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DIABETIC NEUROPATHY: COMPREHENSIVE INSIGHTS INTO MECHANISMS, DIAGNOSIS, AND THERAPEUTIC APPROACHES

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ABSTRACT

Background: Diabetic neuropathy (DN) is one of the most prevalent complications of diabetes mellitus, affecting up to half of patients over their lifetime. It encompasses a spectrum of peripheral and autonomic nerve disorders resulting from chronic hyperglycemia, and significantly impairs quality of life while contributing to high morbidity (e.g. foot ulcers, amputations) and mortality. **Objective:** This review provides a comprehensive overview of DN, including global epidemiology, underlying mechanisms, clinical diagnosis, current treatments, ongoing challenges, and future directions. **Methods:** We synthesized recent (2019–2024) clinical research and review literature on DN, emphasizing human studies and global perspectives. **Results:** Globally, an estimated 22–47% of diabetes patients have peripheral neuropathy, with higher rates in long-standing and poorly controlled disease. Chronic hyperglycemia induces metabolic and microvascular changes (e.g. oxidative stress, inflammation, ischemia) that damage nerve fibres. Diagnosis relies on clinical evaluation (symptoms, sensory testing) and should be performed at diabetes diagnosis and annually thereafter. There are no curative treatments; tight glycemic control can prevent or slow neuropathy, especially in type 1 diabetes. Symptomatic management of neuropathic pain includes medications like duloxetine, pregabalin, gabapentin, and tricyclic antidepressants, which provide partial relief in about 50% of patients. **Conclusions:** DN remains a challenging condition with substantial global impact. Key challenges include underdiagnosis in primary care and lack of disease-modifying therapies. Future directions involve early detection (e.g. via biomarkers or corneal imaging) and development of novel treatments targeting pathogenic pathways and nerve regeneration. Multidisciplinary strategies are needed to improve patient outcomes.

KEYWORDS: Diabetic neuropathy; Diabetic peripheral neuropathy; Diabetes complications; Neuropathic pain; Pathophysiology; Diagnosis; Treatment; Future directions.

INTRODUCTION AND BACKGROUND

Diabetic neuropathy (DN) is a **common chronic complication** of diabetes mellitus, affecting both type 1 and type 2 diabetes patients worldwide. It encompasses various syndromes, of which **diabetic peripheral neuropathy (DPN)** – a distal symmetric polyneuropathy – is the most prevalent form, characterized by length-dependent degeneration of nerve fibers in the feet and hands. Other forms include autonomic neuropathies (e.g. cardiovascular, gastrointestinal, genitourinary), proximal motor neuropathy, and focal mononeuropathies, but DPN accounts for the majority of cases.[1] DN significantly **compromises quality of life** through chronic pain, sensory loss, and weakness, and it contributes to elevated rates of foot ulcers and amputations. In fact, DPN is the leading cause of neuropathic foot ulcers and non-traumatic lower extremity amputations in diabetes. Nearly 30–50% of people with diabetes will develop DPN over their lifetime, and DPN is implicated in ~80% of diabetic foot ulcers and up to 75% of non-traumatic amputations. These complications translate into substantial healthcare burdens and mortality; for example, a five-year mortality rate after a diabetic foot ulcer is over twice as high compared to diabetic patients without foot ulcers.[2]

Global epidemiology: As diabetes prevalence rises globally, the burden of DN is increasing in tandem. An estimated **537 million adults** were living with diabetes in 2021, projected to reach **783 million** by 2045. Correspondingly, DPN is a global public health issue, with prevalence estimates ranging from about **22% up to 47%** of the diabetes population worldwide. Regional variations are noted – for instance, studies in Africa report DPN prevalence as high as 60% in some cohorts.[3] A large multi-country study (INTERPRET-DD) found an overall DPN prevalence of **26.7%** among middle-aged type 2 diabetics, with considerable between-country variation. Higher rates of neuropathy are generally observed in patients with longer diabetes duration, older age, poor glycemic control, obesity, hypertension, and co-existing diabetic complications. Notably, **underdiagnosis** is a challenge in many settings; in developing countries, limited screening and healthcare resources lead to late detection of DPN and consequently higher rates of advanced neuropathic complications. This underscores the need for improved awareness and routine screening for neuropathy in all diabetes care settings.[4]

