Medical News & Perspectives

# Diabetic Foot Infections and Amputations Are All Too Common—Here's What Could Move the Needle

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With a mobile app powered by artificial intelligence (AI), Caitlin Hicks, MD, MS, reviews selfies of patients' feet in real time to track their wounds as part of a clinical trial. The app saves time for Hicks, a vascular surgeon at Johns Hopkins Medicine, but also reduces clinic trips for her patients with diabetes in inner-city Baltimore, many of whom are elderly and less mobile or have other socioeconomic barriers to care. Hicks knows that for these patients, wound vigilance is the linchpin to preventing infection, hospitalization, or, worse, amputation or even death.

Medical News website

One-third of those hospitalized for a diabetic foot infection will require some form of amputation. And roughly half of people who have a lower-limb amputation will die within 5 years.

Despite their crushing toll, diabetic foot infections remain stubbornly hard to treat, but multidisciplinary care teams, new drugs and devices on the horizon, and practical solutions to socioeconomic factors could budge the needle.

"We need more attention paid to this problem, and we need more innovation at the same time, and both can be done even as we're being really good stewards with antimicrobials," David Armstrong, DPM, MD, PhD, a podiatric surgeon at Keck Medicine at the University of Southern California, said in an interview with *JAMA*.

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## New FDA Guidelines

Upcoming guidelines from the US Food and Drug Administration (FDA) focus on developing drugs to treat diabetic foot infections without concomitant bone and joint involvement, in the context of increasing antimicrobial resistance. The guidelines were published in draft form in October ahead of a 3-month comment period.

They will be the first of their kind to focus on diabetic foot infections, an FDA spokesperson told *JAMA* in an email. These infections are often excluded from clinical trials because they are polymicrobial and may require treatment with concurrent antibiotics, confounding safety and efficacy assessments of the study drug.

"We do not have a lot of options for our patients," said Armstrong, who last year coauthored a review on diabetic foot ulcers in *JAMA*. "Sometimes we're treating people with drugs that are 50 or 60 years old and are grossly ineffective, and even harmful."

"We are using antibiotics that should be sitting at home collecting Medicare and Social Security instead of being used in patients," Warren S. Joseph, DPM, an adjunct clinical professor at the Arizona College of Podiatric Medicine at Midwestern University, said in an email. Only 3 antibiotic regimens—ertapenem, piperacillin and tazobactam, and linezolid—are FDA-approved for treating diabetic foot infections, although newer drugs that are safer and more effective are also used off-label, Joseph noted. "Hopefully, that will change as companies recognize the scope of this problem and the need for clinical trials directly involving these complicated patients," he added.

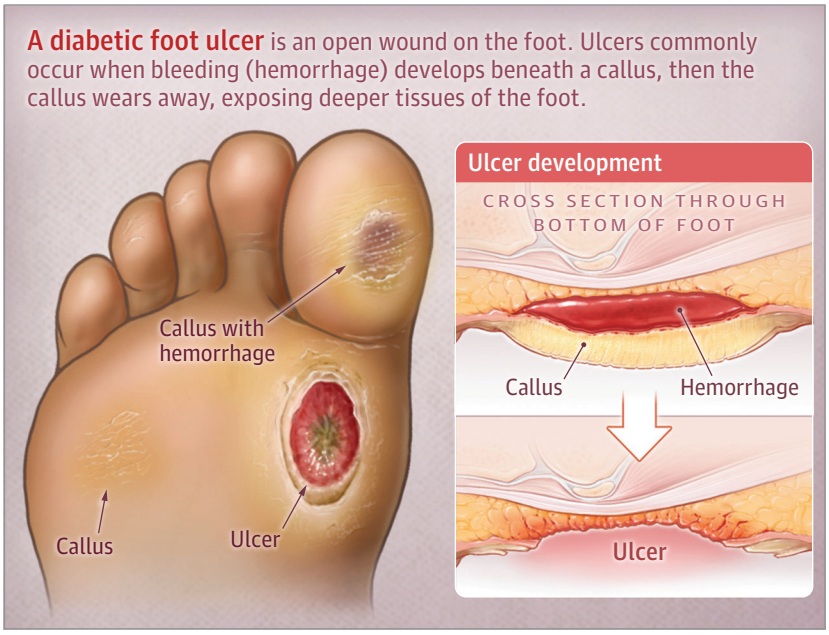
Nicolas Cortes-Penfield, MD, an infectious disease specialist at the University of Nebraska Medical Center, said he hopes the FDA guidelines improve the quality and volume of research on antibiotics for diabetes-related foot infections.

The FDA spokesperson said the agency anticipates that most drug development will focus on systemic antibiotics. The drugs traditionally have been administered intravenously, but recent studies suggest that antibiotics can be efficacious in pill form, even when given for shorter durations, according to guidelines issued in October by the International Working Group on the Diabetic Foot (IWGDF) and the Infectious Diseases Society of America.

## Multidisciplinary Teams

Upstream drivers of diabetic foot infections—vascular disease, nerve damage, uncontrolled blood glucose—make them vexing to treat. And treatment requires a multidisciplinary approach from podiatrists, infectious disease specialists, vascular surgeons, primary care clinicians or endocrinologists, and those who specialize in wound care.

