

Preventive Foot Care in People With Diabetes

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Diabetic foot ulcers and lower-extremity amputations are serious and expensive complications that befall up to 15% of people with diabetes during their lifetime. Relatively simple and inexpensive interventions may decrease the amputation rate up to 85% (1–5). This Technical Review was undertaken to update the evidence for various preventive and therapeutic modalities to decrease diabetic foot ulcers and lower-extremity amputations and to develop the clinical practice recommendations for preventive foot care of people with diabetes.

The Technical Review is organized into three parts: 1) major demographic and comorbidity risk factors, 2) foot-related risk factors, and 3) preventive strategies. The clinical implications of this review will appear in a separate American Diabetes Association (ADA) Position Statement on preventive care of the foot (6a). This Technical Review covers only the care of the nonulcerated foot. The assessment and management of diabetic foot ulcers and Charcot arthropathy, including surgical management, will be covered in a later review.

This Technical Review is based on original research published in the peer-reviewed literature in the English language.

The research quality was graded using a modification of the system used by the U.S. Preventive Services Task Force (APPENDIX (6b,7)). Preference was always given to studies that provided patient-oriented outcomes or clinically relevant care, rather than disease-oriented outcomes. For example, a study that predicted foot ulcer risk was preferred over a study that predicted a decrease in nerve conduction velocity.

Importance

Although only 3% of the population have diagnosed diabetes, half of all nontraumatic lower-extremity amputations in the U.S. occur in people with diabetes (8). The annual age-adjusted amputation rate between 1980 and 1990 varied from 5.1 to 8.1 per 1,000 people with diabetes, but the number of amputations increased 29% over that decade to 54,000 in 1990 (9). Nontraumatic lower-extremity amputation occurred in 1.9% of all hospital discharges of diabetic people between 1983 and 1990 (10). About half of the amputations are of the toes or foot; the other half (43–65%) are amputations at the transtibial (below-the-knee) or transfemoral (above-the-knee) level (8). The prevalence of amputation in the U.S. in 1989 was 2.8% for people with diabetes (8).

Approximately 85% of all amputations are preceded by a nonhealing foot ulcer (11,12). Foot ulcers affect up to 15% of all people with diabetes sometime in their lifetime (13). The annual incidence of self-reported foot ulcers in diabetic people ranges from 2.4 to 2.6% (14), and the prevalence of foot ulcers ranges from 4 to 10% (15–18), reflecting differences in populations and wound management strategies across geographic regions. Almost 6% of all U.S. hospital discharges with a diabetes diagnosis between 1983 and 1990 included a lower-extremity ulcer diagnosis; 46% of all ulcer hospitalizations were in people with diabetes (10). The direct costs for care of foot ulcers was estimated to be \$145 million in 1986 (19). An extensive review of the epidemiological literature on diabetic foot ulcers and amputation is available in *Diabetes in America* (8) (also at <http://diabetes-in-america.s-3.com/default.htm>).

DEMOGRAPHIC AND COMORBIDITY RISK FACTORS

— The risk factors for diabetic foot ulcers and lower-extremity amputation are similar and will be described together in this review and noted separately when they differ. Also, the risk factors are similar for people with type 1 (IDDM) and type 2 (NIDDM) diabetes, so data on these populations are reported together and noted separately only when they differ. (All references to the type of diabetes have been updated to the preferred terminology of “type 1” and “type 2.”) These risk factors include demographic characteristics, comorbid conditions, and foot pathology. Multivariable analyses of risk factors are shown in Table 1.

Age and duration of diabetes

The risk of ulcers and amputation increases two- to fourfold with both age and duration of diabetes (8,14,20). In the U.S., between 1989 and 1993, the prevalence of amputations was 1.6% for diabetic people age 18–44 years, 2.4% for people age 45–64 years, and 3.6% for people age ≥ 65 years (8). In Wisconsin, the prevalence of amputation was 2.4% for people with diabetes onset before 30 years, and 4.4% for people with older onset diabetes (14). Age and

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Abbreviations: AAI, ankle-arm index; MAC, medial arterial calcinosis; OR, odds ratio; pack-year, smoking one pack of cigarettes per day for one year.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—Comparison of significant risk factors for amputation in multivariable models

Characteristics and risk factors	Study and population								
	Moss et al. (14)		Nelson et al. (20), Pima Indians	Selby and Zhang (22), HMO (San Francisco)	Lehto et al. (23), type 1 (Finland)	Lee et al. (27), type 2 (Oklahoma Indians)		Reiber et al. (25), Male veterans	Mayfield et al. (21), Pima Indians
	Wisconsin (early onset)	Wisconsin (late onset)				Men	Women		
Design	Cohort		Cohort	Nested case-control	Cohort	Cohort		Case-control	Case-control
Data collection	Self-report, exam		Exam	Chart review	Exam	Exam		Chart review, exam	Chart review
Sample size (n)	1,210	1,780	4,399	150 + 278	1,044	332	543	80 + 236	63 + 183
Analysis	Logistic regression		Mantel-Haenszel	Logistic regression	Cox regression	Cox proportional hazard model		Logistic regression	Logistic regression
Measure	OR		Incidence rate ratio	OR	RR	Rate ratio		OR	OR
Male versus female	NS	2.8	Adjusted	Matched	Adjusted	NA	NA	NA	6.5
Nonwhite versus white	NS	—	NA	NS	—	NA	NA	NS	NA
Diabetes duration (per x years)	NS	1.8 per 10	Adjusted	NS	2.2 for 9	1.05 per 1	1.08 per 1	Adjusted	1.4 per 5
Age (per x years)	2.0 per 10	NS	Adjusted	Matched	Adjusted	NS	NS	Adjusted	1.3 per 5
Glycemic control (per x units)	1.4 per 2% GHb	1.5 per 2% GHb	—	1.75 per glucose score*	2.5 for HbA _{1c} >13.4%	1.08 per mmol/l	NS	Adjusted	1.6 per 50 mg/dl
Insulin use	—	—	—	—	—	2.56	NS	—	—
Retinopathy	1.4 per 2 steps†	NS	2.1	3.68	3.6	3.19	3.33	Adjusted	4.6‡
Renal disease	—	—	2.2	—	NS	NS	NS	Adjusted	4.6‡
Proteinuria	NS	4.3	—	NS	1.3	NS	NS	—	NS
Hypertension (per mmHg of dBP or sBP)	2.1 per 10 dBP	NS	NS	1.02 per 1 sBP	NS	1.15 per 10 sBP	1.28 per 10 dBP	—	NS
Cholesterol	—	—	NS	NS	1.8 for >6.2 mmol/l	NS	1.18 per mmol/l	6.4 for HDL <1.3 µmol/l	NS
Smokers	NS	NS	NS	NS	NS	NS	NS	NS	NS
Stroke	—	—	—	2.7	—	—	—	—	4.6‡
Heart disease	—	—	—	NS	NS	NS	NS	—	4.6‡
Neuropathy	—	—	2.0 patellar reflex	4.05	4.3 Achilles reflex	—	—	—	2.1 any diagnosis
Vibratory sense	—	—	—	—	2.7	—	—	12.9	—
MAC	—	—	4.8	—	—	—	—	—	—
Peripheral vascular disease	—	—	—	—	3.9 absent pulses	—	—	—	2.1 any diagnosis
Foot deformities	—	—	—	—	2.1 femoral bruit	—	—	—	2.1
Ulcer history	10.5	4.6	—	—	—	—	—	—	2.1
No outpatient education	—	—	—	—	—	—	—	16.5	—

Most ORs or RRs compare with a baseline group without the feature. dBP, diastolic blood pressure; NA, not applicable; sBP, systolic blood pressure; RR, relative risk. Data from Nelson et al. (20) are adjusted for age/sex. *Glucose score = 50 mg/dl fasting glucose or 68 mg/dl random glucose; †2 steps in grade of retinopathy; ‡retinopathy, renal disease, stroke, and heart disease were combined.

duration of diabetes are highly correlated. In populations with accurate ascertainment of the onset of diabetes (i.e., Pima Indians with type 1 diabetes), duration of diabetes becomes the predominant predictor of ulcer and amputation risk (14,20,21). The relationship of the duration to prevalence of ulceration and amputation appears to be similar for people with type 1 and type 2 diabetes (14).

Sex

Male sex has been associated with 1.6 increased risk of ulcers (8,14) and 2.8- to

6.5-fold higher risk of amputation (14,20–22) in most studies of people with type 2 diabetes. No difference between the sexes was reported for people with type 2 diabetes in Finland (23) or people with type 1 diabetes (14). The mechanism of the increased risk for men has yet to be investigated.

Race and socioeconomic status

Analysis of hospital discharges for diabetic foot ulcers suggest no difference by race (8). A twofold higher risk of amputation has been described for Hispanics and

blacks as compared to whites (8,24) and up to a fourfold higher rate in the Pima Indians (20). However, an evaluation of a California health maintenance organization found no difference by race (22), suggesting that the observed differences may be due to socioeconomic issues or a lack of access to health care.

Social factors

The lack of “social connectedness” (defined as living alone, no visits from a friend or relative in the past month, no attendance at social or religious gatherings, and personal

life dissatisfaction) is associated with a 2.1- to 3.8-fold higher risk of amputation (25). People presenting with a foot ulcer were more likely to live alone or be from a lower social class (26).

Glycemic control

Poor glycemic control increases the risk of neuropathy (see below) and amputation (14,20,22,23,27). The increased risk for amputation is observed even when neuropathy is controlled in multivariable analysis. An HbA_{1c} level >13.4% was associated with a 2.2 relative risk of amputation in a Finnish population with type 2 diabetes (23), and a 50 mg/dl increase in the mean random glucose in the Pima Indians was associated with a 1.6 odds ratio (OR) for amputation (21). Only one study has reported an association of glycemia with ulcers. A 1.4–1.5 increased risk of self-reported ulcers was associated with a glycosylated hemoglobin increase of 2% in people with both type 1 and type 2 diabetes in Wisconsin; however, the models did not control for neuropathy (14).

Comorbid conditions

The risk of diabetic foot disease is associated with diabetic complications in other organ systems, including microvascular disease (e.g., diabetic retinopathy, renal disease) and macrovascular disease (e.g., coronary artery disease) (14,17,20–23,25,27).

Patient education and self-care practices

The lack of patient education on foot care has been associated with a 3.2 increased risk of amputation (25). In a survey of patients with ulcers, only 29% previously considered they were at risk for foot problems, compared with 59% of the control subjects without ulcers, although 30% in both groups reported they had been given information on foot care (26). Approximately 70% of both groups had not had their foot remeasured for footwear in the past 10 years.

Tobacco and alcohol use

Cigarette smoking is a major risk factor for peripheral vascular disease (a major risk factor for amputation) and amputation in nondiabetic people. In diabetic people, the evidence for a relationship between tobacco and ulcers or amputation is variable. Tobacco use has been associated with microvascular disease (e.g., retinopathy, nephropathy) in people with diabetes (28)

and cardiovascular disease (29). Most studies of people with diabetes have failed to show an association of cigarette smoking with an increased risk of macrovascular disease (30), peripheral vascular disease (31–33), diabetic foot ulcers (34,35), or amputation (22,23,25,31). However, a few studies show a weak relationship between smoking and peripheral vascular disease, ulcers, or amputation risk. A clinic-based study found an association of smoking with proximal (pelvic, femoropopliteal) peripheral vascular disease, but not with distal disease (below-the-knee) in people with diabetes (36). A population-based cohort study in Wisconsin of people with type 1 diabetes age ≥18 years found an association between ulcers and 10+ pack year history of smoking (OR 1.3) and current smokers (OR 2.3); however, these findings were of borderline statistical significance (CI included 1.0), and no increased risk was found for smokers with type 2 diabetes in the same population (14). A study of people with diabetes in three English communities found more peripheral vascular disease (OR 2.16) in smokers compared with nonsmokers (37).

Alcohol consumption has been associated with an increased risk of foot ulcers in British men with diabetes and impotence (38). Although one study found an association between CAGE scores and neuropathy (39), most studies have not found alcohol to be a major risk factor for neuropathy (37,40), diabetic foot ulcers (35), or amputation (22,23,25). (The CAGE screening instrument is a brief questionnaire and stands for cut down, annoyed by criticism, guilty about drinking, eye-opener drinks.)

FOOT PATHOLOGY AND ASSESSMENT

The major foot-related conditions that increase the risk of ulcers and amputations are peripheral neuropathy, altered biomechanics, peripheral vascular disease, and skin pathology, as well as a history of foot ulcers.

Peripheral neuropathy

Peripheral neuropathy is defined as symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes (41). The prevalence of neuropathy depends on the definition and population investigated. The prevalence of neuropathy increases with age, duration of diabetes, presence of microvascular complications, and poor glycemic control (42–45). Macrovascular

risk factors (i.e., hypertension, hyperlipidemia) do not appear to be associated with the risk of neuropathy (39,44). The most common form of clinical neuropathy, distal symmetric sensorimotor polyneuropathy, affects up to 50% of people who have had diabetes ≥15 years (37,43,44) and affects the motor and sensory modalities in a “stocking-glove” pattern. Autonomic neuropathy frequently develops concurrently.

