National Evidence Based Guidelines for the Management of Type 2 Diabetes Mellitus

Part 6

Detection and Prevention of Foot Problems in Type 2 Diabetes

Prepared by
the Australian Centre for Diabetes Strategies
Prince of Wales Hospital, Sydney
for the Diabetes Australia Guideline Development Consortium

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PART 6

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2.0 Guideline for the Detection and Prevention of Foot Problems in Type 2 Diabetes

2.1 Introduction

Aim of the guideline

This guideline covers issues relating to how foot problems should be defined, assessed, prevented and managed in people with Type 2 diabetes. Its aim is to inform all categories of health professionals of the problems associated with diabetes foot problems and to specifically target general practitioners with this information.

Methods

The Methods used to develop this Guideline are detailed in Part 1. The search terms and results of the literature search are shown in Section 6.1.6.

Quality Assurance

In addition to the methods used to identify and critically appraise the evidence to formulate the guideline recommendations which are described in detail in *Part 1* of this document, the Project Management Team reviewed and checked each step of the methods process and:

- repeated a selection of the searches
- double culled the yield from a selection of the database searches
- double reviewed all articles used as evidence references
- checked all recommendations, evidence statements, evidence tables and search strategy and yield tables

The draft document was reviewed at each step by the Medical Advisor who also reviewed the entire final draft before submission.

Guideline Format

Issues identified by the Expert Working Group (EWG) and from the literature as critical to the impact of foot problems in Type 2 diabetes are shown in point 6.1.2 (next page).

Each of these issues is addressed in a separate section in a format presenting:

- ***Recommendation(s)***
- ***Evidence Statements*** - supporting the recommendations
- ***Background*** **-** to issues for the guideline
- ***Evidence*** - detailing and interpreting the key findings
- ***Summary*** **-** of major evidence found
- ***Evidence tables*** - summarising the evidence ratings for the articles reviewed

The Evidence Tables are important in providing a summary of the key information of studies used to support the Evidence Statements which were used to formulate the Recommendations.

For all issues combined, supporting material appears at the end of the guideline and includes:

- ***Evidence references***
- ***General references***
- ***Other references identified***
- ***Search Strategy and Yield Tables*** documenting the identification of the evidence sources

2.2 Issues for Foot Problems in Type 2 Diabetes

- Is peripheral neuropathy a risk factor for ulceration or amputation?
- Is peripheral vascular disease a risk factor for ulceration or amputation?
- Is foot deformity or a previous amputation a risk factor for ulceration or amputation?
- Is a current or previous ulcer a risk factor for amputation?
- What is the most practical method for detecting loss of protective foot sensation in the primary care setting?
- How should peripheral vascular disease be assessed clinically?
- What should be the frequency of foot examination?
- Does patient education improve footcare and outcomes?
- Does improved glycaemic control decrease the development or progression of peripheral neuropathy?
- Does appropriate footwear reduce ulceration and amputation?
- Do specialist foot clinics and multi-disciplinary teams decrease amputation?
- What are the economic consequences of diabetes foot problems?
- What are the socioeconomic influences on diabetes foot problems?

2.3 Summary of Recommendations

Recommendations
• People with Type 2 diabetes who have peripheral neuropathy should be identified because they are at risk of foot ulceration and amputation
• People with diabetes should be assessed regularly for peripheral vascular disease

• People with diabetes who have had a previous amputation are at high risk of ulceration and further amputation and therefore require regular and frequent review
 	
• People with diabetes should be assessed regularly to detect foot deformities including:
  • Hallux deformities
  • Hammer or claw toes
  • Callus
  • Charcot's foot

• People with diabetes and a current foot ulcer are at high risk for amputation and preventative interventions to lower that risk should be instituted promptly • People with diabetes and a history of a healed previous diabetic foot ulcer should be recognised as having a life long increased risk of recurrent ulceration and amputation
• People with Type 2 diabetes should be routinely assessed with the 10g Semmes-Weinstein monofilament to detect loss of protective foot sensation

• People with diabetes should be assessed for peripheral vascular disease by:
  • enquiring about symptoms of intermittent claudication
  • palpation of pedal pulses

• The routine surveillance for foot problems in people with diabetes should be performed in the following way:
  • in people without established foot problems, the minimum frequency of foot examination should be once a year
  • in people with at risk feet but without a current active problem, foot examination should be performed every 3 to 6 months

• People with diabetes should receive specific footcare education

• Aim to achieve the best possible glycaemic control in people with Type 2 diabetes in order to prevent or reduce the development of peripheral neuropathy which is a major risk factor for foot ulceration and amputation
• People with diabetes should be encouraged to wear properly fitted, cushioned footwear and padded socks • People with diabetes and high risk feet require special attention to footwear
• People with diabetes who have foot ulcers or with high risk feet should be cared for by a multi-disciplinary service which should include a physician and podiatrist and have ready access to a specialist nurse, orthotist and surgeon
• The cost effectiveness of intensified interventions should be considered in the prevention and management of diabetes foot problems
• The influence of socioeconomic factors should be considered in the prevention and management of diabetes foot problems

2.4 Overview of Foot Problems in Diabetes

The most common reason for hospital admission for diabetes is a diabetic foot complication (Young et al, 1993a). People with diabetes are more likely to have an amputation than those without diabetes: 3-fold more likely at age 45-74 and 7-fold more likely for people aged over 75 (Reiber, 1993). About half those having a leg amputation will have a subsequent amputation on the other side (Apelqvist et al, 1993). Half of all non-traumatic amputations are performed in people with diabetes (Pecoraro et al, 1990). Almost all amputations are preceded by an ulcer. Peripheral neuropathy, with or without peripheral vascular disease (PVD), is a major underlying risk factor in people with diabetes developing a foot ulcer. About half of the lower extremity amputations are “major” (below or above knee), while the other half involving the foot or toes are designated “minor”. In Australia there are at least 2600 diabetes-related lower limb amputations each year (Payne, 2000). The Australian National Diabetes Information Audit and Benchmarking (ANDIAB) 2002 survey showed that 24% of people with diabetes attending specialist diabetes centres had peripheral neuropathy, 13% had PVD, 3% had a foot ulcer, 2% had had an amputation in the past and the annual incidence of lower limb amputation was 0.7% (NADC, 2002). The AusDiab Study (Tapp et al, 2003) reported that the prevalence of peripheral neuropathy was 13.1% in those with known diabetes (KDM) and 7.1% in those with newly diagnosed diabetes (NDM). The prevalence of PVD was 13.5% in KDM and 6.9% in NDM.

The St Vincent Declaration called for a 50% reduction in amputation from diabetic gangrene (Krans et al, 1992) and a similar target has been advocated for Australia (Colagiuri et al, 1998). To achieve this goal, the identification of people with diabetes who are at increased risk of subsequent amputation is a major priority. Health professionals require knowledge and resources to identify those at risk and to implement strategies which have been shown to prevent subsequent morbidity in this population. Further research is required into the impact of education in the “at risk” person with diabetes in preventing amputation, the role of a multi-disciplinary team, and the minimum resources needed to provide an effective diabetic foot service.

This guideline has adopted the following definitions to describe risk categories for diabetes foot problems:

“at risk” - people with
- neuropathy **or**
- peripheral vascular disease **or**
- foot deformity

‘high risk’ - people with
- foot deformity with neuropathy or peripheral vascular disease **or**
- previous ulcer **or**
- previous amputation

2.5 Recommendations

Section 1: Diabetes Foot Problems

Issue

Is peripheral neuropathy a risk factor for ulceration or amputation?

Recommendation

People with Type 2 diabetes who have peripheral neuropathy should be identified because they are at risk of foot ulceration and amputation.

Evidence Statements

- Peripheral neuropathy is associated with diabetic foot ulceration and amputation
  Evidence Level III-2

- Peripheral neuropathy predicts diabetic foot ulceration and amputation
  Evidence Level III-2

- Other factors contribute to the increased risk of ulceration and amputation in people with diabetes and peripheral neuropathy
  Evidence Level III-2

Background - Peripheral Neuropathy as a Risk Factor

Fifteen percent of people with diabetes will develop a foot ulcer during their lifetime (Reiber et al, 1998). Half of all non-traumatic amputations are performed in people with diabetes (Pecoraro et al, 1990). Foot ulcers precede 84% of all lower limb amputations in diabetic people in the United States (Pecoraro et al, 1990). While the cause of ulceration is multifactorial, understanding the main factors in the aetiology of the ulcer will increase the likelihood of reducing ulceration and amputation despite the rising prevalence of diabetes.

In the UKPDS study damage to the peripheral nerves from prolonged hyperglycaemia and its metabolic consequences was present in 12.3% at diagnosis and in 30% after 12 years of diabetes (UKPDS 33, 1998). The commonest form is a distal symmetrical polyneuropathy with a glove and stocking distribution of loss of sensation. However the loss of protective sensation is postulated to be the major factor in subsequent ulceration. Coexistence of autonomic neuropathy can contribute partly by inducing dry skin and foot oedema (Boyko et al, 1999). Muscle wasting and foot deformity resulting from peripheral neuropathy are also thought to contribute to the risk of ulceration. Severe peripheral neuropathy can lead to joint disorganisation from repeated trauma with loss of protective sensation resulting in a Charcot joint (most frequently the tarsometatarsal joint). The resulting foot disorganisation and deformity contribute to recurrent ulceration (Sims et al, 1988). However it is also clear that precipitating factors are also necessary for the development of diabetic foot ulcers. Knowing the relative risk of peripheral neuropathy as an underlying risk factor for ulceration and amputation can help in targeting those with diabetes who are at risk and implementing preventative interventions to reduce subsequent ulceration and amputation (Shaw & Boulton, 1997).

Evidence - Peripheral Neuropathy as a Risk Factor

Peripheral neuropathy is associated with diabetic foot ulceration and amputation

Several studies in people with Type 2 diabetes have related reduction of foot sensation and risk of ulceration or amputation.

Coppini et al (1998) reported the incidence of foot ulcers or amputations in 405 subjects without prior amputation attending St Thomas' Hospital Diabetic Clinic. The records were examined retrospectively, and 20 people who developed foot ulcer or amputation over the 14 year follow-up period were each matched with 3 people without ulcers. The population was 60% males with cases being of similar mean age to the controls (50.5 v 50.1 years) however they had a much longer duration of diabetes (9.7 v 4.1 years, p=0.02). A raised VPT at baseline was a predictor of foot complications developing with OR 4.38 (CI 1.1-17.26, p=0.01).

In 811 people with Type 2 diabetes in a community based cross-sectional study from 37 UK general practices, neuropathy was diagnosed by clinical scoring. The population was 50% males with a mean age of 65.4 years (range 34-90 years) and had a duration of diabetes of 7.4 years (range 0-50 years). Those with neuropathy were significantly more likely to have a current or past ulcer than those without (9.8% versus 2.1%, $p \leq 0.01$) (Kumar et al, 1994). In a case-control study of people with diabetes, 76 people with ulceration were compared with 149 control subjects who had never had a foot ulcer. People with an ulcer were similar to the control group in that most had Type 2 diabetes (95 v 93%) and were similar in age (52.7 v 51.8 years) but duration of diabetes was non-significantly longer in the ulcer group (14.5±9.1 v 9.2±8.1 years). In multivariate analysis loss of protective sensation (VPT ≥25 V) had an OR of 32.5 (no CI reported) for ulceration ($p \leq 0.001$) (Lavery et al, 1998).

In a cross-sectional study of African Americans (14.3%), Hispanics (37.5%), and Caucasians (48.2%), Frykberg and coworkers (1998) found peripheral sensory neuropathy (assessed by VPT or monofilament) independently predicted current or past ulceration, OR 4.1 and 4.4 respectively ($p<0.001$ for both groups). The study population was 50% male, had a mean age of 58.5±12.5 years, diabetes duration of 14.3±10.6 years and 80.5% of people had Type 2 diabetes.

In another analysis from the Seattle Veterans Study in people with diabetes, 46 people with an ulcer between 1987 and 1992 were compared with 322 controls from the medical clinic without an ulcer. The control and ulcer cases had a similar proportion of people with Type 2 diabetes (87.0 v 92.7%) and a similar duration of diabetes (13.2 v 12.4 years) but the cases were significantly younger 60.4 v 64.2 years ($p=0.02$). Both vibration sense and monofilament sensation were tested together with ankle-arm blood pressure index and transcutaneous oxygen tension ($TcPO_2$) to assess peripheral circulation. Being insensate to the monofilament gave an adjusted OR of 18.42 (CI 3.83-88.47) for ulceration. The other two independent predictors for ulceration were the absence of the Achilles tendon reflex and a low $TcPO_2$ (McNeeley et al, 1995).

Eighty six people with diabetes and an ulcer presenting to a foot clinic were compared with 49 controls referred to general medical clinics who had diabetes but did not have an ulcer. Those who had an ulcer were similar in age to those who did not (55.3±1.5 v 52.3±2.2 years, p=NS) however they had a longer duration of diabetes (16.1±1.0 v 10.4±1.1 years, $p<0.001$). Abnormal vibratory perception was strongly related to diabetic foot ulceration (OR 10.77, CI 4.59-25.73; $p<0.001$). There was a pattern of increasing odds ratio for ulceration with increasing vibration perception abnormality ($p<0.001$ for trend). The association remained after adjustment for confounding variables (Boulton et al, 1986).

