Preventing Foot Ulcers in Patients With Diabetes

Nalini Singh, MD
David G. Armstrong, DPM, MSc, PhD
Benjamin A. Lipsky, MD

Among persons diagnosed as having diabetes mellitus, the lifetime risk of developing a foot ulcer is estimated to be 15%.1 Based on recent studies, the annual population-based incidence ranges from 1.0% to 4.1%2 and the prevalence ranges from 4% to 10%, which suggests that the lifetime incidence may be as high as 25%.3,4 Lower extremity disease, including peripheral arterial disease, peripheral neuropathy, foot ulceration, or lower extremity amputation, is twice as common in diabetic persons compared with nondiabetic persons and it affects 30% of diabetic persons who are older than 40 years.5 Foot ulcers cause substantial emotional, physical, productivity, and financial losses.6-9 The estimated costs of treating a diabetic foot ulcer were $28,000 in a 1999 US study,10 and $18,000 (with no amputation) and $34,000 (with amputation) in a 2000 Swedish study.11

The most costly and feared consequence of a foot ulcer is limb amputation, which occurs 10 to 30 times more often in diabetic persons than in the general population.12,13 Diabetes underlies up to 8 of 10 nontraumatic amputations, of which 85% follow a foot ulcer.1,3,14 The age-adjusted annual incidence for nontraumatic lower limb amputations in diabetic persons ranges from 2.1 to 13.7 per 1000 persons.2 Mortality following amputation ranges from 13% to 40% at 1 year, 35% to 65% at 3 years, and 39% to 80% at 5 years—worse than for most malignancies.2

Context Among persons diagnosed as having diabetes mellitus, the prevalence of foot ulcers is 4% to 10%, the annual population-based incidence is 1.0% to 4.1%, and the lifetime incidence may be as high as 25%. These ulcers frequently become infected, cause great morbidity, engender considerable financial costs, and are the usual first step to lower extremity amputation.

Objective To systematically review the evidence on the efficacy of methods advocated for preventing diabetic foot ulcers in the primary care setting.

Data Sources, Study Selection, and Data Extraction The EBSCO, MEDLINE, and the National Guideline Clearinghouse databases were searched for articles published between January 1980 and April 2004 using database-specific keywords. Bibliographies of retrieved articles were also searched, along with the Cochrane Library and relevant Web sites. We reviewed the retrieved literature for pertinent information, paying particular attention to prospective cohort studies and randomized clinical trials.

Data Synthesis Prevention of diabetic foot ulcers begins with screening for loss of protective sensation, which is best accomplished in the primary care setting with a brief history and the Semmes-Weinstein monofilament. Specialist clinics may quantify neuropathy with biothesiometry, measure plantar foot pressure, and assess lower extremity vascular status with Doppler ultrasound and ankle-brachial blood pressure indices. These measurements, in conjunction with other findings from the history and physical examination, enable clinicians to stratify patients based on risk and to determine the type of intervention. Educating patients about proper foot care and periodic foot examinations are effective interventions to prevent ulceration. Other possibly effective clinical interventions include optimizing glycemic control, smoking cessation, intensive podiatric care, debridement of calluses, and certain types of prophylactic foot surgery. The value of various types of prescription footwear for ulcer prevention is not clear.

Conclusions Substantial evidence supports screening all patients with diabetes to identify those at risk for foot ulceration. These patients might benefit from certain prophylactic interventions, including patient education, prescription footwear, intensive podiatric care, and evaluation for surgical interventions.

JAMA. 2005;293:217-228 www.jama.com

See also Patient Page.
CME available online at www.jama.com

Author Affiliations: Department of Medicine, Division of Endocrinology and Metabolism (Dr Singh) and General Internal Medicine and Infectious Diseases (Dr Lipsky), Veterans Affairs Puget Sound Healthcare System, and University of Washington School of Medicine, Seattle (Drs Singh and Lipsky); and Center for Lower Extremity Ambulatory Research, Dr William M. Scholl College of Podiatric Medicine, Rosalind Franklin University of Medicine and Science, Chicago, Ill (Dr Armstrong).

Financial Disclosure: Dr Armstrong has participated in research funded by the National Institutes of Health using devices manufactured by Xilas Medical Inc (makers of the biothesiometer).

Corresponding Author: Nalini Singh, MD, VA Puget Sound Healthcare System, Mailcode: S-111-ENDO, 1660 S Columbian Way, Seattle, WA 98108 (Nalini .Singh2@med.va.gov).

Clinical Review Section Editor: Michael S. Lauer, MD. We encourage authors to submit papers for consideration as a “Clinical Review.” Please contact Michael S. Lauer, MD, at lauerm@ccf.org.

©2005 American Medical Association. All rights reserved.
to know if they are preventable. This review summarizes and critically evaluates evidence on the efficacy of identifying diabetic persons at high risk for foot ulcers and of interventions designed to prevent them.