Peripheral neuropathy is associated with an 8- to 18-fold higher risk of ulceration (34,35) and a 2- to 15-fold higher risk of amputation (8,20–23). Peripheral neuropathy is thought to be the underlying pathophysiological alteration leading to Charcot arthropathy. The increased risk for these adverse outcomes is imparted through several different mechanisms. First, the loss of protective sensations that include pain, pressure, and temperature, removes the signals of damaging stimuli or conditions. Second, the motor component of polyneuropathy results in atrophy of the intrinsic muscles (interosseous, lumbricals), resulting in a flexion deformity, which creates areas of increased pressure under the metatarsal heads and tips of the toes. Third, the peripheral sympathetic autonomic neuropathy that often accompanies polyneuropathy causes dyshidrosis and dry skin, which can readily crack. Autonomic neuropathy may also be involved with arteriovenous shunting leading to altered skin and bone perfusion (46,47).

The onset of the loss of protective sensation is usually insidious and may progress at different rates in different types of nerves (sensory [proprioception, touch, vibration, pain, temperature], motor, and autonomic). Abnormalities of nerve function and symptoms are only moderately correlated (38,48,49), with no one modality clearly serving as a gold standard to predict adverse patient outcome. Various methods to aggregate symptoms and signs have been developed and used for research purposes (49,50). An American Diabetes Association consensus conference (41) on diabetic neuropathy recommended that at least one measure from clinical symptoms, clinical examination, electrodiagnostic studies, quantitative sensory testing, and autonomic function testing should be used to define diabetic neuropathy for research purposes.

Electrophysiological tests (e.g., nerve conduction studies) have moderate sensitivity for nerve dysfunction but detect subclinical disease, with little clinical or prognostic significance (51). On the other hand, the tra-

ditional clinical assessment of peripheral neurological function (e.g., reflexes, pinprick, vibration with a tuning fork, and light touch to cotton wisp) are highly subjective and have poor interobserver reproducibility ($\kappa < 0.75$) (52). Tests of autonomic function are not standardized and have poor reproducibility and only fair predictive ability for ulcers or amputation (53).

Psychophysical somatosensory threshold tests for vibration and light touch provide the best discrimination in the clinical setting to identify the loss of protective sensation. The vibratory perception threshold can be determined using an electronic tuning fork that vibrates at 120 Hz. The amplitude of vibration is varied from 10 to 50 volts with the Bio-thesiometer (Bio-medical Instruments, Newbury, OH) or the Horwell Neurothesiometer (Scientific Laboratory Supplies, Nottingham, U.K.). A more sophisticated instrument, the Vibrometer (Somedic, Stockholm), adjusts for the pressure of the probe on the skin, and tests from 0.05- to 399- μ m amplitude (54). The decrease in vibratory perception (i.e., increased threshold) is highly predictive of subsequent ulceration. People with ulcers were almost 11 times more likely to have vibratory thresholds >25 V than people without ulcers (55). In a prospective study of people without a history of ulcers, those with vibratory threshold >25 V had a 6.8 odds of developing an ulcer over the next 4 years, compared with those with vibration thresholds <25 V (34). The Bio-thesiometer costs several hundred dollars and takes at least 5 to 10 min to perform. Other threshold tests, generally used in a research setting, evaluate temperature (hot and cold) (56) and pain, using pinprick thresholds (57). One prospective study found the risk of minor skin lesions increased with impaired thermal sensitivity (58). The use of the "yes/no" method of limits for sensory thresholds (59) has been shown to be faster and more reliable than the traditional two alternative forced-choice method (60).

The Rydel-Seiffer tuning fork (Gebueder Martin, Tuttlingen, Germany) provides a simpler and less expensive semiquantitative measure of vibratory sense (54). This 128-Hz tuning fork is calibrated on an arbitrary scale of 0–8 by moving weights at the extremities of the prongs. In a selected high-risk population, 95% of the people with ulcers had scores of ≤ 4 . The graduated tuning fork was highly correlated with the electronic vibrometer ($r = -0.90$, $P < 0.001$), and had a coefficient of variation

of 6–8% in the same day by different examiners (61) and 24% over several weeks time by a single examiner (54). Results from inexperienced examiners correlated well with the experienced examiner ($r = 0.87$, $P < 0.001$). The tuning fork can be carried in a pocket, is easy and painless to use, and costs approximately \$100. However, no prospective data are available linking the graduated tuning fork to later ulceration or amputation.

The Semmes-Weinstein monofilament assesses the threshold for light touch/pressure in a semiquantitative fashion (62). This instrument, a nylon fiber several centimeters long embedded in a handle, capitalizes on the unique physical properties of a buckling column to produce a quantifiable pressure (63). A range of monofilaments are available. The monofilaments are identified by a number that equals the logarithm of 10 times the force in milligrams required to bow the monofilament. Inter- and intra-rater agreement κ values are 0.72 and 0.83 (52). Testing of the plantar surface of the toes and metatarsal heads provides most of the discriminatory ability; the dorsum and heel provide little additional information (64). Two studies found the 5.07 monofilament (10 g) correlated best with the presence or history of an ulcer (64,65), while two other studies suggested the 4.21 monofilament (1 g) to be a better discriminator (66,67). The proposed cutoffs for defining an insensitive foot range from one to three out of six sites, providing a sensitivity of 0.84–1.00 and specificity of 0.77–1.00 to predict a current or future ulcer. In a prospective, population-based study, the inability to appreciate a 5.07 monofilament in one or more standardized sites on the foot was associated with an increased risk of ulceration (9.9 [4.8–21.0]; OR [95% CI]) and amputation (17 [4.5–95]) (68).

Self-reported symptoms of neuropathy (pain, numbness, tingling) affect 30–40% of all people with diabetes. In a U.S. population survey, 28% reported numbness and 27% reported pain or tingling (45). About 20% of the diabetic population with peripheral neuropathy defined by multiple measures reported painful symptoms (43). Pain is associated with measures of small-fiber neuropathy (69) but has only fair correlation with large-fiber neuropathy and foot ulceration (38,70). Thus, the presence or absence of symptoms should not be used to assess the risk of ulcers or amputation (70).

Painful diabetic neuropathy tends to improve within 1–2 years (71–73), espe-

cially if the onset was associated with a recent metabolic disturbance (72); however, the longer the pain has been present, the more likely it is to persist (73–75). Signs of large fiber neuropathy (vibration, ankle jerks, pain sensation) tend to remain stable or worsen over time (71,74). The impact of improved glycemic control on symptomatic neuropathy remains controversial and is reviewed elsewhere (76).

Altered biomechanics

An increased risk of ulceration and amputation has been associated with alterations in the normal biomechanics of the foot, including increased plantar pressure, bony abnormalities, and limited joint mobility. An extensive review of the role of biomechanics in the diabetic foot was recently published (77).

Increased plantar pressure has been associated with recent or current ulcers (65,78,79) and with risk of amputation. In a prospective study, plantar ulcers developed in 35% of the people with static pressures >12.3 kg/cm² measured on an optical pedobarograph, while no ulcers developed in people with pressures <12.3 kg/cm² (80). Pressures >10 kg/cm² (98.1 kPa) have been associated with increased ulceration (81). Static plantar pressure can be measured using a Harris mat or a polytechnic modified force plate; dynamic pressures can be measured with a pedobarograph, instrumented shoes, and in-shoe or in-sole pressure transducers; shear stress can be measured with in-shoe transducers. Normal ranges and risk level cutoffs have not been standardized because different devices give different results under the same foot, and the transducers wear quickly with repeated measurements. Furthermore, plantar pressure patterns appear to change over time (82). Dynamic and shear pressures are probably more informative than static pressures, but are more difficult to measure. An extensive review of pressure measurement methodologies is available (83).

The causes of the increased plantar pressure in diabetic people include increased body mass, structural alterations of the bone and connective tissue, limited joint mobility, changes in skin and callus formation, and changes in posture and gait. Body weight is associated with $<14\%$ of the variance of peak plantar pressure in diabetic people (84).

Increased plantar pressure is often noted in the presence of bony deformities. Up to half of all people with diabetes have

a hammer toe or claw toe deformity (15,16,85) created by motor neuropathy, which causes atrophy of the interosseous and lumbricals muscles, thus leading to unopposed hyperextension of the toes (86). This hyperextension deformity exposes the metatarsal heads to increased pressure, resulting in higher rates of ulceration, particularly under the first metatarsal head and the great toe (~50% of all plantar ulcers) (65,87). Migration of the plantar fat pad anteriorly with the flexor tendons intensifies the local pressure (85). The foot pad is thinner in people with diabetes, thus increasing the problems with bony deformities causing increased pressure (88). Increased metatarsal head pressure is highly associated with the presence of neuropathy (89). Increased pressure can also occur with common foot deformities, such as bunions and hallux rigidus, and after a lower-extremity amputation (90).

Limited joint mobility, first described in the hands (91) is associated with increased pressure, current ulcer, and a history of past ulcers (92–95). The limitation develops over time in people with diabetes because of glycosylation of the skin, soft tissue, and joints (91,96,97). Diabetic people with limited joint mobility at the subtalar and first metatarsophalangeal joint had higher plantar pressures than those with normal mobility, and were more likely to have a history of ulcers (93,94). Ankle dorsiflexion $<5^\circ$, and subtalar joint motion $<30^\circ$ are significantly associated with plantar ulceration (92). However, the reliability of measurement of these joints was fairly low when assessed by 14 physical therapists (intra-rater reliability coefficient of 0.79–0.90 and inter-rater reliability of coefficient of 0.22–0.05) (98), suggesting limitations in the clinical utility of joint mobility assessment.

People with diabetes and neuropathy are more likely to have gait abnormalities (99), postural instability, and sway (100) and are 15 times more likely to suffer some type of injury during ambulation than those without neuropathy (101).

Bony deformities or limited joint mobility alone may not be sufficient to place a person at increased risk of ulcers. Rather, the combination of altered biomechanics with peripheral neuropathy appears to cause the increased risk. In a study of people with limited joint mobility, all of the people who had a history of ulcers also had neuropathy (93). In another study that compared foot conditions in people with either diabetes or rheumatoid arthritis, sim-

ilar rates of bony deformity were noted; however, the people with diabetes had significantly more neuropathy (102). Of the people with diabetes, 32 had a history of ulcers, while none of those with rheumatoid arthritis had an ulcer history. In a prospective study, limited joint mobility measured by the “praying hand” method (91) was associated with a threefold higher rate of foot ulceration; however, this association disappeared when abnormal vibratory sense was taken into account (55). Bony deformities from any cause were associated with a twofold higher risk of amputation in the Pima Indians and were an independent risk factor, even after controlling for demographic risk factors, neuropathy, peripheral vascular disease, and history of ulcers (21); however, the retrospective chart review probably had an incomplete ascertainment of patients’ neuropathy status.

Alterations in skin properties may also contribute to altered biomechanics and increased pressures. The skin in people with diabetes is less pliable, because of the nonenzymatic glycosylation of collagen and keratin, which creates cross-linkage within the tissue (103). Glycosylation of keratin from the sole of the foot was increased in people with diabetes and was strongly correlated to glycemic control. Callus formation is a normal physiological response to chronic direct pressure and shear stress on the skin. Little information is available to support the common belief that callus formation is more common in people with diabetes. A small case-control study found no increased prevalence of calluses, compared with the general population (16), but a study of people with limited joint mobility causing increased pressure under the first metatarsal joint found increased callus formation as compared with those without increased pressure (105). A callus may function as a foreign body at the skin surface and further increase localized pressure by up to 29% (106). Hemorrhages and early ulcers can form underneath callus and are commonly mistaken for plantar warts by naive examiners (107). Hemorrhagic ulcers were found in 27% of the ulcers in neuropathic feet in one clinic series (2). Calluses were associated with an 11-fold higher risk of ulcers and were more predictive of ulceration than increased plantar pressure alone in a clinic population (29).

Increased pressure alone does not appear to cause tissue damage; rather, it is the cumulative action of moderate levels of pressure applied repeatedly over time that

results in tissue damage. With ambulation, the foot experiences repetitive low-stress impact, which accumulates into tissue damage leading to ulceration. P.W. Brand, a pioneer in the research and management of the neuropathic foot, hypothesized that the person with intact sensation subconsciously perceives inflammation from repetitive low-level trauma and unconsciously alters the gait to redistribute the pressure (108). The person with a loss of protective sensation does not appreciate the increasing damage occurring to the foot, and continues to traumatize the same tissue. He tested this theory using a runner with normal sensation, measuring thermal patterns periodically. Increased temperature was initially noted at points of maximum pressure, but the thermal pattern changed over time, suggesting that the runner had altered his gait (108). This same change was not seen in people with neuropathy. Another investigator was unable to demonstrate an increased variability in the gait pattern between neuropathic and non-neuropathic patients using dynamic gait measurement; however, the subjects were observed for only 15 min of walking, which may not be sufficient trauma to cause tissue damage and prompt gait alterations (77). Further investigation is needed to establish the mechanism by which increased pressure leads to ulcers and amputation.