A less rigorous assessment of neuropathy was also performed in another analysis of the Seattle Veterans Study which examined patients at admission for first amputation. This case control analysis assessed 80 consecutively recruited males who were admitted for amputation compared with 236 concurrently selected males who were similar for age 63.4±11.9 v 61.1±10.0 years and duration of diabetes 13.3±10.5 v 10.9±9.7. Neuropathy was considered to be the main underlying factor in 61% of cases (Pecoraro et al, 1990).

A case-control study in Pima Indians by Mayfield and coworkers (1996) compared the medical records of 61 people with amputations over a 9-year period with 183 controls not having amputation over that period. There were significant differences between the cases and the controls with the cases being more likely to be male (53% v 37%, $p=0.05$), be over 65 years of age (20% v 10%, $p=0.001$) and have a greater proportion of subjects with a duration of diabetes ≥25 years (25 v 5%, p<0.001). Peripheral neuropathy was one of the four major contributing risk factors (including PVD, bone deformity and a history of foot ulcers). Each risk factor conveyed an OR for amputation of 2.1 (CI 1.4-3.3) (Mayfield et al, 1996).

Recurrence of foot ulceration is also associated with peripheral neuropathy. In a study from the UK, 26 people with diabetes and relapsing foot ulcers were compared with a group which did not relapse (n=25). Both groups were similar in age (66.4 v 64.6 years), gender (53.8 v 52.0 % male) and duration of diabetes (21.7 v 20.7 years). Those with a relapsing ulcer had a significantly higher vibration threshold compared with those without relapse of ulcer (VPT ≥38 v ≥25, p=0.003) (Mantey et al, 1999).

Peripheral neuropathy predicts diabetic foot ulceration and amputation

Several prospective studies have examined the relationship between peripheral neuropathy and future risk of ulceration or amputation.

Rith-Najarian et al (1992) stratified 406 Native American Indians with diabetes into risk categories based on sensation status using a 5.07 Semmes-Weinstein monofilament at 8 points on the plantar surface of each foot. Those failing to sense the monofilament at one or more locations were retested twice before being classified as insensate. In a follow up of the cohort for 32 months, an ulcer was five times more likely to occur in a person with either a history of ulceration or amputation or loss of monofilament sensation, than in a person without. Comparing those with sensory loss with those without provided a test sensitivity of 90% and specificity of 86% for predicting ulceration with likelihood ratios for a positive test of 5.2 (95% confidence interval (CI) 4.0-6.7) and 0.12 (CI 0.05-0.27) for a negative test. Amputation risk was increased 17 times (CI 4.5-9.5).

A diabetes foot clinic in Manchester used a biothesiometer to categorise subjects without previous ulcer or significant ischaemia at enrolment (Young et al, 1994). In up to 4 years of follow up, using a biothesiometer threshold of > 25V, the test sensitivity for developing a first ulcer was 83% with a specificity of 62% with likelihood ratio for a positive test of 2.2 (CI 1.8-2.5) and for a negative test of 0.27 (CI 0.14-0.48). In these 469 subjects with both Type 1 and Type 2 diabetes without previous ulceration, a vibration perception threshold (VPT) > 25V was associated with a 7.99 (CI 3.65-17.5; p < 0.01) times increased risk of ulceration compared with people who had a VPT < 15V. Recurrent ulceration only occurred in those with VPT > 25V, who had a cumulative 4-year ulcer incidence of 19.8% or 8.3% per year (Young et al, 1994).

In a prospective study of 352 people with Type 2 diabetes, foot lesions were assessed using the Seattle Wound Classification system. Monofilament testing and thermal sensitivity testing were used to identify neuropathy. In this predominantly African American female group (76%) with a mean age 60 years, using multivariate modelling, neuropathy predicted both minor wounds and ulceration (OR 5.23 [CI 2.26-12.13], p≤0.001) (Litzelman et al, 1997a).

Abbott et al (1998) prospectively investigated the incidence of foot ulcer over one year in 1,033 people with Type 1 or Type 2 diabetes with established neuropathy

(VPT ≥ 25 V on at least one foot and VPT ≤ 50 V on both feet) in the UK, US and Canada. For each 1 unit increase in VPT at baseline the risk of ulcer increased by 5.6% and a VPT > 25V carried a sevenfold risk of ulceration over 4 years. Abnormal VPT carried a 7% annual risk of foot ulcer (Abbott et al, 1998).

In a prospective case control study, 213 people with diabetes (both Type 1 and 2) were evaluated for the usefulness of the International Working Group on the Diabetic Foot Classification System (Peters & Lavery, 2001). They were stratified into four risk category groups: no neuropathy (Group 0, n=79), neuropathy without PVD or deformity (Group 1, n=21), neuropathy and/or PVD and/or deformity (Group 2, n=51) and previous history of foot ulcer or a lower-extremity amputation (Group 3, n=62), followed for 3 years and assessed for the development of foot problems. Mean age and duration of diabetes increased significantly with increasing severity of risk classification. Foot ulcers occurred in 5.1, 14.3, 18.8, and 55.8% of people in each of the four groups respectively ($p<0.001$).

In another study by Abbott et al (2002), a cohort of 9,710 people in the UK was assessed at baseline and the final ulceration status of 6,613 people was assessed by postal questionnaire 2 years later. Respondents had a mean age of 61.7±13.3 years, duration of diabetes of 8.6±10.4 and 53.2% were men which was similar to the baseline population. There were 219 people who developed a new foot ulcer during the study period with an annual incidence rate of 2.2%. Univariate analysis found the relative risk (RR) of foot ulcer in those who had a high neuropathy symptom score (5-9) was 1.94 (CI 1.54-2.43, $p<0.0001$) and for those with a high neuropathy disability score (6-10) was 6.28 (CI 4.93-7.99, $p<0.0001$).

A cohort study was conducted in 733 people with diabetes (aged 10-79 years) over a 7-year period (Hamalainen et al, 1999). At baseline, a podiatric examination, neurophysiological and circulatory measurements were performed. 25 people had one or more amputations during the follow-up period. People who had an amputation were more likely to be older ($p<0.001$), have a history of retinopathy ($p<0.001$) and nephropathy ($p=0.023$), and have one or more peripheral pulses absent ($p<0.001$) when compared with people without an amputation. Reduced VPT (OR 14.5 [CI 3.6-57.8], $p=0.0001$), reduced ABI (OR 8.2 [CI 2.8-24.0], $p=0.0001$), and history of retinopathy (OR 6.1 [CI 1.9-19.6], $p=0.0024$) were independently associated with lower extremity amputation.

In a prospective cohort study in the UK, 185 people with diabetic foot ulcers were followed for a mean of 34 months to assess the relative risk of amputation (Moulik et al, 2003). The mean age was 65±13 years, with 64% male, 84% with Type 2 diabetes, 61% with neuropathy and 41% with PVD. Ulcers were categorised as 45% neuropathic, 24% ischaemic and 30% neuroischaemic. At the end of follow-up 30 people had had amputations and the 5 year amputation rates were 11%, 29% and 25% respectively for the above ulcer categories.

The prospective Seattle Foot Study followed 776 US veterans with diabetes until first lower extremity amputation. The subjects were white males with a median age of 65 years (28-91), the majority had Type 2 diabetes (93%) with a median duration of 9 years. The participants were followed for a median of 3.3 years. Neuropathy assessed by insensitivity to the monofilament was associated with a RR for amputation of 2.9

and an OR 1.1-7.8. This study also found that PVD, foot ulcers, former amputation and treatment with insulin were independent risk factors (Adler et al, 1999). As part of this ongoing Seattle Foot Study 749 people were followed with monofilament testing for a median of 3.7 years. These study participants had a mean age of 63.2 years, were 98% mean and 93.6% had had Type 2 diabetes for a mean duration of 11.4 years. Insensitivity to the monofilament remained an independent risk factor for foot ulcer with a RR of 2.2 (CI 1.5-3.1) (Boyko et al, 1999).

Kastenbauer et al (2001) reported predictors for foot ulceration in a prospective study of people (aged <75 years) with Type 2 diabetes and without a history of foot ulceration. 135 people had a normal VPT, while 52 had an elevated VPT at baseline. During a mean of 3.6 years of follow-up, 10 people including 9 with elevated VPT at baseline developed 18 forefoot ulcerations. A multiple Cox proportional hazards regression analysis showed both elevated VPT and elevated mean plantar pressure (MPP) were significant risk factors for foot ulceration, with a RR of 25.4 (CI 3.1-205, p=0.0024) and 6.3 (CI 1.2-32.7, p=0.029), respectively.

Other factors contribute to the increased risk of ulceration and amputation in people with diabetes and peripheral neuropathy

While peripheral neuropathy is a major independent predictor of diabetic foot ulceration and amputation, the path to ulceration and amputation is variable. The role of vascular insufficiency, deformity, inadequate patient education and use of inappropriate footwear are all dealt with in subsequent Sections. There are also other important precipitating factors such as injury.

Some researchers have attempted to analyse the causal pathways responsible for ulceration by mathematical methods. Reiber et al (1999) used the Rossman model of causation to examine the histories of individuals with incident foot ulcers in Manchester and Seattle between 1990 and 1994. The study participants from Manchester were similar in demographic characteristics to those from Seattle with no significant difference in the age (64.7 v 64.7 years) or diabetes duration (14.8 v 11.6 years). However the Seattle cohort was 100% male, significantly different to the 67.4 % males in the Manchester cohort (p<0.001). A multi-disciplinary team examined the data blinded to patient identity. Peripheral neuropathy assessed by VPT or monofilament was present in 78% (Reiber et al, 1999). In 63% of cases of foot ulceration, a critical triad was present including peripheral neuropathy, foot deformity and minor foot trauma but 32 unique causal pathways were identified.

Another analysis from the Seattle study by Reiber et al (1992) studied 80 consecutive male veterans with diabetes in Seattle admitted for amputation where it was found that loss of vibration sense resulted in an OR for amputation of 15.5 (CI 8.3-28.7). Loss of distal touch sensation in the 316 males, with both types of diabetes, gave a risk of amputation OR 5.1 (CI 2.6-10.2) compared with 236 male controls with diabetes. While pointing out multiple statistically significant risk factors for amputation from the analysis, the authors comment that while there are important underlying conditions such as sensory neuropathy, other risk factors also contribute, including the events following a minor injury to a neuropathic foot (Reiber et al, 1992).

Apelqvist et al (1990) studied a cohort of 314 consecutive people with diabetes referred to a Swedish department of medicine because of foot ulcers. The study participants had a mean age of 64±17 and duration of diabetes of 17±12 years and 96% had sensory and muscular disturbances of neuropathy. Neuropathy was more common in those progressing to amputation than in those who did not. However, consistent with other studies, additional precipitating factors were again found in 84% of subjects, such as wearing ill fitting shoes or acute mechanical trauma.

In a case-control study, Masson et al (1989) found that among people with diabetes (n= 38) or with rheumatoid arthritis (n=37) who presented with similar forefoot deformity. 32% of the diabetic group had a history of plantar ulceration compared with none of the rheumatoid group (p<0.01). The groups were similar in age (56 v 54 years) and duration of disease (19 v 15 years). Elevated plantar pressure (>10 kg/cm^2) was very common in both groups (61.0 v 51.0%, respectively, p=NS). However, the diabetic group had more severe neuropathy (85.0 v 35.0% with absent ankle reflexes, p<0.01; 56.0 v 27.0% with reduced vibration perception, p<0.01; VPT 33.5±13.4 v 16.9±10.9, p<0.001). These data suggest that high pressure alone is not sufficient for ulceration and loss of sensory awareness plays an important role in diabetic foot ulceration.