**METHODS**

Assisted by a medical librarian, we conducted a systematic literature search using the EBSCO (EBSCO Information Services, Birmingham, Ala), MEDLINE, and the National Guideline Clearinghouse databases for articles published between January 1980 and April 2004 and used the following phrases: *diabetes or diabetic, foot ulcer or infection, and prevention or preventing*. The EBSCO database includes the American Medical Association Collection, Comprehensive Biomedical Reference Collection, Cumulative Index to Nursing and Allied Health Literature, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, Database of Abstracts of Reviews of Effectiveness, Health Business Fulltext Elite, International Pharmaceutical Abstracts, Comprehensive Nursing and Allied Health Collection, and the American Medical Association's Archive. We also searched (1) the bibliography of each identified article; (2) the National Guideline Clearinghouse Web site (http://www.guidelines.gov); (3) an extensive printed diabetic foot reference collection; and (4) several Web sites specializing in issues related to the diabetic foot.

This search identified 165 articles that addressed preventing diabetic foot ulcers, including 22 randomized controlled studies, most of which measured changes in the rates of foot ulceration and amputations related to various interventions. For topics on which there were only a few randomized controlled studies, we focused on selected case-control and cohort studies.

**Pathophysiology of Diabetic Foot Ulcers**

**Causative Factors.** The causal pathways leading to foot ulceration include several component causes, the most important of which is peripheral neuropathy. This is present to some degree in more than 50% of diabetic persons older than 60 years. Peripheral neuropathy must usually be profound before leading to loss of protective sensation; the consequent vulnerability to physical and thermal trauma increases the risk of foot ulceration 7-fold. A second causative factor in foot ulceration is excessive plantar pressure. This is related to both limited joint mobility (at the ankle, subtalar, and first metatarsophalangeal joints) and to foot deformities. In one study of patients with peripheral neuropathy, 28% with high plantar pressure developed a foot ulcer during a 2.5-year follow-up compared with none with normal pressure. A third component cause is trauma, especially when repetitive. Among 669 persons with a foot ulcer, 21% were attributed to rubbing from footwear, 11% were linked to injuries (mostly falls), 4% to cellulitis complicating tinea pedis, and 4% to self-inflicted trauma (eg, cutting toenails). Persons who had a previous foot ulceration could withstand fewer cycles of stress to their feet before an ulcer recurred.

**Contributeory Factors.** Once a foot ulcer develops, several factors may contribute to adverse outcomes. The most important is atherosclerotic peripheral vascular disease, which is twice as common in persons with diabetes as in persons without diabetes and particularly affects the femoropopliteal and smaller vessels below the knee, while frequently sparing the pedal vessels. Diabetes is also associated with several intrinsic wound-healing disturbances, including impaired collagen cross-linking and matrix metalloproteinase function, and immunologic perturbations, especially in polymorphonuclear leukocyte function. Furthermore, persons with diabetes have a higher rate of onychomycosis and toe-web tinea infections that can lead to skin disruption.

Having a foot ulcer dramatically worsens physical, psychological, and social quality of life. The obesity and poor vision that are associated with diabetes may also impair self-care. Optimal prevention (and treatment) outcomes require both a motivated patient and an effective medical care system.

**Screening to Identify Patients at Risk for Diabetic Foot Ulcers**

Preventing foot complications begins with identifying those at risk. Primary care clinicians should inquire about factors known to be associated with foot ulcers, namely, previous foot ulceration (relative risk [RR], 1.6; 95% confidence interval [CI], 1.2-2.3; *P*=.004), prior lower extremity amputation (RR, 2.8; 95% CI, 1.8-4.3; *P*<.001), long duration (>10 years) of having diabetes (odds ratio [OR], 3.0; *P*<.04), poor glycemic control (glycosylated hemoglobin >9%; OR, 3.2; 95% CI, 1.4-6.2; *P*<.001). Clinicians should also examine the feet for structural abnormalities (eg, calluses, hammer or claw toes, flat feet, bunions), reduced joint mobility, dry or fissured skin, tinea, or onychomycosis, and also inspect footwear to ensure proper fit.

**Screening for Loss of Protective Sensation.** Nerve conduction studies are generally considered the criterion standard for diagnosing peripheral neuropathy. They are less useful in screening for loss of protective sensation (ie, degree of neuropathy beyond which the patient has a measurably increased risk for diabetic foot ulceration), and are not widely available.

**Monofilament.** The most frequently used instrument for detecting neuropathy is the nylon Semmes-Weinstein monofilament. Inability to perceive the 10g of force a 5.07 monofilament applies is associated with clinically significant large-fiber neuropathy (Figure). In 3 prospective studies, the Semmes-Weinstein monofilament identified persons at increased risk of foot ulceration with a sensitivity of 66% to 91%, a specificity of 34% to 86%, a positive predictive value of 18% to 39%, and a negative predictive value of 94% to 95%. Certain brands of monofilaments are more accurate than others and should not be used on more than 10 patients without a recovery period of 24 hours.

**Figure**

**Comparison of monofilament test results**

<table>
<thead>
<tr>
<th>Monofilament Strength</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.4-2.6</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>2.0-2.6</td>
<td>.81-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>2.6-3.6</td>
<td>.71-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>3.6-4.6</td>
<td>.61-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>4.6-5.0</td>
<td>.51-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
</tbody>
</table>

**Note:** These values are approximate.

**Screening to Identify Patients at Risk for Diabetic Foot Ulcers**

Preventing foot complications begins with identifying those at risk. Primary care clinicians should inquire about factors known to be associated with foot ulcers, namely, previous foot ulceration (relative risk [RR], 1.6; 95% confidence interval [CI], 1.2-2.3; *P*=.004), prior lower extremity amputation (RR, 2.8; 95% CI, 1.8-4.3; *P*<.001), long duration (>10 years) of having diabetes (odds ratio [OR], 3.0; *P*<.04), poor glycemic control (glycosylated hemoglobin >9%; OR, 3.2; 95% CI, 1.4-6.2; *P*<.001). Clinicians should also examine the feet for structural abnormalities (eg, calluses, hammer or claw toes, flat feet, bunions), reduced joint mobility, dry or fissured skin, tinea, or onychomycosis, and also inspect footwear to ensure proper fit.