The severity and location of the tissue trauma in an insensitive foot may be identified by temperature differentials across the foot (108). In the normal foot, the highest temperatures occur in the medial arch in a “butterfly” pattern, with a mean temperature of 25.7 ± 2.1 to $27.2 \pm 2.1^\circ\text{C}$ (109,110). When tissue is exposed to repetitive, increased focal pressure, the local temperature increases (111). Increased temperature has been described over prominent metatarsal heads (112). In a 3-year prospective study of people with symptomatic neuropathy, areas with elevated temperature experienced an increased incidence of plantar ulceration (109).

However, several aspects of diabetic foot pathology limit the usefulness of temperature assessment of the neuropathic foot. In people with peripheral neuropathy, marked arteriovenous shunting increases the blood flow in the skin (46). This alteration, which may be due to involvement of the autonomic nerves, increases the overall temperature of the foot and ameliorates the ability to increase local blood flow. Diabetic people with sensory and painful neuropathy had a

Table 2—Percentage of ulcers and amputations associated with specified pivotal or precipitating events

	Ulcers		Amputation	
	Edmonds et al. (150)	Apelqvist et al. (87)	Pecoraro et al. (11)	Mayfield et al. (21)
Population (n)	386 ulcers in 239 patients	314 patients	80 veterans	63 Pima Indians
Accidental cuts	5	18	8	26
Shoe trauma	47	40	36	8
Mal perforans*	—	12	—	38
Thermal trauma	1	—	8	5
Decubitus	2	4	8	1
Iatrogenic	—	—	3	5
Vascular occlusion	—	—	8	7
Paronychia and dermatologic conditions	3	6	3	7
Unknown/unspecified	32	16	14	3
Edema	13	—	—	—
Miscellaneous	—	4	12	0

*Also called a repetitive stress ulcer. Usually a new ulcer located on the plantar surface, but could include ulcers on the dorsum of toes or lateral border of shoes. Some authors combined this category with shoe trauma.

mean foot temperature 2–7°C warmer, compared with diabetic people without neuropathy or nondiabetic people (110,112). Conversely, foot temperature does not increase in people who have significant peripheral vascular disease (111).

A skilled clinician can detect a change of ~2°C using the hand (108). Quantitative techniques to measure temperature include thermistors, liquid-crystal contact thermography, thermography detectors, and infrared thermography. The reproducibility of thermography over 3–6 months had a correlation coefficient of 0.82 (112). A 2° difference has been suggested as clinically significant, indicating an inflammatory process leading to ulceration or Charcot arthropathy (108). A prospective study of people with healed ulcers and no peripheral vascular disease found a mean 3.6°C difference between the foot with the prior ulcer and the contralateral foot at the visit just before a subsequent ulceration (113). Further studies are needed on the effectiveness of prospective temperature screening for impending ulcers and Charcot arthropathy.

Although quantitative plantar pressure measurement is being used increasingly in the clinical setting to customize footwear, no studies to date have demonstrated the effectiveness of this modality over the traditional clinical exam, which uses clues of bony deformities, erythema, increased warmth, and callus to identify areas of increased pressure (114).

Peripheral vascular disease

Peripheral vascular disease, defined as atherosclerosis of the peripheral blood vessels, is 2–3 times more likely to develop in people with diabetes than in the general population (115). The prevalence depends on the definition and population surveyed. Peripheral vascular disease, defined as at least one absent pulse, was noted in 15% of people at 10 years and 45% of people at 20 years after diagnosis of diabetes (116). In the University Group Diabetes Program (UGDP) study, the cumulative incidence of nonpalpable dorsalis pedis pulse, intermittent claudication, and arterial calcification was 35, 38, and 61% (men) and 38, 24, and 32% (women), respectively, after diabetes diagnosis (117). The age-adjusted incidence per thousand of claudication for people with diabetes in the Framingham Study was 12.6 and 8.4 for men and women, respectively (115). Peripheral vascular disease is highly correlated with age and duration of diabetes (115–117). Controversial associations include smoking (see earlier discussion) and glycemic status (31,117,118). Peripheral vascular disease affects the femoral and iliac arteries in a similar rate in people with and without diabetes; however, those with diabetes are much more likely to have involvement of the peroneal and tibial vessels and to spare the vessels in the foot (119,120).

Peripheral vascular disease is an infrequent precipitating event (~5–7%) for

ulcers or amputations (11,21,87) (Table 2). However, peripheral vascular disease plays a major role in delayed wound healing and gangrene and is a contributing factor to almost half of the amputations (11).

Traditionally, the gold standard for the diagnosis of peripheral vascular disease has been the angiogram. In the clinical setting, the ratio of blood pressures of the lower extremity to arm pressure, called ankle-arm index (AAI) or ankle-brachial index (ABI), is easier to obtain and has fair predictive value for delayed wound healing (121) and amputation (122). The lower normal limit has been variably defined as 0.94–0.97 (123,124). Critical ischemia includes an AAI <0.5. (125). An AAI <0.9 is 95% sensitive and almost 100% specific in detecting angiogram-positive disease (126). The variability of AAI can be attributed mainly to biological variability, and to a lesser degree, observer variation. The European community prefers the absolute blood pressure of the ankle and toe instead of the AAI (125).

The symptoms of peripheral vascular disease are claudication or rest pain. Claudication is defined as pain in the calf that develops upon walking and is relieved within 10 min of rest (127). Rest pain is defined as pain that occurs at rest and is relieved by dependent positioning of the legs. Chronic critical ischemia has recently been defined as persistently recurring ischemic rest pain requiring regular analgesia for more than 2 weeks, with an ankle systolic pressure ≤50 mmHg and/or a toe systolic pressure of ≤30 mmHg (125) (chronic critical ischemia also includes obvious tissue loss such as gangrene). Claudication and rest pain may be more difficult to assess in the person with diabetes because of the frequent coexistence of nociception or hyperesthesia caused by neuropathy. In addition, the distal location of the vascular lesions is less likely to produce classic symptoms. Claudication, as defined by the Rose criteria (98), has a poor sensitivity (9–20%) but excellent specificity (96–99%) to predict AAI ≤0.8 in a nondiabetic population (128). The symptoms of claudication had a sensitivity/specificity of 22/96% against a gold standard of blood pressure, treadmills, and Doppler studies in 458 volunteers with diabetes (129). In a population of veterans with diabetes, the inability to walk one city block had a sensitivity/specificity of 0.5/0.87 to predict an AAI ≤0.5 (33).

The clinical exam for early peripheral vascular disease remains an inexact art.

Detection of the dorsalis pedis and posterior tibial artery by palpation is greatly affected by room temperature, biological variation, and provider skill. The dorsalis pedis is congenitally absent in up to 12% of the white population and <5% of the black population (130,131). The probability of agreement on an absent pulse between experienced examiners has been reported to range from 0.49 to 0.59 (132,133) but can be improved from a κ of 0.3–0.6 to 0.6–0.7 with training and practice (134,135). The sensitivity/specificity of a decreased or absent posterior tibial pulse was 71/91% for an AAI ≤ 0.9 in a nondiabetic population (128). In another study, palpable pedal pulses were always present when toe blood pressure was >40 mmHg and AAI >0.5 ; patients who lacked palpable pulses in both feet had an AAI <0.9 (136). Pulse palpation in 458 volunteers with diabetes had a sensitivity/specificity of 67/69%, using a gold standard of blood pressures, treadmills, and Doppler studies (129). Simple clinical exams or signs with poor predictive value include capillary refill time, foot skin coolness, diminished lower limb hair growth, and blue/purple foot skin color (33). Tests of reactive hyperemia provided no more accuracy than the AAI and were not tolerated by half of the subjects in one study (123). The best ancillary vascular test appeared to be venous filling ≥ 20 s, which had a sensitivity/specificity of 22/94% to predict an AAI ≤ 0.5 (33). Stress testing may provide additional information to the AAI, but has low reproducibility (137).

The vascular assessment of people with diabetes is further complicated by the presence of medial arterial calcinosis (MAC) or Monckeberg's sclerosis. In MAC, the medial wall of the blood vessels become calcified, producing a "lead-pipe" condition, which may increase blood pressure readings, and at extreme levels, prevent blood pressure assessment because the vessel becomes non-compressible (138). MAC is observed radiographically in 60–80% of people with diabetes for ≤ 10 years (20,117). The condition is progressive, developing first in the feet and moving proximally, and is highly related to age, duration of diabetes, loss of vibration perception, and poor glycemic control (139,140). MAC has been noted in both diabetic and nondiabetic people with sympathetic denervation (141). MAC is generally associated with increased ankle systolic blood pressures and AAI ($r = 0.40$, $r = 0.35$, respectively) (140). Although AAI >1.3 is highly specific for MAC, MAC is

present at normal ranges of AAI and in up to one third of diabetic people with AAI ≤ 1.0 (140,142). In view of the frequency of MAC in patients with diabetes, segmental pressures, and therefore AAI ≥ 1.0 , may be artificially elevated and may require further evaluation.

Toe pressures measured with plethysmography may be a more accurate reflection of blood supply to the foot (143) and may provide better prediction of wound healing than ankle pressure or AAI (122,144,145). However, toe pressures measured with pulse-volume recordings are thought to have poor reproducibility (137), especially in the presence of autonomic neuropathy (146). The impact of MAC on the accuracy of blood pressure measurements and the preferred vascular assessment measured in the person with diabetes remains controversial.

Finally, several studies suggest that skin perfusion is an important and independent predictor of ulceration and wound healing in diabetes (35,121). In a case-control study of a veterans population, multivariate analysis revealed the most important risk factors for ulceration were transcutaneous oxygen <30 mmHg (OR 58 [95% CI 5.08–658]), absence of Achilles tendon reflexes (OR 6.5), and being insensate to 5.07 monofilament (OR 18) (35).

After consideration of these many difficulties in vascular evaluation, experts at a recent consensus conference recommended that AAI be used in addition to claudication history and pulse palpation for screening people with diabetes. They recommended that a screening AAI be performed for all people with type 1 diabetes ≥ 35 years old or with ≥ 20 years duration of diabetes, and for all people with type 2 diabetes and aged >40 years (147). The value of these recommendations has yet to be demonstrated in a population-based study.

The gold standard for confirmation of vascular disease has been the angiogram, but this test is expensive, invasive, and may cause renal and anaphylactic complications. Noninvasive tests using Doppler wave form analysis, duplex ultrasound scanning, and nuclear magnetic resonance can provide information on the flow and pressures at each segment of the lower extremity with less risk to the patient, but cannot provide as much information on collaterals or runoff before graft placement (148). The value of noninvasive laboratory testing in the screening, diagnosis, and management of peripheral vascular disease needs further study.

Ulcers and other skin pathology

Ulcers are defined as any break in the cutaneous barrier (in clinical studies the break must extend through the full thickness of the dermis). The site of ulceration is highly related to the associated foot pathology and precipitating event (65,87). In the neuropathic foot experiencing increased plantar pressure, ulcers are more common under the tips of the toes and plantar surface of the metatarsal heads, especially under the first and fifth, and under any bony deformity. In the ischemic foot, ulcers are more likely to occur on the tips of the toes and lateral border of the foot.

Approximately 5% of people with diabetes for <20 years reported a current or past foot ulcer (37). A randomized controlled trial found that the history of an ulcer increased the risk of ulceration 1.3-fold (58). In another prospective study, the risk of foot ulceration was more highly associated with a history of a previous ulcer (56.8 [5.08–658]; OR [95% CI]) than with callus (OR 11) or plantar pressure >10 kg/cm² (OR 4.7) (35). A history of a prior foot ulcer is associated with a 2- to 10.5-fold higher risk of amputation (14,21,25,27).

Foot ulcers recurred in 30–40% per year of people who returned to their own usual shoes, thus highlighting the important role increased pressure and footwear play in the development of ulcers (2,149). A number of minor skin conditions are thought to increase the risk of ulceration or amputation. These include dry skin (16), edema (2), improper nail care (17), and ingrown toenails (87,150). In a prospective study, dry skin, ingrown nails, improperly trimmed nails, edema, and onychomycosis were not associated with an increased risk of ulceration in the following year, but fungal dermatitis was associated with a three-fold increased risk of a minor, nonulcerated skin lesion (58).

Causal pathways

Each of the risk factors discussed above are rarely the sole cause of amputation. The causal pathway to amputation includes many component causes. These may include pathophysiological components (ischemia, neuropathy, infection, faulty wound healing), pathological components (ulceration, gangrene), and environmental components (minor trauma). In one case series, absent protective sensation was a component cause in 82%, ischemia in 46% of the cases, and ulceration complicated by failure to heal was present in 72% of the cases (11).

Pivotal or precipitating events

In almost all amputations, an event can be identified that sets off the cascade of consequences, which culminates in amputation. This event, often called the "pivotal event" or "precipitating event," has been identified and categorized in several case series of amputations (Table 2). Shoe-related trauma is the most frequent event leading to ulcers and amputation. Many of the events listed in Table 2 could be prevented by proper protective foot wear and foot care practices.

