussion of leucocyte, fibrin and platelet patch, and placental-derived products. No other specific types of dressings, including those containing topical antimicrobials, antiseptics, honey, collagen, alginate, herbal remedies, cell therapies, or hyaluronic acid, are recommended based on current evidence.[55] [56]

Split-thickness skin grafting may be considered an option for achieving wound healing in patients with a large epithelial defect that has a tissue bed with healthy granulation. The success rate for autologous skin grafting is high; however, its use over high-pressure areas (namely, the heel and the plantar forefoot overlying the metatarsal heads) may be limited.

There are also several skin substitutes (i.e., non-autologous xenogenic or allogenic tissues) that have been approved for use on diabetic foot wounds. In contrast to autologous skin grafts, several applications of the skin substitute are generally needed at 1- to 2-week intervals to achieve complete re-epithelialisation. There is currently little evidence to support the use of skin substitutes for diabetic foot wounds and they are not recommended by the IWGDF.[55]

NICE recommends that dermal or skin substitutes should only be considered when healing is not progressing and following advice from the multidisciplinary foot care service.[9]

Offloading footwear and devices

Repetitive trauma sustained during ambulation is the most common cause of foot ulcers in patients with diabetes. All patients with diabetes should be encouraged to routinely wear appropriate footwear, even if they do not have any signs of active foot ulceration. See Screening and Prevention sections for more information.

For those with active ulceration, offloading the foot is essential to minimise or avoid this repetitive trauma, in order to achieve ulcer healing.

Total contact casts and non-removable cast-walkers are the most effective options for offloading footwear, although removable cast-walkers and modified footwear can be considered if frequent access to the wound is required.[28] Non-removable devices are contraindicated when there is both mild infection and mild ischaemia, or moderate infection or ischaemia, or heavy exudate present.[28]

NICE recommends non-removable casting to offload plantar neuropathic, non-ischaemic, uninfected forefoot, and midfoot diabetic ulcers. Offer an alternative casting device until casting can be provided.[9]

The IWGDF recommends the following:[28]

- In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, a non-removable knee-high device should be used as the first choice of offloading treatment: either a total contact cast or non-removable knee-high walker depending on the resources available, technician skills, patient preferences, and the extent of any foot deformity present.
- If non-removable knee-high device is not tolerated or is contraindicated, a removable knee-high or ankle-high device is recommended second-line, with the patient encouraged to wear the device during all weight-bearing activities.
- For neuropathic plantar rearfoot ulcers, consider a non-removable knee-high offloading device over a removable device.
- For non-plantar foot ulcers, use a removable offloading device, footwear modifications, toe spacers, orthoses, or digital flexor tenotomy, depending on the type and location of the foot ulcer.
- In any patient using a knee-high or ankle-high offloading device, consider adding a shoe lift on the contralateral limb to improve comfort and balance.

Nutritional support

Malnutrition, including sarcopenia, is very common in patients with diabetes and may impair wound healing. There is a clear correlation with nutritional status and healing, and as such, a balanced diet with adequate fluids, calories, proteins, and nutrients is fundamental to the healing process.[52] Patients should be screened for risk of malnutrition, and if present, malnutrition should be addressed with dietary counselling and supplementation as needed. Discuss individual nutritional goals with patients who have, or are at risk of, malnutrition, ideally within the context of a multidisciplinary team, which may include professionals such as podiatrists, dietitians, surgeons, general practitioners, dermatologists, wound care specialists, etc.[52]

Caloric needs are high when a diabetic foot ulcer is present. Use indirect calorimetry as the gold standard for identifying energy needs. If indirect calorimetry is unavailable, there are other formulas available that can provide a starting point.[52] As a general guide, offer most people at risk of nutritional deficiencies a minimum of 25-30 calories per kg body weight per day, 1.25 to 1.50 g of protein per kg body weight per day, and 1 mL/kcal/day of fluid intake. For people with a high body mass index, lower calorie intake while still meeting protein goals may be appropriate.[52] Give priority to nutrient dense foods. Oral nutrition supplements (ONSs) can be taken between meals as needed to help provide additional protein and micronutrients. If a patient is unable to meet estimated nutrient, energy, protein, and hydration needs despite nutrition interventions, discuss with them the benefits and harms of enteral or parenteral feeding to provide additional or an alternative source of nutrition support.[52] Vitamins and minerals are essential to the health of the body and should be included in all nutritional assessments and supplementation programmes.[52]

Antibiotic therapy

Culturing a specimen from a diabetic foot infection allows selection of appropriate antibiotic therapy. For guidance on collecting samples for microbiological culture, see Investigations .

Do not start antibiotics if there are no active signs or symptoms of infection, for example with the goal of reducing the risk of future infection, or to promote healing.[9][40]

Prompt initiation of an empirical antibiotic regimen is recommended when there are signs of infection: the choice of antibiotic should be based on the severity of the infection and the likely aetiological agents, with guidance from local agencies if available.[9] [40] When choosing an antibiotic for people with a suspected diabetic wound infection, take account of:[9]

- The severity of the diabetic foot infection according to IWGDF/IDSA or NICE classification (mild, moderate, or severe; see Criteria for more details)[40]
- The risk of developing complications
- Previous microbiological results (including previous multiresistant organisms)
- Previous antibiotic use
- Patient preferences

Always take local antibiotic prescribing policies into account. If your patient with a suspected diabetic foot infection is under 18 years of age, seek specialist advice on the most appropriate antibiotic regimen.[9]

Mild infection in an adult

- Treat with oral antibiotics; gram-positive cocci (staphylococci and streptococci) are the most common pathogens in acute infection and narrow-spectrum therapy is appropriate.[9][51]
- NICE recommends flucloxacillin as the first-line option for mild infection; if the patient has a penicillin allergy or flucloxacillin is unsuitable, clarithromycin or doxycycline are alternative options.[9] Flucloxacillin may need to be used at a higher-than-standard dose because of poor bioavailability in people with diabetes who have impaired circulation.[9]
- Options recommended by the International Working Group on the Diabetic Foot (IWGDF) include cloxacillin or cefalexin if there are no complicating features. Alternative options are recommended for patients with allergy/intolerance, in those who have had recent antibiotic exposure and if they are at risk of MRSA.[40]
- Most patients with mild infection can be treated in the community.[40]

Moderate or severe infection in an adult

NICE and the IWGDF both group their treatment recommendations for moderate and severe infections together.[9] [40] Local antibiotic policy should apply and the advice of a microbiologist should be sought on the most appropriate regimen according to microbiological results.

- NICE recommends the following options: flucloxacillin with or without gentamicin and/or metronidazole; or amoxicillin/clavulanate with or without gentamicin; or ceftriaxone plus metronidazole. If the patient has a penicillin allergy, trimethoprim/sulfamethoxazole with or without gentamicin and/or metronidazole is recommended. Oral or intravenous antibiotics are recommended. Oral antibiotics are first-line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.[9]
- The IWGDF recommends amoxicillin/clavulanate, ampicillin/sulbactam, cefuroxime, cefotaxime, or ceftriaxone if there are no complicating features. Alternative options are recommended for patients who have had recent antibiotics, for a macerated ulcer or warm climate, for ischaemic limb/

necrosis/gas forming, and for patients with risk factors for extended-spectrum beta-lactamase drug resistance.[40]

- Consider hospital admission if the patient has a moderate infection that is complex (e.g., wound penetrates to subcutaneous tissues, contains a foreign body, or has discoloration, necrosis, or gangrene), associated with severe foot ischaemia or metabolic or haemodynamic instability, or if outpatient management has failed or is inappropriate, for example requiring intravenous therapy or frequent dressing changes.[40]
- Severe infections are usually treated as an inpatient with parenteral, broad-spectrum, empirical antibiotics.
- IWGDF recommend that oral antibiotics should generally not be used for severe infections, except as follow-on (switch) after initial parenteral therapy.[40]

Ensure review of intravenous antibiotics by 48 hours after initiation and consider switching to an oral regimen if possible.[9]

Review microbiology results when available and adjust antibiotic treatment choice as necessary. Definitive therapy should be based on culture results and clinical response to the empirical regimen.

If *Pseudomonas aeruginosa* is suspected or confirmed, NICE recommends the following additional antibiotics as suitable options: piperacillin/tazobactam; clindamycin plus ciprofloxacin (consider safety issues - see below) and/or gentamicin.[9]

In temperate climates, do not empirically target antibiotic therapy against *P aeruginosa* . But do use empirical treatment of *P aeruginosa* if it has been isolated from cultures of the affected site within the previous few weeks, in a person with moderate or severe infection who resides in tropical/subtropical climates.[40]

If MRSA is suspected or confirmed:

- NICE recommends adding one of vancomycin, teicoplanin, or linezolid (with specialist advice) to the standard antibiotic options.[9]
- For mild infections, the IWGDF recommends linezolid, trimethoprim/sulfamethoxazole, clindamycin, levofloxacin, moxifloxacin, or doxycycline. For moderate or severe infections, consider adding or substituting with vancomycin, teicoplanin, linezolid, daptomycin, fusidic acid, trimethoprim/sulfamethoxazole, or doxycycline.

Systemic fluoroquinolone antibiotics, such as ciprofloxacin, levofloxacin, and moxifloxacin, may cause serious, disabling, and potentially long-lasting or irreversible adverse events. This includes, but is not limited to, tendinopathy/tendon rupture; peripheral neuropathy; arthropathy/arthralgia; aortic aneurysm and dissection; heart valve regurgitation; dysglycaemia; and central nervous system effects including seizures, depression, psychosis, and suicidal thoughts and behaviour.[59]

- Prescribing restrictions apply to the use of fluoroquinolones, and these restrictions may vary between countries. In general, fluoroquinolones should be restricted for use in serious, life-threatening bacterial infections only. Some regulatory agencies may also recommend that they must only be used in situations where other antibiotics, that are commonly recommended for the infection, are inappropriate (e.g., resistance, contraindications, treatment failure, unavailability).
- Consult your local guidelines and drug formulary for more information on suitability, contraindications, and precautions.

Course length of antibiotic therapy should be based on clinical assessment for a minimum of 7 days.[9] Consider extending to 3-4 weeks if the infection is improving but extensive and resolving slower than

expected, or if the patient has severe peripheral artery disease.[40] Six weeks of treatment may be required for osteomyelitis.[9]

Further diagnostic tests or alternative treatments may need to be considered if the infection has not resolved after 4 weeks.[40]

Surgery

For pressure offloading in patients with active ulceration, where conservative measures have failed, the IWGDF advises surgery can be considered as follows (to be used in combination with an offloading device):[28]

- Achilles tendon lengthening or metatarsal head resection for neuropathic plantar metatarsal head ulcers
- Joint arthroplasty for neuropathic hallux ulcers
- Metatarsal osteotomy for neuropathic plantar ulcers on metatarsal heads 2-5
- Digital flexor tenotomy for neuropathic plantar or apex ulcers on digits 2-5, secondary to a flexible toe deformity
- Digital flexor tenotomy for non-plantar foot ulcers (depending on its location)

A revascularisation procedure should be considered for anyone with peripheral artery disease, a foot ulcer, and clinical findings of ischaemia (absent pulses, monophasic, or absent pedal Doppler waveforms, ankle pressure <100 mmHg or toe pressure <60 mmHg), and for those with ulcers that do not improve within 4 weeks despite appropriate management.[11] Seek an urgent vascular opinion if there are signs of severe ischaemia: ankle-brachial pressure index <0.4, ankle pressure <50 mmHg, toe pressure <30 mmHg, or transcutaneous oxygen pressure <30mmHg.