**Screening for Loss of Protective Sensation.** Nerve conduction studies are generally considered the criterion standard for diagnosing peripheral neuropathy. They are less useful in screening for loss of protective sensation (ie, degree of neuropathy beyond which the patient has a measurably increased risk for diabetic foot ulceration), and are not widely available.

**Monofilament.** The most frequently used instrument for detecting neuropathy is the nylon Semmes-Weinstein monofilament. Inability to perceive the 10g of force a 5.07 monofilament applies is associated with clinically significant large-fiber neuropathy (Figure). In 3 prospective studies, the Semmes-Weinstein monofilament identified persons at increased risk of foot ulceration with a sensitivity of 66% to 91%, a specificity of 34% to 86%, a positive predictive value of 18% to 39%, and a negative predictive value of 94% to 95%. Certain brands of monofilaments are more accurate than others and should not be used on more than 10 patients without a recovery period of 24 hours.

**Figure**

**Comparison of monofilament test results**

<table>
<thead>
<tr>
<th>Monofilament Strength</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.4-2.6</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>2.0-2.6</td>
<td>.81-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>2.6-3.6</td>
<td>.71-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>3.6-4.6</td>
<td>.61-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
<tr>
<td>4.6-5.0</td>
<td>.51-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
<td>.91-1.00</td>
</tr>
</tbody>
</table>

**Note:** These values are approximate.
While authorities recommend testing 8 to 10 anatomic sites, testing just 4 plantar sites on the forefoot (great toe and base of first, third, and fifth metatarsals) identifies 90% of patients with an insensate site. Most consider a lack of perception at any site(s) to be abnormal, but as the threshold for an abnormal test is raised from 1 to 4 insensate sites, the sensitivity remains higher than 90% while the specificity improves from 60% to 80%. Asking the patient to say “yes” or “no” when asked if he/she believes the Semmes-Weinstein monofilament is being applied is equally accurate and quicker than the “forced-choice” method (asking the patient to correctly identify whether it was at time “A” or “B” that the monofilament was applied).

Biothesiometer. A biothesiometer (Xilas Medical, San Antonio, Tex) is a handheld device that assesses vibration-perception threshold. A rubber tacttor is applied to the distal aspect of the toe and the amplitude is increased to a maximum of 100 V (converted from microns). In one study, a vibration-perception threshold of more than 25 V had a sensitivity of 83%, a specificity of 63%, a positive likelihood ratio of 2.2 (95% CI, 1.8-2.5), and a negative likelihood ratio of 0.27 (95% CI, 0.14-0.48) for predicting a foot ulceration over 4 years. A case-control study with 255 diabetic persons found that having either abnormal Semmes-Weinstein monofilament perception or a vibration-perception threshold of more than 25 V predicted foot ulceration with a sensitivity of 100% and a specificity of 77%.

Tuning Fork. The tuning fork provides an easy and inexpensive test of vibratory sensation. With a conventional fork, an abnormal response occurs when the patient loses vibratory sensation while the examiner still perceives it. With a graduated (Rydel-Seiffer) fork (Gebrueder Martin, Tuttingen, Germany), persons indicate first loss of vibration at the plantar halluc as the intersection of 2 virtual triangles moves on a scale exponentially from 0 to 8 in a mean (SD) of 39.8 (1) seconds. This test correlates more strongly with biothesiometer results ($r$, –0.90; $P<.001$) than the conventional tuning fork, but the latter predicted foot ulceration in 2 studies. Tuning fork results are less predictive of ulceration than results from using the monofilament.

Screening for Patients With Elevated Plantar Pressure. Devices identifying high plantar pressure include mats to measure barefoot plantar load distribution and transducers distributed in a removable shoe insole to measure pressure inside footwear. The numerical values generated are often device-specific and cannot easily be compared. There is no generally accepted plantar pressure level associated with an increased risk of diabetic foot ulceration. In case-control studies using the EMED pressure platform system (Novell, Minneapolis, Minn), a peak barefoot dynamic pressure of 70 N/cm² had a sensitivity of 70.0% and a specificity of 65.1%, while a cutoff of 87.5 N/cm² had a sensitivity of 64%, a specificity of 46%, a positive predictive value of 17%, and a negative predictive value of 90% (Table 1).