Pathophysiology and mechanisms

The pathogenesis of diabetic neuropathy is **multifactorial**, driven by chronic hyperglycemia and associated metabolic disturbances. Persistent **hyperglycemia** triggers a cascade of biochemical changes within nerve cells and supporting Schwann cells, collectively causing nerve fiber injury. Major mechanisms include:[5]

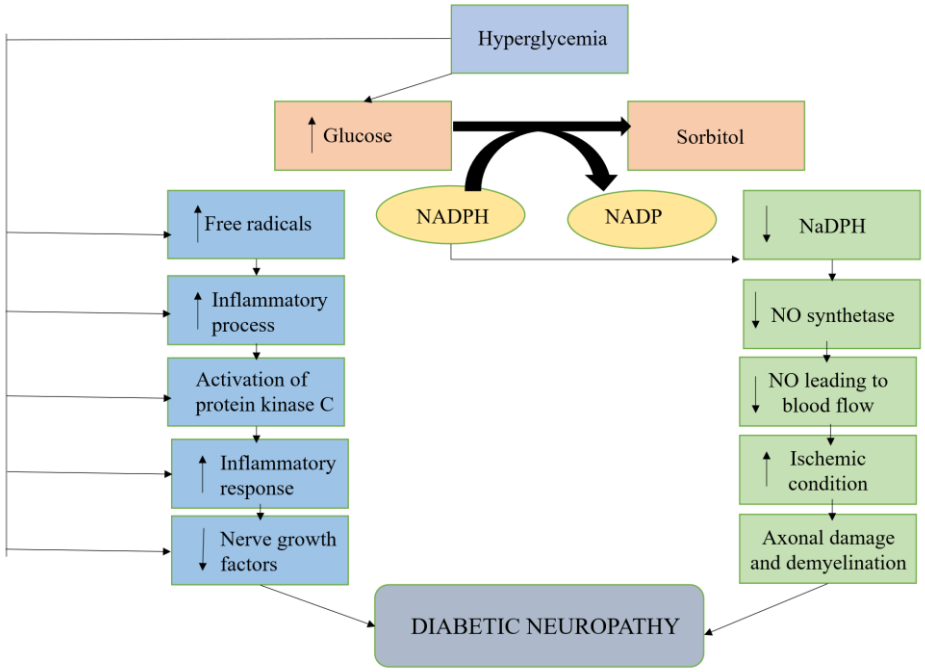

Fig. 1: Pathophysiology of diabetic neuropathy.

- **Polyol pathway flux:** Excess intracellular glucose is shunted into the sorbitol pathway, consuming NADPH and leading to oxidative stress. Sorbitol accumulation and reduced myoinositol can disrupt neuronal osmolar balance and signaling.
- **Advanced glycation end-products (AGEs):** Hyperglycemia promotes non-enzymatic glycation of proteins and lipids, forming AGEs that alter protein function and engage receptors (RAGE) to induce inflammation and oxidative damage.
- **Oxidative stress and inflammation:** Mitochondrial dysfunction and endoplasmic reticulum stress from hyperglycemia and dyslipidemia generate reactive oxygen species (ROS). ROS activate stress pathways (e.g. PKC, NF-κB) and drive chronic inflammation. In diabetic nerves, accumulation of macrophages and pro-inflammatory cytokines further damages fibers.[6]
- **Ischemia and vascular insufficiency:** Diabetes causes **microvascular dysfunction** in vasa nervorum (the small vessels supplying peripheral nerves). Endothelial dysfunction and reduced nitric oxide lead to nerve ischemia, compounding metabolic injury. This neurovascular impairment impedes nerve repair and contributes to axonal degeneration.
- **Demyelination and axonal degeneration:** Metabolic and ischemic stress results in distal axonal degeneration (especially of long sensory fibers) and segmental demyelination. Small unmyelinated and thinly myelinated fibers (pain and temperature sensations) are often affected earliest, followed by larger myelinated fibers (vibration, proprioception).[7]