Revascularisation should aim to restore adequate arterial blood flow to at least one of the foot arteries. The main options for this type of procedure are endovascular (usually balloon angioplasty with or without stent placement), open (surgical bypass or endarterectomy), or hybrid (a combination of both). The choice of procedure should be based on the patient's individual risks and preferences, limb threat severity, anatomical distribution of peripheral artery disease, and the availability of an autogenous vein for bypass.[11] In patients with infrapopliteal disease undergoing endovascular intervention by percutaneous transluminal angioplasty, addition of a stent probably increases rates of technical success of the procedure compared to no stenting, although the impact on complications, longer-term success rates and mortality is uncertain.

Seek an urgent surgical opinion in cases of severe infection, or moderate infection with extensive gangrene, necrotising infection, suspected deep abscess, compartment syndrome, or severe lower limb ischaemia.[40] Prompt removal of infected and necrotic tissues (within 24-48 hours), including bone if there is osteomyelitis, in combination with antibiotics has been shown to improve wound healing rates and lower major amputation rates.[40]

Minor amputations (i.e., toe or partial foot resections) may be performed on areas with irreversible gangrene, osteomyelitis, or deep-tissue infection. Major amputation is determined on a patient-by-patient basis but is generally reserved for the following situations:

- Infection or gangrene that is so extensive that reconstruction either is not possible or will not preserve meaningful function in the affected limb
- Patients who have very little or no function in the limb (excluding previous history of stroke or paralysis)

- Severe peripheral arterial disease which cannot be revascularised

Management of cardiovascular risk factors and considerations for associated comorbidities

In addition to optimising glycaemic control, management of other risk factors and associated conditions is important for course and outcomes.

Chronic kidney disease

- Renal function should be considered when selecting antibiotic therapy. Check your local drug information source.
- End-stage renal disease and renal replacement therapy in patients with diabetes-related foot disease is associated with high rates of amputation and mortality.[60] [61] [62]
- In patients with diabetes receiving renal replacement therapy, feet should be protected during the haemodialysis session (e.g., offloading with protective boot).[39]

Cardiovascular disease and risk factors

- Patients with diabetic foot ulcers are at increased risk of cardiovascular-related morbidity and mortality compared with patients with diabetes without foot ulcers.[63] [64] [65]
- Control of blood pressure and lipid levels may reduce risk of vascular complications.[18] All patients should receive regular blood pressure and lipid monitoring along with lifestyle advice and optimal pharmacological management.
- Aggressive cardiovascular risk management (blood pressure, lipids, glycaemic control) has been demonstrated to reduce mortality in patients with diabetic foot ulcers in one study.[66]
- Note that overly aggressive antihypertensive treatment may result in reduced limb perfusion, increasing the risk of complications.[67]

Heart failure

- Patients with diabetic foot ulcers have a higher prevalence of heart failure compared with patients with diabetes without foot ulcers, and the prevalence increases with increasing severity.[68]
- Comorbid heart failure is associated with a worse prognosis, with lower healing rates, and increased risk of recurrence and amputations.[68]
- Oedema (associated with heart failure) may affect tissue perfusion and wound healing and should be treated where present.[36]

Depression

- Depression and other mental health issues such as anxiety are common comorbidities in those with diabetes-related foot disease.[69]
- Depression has been associated with a higher risk of developing diabetic foot ulcers and also a higher risk of major lower-limb amputation and mortality.[70] [71] [72] [73]
- Screening for depression is recommended.[67]

Follow-up and referral

Non-healing foot ulcers and foot infections have the potential to progress suddenly, with few warning signs. Multidisciplinary or interdisciplinary care has repeatedly been demonstrated to significantly lower leg amputation rates.[74] [75] [76] [77]

In the UK, NICE recommends that any patient with an active diabetic foot problem is referred to a multidisciplinary clinic within 1 working day.[9] In healthcare systems in some other countries, primary

care physicians may provide basic clinical care at an initial visit for a new diabetic foot ulcer, but they should have a low threshold to refer to interdisciplinary foot clinics or inpatient units for more focused care.

Lack of recognition of ischaemia and infection are two major, but avoidable, pitfalls that lead to delayed referral.[78]

Reassess patients with a suspected diabetic foot infection if:[9]

- Symptoms worsen rapidly, or significantly
- Symptoms do not start to improve within 1-2 days
- The patient becomes systemically unwell or has pain out of proportion to the infection

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute (summary)		
at initial presentation		
	1st	**multidisciplinary care**
	plus	**wound debridement**
	plus	**wound dressing**
	plus	**offloading footwear and devices**
	adjunct	**nutritional support**
with mild infection	**plus**	**oral empirical antibiotic therapy**
with moderate or severe infection	**plus**	**oral or intravenous empirical antibiotic therapy**
	adjunct	**Pseudomonas antibiotic cover**
	adjunct	**MRSA antibiotic cover**
	adjunct	**surgical drainage and/or debridement**

Ongoing		(summary)
after initial definitive treatment		
	1st	follow-up and continuing diabetic care
	plus	offloading footwear
	adjunct	offloading surgery
	adjunct	surgical bypass and/or endovascular intervention
	adjunct	amputation
	adjunct	management of cardiovascular risk factors and associated long-term comorbidities

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute

at initial presentation

1st **multidisciplinary care**

» Make an immediate referral to acute services for any patient who has a limb-threatening or life-threatening diabetic foot problem.[9] In the UK, the National Institute for Health and Care Excellence recommends informing the multidisciplinary foot care service so the patient can be assessed and an individualised treatment plan put in place.

» If the patient is already in hospital when the foot complication is identified, ensure the multidisciplinary foot care team is alerted and involved in their care.

» Examples of limb-threatening and life-threatening diabetic foot problems include ulceration with fever or any signs of sepsis; ulceration with limb ischaemia; clinical concern that there is a deep-seated soft-tissue or bone infection (with or without ulceration); or gangrene (with or without ulceration).

» For any other patient with an active diabetic foot problem, refer within 1 working day to the multidisciplinary foot care/foot protection service (according to local protocols).[9] The foot care service should triage the patient within 1 further working day.

» The multidisciplinary foot care team should be led by a named healthcare professional, and consist of specialists with skills in podiatry, wound care nursing, diabetology, diabetes specialist nursing, vascular surgery, orthopaedic surgery, infectious disease, biomechanics and orthoses, interventional radiology, and casting, as well as other allied health professionals who work together to optimise patient care.[9]

» The American Diabetes Association also advocates an interprofessional approach for all patients with foot ulcers and high-risk feet, ideally facilitated by a podiatrist.[37]

plus **wound debridement**

Treatment recommended for ALL patients in selected patient group

Acute

» Debridement of slough, necrotic tissue, and surrounding callus of the ulcer is recommended, after taking account of relative contraindications such as pain or severe ischaemia.[55] The goal of debridement is to create a clean wound bed and promote wound healing.

» Sharp debridement of ulcers using surgical instruments remains the standard of care, despite a lack of high-quality clinical trials to support its use.

» Neuropathic ulcers can usually be debrided without the need for local anaesthesia.[36]

» Numerous alternative debridement techniques exist, including using enzymes, larvae, hydrogels, lasers, and ultrasound; however, there is currently insufficient evidence to support the routine use of any of these over sharp debridement, according to the International Working Group on the Diabetic Foot (IWGDF).[55]

» Debridement of diabetic foot ulcers in a hospital setting should only be done by members of the multidisciplinary foot care team, using the technique that best matches their specialist expertise and clinical experience, the site of the diabetic foot ulcer, and the patient's preference.[9] Community-based debridement should only be done by healthcare professionals with the relevant skills and training.[9]

» There is reasonable-quality evidence that negative pressure wound therapy after surgical debridement may decrease the time to healing, and both the UK National Institute for Health and Care Excellence and the IWGDF recommend its use in this circumstance.[9] [55]

» See Emerging treatments for discussion of adjunctive therapies to promote wound healing in diabetic foot ulcers, including hyperbaric and topical oxygen therapy.

» Topical medications, vitamins, physical therapies, and gasses other than oxygen are not currently recommended for this purpose.[55]

plus **wound dressing**

Treatment recommended for ALL patients in selected patient group

» The choice of wound dressing when treating diabetic foot ulcers should depend on the clinical assessment of the wound.[9]

Acute

» Evidence is sparse to inform decisions about the best choice of wound dressing for diabetic foot ulcers. Dressings that maintain a moist environment, including non-adherent dressings covered with a layer of gauze or other absorptive material, are commonly used.[56]

» The UK National Institute for Health and Care Excellence (NICE) and the International Working Group on the Diabetic Foot (IWGDF) have concluded that evidence supports the use of a sucrose octasulfate-impregnated wound dressing on diabetic foot wounds after other modifiable factors such as infection have been treated.[55] [57] [58]

» See Emerging treatments for discussion of leucocyte, fibrin and platelet patch, and placental-derived products.

» No other specific types of dressings, including those containing topical antimicrobials, antiseptics, honey, collagen, alginate, herbal remedies, cell therapies, or hyaluronic acid, are recommended based on current evidence.[55] [56]

» Split-thickness skin grafting may be considered an option for achieving wound healing in patients with a large epithelial defect that has a tissue bed with healthy granulation. The success rate for autologous skin grafting is high; however, its use over high-pressure areas (namely, the heel and the plantar forefoot overlying the metatarsal heads) may be limited.

» There are also several skin substitutes (i.e., non-autologous xenogenic or allogenic tissues) that have been approved for use on diabetic foot wounds. In contrast to autologous skin grafts, several applications of the skin substitute are generally needed at 1- to 2-week intervals to achieve complete re-epithelialisation. There is currently little evidence to support the use of skin substitutes for diabetic foot wounds and they are not recommended by the IWGDF.[55]

» NICE recommends that dermal or skin substitutes should only be considered when healing is not progressing and following advice from the multidisciplinary foot care service.[9]

plus **offloading footwear and devices**

Treatment recommended for ALL patients in selected patient group

» Repetitive trauma sustained during ambulation is the most common cause of foot ulcers

MANAGEMENT

Acute

in patients with diabetes. All patients with diabetes should be encouraged to routinely wear appropriate footwear, even if they do not have any signs of active foot ulceration. For those with active ulceration, offloading the foot is essential to minimise or avoid this repetitive trauma, in order to achieve ulcer healing.

» Total contact casts and non-removable cast-walkers are the most effective options for offloading footwear, although removable cast-walkers and modified footwear can be considered if frequent access to the wound is required.[28] Non-removable devices are contraindicated when there is both mild infection and mild ischaemia, or moderate infection or ischaemia, or heavy exudate present.[28]

» The UK National Institute for Health and Care Excellence (NICE) recommends non-removable casting to offload plantar neuropathic, non-ischaemic, uninfected forefoot and midfoot diabetic ulcers. Offer an alternative casting device until casting can be provided.[9]

» The International Working Group on the Diabetic Foot (IWGDF) recommends that in a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, a non-removable knee-high device should be used as the first choice of offloading treatment: either a total contact cast or non-removable knee-high walker, depending on the resources available, technician skills, patient preferences, and the extent of any foot deformity present.[28] If non-removable knee-high device is not tolerated or is contraindicated, a removable knee-high or ankle-high device is recommended second-line, with the patient encouraged to wear the device during all weight-bearing activities.