Summary - Peripheral Neuropathy as a Risk Factor

- Prospective studies show a strong relationship between the presence of peripheral neuropathy (assessed by a biothesiometer or Semmes-Weinstein monofilament) and subsequent ulceration

- There is a similarly strong relationship between peripheral neuropathy and subsequent amputation

- Cross-sectional studies have consistently demonstrated that peripheral neuropathy is an independent risk factor for foot ulceration and amputation in people with diabetes

- The presence of peripheral neuropathy requires other permissive factors and/or a series of events (some of which may be preventable or reversible) to culminate in an ulcer or amputation

- More research is required to clarify the factors which influence the different pathways from peripheral neuropathy to ulceration and amputation

Evidence Table: Section 1

Peripheral neuropathy as a risk factor for ulceration and amputation

Author	Evidence				
	Level of Evidence		Quality Rating	Magnitude Rating	Relevance Rating
	Level	Study Type			
Abbott C (1998) (Adults – Canada; UK; US)	III-2	Cohort	High	High +	High
Abbott C (2002) (Adults – UK)	III-2	Cohort	High	High +	High
Adler AI (1999) (Adults – US)	III-2	Cohort	High	High +	High
Apelqvist J (1990) (Adults – UK)	III-2	Cohort	Medium	High +	High
Boulton AJM (1986) (Adults – US)	III-2	Case-control	Medium	High +	High
Boyko EJ (1999) (Adults – US)	III-2	Cohort	High	High +	High
Coppini DV (1998) (Adults – UK)	III-2	Case-control	Medium	High +	High
Frykberg RG (1998) (Adults – US)	III-2	Cross-sectional	High	High +	High
Hamalainen H (1999) (Adults – Finland)	III-2	Cohort	High	High +	High
Kastenbauer T (2001) (Adults – Austria)	III-2	Cohort	Medium	High +	High
Kumar S (1994) (Adults – UK)	III-2	Cross-sectional	Medium	High +	High
Lavery LA (1998) (Adults – US)	III-2	Case-control	High	High +	High
Litzelman DK (1997a) (Adults – US: African American, Multiethnic)	III-2*	RCT	Low	High +	Low
Mantey I (1999) (Adults – UK)	III-2	Cross-sectional	High	Low	High
Masson EA (1989) (Adults – UK)	III-2	Case-control	High	High +	High
Mayfield JA (1996) (Adults – US: Gila River Indians)	III-2	Case-control	High	High +	Low
McNeely MJ (1995) (Adults – US)	III-2	Case-control	High	High +	High
Moulik PK (2003) (Adults – UK)	III-2	Cohort	High	High +	High
Pecoraro RE (1990) (Adult males – US)	III-2	Case-control	High	Low	High
Peters EJG (2001) (Adults – US)	III-2	Case-control	Medium	High +	High
Reiber GE (1992) (Adult male – US)	III-2	Case-control	High	High +	High
Reiber GE (1999) (Adults – UK; US)	III-2	Cohort	Medium	Low	High
Rith-Najarian S (1992) (Adults – US: Red Lake Chippewa Indians)	III-2	Cohort	High	High +	Low
Young (1994) (Adults – UK)	III-2	Cohort	High	High +	High

For magnitude rating:
+ peripheral neuropathy is a risk factor for ulceration and amputation. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.
*RCT but only the epidemiological data from this study were used for the relevant evidence statement

Section 2: Diabetes Foot Problems

Issue

Is peripheral vascular disease a risk factor for ulceration or amputation?

Recommendation

People with diabetes should be assessed regularly for peripheral vascular disease.

Evidence Statements

- Peripheral vascular disease is a risk factor for amputation
  Evidence Level III-2

- Studies on the relationship between peripheral vascular disease and foot ulcers have given variable results
  Evidence Level III-2

Background - Peripheral Vascular Disease as a Risk Factor

Peripheral vascular disease (PVD) is common in people with Type 2 diabetes being present in 8% at the time of diagnosis and in 45% of people who have had diabetes for 20 years (Hiatt & Sussman, 1994). The prevalence of PVD at diagnosis of diabetes and the risk of developing PVD over time increase with increasing age (Davis et al, 1997).

PVD is considered to be the most important factor related to outcome of a diabetic foot ulcer (International Working Group on the Diabetic Foot, 1999) and is a major contributor to the high rates of amputation in people with diabetes as well as predicting increased risk of cardiovascular mortality (Orchard & Strandness, 1993).

Vascular assessment in the general practice setting is, by necessity, based on history and clinical examination. More sophisticated bedside investigations are available and have been shown to predict ulceration and amputation. The ankle-arm index (AAI) or ankle-brachial index (ABI), is a ratio of blood pressure measured in the arm and in the ankle by a hand-held ultrasound doppler. A ratio of less than 0.50 indicates severe PVD. Calcification of pedal arteries, which is common in people with diabetes, results in a falsely high blood pressure reading in the feet and consequently a falsely high ratio. In addition, the repeatability of the AAI/ABI measure has a coefficient of variation of 10 to 15% and therefore requires duplicate readings. In view of the equipment and time required to perform the examination, AAI/ABI may be used in a specialist practice but has limited application in a busy general practice.

Transcutaneous oximetry ($TcPO_2$) is a measurement of partial pressure of oxygen at the skin surface. Levels less that 50mmHg are associated with PVD and a reduced healing ability (McNeely et al, 1995).

Invasive techniques such as angiography are more specific in demonstrating PVD but are also associated with significant morbidity. In a study of 104 people with diabetes, both a score based on the results of an angiogram (OR 2.32 [CI 1.40-3.84]) and the ABI (OR 1.84 [CI 1.10-3.06]) were predictive of major amputation (Faglia et al, 1998).

Evidence - Peripheral Vascular Disease as a Risk Factor

Peripheral vascular disease is a risk factor for amputation

In the prospective Seattle Diabetic Foot Study of 776 veterans with diabetes, PVD has been shown to be an independent risk factor for amputation (RR 3.0, CI 1.3-7.1) (Adler et al, 1999). In a multivariate model relative to a reference hazard ratio (HR) of 1 for an individual with neither PVD (as indicated by absent or diminished pulses) nor neuropathy, individuals with PVD in either leg but without neuropathy had an HR for amputation of 20.5 compared with an HR of 9.3 for neuropathy alone and HR 19.0 when both PVD and neuropathy were present. When different measures of PVD were used in a multivariate hazards model, AAI ≤ 0.8 in either lower extremity, $TcPO_2 \leq 50$ mmHg in either foot and absence/diminished peripheral pulses gave a similar HR for predicting risk of amputation, 2.9 (CI 1.3-6.2), 3.0 (CI 1.3-7.1) and 3.0 (1.4-6.5), respectively.

Lehto et al (1996) prospectively followed for 7 years 1,044 people aged 45 to 64 years with Type 2 diabetes. During the 7-year follow-up, the incidence of amputation was 5.6% in men and 5.3% in women. Compared with people without an amputation during the follow-up, people who had an amputation were more likely to have absence of two or more peripheral pulses ($p<0.001$). The age- and sex-adjusted RR for lower extremity amputation was 3.9 (CI 2.3-6.8, $p<0.001$) in people with two or more peripheral artery pulses absent.

Del Aguila et al (1994) conducted a case-control study in people with diabetes who had an amputation (n=67) compared with a control group of people with diabetes who had another type of surgery unrelated to diabetes (n=236). PVD was determined by patient report of claudication or clinician diagnosis. More case subjects had a history of PVD (52.2%) and prior ulcer (29.9%) compared with control subjects (29.7% and 3.8%, respectively) ($p<0.001$, and $p<0.0001$). The risk of lower-extremity amputation was associated with a history of PVD (OR 2.6, CI 1.5-4.5) and prior ulceration (OR 10.7, CI 4.6-25.0).

A case-control study of Pima Indians with diabetes compared 61 people with amputation to 183 controls as described in Section 1. The OR for first amputation in people with PVD was 6.9 (CI 2.6-18.3) which decreased to an OR of 3.4 (CI 1.2-9.4) after adjustment for demographic factors and diabetes severity (Mayfield et al, 1996).

In a prospective cohort study in the UK 185 people with diabetic foot ulcers were followed for a mean 34 months to assess the relative risk of amputation (Moulik et al, 2003). The mean age was 65±13 years, with 64% male, 84% with Type 2 diabetes, 61% with neuropathy and 41% with PVD. The ulcers were categorised as 45% neuropathic, 24% ischemic and 30% neuroischemic. At the end of follow-up 30 people had had amputations and the 5 year amputation rates were 11%, 29% and 25% respectively for the above groups. The study indicated that people with PVD and therefore ischemic ulcers were more likely to have an amputation than someone with a neuropathic ulcer.

As described in Section 1, Hamalainen and coworkers (1999) conducted a cohort study of 733 people with diabetes (aged 10-79 years). At baseline, a podiatric examination, neurophysiological and circulatory measurements were performed. 25 people had one or more amputations during the 7 year follow-up period. People who had an amputation were more likely to be older ($p<0.001$), have a history of retinopathy ($p<0.001$) and nephropathy ($p=0.023$), and have one or more peripheral pulses absent ($p<0.001$) compared with people without amputation. However in logistic regression the absence of a peripheral pulse was not independently associated with lower extremity amputation.

Studies on the relationship between peripheral vascular disease and foot ulcers have given variable results

In a study by Abbott et al (2002) a cohort of 9,710 people in the UK were assessed at baseline and the final ulceration status of 6,613 people was established by postal

questionnaire two years later. There were 219 people who developed a new foot ulcer during the study period with an annual incidence rate of 2.2%. In this group univariate analysis showed that the RR of foot ulcer increased as the number of pedal pulses diminished. Compared with those with 4 pedal pulses those who had 3, 2, 1 and 0 pedal pulses had RR of 1.52 (CI 1.02-2.26), 2.51 (CI 1.87-3.37), 4.03 (CI 2.54-6.37) and 4.72 (CI 3.28-6.78), with $p<0.0001$ across all groups. There was also a higher risk of amputation associated with a history of peripheral vascular disease - RR 2.31 (CI 1.46-3.64), $p=0.0003$.
Other previously described studies have also reported an association between ulceration and measures of PVD. The Seattle Veterans population failed to demonstrate a risk of ulceration with low AAI, but reported increased risk with low $TcPO_2$ (OR 57.87, CI 5.08 – 658.96) after adjusting for age, sex, serum glucose levels, marital status, history of treatment for alcohol abuse, prior LEA and prior revascularisation (McNeely et al, 1995). In a more recent publication from this group in a prospective study of 749 people, both diminished large vessel perfusion as measured by AAI, and tissue oxygen perfusion were associated with increased risk for ulceration [AAI<0.5, RR 1.94 (1.07-3.52); $TcPO_2$ RR 0.80 (0.69-0.93)] (Boyko et al, 1999). In a prospective cohort of 358 American-Indians, the incidence of plantar ulceration was related to ABI but in all ranges of vascular indices, ulceration rates were significantly higher among people who had lost protective sensation (Rith-Najarian et al, 1992).

However other studies have not shown this association. In the previously described model developed to clarify causal pathways for incident foot ulcers, lower limb ischaemia was a component cause in 35% of study pathways, but not a sufficient cause of ulceration for any of the 147 people (Reiber et al, 1999). In the case-control study by Lavery et al (1998) there were no significant multivariate associations between ulceration and vascular disease as measured by ABI, pedal pulses or $TcPO_2$ <30mm Hg in a Texan study of 76 cases and 149 controls. Pham et al (2000) conducted a prospective study of foot ulceration in 248 people with diabetes in three diabetic foot centres, followed for a mean 30 months. The cohort had a mean age of 58 ± 12 years, 50% were males, 80% had Type 2 diabetes and they had a mean duration of diabetes of 14±11 years. PVD assessed by absent pedal pulses was not an independent risk factor for foot ulceration.

Summary - Peripheral Vascular Disease as a Risk Factor

- Peripheral vascular disease is common in people with Type 2 diabetes
- Peripheral vascular disease is associated with a 2-4 fold increased risk of amputation
- The role of peripheral vascular disease as a independent risk factor for foot ulceration remains uncertain

Evidence Table: Section 2

Peripheral vascular disease as a risk factor

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Abbott C (2002) (Adults – UK)	III-2	Cohort	High	High +	High
Adler AI (1999) (Adults – US)	III-2	Cohort	High	High +	High
Boyko EJ (1999) (Adults – US)	III-2	Cohort	High	High +	High
del Aguila MA (1994) (Adults – US)	III-2	Case-control	Medium	High +	High
Hamalainen H (1999) (Adults – Finland)	III-2	Cohort	High	High +	High
Lavery LA (1998) (Adults – US)	III-2	Case-control	High	High +	High
Lehto S (1996) (Adults – Finland)	III-2	Cohort	High	High +	High
Mayfield JA (1996) (Adults – US: Gila River Indians)	III-2	Case-control	High	High +	Low
McNeely MJ (1995) (Adults – US)	III-2	Case-control	High	High +	High
Moulik PK (2003) (Adults – UK)	III-2	Cohort	High	High +	High
Pham H (2000) (Adults – US)	III-2	Cohort	High	High +	High
Reiber GE (1999) (Adults – US; UK)	III-2	Cohort	Medium	Low	High
Rith-Najarian S (1992) Adults – US: Red Lake Chippewa Indians	III-2	Cohort	High	High +	Low

For magnitude rating:
+ peripheral vascular disease is a risk factor for diabetic foot disease. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 3: Diabetes Foot Problems

Issue

Is foot deformity or a previous amputation a risk factor for ulceration or amputation?