A quality interdisciplinary team is more important than any single drug in treating infection, Armstrong said. A 2021 analysis found that multidisciplinary teams reduced




the risk of major—or above the ankle—amputation by an average of 2.5-fold compared with usual care.

At the decade-old Johns Hopkins Diabetic Foot and Wound Clinic, patients meet with 4 specialists at the same time: a podiatrist, a vascular surgeon, an endocrinologist, and a wound care nurse. This upfront investment in care helps patients present with smaller, less severe wounds and reduces the risk of amputation, Hicks said.

She admits it's "a heavy lift for health systems" in terms of coordination and billing but says that improved patient outcomes could reduce long-term spending. A major amputation costs roughly $115 000 in the US, and the national inpatient and emergency department costs of diabetic foot ulcers were $8.78 billion annually, according to an analysis of 2006-2010 data.

"Having a longitudinal relationship and multidisciplinary team who regularly work together to take care of these really complex patients is the optimal model," Cortes-Penfield said in an interview.

Cortes-Penfield is conducting what he thinks is the first US survey of diabetic foot infection care teams. Although these teams are increasing, they're not as prevalent as they should be, he said. He estimates there are fewer than 20 nationwide and, in most cases, no more than 1 per state.

A larger effort to build multidisciplinary teams is the mission of the American Limb Preservation Society, which Armstrong founded in 2020 and calls "a dating app and a marriage counselor" for its 1000 members to find other clinicians working in their region or collaborate on research.

## New Tech to Treat Wounds

Beyond better care teams, clinical trials are testing new topical treatments for diabetic foot ulcers. Phase 3 trials, for example, have demonstrated significantly better wound closure in patients who received an esmolol hydrochloride gel or a macrophage cream compared with standard of care alone. Researchers told *JAMA* that the macrophage cream has been approved for use in China, Malaysia, Singapore, and Taiwan and that the esmolol hydrochloride gel is expected to enter the market in India later this year.

There's also a plethora of new technology in clinical trials to monitor diabetic wounds, relieve pressure on feet, clean wounds more efficiently, and improve dressings.

"Digital monitoring is a very hot thing right now," said Hicks, who is testing the foot selfie app in a National Institutes of Health–funded randomized clinical trial involving 120 patients. The trial follows a feasibility study of the app that showed efficacy and high satisfaction among 25 patients. After a patient uploads an image, AI delivers analytics to Hicks and her team about the wound size and tissue composition, allowing them to tailor treatment remotely while reducing clinic visits to an as-needed basis rather than every 1 to 2 weeks.

Affordability of new technology is critical, Hicks said. For example, effective remote monitoring technology, particularly for use in rural areas that don't have wound care centers, would be a huge benefit for patients and incentive for payers, she said. People in rural areas have higher rates of amputation from diabetic foot infections than those in urban areas, and less access to specialists.

Remote monitoring is also being used in the design of a "SmartBoot" that relieves pressure from wounds and provides adherence and activity data via embedded sensors and smartwatches. So far, the boot has been tested in a small study of 14 people and is now being investigated in a larger clinical trial, according to Armstrong, the trial's principal investigator.

Armstrong and his colleagues are also developing a device that could better clean wounds with micro water jets, while other researchers are pursuing a technology using specialized polymers applied like adhesive tape that mechanically shrinks wounds.

Today, standard wound care includes basic wound dressings to absorb secretions and maintain a moist environment, according to the IWGDF. In guidelines updated in 2023 that included an analysis of 400 studies, the group conditionally recommended the use of newer technology for hard-to-heal wounds, such as placental-derived products, sucrose-octasulfate dressings, a patch made from a patient's own blood, negative pressure wound therapy, and topical oxygen.

The group noted that cost and cost-effectiveness received little attention in many studies. "We encourage not more, but better quality trials including those with a health economic analysis, into this area," the authors wrote.

## Addressing Social Barriers

Armstrong, Cortes-Penfield, and Hicks all said that new developments to treat diabetic foot infections must address socioeconomic disparities. People from racial or ethnic minority groups, for example, are more likely to experience diabetic foot ulcers and to undergo subsequent amputations.

Diabetes and its complications disproportionately affect those who have fewer resources, belong to marginalized social groups, or live in rural areas with limited access to care or in states that have turned down access to federal funding like Medicaid, Cortes-Penfield said.

States like Massachusetts and New York that were early to expand Medicaid under the Affordable Care Act saw a relative improvement in major amputation rates among African American, Hispanic, and other racial and ethnic minority adults compared with states that did not expand Medicaid, according to a 2022 study.

"These folks often have some kind of social barriers to care," Cortes-Penfield said. He urges clinicians to build a rapport with patients to address these hurdles together. For clinicians, this could include asking patients if they need financial and housing support, vouchers for transportation to appointments, or translation services for those who don't speak English.

"Access to advanced care—which means multidisciplinary care—digital monitoring technologies, and cost-effective ways that patients can access care, without having to pay out of pocket, is critical to reducing the disparities in amputation rates that we see in the US," Hicks said. ■

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**Note:** Source references are available through embedded hyperlinks in the article text online.