» For neuropathic plantar rearfoot ulcers, consider a non-removable knee-high offloading device over a removable device. For non-plantar foot ulcers, use a removable offloading device, footwear modifications, toe spacers, orthoses, or digital flexor tenotomy, depending on the type and location of the foot ulcer.[28]

» In any patient using a knee-high or ankle-high offloading device, consider adding a shoe lift on the contralateral limb to improve comfort and balance.[28]

adjunct **nutritional support**

Treatment recommended for SOME patients in selected patient group

MANAGEMENT

Acute

» Malnutrition, including sarcopenia, is very common in patients with diabetes and may impair wound healing. There is a clear correlation with nutritional status and healing, and as such, a balanced diet with adequate fluids, calories, proteins, and nutrients is fundamental to the healing process.[52] Patients should be screened for risk of malnutrition, and if present, malnutrition should be addressed with dietary counselling and supplementation as needed. Discuss individual nutritional goals with patients who have, or are at risk of, malnutrition, ideally within the context of a multidisciplinary team, which may include professionals such as podiatrists, dietitians, surgeons, general practitioners, dermatologists, wound care specialists, etc.[52] Optimal glycaemic control is essential.

» Caloric needs are high when a diabetic foot ulcer is present. Use indirect calorimetry as the gold standard for identifying energy needs. If indirect calorimetry is unavailable, there are other formulas available that can provide a starting point.[52] As a general guide, offer most people at risk of nutritional deficiencies a minimum of 25-30 calories per kg body weight per day, 1.25 to 1.50 g of protein per kg body weight per day, and 1 mL/kcal/day of fluid intake. For people with a high body mass index, lower calorie intake while still meeting protein goals may be appropriate.[52] Give priority to nutrient dense foods. Oral nutrition supplements (ONSs) can be taken between meals as needed to help provide additional protein and micronutrients. If a patient is unable to meet estimated nutrient, energy, protein, and hydration needs despite nutrition interventions, discuss with them the benefits and harms of enteral or parenteral feeding to provide additional or an alternative source of nutrition support.[52] Vitamins and minerals are essential to the health of the body and should be included in all nutritional assessments and supplementation programmes.[52]

with mild infection **plus** **oral empirical antibiotic therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

» flucloxacillin: 0.5 to 1 g orally four times daily

Secondary options

» clarithromycin: 500 mg orally twice daily

Acute

OR

» doxycycline: 200 mg orally on the first day, followed by 100-200 mg once daily

» Mild infection is defined as the presence of ≥2 of the following: local swelling or induration, erythema 0.5 to <2.0 cm around the wound, local tenderness or pain, local increased warmth, or purulent discharge (exclude other causes of inflammatory response, such as trauma, gout, acute Charcot's neuro-osteoarthropathy, fracture, thrombosis, and venous stasis).[40]

» For guidance on collecting samples for microbiological culture, see Investigations .

» Do not start antibiotics if there are no active signs or symptoms of infection, for example with the goal of reducing the risk of future infection, or to promote healing.[9] [40]

» Prompt initiation of an empirical antibiotic regimen is recommended when there are signs of infection: the choice of antibiotic should be based on the severity of the infection and the likely aetiological agents, with guidance from local agencies if available.[9] [40] If your patient with a suspected diabetic foot infection is under 18 years, seek specialist advice on the most appropriate antibiotic regimen.[9]

» When choosing an antibiotic for people with a suspected diabetic wound infection, take account of the severity of the diabetic foot infection according to IWGDF/IDSA or NICE classification (mild, moderate, or severe; see Criteria for more details), the risk of developing complications, previous microbiological results (including previous multiresistant organisms), previous antibiotic use, and patient preferences.[9] [40]

» Treat with oral antibiotics; gram-positive cocci (staphylococci and streptococci) are the most common pathogens in acute infection and narrow-spectrum therapy is appropriate.[9] [51]

» NICE recommends flucloxacillin as the first-line option for mild infection; if the patient has a penicillin allergy or flucloxacillin is unsuitable, clarithromycin or doxycycline are alternative options.[9] Flucloxacillin may need to be used at a higher-than-standard dose because of poor bioavailability in people with diabetes who have impaired circulation.[9]

» Other options recommended by the International Working Group on the Diabetic

Acute

Foot include cloxacillin or cefalexin if there are no complicating features. Alternative options are recommended for patients with allergy/ intolerance, in those who have had recent antibiotic exposure and if they are at risk of MRSA.[40]

» Review microbiology results when available and adjust antibiotic treatment choice as necessary. Definitive therapy should be based on culture results and clinical response to the empirical regimen.

» Most patients with mild infection can be treated in the community.[40]

» Course length of antibiotic therapy should be based on clinical assessment for a minimum of 7 days.[9] Consider extending to 3-4 weeks if the infection is improving but extensive and resolving slower than expected, or if the patient has severe peripheral artery disease.[40] Six weeks of treatment may be required for osteomyelitis.[9]

» Further diagnostic tests or alternative treatments may need to be considered if the infection has not resolved after 4 weeks.[40]

with moderate or severe infection — **plus** — **oral or intravenous empirical antibiotic therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

» flucloxacillin: 1 g orally four times daily; 1-2 g intravenously every 6 hours

OR

» flucloxacillin: 1 g orally four times daily; 1-2 g intravenously every 6 hours

--AND--

» gentamicin: 5-7 mg/kg intravenously every 24 hours

Adjust dose according to serum gentamicin level.

-and/or-

» metronidazole: 400 mg orally three times daily; 500 mg intravenously every 8 hours

OR

» amoxicillin/clavulanate: 500/125 mg orally three times daily; 1.2 g intravenously every 8 hours

Acute

Intravenous dose consists of 1 g of amoxicillin plus 0.2 g of clavulanate.

OR

» amoxicillin/clavulanate: 500/125 mg orally three times daily; 1.2 g intravenously every 8 hours
Intravenous dose consists of 1 g of amoxicillin plus 0.2 g of clavulanate.

--AND--

» gentamicin: 5-7 mg/kg intravenously once daily
Adjust dose according to serum gentamicin level.

OR

» trimethoprim/sulfamethoxazole: 160/800 mg orally twice daily; 160/800 mg intravenously every 12 hours, may increase to 240/1200 mg every 12 hours in severe infections

OR

» trimethoprim/sulfamethoxazole: 160/800 mg orally twice daily; 160/800 mg intravenously every 12 hours, may increase to 240/1200 mg every 12 hours in severe infections

--AND--

» gentamicin: 5-7 mg/kg intravenously every 24 hours
Adjust dose according to serum gentamicin level.

-and/or-
» metronidazole: 400 mg orally three times daily; 500 mg intravenously every 8 hours

OR

» ceftriaxone: 2 g intravenously every 24 hours
-and-
» metronidazole: 400 mg orally three times daily; 500 mg intravenously every 8 hours

» Moderate infection in an adult is defined as a patient with no systemic manifestations and involving erythema extending ≥2 cm from the wound margin, and/or tissue deeper than skin and subcutaneous tissues (e.g., tendon, muscle, joint, and bone).[40]

Acute

» Severe infection in an adult is defined as any foot infection with associated manifestations of systemic inflammatory response syndrome, as manifested by ≥2 of the following: temperature >38°C or <36°C, heart rate >90 beats/minute, respiratory rate >20 breaths/minute or $PaCO_2$ < 4.3 kPa (32 mmHg), WBC count >12 × 10^9 cells/L (12,000/microlitre) (leukocytosis) or <4 × 10^9 cells/L (4000/microlitre) (leukopenia); or a normal WBC count with >10% immature (band) forms.[40]

» For guidance on collecting samples for microbiological culture, see Investigations .

» Prompt initiation of an empirical antibiotic regimen is recommended when there are signs of infection, with the choice of antibiotic based on the severity of the infection and the likely aetiological agents, with guidance from local agencies if available.[9] [40]

» NICE recommends the following options for moderate or severe infection: flucloxacillin with or without gentamicin and/or metronidazole; or amoxicillin/clavulanate with or without gentamicin; or ceftriaxone plus metronidazole. If the patient has a penicillin allergy, trimethoprim/sulfamethoxazole with or without gentamicin and/or metronidazole is recommended. Oral or intravenous antibiotics are recommended. Oral antibiotics are first-line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.[9] In severe infection, NICE recommends intravenous administration of antibiotics for at least 48 hours (until stabilised).[9]

» The IWGDF recommends amoxicillin/clavulanate, ampicillin/sulbactam, cefuroxime, cefotaxime, or ceftriaxone if there are no complicating features. Alternative options are recommended for patients who have had recent antibiotics, for a macerated ulcer or warm climate, for ischaemic limb/necrosis/gas forming, MRSA infection, and for patients with risk factors for extended-spectrum beta-lactamase drug resistance.

» Consider hospital admission if the patient has a moderate infection that is complex (e.g., wound penetrates to subcutaneous tissues, contains a foreign body, or has discoloration, necrosis, or gangrene), associated with severe foot ischaemia or metabolic or haemodynamic instability, or if outpatient management has failed or is inappropriate, for example, requiring

Acute

intravenous therapy or frequent dressing changes.[40]

» Severe infections are usually treated as an inpatient with parenteral, broad-spectrum, empirical antibiotics. Local antibiotic policy should apply and the advice of a microbiologist on the most appropriate regimen according to microbiological results should be sought.

» The IWGDF recommends that oral antibiotics should generally not be used for severe infections, except as follow-on (switch) after initial parenteral therapy.[40]

» Ensure review of intravenous antibiotics by 48 hours after initiation and consider switching to an oral regimen if possible.[9]

» Review microbiology results when available and adjust antibiotic treatment choice as necessary. Definitive therapy should be based on culture results and clinical response to the empirical regimen.

» Course length of antibiotic therapy should be based on clinical assessment for a minimum of 7 days.[9] Consider extending to 3-4 weeks if the infection is improving but extensive and resolving slower than expected, or if the patient has severe peripheral artery disease.[40] Six weeks of treatment may be required for osteomyelitis.[9]

» Further diagnostic tests or alternative treatments may need to be considered if the infection has not resolved after 4 weeks.[40]

adjunct **Pseudomonas antibiotic cover**

Treatment recommended for SOME patients in selected patient group

Primary options

» piperacillin/tazobactam: 4.5 g intravenously every 8 hours, may increase to 4.5 g every 6 hours in severe infections
Dose consists of 4 g of piperacillin plus 0.5 g of tazobactam.

Secondary options

» clindamycin: 150-450 mg orally four times daily; 600-2700 mg/day intravenously given in 2-4 divided doses, may increase to 1200 mg every 6 hours in life-threatening infections

--AND--

» ciprofloxacin: 500 mg orally twice daily; 400 mg intravenously every 8-12 hours

Acute

-and/or-

» gentamicin: 5-7 mg/kg intravenously every 24 hours

Adjust dose according to serum gentamicin level.

» If *Pseudomonas aeruginosa* is suspected or confirmed, the UK National Institute for Health and Care Excellence recommends the following additional antibiotics as suitable options: piperacillin/tazobactam; clindamycin plus ciprofloxacin (consider safety issues - see below) and/or gentamicin.[9]

» In temperate climates, do not empirically target antibiotic therapy against *P aeruginosa* . But do use empirical treatment of *P aeruginosa* if it has been isolated from cultures of the affected site within the previous few weeks, in a person with moderate or severe infection who resides in tropical/subtropical climates.[40]

» Systemic fluoroquinolone antibiotics, such as ciprofloxacin, may cause serious, disabling, and potentially long-lasting or irreversible adverse events. This includes, but is not limited to, tendinopathy/tendon rupture; peripheral neuropathy; arthropathy/arthralgia; aortic aneurysm and dissection; heart valve regurgitation; dysglycaemia; and central nervous system effects including seizures, depression, psychosis, and suicidal thoughts and behaviour.[59] Prescribing restrictions apply to the use of fluoroquinolones, and these restrictions may vary between countries. In general, fluoroquinolones should be restricted for use in serious, life-threatening bacterial infections only. Some regulatory agencies may also recommend that they must only be used in situations where other antibiotics, that are commonly recommended for the infection, are inappropriate (e.g., resistance, contraindications, treatment failure, unavailability).