Recommendation

People with diabetes who have had a previous amputation are at high risk of ulceration and further amputation and therefore require regular and frequent review

People with diabetes should be assessed regularly to detect foot deformities including:

- Hallux deformities
- Hammer or claw toes
- Callus
- Charcot's foot

Evidence Statements

- A previous amputation is a risk factor for ulceration and further amputation
  Evidence Level III-2

- Foot deformity is a risk factor for ulceration, especially in people with neuropathy
  Evidence Level III-2

- Callus is a risk factor for ulceration, especially in people with neuropathy
  Evidence Level III-2

Background – Foot Deformity and Previous Amputation as Risk Factors for Ulceration and Amputation

Mechanical factors play a critical role in the aetiology of neuropathic foot ulcers (Cavanagh et al, 1996; Mayfield et al, 1998). Alterations in the normal biomechanics of the foot result from alterations in foot structure and non-enzymatic glycosylation which alters foot tissue properties. These combine to increase plantar pressure, a consistent finding in people with diabetes, which has been associated with increased risk of ulceration (Veves et al, 1992). Plantar pressures are difficult to measure in a routine practice setting as sophisticated technology is required, however callus, a sign of increased foot pressure, is more predictive of ulceration than increased plantar pressure alone (Mayfield et al, 1998).

Plantar pressures during walking and standing in the normal foot are sufficient to occlude capillary blood flow and it has been suggested that local reflexes including the hyperaemic response are abnormal in people with neuropathy and that capillary fragility may be greater in people with diabetes (Cavanagh et al, 1996). People who have lost protective sensation may not appreciate increasing damage to the foot due to increased pressure and continue to traumatise the same tissue (Mayfield et al, 1998).

Causes of increased plantar pressures in people with diabetes include increased body mass (however this contributes less than 14% of variance in peak plantar pressure), changes in posture, gait, soft tissues and bone structure. Limited joint mobility occurs in the absence of neuropathy but only becomes a risk for ulceration with the loss of protective sensation. Glycosylation of soft tissues is thought to predispose to the excess callus formation seen in people with diabetes in response to abnormal plantar pressures. Bony deformities caused by motor neuropathy, hammer toe or claw toe deformity are present in up to half of all people with diabetes (Mayfield et al, 1998).

Foot deformity is a major contributor to increasing foot pressures. Foot deformities in people with diabetes range from minor abnormalities in joint mobility to the severe deformity seen in advanced Charcot’s foot. A previous amputation, particularly a minor amputation, frequently results in abnormal plantar pressures and increases the risk of subsequent amputation.

Callus is a diffuse hyperkeratotic area which develops in response to shear stresses, usually in proximity to a bony prominence (Reiber et al, 1999). Callus is not only a sign of increased foot pressures but also contributes to further increase plantar foot pressures by acting as a foreign body and predispose to the formation of ulcers beneath such lesions.

Reducing plantar pressures is the basis of treating foot ulcers and preventing ulceration in at risk feet (Cavanagh et al, 1996). Several measures have been shown to reduce abnormal pressures, protect the foot from external trauma and reduce the formation of callus and ulcers. Conservative management of increased plantar pressures involves debridement of callus and footwear modification.

Evidence – Foot Deformity and Previous Amputation as Risk Factors for Ulceration and Amputation

Previous amputation is a risk factor for ulceration and further amputation

A history of previous lower extremity event (ulceration or amputation) determined by interview, medical record review and examination, was used to classify risk in a prospective study of 358 American Indians (Rith-Najarian et al, 1992). People in the risk category, including previous amputation had the highest level of risk for ulceration (OR 78) and further amputation (rate 180/1000 diabetic person-year). The trend for increasing risk of amputation and ulceration with the risk category which included neuropathy, deformity and a history of ulceration or amputation, was highly significant ($p<0.00001$). Increased risk associated with a history of amputation was also confirmed in the previously described Seattle Veterans study (RR 2.8 [CI 1.84-7.29], $p<0.001$) (Boyko et al, 1999). People who experienced a lower extremity amputation during follow-up were more likely to have had a history of previous amputation (Adler et al, 1999).

In a 5 year prospective study, 189 people with diabetes who had achieved healing after an index amputation (93 with a minor amputation and 96 with a major amputation) were studied. Over the study period there were 72 new amputations, 48 minor and 24 major amputations (Larsson et al, 1998). The rates of new major amputations after 1, 3 and 5 years were 9%, 13% and 23% respectively and the rates for mortality were 15%, 38%, and 68% respectively.

In the prospective Seattle Diabetic Foot Study of 776 veterans with diabetes, previous amputation was an independent risk factor for amputation (HRs ranged from 3.0 – 3.4) in multivariate models which incorporated different measures of PVD (Adler et al, 1999).

Lavery et al (1998) conducted a case-control study to evaluate risk factors for foot ulceration in people with diabetes (mean age 52 years). Among 225 people, 76 case subjects were defined as having an existing or a recently healed foot ulcer and 149 control subjects were defined as never having had a foot ulcer. In a multivariate model, the following were significant risk factors for foot ulceration: history of amputation (OR 10.0, $p<0.02$); loss of protective sensation (OR 15.2, $p<0.001$); and elevated plantar pressure >65 N/cm^2 (OR 5.9, $p<0.001$). A group of 25 people who had had an amputation of the great toe were assessed for deformity, using the contralateral extremity as the control. The group had a mean age of 56.5±9.8 years and a duration of diabetes of 16.7±8.9 years. Deformity of the second and third toes was more common ($p=0.012$ and $p=0.002$ respectively) as was new ulcers in feet that had had an amputation ($p=0.002$) (Quebedeaux et al, 1996). In a community-based cross-sectional study of 811 people (aged 34 to 90 years) with diabetes (Kumar et al, 1994), 43 people (5.3%, CI 3.8-6.8%) had current or past foot ulcers. A multiple logistic regression analysis showed history of previous amputation and presence of PVD increased the risk of ulceration (OR 12.7, $p<0.01$; OR 2.6, $p<0.01$, respectively).

Foot deformity is a risk factor for ulceration, especially in people with neuropathy

Abbott and coworkers (2002) followed a cohort of 9,710 people in the UK for 2 years assessing the final ulceration status of 6,613 people by postal questionnaire. There were 219 people who developed a new foot ulcer during the study period with an annual incidence rate of 2.2%. Foot deformity was defined as the presence of 3 or more of muscle wasting, hammer and claw toes, bony prominences, prominent metatarsal heads, Charcot arthopathy and limited joint mobility. Foot deformity was associated with a RR for foot ulceration of 2.54 (CI 2.04-3.22, p<0.0001). Increasing deformity was also found to be an independent predictor of foot ulcer with a RR of 1.57 (CI 1.22-2.02, p=0.0004).

Foot deformity, defined as hallux rigidus, hallux valgus, or toe deformities, was shown to eb a significant risk factor for foot ulceration in 225 people with diabetes which included 76 case subjects and 149 control subjects (OR 3.3, p<0.03) (Lavery et al (1998). In a cohort of Veterans in Seattle followed for over 3 years, Charcot's deformity was associated with an increased risk of foot ulceration (RR 3.5, CI 1.2-9.9, p=0.019). Hallux limitus and severe hammer/claw toe deformity were also associated with an increased risk of foot ulcer (RR 1.7, CI 1.2-2.3, p=0.003; RR 1.8, CI 1.2-2.5, p=0.002, respectively). There was no statistically significant association with other deformities, prominent metatarsal heads, hallus valgus, or bony prominences in this population (Boyko et al, 1999).

The importance of the combined effects of neuropathy and deformity is illustrated by a case-control study which compared people with diabetes and people with rheumatoid arthritis as described in Section 1. Masson et al (1989) found that among people with diabetes (n= 38) or with rheumatoid arthritis (n=37) who presented with similar forefoot deformity. 32% of the diabetic group had a history of plantar ulceration compared with none of the rheumatoid group (p<0.01). The groups were similar in age (56 v 54 years) and duration of disease (19 v 15 years). Elevated plantar pressure (>10 kg/cm^2) was very common in both groups (61.0 v 51.0%, respectively, p=NS). However, the diabetic group had more severe neuropathy (85.0 v 35.0% with absent ankle reflexes, p<0.01; 56.0 v 27.0% with reduced vibration perception, p<0.01; VPT 33.5±13.4 v 16.9±10.9, p<0.001). These data suggest that high pressure alone is not sufficient for ulceration and loss of sensory awareness plays an important role in diabetic foot ulceration.

Deformity, including hallux varus or valgus, claw and hammer-toes, bony prominence, and Charcot foot, was assessed in a cohort of 406 diabetic American Indians. In the presence of peripheral neuropathy in which protective sensation was lost, the rate of ulceration in people with deformed feet was twice that of people without deformity (OR 32) (Rith-Najarian et al, 1992).

In a study of 65 people with diabetes (Fernando et al, 1991), people with limited joint mobility (LJM) and neuropathy (n=12) and people with LJM but no neuropathy (n=11) had significantly higher plantar pressure compared with those without LJM (n=42) (p<0.001). There was a strong correlation between plantar pressure and joint mobility in the foot (r= -0.7, p<0.001). Previous foot ulceration was present in 65% of people with both LJM and neuropathy compared with none in people with LJM but no neuropathy, and only 5% in people with neuropathy but no LJM.

Data on foot deformity and risk of amputation are limited. In a case-control study of 244 people with diabetes foot deformity was found to have a risk equal to neuropathy and PVD in predicting amputation but the risk increased with increasing number of risk factors (Mayfield et al, 1996). After adjusting for demographic factors and disease severity, and independent of other risk factors, there was a significant association between foot deformity and first amputation in a Native American Indian population (OR 3.0, CI 1.02-8.7). This study was a retrospective review of medical records, which could have underestimated the prevalence of significant peripheral neuropathy in the control group.

A longitudinal outcome study (Lavery et al, 2003a) evaluated the effectiveness of dynamic plantar pressure assessment in determining people at high risk for neuropathic ulceration. A total of 1,666 people with diabetes (mean age 69 years) were enrolled in this 2-year study. Lower-extremity screening involved sensory (using 10g Semmes-Weinstein monofilament and vibration perception threshold testing) and musculoskeletal examination, as well vascular status assessment. Based on screening results, people were categorised by their risk of diabetic foot complications. 263 people (15.8%) either presented with or developed an ulcer during the 24-month follow up period. The baseline peak pressure was significantly higher in the ulcerated group compared with those who did not develop ulcers (n=1,403) (95.5±26.4 v 85.1±27.3 N/cm^2, p<0.001). People with neuropathy and deformity (risk group 2) and with a history of ulceration or amputation (risk group 3) had significantly higher peak plantar pressure than people without neuropathy (risk group 0) (p=0.001 for both associations). People with forefoot deformity were more likely to have elevated foot pressures than those without deformity (OR 1.5 for people with hallux valgus, CI 1.1-2.0; p=0.005; OR 1.5 for people with hammer or claw toe deformity, CI 1.1-1.9, p=0.002). By using ROC analysis, the optimal cut point of 87.5 N/cm^2 yielded a sensitivity of 63.5% and a specificity of 46.3%. The authors concluded that elevated foot pressure is an important risk factor for foot complications, but by itself is a poor predictor of foot ulcers.

Callus is a risk factor for ulceration, especially in people with neuropathy

In a prospective study of 63 people (median age 62 years) with diabetes (duration median 17 years) and neuropathy assessed on the basis of VPT, the presence of plantar callus was highly predictive of ulceration in a callused area (RR 11.0 [CI 2.8-43.2], p=0.004). This compared with a RR for ulceration in an area of elevated plantar pressure but without callus of 4.7 (CI 1.2-18.9), p=0.04 (Murray et al, 1996). The authors concluded that callus should be recognised as a risk factor for foot ulceration.

Reiber et al (1999) used the Rothman model of causation to determine the causal pathways of incident foot ulcers in 146 people with diabetes from Manchester, UK (n=92) and Seattle, US (n=56). There were no statistically significant differences by study sites in age, diabetes duration or HbA_{1c} values. Foot deformity and callus were among the component causes leading to ulceration in 63% and 30% of subjects, respectively.

Among 157 diabetic people (mean age 61.2 years) with neuropathy (VPT >25V) without either PVD or foot ulcer history, Abouaesha et al (2001) found that people with callus under the forefoot had significantly increased peak pressures at all metatarsal heads (MTH) ($p<0.0001$) and reduced plantar tissue thickness at the second to the fifth MTH ($p<0.0001$ to <0.05) compared with people without callus. A significant association was observed between peak plantar pressure and plantar tissue thickness at all MTHs ($r= -0.26$ to -0.61, $p<0.001$ for the first MTH, $p<0.0001$ for the rest MTHs), with the least pronounced association at the first MTH.

In a case control study of 33 people with diabetes, Pataky et al (2002) reported that both maximum peak plantar pressure (PP) and duration of PP were significantly higher in people with callus (n=10) than people without callus (n=10) (314±52 v 128±16 kPa, $p<0.005$; 621±27 v 505±27 ms, $p<0.05$; respectively). In another group of 13 people, the peak PP decreased by 58% after callus removal (340±33 v 141±23 kPa, $p<0.0001$), duration of PP also reduced ($p<0.05$).

The effect of regular callus removal on foot pressure was examined by Pitei et al (1999) among 24 people age 51 to 69 years with diabetes and neuropathy. The plantar pressure was reduced by 32.1±8.4% ($p=0.014$) after callus removal in 6 people who did not have a history of ulceration. There was a significant reduction of 30.9±4.5% ($p<0.005$) in 10 people who had a history of previous ulceration who received regular callus removal at a 6 to 8 week interval and a reduction of 24.8±4.0% ($p=0.005$) in 8 people with a previous history of foot ulcer who received regular callus removal at a 3 to 4 week interval, respectively.