Figure. Monofilament Test for Light Touch Sensation

<table>
<thead>
<tr>
<th>Place Monofilament Perpendicular to Skin</th>
<th>Apply Pressure Until Monofilament Buckles</th>
<th>Release</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Semmes-Weinstein Monofilament Test</td>
<td><strong>B</strong> Testing Sites</td>
<td><strong>Sites Shown to Identify 90% of Patients With Abnormal Monofilament Test</strong></td>
</tr>
<tr>
<td>First Metatarsal</td>
<td>Third Metatarsal</td>
<td>Fifth Metatarsal</td>
</tr>
</tbody>
</table>

The 5.07 Semmes-Weinstein monofilament consists of a plastic handle supporting a nylon filament. The filament is placed perpendicular to the skin, and pressure is applied until the filament buckles. The filament is held in place for approximately 1 second, then released. Inability to perceive the 10g of force it applies is associated with clinically significant large-fiber neuropathy. Testing 10 sites (as shown) evaluates all dermatomes of the foot and may improve the sensitivity and specificity compared with testing a single site.
Screening for Peripheral Vascular Disease. Peripheral vascular disease is most easily detected by the ankle-brachial index (ABI), which is the ratio of systolic blood pressure in the ankle to that in the brachial artery. An ABI of 0.90 or less suggests peripheral vascular disease, while higher than 1.1 may represent a falsely elevated pressure caused by medial arterial calcinosis.59 This test is easily performed, objective, and reproducible.59 One large study found that the ABI was strongly related to the risk of foot ulceration (0.3 lower ABI is associated with an RR of 0.80; 95% CI, 0.69-0.93; P = .01).37

Arterial oxygen supply can also be measured by transcutaneous oximetry.59 A transcutaneous oxygen tension higher than 30 mm Hg correlates with a high likelihood of wound healing.59 Transcutaneous oxygen tension is also inversely associated with the risk of foot ulceration (15 mm Hg higher dorsal foot ulceration (15 mm Hg higher dorsal foot pressure is associated with an RR of 0.80; 95% CI, 0.69-0.93; P = .004).37 Because accurately measuring transcutaneous oxygen tension requires expensive equipment and a trained technician, it is not routinely used.

Educational Interventions to Prevent Foot Ulceration

Patient Education. Most patient education studies emphasize foot care, but have been short-term and have measured changes in behavior and cognition rather than the incidence of relevant clinical outcomes such as ulceration. Patient education formats have included lectures, hands-on workshops, skills exercises, behavioral modification programs, and telephone reminders (Table 2).

Two recent reviews concluded that patient education improves short-term knowledge and may modestly reduce risk of foot ulcerations and amputations.31,67 Larger randomized clinical trials are needed to assess which patient education formats are the most effective, how often periodic reinforcement is required, and the long-term effectiveness of various programs.

Physician Education. Health care organizations have used various strategies to improve clinicians’ performance with patient education.68,69 In one strategy, a computerized registry reminded physicians to enter the patient's risk status for lower extremity amputation. After 28 months, the percentage of patients who had received foot screening and risk assessment increased from 15% to 76%.68 Project LEAP (Lower-Extremity Amputation Prevention), developed by the US Department of Health and Human Services, is a 1-day workshop on diabetes foot care. When given to 560 clinicians from 85 organizations, it improved the rate of documenting foot care education from a baseline of 38% to 62% after 9 months.70 More importantly, appropriate foot care self-management increased from 32% to 48%, and there was a trend toward reduced lower extremity amputations.70

Another approach is implementing foot care clinical practice guidelines. An Indian Health Service diabetes program observed 669 patients during a standard care period (1986-1989) with routine foot screening; a public health period (1990-1993) with an annual foot examination and initial risk stratification to give those at high-risk special interventions; and a staged diabetes management period (1994-1996) during which clinicians used clinical practice guidelines.71 The average lower-extremity amputation incidence per 1000 diabetic person-years was 29 during the standard care period, 21 during public health, and 15 during staged management. The overall reduction in lower extremity amputation was 48% (P = .02), and the incidence of first amputation decreased from 21 per 1000 to 6 per 1000 from the first to the third period (P < .001).71

Clinical Practice Guidelines on the Diabetic Foot. Published guidelines72-77 (Table 3) uniformly recommend that all diabetic persons have an

**Table 1. Screening Methods to Identify Persons With Diabetes at Increased Risk for Foot Ulceration**

<table>
<thead>
<tr>
<th>Method</th>
<th>Monofilament (Light Touch Sensation)</th>
<th>Pressure Mat or Platform (Plantar Pressure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. and type of studies</td>
<td>3 Prospective cohort studies</td>
<td>1 Case-control study66; 2 prospective cohort studies87,96</td>
</tr>
<tr>
<td>Criteria for positive screening test</td>
<td>&gt;=1 Insensate site</td>
<td>Cutoffs: &gt;= 59 N/cm²; &gt;= 70 N/cm²; &gt;= 87.5 N/cm²</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>66-91</td>
<td>57-70; 64</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>34-86</td>
<td>70; 65; 46</td>
</tr>
<tr>
<td>Predictive value, %</td>
<td>Positive: 18-39; Negative: 94-95</td>
<td>16*; 31; 49; 17</td>
</tr>
<tr>
<td>Likelihood ratio</td>
<td>Positive: 1.4-4.7; Negative: 0.3-0.5</td>
<td>1.9; 2.0; 1.2</td>
</tr>
<tr>
<td>Comment</td>
<td>Inexpensive, quick, widely available, validated; number of test sites needed unclear</td>
<td>Numerical value of plantar pressure is device-specific; optimal cutoff unknown</td>
</tr>
</tbody>
</table>