Risk stratification

Risk classification systems aggregate risk conditions with similar prognosis or treatment requirements. No formal risk classification system has been developed to predict diabetic foot ulceration, and few multivariate analyses of ulcer risk have been published. In one descriptive study, ulcers were more highly associated with a vibratory threshold >25 V than with low ankle blood pressure or elevated plantar pressure (55). In a case-control study of a veterans population, the most important risk factors for ulceration were absence of Achilles tendon reflexes (OR 6.5), being insensate to 5.07 monofilament (OR 18), and transcutaneous oxygen <30 mmHg (58 [5.08–658]; OR [95% CI]) (35). Several risk classification systems have been published to predict the risk of amputation (21,114,151–153). Most systems were based on expert opinion, but one system was later validated in a prospective fashion (68) and another was developed using multivariate analyses of retrospective chart review (21). Although each system assigns different weights to the various risk factors, all incorporate the same basic risk factors of peripheral neuropathy, peripheral vascular disease, bony deformities, evidence of increased plantar pressure, and a history of ulcers.

PREVENTIVE INTERVENTIONS

Diabetic foot care programs can decrease the rate of ulcers and amputations by 44 to 85% according to one randomized controlled trial (1) and a number of pre-post-design studies (2–5). These programs have usually included a thorough foot risk assessment, callus and nail care, customized footwear, wound care, and patient education provided by a multidisciplinary team with a special interest and expertise in the foot. Most of the interventions also incorporated system changes of standardized records, chart reminders,

patient-tracking data, and increased clinic access. These studies implemented the various interventions simultaneously, making it difficult to assess the relative impact of each component to the overall success of the program. The evidence for specific interventions is reviewed below.

Glycemic control

In the Diabetes Complications and Control Trial (DCCT), people with type 1 diabetes who achieved near-normal glycemic control experienced a 69% reduction in the subclinical neuropathy and a 57% reduction in clinical neuropathy, as compared with the control subjects who received the usual treatment and who had higher levels of glycemia (118). The specific impact of normalizing blood glucose, lipids, or blood pressure on the development of peripheral vascular disease in people with either type of diabetes is untested.

Foot exams

Examination of the foot is an obvious, fundamental step to identifying certain foot risk factors that can be modified, thus reducing the risk of ulceration and amputation. Little standardization exists on what constitutes an adequate foot exam, and no data are available to support either the effectiveness or optimum frequency of foot exams.

The most rudimentary exam consists of a visual scan of the skin surface for breaks in the cutaneous barrier, increased warmth, and callus formation. The visual scan at each contact with a health care provider can identify new, unsuspected foot lesions. In a community survey of diabetic people, 9% of foot ulcers were unknown to the patient (18). The ritual of a foot exam at each visit may emphasize the importance of this activity to the patient and might provide a teaching opportunity to reinforce self-care, but this has yet to be evaluated rigorously.

A comprehensive examination of the foot, including an assessment of the neurological, vascular, and biomechanical status is fundamental to identifying patients with risk factors and to implementing interventions. The optimum interval for screening asymptomatic diabetic people has not been studied. A 1-year interval has been suggested by experts, based on the natural history of neuropathy and peripheral vascular disease. The optimum interval for assessment of the person with high-risk conditions has also not been evaluated.

Approximately 40–60% of people with diagnosed diabetes have received a foot exam within the past year (154–157). Foot exams are more likely to be performed if there are medical record reminders (1) or if the patient's socks and shoes are removed before the physician enters the exam room (158). Primary care providers currently recognize the prognostic significance of foot ulcers and are twice as likely to refer patients with foot ulcers for podiatric foot care and education, compared with patients with bony deformities or peripheral neuropathy (159). When health care providers are provided with education and practice guidelines, the foot examination tends to be more complete and podiatric referral is more likely (1).

Peripheral neuropathy

The primary preventive strategy for neuropathy is to maintain glycemic control at as near-normal levels as possible (118). Secondary prevention involves early detection of foot risk factors so that preventive footwear and patient education can be provided (see below). No tertiary preventive strategy is yet available; that is, no treatment is currently available in the U.S. to reverse neuropathy. A number of pharmacological agents, however, are under development and assessment. A complete discussion on the medical management of peripheral neuropathy is beyond the scope of this paper.

Altered biomechanics

Management of the person with abnormal biomechanics depends primarily on debridement of callus and nails and on provision of footwear tailored to the specific pathology (see FOOTWEAR section below). Conservative management of increased plantar pressure involves debridement of callus and footwear modification. Removal of the callus under the forefoot using a scalpel or abrasive device can reduce mean peak pressures on the foot by 29% (106). The rate of callus formation can also be decreased by appropriate footwear (see below). Physical therapy has been suggested for limited joint mobility and balance problems but has not been evaluated for effectiveness. Surgical modification of the bony deformities of the foot, including resection of the metatarsal head, have been associated with decreased pressures and improved ulcer healing (160,161), but have not been rigorously evaluated against other management strategies.

Peripheral vascular disease

People in the general population with symptoms of claudication rarely progressed to amputation over 10–15 years (1.6 to 1.8%) (162,163), but the rate of progression appears to be somewhat higher in diabetic populations (15–20%) (117).

Patients with claudication have been successfully treated with a graduated exercise program (164,165). However, some providers are now advocating angioplasty or vascular bypass (166). Patients with severe rest pain that qualifies as critical ischemia have been treated with amputation in the past, but now may be offered vascular bypass or angioplasty. People with claudication or rest pain in the general population treated with bypass and angioplasty reported improved functional status in several descriptive studies (167). A study of Veterans Administration general population patients with claudication or rest pain randomized to angioplasty or bypass surgery found equal improvement in the quality of life and functional status (168). A subanalysis of patients with diabetes was not possible because of the small sample size. The few studies that have reported outcomes separately for the diabetic population note more complications and adverse outcomes as compared with the nondiabetic population. Institutional-based reports suggest a decrease in amputation rates after the introduction of angioplasty and vascular bypass to the pedal vessels (169,170). Epidemiological studies of large populations have not detected a decrease in the number of amputations since the adoption of these surgical approaches (171).

The value of early detection and intervention for peripheral vascular disease in the asymptomatic person with diabetes remains unknown. A complete discussion on the medical management of peripheral vascular disease is beyond the scope of this paper.

Abnormal skin conditions and foot ulcer history

Experts suggest that patients should be taught to avoid foot soaks, to dry the foot thoroughly, and to use skin moisturizers liberally, but little research is available on the effectiveness of these self-care practices. In a survey of self-care practices, dry skin and maceration were found as frequently in people who reported soaking their feet as in those who did not (172). Experts also suggest that the nails should be trimmed to the contour of the toe and extend 2 mm beyond the nail bed. The edges should be

gently filed to prevent catching on socks and bedding. A health care professional should trim nails that are exceptionally thick or deformed or for people with peripheral vascular disease or peripheral neuropathy. However, little research is available to support these recommendations.

Tinea pedis can be treated effectively with good hygiene and topical antifungal agents. Until recently, the only cure for onychomycosis (mycotic nails) was nail ablation, but now itraconazole and terbinafine provide culture cure rates of 70–80% and cosmetic improvement in ~50% (173,174). Itraconazole may interact with sulfonyleureas, cisapride, statin drugs, warfarin, digoxin, and calcium-channel blockers, while terbinafine does not. The high recurrence rates are probably due to immunological factors. Because of the high cost of the medications and high recurrence rate, their cost-effectiveness is questionable and has yet to be explored for people with diabetes. Pulse dosing protocols, which use medications only a few days per month and thus reduce cost, are available for itraconazole (175) and are under investigation for terbinafine.

Footwear

When fitted properly, footwear can reduce abnormal pressures, reduce the formation of callus and ulcers, and protect the foot from external trauma. The composition and design of the sole and insert can affect pressures and callus formation. In one study of people with diabetes, peak pressures on the sole were highest when walking barefoot and were significantly lowered when measured in properly selected and fitted shoes (176). Plantar pressure in the midfoot was decreased by 31–51% in tennis shoes with a firm rubber sole, compared with a flat, flexible sole with no cushion (177,178). Rocker and wedge sole modifications can reduce the pressure under the metatarsal heads up to 30% (177,179). Athletic running shoes decreased plantar callus formation in a group of people with diabetes, reducing the need for debridement by threefold and reducing the number of people complaining of painful callus from 70 to 9% (180). Cushioned inserts of viscoelastic polymer decreased focal pressure by about half (181). A customized molded insert allows maximum foot and insole contact, reducing focal areas of increased pressure more than a flat insert (182). For diabetic people with a transmetatarsal amputation, a cus-

tom-made full-length shoe with a total contact insert and a rocker bottom sole has been shown to improve functional mobility and reduce plantar pressure better than regular footwear or a short shoe (183). A number of materials are available and vary in their compressibility and durability (184). Thick, padded socks also decrease peak forefoot pressure and the area under the time-pressure curve by a mean of 25 and 29%, respectively (185), and were well accepted by patients. However, several patients developed ulcers from wearing the socks in shoes that did not accommodate the extra thickness (186).

Tovey (187) has summarized the principles of proper footwear selection. Footwear should relieve areas of excessive plantar pressure, reduce shock and shear, and accommodate, stabilize, and support deformities. Shoes should fit both the foot shape and size. The first metatarsophalangeal joint should be accommodated in the widest part of the shoe and the length should allow 3/8 to 1/2 inch between the end of the shoe and the longest toe. The shoe should have sufficient room in the toe area and over the instep. Shoes with laces can adjust for edema and deformities. The heel should fit snugly without undue motion. In certain feet, limitation of joint mobility may add to stability and pain reduction. People with balance problems may benefit by footwear with wide, low heels to improve stability and assistive devices such as canes.

Therapeutic footwear, selected according to Tovey's principles, has been shown to be effective in the prevention of ulceration for people at high risk. People with neuropathy and a history of prior ulceration were randomized to either a depth shoe with insert padding per Tovey's specifications made by a major Italian shoe manufacturer or to their own usual footwear. After 1 year, the foot ulcer relapses were significantly lower (28 vs. 58%, $P = 0.009$) in the specially padded shoe (188).

The effectiveness of footwear is heavily dependent on footwear acceptability and use. In a cohort of high-risk patients who were provided therapeutic footwear (protective cushioned footwear with padded insoles), patients who wore their shoes >60% of the time reduced the ulcer relapse rate by >50%, compared with patients who wore their shoes for less time (149). Patients who wore the shoes were free of ulcer recurrence for up to 20 months, whereas 38% of patients who did

Table A1—Type of evidence, study designs, and inferences for technical review

Type	Study design	Inferences
I-A	Randomized controlled trial, crossover trials	Causation, efficacy of treatment or risk modification
I-B	Controlled trial, nonrandomized	
II-A	Cohort, case-control	Association
II-B	Time series, pre-post studies, repeated panel	
II-C	Cross-sectional population-based data	
III	Descriptive studies	Hypothesis generation
	Case series, case reports	
IV	Expert opinion and consensus opinion	Test characteristics
X	Meets all of the screening and diagnosis criteria*	
Y	Meets part of the screening and diagnosis criteria*	

*Screening and diagnostic test criteria: 1) gold standard, preferably a patient outcome that matters rather than a disease; 2) definitions of the test and the outcomes are clear and easily reproduced; 3) test characteristics: sensitivity, specificity, reproducibility provided; 4) subjects: population-based preferred over selected populations; and 5) tests that provided results early in the disease course are preferred to ones that can only be used late in the course, especially if effective early intervention is possible.

not use the shoes experienced another foot ulcer within 1 year. These high-use patients were also more likely to receive debridement of callus and nails (2.0 SD [1.7–2.3] vs. 1.3 [0.9–1.7]) times per month ($P < 0.05$), suggesting a selection bias. After 40 months, this protective effect leveled off, and 54% of the high-use patients versus 100% of the low-use patients had experience ulcer relapses, suggesting that the footwear may have lost its ability to absorb shock after 2 years. The cosmetic acceptability of the extra-depth shoe and rocker bottom limits the effectiveness of therapeutic footwear. In a study of 85 high-risk diabetic patients who were prescribed therapeutic footwear, only 49 patients wore their prescribed shoes to a subsequent clinic visit. Those who failed to purchase or wear the prescribed shoe cited the unattractive appearance of the shoes (189).

Most people with diabetes and neuropathy alone can wear commercial footwear such as walking shoes and athletic shoes that meet Tovey's principles. People with hammer toes, bunions, or evidence of high plantar pressure will need extradePTH, depth-inlay, or custom shoes that provide a slightly wider and deeper toe box. A number of styles are available from specialty shoe distributors for less than \$200. Commercial and custom insoles may be needed to redistribute the pressure, and sole modifications, including a rocker or wedge, may be needed for people with limited joint mobility. Custom-molded shoes are usually required for people with severe deformities such as Charcot arthropathy, severe arthritis, or postamputation. These shoes are fabricated over a plas-

ter replica of the patient's foot by a specialist and are often very expensive.