These processes result in a **length-dependent peripheral polyneuropathy**, where the longest nerves (feet > hands) are affected first. Clinically, this explains why symptoms like tingling, numbness, or burning pain start in the toes and ascend ("stocking-glove" distribution). Both **sensory and motor fibers** can be involved, but sensory loss and neuropathic pain are the predominant manifestations in DPN. Autonomic nerve fibers are also vulnerable, leading to diabetic autonomic neuropathies (e.g. cardiovascular autonomic neuropathy, gastroparesis, erectile dysfunction) that significantly impact morbidity.[8]

Importantly, **hyperglycemia is the primary driver** of DN, as evidenced by landmark trials showing risk reduction with intensive glycemic control. In the Diabetes Control and Complications Trial (DCCT) for type 1 diabetes, tight glycemic control reduced neuropathy incidence by ~78%, whereas in type 2 diabetes (UKPDS), intensive control had a more modest ~5–10% risk reduction. This difference reflects that type 2 patients often have long periods of undiagnosed hyperglycemia before diagnosis. Nonetheless, these data underscore that maintaining **good glycemic control** is crucial to prevent or slow neuropathy. Beyond glucose, other factors like dyslipidemia, hypertension, and smoking also contribute to neuropathy risk – likely via exacerbating oxidative and vascular stress – and thus comprehensive cardiovascular risk management is recommended to mitigate progression of DN.[9]

Clinical diagnosis

Early **diagnosis of diabetic neuropathy** is vital for preventing severe complications. However, DN can be insidious in onset; many patients are asymptomatic in early stages, and up to 50% of DPN cases may go unrecognized until advanced. **Screening and assessment** for neuropathy should therefore be a routine part of diabetes care. Guidelines (e.g. American Diabetes Association) recommend that all patients with type 2 diabetes be evaluated for peripheral neuropathy at the time of diagnosis and *at least annually* thereafter; for type 1 diabetes, screening should begin five years after diagnosis and then annually. Regular screening allows for early detection and intervention before ulcerations or injuries occur.[10]

Clinical evaluation: The diagnosis of DPN is primarily clinical. It begins with a thorough history for neuropathic symptoms – common complaints include distal limb **numbness**, tingling ("pins and needles"), burning or **shooting pain**, electric shock-like sensations, or heightened pain response to light touch (allodynia). Symptoms typically start in the toes or soles and progress proximally. Some patients have predominantly painless numbness, which is high-risk for injuries, while others suffer from debilitating neuropathic pain. Autonomic symptoms (e.g. dizziness from orthostatic hypotension, gastroparesis, erectile dysfunction) should also be queried, as they suggest autonomic neuropathy.[11]

Physical examination focuses on the lower extremities. A **neurological foot exam** should assess:[12]

- **Light touch sensation:** using a 10-g monofilament on plantar surfaces – inability to feel it at designated sites indicates loss of protective sensation and risk of ulceration.
- **Vibration sense:** tested with a tuning fork (128 Hz) on bony prominences (e.g. great toe) to gauge large-fiber function.
- **Pinprick or temperature sensation:** to assess small-fiber function (pain and temperature perception).
- **Ankle reflexes:** typically reduced or absent in DPN.
- **Inspection:** look for dry or cracked skin (can indicate autonomic denervation), muscle atrophy (if motor fibers affected), foot deformities (e.g. claw toes, Charcot joints), and any ulcers or calluses. Foot deformities and high-pressure callus areas signal risk for ulcer development.

Using simple clinical scoring tools (e.g. Michigan Neuropathy Screening Instrument or Neuropathy Disability Score) can improve detection. A combination of abnormal sensory tests (such as insensitivity to monofilament plus reduced vibration) strongly suggests DPN in the context of diabetes.