*Data not available in case-control study to calculate a positive and a negative predictive value.
annual foot examination that includes assessing for anatomic deformities, skin breaks, nail disorders, loss of protective sensation, diminished arterial supply, and improper footwear. The clinician should then assign the patient to a risk category by using any of several systems. The recommended interventions for various risk groups differ slightly among the guidelines, but persons at higher risk for foot ulceration should have more frequent foot examinations.73-77

Clinical Interventions to Prevent Foot Ulceration

Optimizing Glycemic Control. The Diabetes Complications and Control Trial reported a 57% reduction in the incidence of clinical neuropathy in patients managed with intensive compared with conventional glycemic treatment.78 In the United Kingdom Prospective Diabetes Study, a 1% mean reduction in hemoglobin A1c was associated with a 25% reduction in microvascular complications, including neuropathy. There was also a nonsignificant reduction in amputations (by 36%) in the intensive compared with the conventional treatment group.79

Smoking Cessation. Some but not all studies have found a direct causal association between tobacco use and foot ulceration or amputation.37 A case-control study of diabetic persons in the United Kingdom found the lower risk of leg amputation in those of South Asian compared with European ancestry (OR, 0.26; 95% CI, 0.11-0.65; Table 2.

Table 2. Studies of Patient Education Programs Directed at Improving Foot Care in Persons With Diabetes

<table>
<thead>
<tr>
<th>Effect Measured</th>
<th>No. of Patients, Intervention/ Control</th>
<th>Intervention</th>
<th>Duration of Intervention</th>
<th>Duration of Follow-up</th>
<th>Main Outcome for Intervention Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge of foot care</td>
<td>Kruger and Guthrie,60 1992</td>
<td>Hands-on session plus lecture vs lecture alone</td>
<td>1 wk</td>
<td>6 mo</td>
<td>No significant difference</td>
</tr>
<tr>
<td></td>
<td>Mazzuca et al,61 1986</td>
<td>Didactic instruction, skills exercises, behavioral modification, telephone follow-up vs usual care</td>
<td>Not stated</td>
<td>11.8-14.3 mo</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Knowledge and incidence of foot lesions</td>
<td>Barth et al,62 1991</td>
<td>4 Weekly =2-hour foot care sessions vs general diabetes mellitus education with 1 hour on foot care</td>
<td>4 wk (total of 9 h)</td>
<td>6 mo</td>
<td>Reduction in foot problems at 1 mo (P&lt;.006)</td>
</tr>
<tr>
<td></td>
<td>Bloomgarden et al,63 1987</td>
<td>9 Educational sessions about diabetes mellitus and foot care vs usual care only</td>
<td>Mean (SD), 1.6 (0.3) y</td>
<td>18 mo</td>
<td>Modestly increased knowledge for intervention group (P = .007)</td>
</tr>
<tr>
<td></td>
<td>Litzelman et al,64 1993</td>
<td>191/205 Sessions on foot care, telephone reminders, postcard reminders vs usual care</td>
<td>12 mo</td>
<td>12 mo</td>
<td>Fewer serious foot lesions (OR, 0.41 [95% CI, 0.16 to 1.00]; P = .05)</td>
</tr>
<tr>
<td></td>
<td>Pieber et al,65 1995</td>
<td>53/55 4 Weekly sessions on diabetes mellitus education and foot care vs usual care</td>
<td>4 wk</td>
<td>6 mo</td>
<td>Significantly reduced callus formation and “poor nail care” compared with baseline</td>
</tr>
</tbody>
</table>

Abbreviations: ARR, absolute risk reduction; CI, confidence interval; OR, odds ratio; RR, relative risk.
*Calculated measures of effect using STATA statistical software (version 8, STATA Corp, College Station, Tex).
†Measure of effect calculated by authors of original study.
FOOT ULCERS IN DIABETIC PATIENTS

7.1% (P = .004) partly attributable to their lower rates of smoking (31% vs 57%; P = .03). Similarly, a cross-sectional study of 1142 patients with type 2 diabetes in Jordan found smoking to be a strong predictor of amputation.81

Foot Examination by a Clinician. Foot examinations did not significantly reduce amputations among 244 diabetic patients in 1 case-control study (OR, 0.55; 95% CI, 0.2-1.7; P = .31).82 These results may reflect the study’s limited sample size, high rates of foot examination in both case and control patients, different degree of risk between the groups, as well as the unusually high rates of diabetes and amputations among the Pima Indian population studied.83 Another randomized study of diabetic persons (N=91) with a previous foot ulceration found a significantly reduced risk for ulceration recurrence (RR, 0.52; 95% CI, 0.29-0.93; P = .03) at 1 year for those who received routine podiatric care.84 Thus, screening foot examinations are unlikely to reduce the incidence of foot complications unless they eventuate in appropriate specialist referrals (eg, for intensive podiatric care and customized footwear; TABLE 4).