Often, people with neuropathy purchase shoes that are too small to have the usual sensation of footwear pressure. Experts suggest that before shoe shopping, the patient should stand on a piece of paper and draw an outline of the foot and use this for comparison with the prospective shoe. Patients with evidence of elevated pressure, neuropathy, bony deformities, or a history of an ulcer should have their footwear fitted by a professional (i.e., pedorthist or other foot care professional) (176). The effectiveness of quantitative pressure measurement systems to customize footwear has yet to be evaluated.

Patient education

Most foot care intervention programs have included patient education along with other interventions, making it difficult to distinguish the relative impact of education in the overall success (1–5). Studies of lecture-style educational sessions on foot care have shown short-term improvements in knowledge, but few changes in foot care practices and foot conditions (190). Educational interventions using motivational techniques (191) or skill-based education (192) tend to show more changes in self-care behaviors. In a randomized trial of a county hospital population, patients received an intensive evaluation and education session, reinforced with behavioral contracts and reminders, and their doctors received education and chart reminders (1). The control population received the usual care and usual provider education. After 1 year,

patients were more likely to report appropriate self-care of the foot behaviors, including inspection of feet and shoes, washing of feet, and drying between toes. However, other behaviors, including testing of bath temperature and reporting foot problems were not significantly altered. Patients with the intervention had fewer serious foot lesions (OR 0.41) including ulcers. Another study randomized primary care sites to usual care or group education provided by the general practitioner. The patient groups had similar demographic and foot pathology at baseline. At 6 months, the intervention group had significant reductions in callus (49 vs. 82%), fewer minor skin pathology (49 vs. 65%), and improper nail trimming (27 vs. 92%) (193). Both of these studies highlight the effectiveness of combining provider and patient education.

Only one randomized controlled study has been conducted of foot education as the sole intervention. Veterans from a high-risk foot clinic were randomized to "usual education" or a 1-h slide lecture showing ulcers and amputations followed by a simple, one-page instruction sheet to take home. After 2 years, people receiving the educational session had a threefold decrease in ulceration ($P < 0.005$) and amputation rates ($P < 0.0025$) (194). Little is known about the effectiveness of education over longer periods of time or for low-risk populations.

The patient's ability to conduct an adequate self-exam of the foot may be limited by poor vision, obesity, poor mobility, or cognitive problems. One study found 71% of the patients in a high-risk foot clinic had poor vision (195). Another study found that 39% of the elderly diabetic people studied were unable to reach their toes to remove a simulated lesion that had been applied to the foot and that only 14% of the elderly subjects could respond appropriately to a plantar lesion (196). Patients should be evaluated for these types of limitations, and if present, family members or nursing services should be recruited to provide foot care and surveillance.

Little research has been conducted on the content of patient education. Frequent surveillance of the foot and early notification of health care professionals is suggested. No inexpensive systems for home monitoring of temperature have been developed. Experts suggest that patients should be taught to palpate the feet with their hands to detect increased warmth, but the effectiveness of this practice has not been

Table A2—Type of evidence for selected foot care examinations and management strategies in diabetic people without a current ulcer

	Evaluation method or management strategy	Type of evidence	References
Foot screening and surveillance			
Frequency and type of exam			
Low-risk patient†	Comprehensive annual exam	IV	*
High-risk patient†	Components of comprehensive exam every 3–6 months	IV	*
Comprehensive foot examination			
History	History of neuropathy, vascular disease or treatment, prior ulcer, or amputation	II-A	14,21,25,35,27,58
Peripheral neuropathy			
LOPS	Semmes-Weinstein monofilament 5.07 (10 g) or threshold tests for vibration	I-A, X	34,35,54,55,61,64,65,68
Other neuropathy	Assessment of motor strength, proprioception, gait, and stability	II-A, III	99–101
Altered biomechanics	Assessment of bony deformities, limited joint mobility, prior amputation	III	93–95
Increased focal pressure	Erythema, callus formation, pre-ulcer (i.e., hemorrhage under callus)	II-A, II-B	103–106
	Temperature assessment by palpation or thermometer		
	Useful in people with deformity or LOPS alone	II-A	109,112,113
	Not useful in people with PVD or autonomic neuropathy	III	110,112
PVD	Symptoms of claudication or rest pain	II-C, X	33,125,128,129
	Palpation of dorsalis pedis and posterior tibial pulses	X	33,128,134–136
Skin pathology	Visual inspection for breaks in the cutaneous barrier (i.e., ulcers) and minor skin abnormalities (thickened or ingrown nails, fissures, fungal infection, erythema, edema, dry skin)	II-A	2,16,17,58,87,150
Risk conditions			
Prevention of:			
Neuropathy	Glycemic levels maintained as near normal as possible	I-A	118
PVD	Smoking cessation	II-A	29
Neuropathy, evidence of increased plantar pressure, or a history of plantar ulcers without bony deformity	Athletic shoe or walking shoe with cushioned soles or inserts, adequate toe box, and lace-up vamp	I-A	176–178
Moderate bony deformities		III	180,181
Toe deformities	Extra-depth shoe ± insert	I-A	182,183,188
Bunions	Extra wide shoe	III	
Marked bony deformities (i.e., Charcot foot, amputation)	Molded shoe to accommodate foot	I-A	181,182
	Surgical modification of foot to fit footwear	II-B	160,161
Limited joint mobility (MTP or ankle)	Rocker sole ± insert	I-A	177,179
Callus	Debridement	II-B	106
	Cushioned soles and inserts	I-A	180
Nail pathology			
Thick, mycotic, or painful	Debridement	IV	*
Ingrown or mycotic	Excision	IV	*
Mycotic	Oral antifungal medications	I-A	173–175
PVD			
Asymptomatic	Observation	II-A	117,162,163
Claudication	Exercise therapy	I-A	164,165
	Bypass surgery or angioplasty	I-A, II-B	166–168
Rest pain (critical ischemia)	Distal bypass, angioplasty, or amputation	II-B, III	168–171
Ulcer history	Determine probable etiology and treat	IV	*
Minor skin abnormalities			
Dry skin	Emollients	IV	*
Fungal infections	Topical agents	IV	*
Therapeutic footwear	Should be fitted by a person with expertise in therapeutic footwear	III	176
Patient education			
Low-risk patient†	Patient education on foot care and footwear (possibly useful)	I-A	190–193
High-risk patient†	Patient education on foot care and footwear (beneficial)	I-A	194
Frequency of education	Annual	IV	*
Education content:	Impact of neuropathy	IV	*
(knowledge and self-management skills)	Foot hygiene	III	193
	Toenail trimming (low-risk foot)	IV	*
	Soaking feet, prohibition	IV	*
	Skin moisturizers	IV	*
	Footwear selection	I-A	176
	Avoidance of foot trauma	II-A	11,21,87,150
	Daily surveillance of the foot	IV	*
	When to consult medical care	IV	*
Educational assessment	Patient's ability to conduct self-foot exam and respond to high-risk conditions	III	195,196

*No references provided for recommendations based on expert opinion (IV). †High-risk (one or more of the following conditions): LOPS, evidence of increased pressure, limited joint mobility, bony deformity including amputation, PVD, or a current or past foot ulcer; low-risk: none of the listed conditions. LOPS, loss of protective sensation; PVD, peripheral vascular disease.

evaluated. Experts also suggest that people with neuropathy should also be advised to break in the new shoes gradually to minimize the formation blisters and ulcers.

Exercise

Exercise is an important management tool for people with diabetes that must be modified for individuals with high-risk foot conditions. Experts recommend non-weight-bearing or low-impact exercise, such as swimming or bicycle riding. These types of exercises will provide cardiovascular and metabolic benefits but may not provide calcium retention for prevention of osteoporosis.

Economic implications

The economic impact of foot-related problems in people with diabetes is considerable. However, cost has been difficult to assess because of the rapid changes in health care over the past 15 years. For example, in 1985, a hospital in southern California charged \$23,500 for a vascular bypass and \$24,700 for an amputation (197) but in 1990, the Deaconess Hospital in Boston, Massachusetts charged on average \$15,981 for a vascular bypass and \$18,341 for an amputation (198). This may reflect geographic differences in charges, but also reflects the shift to shorter length of stay and cost-containment efforts. In 1992, the average hospital reimbursement for a lower-extremity amputation from the Medicare program was \$10,969, compared with \$26,940 from private insurers. During this same period, rehabilitation was moved from the acute care hospital to rehabilitation facilities and nursing homes, and was reimbursed in 1992 at a rate of \$7,000 to \$21,000 per person.

In contrast, the costs for the preventive strategies listed above are negligible. Foot exams take less than 5 min of a primary care provider's time and monofilaments cost less than \$25. Patient education and debridement of the nails and callus are generally reimbursed and have a low cost. In 1998, insoles off the shelf cost \$5 to \$20, custom insoles cost up to \$200, depth shoes (\$150 to \$200), and custom-molded shoes up to \$500. Medicare's evaluation of therapeutic footwear for diabetic people with high-risk conditions found the program to be cost neutral (199). No formal cost-benefit analyses or modeling of preventive foot care has been published yet, but would be valuable.

SUMMARY — A number of effective, low-cost strategies are available to identify

and treat the person at risk for diabetic foot ulcers and lower-extremity amputation. These strategies must be more widely adopted by all diabetic care providers to maintain the integrity and function of the lower limb, and thus improve the quality of life for people with diabetes.

APPENDIX

Methods for the Technical Review on foot care

This Technical Review is based on original research published in English peer-reviewed literature. The articles were restricted to human subjects and excluded abstracts and unpublished work. Emphasis was given to clinically important outcomes, especially those that matter to patients, rather than disease-oriented outcomes.

The type of evidence for studies on prognosis, risk factor identification, and interventions was scored using a modification of the U.S. Preventive Services Task Force Criteria (Table A1). The highest level of evidence was used for scoring; however, if only one small study was available, the next lower level was included in the designation.

Interventional studies under the control of the investigator were graded as level I. Randomized controlled trials and well-designed crossover studies were coded as I-A. Controlled, nonrandomized studies, coded as II-1 in the U.S. Preventive Task Force classification system, were graded as I-B because the quality and inferences were more similar to I-A studies.

Level II involved various observational study designs that permit the association of a risk or treatment with outcomes, but cannot confirm causation or efficacy of treatment. Analytic studies (i.e., case-control, cohort data) were coded as II-A. Data from population-based time series data, such as vital statistics or utilization data (i.e., hospital discharge records) were coded as II-B. Population-based cross sectional data (i.e., National Health Interview Study) were coded as II-C.

Studies involving descriptive cases, case series, or comparisons of case series, even if the study called one group "controls," were coded as level III. Evidence entirely based on expert opinion was identified as level IV. Both of these categories of data are used for hypothesis generation.

Data for the clinical management of the foot in diabetic patients without a current ulcer are given in Table A2.

Screening and diagnostic tests do not fit into the U.S. Preventive Services Task Force Classification system, so were evaluated differently. All tests had to have a gold standard and a clear outcome, preferably a patient-oriented rather than disease-oriented outcome. An example of this would be the preference for a screening test that predicted the risk of ulceration over a test that predicted a nerve conduction value <2 SDs. The evaluation had to provide clear definitions for the test and outcomes, and provide details on the test characteristics, including sensitivity, specificity, and reproducibility. The more generalized the population, the better; or the replication of the study was also counted. Studies of test characteristics that met all of the criteria were coded as (X); those that met at least half, but not all, of the criteria were coded as (Y).