» Consult your local guidelines and drug formulary for more information on suitability, contraindications, and precautions.

adjunct **MRSA antibiotic cover**

Treatment recommended for SOME patients in selected patient group

Primary options

» vancomycin: 15-20 mg/kg intravenously every 8-12 hours, maximum 2000 mg/dose

Acute

Adjust dose according to serum vancomycin level.

OR

» teicoplanin: 6 mg/kg intravenously every 12 hours for 3 doses, followed by 6 mg/kg every 24 hours
Monitor serum teicoplanin level during treatment.

Secondary options

» linezolid: 600 mg intravenously/orally every 12 hours

» If MRSA is suspected or confirmed, the UK National Institute for Health and Care Excellence recommends adding one of vancomycin, teicoplanin, or linezolid (with specialist advice) to the standard antibiotic options.[9]

» The International Working Group on the Diabetic Foot also recommends other options for MRSA (e.g., daptomycin, trimethoprim/sulfamethoxazole, doxycycline).[40]

adjunct **surgical drainage and/or debridement**

Treatment recommended for SOME patients in selected patient group

» Seek an urgent surgical opinion in cases of severe infection, or moderate infection with extensive gangrene, necrotising infection, suspected deep abscess, compartment syndrome, or severe lower limb ischaemia.[40] Prompt removal of infected and necrotic tissues (within 24-48 hours), including bone if there is osteomyelitis, in combination with antibiotics has been shown to improve wound healing rates and lower major amputation rates.[40]

Ongoing

after initial definitive treatment

1st **follow-up and continuing diabetic care**

» Non-healing foot ulcers and foot infections have the potential to progress suddenly, with few warning signs.

» Multidisciplinary or interdisciplinary care has repeatedly been demonstrated to significantly lower leg amputation rates.[74] [75] [76] [77]

» In the UK, the National Institute for Health and Care Excellence recommends that any patient with an active diabetic foot problem is referred to a multidisciplinary clinic within 1 working day.[9] In healthcare systems in some other countries, primary care physicians may provide basic clinical care at an initial visit for a new diabetic foot ulcer, but they should have a low threshold to refer to interdisciplinary foot clinics or inpatient units for more focused care.

» Lack of recognition of ischaemia and infection are two major, but avoidable, pitfalls that lead to delayed referral.[78]

» Reassess patients with a suspected diabetic foot infection if: symptoms worsen rapidly, or significantly; symptoms do not start to improve within 1 to 2 days; or the patient becomes systemically unwell or has pain out of proportion to the infection.[9]

» It is important to remember the need for proper follow-up of the diabetes itself (e.g., regular check-ups, maintenance of target blood glucose levels, blood pressure and lipid management) according to current guidelines. These goals do not change in the presence or absence of diabetes-related foot disease.

» Sodium-glucose cotransporter-2 (SGLT2) inhibitors should not be started in drug-naïve people with a diabetes-related foot ulcer or gangrene, and temporary discontinuation should be considered in people who develop a foot ulcer or gangrene while already using them, until the foot is healed, according to joint guidelines from the IWGDF, European Society for Vascular Surgery and Society for Vascular Surgery.[11]

plus **offloading footwear**

Treatment recommended for ALL patients in selected patient group

» Repetitive trauma sustained during ambulation is the most common cause of foot ulcers

Ongoing

in patients with diabetes. All patients with diabetes should be encouraged to routinely wear appropriate footwear, even if they do not have any signs of active foot ulceration.[24]

» The use of specialised therapeutic footwear is recommended for high-risk patients with diabetes, such as those with loss of protective sensation, poor peripheral circulation, ulcers, callus formation, foot deformities, a history of amputation, or those on renal replacement therapy.[9][37]

» The International Working Group of the Diabetic Foot recommends therapeutic footwear that accommodates the shape of the feet and fits properly.[24] The inside length of the shoe should be 1-2 cm longer than the foot and should not be too tight or too loose. The internal width should equal the width of the foot at the metatarsal-phalangeal joints or the widest part of the foot, and the height should allow enough room for all the toes. Evaluate the fit with the patient in the standing position, preferably later in the day.

» If there is no appropriate off-the-shelf footwear, or if they have an existing foot deformity, consider prescribing therapeutic footwear such as extra-depth shoes, custom-made footwear, insoles and/or toe orthoses.[24]

» Patients with a healed plantar foot ulcer should be prescribed therapeutic footwear that has a demonstrated plantar pressure relieving effect during walking, to help prevent a recurrent plantar foot ulcer. Encourage the person to consistently wear this prescribed footwear, both indoors and outdoors.[24]

» Prompt treatment of any pre-ulcerative lesions, excess callus, ingrown toenails, or fungal infections is important.[24]

adjunct **offloading surgery**

Treatment recommended for SOME patients in selected patient group

» For pressure offloading in patients with active ulceration, where conservative measures have failed, the International Working Group on the Diabetic Foot advises surgery can be considered as follows (to be used in combination with an offloading device): Achilles tendon lengthening or metatarsal head resection for neuropathic plantar metatarsal head ulcers; joint arthroplasty for neuropathic hallux ulcers; metatarsal osteotomy for neuropathic plantar ulcers on

Ongoing

metatarsal heads 2-5; digital flexor tenotomy for neuropathic plantar or apex ulcers on digits 2-5, secondary to a flexible toe deformity; and digital flexor tenotomy for non-plantar foot ulcers (depending on its location).[28]

adjunct **surgical bypass and/or endovascular intervention**

Treatment recommended for SOME patients in selected patient group

» A revascularisation procedure should be considered for anyone with peripheral artery disease, a foot ulcer, and clinical findings of ischaemia (absent pulses, monophasic or absent pedal Doppler waveforms, ankle pressure <100 mmHg or toe pressure <60 mmHg), and for those with ulcers that do not improve within 4 weeks despite appropriate management.[11] Seek an urgent vascular opinion if there are signs of severe ischaemia: ankle-brachial pressure index <0.4, ankle pressure <50 mmHg, toe pressure <30 mmHg, or transcutaneous oxygen pressure <30 mmHg.

» Revascularisation should aim to restore adequate arterial blood flow to at least one of the foot arteries. The main options for this type of procedure are endovascular (usually balloon angioplasty with or without stent placement), open (surgical bypass or endarterectomy), or hybrid (a combination of both). The choice of procedure should be based on the patient's individual risks and preferences, limb threat severity, anatomical distribution of peripheral artery disease, and the availability of an autogenous vein for bypass.[11] In patients with infrapopliteal disease undergoing endovascular intervention by percutaneous transluminal angioplasty, addition of a stent probably increases rates of technical success of the procedure compared to no stenting, although the impact on complications, longer-term success rates and mortality is uncertain.

adjunct **amputation**

Treatment recommended for SOME patients in selected patient group

» Minor amputations (i.e., toe or partial foot resections) may be performed on areas with irreversible gangrene, osteomyelitis, or deep-tissue infection. Major amputation is determined on a patient-by-patient basis but is generally reserved for the following situations: infection or gangrene that is so extensive that reconstruction either is not possible or will not preserve meaningful function in the affected limb;

Ongoing

patients who have very little or no function in the limb (excluding previous history of stroke or paralysis); or severe peripheral arterial disease which cannot be revascularised.

adjunct **management of cardiovascular risk factors and associated long-term comorbidities**

Treatment recommended for SOME patients in selected patient group

» In addition to optimising glycaemic control, management of other risk factors and associated conditions is important for course and outcomes.

» Chronic kidney disease: renal function should be considered when selecting antibiotic therapy. Check your local drug information source. In patients with diabetes receiving renal replacement therapy, feet should be protected during the haemodialysis session (e.g., offloading with protective boot).[39]

» Cardiovascular disease and risk factors: patients with diabetic foot ulcers are at increased risk of cardiovascular-related morbidity and mortality compared with patients with diabetes without foot ulcers.[63] [64] [65] Control of blood pressure and lipid levels may reduce risk of vascular complications.[18] All patients should receive regular blood pressure and lipid monitoring along with lifestyle advice and optimal pharmacological management. Aggressive cardiovascular risk management (blood pressure, lipids, glycaemic control) has been demonstrated to reduce mortality in patients with diabetic foot ulcers in one study.[66] Note that overly aggressive antihypertensive treatment may result in reduced limb perfusion, increasing the risk of complications.[67]

» Heart failure: oedema (associated with heart failure) may affect tissue perfusion and wound healing and should be treated where present.[36]

» Depression: depression has been associated with a higher risk of major lower-limb amputation and mortality.[70] [71] [72] [73] Screening is recommended.[67]

Emerging

Adjunctive therapies for diabetic foot ulcers

A wide range of adjunctive therapies are in development for the treatment of diabetic foot ulcers, some of which are already available in some healthcare systems.[79] [80] The American Diabetes Association refers to these collectively as 'advanced wound therapy', of which there are nine broad categories: negative-pressure wound therapy (standard electrically powered and mechanically powered); oxygen therapies (hyperbaric oxygen therapy, topical oxygen therapy, oxygen-releasing sprays, and dressings); biophysical therapies (electrical stimulation, diathermy, pulsed electromagnetic fields, pulsed radiofrequency energy, low-frequency non-contact ultrasound, and extracorporeal shock wave therapy); growth factors (platelet-derived growth factor, fibroblast growth factor, and epidermal growth factor); autologous blood products (platelet-rich plasma, whole blood clot, and leukocyte, platelet, and fibrin multilayered patches); acellular matrix tissues (xenograft dermis and xenograft acellular matrices, including placental-derived amniotic tissues, amniotic fluid, and umbilical cord); bioengineered allogeneic cellular therapies (bilayered skin equivalent such as human keratinocytes and fibroblasts, and dermal replacement therapy with human fibroblasts); stem cell therapies (autogenous bone marrow–derived stem cells, and allogeneic amniotic matrix with mesenchymal stem cells); and miscellaneous active dressings including hyaluronic acid, honey dressings, and sucrose octasulfate dressing.[37] The International Working Group on the Diabetic Foot (IWGDF) conducted a comprehensive literature review on adjunctive therapies as part of its 2023 guidelines update.[55] It concluded there is evidence to support the use of negative-pressure wound therapy for post-operative wounds, as well as topical and hyperbaric oxygen therapy, placental derived products and a leucocyte, fibrin, and platelet patch (the 3C Patch). See Management approach (Wound debridement) for discussion of negative-pressure wound therapy, and below for discussion of oxygen therapy, placental-derived products, and the 3C Patch. However, for all other adjunctive therapies, the IWGDF concluded there is currently insufficient evidence from clinical trials to support their use, and none are recommended at present.[55]

Topical and hyperbaric oxygen therapy

Hyperbaric oxygen therapy (breathing 100% oxygen at twice the atmospheric pressure of sea level) and topical oxygen therapy have both been found to improve healing of diabetic foot ulcers in some randomised controlled trials, albeit of low-quality evidence.[55] [81][82] [83] The IWGDF cautiously recommends their use as an adjunctive therapy where standard of care alone has failed, in places where the appropriate resources and equipment exist to provide them. In the UK, however, NHS England does not recommend use of hyperbaric oxygen based on current evidence.[84] Neither NHS England nor NICE currently makes any recommendations about the use of topical oxygen therapy. The cost effectiveness of hyperbaric oxygen therapy remains uncertain.[85]