Electrodiagnostic testing: Nerve conduction studies (NCS) and electromyography are not required for routine diagnosis if the presentation is typical of diabetic polyneuropathy. They can document the neuropathy and quantify its severity (often showing reduced sural nerve amplitudes and slowed conduction in a length-dependent pattern). NCS are mainly indicated if the clinical picture is atypical (asymmetric symptoms, motor-predominant deficits, acute onset) to exclude other causes. In long standing diabetics, NCS often confirm a sensorimotor polyneuropathy but may be normal in purely small-fiber neuropathy.[13]

Advanced and emerging diagnostics: New techniques are being explored to detect neuropathy at earlier or subclinical stages. For instance, **corneal confocal microscopy** is a noninvasive imaging method that can visualize small nerve fibers in the cornea; early small-fiber damage due to diabetes can be quantified by reduced corneal nerve fiber density. Skin biopsy with intraepidermal nerve fiber density measurement is another tool to diagnose small-fiber neuropathy even when NCS are normal. These advanced tests and **biomarker studies** (looking at inflammatory or neural injury markers in blood/skin) are part of research efforts to enable **early diagnosis** and intervention. While promising, such techniques are not yet in widespread clinical use. At present, **vigilant clinical screening remains the cornerstone** of DN diagnosis. Prompt recognition of neuropathy allows clinicians to intensify glycemic control and implement foot care measures to avert ulceration and amputation.[14]

TREATMENT AND MANAGEMENT

Management of diabetic neuropathy involves a **multifaceted approach** addressing the underlying disease process, mitigating neuropathic symptoms (especially pain), and preventing complications. Key elements include: (1) **glycemic control and risk factor management** to slow neuropathy progression, (2) **pharmacologic and non-pharmacologic therapies** for neuropathic pain, and (3) **foot care and patient education** to prevent injury.[15]

Glycemic control: Tight control of blood glucose remains the only proven strategy to prevent or delay diabetic neuropathy. Especially in type 1 diabetes, early intensive glycemic management markedly reduces the long-term risk of DN. In type 2 diabetes, glucose control is beneficial, though its impact on neuropathy is more modest once neuropathy is established. Nonetheless, all patients should aim for individualized glycemic targets to minimize chronic hyperglycemic exposure. Additionally, aggressive management of **hypertension and dyslipidemia** is recommended given their role in microvascular complications. Some newer diabetes medications (e.g. **SGLT2 inhibitors** and **GLP-1 agonists**) not only improve glycemic control but also promote weight loss and may have neuroprotective effects; ongoing studies are evaluating whether these agents confer specific benefits in DN.[16]

Lifestyle and supportive measures: Patients should be counseled on diet and exercise, as improved fitness and weight control can help metabolic parameters and potentially neuropathic symptoms. Avoidance of smoking (a vasoconstrictor that can worsen nerve ischemia) is also advised. Deficiencies such as vitamin B12 (especially in metformin users) should be corrected. While various vitamins and supplements (e.g. alpha-lipoic acid, acetyl-L-carnitine) have been studied for DN, evidence is mixed and they are not standard care.[17]

Pain management: Neuropathic pain can be the most debilitating aspect of DN for patients. Effective relief usually requires pharmacotherapy. International guidelines uniformly recommend certain antidepressant and anticonvulsant medications as first-line agents for **painful diabetic peripheral neuropathy (PDN)**. These drugs modulate neurotransmitters and ion channels involved in pain signaling. Table 1 compares the major pharmacologic options for PDN.[18]

Figure 1: Global trends in diabetes and diabetic neuropathy. The rising number of people with diabetes (blue line) portends a growing burden of diabetic peripheral neuropathy (DPN). Bars show estimated global diabetes prevalence in 2000, 2010, 2021, with projections for 2030 and 2045. The red line estimates the corresponding number of individuals with DPN (assuming ~30% of diabetics are affected). As of 2021, over 500 million people have diabetes worldwide, and hundreds of millions suffer from DPN.[19]

Table 1: Comparison of pharmacologic treatments for painful diabetic neuropathy.[20]