Summary - Foot Deformity and Previous Amputation as Risk Factors for Ulceration and Amputation

- Previous amputation is a risk factor for ulceration and further amputation and is associated with a 68% mortality rate after 5 years
- In the presence of diabetic neuropathy, limited joint mobility and bony deformities increase the risk of ulceration
- Deformity increases the risk of ulceration by at least 3 fold
- The deformity caused by previous amputation also increases the risk of ulceration by at least 3 fold
- Callus is common in people with diabetes and in the presence of neuropathy increases the risk of ulceration

Evidence Table: Section 3

Deformity as a risk factor for ulceration and amputation

Author	Evidence				
	Level of Evidence		Quality Rating	Magnitude Rating	Relevance Rating
	Level	Study Type			
Abbott C (2002) (Adults – UK)	III-2	Cohort	High	High +	High
Abouaesha F (2001) (Adults – UK)	III	Cross-sectional	Medium	High+	Medium
Adler AI (1999) (Adults – US)	III-2	Cohort	High	High +	High
Boyko EJ (1999) (Adults – US)	III-2	Cohort	High	High +	High
Fernando JS (1991) (Adults – UK)	III-2	Cross-sectional	Medium	High +	High
Kumar S (1994) (Adults – UK)	III-2	Cross-sectional	Medium	High +	High
Larsson J (1998) (Adults – Sweden)	III-2	Cohort	High	High +	High
Lavery LA (1998) (Adults – US)	III-2	Case-control	High	High +	High
Lavery LA (2003a) (Adults – US)	III-2	Cohort	Medium	High +	High
Masson EA (1989) (Adults – UK)	III-2	Case-control	High	High +	High
Mayfield JA (1996) (Adults – US: Gila River Indians)	III-2	Case-control	High	High +	Low
Murray HJ (1996) (Adults – UK)	III-2	Cohort	Medium	High +	High
Pataky Z (2002) (Adults – Switzerland)	III-2	Case-control	Medium	High +	High
Pitei DL (1999) (Adults – Denmark)	III-2	Case-control	Medium	High +	High
Quebedeaux TL (1996) (Adults – US)	III-2	Case-control	High	High +	High
Reiber GE (1999) (Adults – US; UK)	III-2	Cohort	Medium	High +	High
Rith-Najarian S (1992) (Adults -US: Red Lake Chippewa Indians)	III-2	Cohort	High	High +	Low
Uccioli L (1995) (Adults – Italy)	II	RCT	High	High +	High

For magnitude rating:
+ deformity is a risk factor for ulceration and amputation. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9

Section 4: Diabetes Foot Problems

Issue

Is a current or previous ulcer a risk factor for amputation?

Recommendation

People with diabetes and a current foot ulcer are at high risk for amputation and preventative interventions to lower that risk should be instituted promptly

People with diabetes and a history of a healed previous diabetic foot ulcer should be recognised as having a life long increased risk of recurrent ulceration and amputation

Evidence Statements

- A healed diabetic foot ulcer is an indicator of high risk for recurrent ulceration and amputation
  Evidence Level III-2

- A current ulcer is a high risk indicator for amputation
  Evidence Level III-2

Background - Ulcer as a Risk Factor for Amputation

Observational studies suggest that 6-43% of people with diabetes who have a foot ulcer eventually progress to amputation (Bild et al, 1989; Apelqvist et al, 1994; Larsson et al, 1995; Moss et al, 1996). Retrospective studies suggest that lower extremity ulcers precede 71-85% of first (Reiber et al, 1992; Larsson et al, 1995; Moss et al, 1996) or second amputation (Larsson et al, 1998). While the presence of a current ulcer leads to an increased risk of amputation, it is important to know the level of risk and whether a healed ulcer is also a risk factor in the assessment of the feet of a person with diabetes for ongoing monitoring and preventative intervention. It has been observed that the most likely site for plantar ulceration in neuropathic feet is at the location of a previous ulcer (Sims et al, 1988).

While sophisticated measurements are sometimes used to assess the high risk foot, the history of an ulcer or the detection of a current ulcer by physical examination are both risk factors capable of detection by all primary care health professionals. Preventative action can then be instituted in an easily identified high risk group (Apelqvist et al, 1993).

Evidence - Ulcer as a Risk Factor for Amputation

A healed diabetic foot ulcer is an indicator of high risk for recurrent ulceration and amputation

A UK prospective study followed 63 neuropathic people (median age 62 years and median duration of diabetes 17 years) with plantar callus and high plantar foot pressures. After 22 months follow-up previous ulceration proved to be the highest risk factor for the development of a new foot ulcer with a RR of 56.8 ($p=0.00001$) (Murray et al, 1996).

A 14 year prospective study followed 984 diabetic individuals (mean age 64.4 years and a duration of diabetes 10.9 years) from a population based cohort from Wisconsin, US. A history of foot ulceration was associated with the highest OR of 3.56 (CI 1.84-6.89, $p \leq 0.0005$) for amputation in a multivariate logistic regression model. Male gender was also a risk factor (OR 2.66 [CI 1.49-4.76], $p<0.001$) (Moss et al, 1999).

In the continuing Seattle Diabetic Foot Study of outpatients in a Veterans Affairs medical clinic, 776 people with diabetes (median age 65 years) were followed for a median of 3.3 years. 30 people underwent surgery for lower extremity amputation (LEA). Compared with people who did not have a LEA during the follow-up, people who had an LEA were more likely to have had a previous LEA ($p<0.0001$) and a previous lower-extremity ulcer ($p=0.0001$). Previous lower-extremity ulcer was associated with an increased risk of LEA in 3 multivariate models which used different methods to assess PVD – AAI model (OR 3.3, CI 1.4-8.1), $TcPO_2$ model (OR 3.4, CI 1.4-8.1) and palpating pulses model (OR 3.0, CI 1.2-7.4) (Adler et al, 1999).

Also in the Seattle study, 67 people with diabetes presenting for initial non-traumatic amputation between 1984 and 1987 were compared with 236 consecutive people with diabetes seen for other unrelated surgery (del Aguila et al, 1994). There was no significant difference between the case or control groups in age (63.6 v 16.1 years) or duration of diabetes (12.4 v 10.9 years). Presence of prior foot ulcer was independently associated with risk of lower extremity amputation (OR 10.9, CI 4.6-25.5). In a population based case-control study, Pima Indians aged 25-85 years having amputations between 1983 and 1992 were compared with those not having an amputation by 1992 (Mayfield et al, 1996). The control group was significantly younger (p=0.001) with a shorter duration of diabetes (p<0.001). There was a similar risk of amputation with peripheral neuropathy, PVD, bone deformity and a history of foot ulcer with adjusted OR 3.1 (CI 1.3-7.0), 3.4 (CI 1.2-9.4), 3.0 (CI 1.02-8.7) and 2.2 (CI 0.95-5.3) respectively. In 875 Oklahoma Indians with no prior amputation at initial examination (mean age 51.6 ± 10.8 years and duration of diabetes 6.6 ± 6.1 years), history of foot ulcer was a strong risk factor for amputation over a 10 year period with a RR in men of 2.96 (CI 0.91-9.61, p=0.06) and in women of 7.08 (CI 2.50-20.01, p<0.001) (Lee et al, 1993).

Poor wound healing and osteomyelitis may play a part in amputation after foot ulcer. In the Seattle Foot Study 80 people with diabetes who had had one amputation were compared with 236 veterans with diabetes not having an amputation, to determine causal pathways using both objective and subjective data. There were no statistically significant differences between cases and controls in age (63.4 v 61.1 years) or duration of diabetes (13.3 v 10.9 years). While 23 causal pathways were identified, a critical triad of injury leading to ulceration and poor wound healing was responsible for 73% of cases. Overall 84% of amputations in this paper were attributed to ulceration (Pecoraro et al, 1990).

A database analysis was performed of 8,905 people with Type 1 or Type 2 diabetes (mean age of 65.8 years) participating in a health maintenance organisation from 1993-1995 (Ramsey et al, 1999). The cumulative incidence of foot ulcers over 3 years was 5.8%. Of these 15.6% required amputation, and a similar proportion (15%) developed osteomyelitis, of whom 36% had a lower extremity amputation during the follow up. This suggested osteomyelitis played a part in some, but not all, amputations following ulcers.

Peters & Lavery (2001) examined outcomes in a 3-year case-control study of 213 people with diabetes (both Type 1 and 2) who were stratified into four risk groups according to risk category: no neuropathy (Group 0, n=79), neuropathy without PVD or deformity (Group 1, n=21), neuropathy and/or PVD and/or deformity (Group 2, n=51) and previous history of foot ulcer or a LEA (Group 3, n=62). People in the high-risk group had longer duration of diabetes (p=0.001) and worse glycaemic control (p=0.02) compared with people in the low-risk groups. During 3 years of follow-up, ulceration occurred in 5.1, 14.3, 18.8, and 55.8% of people in each of the four groups respectively (p<0.001). All amputations occurred only in groups 2 and 3 (3.1 and 20.9%, p<0.001). People in the high risk group (Group 3) were 34.1 times (CI 11.0-105.8) more likely to develop an ulcer, and 2.7 times (CI 2.2-3.4) more likely to have a lower-extremity amputation in the follow-up period.

A current ulcer is a high risk indicator for amputation

197 people with diabetes (89% with Type 2 diabetes) who presented with a new foot ulcer were followed up until outcome was noted eg healing, amputation (Oyibo et al, 2001). The mean age and duration of diabetes was 56.6 ± 12.6 and 15.4 ± 9.9 years respectively. At the end of the study 65% of ulcers healed completely, 16% were still unhealed and 15.5% had resulted in an amputation. The remaining 3.5% of patients died. The size of the ulcer at presentation was significantly higher in the group who required amputation compared with the group who did not 3.9 (1.4-5.4) cm v 1.1 (0.5-2.6) cm ($p<0.0001$).

A prospective Swedish study followed 108 men and 81 women with diabetes aged between 32 and 94 years, who had achieved healing after an index amputation – 93 below ankle amputations and 96 above ankle amputaations. After a mean 6.3 years of follow up, 85% of new amputations were preceded by a foot ulcer (Larsson et al, 1998).

In the continuing Seattle Diabetic Foot Study of outpatients in a Veterans Affairs medical clinic, 776 people with diabetes (median age 65 years) were followed for a median of 3.3 years. All people who had an amputation, but only 27% of people who did not, had a preceding ulcer at sometime before or during the study ($p<0.001$) (Adler et al, 1999). Embedded in this study was a paired case control analysis which included 20 people without amputation before study entry who had an amputation during follow up - 17 ipsilateral LEA and 3 contralateral amputation. The OR associated with first ulcer for subsequent ipsilateral amputation was 5.7 (CI 1.6-30.2) (Adler et al, 1999).

Summary - Ulcer as a Risk Factor for Amputation

- History of past diabetic foot ulcer indicates an increased life long risk of recurrent foot ulceration or amputation

- A current foot ulcer increases the risk of amputation.

- A second amputation after either a major or minor amputation has occurred is preceded by an ulcer in 85% of cases

Evidence Table: Section 4

Ulcer as a risk factor for amputation

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Adler AI (1999) (Adult men – US)	III-2	Cohort	High	High +	High
del Aguila MA (1994) (Adult men – US)	III-2	Case-control	Medium	High +	High
Larsson J (1998) (Adults – Sweden)	III-2	Cohort	High	High +	High
Lee JS (1993) (Adults – US: Oklahoma Indians)	III-2	Cohort	Medium	High +	Low
Mayfield JA (1996) (Adults – US: Gila River Indians)	III-2	Case-control	High	High +	Low
Moss SE (1999) (Adults – US)	III-2	Cohort	High	High +	High
Murray HJ (1996) (Adults – UK)	III-2	Cohort	Medium	High +	High
Oyibo SO (2001) (Adults – US)	III-2	Cohort	Medium	High +	High
Pecoraro RE (1990) (Adult men – US)	III-2	Case-control	High	High +	High
Peters EJG (2001) (Adults – US)	III-2	Case-control	Medium	High +	High
Ramsey SD (1999) (Adults – US)	III-2	Cohort	High	High +	High

For magnitude rating:
+ ulcer is a risk factor for amputation. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 5: Diabetes Foot Problems

Issue

What is the most practical method for detecting loss of protective foot sensation in the primary care setting?

Recommendation

People with Type 2 diabetes should be routinely assessed with the 10g Semmes-Weinstein monofilament to detect loss of protective foot sensation.