Custom Footwear and Orthotics. Prescription shoes for high-risk patients should reduce areas of high plantar pressure and friction and accommodate foot deformities (eg, with a deep, wide toe box and ample padding).85 Similarly, shoe inserts should cushion the plantar surface and redistribute pressure over a greater surface area.86 Clinical data supporting the benefits of prescription footwear are surprisingly

---

**Table 3. Summary of Available Recommendations From Professional Organizations on Screening to Prevent Diabetic Foot Ulcers in Persons With Diabetes**

<table>
<thead>
<tr>
<th>Organization</th>
<th>Risk Stratification Category</th>
<th>Description of Risk Category</th>
<th>Recommended Interventions for Various Risk Strata</th>
<th>Recommended Footwear</th>
</tr>
</thead>
<tbody>
<tr>
<td>International Working Group on the Diabetic Foot†</td>
<td>0</td>
<td>No sensory neuropathy</td>
<td>Annual foot examination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Sensory neuropathy only</td>
<td>Foot examination every 6 mo</td>
<td>Special footwear (including insoles and orthoses)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Sensory neuropathy plus peripheral vascular disease and/or foot deformities</td>
<td>Foot examination every 3 mo</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Previous foot ulcer</td>
<td>Foot examination every 1-3 mo</td>
<td>Special footwear (including insoles and orthoses)</td>
</tr>
<tr>
<td>American Diabetes Association†</td>
<td>Low risk</td>
<td>No risk factors for foot ulcer</td>
<td>More frequent evaluation, patient and family education</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Peripheral neuropathy, altered biomechanics, increased pressure, bony deformity, peripheral vascular disease, history of foot ulcer or amputation, or severe nail pathology</td>
<td>Neuropathy or increased plantar pressure; well-fitted walking shoes or athletic shoes</td>
<td></td>
</tr>
<tr>
<td>US Veterans Health Agency and Department of Defense†</td>
<td>High risk</td>
<td>Lack of protective sensation, peripheral vascular disease, foot deformities, history of foot ulcer or nontraumatic amputation</td>
<td>Refer to foot care specialist</td>
<td>Foot deformities and neuropathy; extradepth shoes and/or pressure-reducing insoles Foot deformities not accommodated by deep shoes; custom-molded shoes</td>
</tr>
<tr>
<td>American College of Foot and Ankle Surgeons†</td>
<td>Low risk</td>
<td>No universally accepted system, but includes International Working Group’s categorization</td>
<td>General recommendations about preventative podiatric care, protective shoes, reducing high pressure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>At risk</td>
<td>Normal sensation, palpable pulses</td>
<td>Elective prophylactic surgery to correct selected deformities</td>
<td>High risk; therapeutic shoes with insoles and high toe box Severe foot deformities; custom-molded shoes</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Neuropathy, absent pedal pulses, or other risk factor</td>
<td>Foot examination every 3 to 6 mo and enhanced education</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk factor plus foot deformity, skin changes, or previous ulcer</td>
<td>Specialist foot examination every 1-3 mo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Special footwear and insoles</td>
<td>Frequent skin and nail care</td>
<td></td>
</tr>
</tbody>
</table>

---

*All organizations recommend at least an annual foot screening for all persons with diabetes.
†Consists of the Royal College of General Practitioners, the British Diabetic Association, the Royal College of Physicians, and the Royal College of Nursing.

©2005 American Medical Association. All rights reserved.
meager. In the largest of several studies, 400 persons with a history of a foot ulcer (but without a severe deformity) were randomized to receive extradeep, extrawide therapeutic shoes with customized neoprene-covered cork insoles; therapeutic shoes with nylon-covered polyurethane inserts; or instructed to wear usual footwear.86 Persons assigned to therapeutic shoes had a similar incidence of foot ulcer recurrence as controls.86 These surprising findings may have resulted from excluding patients with severe foot deformities, a person’s low baseline prevalence of “foot insensitivity,”87 and defining a foot ulcer as existing for 30 days or longer. This and other studies suggest that patients at low risk for foot complications may safely wear well-fitting, good-quality over-the-counter athletic or walking shoes, whereas those with neuropathy and foot deformities may benefit from custom shoes (Table 5). Larger randomized studies should explore which type of therapeutic footwear (including stockings) may best reduce ulceration in patients with neuropathy and deformities and whether patients with only neuropathy require prescription footwear.

Debridement of Calluses. Calluses (hyperkeratotic lesions caused by pressure) further increase pressure, which is a component cause of ulceration. Because debriding hyperkeratoses can reduce peak plantar pressure by 26%,91 this should be routinely provided by trained personnel. Wearing proper footwear may not only prevent but also reduce development of calluses. Among 78 diabetic persons, the mean size of plantar calluses decreased in direct proportion with the amount of time spent wearing running shoes.92 Similarly, among high-risk persons, those who visited podiatrists most frequently (every 3-4 weeks) had the lowest mean plantar pressure before and after callus removal.93 The optimal frequency of podiatric evaluation and management is uncertain.