Placental derived products

Numerous products have been derived from human placenta to assist with healing of diabetic foot ulcers, including dehydrated amnion/chorion graft, dehydrated amniotic membrane, cryopreserved placental membrane, and dehydrated umbilical cord. Several studies have suggested these can improve and speed up healing of ulcers, and they can be considered as an adjunctive treatment where standard of care alone has failed, according to the IWGDF. However, the quality of evidence is low and the cost effectiveness of these products remains unclear.[55]

3C Patch®

The 3C Patch® (previously known as LeucoPatch®) is a single-use medical device that is used as part of wound care for foot ulcers in people with diabetes. It uses a centrifuge device to create a biological patch from a person's own blood. The patch is a disc-shaped layered matrix of fibrin, leukocytes, and platelets and acts as a concentrated source of cells, growth factors, and signalling molecules, which are thought to promote wound healing. 3C Patch is under assessment for the management of recalcitrant wounds. Randomised controlled trial evidence suggests that using 3C Patch led to more ulcers healing at 20 weeks compared with standard care, and median time to ulcer healing of 72 days compared with 84 days in the standard care group.[86] The IWGDF supports its use as an adjunctive therapy where best standard of

care alone has been ineffective, and where the resources and expertise exist for the regular venepuncture required.[55] The National Institute for Health and Care Excellence does not recommended the 3C patch as a cost-saving option for diabetic foot ulcers.[87]

Local/rotational soft-tissue flaps and skin grafting

Many advanced soft-tissue and/or bone reconstruction options have been described for patients with large foot wounds; however, they are not commonly used in clinical practice. The goal of these options is to achieve an intact skin surface in a functional, weight-bearing surface on the residual foot, thereby avoiding major (above-ankle) amputation. The outcomes of these procedures can be excellent. A theme throughout the studies is the agreement that diabetic foot wounds may be suitable for closure with local random flaps after infection has been addressed through surgical debridement and antibiotic therapy, after devitalised tissue has been removed, and when lower-extremity vascular status is intact.[88] Patients should be referred to an interdisciplinary diabetic foot clinic for evaluation for these procedures.

Primary prevention

Regular foot checks by healthcare professionals are essential for the prevention of diabetes-related foot disease. In the UK, the National Institute for Health and Care Excellence (NICE) guidelines recommend assessing the risk of foot problems in adults with diabetes:[9]

- At time of diagnosis of diabetes, and then at least annually
- When any foot problems arise
- On any admission to hospital, and if there is any change in the patient's status when in hospital

Patients aged 12-17 years with diabetes should have their feet assessed annually by an appropriately skilled team (in the UK, this should be the paediatric care or transitional care team).[9]

See Diagnosis approach (Physical examination) for more advice on how to perform a foot examination on a person with diabetes. See Screening for more advice on how to stratify a patient's risk of developing diabetes-related foot disease, including the IWGDF scoring system, and the recommended frequency of foot checks.

The International Working Group on the Diabetic Foot (IWGDF) has produced comprehensive guidelines on the prevention of foot complications in people with diabetes, most recently updated in 2023.[24]

People with an IWGDF score of 0 (very low risk) should be screened and examined annually, but otherwise they do not need any specific interventions to prevent foot complications.[24]

For those with an IWGDF score of 1-3 (low, moderate, and high risk), the following primary prevention measures are recommended:[24] [36]

- Self-care advice: do not walk barefoot, or in socks without shoes, or in thin-soled slippers, either indoors or outdoors. Wash feet daily with careful drying between toes, apply emollients to dry skin, and cut toenails straight across. Self-examine feet daily and contact a healthcare professional promptly if suspecting any pre-ulcerative lesion.
- Provide structured education about appropriate foot self-care to prevent ulceration.
- Footwear advice: wear footwear that accommodates the shape of the feet and fits properly. The inside length of the shoe should be 1-2 cm longer than the foot, and should not be too tight or too loose. The internal width should equal the width of the foot at the metatarsal-phalangeal joints or the widest part of the foot), and the height should allow enough room for all the toes. Evaluate the fit with the patient in the standing position, preferably later in the day.
- If there is no appropriate off-the-shelf footwear, or if they have an existing foot deformity, consider prescribing therapeutic footwear such as extra-depth shoes, custom-made footwear, insoles and/or toe orthoses.
- Prompt treatment of any pre-ulcerative lesions, excess callus, ingrown toenails or fungal infections.

- If they have a non-rigid hammertoe with nail changes, excess callus or a pre-ulcerative lesion on the apex or distal part of this toe, consider toe orthotics and/or digital flexor tenotomy.
- Consider referral to an 8-12 week foot and ankle exercise program, and/or advising them that walking an extra 1000 steps per day in appropriate footwear is likely to be safe (IWGDF risk 1-2 only).
- Referral to an integrated foot care program for ulcer prevention (IWGDF risk 2-3 only).

At-risk patients should be encouraged to examine their feet on a daily basis, according to the ADA.[37] The integrity of the skin on all areas of the foot should be examined for calluses, bunions, blisters, ulcers, or other changes. Socks should be visually inspected before wearing to identify any fabric defects. The inside and outside of shoes should be examined for the integrity of the insole, as well as the presence of any foreign bodies. Patients who cannot see the plantar aspects of their feet because of body shape, poor strength, or poor range of motion can inspect this area by placing a hand mirror on the floor. Those with poor vision should enlist the help of family members or neighbours for frequent visual inspections.[37]

Daily foot thermography has been demonstrated to significantly reduce the risk of developing ulcers in high-risk diabetic feet, and is recommended by the IWGDF for those with a score of 2-3 (moderate and high risk).[24] This consists of using an infrared thermometer to check the cutaneous temperature of the foot for areas which are warmer than surrounding skin. Patients who undertake this type of monitoring should be encouraged to contact their usual footcare team promptly if they notice a persistent temperature difference of more than 2.2°C (4.0°F) on two consecutive days. However, this approach is not widely used at present due to the additional burden it places on patients, limited access to infrared thermometers and a lack of data on cost effectiveness and feasibility.[24]

Considerations for comorbidities and risk factors

Optimal care of patients should include management of cardiovascular risk factors to within recommended treatment goals. This includes:[36] [37]

- Glycaemic control
- Blood pressure control
- Lipid control
- Smoking cessation
    - All patients should completely abstain from tobacco use. If this is not feasible, the American Diabetes Association (ADA) recommends referral to a foot care specialist for ongoing preventive care and lifelong surveillance for all patients who smoke and who have additional risk factors for diabetes-related foot disease (e.g., a history of prior lower-extremity complications, loss of protective sensation, structural abnormalities, or peripheral arterial disease).[37]
- Peripheral arterial disease
    - Optimise management with pharmacotherapy (antiplatelets, statins) and revascularisation as needed[38]
- End-stage renal disease
    - In patients with diabetes receiving renal replacement therapy, feet should be protected during the haemodialysis session (e.g., offloading with protective boot).[39]
    - Foot checks should be carried out regularly during haemodialysis sessions.[39]

Secondary prevention

Close monitoring is essential for people with established diabetic foot problems, as recurrence rates are high: after successful healing of a diabetes-related foot ulcer the recurrence rate is 40% within a year and 65% within 3 years.[21]

As per the IWGDF risk stratification system (see Screening), all patients with existing foot deformities are classed in category 2 (moderate risk of ulceration) and should undergo foot screening and examination once every 3-6 months.[24] All those with a history of a foot ulcer are in category 3 (high risk) and should undergo foot screening and examination once every 1-3 months. These patients should also follow the prevention advice outlined in the Primary prevention section including referral to an integrated foot care programme.

Furthermore, those with a healed plantar foot ulcer should be prescribed therapeutic footwear that has a demonstrated plantar pressure relieving effect during walking, to help prevent a recurrent plantar foot ulcer. Encourage the person to consistently wear this prescribed footwear, both indoors and outdoors.[24]

Offloading devices and surgery can also be considered for the prevention of recurrent ulcers, see Management approach for more information.

Considerations for comorbidities and risk factors

As in primary prevention, management of cardiovascular risk factors is also important for secondary prevention. Considerations include glycaemic control, blood pressure control, lipid control, and smoking cessation.[37] [38]

In those with peripheral arterial disease, management with pharmacotherapy (antiplatelets, statins) should be optimised with revascularisation as needed.[38]

In patients with diabetes and end-stage renal disease receiving renal replacement therapy, feet should be protected during the haemodialysis session (e.g., offloading with protective boot).[39] Foot checks should also be carried out regularly during haemodialysis sessions.[39]

Patient discussions

Patient education is considered an important part of the prevention and management of diabetes-related foot disease, despite a lack of strong supporting evidence. Studies suggest that education about diabetes-related foot problems improves knowledge and self-care, but it is unclear whether this translates to improved quality of life or reduced incidence of ulcers or amputation incidence.[99] Evidence also suggests that while education for people with diabetes and their families is important, the knowledge is quickly forgotten and needs to be reinforced regularly.[100]

The UK National Institute for Health and Care Excellence (NICE) recommends that people with diabetes and/or their family members or carers be provided with information and clear explanations of the potential for the development of foot disease at initial assessment, at annual assessment, or if problems arise. This should include oral and written advice on:[9]

- Basic foot care advice and the importance of footcare
- Foot emergencies and who to contact
- Footwear advice
- The person's individual risk of developing a foot problem (low, moderate, or high risk)
- Information about diabetes and the importance of blood glucose control

It is very important to reiterate to patients the need for adherence to any offloading restrictions. Specifically, the need to wear any protective offloading footwear or removable cast-walkers for any steps taken (even within the home) should be emphasised.

If a diabetic foot problem does develop, NICE recommends providing the patient with oral and written information including:[9]

- A clear explanation of the foot problem
- Pictures of diabetic foot problems
- Advice on care of the other leg
- How to recognise a foot emergency and who to contact
- Wound care
- Footwear advice

[Diabetes UK: putting feet first] (https://www.diabetes.org.uk/Get_involved/Campaigning/Putting-feet-first)

[National Diabetes Foot Care Audit: are services providing effective diabetes foot care?] (https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/public/2023-03/NDA_Footcare_Summary_2014-21_v1.pdf)

[Diabetes Australia: diabetes and your feet] (https://www.diabetesaustralia.com.au/living-with-diabetes/preventing-complications/foot-care)

[American Podiatric Medical Association: diabetic wound care] (https://www.apma.org/patients-and-the-public/conditions-affecting-the-foot-and-ankle/diabetic-wound-care)

[ADA: diabetic foot complications] (https://www.diabetes.org/diabetes/foot-complications)

[JAMA Patient Page: what are diabetic foot ulcers?] (https://jamanetwork.com/journals/jama/fullarticle/2812203)

FOLLOW UP

Monitoring

Monitoring

Follow-up of a wound is required until a durable and 100% intact skin surface has been achieved. The frequency of review should be according to local protocols and guidelines and the necessity of redressing according to wound status. When wound healing is complete, follow-up frequency should be according to risk status by the foot protection service.[9] Once healed, patients are at very high risk for recurrence. For this reason the term diabetic foot remission, rather than healing, is often used to communicate this risk to both patients and carers.[21] [97] [98]

Monitoring of blood glucose, blood pressure, and serum lipids, and monitoring for other complications is part of the general management of diabetes in all patients. Annual assessment of renal function is recommended.

See Screening and Secondary prevention for more information.