Medication (Class)	Mechanism of Action	Clinical Use and Efficacy
Duloxetine (SNRI)	Inhibits serotonin and norepinephrine reuptake, enhancing descending pain inhibition in the CNS.	First-line for painful DPN; FDA-approved. Reduces neuropathic pain in ~50% of patients (moderate pain relief).
Pregabalin (Gabapentinoid)	Binds α2δ subunit of voltage-gated calcium channels, reducing excitatory neurotransmitter release.	First-line for painful DPN; FDA-approved. Similar efficacy to duloxetine in relieving neuropathic pain. Often improves sleep quality.
Gabapentin (Gabapentinoid)	Mechanism similar to pregabalin (calcium channel modulation); also enhances GABA activity indirectly.	First-line alternative to pregabalin (off-label use for DPN). Effective for many patients, though may take weeks to titrate to effective dose.
Amitriptyline (Tricyclic antidepressant)	Inhibits norepinephrine and serotonin reuptake; also blocks sodium channels and NMDA receptors, providing analgesic effect.	Widely used off-label for PDN (guideline-supported first-line). Particularly useful if coexistent insomnia. Efficacy comparable to SNRIs/gabapentinoids.
Tapentadol (Opioid analgesic)	μ-opioid receptor agonist and norepinephrine reuptake inhibitor, providing dual analgesic action.	Second-line for refractory PDN pain. Tapentadol is approved for diabetic neuropathic pain in some regions. Tramadol (a weaker opioid agonist) is another option for short-term use.
Capsaicin 8% patch (Topical)	Activates TRPV1 receptors on peripheral nerves, causing an initial release and subsequent depletion of substance P (a pain neurotransmitter). Leads to reversible desensitization of pain fibers.	Used for localized neuropathic pain in PDN (e.g. feet). Provides moderate pain relief in some patients. Applied in clinic as a high-concentration patch for 30–60 minutes for prolonged effect (months).

Note: All patients with DPN should also receive **education on foot care** and injury prevention. This includes daily foot inspections, wearing protective footwear, and prompt treatment of any foot lesion. While the medications above can relieve pain, they do not reverse nerve damage. **Combination therapy** may be

considered if monotherapy is insufficient, although trials (e.g. OPTION-DM) suggest rotating first-line agents may be as effective as combining them. Importantly, treatment must be individualized, balancing pain relief with side effect tolerability for each patient.[21,22]

Non-pharmacologic therapies: Several non-drug modalities can complement medical treatment of DN. **Exercise and physical therapy** may improve neuropathic symptoms and functional capacity. For patients with balance issues or foot deformities, physiotherapy and orthotic interventions help prevent falls and ulcers. **Transcutaneous electrical nerve stimulation (TENS)** and acupuncture have shown some benefit for neuropathic pain in small studies, though results vary.[23] **Neuromodulation techniques** are emerging for refractory pain: notably, **spinal cord stimulation (SCS)** has recently been approved by the FDA for painful diabetic neuropathy. High-frequency (10 kHz) SCS via an implanted device can substantially reduce neuropathic pain in patients not responding to conventional drugs. While SCS involves surgery and is costly, studies report significant pain relief in a majority of properly selected patients, without the systemic side effects of medications. As real-world experience grows, SCS may become a valuable option in severe PDN cases.[24]

Challenges in management

Despite the variety of therapies, **diabetic neuropathy remains challenging to manage**. One major challenge is the **lack of disease-modifying treatments** that can halt or reverse neuropathic progression. Current therapies mostly provide symptomatic relief; strict glucose control is the only intervention proven to affect neuropathy onset/progression, and it is preventive rather than restorative. Once nerve damage is established, we can often only alleviate symptoms and try to protect the feet from injury. The **incomplete efficacy** of available treatments is problematic – even the best first-line drugs achieve meaningful pain reduction in only about half of patients, and seldom eliminate pain entirely. Many patients have residual pain or develop intolerable side effects, requiring switches in therapy. Furthermore, certain medications (e.g. tricyclics or opioids) are limited by safety concerns in older patients or those with comorbidities.[25]