**Foot Specialist and Multidisciplinary Team Care.** A few studies have assessed the role of foot specialist care as the main intervention in preventing diabetic foot ulcers.84,94 Among 91 diabetic persons with a healed foot ulcer, there were 20 ulcer recurrences in those randomized to podiatric care and 32 in the control group after a median follow-up of 386 days (RR, 0.52; 95% CI, 0.30-0.93; P = .03).94 In another trial of diabetic persons with neuropathy, 235 were randomized to receive podiatric care at least twice a year and 263 to receive no podiatric treatment.95 During the study period (≤3 years), there was no difference in the incidence of foot ulcers, but the podiatric care group had fewer deep ulcers (6 vs 12), infected ulcers (1 vs 10; P<.01), and hos-

<table>
<thead>
<tr>
<th>Table 4. Prevention of Foot Ulceration in Persons With Diabetes: Recommended Management Based on Results of Clinical Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Evaluation</strong></td>
</tr>
<tr>
<td>Inquire about factors associated with foot ulcers</td>
</tr>
<tr>
<td>Prior lower extremity amputation</td>
</tr>
<tr>
<td>Duration of diabetes &gt;10 y</td>
</tr>
<tr>
<td>Poor glycemic control (hemoglobin A1c &gt;9%)</td>
</tr>
<tr>
<td>Impaired vision (visual acuity &lt;20/40)</td>
</tr>
<tr>
<td>Presence of gross structural abnormalities (calluses, hammer or claw toes, flat feet, bunions) or reduced joint mobility</td>
</tr>
<tr>
<td>Presence of dry or fissured skin</td>
</tr>
<tr>
<td>Tinea pedis or onychomycosis</td>
</tr>
<tr>
<td>Loss of protective sensation† with monofilament or biothesiometer</td>
</tr>
<tr>
<td>Peripheral vascular disease (abnormal pedal pulses or ankle-brachial indices)</td>
</tr>
<tr>
<td>Counsel</td>
</tr>
<tr>
<td>Plan schedule of follow-up clinical foot examinations according to foot risk status</td>
</tr>
<tr>
<td>No neuropathy, deformities, history of foot ulcer or amputation</td>
</tr>
<tr>
<td>Peripheral neuropathy only</td>
</tr>
<tr>
<td>Peripheral neuropathy and foot deformities</td>
</tr>
<tr>
<td>Peripheral neuropathy, foot deformities, and Charcot arthropathy, or history of ulcer or amputation</td>
</tr>
</tbody>
</table>

*Podiatrist, orthopedic surgeon, or wound care specialist.†See prophylactic surgery and proper footwear sections in text.‡These represent standard recommendations advocated in most guidelines; not all are supported by research studies.
FOOT ULCERS IN DIABETIC PATIENTS

After 3 years, the schedule follow-up foot examinations with the team were 54 times more likely to develop an ulcer and 20 times more likely to require an amputation than those who kept most appointments.97

Prospective cohort study

and podiatric care.97 After 3 years, the incidence of lower-extremity amputation was only 1.1 per 1000 persons per year. Among high-risk persons, those who missed more than 50% of their appointments with the team were 54 times more likely to develop an ulcer and 20 times more likely to require an amputation than those who kept most appointments.97

Prophylactic Foot Surgeries. A dramatically increased interest in reconstructive surgery has occurred in the past 2 decades.72,98-113 One proposed classification system divides nonvascular foot surgery into elective (to alleviate pain), prophylactic (to reduce risk of ulceration), curative (to heal an open wound), and emergent (to help control a limb-threatening infection).114 Only a few small studies have reported long-term outcomes for prophylactic procedures, generally aimed at correcting deformities that increase plantar pressure (Table 6).

Revascularization Surgery. Vascular surgeons have developed tech-

### Table 5. Studies of Therapeutic Footwear Directed at Preventing Foot Ulceration in Persons With Diabetes

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Intervention</th>
<th>Duration of Intervention</th>
<th>Duration of Follow-up</th>
<th>Main Outcome for Intervention Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized controlled trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Intervention and 11 control patients had foot calluses but no history of ulceration</td>
<td>1 y</td>
<td>1 y</td>
<td>Reduction in mean callus grade in those using orthoses (from 1.9 to 1.2), but not in those receiving podiatric care (increased from 1.6 to 1.7)</td>
</tr>
<tr>
<td>Colagiuri et al,96 1995</td>
<td>Custom-made rigid orthotic device for ≥7 h/d vs routine podiatric care every 3 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reiber et al,10 2002</td>
<td>All had previous foot ulcer but without severe deformity</td>
<td>2 y</td>
<td>2 y</td>
<td>No significant difference in 2-y cumulative foot ulcer recurrence (No. of persons with ≥1 ulcer per person-years of follow-up)</td>
</tr>
<tr>
<td>121</td>
<td>3 Pairs of extradeep and extrawide therapeutic shoes with customized cork inserts and neoprene cover</td>
<td>7.6% vs 9.0%; RR, 0.85 (95% CI, 0.44 to 1.59); ARR, –0.013 (95% CI, –0.063 to 0.035); P = .59*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>119</td>
<td>3 Pairs of therapeutic shoes with polyurethane inserts and nylon cover</td>
<td>7.6% vs 9.0%; RR, 0.84 (95% CI, 0.43 to 1.61); ARR, –0.013 (95% CI, –0.063 to 0.035); P = .59*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>180</td>
<td>Usual footwear</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prospective pseudorandomized (alternate allocation) study

Uocioli et al,99 1995

33 Intervention and 36 control patients had a history of foot ulcer

Therapeutic extradeep, soft leather semirocker soles vs usual footwear

1 y | 1 y | Lower foot ulcer relapse with therapeutic shoes: 27.3% vs 58.3%; RR, 0.47 (95% CI, 0.25 to 0.87); ARR, –0.31 (95% CI, –0.53 to –0.09); P = .02*

Prospective cohort study

Busch and Chantelau,96 2003

60 Intervention and 32 control patients had a history of foot ulcer

“Stock” diabetic shoe: rocker-shaped sole, standardized shock absorption sole, and soft upper without stiff toe-cap vs usual footwear

≤42 mo or ulcer relapse ≤42 mo or ulcer relapse Lower rate of foot ulcer recurrence in diabetic shoe group: 15% vs 69%; RR, 0.25 (95% CI, 0.13 to 0.49); ARR, –0.44 (95% CI, –0.83 to –0.25); P <.001*

Abbreviations: ARR, absolute risk reduction; CI, confidence interval; RR, relative risk.