Complications

Complications	Timeframe	Likelihood
delayed wound healing	**short term**	**medium**

The desired healing rate is at least a 50% wound area reduction within 4 weeks. The most common reasons for delayed wound healing are subtle infection (especially osteomyelitis), inadequate arterial perfusion, and inadequate offloading.

Clinicians should consider further evaluation for these aetiologies using tests with higher sensitivity (e.g., magnetic resonance imaging or bone biopsy if plain x-ray alone does not suggest osteomyelitis; diagnostic angiogram if non-invasive testing does not suggest arterial insufficiency; non-removable offloading footwear such as a total contact cast or non-removable cast-walker in patients previously provided removable footwear).

osteomyelitis	**long term**	**medium**

Osteomyelitis (infection of the cortical and/or trabecular bone) may occur when chronic ulcers allow for the entry of bacteria into bone. Osteomyelitis is particularly likely in wounds that are wide, deep, have been present for many weeks, are located over a bony prominence, show visible bone, or are accompanied by an erythematous, swollen ('sausage') toe.[40]

Most cases are polymicrobial, and involvement of gram-positive and -negative organisms is common.

If osteomyelitis is suspected, the wound may be probed gently with a blunt sterile metal instrument (probe-to-bone test), although this must only be done by skilled clinicians as it can cause harm. The feeling of gritty bone at the base of the ulcer is a positive probe-to-bone test, which supports the diagnosis.

Making an accurate diagnosis of osteomyelitis in a diabetic foot can be challenging as there is no universally accepted definition or criteria, and low levels of agreement between commonly used diagnostic tests. Nevertheless, based on current evidence, the IWGDF and IDSA recommend a combination of probe-to-bone test, plain x-ray (and/or further imaging such as MRI), and serum inflammatory markers to support the diagnosis.[40] Bone biopsy is potentially definitive but not widely available, and lacks data demonstrating clear benefits to its use.[40]

The probe-to-bone test cannot be used in isolation to diagnose or rule out osteomyelitis.[90] The UK National Institute for Health and Care Excellence indicates that osteomyelitis may be present in a person with diabetes despite a negative probe-to-bone test.[9]

Management of osteomyelitis may consist of surgical resection of the bone, but oral or parenteral antibiotics alone may be appropriate in selected patients. Up to 6 weeks of antimicrobial therapy is recommended and appears to be as effective as 12 weeks.[9] [91] However, a prospective randomised non-inferiority pilot trial found a post-debridement systemic antibiotic therapy course for diabetic foot osteomyelitis of 3 weeks gave similar (and statistically non-inferior) incidences of remission and adverse events to a course of 6 weeks.[92]

ulcer recurrence	**long term**	**low**

Should be identified by the patient (during daily foot exams) or the provider (during clinic follow-up).

Recurrence in the location of a previous ulcer that had completely healed is often due to suboptimal foot biomechanics (i.e., an improper distribution of pressure across the weight-bearing surfaces of the foot).

FOLLOW UP

Complications	Timeframe	Likelihood
Management should be similar to that of an initial foot ulcer.		
Charcot's neuro-osteoarthropathy	**long term**	**low**

Charcot's neuro-osteoarthropathy (CNO) is a complex disorder that occurs in people with diabetes who have some form of peripheral neuropathy. It is characterised by inflammation and varying degrees of structural damage to the bones, joints, and soft tissue of the foot. The true prevalence is unknown as it is thought to be under-reported; however, estimates range from 0.04% to 0.53% of people with diabetes.[29] The condition can lead to permanent bone and joint deformities, including collapse of the longitudinal and transverse arches of the foot.[93] These deformities predispose to ulceration and infection, which in turn increase the risk of major lower limb amputation.[29]

The diagnosis of CNO should be considered if there is swelling, redness, warmth, or deformity (particularly if the skin is intact). It should be considered even if pain is not present or deformity is not apparent.[9] It may be triggered by trauma, preceding foot surgery, an infected foot ulcer, or offloading the contralateral foot.[94] Pain, erythema, and redness may appear acutely, mimicking a foot infection. Chronic deformation may lead to repetitive trauma of the midfoot (arch) during walking, leading to ulceration in this area.

In the UK, the National Institute for Health and Care Excellence recommends that to confirm the diagnosis the person should be referred within 1 working day to the multidisciplinary foot care service for triage within 1 further working day. Non-weight-bearing should be instituted until definitive treatment can be started. If Charcot's neuro-osteoarthropathy is suspected, a weight-bearing x-ray of the foot and ankle should be performed. If this is normal and CNO is still suspected, magnetic resonance imaging should be performed.[9] [95] The mainstay of treatment is offloading with a non-removable offloading device. If a non-removable device is not advisable because of clinical or other circumstances, treatment with a below-knee removable device can be considered.[9] Bisphosphonates should not be offered except as part of a clinical trial.[9]

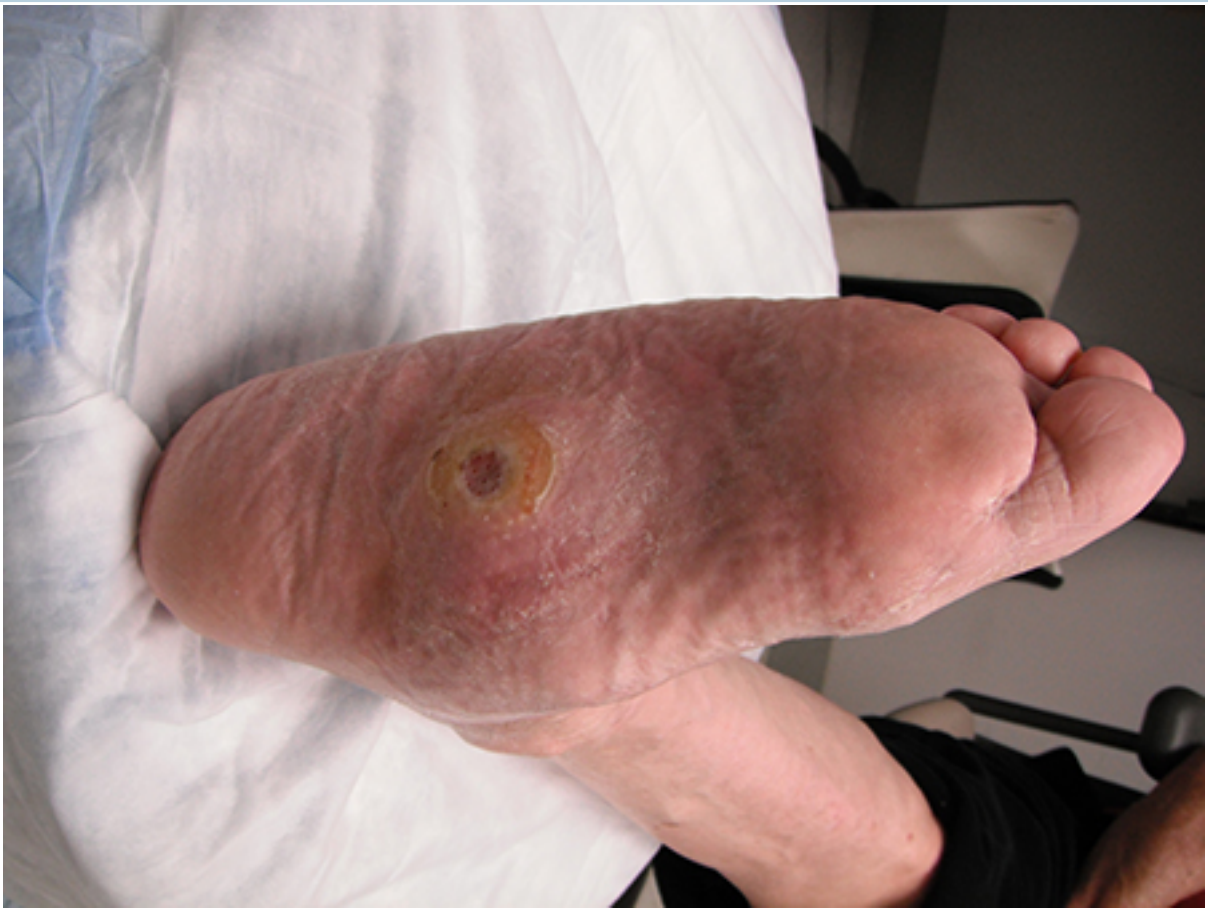
Monitoring of treatment should be done by clinical assessment, temperature monitoring, and/or repeated x-rays. People who develop subsequent deformity are considered at high risk for future foot ulceration and, once the active CNO arthropathy has become inactive, should have foot orthoses provided, and should be followed-up by a foot protection service.[9]

The International Working Group on the Diabetic Foot (IWGDF) advises using infrared thermometry to calculate the temperature difference between both legs, if suspecting a diagnosis of CNO.[29] Serial skin temperature measurements can also be used to monitor disease activity and help decide when CNO is in remission, in combination with imaging and the presence of soft tissue oedema.

If MRI is unavailable or contraindicated, a nuclear imaging (scintigraphy), computed tomography, or SPECT-CT (single photon emission computed tomography) scan can be used to support the diagnosis of CNO when x-rays are normal but clinical suspicion remains high.[29] Serum biomarkers such as c-reactive protein, erythrocyte sedimentation rate, or white blood cell count, should not be used to diagnose or exclude CNO.[29]

The IWGDF recommends using a non-removable knee-high device to immobilise and offload the foot to promote remission in patients with active CNO and intact skin.[29] Alternative options include a total contact cast, a knee-high walker rendered non-removable, or a removable knee-high device. However below-the-ankle offloading devices, such as surgical or custom-moulded shoes, should not be used as they do not sufficiently offload the diseased bone and joints.[29]

Complications	Timeframe	Likelihood



Midfoot ulcer in a patient with Charcot arthropathy (midfoot collapse)
From the collection of Dr Neal R. Barshes; used with permission

graft stenosis or thrombosis	variable	low

Stenosis requiring endovascular or surgical intervention occurs in about 20% of vein graft bypasses within the first 2 years after creation.[96] Most vascular surgeons will perform routine ultrasound surveillance to identify such stenosis, although the benefits of this approach remain uncertain and local protocols vary.[11]

Although graft thrombosis is often asymptomatic, it may occasionally cause obvious signs of ischaemia, including delayed wound healing, ischaemic rest pains, clinical signs of acute limb ischaemia such as acute-onset weakness, paraesthesias, or limb pain (especially if the vascular reconstruction was done with a prosthetic vascular graft). Incidence may be as high as 10% to 15% during the first year after revascularisation and <5% per year during subsequent years.[96]

Prognosis

Outcomes, including the avoidance of leg amputation, can be quite favourable, especially in healthcare settings with multidisciplinary or interdisciplinary teams that work together to optimise patient care.

Neuropathic foot ulcer

Typically requires 2 to 3 months for complete wound healing. Patients should anticipate the need to minimise weight-bearing on the affected foot, adhere to offloading instructions, and wear offloading footwear or cast-walkers for this period of time. Follow-up may occur on a weekly or twice-weekly frequency.

Non-healing foot ulcer associated with severe peripheral arterial disease

Typically requires approximately 6 months for complete wound healing. Endovascular interventions may be performed on an outpatient or short-stay basis. Surgical revascularisation in this setting may require hospitalisation for about 1 week. Subsequent foot debridement or reconstructive procedures are common and often done on an outpatient basis.

Foot infection

May require 3 to 4 months for complete wound healing in patients with no peripheral artery disease, or 6 to 12 months in patients with peripheral artery disease.