Evidence Statements

- Loss of sensation to the 10g Semmes-Weinstein monofilament predicts foot ulceration and amputation
  Evidence Level III-2

- The 10 g Semmes-Weinstein monofilament is clinically reliable
  Evidence Level III-2

Background - Detection of Loss of Protective Foot Sensation

Peripheral neuropathy is common in people with Type 2 diabetes and was present in 12.3% of people participating in the United Kingdom Prospective Diabetes Study at diagnosis and in approximately 30% after 12 years (UKPDS 33, 1998). As reviewed in Section 1 peripheral neuropathy is a major risk factor for both foot ulceration and amputation. Therefore its clinical detection is important in identifying feet at risk of ulceration and is pivotal for effective strategies to prevent foot ulceration and amputation.

One of the main objectives of the foot examination in the primary care setting is to detect a level of peripheral neuropathy which significantly increases the risk of sustaining a foot wound, which is defined as 'loss of protective sensation'. This is one of the most important criteria in identifying people at high-risk of foot problems and is paramount in implementing a structured management plan to prevent lower extremity complications (Armstrong et al, 1998). The detection of loss of protective sensation is an important indicator to both the person with diabetes and the primary carer that more frequent review and suitable preventative actions should be instituted and necessitates behavioural change in both the person with diabetes and the doctor.

Several methods have been used to assess peripheral neuropathy in clinical studies and include:

- the 10g Semmes-Weinstein monofilament
- vibration perception threshold (VPT) measured using a biothesiometer or 128Hz tuning fork
- calculation of a neuropathy score based on:
  - symptoms - the University of Texas Subjective Peripheral Neuropathy questionnaire which relies on 4 questions of symptoms of neuropathy (Dyck, 1988) or
  - clinical examination - the neuropathy disability score derived from a combination of testing for pain, temperature and vibration threshold with the presence or absence of ankle reflexes (Young et al, 1993b)

Symptoms alone are not considered reliable because a significant proportion of people with diabetes who have neuropathy are asymptomatic (Young & Matthews, 1998). Similarly testing of ankle jerks alone is of little value since they are frequently absent in the elderly population, with or without diabetes (de Hens-van Putten et al, 1996) and has not been as successful as the more objective measures (eg VPT) in predicting ulceration or amputation in people with diabetes.

The primary care setting requires a simple, cheap and reliable means of identification of the foot which has lost protective sensation (the insensate foot) and has led to the increasing popularity of the 10g Semmes-Weinstein monofilament. The monofilament consists of a pressure sensitive nylon filament attached to a rod. The monofilament buckles at a reproducible pressure of 10g force which has been identified as the level of sensation protective against foot ulceration, initially in leprosy (Birke & Sims, 1986; Halar et al, 1987). The loss of this protective sensation at one site is taken as indicating an abnormal monofilament test. The test must be performed in areas free of callus which may impair the ability to feel the monofilament.

The other frequently reported method is the biothesiometer. This is a handheld device which vibrates at 100Hz and connects by an electrical cord to a base unit which allows the voltage to be increased by the operator through a range of 0 to 50V which is displayed on a scale. This instrument is popular in specialist diabetes units but is infrequently used in the primary care setting.

Foot examination of people with diabetes is often inadequate. One study of people admitted to a teaching hospital with diabetes foot problems reported that less than 15% received a minimally competent lower limb examination as part of their routine care (Armstrong et al, 1998).

Evidence – Detection of Loss of Protective Foot Sensation

Loss of sensation to the 10g Semmes-Weinstein monofilament predicts foot ulceration and amputation

In a systematic review, Mayfield and Sugarman (2000) identified 6 prospective studies using the 10g Semmes-Weinstein monofilament and 4 using VPT to predict the risk of foot ulceration and amputation. Among people who were unable to feel the Semmes-Weinstein monofilament which was tested in 1 to 4 sites including the plantar surface of the toes, metatarsal heads, insole, and heel, and the dorsum of the foot, the odds ratio (OR) of increased risk of ulceration ranged from 4.1 (CI 1.89-8.87) to 18.4 (CI 3.83-88.47), and the relative risk (RR) of amputation ranged from 2.2 (CI 1.5-3.1) to 9.9 (CI 4.8-21.0). Similarly, the risk of ulceration increased in people with VPT >25, with an OR ranging from 4.4 (CI 1.1-17.3) to 10.8 (CI 4.6-25.7).

The following provides more details on studies included in the above systematic review. In prospective studies, the 10g Semmes-Weinstein monofilament has emerged as the most sensitive test for peripheral neuropathy in predicting foot ulcer risk. Boyko and coworkers (1999) studied 749 US veterans with diabetes who were followed up for a mean of 3.7 years. 163 ulcers developed during the follow-up. The risk of developing a foot ulcer was significantly higher for inability to perceive the 10g Semmes-Weinstein monofilament at one or more of 9 sites (RR 3.37, CI 2.45-4.63; p<0.001) compared with loss of vibration sensation with the 128 Hz tuning fork (RR 2.33, CI 1.66-3.28; p<0.001) and absence of Achilles tendon reflex (RR 1.40, CI 1.03-1.90; p=0.030). However in multivariate logistic regression analysis, only the 10g Semmes-Weinstein monofilament was an independent predictor of future foot ulceration (RR 2.2, CI 1.5-3.1; p<0.001).

McNeely et al (1995), in a prospective case-control study in the Seattle Veterans Affairs Medical Centre, compared 46 people with diabetes and foot ulcers to 322 control subjects without foot ulcers. Neuropathy was determined by vibration sensation with 128Hz tuning fork, a 10g Semmes-Weinstein monofilament and Achilles tendon reflexes. Vascular indices included ankle/arm blood pressure and $TcPO_2$ on the dorsal foot. In multivariate logistic regression analysis, the 10g Semmes-Weinstein monofilament was the single most practical measure of risk assessment. The adjusted OR for not feeling the 10g Semmes-Weinstein monofilament was 18.42 (CI 3.83-88.47) compared with an OR for absent Achilles tendon reflexes (OR 6.48, CI 2.37–18.06), while absent vibration sensation was not a significant independent risk factor (McNeely et al, 1995).

In another prospective study of native American Indians, sensory status was determined by the 10g Semmes-Weinstein monofilament applied to 8 points on the plantar surface of each foot. The 358 subjects were blindfolded and retested twice before being classified as insensate (if they consistently failed to feel the filament at one or more locations). 68 subjects were unable to feel the monofilament at screening. Among this group, there was a significantly increased risk of subsequent ulceration (OR 9.9, CI 4.8-21.0) and amputation (OR 17, CI 4.5-95.0) compared with those who retained sensation (Rith-Najarian et al, 1992).

In another case-control, 30 people with recent or current foot ulceration were compared with 85 controls without a history of foot ulcer (Armstrong et al, 1998). The sensitivity and specificity of VPT testing assessed using a biothesiometer, the 10g Semmes-Weinstein monofilament and a 4-question verbal neuropathy score were compared. Overall, VPT > 25V or four or more of eight imperceptible monofilament sites had higher sensitivity (100%) and specificity (76.5%) than the symptom score. However combining the modalities increased specificity (88.2%) but sensitivity decreased to 88.2%. Armstrong and coworkers recommend the monofilament as an inexpensive and reliable method for use in primary care, nursing or specialist practice.

The different screening techniques to identify diabetic people at high risk of foot ulceration were compared by Pham and coworkers (2000) in 248 people who were followed up for 30 months. Foot ulcers developed in 73 people or 95 feet during the study. People with foot ulcer were more likely to be insensate to the 10g Semmes-Weinstein monofilament (p=0.000), had a higher neuropathy symptom score (NDS) (p=0.000), a high VPT (p=0.000), and high foot pressure (p=0.000) compared with people who did not develop a foot ulcer. Of these techniques, inability to feel the monofilament combined with high NDS had a sensitivity of 99% for foot ulcer development, while the best specificity of 78% was seen with the combination of high NDS and foot pressure. A multivariate analysis showed that significant factors for developing foot ulcer were high NDS (OR 3.1, CI 1.3-7.6, p=0.013), high VPT (OR 3.4, CI 1.7-6.8, p=0.001), inability to detect the monofilament (OR 2.4, CI 1.1-5.3, p=0.036), and high foot pressure (OR 2.0, CI 1.2-3.3, p=0.007). The authors concluded that clinical examination combined with testing with the 10g Semmes-Weinstein monofilament is the most sensitive test in identifying people at high risk for foot ulceration.

The 10g Semmes-Weinstein monofilament is clinically reliable

In 1,001 people attending a UK diabetes clinic, foot examination was performed with the 10g Semmes-Weinstein monofilament, biothesiometer and pulse palpation (Klenerman et al, 1996). 229 people with an initial abnormal test were invited for a second test. Of this group, 21.8% had loss of protective sensation as judged by the absence of some or all protective sensation to the monofilament; 7.7% had absent pedal pulses and 4% had combined vascular and sensory loss. Between the two testings the biothesiometer variation was considered clinically unacceptable. The results for palpation of pedal pulses were more stable, with 81% of people having the same results for the posterior tibial pulse on the right, compared to 70% on the left side; and 82% having the same results for the dorsalis pedis on the right, while only 68% on the left side. The monofilament gave the same result in the first and second tests for 88% of people on the right, and 85% on the left side. The stability of testing with the monofilament prompted the authors to recommend its routine use in screening for at risk feet.

There is no universal consensus on the optimal testing sites for the 10g Semmes-Weinstein monofilament with various studies recommending between 1 and 10 different sites. McGill et al (1999) addressed this question in a study of 132 randomly selected Australian people with diabetes by calculating the sensitivity and specificity of the 10g Semmes-Weinstein monofilament assessed at 5 different sites in identifying people with a VPT >40V using the biothesiometer. Inability to detect the monofilament at either of the sites over the first and fifth metatarsal heads gave a sensitivity and specificity of 80% and 86% respectively for a VPT >40V. While providing a practical approach to screening large numbers of people with diabetes it should be noted that in this study the choice of a VPT >40V was arbitrary and that ulceration was not a study endpoint (McGill et al, 1999).

Summary - Detection of Loss of Protective Foot Sensation

- A loss of sensation to the 5.07 Semmes-Weinstein monofilament which exerts a 10g pressure at buckling point indicates loss of protective foot sensation

- Failure to feel the 10g Semmes-Weinstein monofilament at one uncallused plantar site is predictive of future foot ulceration

- The 10g Semmes-Weinstein monofilament is equivalent to or better than other simple tests of neuropathy for the primary care setting

- The Semmes-Weinstein monofilament test is simple and its reliability is clinically acceptable

- Data on the optimal number and location of sites for testing with 10g Semmes-Weinstein monofilament are limited and further research is required

- The limited available data suggest that testing at two sites, over the first and fifth metatarsal heads, is sufficient to identify loss of protective sensation

Evidence Table: Section 5

Detection of Loss of Protective Foot Sensation

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Armstrong DG (1998) (Adults – US)	III-2	Case-control	Medium	High +	High
Boyko EJ (1999) (Adults – US)	III-2	Cohort	High	High +	High
Klenerman L (1996) (Adults – UK)	III-2	Cross-sectional	High	High +	High
Mayfield JA (2000)	III-2	Systematic review of Cohort studies	Medium	High +	High
McGill M (1999) (Adults – Australia)	III-2	Cross-sectional	Medium	High +	High
McNeely MJ (1995) (Adults – US)	III-2	Case-control	High	High +	High
Pham H (2000) (Adults – US)	III-2	Cohort	High	High +	High
Rith-Najarian S (1992) (Adults – Red Lake Chippewa Indians)	III-2	Cohort	High	High +	Low

For magnitude rating:
+ Semmes-Weinstein monofilament predicts foot ulceration. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 6: Diabetes Foot Problems

Issue

How should peripheral vascular disease be assessed clinically?

Recommendation

People with diabetes should be assessed for peripheral vascular disease by:
- enquiring about symptoms of intermittent claudication
- palpation of pedal pulses

Evidence Statements

- Intermittent claudication is indicative of peripheral vascular disease
  Evidence Level III-2

- The absence of intermittent claudication does not exclude peripheral vascular disease
  Evidence Level III-2

- Palpable foot pulses in people with diabetes make significant peripheral vascular disease unlikely
  Evidence Level III-2

- The absence of foot pulses increases the likelihood of amputation
  Evidence Level III-2

Background - Clinical Detection of Peripheral Vascular Disease

Peripheral vascular disease (PVD) is common in people with Type 2 diabetes being present in 8% at the time of diagnosis and in 45% of people who have had diabetes for 20 years (Hiatt & Sussman, 1994). The prevalence of PVD at diagnosis of diabetes and the risk of developing PVD over time increase with increasing age (Davis et al, 1997). As reviewed in Section 2, PVD is an important risk factor for amputation. Although various factors predict the outcome of foot ulcers in people with diabetes, the severity of existing lower extremity arterial disease is considered to be the main independent risk factor for major amputation (Pecoraro et al, 1990).

While sophisticated and invasive tests are now available to quantify the extent of PVD in people with diabetes, clinical means of identifying those with PVD remain important in the primary care setting. A history of intermittent claudication is a well recognised feature of PVD. Claudication pain arises in an exercising muscle when the perfusion pressure of the blood during exercise is insufficient to remove anaerobic metabolites and maintain muscle function. In contrast to those without diabetes, the arteries below the knee are more severely affected in people with diabetes (LoGerfo & Coffman, 1984). Exercise-induced leg pain most commonly begins in the calf but can extend to the thigh or buttocks if exercise is continued. Severe claudication is most often the result of multilevel arterial disease.