Another challenge is **timely diagnosis and intervention**. As mentioned, DN is frequently underdiagnosed – patients may not report mild symptoms, and busy clinicians might not screen rigorously for neuropathy. Consequently, some patients present with advanced insensate neuropathy only after they develop an ulcer or Charcot foot. Especially in resource-limited settings, there may be a "paucity of screening and diagnostic resources" and suboptimal diabetes care services, resulting in a high prevalence of undetected DPN and its complications in developing countries. Improving provider and patient awareness about neuropathy is an ongoing need. Routine annual foot exams and early referrals to specialists (e.g. podiatry, neurology) for neuropathy evaluation should be standard, but implementation is inconsistent globally.[26]

Global disparities in neuropathy management are notable. In high-income countries, patients often have access to the full range of medications and devices (like SCS), whereas in low- and middle-income countries, even basic pain medications or proper footwear may be lacking. The cost of newer drugs (such as duloxetine or pregabalin) can be prohibitive for uninsured patients. This leads to continued use of older, sometimes less effective treatments or even unchecked use of opioids or traditional remedies with their own risks. Harmonizing care standards and improving access to neuropathy treatments worldwide is a public health challenge.[27]

Additional challenges include managing the **diverse manifestations** of DN. For instance, autonomic neuropathy (e.g. cardiovascular autonomic neuropathy, CAN) can cause resting tachycardia, orthostatic hypotension, and exercise intolerance, which are difficult to treat and associated with increased mortality. Gastrointestinal neuropathy (gastroparesis) and genitourinary neuropathies (bladder dysfunction, erectile dysfunction) require specialized management beyond typical neuropathic pain medications. A comprehensive neuropathy management plan thus often involves multiple specialists and therapies, underscoring the need for a multidisciplinary approach. Psychological support is also important, as chronic neuropathic pain and disability can lead to depression and anxiety.[28]

Future directions

Looking ahead, research is actively exploring **new avenues to better prevent, detect, and treat** diabetic neuropathy:[29]

- **Disease-modifying therapies:** A top priority is developing treatments that target the root causes of nerve degeneration rather than just symptoms. Various approaches under investigation include **agents that reduce oxidative stress or inflammation** in nerves, **mitochondria-targeted antioxidants**, and **pathway inhibitors** (for PKC, AGE formation, etc.). While prior trials of aldose reductase inhibitors and nerve growth factor were disappointing, newer compounds and biologics are being tested in clinical trials. For example, research into **gene therapy and stem cell therapy** aims to promote nerve regeneration or protect neurons from hyperglycemic damage, though these are in early stages.[30]
- **Metabolic therapies:** As our understanding of diabetic neurodegeneration expands, there is interest in repurposing certain metabolic drugs for neuropathy. For instance, **GLP-1 receptor agonists** and **SGLT2 inhibitors**, beyond glucose-lowering, have shown potential neuroprotective effects in preclinical models (possibly through anti-

inflammatory and weight loss mechanisms). Similarly, **omega-3 fatty acids**, **vitamin D**, and other supplements are being studied for any neuropathy benefit. Large randomized trials are needed to confirm any disease-modifying impact.[31]