References

1. Litzelman DK, Slemenda CW, Langefeld CD, Hays LM, Welch MA, Bild DE, Ford ES, Vinicor F: Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitus. *Ann Intern Med* 119:36-41, 1993
2. Edmonds ME, Foster A, Watkins PJ: Can careful foot care in the diabetic patient prevent major amputation? In *Limb Salvage and Amputation for Vascular Disease*. Greenhalgh RM, Jamieson CW, Nicolaidis AN, Eds. Philadelphia, WB Saunders, 1988, p. 407-417
3. Davidson JK, Alogna M, Goldsmith M, Borden J: Assessment of program effectiveness at Grady Memorial Hospital - Atlanta. In *Educating Diabetic Patients*. Steiner G, Lawrence PA, Eds. New York, Springer, 1981, p. 329-348
4. Runyan JW Jr, Vander Zwaag R, Joyner MB, Miller ST: The Memphis Diabetes Continuing Care Program. *Diabetes Care* 3:382-386, 1980
5. Assal JP, Muhlhauser I, Pernet A, Gfeller R, Jorgens V, Berger M: Patient education as the basis for diabetes care in clinical practice and research. *Diabetologia* 28:602-613, 1985
- 6a. American Diabetes Association: Preventive care of the foot in people with diabetes (Position Statement). *Diabetes Care* 21: 2178-2179, 1998
- 6b. U.S. Preventive Task Force: *Guide to Clinical Preventive Services, Report of the U.S. Preventive Services Task Force*. Baltimore, MD, Williams & Wilkins, 1996
7. Woolf SH, Diguseppi CG, Atkins D, Kamerow DB: Developing evidence-based clinical practice guidelines: lessons learned by the U.S. Preventive Services Task Force. *Ann Rev Public Health* 17:511-538, 1996

8. Reiber GE, Boyko EJ, Smith DG: Lower extremity foot ulcers and amputations in diabetes. In *Diabetes in America*. 2nd ed. Harris MI, Cowie CC, Stern MP, Boyko EJ, Reiber GE, Bennett PH, Eds. Washington, DC, U.S. Govt. Printing Office, 1995 (NIH publ. no. 95-1468)
9. Centers for Disease Control: *Diabetes Surveillance, 1993*. Atlanta, GA, U.S. Department of Health and Human Services, 1993
10. Preston SD, Reiber GE, Koepsell TD. *Lower Extremity Amputations and Inpatient Mortality in Hospitalized Persons With Diabetes: National Population Risk Factors and Associations*. PhD thesis. University of Washington, 1993
11. Pecoraro RE, Reiber GE, Burgess EM: Pathways to diabetic limb amputation: basis for prevention. *Diabetes Care* 13:513-521, 1990
12. Larsson J: Lower extremity amputation in diabetic patients. PhD thesis. Lund University, 1994
13. Palumbo JP, Melton LJ: Peripheral vascular disease and diabetes. In *Diabetes in America*. Harris M, Hamman R, Eds. Washington, U.S. Govt. Printing Office, 1985, p. XV 1-21
14. Moss SE, Klein R, Klein BEK: The prevalence and incidence of lower extremity amputation in a diabetic population. *Arch Intern Med* 152:610-616, 1992
15. Rosenqvist U: An epidemiological survey of diabetic foot problems in Stockholm County 1982. *Acta Med Scand* 687 (Suppl.):55-60, 1984
16. Borssen B, Bergenheim T, Lithner F: The epidemiology of foot lesions in diabetic patients aged 15-50 years. *Diabet Med* 7:438-444, 1990
17. Neil HAW, Thompson AV, Thorogood M, Fowler GH, Mann JI: Diabetes in the elderly: the Oxford Community Diabetes Study. *Diabet Med* 6:608-613, 1989
18. Walters DP, Gatling W, Mullee MA, Hill RD: The distribution and severity of diabetic foot disease: a community study with comparison to a non-diabetic group. *Diabet Med* 9:354-358, 1992
19. Huse DM, Oster G, Killen AR, Lacey MJ, Colditz GA: The economic costs of non-insulin-dependent diabetes mellitus. *J Am Med Assoc* 262:2708-2713, 1989
20. Nelson R, Gohdes D, Everhart J, Hartner J, Zwemer F, Pettitt D, Knowler W: Lower-extremity amputations in NIDDM: 12-yr follow-up study in Pima Indians. *Diabetes Care* 11:8-16, 1988
21. Mayfield JA, Reiber GE, Nelson RG, Greene T: A foot risk classification system to predict diabetic amputation in Pima Indians. *Diabetes Care* 19:704-709, 1996
22. Selby JV, Zhang D: Risk factors for lower extremity amputation in persons with diabetes. *Diabetes Care* 18:509-516, 1995
23. Lehto S, Pyorala K, Ronnema T, Laakso M: Risk factors predicting lower extremity amputations in patients with NIDDM. *Diabetes Care* 19:607-612, 1996
24. Lavery LA, Ashry HR, vanHoutum W, Pugh JA, Harkless LB, Basu S: Variation in the incidence and proportion of diabetes-related amputations in minorities. *Diabetes Care* 19:48-52, 1996
25. Reiber GE, Pecoraro RE, Koepsell TD: Risk factors for amputation in patients with diabetes mellitus. *Ann Intern Med* 117:97-105, 1992
26. Masson EA, Angle S, Roseman P, Soper C, Wilson I, Cotton M, Boulton AJM: Diabetic foot ulcers: do patients know how to protect themselves? *Practical Diabetes* 6:22-23, 1989
27. Lee J, Lu M, Lee V, Russel D, Bahr C, Lee E: Lower extremity amputation: incidence, risk factors, and mortality in the Oklahoma Indian Diabetes Study. *Diabetes* 42:876-882, 1993
28. Chaturvedi N, Stephenson JM, Fuller JH, The EURODIAB IDDM Complications Study Group: The relationship between smoking and microvascular complications in the EURODIAB IDDM Complications Study. *Diabetes Care* 18:785-792, 1995
29. *Smoking and Health: A Report of the Surgeon General*. Office of Smoking and Health, U.S. Department of Health, Education, and Welfare. Washington, DC, U.S. Govt. Printing Office, 1979
30. Janka HU, Ziegler AG, Standl E, Mehnert H: Daily insulin dose as a predictor of macrovascular disease in insulin treated non-insulin-dependent diabetics. *Diabetologia* 13:359-64, 1987
31. West KM, Ahuja MMS, Bennett PH, Czyzyk A, Mateo de Acosta O, Fuller JH, Grab B, Grabauskas V, Jarrett RJ, Kosaka K, Keen H, Krolewski AS, Miki E, Schiack V, Teuscher A, Watkins PJ, Stober JA: The role of circulating glucose and triglyceride concentrations and their interactions with other "risk factors" as determinants of arterial disease in nine diabetic population samples from the WHO Multinational Study. *Diabetes Care* 6:361-369, 1983
32. World Health Organization Multinational Study of Vascular Disease in Diabetics, Diabetes Drafting Group: Prevalence of small vessel and large vessel disease in diabetic patients from 14 centres. *Diabetologia* 28:615-640, 1985
33. Boyko EJ, Ahroni JH, Davignon DSV, Prigeon RL, Smith DG: Diagnostic utility of the history and physical examination for peripheral vascular disease among patients with diabetes mellitus. *J Clin Epidemiol* 50:659-668, 1997
34. Young MJ, Breddy JL, Veves A, Boulton AJM: The prediction of diabetic neuropathic foot ulceration using vibration perception thresholds: a prospective study. *Diabetes Care* 17:557-560, 1994
35. McNeely MJ, Boyko EJ, Ahroni JH, Stensel VL, Reiber GE, Smith DG, Pecoraro RE: The independent contributions of diabetic neuropathy and vasculopathy in foot ulceration. *Diabetes Care* 18:216-219, 1995
36. Janka HU, Standl E, Mehnert H: Peripheral vascular disease in diabetes mellitus and its relation to cardiovascular risk factors: screening with the Doppler ultrasonic technique. *Diabetes Care* 3:207-213, 1980
37. Kumar S, Ashe HA, Fernando DJS, Tsigos C, Young RJ, Ward JD, Boulton AJM: The prevalence of foot ulceration and its correlates in type 2 diabetic patients: a population-based study. *Diabet Med* 11:480-484, 1994
38. Young RJ, Zhou YQ, Rodriguez E, Prescott RJ, Ewing DJ, Clarke BF: Variable relationship between peripheral somatic and autonomic neuropathy in patients with different syndromes of diabetic polyneuropathy. *Diabetes Care* 35:192-197, 1986
39. Adler AI, Boyko EJ, Ahroni JH, Stensel V, Forsberg RC, Smith DG: Risk factors for diabetic peripheral sensory neuropathy. *Diabetes Care* 20:1162-1167, 1997
40. Franklin GM, Shetterly SM, Cohen JA, Baxter J, Hamman RF: Risk factors for distal symmetric neuropathy in NIDDM. *Diabetes Care* 17:1172-1177, 1994
41. American Diabetes Association, American Academy of Neurology: Report and recommendations of the San Antonio Conference on Diabetic Neuropathy. *Diabetes Care* 11:592-597, 1988
42. Pirart J: Diabetes mellitus and its degenerative complications: a prospective study of 4,400 patients observed between 1947 and 1973. *Diabetes Care* 1:168-262, 1978
43. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, Wilson DM, O'Brien PC, Melton LJ: The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. *Neurology* 43:817-824, 1993
44. Franklin GM, Kahn LB, Baxter J, Marshall JA, Hamman RF: Sensory neuropathy in non-insulin-dependent diabetes mellitus: the San Luis Valley Diabetes Study. *Am J Epidemiol* 131:633-643, 1990
45. Harris M, Eastman R, Cowie C: Symptoms of sensory neuropathy in adults with NIDDM in the U.S. population. *Diabetes Care* 16:1446-1452, 1993
46. Edmonds ME, Roberts VC, Watkins PJ: Blood flow in the diabetic neuropathic foot. *Diabetologia* 22:9-15, 1982
47. Corbin DOC, Young RJ, Morrison DC, Hoskins P, McDicken WN, Housley E, Clarke BF: Blood flow in the foot, polyneuropathy and foot ulceration in diabetes mellitus. *Diabetologia* 30:468-473, 1987