Palpation of foot pulses is a routine part of the assessment of the peripheral circulation in people with diabetes. Pedal pulse palpation is a simple and adequately reliable clinical method (Meade et al, 1968). Other clinical signs which may be useful include atrophic skin and loss of hair, pallor on elevation followed by dusky colour on dependency and a prolonged capillary filling time.

Several studies have reported that clinical signs of PVD correlate well with future risk of amputation although it should be remembered that the absence of claudication does not exclude a diagnosis of PVD since pain may not be a feature if peripheral neuropathy is also present. Also some of the controversy about the usefulness of routine clinical examination of peripheral pulses is in part related to inter-observer variation and a relatively high false-positive rate for the presence of PVD.

Evidence - Clinical Detection of Peripheral Vascular Disease

Intermittent claudication is indicative of peripheral vascular disease

A cross-sectional study in 631 predominantly male veterans (mean age 63.4 years) with diabetes in a general medical clinic compared the accuracy of data from history and physical examination on the detection of severe PVD, assessed by an ankle-arm index (AAI) ≤0.5 using Doppler blood pressure measurements (Boyko et al, 1997). The study showed that 46 people had severe PVD (AAI ≤0.5) in the right leg, 44 in the left leg, and 26 in both legs. Claudication symptoms had a sensitivity of 50% and a specificity of 87% for PVD by AAI, compared with 65% and 78% for absent or diminished peripheral pulses and 22% and 93% for venous filling time >20 seconds. A stepwise logistic regression model identified age, symptom of claudication, self-reported history of PVD, absent or diminished peripheral pulses and prolonged venous filling time as significantly associated with AAI ≤0.5 (all p<0.05). The use of AAI has some limitations because of the potential for a falsely high result due to arterial calcification, however a conservatively low cutoff of 0.5 was used to diagnose PVD in this study (Boyko et al, 1997).

Walters et al (1992) studied the predictive values of a history of claudication or the absence of 2 or more pedal pulses in identifying PVD defined in terms of an ABI ≤0.9. In 1,058 people with diabetes (mostly Type 2 diabetes), 34% had claudication. A history of intermittent claudication had a sensitivity of 34%, specificity of 97% and positive predictive value of 72% for PVD.

In a cross-sectional study, Taniwaki et al (2001) evaluated 315 people with Type 2 diabetes. Intermittent claudication and/or leg pain at rest and reduced ABI (<0.9) were used as subjective and objective measures of PVD, respectively. Overall, 49 people had intermittent claudication and 9 had leg pain at rest. Of the 56 people with a low ABI (<0.9), 26 who had PVD symptoms.

The absence of intermittent claudication does not exclude peripheral vascular disease

Asymptomatic PVD is common in people with diabetes. In a study of 104 people with diabetes admitted for current foot ulcers from 1993 to 1995, PVD was assessed by digital subtraction angiography (DSA) (Faglia et al, 1998). Of the 103 subjects in whom DSA detected a haemodynamically significant vascular stenosis, ischaemic pain was present in only 26.2% and in the remaining 73.8% pain was completely absent.

Elhadd et al (1999) assessed 48 people with diabetes (n=45 with Type 2 diabetes) who had no symptoms or history of PVD using the ABI and peripheral pulse palpation. An ABI <0.9 was considered abnormal. Of the 48 people, 12 had palpable dorsalis pedis and posterior tibial pulse, while 36 had absent pulses. The 12 people who had palpable pulses had an ABI >1.0 with a median of 1.10 (1.01-1.30). Among the 36 people with absent peripheral pulses, only 18 people had evidence of PVD, with a median ABI of 0.76 (0.49-0.89), while the other 18 people had a normal ABI with median of 1.08 (0.92-1.05). Despite these people being asymptomatic, 37.5% were found to have PVD based on a low ABI.

Walters et al (1992) found PVD, which was defined as an ABI of 0.9 or less, present in 23.5% of people with Type 2 diabetes (n=864), of whom only 34% complained of claudication.

Summarising the above two evidence statements, the presence of intermittent claudication is strongly suggestive of PVD, but less than half of people with diabetes who have PVD experience intermittent claudication.

Palpable foot pulses in people with diabetes make significant peripheral vascular disease unlikely

Congenital absence of peripheral pulses is rare. In a study of 548 healthy young people, the posterior tibial pulse was absent in only 0.18%, while the dorsalis pedis pulse was bilaterally absent in 1.8% and unilaterally absent in 3.0% (Robertson et al, 1990).

McGee and Boyko (1998) reviewed papers published between 1966 and 1997 regarding bedside diagnosis of PVD. The majority of the 17 studies identified was on people without diabetes. The authors concluded that the following positive findings were helpful in diagnosing PVD: abnormal pedal pulses, a unilateral cold extremity, prolonged venous filling time and a femoral bruit. In deciding whether a pulse is present or absent, clinicians demonstrated fair to almost perfect agreement (McGee & Boyko, 1998).

In a cross-sectional study of 631 veterans with diabetes attending a general medical clinic in the US, history and clinical examination were evaluated in detecting PVD (Boyko et al, 1997). The criterion used for PVD was an ABI ≤0.5, derived from Doppler blood pressure measurements of ankle and brachial systolic pressures. Pulses were recorded as absent in one foot only if both pulses were absent. Absent peripheral foot pulses had a sensitivity of 65% and a specificity of 78% for detecting an ABI with ≤0.5. Diminished foot pulses and delayed venous filling were associated with the highest positive likelihood ratios. Classical signs such as decreased hair, or skin atrophy were not clinically useful. Diminished or absent peripheral pulses in a leg had a sensitivity of 65.2% and a specificity of 78.3% with a positive likelihood ratio of 3 (CI 2.3-3.9) and a negative likelihood ratio of 0.4 (CI 0.3-0.7) for an ABI < 0.5. In multivariate analysis a negative history of PVD and palpable peripheral pulses effectively ruled out the presence of PVD (Boyko et al, 1997).

A prospective study in Denmark examined the relationship between pedal pulses and measurement of distal systolic pressure in a group of 132 people without diabetes suspected of having PVD (data on 15 people with only one leg were not included) (Christensen et al, 1989). The group was aged 62 years, half were men and all had claudication, rest pain or ulcers of presumed arteriosclerotic origin. The presence of palpable pedal pulses was usually associated with an ankle index >50% (ankle systolic pressure as a percentage of systemic systolic pressure) and a toe systolic pressure >40 mmHg.. The median ankle index was 94% in the 52 people with palpable pulses in both feet, 50% in the 38 people without palpable pulses in both feet, and 54% in the 27 people with palpable pulses in only one foot. Repeated assessment of the pulses in the feet over time was found to be useful in following the progress of peripheral arterial disease as well as healing of any ulcer present.

The absence of foot pulses increases the likelihood of amputation

The absence of peripheral pulses has prognostic significance. In a study of 314 people with mainly Type 2 diabetes and foot ulceration who were followed prospectively, the absence of pedal pulses was more common in people who underwent amputation than in those who had an ulcer which healed (77 v 44%, p<0.001) (Apelqvist et al, 1990).

In a Finnish cohort study, Lehto et al (1996) reported that the absence of palpable peripheral pulses predicted amputation in 1,044 people aged 45-64 years with Type 2 diabetes. During 7-year follow-up, amputation occurred in 5.6% of men and 5.3% in women. The age- and sex-adjusted RR for lower extremity amputation was 3.9 (2.3-6.5, p<0.001) in people with two or more absent peripheral pulses.

Summary - Clinical Detection of Peripheral Vascular Disease

- Peripheral vascular disease is common in people with Type 2 diabetes and is an important risk factor for amputation
- The presence of symptoms of intermittent claudication has a sensitivity of 50% and a specificity of 87% for peripheral vascular disease determined by an ankle arm index ≤0.5
- Less than half of people with diabetes and peripheral vascular disease experience intermittent claudication
- The presence of palpable pedal pulses is a good predictor of adequate peripheral circulation but their absence is only a moderate predictor of peripheral vascular disease.
- Both dorsalis pedis and posterior tibial pulses should be impalpable for the designation "absent foot pulses"
- A negative history of peripheral vascular disease together with palpable peripheral pulses usually excludes a critical reduction in limb perfusion
- History of claudication and palpation of peripheral pulses are reliable in detecting peripheral vascular disease in a routine practice setting
- The absence of peripheral pulses has prognostic significance for future amputation in people with diabetes with and without foot ulceration

Evidence Table: Section 6

Clinical detection of peripheral vascular disease

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Apelqvist J (1990) (Adults – Sweden)	III-2	Cohort	Medium	High P+	High
Boyko EJ (1997) (Adults – US)	III-2	Cross-sectional	Medium	High I+P+	High
Christensen JH (1989) (Adults – Denmark)	III-2	Cross-sectional	Medium	Low	Low
Elhadd TA (1999) (Adults – UK)	III-2	Cross-sectional	High	High I-P+	High
Faglia E (1998) (Adults – Italy)	III-2	Cross-sectional	Medium	High I-	High
Lehto S (1996) (Adults – Finland)	III-2	Cohort	High	High P+	High
McGee SR (1998)	III-2	Systematic review of cohort studies	High	High P+	Low
Robertson GSM (1990) (Adults & Adolescents – UK)	III-2	Cross-sectional	Low	High P+	Low
Taniwaki H (2001) (Adults – Japan)	III-2	Cross-sectional	High	High I+	High
Walters DP (1992) (Adults – UK)	III-2	Cross-sectional	High	High I+	High

For magnitude rating:
+ indicates positive clinical detection of peripheral vascular disease. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 7: Diabetes Foot Problems

Issue

What should be the frequency of foot examination?

Recommendation

The routine surveillance for foot problems in people with diabetes should be performed in the following way:

- in people without established foot problems, the minimum frequency of foot examination should be once a year
- in people with at risk feet but without a current active problem, foot examination should be performed every 3 to 6 months

Evidence Statements

- Routine examination of the feet of people with diabetes is frequently not performed
  Evidence Level III-2

- The optimal frequency of foot examinatin has not been established but there is general international consensus
  Evidence Level I

Background - Frequency of Foot Examination

While people with diabetes who have peripheral neuropathy, foot deformity, history of previous ulceration or amputation and/or PVD are a group at increased risk of ulceration and amputation, no studies have been done to assess the impact of the frequency of examination on outcomes. It is generally accepted that regular surveillance for foot problems is good clinical practice. The benefits of monitoring people with diabetes arise from the ability to detect feet at increased risk and from the identification of specific foot problems which can be treated early which has the potential to reduce subsequent morbidity.

Evidence – Frequency of Foot Examination

Routine examination of the feet of people with diabetes is frequently not performed

The lack of routine foot examination is a major issue in the care of people with diabetes. A UK retropective survey (Deerochanawong et al, 1992) showed that 47% of people who were under the care of a hospital service for diabetes had incomplete foot examination and assessment. 15% of people with diabetes had their diabetes first diagnosed when they were admitted for amputation.

In a New Zealand survey of 540 people with diabetes (Simmons et al, 1995), major lesions (amputation, ulcer) and perdisposing lesions (callus or fugual infection) were present in 48.5% of people. However, 40% of people (n=214) reported they had not had their feet examined over the previous 12 months.

Wylie-Rosett et al (1995) reviewed foot examination in 350 people with diabetes (86% were black or Hispanic, mean age 57.7 years). A documented foot examination was defined as assessing at least two of the three components (circulation, skin and neurological status) of a foot examination. People had a mean duration of diabetes of 8.8 years, but there was no indication of foot examination or referral for foot examination for 56% of people in their primary care clinics during a 2-year period.

The optimal frequency of foot examination has not been established but there is general international consensus

Although regular foot examination is considered necessary in all people with diabetes, no studies were found which directly addressed the optimal frequency of foot examination in people with diabetes. However recommendations about the frequency of foot examination have been made in several guidelines in Australia and overseas.