Amputation

The 5-year mortality rate for people who undergo lower extremity amputation due to a diabetic foot ulcer remains alarming at 30.5%, whereas those with major amputation have a 5-year mortality of 56.6%.[89] The high rate is thought to be associated with cardiovascular disease.

Impact of long-term comorbidities

Chronic kidney disease (CKD): renal failure has a significant impact on the course and outcome of the diabetes-related foot disease. Presence of CKD increases risk of amputation and all-cause mortality.[42][43]

Cardiovascular disease (CVD): patients with diabetic foot ulcers are at increased risk of cardiovascular-related morbidity and mortality compared with patients with diabetes without foot ulcers.[63][64] [65] CVD is one of the leading causes of death in those with diabetes-related foot disease (and in those with diabetes generally).[43]

Heart failure: comorbid heart failure is associated with a worse prognosis, with lower healing rates, and increased risk of recurrence and amputations.[68]

Depression: patients with depression and diabetic foot ulcers are at higher risk of major lower-limb amputation and mortality.[71][72][73]

Diagnostic guidelines

United Kingdom

Diabetic foot problems: prevention and management (https://www.nice.org.uk/guidance/NG19)

Published by: National Institute for Health and Care Excellence **Last published:** 2019 (reaffirmed 2023)

Diabetes at the front door (https://www.diabetes.org.uk/for-professionals/improving-care/good-practice/inpatient-and-hospital-care/joint-british-diabetes-society-for-inpatient-care)

Published by: Joint British Diabetes Societies for Inpatient Care **Last published:** 2023

International

Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2023 update) (https://iwgdfguidelines.org/prevention-guideline-2023/)

Published by: International Working Group on the Diabetic Foot **Last published:** 2023

Practical guidelines on the prevention and management of diabetes-related foot disease (IWGDF 2023 update) (https://iwgdfguidelines.org/practical-guidelines-2023/)

Published by: International Working Group on the Diabetic Foot **Last published:** 2023

Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF/IDSA 2023 update) (https://iwgdfguidelines.org/infection-guideline-2023)

Published by: International Working Group on the Diabetic Foot and the Infectious Diseases Society of America **Last published:** 2023

Guidelines on the classification of foot ulcers in people with diabetes (IWGDF 2023 update) (https://iwgdfguidelines.org/classification-2023)

Published by: International Working Group on the Diabetic Foot **Last published:** 2023

The intersocietal IWGDF, ESVS, SVS guidelines on peripheral artery disease in patients with diabetes mellitus and a foot ulcer (https://iwgdfguidelines.org/pad-guideline-2023/)

Published by: International Working Group on the Diabetic Foot, European Society for Vascular Surgery, and Society for Vascular Surgery **Last published:** 2023

Guidelines on the diagnosis and treatment of active Charcot neuro-osteoarthropathy in persons with diabetes mellitus (https://iwgdfguidelines.org/charcot-2023/)

Published by: International Working Group on the Diabetic Foot **Last published:** 2023

IDF clinical practice recommendations on the diabetic foot (https://www.idf.org/e-library/guidelines.html)

Published by: International Diabetes Federation **Last published:** 2017

North America

Standards of care in diabetes - 2024 (https://diabetesjournals.org/care/issue/47/Supplement_1)

Published by: American Diabetes Association **Last published:** 2023

Best practice recommendations for the prevention and management of diabetic foot ulcers (https://www.woundscanada.ca/health-care-professional/publications/dfc-2)

Published by: Wounds Canada **Last published:** 2019 (reaffirmed 2021)

Clinical practice guidelines for the prevention and management of diabetes in Canada (http://guidelines.diabetes.ca/cpg)

Published by: Diabetes Canada **Last published:** 2018

Asia

Prevention and management of diabetic foot (http://clinicalestablishments.gov.in/En/1068-standard-treatment-guidelines.aspx)

Published by: Ministry of Health and Family Welfare, Government of India **Last published:** 2016

Oceania

2021 evidence-based Australian guidelines for diabetes-related foot disease (https://www.diabetesfeetaustralia.org/new-guidelines)

Published by: Diabetes Feet Australia **Last published:** 2021

National evidence-based guideline: prevention, identification and management of foot complications in diabetes (https://baker.edu.au/-/media/documents/impact/diabetes-foot-guidelines/baker-institute-foot-complications-full-guideline.pdf)

Published by: Australian Government National Health and Medical Research Council; Baker IDI Heart & Diabetes Institute **Last published:** 2011

Treatment guidelines

United Kingdom

Diabetic foot problems: prevention and management (https://www.nice.org.uk/guidance/ng19)

Published by: National Institute for Health and Care Excellence **Last published:** 2019 (reaffirmed 2023)

International

Practical guidelines on the prevention and management of diabetes-related foot disease (IWGDF 2023 update) (https://iwgdfguidelines.org/practical-guidelines-2023/)

Published by: International Working Group on the Diabetic Foot **Last published:** 2023

The intersocietal IWGDF, ESVS, SVS guidelines on peripheral artery disease in patients with diabetes mellitus and a foot ulcer (https://iwgdfguidelines.org/pad-guideline-2023/)

Published by: International Working Group on the Diabetic Foot, European Society for Vascular Surgery, and Society for Vascular Surgery **Last published:** 2023

Guidelines on interventions to enhance healing of foot ulcers in people with diabetes (IWGDF 2023 update) (https://iwgdfguidelines.org/wound-healing-2023/)

Published by: International Working Group on the Diabetic Foot **Last published:** 2023

Guidelines on offloading foot ulcers in persons with diabetes (IWGDF 2023 update) (https://iwgdfguidelines.org/offloading-guideline-2023/)

Published by: International Working Group on the Diabetic Foot **Last published:** 2023

North America

Standards of care in diabetes - 2024 (https://diabetesjournals.org/care/issue/47/Supplement_1)

Published by: American Diabetes Association **Last published:** 2023

Nutrition interventions in adults with diabetic foot ulcers (https://www.guidelinecentral.com/guidelines/ALPS)

Published by: American Limb Preservation Society **Last published:** 2023

Best practice recommendations for the prevention and management of diabetic foot ulcers (https://www.woundscanada.ca/health-care-professional/publications/dfc-2)

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Clinical practice guidelines for the prevention and management of diabetes in Canada (http://guidelines.diabetes.ca/cpg)

Published by: Diabetes Canada **Last published:** 2018

The management of diabetic foot (https://vascular.org/research-quality/guidelines-and-reporting-standards/clinical-practice-guidelines)

Published by: Society for Vascular Surgery; American Podiatric Medical Association; Society for Vascular Medicine **Last published:** 2016

Inpatient management of diabetic foot disorders: a clinical guide (http://care.diabetesjournals.org/content/36/9/2862)

Published by: American Diabetes Association **Last published:** 2013

Asia

Prevention and management of diabetic foot (http://clinicalestablishments.gov.in/En/1068-standard-treatment-guidelines.aspx)

Published by: Ministry of Health and Family Welfare, Government of India **Last published:** 2016

Oceania

2021 evidence-based Australian guidelines for diabetes-related foot disease (https://www.diabetesfeetaustralia.org/new-guidelines/)

Published by: Diabetes Feet Australia **Last published:** 2021

National evidence-based guideline: prevention, identification and management of foot complications in diabetes (https://baker.edu.au/-/media/documents/impact/diabetes-foot-guidelines/baker-institute-foot-complications-full-guideline.pdf)

Published by: Australian Government National Health and Medical Research Council; Baker IDI Heart & Diabetes Institute **Last published:** 2011

Online resources

1. NHS National Diabetes Foot Care Audit (https://digital.nhs.uk/data-and-information/clinical-audits-and-registries/national-diabetes-foot-care-audit) *(external link)*

2. Diabetes UK: putting feet first (https://www.diabetes.org.uk/Get_involved/Campaigning/Putting-feet-first) *(external link)*

3. National Diabetes Foot Care Audit: are services providing effective diabetes foot care? (https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/public/2023-03/NDA_Footcare_Summary_2014-21_v1.pdf) *(external link)*

4. Diabetes Australia: diabetes and your feet (https://www.diabetesaustralia.com.au/living-with-diabetes/preventing-complications/foot-care) *(external link)*

5. American Podiatric Medical Association: diabetic wound care (https://www.apma.org/patients-and-the-public/conditions-affecting-the-foot-and-ankle/diabetic-wound-care) *(external link)*

6. ADA: diabetic foot complications (https://www.diabetes.org/diabetes/foot-complications) *(external link)*

7. JAMA Patient Page: what are diabetic foot ulcers? (https://jamanetwork.com/journals/jama/fullarticle/2812203) *(external link)*

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Images

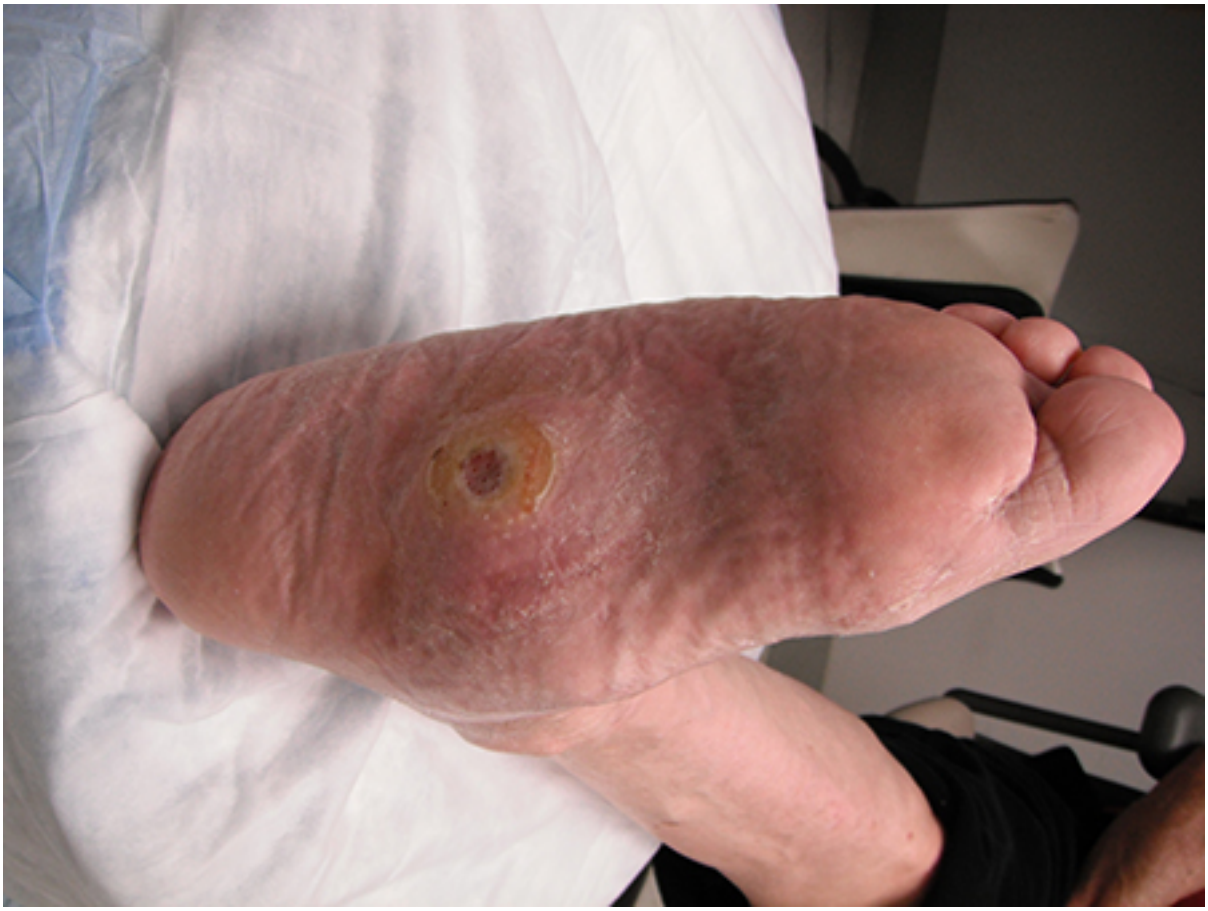

Figure 1: Midfoot ulcer in a patient with Charcot arthropathy (midfoot collapse)