- 1987
48. Dyck PJ, Bushek W, Spring EM, Karnes JL, Litchy WJ, O'Brien PC, Service FJ: Vibratory and cooling detection thresholds compared with other tests in diagnosing and staging diabetic neuropathy. *Diabetes Care* 10:432-440, 1987
 49. Dyck PJ, Karnes JL, Daube J, O'Brien PSFJ: Clinical and neuropathological criteria for the diagnosis and staging of diabetic polyneuropathy. *Brain* 108:861-880, 1985
 50. Dyck PJ: Evaluation procedures to detect, characterize, and assess the severity of diabetic neuropathy. *Diabet Med* 8:48-51, 1991
 51. Dyck PJ: Quantitating severity of neuropathy. In *Peripheral Neuropathy*. 3rd ed. Dyck PJ, Thomas PK, Griffin JW, Low PA, Poduslo JF, Eds. Philadelphia, WB Saunders, 1993, p. 686-697
 52. Maser RE, Nielsen VK, Bass EB, Manjoo Q, Dorman JS, Kelsey SF, Becker DJ, Orchard TJ: Measuring diabetic neuropathy, assessment and comparison of clinical examination and quantitative sensory testing. *Diabetes Care* 12:270-275, 1989
 53. Neumann C, Branchtein L, Schmid H: Severe autonomic neuropathy: how many symptoms? *Diabetes Care* 18:133-134, 1995
 54. Liniger C, Albeanu A, Bloise D, Assal J: The tuning fork revisited. *Diabet Med* 7:859-864, 1990
 55. Boulton AJM, Kubrusly DB, Bowker JH, Gadia MT, Quintero L, Becker DM, Skyler JS, Sosenko JM: Impaired vibratory perception and diabetic foot ulceration. *Diabet Med* 3:335-337, 1986
 56. Fruhstorfer H, Lindblom U, Schmidt WG: Method for quantitative estimation of thermal thresholds in patients. *J Neurol Neurosurg Psychiatry* 39:1071-1075, 1976
 57. Chan AW, MacFarlane IA, Bowsher D, Campbell JA: Weighted needle pinprick sensory thresholds: a simple test of sensory function in diabetic peripheral neuropathy. *J Neurol Neurosurg Psych* 55:56-59, 1992
 58. Litzelman DK, Marriott DJ, Vinicor F: Independent physiological predictors of foot lesions in patients with NIDDM. *Diabetes Care* 20:1273-1278, 1997
 59. Gerr FE, Letz R: Reliability of a widely used test of peripheral cutaneous vibration sensitivity and a comparison of two testing protocols. *Br J Ind Med* 45:635-639, 1988
 60. Sekuler R, Nash D, Armstrong R: Sensitive, objective procedure for evaluating response to light touch. *Neurology* 23:1282-1291, 1973
 61. Thivolet C, El Farkh J, Petiot A, Simonet C, Tourniaire J: Measuring vibration sensations with graduated tuning fork. *Diabetes Care* 13:1077-1080, 1990
 62. Bell-Krotoski JA: Sensibility testing: current concepts. In *Rehabilitation of the Hand: Surgery and Therapy*. 3rd ed. Hunter JM, Schneider LH, Mackin EJ, Callahan AD, Eds. St. Louis, MO, CV Mosby, 1989, p. 109-128
 63. Levin S, Pearsall G, Ruderman RJ: Von Frey's method of measuring pressure sensibility in the hand: an engineering analysis of the Weinstein-Semmes pressure aesthesiometer. *J Hand Surg* 3:211-216, 1978
 64. Holewski JJ, Stess RM, Graf PM, Grunfeld C: Aesthesiometry: quantification of cutaneous pressure sensation in diabetic peripheral neuropathy. *J Rehabil Res Dev* 25:1-10, 1988
 65. Birke JA, Sims DS: Plantar sensory threshold in the ulcerative foot. *Lepr Rev* 57:261-267, 1986
 66. Sosenko JM, Kato M, Soto R, Bild DE: Comparison of quantitative sensory-threshold measures for their association with foot ulceration in diabetic patients. *Diabetes Care* 13:1057-1061, 1990
 67. Kumar S, Fernando DJS, Veves A, Knowles EA, Young MJ, Boulton AJM: Semmes-weinstein monofilaments: a simple, effective and inexpensive screening device for identifying diabetic patients at risk of foot ulceration. *Diabetes Care* 13:63-68, 1991
 68. Rith-Najarian SJ, Stolusky T, Gohdes DM: Identifying diabetic patients at high risk for lower-extremity amputation in a primary health care setting. *Diabetes Care* 15:1386-1389, 1992
 69. Tsigos C, White A, Young RJ: Discrimination between painful and painless diabetic neuropathy based on testing of large somatic nerve and sympathetic nerve function. *Diabet Med* 9:359-365, 1992
 70. Veves A, Manes C, Murray HJ, Young MJ, Boulton AJM: Painful neuropathy and foot ulceration in diabetic patients. *Diabetes Care* 16:1187-1189, 1993
 71. Mayne N: The short-term prognosis in diabetic neuropathy. *Diabetes* 17:270-273, 1968
 72. Young RJ, Ewing DJ, Clarke BF: Chronic and remitting painful diabetic polyneuropathy. *Diabetes Care* 11:34-40, 1988
 73. Benbow SJ, Chan AW, Bowsher D, MacFarlane IA, Williams G: A prospective study of painful symptoms, small-fibre function and peripheral vascular disease in chronic painful diabetic neuropathy. *Diabet Med* 11:17-21, 1994
 74. Bischoff A: The natural course of diabetic neuropathy: a follow-up. *Horm Metab Res* 9:98-100, 1980
 75. Boulton AJM, Armstrong WD, Scarpello JHB, Ward JD: The natural history of painful diabetic neuropathy: a 4 year study. *Postgrad Med J* 59:556-559, 1983
 76. Boulton A: What causes neuropathic pain? *J Diabetes Complications* 6:58-63, 1992
 77. Cavanagh PR, Simoneau GG, Ulbrecht JS: Ulceration, unsteadiness, and uncertainty: the biomechanical consequences of diabetes mellitus. *J Biomechanics* 26:23-40, 1993
 78. Ciercteko GC, Dhanendran M, Hutton WC, Lequesne LP: Vertical forces acting on the feet of diabetic patients with neuropathic ulceration. *Br J Surg* 68:608-614, 1981
 79. Veves A, Van Ross ER, Boulton AJ: Foot pressure measurements in diabetic and nondiabetic amputees. *Diabetes Care* 15:905-907, 1992
 80. Veves A, Murray HJ, Young MJ, Boulton AJM: The risk of foot ulceration in diabetic patients with high foot pressure: a prospective study. *Diabetologia* 35:660-663, 1992
 81. Boulton AJM, Hardisty CA, Betts RP, Franks CI, Worth RC, Ward JD, Duckworth T: Dynamic foot pressure and other studies as diagnostic and management aids in diabetic neuropathy. *Diabetes Care* 6:26-33, 1983
 82. Boulton AJM, Betts RP, Franks CI, Ward JD, Duckworth T: The natural history of foot pressure abnormalities in neuropathic diabetic subjects. *Diabetic Res* 5:73-77, 1987
 83. Cavanagh PR, Hewitt FG Jr, Perry JE: Inshoe plantar pressure measurement: a review. *Foot* 2:185-194, 1992
 84. Cavanagh PR, Sims DS Jr, Sanders LJ: Body mass is a poor predictor of peak plantar pressure in diabetic men. *Diabetes Care* 14:750-755, 1991
 85. Coughlin MS: Mallet toes, hammer toes, claw toes, and corns: causes and treatments of lesser toe deformities. *Postgrad Med* 75:191-198, 1984
 86. Habershaw G, Donovan JC: Biomechanical considerations of the diabetic foot. In *Management of Diabetic Foot Problems*. Kozak GP, Hoar CS, Rowbotham JL, Wheelock FC, Gibbons GW, Campbell D, Eds. Philadelphia, WB Saunders, 1984, p. 32-44
 87. Apelqvist J, Larsson J, Agardh CD: The influence of external precipitating factors and peripheral neuropathy on the development and outcome of diabetic foot ulcers. *J Diabetes Complications* 4:21-25, 1990
 88. Gooding GAW, Stess RM, Graf PM: Sonography of the sole of the foot: evidence for loss of foot pad thickness in diabetes and its relationship to ulceration of the foot. *Invest Radiol* 21:45-48, 1986
 89. Boulton AJM, Betts RP, Franks CI, Newrick PG, Ward JD, Duckworth T: Abnormalities of foot pressure in early diabetic neuropathy. *Diabet Med* 4:225-228, 1987
 90. Lavery LA, Lavery DC, Quebedeaux-Farnham TL: Increased foot pressures after great toe amputation in diabetes. *Diabetes Care* 18:1460-1462, 1995
 91. Rosenbloom AL, Silverstein JH, Lezotte DC, Riley WJ, Maclaren NK: Limited joint

- mobility in childhood diabetes mellitus indicates increased risk of microvascular disease. *N Engl J Med* 305:191-194, 1982
92. Mueller MJ, Diamond JE, Delitto A, Sina-core DR: Insensitivity, limited joint mobility, and plantar ulcers in patients with diabetes mellitus. *Phys Ther* 69:453-462, 1989
 93. Fernando DJS, Masson EA, Veves A, Boulton AJM: Relationship of limited joint mobility to abnormal foot pressures and diabetic foot ulceration. *Diabetes Care* 14:8-11, 1991
 94. Birke JA, Franks BD, Foto JG: First ray joint limitation, pressure, and ulceration of the first metatarsal head in diabetes mellitus. *Foot Ankle Int* 16:277-284, 1995
 95. Delbridge L, Perry P, Marr S, Arnold N, Yue DK, Turtle JR, Reeve TS: Limited joint mobility in the diabetic foot: relationship to neuropathic ulceration. *Diabet Med* 5:333-337, 1988
 96. Grgic A, Rosenbloom AL, Weber FT, Giordano B, Malone JL, Shuster JJ: Joint contracture: common manifestation of childhood diabetes mellitus. *J Pediatr* 88:584-588, 1976
 97. Shinabarger NI: Limited joint mobility in adults with diabetes mellitus. *Phys Ther* 67:215-218, 1987
 98. Elveru RA, Rothstein JM, Lamb RL: Goniometric reliability in a clinical setting. *Phys Ther* 68:672-677, 1988
 99. Mueller MJ, Minor SD, Sahrman SA, Schaaf JA, Strube MJ: Differences in the gait characteristics of patients with diabetes and peripheral neuropathy compared with age-matched controls. *Phys Ther* 74:299-313, 1994
 100. Simoneau GG, Ulbrecht JS, Derr JA, Becker MB, Cavanagh PR: Postural instability in patients with diabetic sensory neuropathy. *Diabetes Care* 17:1411-1421, 1994
 101. Cavanagh PR, Derr JA, Ulbrecht JS, Maser RE, Orchard TJ: Problems with gait and posture in neuropathic patients with insulin-dependent diabetes mellitus. *Diabet Med* 9:469-474, 1992
 102. Masson EA, Hay EM, Stockley I, Veves A, Betts RP, Boulton AJM: Abnormal foot pressures alone may not cause ulceration. *Diabet Med* 6:426-428, 1989
 103. Delbridge L, Ellis CS, Robertson K, Lequesne LP: Non-enzymatic glycosylation of keratin from the stratum corneum of the diabetic foot. *Br J Dermatol* 112:547-554, 1985
 104. Gibbs RC, Boxer MC: Abnormal biomechanics of feet and their cause of hyperkeratoses. *J Am Acad Dermatol* 6:1061-1069, 1982
 105. Murray HJ, Young MJ, Hollis S, Boulton AJM: The association between callus formation, high pressures and neuropathy in diabetic foot ulceration. *Diabet Med* 13:979-982, 1996
 106. Young MJ, Cavanagh PR, Thomas G, Johnson MM, Murray H, Boulton AJM: The effect of callus removal on dynamic plantar foot pressures in diabetic patients. *Diabetes Med Suppl* 9:55-57, 1992
 107. Rosen RC, Davids MS, Bohanske LM, Lemont H: Hemorrhage into plantar callus and diabetes mellitus. *Cutis* 35:339-341, 1985
 108. Brand PW: Repetitive stress in the development of diabetic foot ulcers. In *The Diabetic Foot*. 4th ed. Levin ME, Davidson JK, Eds. St. Louis, MO, Mosby, 1988, p. 83-90
 109. Benbow SJ, Chan AW, Bowsher DR, Williams G, Macfarlane IA: The prediction of diabetic neuropathic plantar foot ulceration by liquid-crystal contact thermography. *Diabetes Care* 17:835-839, 1994
 110. Archer AG, Roberts VC, Watkins PJ: Blood flow patterns in painful diabetic neuropathy. *Diabetologia* 27:563-567, 1984
 111. Clark RP, Goff MR, Hughes J, Klenerman L: Thermography and pedobarography in the assessment of tissue damage in neuropathic and atherosclerotic feet. *Thermology* 3:15-20, 1989
 112. Chan AW, MacFarlane IA, Bowsher DR: Contact thermography of painful diabetic neuropathic foot. *Diabetes Care* 14:918-922, 1991
 113. Armstrong DG, Lavery LA, Liswood PJ, Todd WF, Tredwell JA: Infrared dermal thermometry for the high-risk diabetic foot. *Phys Ther* 77:169-177, 1997
 114. Birke JA, Sims DS: The insensitive foot. In *Physical Therapy of the Foot and Ankle*. Hunt GC, Ed. New York, Churchill Livingstone, 1988, p. 133-168
 115. Kannel WB, McGee DL: Diabetes and cardiovascular disease: the Framingham Study. *J Am Med Assoc* 241:2035-2038, 1979
 116. Melton LJ III, Macken KM, Palumbo PJ, Elveback LR: Incidence and prevalence of clinical peripheral vascular disease in a population-based cohort of diabetic patients. *Diabetes Care* 3:648-654, 1980
 117. Kreines K, Johnson E, Albrink M, Knatterud GL, Levin ME, Lewitan A, Newberry W, Rose FA: The course of peripheral vascular disease in non-insulin-dependent diabetes. *Diabetes Care* 8:235-243, 1985
 118. Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977-986, 1993
 119. Strandness DE Jr, Priest RE, Gibbons GE: Combined clinical and pathologic study of diabetic and nondiabetic peripheral arterial disease. *Diabetes* 13:366-372, 1964
 120. Conrad MC: Large and small artery occlusion in diabetics and nondiabetics with severe vascular disease. *Circulation* 36:83-91, 1967
 121. Pecoraro RE, Ahroni JH, Boyko EJ, Stensel VL: Chronology and determinants of tissue repair in diabetic lower-extremity ulcers. *Diabetes Care* 40:1305-1313, 1991
 122. Holstein P: The distal blood pressure predicts healing of amputations on the feet. *Acta Orthop Scand* 55:227-233, 1984
 123. Hiatt WR, Marshall JA, Baxter J, Sandoval R, Hildebrandt W, Kahn LR, Hamman RF: Diagnostic methods for peripheral arterial disease in the San Luis Valley Diabetes Study. *J Clin Epidemiol* 43:597-606, 1990
 124. Carter SA: Clinical measurement of systolic pressures in limbs with arterial occlusive disease. *JAMA* 207:1869-1874, 1969
 125. European Society of Vascular Surgery: Chronic Critical Leg Ischaemia. *Eur J Vasc Surg* 6:1-3, 1992
 126. Fowkes F: The measurement of atherosclerotic peripheral arterial disease and epidemiologic surveys. *Int J Epidemiol* 17:248-254, 1988
 127. Rose GA, Blackburn H, Gillum RF, Prineas RJ: *Cardiovascular Survey Methods*. Geneva, Switzerland, World Health Org., 1982 (WHO Monograph Series, no. 56)
 128. Criqui MH, Fronek A, Klauber MR, Barrett-Connor E, Gabriel S: The sensitivity, specificity, and predictive value of traditional clinical evaluation of peripheral arterial disease: results from noninvasive testing in a defined population. *Circulation* 71:516-522, 1985
 129. Marinelli MR, Beach KW, Glass MJ, Primozich JF, Strandness DE Jr: Noninvasive testing versus clinical evaluation of arterial disease. *J Am Med Assoc* 241:2031-2034, 1979
 130. Barnhorst DA, Barner HB: Prevalence of congenitally absent pedal pulses. *N Engl J Med* 278:264-265, 1968
 131. Silverman JJ: Incidence of palpable dorsalis pedis and posterior tibial pulsations in soldiers. *Am Heart J* 32:82-87, 1946
 132. Ludbrook J, Clarke AM, McKenzie JK: Significance of absent ankle pulse. *Br Med J* (No. 5294):1724-1726, 1962
 133. Meade TW, Gardner MJ, Cannon P, Richardson PC: Observer variability in recording the peripheral pulses. *Br Heart J* 30:661-665, 1968
 134. Lawson IR, Ingman SR, Masih Y, Freeman B: Reliability of palpation of pedal pulses as ascertained by the kappa statistic. *J Am Geriatrics Soc* 28:300-303, 1980
 135. Brearley S, Shearman CP, Simms MH: Peripheral pulse palpation: an unreliable physical sign. *Ann R Coll Surg Engl* 74:169-171, 1992
 136. Christensen JH, Freundlich M, Jacobsen BA, Falstie-Jensen N: Clinical relevance of pedal pulse palpation in patients suspected of peripheral arterial insufficiency. *J Intern Med* 226:95-99, 1989
 137. Osmundson PJ, O'Fallon WM, Clements