- **Early detection and biomarkers:** Future management of DN may be transformed by tools that catch neuropathy at a subclinical stage. **Corneal confocal microscopy** and **skin biopsies** for nerve fiber density are moving towards wider clinical adoption to identify small-fiber neuropathy early. Researchers are also investigating blood biomarkers (such as inflammatory cytokines, neuronal injury markers like NF-L) that could signal early nerve damage or track disease progression. If validated, such biomarkers could enable screening of diabetic patients for early neuropathy and monitoring response to therapies, analogous to how HbA1c tracks glycemic control.[32]
- **Advanced neuroimaging:** Imaging techniques like **MRI neurography (MRN)** are improving, allowing visualization of nerve trunks and even distal nerve degeneration. MRN and high-resolution ultrasound might help differentiate diabetic neuropathy from other neuropathies and assess nerve edema or compression sites, guiding more targeted interventions in the future.[33]
- **Emerging pain therapies:** On the symptomatic side, research continues into novel analgesics for neuropathic pain. **Sodium channel blockers** selective for nociceptive fibers (e.g. Nav1.7 blockers) are one promising class in development, aiming to provide pain relief without systemic side effects. Topical agents are also being refined – for example, new formulations of capsaicin or resiniferatoxin to achieve longer-lasting analgesia with a single application. Non-invasive brain and spinal stimulation techniques (transcranial magnetic stimulation, transcutaneous spinal stimulation) are being explored for neuropathic pain relief as well.[34]
- **Technology and remote care:** Diabetes technology may contribute to neuropathy care as well. Continuous glucose monitors and insulin pumps help maintain tighter glucose control, potentially reducing risk of neuropathy over time. Wearable sensors are being developed to detect early signs of foot ulcer formation (through temperature or pressure changes), which could be especially useful for neuropathic patients with loss of protective sensation. Telemedicine and mobile health apps might enable broader implementation of annual neuropathy screenings and patient education, especially in remote or underserved regions.[35]
- **Comprehensive care models:** Future management is likely to emphasize multidisciplinary clinics that address diabetes and its complications in an integrated fashion. For neuropathy, this means closer collaboration between endocrinologists, neurologists, podiatrists, pain specialists, and rehabilitation teams. Such models can ensure that patients receive holistic care – glycemic optimization, pain management, orthotic support, and self-care education – in a coordinated way. Health systems around the world are recognizing the need to invest in complication prevention programs, which include foot care services and patient education initiatives to reduce the burden of neuropathy-related amputations.[36]

In summary, diabetic neuropathy remains a **global challenge**, but advances on multiple fronts offer hope. Continued research into the complex mechanisms of DN will ideally yield targeted treatments to **prevent nerve damage or even promote nerve repair** – something currently elusive. Meanwhile, enhancing early detection and patient-centered care can significantly improve outcomes with existing tools. As the diabetes epidemic grows, addressing neuropathy through innovation and system-level strategies will be critical to reduce suffering and healthcare costs associated with this complication.

CONCLUSION

Diabetic neuropathy is a prevalent and debilitating complication of diabetes that affects millions of patients worldwide. It results from chronic hyperglycemia-induced nerve injury through metabolic and microvascular mechanisms, and it manifests most commonly as distal symmetric polyneuropathy causing pain and sensory loss in the extremities. DN carries a tremendous global health burden – it is a leading cause of foot ulcers and amputations, and it impairs quality of life through chronic pain and disability. Early recognition of neuropathy is essential: clinicians should regularly screen diabetic patients for neuropathic signs and symptoms, given that early intervention can prevent ulcers and mitigate pain.

Management of diabetic neuropathy requires a comprehensive approach. **Optimal glycemic control** remains the cornerstone for preventing neuropathy progression, along with control of coexisting risk factors. For neuropathic pain, several evidence-based medications (duloxetine, pregabalin, gabapentin, tricyclic antidepressants) are available and provide partial relief for many patients, though side effects and incomplete responses are common. Non-pharmacologic modalities and careful foot care are important supportive measures. **Challenges** persist in that no therapy can reverse established neuropathy, and a significant proportion of patients continue to suffer pain despite our best treatments. Moreover, gaps in care – especially in low-resource settings – lead to late diagnoses and high complication rates.

Encouragingly, ongoing **research and innovation** promise improvements in neuropathy care. Emerging diagnostic tools (such as corneal microscopy and novel biomarkers) may enable earlier and more precise detection of nerve damage. A pipeline of investigational treatments targeting the underlying pathogenic pathways

offers hope that future therapies could slow, halt, or even repair diabetic neuropathy, moving care beyond mere symptom management. Furthermore, new pain management strategies like spinal cord stimulation have expanded options for refractory cases. To fully realize these advances, increased awareness and education about DN are needed among both healthcare providers and patients. By integrating cutting-edge research findings with global public health efforts (for instance, improving access to neuropathy screening and standardizing treatment guidelines across regions), we can better address the burden of diabetic neuropathy. Ultimately, preventing and effectively treating DN will be integral to improving the lives of people with diabetes worldwide.

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