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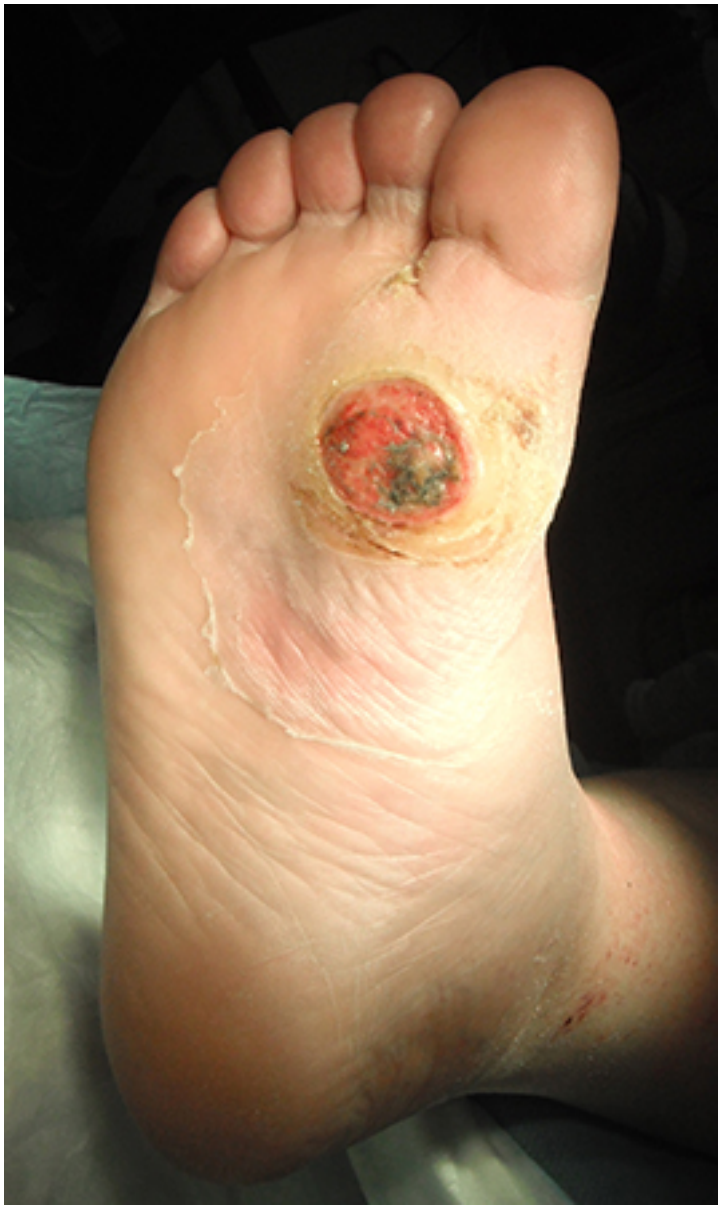

Figure 2: Uninfected foot ulcer overlying the plantar aspect of the first metatarsophalangeal joint. Note the hyperkeratotic skin (callus) surrounding the wound edge

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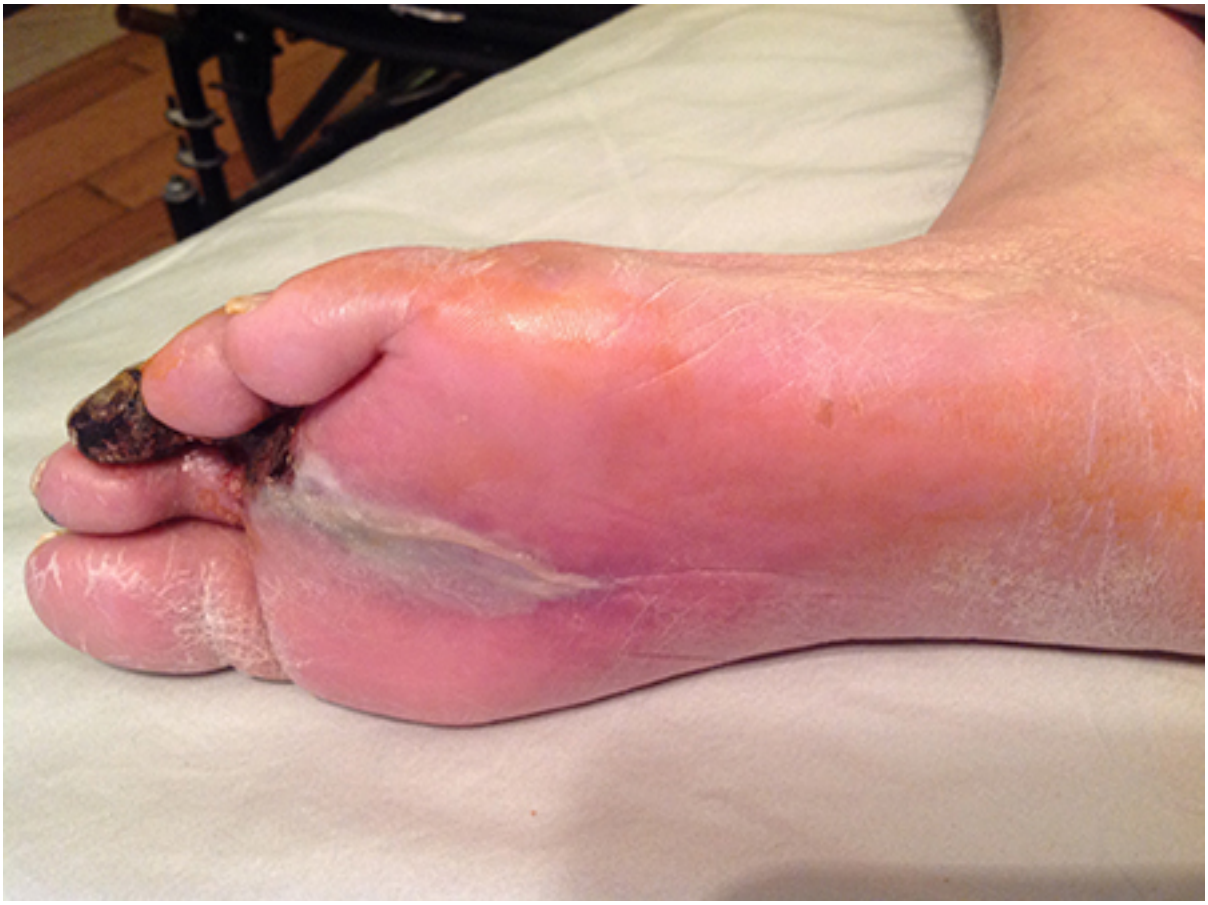

Figure 3: A foot infection originating from a gangrenous third toe. Note the erythema and fluctuance in the midfoot. An abscess cavity was found tracking under the longitudinal section of macerated skin

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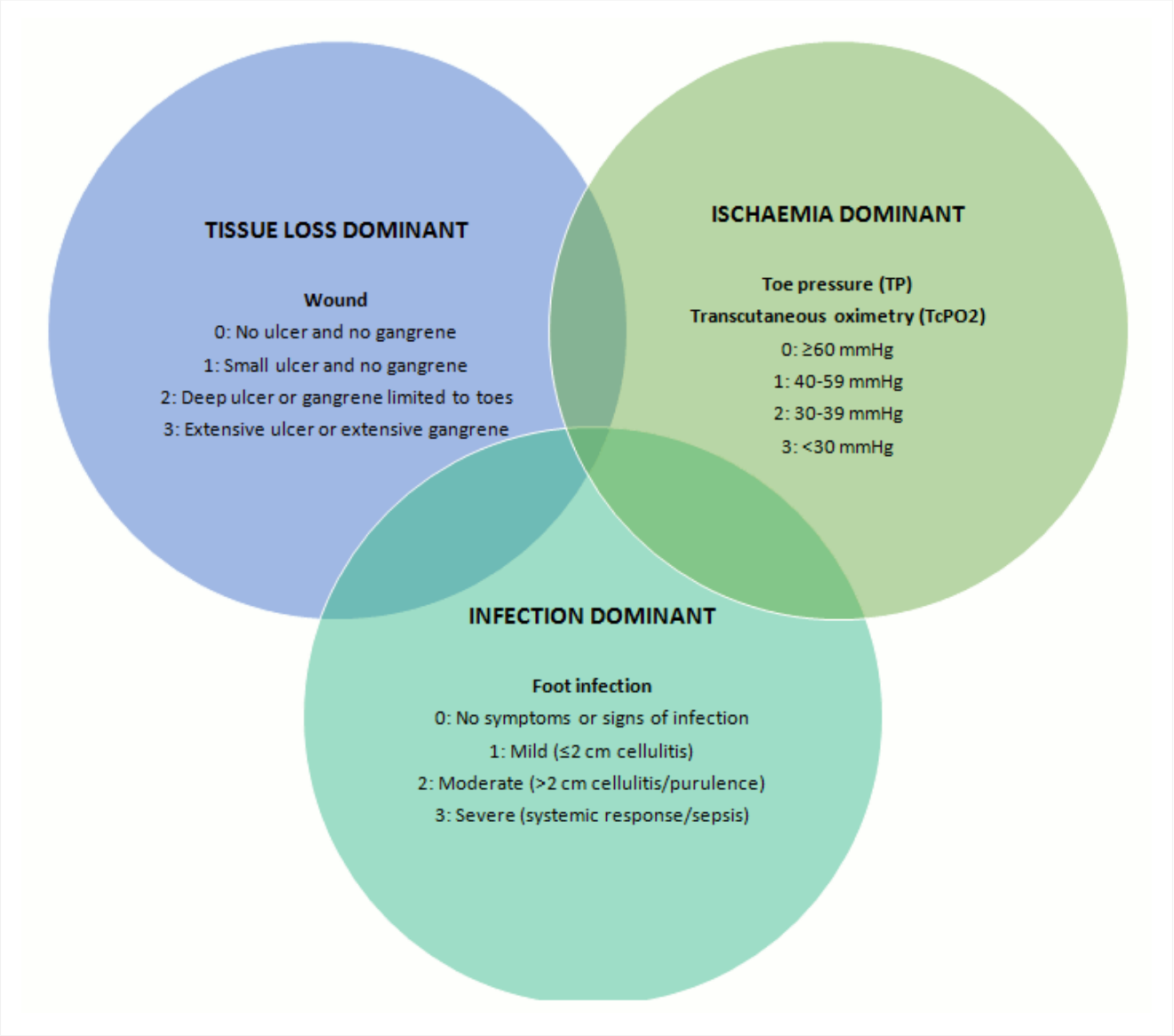

Figure 4: Diabetic foot problems can be related to the presence of a wound, ischaemia, or infection (WIfI). Which of these parameters is dominant can vary, and a flexible long-term management approach is needed. The Venn diagram shows intersecting rings of dominance for these three parameters, with gradings listed for each. The shaded areas represent combinations of these parameters of dominance

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This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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