*Calculated measures of effect using STATA statistical software (version 8, STATA Corp, College Station, Tex).

©2005 American Medical Association. All rights reserved.
niques (eg, bypass grafts from femoral
to pedal arteries and peripheral angi-
plasty) to improve blood flow to an is-
chemic foot. While these procedures
help heal ischemic ulcers, no prospec-
tive study shows that they reduce foot
ulceration.121 The reported effect of re-
vascularization procedures on the in-
cidence and site of amputations var-
ies, but most recent studies suggest
benefits.122-124

Cost-Effectiveness. A recent cost of
illness model, based on published data
about diabetic complications and the
value of health resources from numer-
ous sources found that the mean an-
nual cost of treatment in 2001 was
$9306 for an uninfected diabetic foot
ulcer, $24582 for an infected foot
ulcer, and $45579 for a foot ulcer with
osteomyelitis.125 Another review com-
piled cost data from 1990 to 1997 from
7 studies—4 conducted in the United
States and 3 in other countries.126 Af-
after inflation adjustment and currency
conversion, the cost of treating foot ul-
cers not requiring amputation ranged
from $993 to $17519, and ap-
proached $30724 in 1 study that spanned 2 years after diagnosis.

A few groups have modeled cost-
utility analyses for strategies to pre-
vent foot ulcers. A Markov model from
Sweden of intensive prevention (pa-
ient education, use of appropriate foot-
wear, and access to therapeutic foot
care) for high-risk patients was cost-
effective if the incidence of foot ulcers
and lower extremity amputations was
reduced by 25%.127 A similar model for
patients with newly diagnosed type 2
diabetes found that implementing a

| Table 6. Studies of Prophylactic Foot Surgeries Directed at Preventing Foot Ulceration in Persons With Diabetes |
|---|---|---|---|---|
| **Case series** | **Intervention** | **Duration of Follow-up** | **Main Outcome for Intervention** |
| Armstrong et al,109 1996 | Single, lesser digital resectional arthroplasty in all | 3 y | 2 Postoperative infections in patients with diabetes vs 0 in controls |
| Armstrong et al,110 1999 | Percutaneous Achilles tendon lengthening in all | 8 wk | Mean (SD) reduction in peak plantar pressure from 86 (9.4) N/cm² preoperatively to 63 (13.2) N/cm²; P < .001 |
| Hybrid case-control study | **Achilles tendon lengthening vs no surgery** | 17 mo | Rapid healing of previously recalcitrant plantar wounds and lower rate of ulcer recurrence in surgical group vs controls (0% vs 19%; ARR, –0.19 [95% CI, –0.35 to –0.02]; P = .13)† |
| Randomized clinical trial | **Percutaneous Achilles tendon lengthening plus total contact cast vs total contact cast alone** | 2 y | Lower ulcer recurrence rate (38% vs 81%; RR, 0.48 [95% CI, 0.28-0.80]; ARR, –0.42 [95% CI, –0.66 to –0.18]; P = .004)† and longer mean (SD) time to ulceration after healing (131.2 [189.9] vs 451.0 [364.4] days; P = .03) in surgical vs control group |
| Retrospective cohort study | **Surgical excision and/or bone segment removal vs nonsurgical treatment** | 6 mo | Improved ulcer healing rate (95% vs 79%; RR, 1.20 [95% CI, 0.96 to 1.51]; P = .19)† and reduced ulcer relapse rate (14% vs 42%; RR, 0.33 [95% CI, 0.11 to 1.19]; ARR, –0.29 [95% CI, –0.54 to –0.01]; P = .38)† in surgical vs control group |

Abbreviations: ARR, absolute risk reduction; CI, confidence interval; OR, odds ratio; RR, relative risk.

*This study was also classified as a gait laboratory study.
†Calculated measures of effect using STATA statistical software (version 8, STATA Corp, College Station, Tex).
‡Measure of effect calculated by the authors of the original study.
FOOT ULCERS IN DIABETIC PATIENTS

Critical revision of the manuscript for important intellectual content: Armstrong, Lipsky. Statistical analysis: Singh.

Administrative, technical, or material support: Singh, Armstrong, Lipsky.

Study supervision: Lipsky.

Role of the Sponsor: There was no sponsor for this study and no agency or company reviewed the manuscript.

Acknowledgment: We thank VA Puget Sound Healthcare System employees Ted Hamilton, MLIS, for his invaluable assistance with the literature searches, and Christopher Pacheco for providing the initial version of the foot ulceration figure. We also thank Edward J. Boyko, MD, MPH, for his time and expertise in calculating measures of effect in the tables.

REFERENCES

FOOT ULCERS IN DIABETIC PATIENTS


In every outthrust headland, in every curving beach, in every grain of sand there is the story of the earth.
—Rachel Carson (1907-1964)