- IP, Kazmier FJ, Zimmerman Br, Palumbo: Reproducibility of noninvasive tests of peripheral occlusive arterial disease. *J Vasc Surg* 2:678-683, 1985
138. Lazarus HM, Albo D Jr, Welling D, Hutto W: Doppler ankle pressures and stiff arteries. In *Noninvasive Cardiovascular Diagnosis Current Concepts*. Diethrich EB, Ed. Baltimore, University Park Press, 1978, p. 127-135
139. Everhart JE, Pettitt DJ, Knowler WC, Rose FA, Bennett PH: Medial arterial calcification and its association with mortality and complications of diabetes. *Diabetologia* 31, 1988
140. Young MJ, Adams JE, Boulton AJM, Cavanagh PR: Medial arterial calcification in the feet of diabetic patients and matched non-diabetic control subjects. *Diabetologia* 36:615-621, 1993
141. Goebel FD, Fuessl HS: Monckeberg's sclerosis after sympathetic denervation in diabetic and non-diabetic subjects. *Diabetologia* 24:347-350, 1983
142. Emanuele MA, Buchanan BJ, Abaira C: Elevated leg systolic pressures and arterial calcification in diabetic occlusive vascular disease. *Diabetes Care* 4:289-292, 1981
143. Duprez D, Missault LWA, Clement DL: Comparison between ankle and toe index in patient with peripheral arterial disease. *Int Angiol* 6:295-297, 1987
144. Bone GE, Pomajzl MJ: Toe blood pressure by photoplethysmography: an index of healing in forefoot amputation. *Surgery* 89:569-574, 1981
145. Carter SA, Strandness DE Jr: Measurement of distal arterial blood pressure: a simple and valuable guide to the diagnosis and therapy of arterial occlusive disease. *Scand J Clin Lab Invest* 128:357-361, 1973
146. Uccioli L, Monticone G, Durola L, Russo F, Mormile F, Mennuni G, Menzinger G: Autonomic neuropathy influences great toe blood pressure. *Diabetes Care* 17:284-287, 1994
147. Orchard TJ, Strandness DE Jr: Assessment of peripheral vascular disease in diabetes: report and recommendations of an international workshop sponsored by the American Diabetes Association and the American Heart Association September 18-20, 1992 New Orleans, *Circulation* 88:819-28, 1993
148. Moneta GL, Strandness GL: Peripheral arterial duplex scanning. *J Card Ultrasound* 115:645-651, 1987
149. Chantelau E, Haage P: An audit of cushioned diabetic footwear: relation to patient compliance. *Diabet Med* 11:114-116, 1994
150. Edmonds ME, Blundell MP, Morris ME, Thomas EM, Cotton LT, Watkins PJ: Improved survival of the diabetic foot: the role of a specialized foot clinic. *Q J Med* 60:763-771, 1986
151. Sims DS Jr, Cavanagh PR, Ulbrecht JS: Risk factors in the diabetic foot. *J Am Phys Ther Assoc* 68:1887-1902, 1988
152. Duffy JC, Patout CA Jr: Management of the insensitive foot in diabetes: lessons learned from Hansen's disease. *Mil Med* 155:575-579, 1990
153. Brill LR, Cavanaugh PR, Doucette, Margaret M, Ulbrecht JS: *Prevention, Protection and Recurrence Reduction of Diabetic Neuropathic Foot Ulcers*. East Setauket, NY, Curative Technologies, 1994
154. Mazze R, Deeb L, Palumbo PJ: Altering Physicians' Practice Patterns: A Nationwide Educational Experiment: evaluation of the Clinical Education Program of the American Diabetes Association. *Diabetes Care* 9:420-425, 1986
155. Deeb LC, Pettijohn FP, Shirah JK, Freeman G: Interventions among primary-care practitioners to improve care for preventable complications of diabetes. *Diabetes Care* 11:275-280, 1988
156. Payne TH, Gabella BA, Michael SL, Young WF, Pickard J, Hofeldt FD, Fan F, Stomberg JS, Hamman RF: Preventive care in diabetes mellitus: current practice in urban health-care system. *Diabetes Care* 12:745-747, 1989
157. Mayfield JA, Rith-Najarian SJ, Acton KJ, Schraer CD, Stahn RM, Johnson MH, Gohdes D: Assessment of diabetes care by medical record review. *Diabetes Care* 17:918-923, 1994
158. Cohen SJ: Potential barriers to diabetes care. *Diabetes Care* 6:499-500, 1983
159. del Aguila MA, Reiber GE, Koepsell TD: How does provider and patient awareness of high-risk status for lower-extremity amputation influence foot-care practice? *Diabetes Care* 17:1050-1054, 1994
160. Tillo TH, Giurini JM, Habershaw GM, Chrzan JS, Rowbotham JL: Review of metatarsal osteotomies for the treatment of neuropathic ulcerations. *J Am Podiatr Med Assoc* 80:211-217, 1990
161. Patel VG, Wieman TJ: Effect of metatarsal head resection for diabetic foot ulcers on the dynamic plantar pressure distribution. *Am J Surg* 167:297-300, 1994
162. Brand FN, Abbott RD, Kannel WB: Diabetes, intermittent claudication, and risk of cardiovascular events. *Diabetes* 38:504-509, 1989
163. Widmer LK, Biland L: Incidence and course of occlusive peripheral artery disease in geriatric patients. *Int Angiol* 4:289-294, 1985
164. Creasy TS, McMillan PJ, Fletcher EWL, Collin J, Morris PJ: Is percutaneous transluminal angioplasty better than exercise for claudication? Preliminary results from a prospective randomized trial. *Eur J Vasc Surg* 4:135-140, 1990
165. Williams LR, Ekers MA, Collins PS, Lee JF: Vascular rehabilitation: benefits of a structured exercise/risk modification program. *J Vasc Surg* 14:320-326, 1991
166. Currie ID, Wilson YG, Baird RN, Lamont PM: Treatment of intermittent claudication: the impact on quality of life. *Eur J Vasc Surg* 10:356-361, 1995
167. Conte MS, Belkin M, Donaldson MC, Baum P, Mannick JA, Whittmore AD: Femortibial bypass for claudication: do results justify an aggressive approach? *J Vasc Surg* 21:873-881, 1995
168. Wolf GL, Wilson SE, Cross AP, Deupree RH, Stason WB: Surgery and balloon angioplasty for peripheral vascular disease: a randomized clinical trial. *J Vasc Interventional Radiol* 4:63-648, 1993
169. Luther M: The influence of arterial reconstructive surgery on the outcome of critical leg. *Eur J Vasc Surg* 8:682-689, 1994
170. LoGerfo FW, Gibbons GW, Pomposelli FB Jr, Campbell DR, Miller A, Freeman DV, Quist WC: Trends in the care of the diabetic foot: expanded role of arterial reconstruction. *Arch Surg* 127:617-621, 1992
171. Tunis SR, Bass EB, Steinberg EP: The use of angioplasty, bypass surgery, and amputation in the management of peripheral vascular disease. *N Engl J Med* 325:556-562, 1991
172. Plummer ES, Albert SG: Foot care assessment in patients with diabetes: a screening algorithm for patient education and referral. *Diabetes Educ* 21:47-51, 1995
173. De Backer M, De Vroey C, Lesaffre E, Scheys I, De Keyser P: Twelve weeks of continuous oral therapy for toenail onychomycosis caused by dermatophytes: a double-blind comparative trial of terbinafine 250 mg/day versus itraconazole 200 mg/day. *J Am Acad Dermatol* 38:S57-S63, 1998
174. Goodfield M: Short-duration therapy with terbinafine for dermatophyte onychomycosis: a multicenter trial. *Br J Dermatol* 126 (Suppl. 39):33-35, 1992
175. De Doncker P, Gupta AK, Maynissen G, Stoffels P, Heremans A: Itraconazole pulse therapy for onychomycosis and dermatomycoses: an overview. *J Am Acad Dermatol* 37:968-974, 1997
176. Samow MR, Veves A, Giurini JM, Rosenblum BI, Chrzan JS, Habershaw GM: Inshoe foot pressure measurements in diabetic patients with at-risk feet and in healthy subjects. *Diabetes Care* 17:1002-1006, 1994
177. Rose NE, Feiwel LA, Cracchiolo A, III: A method for measuring foot pressures using a high resolution, computerized insole sensor: the effect of heel wedges on plantar pressure distribution and center of force. *Foot Ankle* 13:263-270, 1992
178. Perry JE, Ulbrecht JS, Derr JA, Cavanagh PR: The use of running shoes to reduce plantar pressures in patients who have diabetes. *J Bone Jt Surg* 77-A:1819-1828, 1995

179. Nawoczenski DA, Birke JA, Coleman WC: Effect of rocker sole design on plantar fore-foot pressures. *J Am Podiatr Med Assoc* 78:455-460, 1988
180. Soulier SM: The use of running shoes in the prevention of plantar diabetic ulcers. *J Am Podiatr Assoc* 76:395-400, 1986
181. Boulton A, Franks C, Betts R, Duckworth T, Ward J: Reduction of abnormal foot pressures in diabetic neuropathy using a new polymer insole material. *Diabetes Care* 7:42-46, 1984
182. Lord M, Hosein R: Pressure redistribution by molded inserts in diabetic footwear: a pilot study. *J Rehabil Res Dev* 31:214-221, 1994
183. Mueller MJ, Strube MJ, Allen BT: Therapeutic footwear can reduce plantar pressures in patients with diabetes and transmetatarsal amputation. *Diabetes Care* 20:637-641, 1997
184. Brodsky JW, Kourosh S, Stills M, Mooney V: Objective evaluation of insert materials for diabetic and athletic footwear. *Foot Ankle* 9:111-116, 1988
185. Veves A, Masson EA, Fernando DJS, Boulton AJM: Use of experimental padded hosiery to reduce abnormal foot pressures in diabetic neuropathy. *Diabetes Care* 12:653-655, 1989
186. Murray HJ, Veves A, Young MJ, Richie DH, Boulton AJM: Role of experimental socks in the care of the high-risk diabetic foot. a multicenter patient evaluation study: American Group for the Study of Experimental Hosiery in the Diabetic Foot. *Diabetes Care* 16:1190-1192, 1993
187. Tovey FI: The manufacture of diabetic footwear. *Diabet Med* 1:69-71, 1984
188. Uccioli L, Faglia E, Monticone G, Favale F, Durola L, Aldeghi A, Quarantiello A, Calia P, Menzinger G: Manufactured shoes in the prevention of diabetic foot ulcers. *Diabetes Care* 18:1376-1378, 1995
189. Breuer U: Diabetic patients' compliance with bespoke footwear after healing of neuropathic foot ulcers. *Diabete Metab* 20:415-419, 1994
190. Bloomgarden ZT, Karmally W, Metzger MJ, Brothers M, Nechemias C, Bookman J, Faierman D, Ginsberg-Fellner F, Rayfield E, Brown WV: Randomized, controlled trial of diabetic patient education: improved knowledge without improved metabolic status. *Diabetes Care* 10:263-272, 1987
191. Barth R, Campbell LV, Allen S, Jupp JJ, Chisholm DJ: Intensive education improves knowledge, compliance, and foot problems in type 2 diabetes. *Diabet Med* 8:111-117, 1991
192. Kruger S, Guthrie D: Foot care: knowledge retention and self-care practices. *Diabetes Educ* 18:487-490, 1992
193. Pieber TR, Holler A, Siebenhofer A, Brunner GA, Semlitsch B, Schattenberg S: Evaluation of a structured teaching and treatment programme for type 2 diabetes in general practice in a rural area of Austria. *Diabet Med* 12:349-354, 1995
194. Malone JM, Snyder M, Anderson G, Bernhard VM, Holloway GA, Bunt TJ: Prevention of amputation by diabetic education. *Am J Surg* 158:520-524, 1989
195. Crausaz FM, Clavel S, Liniger C, Albeanu A, Assal J-P: Additional factors associated with plantar ulcers in diabetic neuropathy. *Diabet Med* 5:771-775, 1988
196. Thomson FJ, Masson EA: Can elderly diabetic patients co-operate with routine foot care? *Age Ageing* 21:333-337, 1992
197. Raviola CA, Nichter LS, Baker JD, Busutil RW: Cost of treating advanced leg ischemia-bypass graft vs primary amputation. *Arch Surg* 123:495-496, 1988
198. Gibbons GW, Marcaccio EJ Jr, Burgess AM, Pomposellil FB Jr, Freeman DV, Campbell DR, Miller A, LoGerfo FW: Improved quality of diabetic foot care, 1984 vs 1990. *Arch Surg* 128:576-581, 1993
199. Wooldridge J, Moreno L: Evaluation of the costs to Medicare of covering therapeutic shoes for diabetic patients. *Diabetes Care* 17:541-547, 1994