The Australian guidelines include:

- the New South Wales Department of Health 'Guidelines for the Clinical Management of Diabetes Mellitus' (1996) which suggests six monthly foot review of people with diabetes or at every visit for people in the "high risk foot" category
- the 'Systematic Review of Existing Evidence and Primary Care Guidelines on the Management of Non-Insulin-Dependent Diabetes in Aboriginal and Torres Strait Islander Populations' (Couzos et al, 1998) proposes that feet should be inspected

at every clinic visit, but more comprehensive (vascular and neurological) examination should be performed annually

- the position statement of the Australian Diabetes Society on the Lower Limb in People with Diabetes (Campbell et al, 2000) states that all people should have annual routine foot screening and people with 'at risk' feet should be inspected at each clinical visit

The following guidelines were formulated by overseas groups:

- The US Veterans Health Administration 'Clinical Guidelines for Management of Patients with Diabetes Mellitus' (1997) recommend that foot examination should be performed at least annually in all people with diabetes who are over 15 years of age and at more frequent intervals for those at high risk
- The Scottish National Clinical Guidelines (The Scottish Intercollegiate Guidelines Network, 1997) recommend annual screening examination of feet with more frequent review of people with identified risk factors
- The European Diabetes Policy Group (1999) states that surveillance for foot problems should be a routine part of the annual review
- International Consensus on the Diabetic Foot guideline (1999) - all people with diabetes should be examined at least once a year for potential foot problems and all people with demonstrated risk factor(s) should be examined more often (every 1-6 months)
- The UK Clinical Guidelines for Type 2 Diabetes - prevention and management of foot problems recommend annual routine screening for foot problems
- The American Diabetes Association (2004) suggests at least annual review with more frequent evaluation once risk factors are detected. People with neuropathy should have a visual inspection of their feet at every visit

As with all recommendations, the frequency of assessment should be modified by clinical judgment. However there is general agreement that good clinical practice in the management of people with diabetes includes the following routine surveillance for foot problems:

- in people where no foot complications have previously been found, the minimum frequency of foot examination should be once a year as part of the annual review
- in people with at risk feet but without a current active problem, a foot examination should be performed every 3 to 6 months

Summary - Frequency of Foot Examination

- A number of studies have shown that routine foot examination is frequently not performed in people with diabetes

- No studies have examined the impact of frequency of foot examination on clinical outcomes in people with diabetes

- There is general agreement that people with diabetes should have their feet examined every year for risk factors and if risk factors are identified feet should be examined more frequently

- ## Summary Table: Section 7

Frequency of foot examination

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
American Diabetes Association (2004)	Not gradeable	Position statement			
Campbell LV (2000)	Not gradeable	Position statement			
Couzos S (1998) (Australia: Aboriginal & Torres Strait Islanders)	I	Systematic review	High	High +	High
Deerochanawong C (1992) (Adults – UK)	III-2	Cross-sectional	Medium	Medium	High
European Diabetes Policy Group (1999)	Not gradeable	Consensus guidelines			
International Consensus on the Diabetic Foot (1999)	Not gradeable	Consensus Guidelines			
New South Wales Dept Health (1996)	Not gradeable	Evidence/ Consensus guidelines			
Scottish Intercollegiate Guidelines Network (1997)	I	Systematic review	High	High +	High
Simmons D (1995) (Adults – New Zealand)	III-2	Cross-sectional	Medium	Medium	High
UK Guidelines (1999)	I	Systematic review	High	High +	High
Veterans Health Administration (1997)	I	Systematic review	High	High +	High
Wylie-Rosett J (1995) (Adult s – US)	III-2	Cross-sectional	Medium	Medium	Low

For magnitude rating:
+ Recommended that the foot is examined regularly. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 8: Diabetes Foot Problems

Issue

Does patient education improve footcare and outcomes?

Recommendation

People with diabetes should receive specific footcare education.

Evidence Statements

- Footcare education for people with diabetes improves knowledge and may improve self care behaviour
  Evidence Level I

- Footcare education for people with diabetes may prevent serious foot lesions and amputation
  Evidence Level I

Background - Patient Education and Foot Disease

An integral part of any strategy to reduce diabetes foot problems requires people with diabetes to have adequate knowledge to be able to take appropriate action to minimise their risk of developing foot complications (Levin, 1995). Deficiencies in self care of feet can occur because people with diabetes have received inadequate information or are not aware of the importance of, or are unable to perform, foot self care behaviour. One study showed that 89% of people with diabetes whose feet are at increased risk were making multiple errors in their foot self care behaviour (Plummer & Albert, 1995). Unfortunately the healthcare system does not currently provide easily accessible education or podiatry services for people with diabetes whose feet are "at risk" (Fletton et al, 1995). Those who are physically unable to practice self footcare due to age or a disability, like visual impairment, are often dependent on family or carers who must also be involved in the educational process. Also people with a lower socio-economic status have increased risk of foot ulceration and poorly fitting (or lack of) footwear (Day & Harkless, 1997).

The extent and nature of the education necessary to prevent the development of diabetic foot problems and the means of selecting an appropriate educational strategy for each person is another important consideration. There is a general lack of consistency of educational interventions which have used different methods, target groups, settings and methods of follow-up which has complicated interpretation of educational studies (Mason et al, 1999).

Even the most successful published footcare education programmes have not always continued to be used in the institutions where they were developed (Pichert & Penha, 1993). Footcare education programmes should be coordinated and not provide education to people with diabetes but staff should also receive education and prompting to perform routine footcare tasks.

Evidence - Patient Education and Foot Disease

Footcare education for people with diabetes improves knowledge and may improve self care behaviour

Valk et al (2002) conducted a Cochrane systematic review through searching Medline, CINAHL and EMBASE, hand searching of wound care journals and relevant conference proceedings and identified 8 prospective randomised controlled trials which evaluated educational programmes for the prevention of foot ulcers in people with Type 1 or 2 diabetes. Four RCTs comparing intensive with brief educational interventions were identified (Barth et al, 1991; Kruger et al, 1992; Ronnemaa et al, 1997; Malone et al, 1989). All four were performed in an outpatient care setting. Patients' knowledge of foot care was reported in 3 of the 4 RCTs (Barth et al, 1991; Kruger et al, 1992; Ronnemaa et al, 1997). This outcome was significantly improved in 2 of the RCTs, at 6 months in one (Barth et al, 1991) and at 1 year in the other (Ronnemaa et al, 1997). In one RCT, foot care knowledge was not improved in the intervention group at 6 months follow up (Kruger et al, 1992). However, this RCT studied small groups (23 patients in the intervention group and 27 in the control group), and also had a relatively high dropout rate.

Behaviour assessment scores, measured in all studies using newly developed and non validated scoring lists, were also reported in those 3 RCTs (Barth et al, 1991; Kruger et al, 1992; Ronnemaa et al, 1997). The foot care behaviour of patients (e.g. washing, creaming, foot inspection, cutting toe nails, use of pumice stone, foot gymnastics) improved significantly at 6 months (Barth et al, 1991; Kruger et al, 1992) and one year (Ronnemaa et al, 1997).

One RCT evaluated the effect of foot care education as part of general diabetes education in primary care (Bloomgarten et al, 1987). No significant effect was found after a follow up of approximately 1.5 years on the behaviour assessment scores (7 questions on diabetes self care of which 1 asked how often the feet were checked for sores). Callus, nail dystrophy and fungal infections were not different between intervention and control groups after 1.5 years.

One RCT evaluated the effect of a complex intervention that included patient education on foot care, in a primary care setting (Litzelman et al, 1993). This intervention was targeted at both patients and doctors. A significant positive effect was found on patients' foot care behaviour.

Two RCTs evaluated the effect of patient education, tailored to the educational needs of the patients (Mazzuca et al, 1986; Rettig et al, 1986). One was performed in primary care (Mazzuca et al, 1986), the other study in the home environment (Rettig et al, 1986). In the first, foot care knowledge only was assessed at 1 year, and no effect was found (Mazzuca et al, 1986). In the second, there was a statistically significant improvement in foot care knowledge at 6 months follow up (Rettig et al, 1986). However, no positive effects were found on foot appearance and foot care skills score.

Mason et al (1999) reviewed 5 randomised footcare educational studies which included people with Type 2 diabetes. They reached the conclusion that since there were no consistent patterns in study methods or findings that it was necessary to interpret the results of each study individually. Therefore studies which have addressesd this question are described in more detail below.

Rettig et al (1986) evaluated the effects of an individualised diabetes self-care home education programme. Of 471 people with Type 2 diabetes enrolled, 228 were assigned to the home education group and 243 to the control group. After 6 months footcare knowledge score was significantly higher among the intervention subjects compared with the control subjects (62.2±1.7 v 53.1±1.8, p=0.001), but there were no differences in footcare skill score (71.8±2.0 v 68.9±1.8, p=NS) or foot appearance score (70.2±0.7 v 68.8±0.7, p=NS). At 12 months there were no differences in diabetes-related hospitalisations between the2 groups.

Bloomgarden et al (1987) evaluated a diabetes clinic education (general and footcare) programme in 266 people with insulin treated diabetes (127 in the education group and 139 in the control group). There were no significant differences between groups in type or duration of diabetes, insulin dosage, and educational background. Knowledge score (which did not include any question related to feet) increased in the education group (5.3±1.6 to 5.8±1.6) but did not change in the control group (5.3±1.7) (p=0.007). The behaviour score (which included 1 question about frequency of foot inspection) improved in both groups (3.4±1.4 to 4.3±1.6; 3.6±1.6 to 4.1±1.6, respectively) (p=0.10). Among 83 people without foot lesion at the initial evaluation in the eduction group, 31 developed mild and 2 developed severe foot lesions during the 18 month period; while among 63 people without foot lesions in the control group, the corresponding number were 28 and 2, respectively (p=0.63).

Barth et al (1991) compared a conventional group eduction programme with a similar programme which included 4 additional footcare sessions based on a cognitive motivational technique in 70 Australian people with Type 2 diabetes with sub-optimal glucose control and who had not attended a diabetes education programme in the past six months. The intensive group showed a greater improvement than the conventional group in footcare knowledge (p<0.001), compliance with the recommended footcare routine (p=0.012), and compliance with advice to consult a podiatrist for further treatment (p=0.008) at 1 month, and these effects were maintained at 6 months.

Kruger et al (1992) evaluated the effectiveness of two education programmes in 50 people with diabetes. The control group received a lecture presentation on foot care, while the experimental group participated in a hands-on footcare session on foot care in addition to the lecture presentation. Daily foot check sheets were given to all participants to encourage daily foot inspection. After 6 months, the experimental group reported improvements in daily foot inspection (52.5 to 66.7%) and trimming toenails regularly (34.8 to 80.0%), but there was no significant increase in footcare knowledge score in the intervention group but knowledge score improved significantly in the control group.

In a randomised controlled trial of 395 people with Type 2 diabetes, Litzelman et al (1993) assessed the effect of a multifaceted intervention in a general practice setting. The 12-month intervention included a footcare session with 1 to 4 people conducted by nurse clinicians which covered footcare behaviours and proper footwear, and follow-up by telephone and postcards reminding people of self footcare. At the end of 12 months, people in the intervention group (n=191) were more likely than those in the control group (n=205) to report appropriate footcare behaviours (53 v 17%, p<0.001), to have their feet examined during regular office visits (68 v 28%, p<0.001), to receive footcare education from health providers (42 v 18%, p<0.001). Meanwhile, physicians assigned to the intervention group were more likely to refer patients to podiatry clinic compared with those assigned to the control group (10.6 v 5.0%, p=0.04).

Ronnemaa et al (1997) randomised 530 people with both Type 1 and Type 2 diabetes who had not visited a podiatrist in the previous 6 months and who were not in obvious need of podiatry care to receive education and primary preventative care from a podiatrist or to receive only written instructions. After 1 year, people in the podiatrist group (n=267) had greater improvements in knowledge scores of diabetic footcare (p=0.004) and self care (p<0.001) compared with control subjects (n=263). The prevalence of callus in regions other than the calcaneal region decreased more in the podiatrist group (54.5 to 39.5%) than in the control group (51.3 to 48.2%) (p=0.009), and the size of callus decreased more in the podiatrist group (p<0.001).

Mazzuca et al (1986) studies 532 people with diabetes (type not stated) in a primary care setting. Subjects were randomised to an intervention group who received instruction on footcare, and a control group. Follow up at between 11.8 and 14.3 months showed no difference in level of knowledge. Of the original cohort 275 (52%) completed the follow up assessment.

Other studies have also examined this question. One hundred people (mean age 65 years) with diabetes and high risk feet attended a two-session education programme conducted by a diabetes educator 3 months apart in this cohort study (Ward et al, 1999). The programme included foot self examination, foot washing, proper footwear, and encouragement in enlisting proper physician foot care. Data on 34 people who attended both sessions showed a significant improvement in knowledge score during the first visit ($p<0.05$), but not during the second visit ($p=0.09$). The footcare behaviour scores also improved during the 3 months between visits ($p<0.02$).

In a prospective study in a rural general practice setting, footcare education was provided to 53 people with Type 2 diabetes as part of a treatment and teaching programme by trained general practitioners and 55 people who did not receive any specific instruction served as the control group (Pieber et al, 1995). The level of footcare was poor in both groups at baseline. At 6 months, people in the intervention group had a significantly higher diabetes-related knowledge score than people in the control group ($p=0.001$), and the number of people with callus formation and interdigital problems decreased in the intervention group (both $p<0.001$) but was unchanged in the control group.

In a study by Donohoe et al (2000), 1,939 people with diabetes (mostly Type 2 diabetes) and 150 health professionals were randomised to an integrated footcare or to a usual footcare group. After 6 months, there was an improvement in patients'overall attitude towards their footcare in both groups (both $p<0.001$ v baseline), with a greater change in the intervention group ($p=0.01$). Patients' knowledge about diabetic foot problems improved significantly in both groups ($p=0.015$ for the intervention group; $p=0.002$ for the control group), but without a difference between groups ($p=0.54$). More people in the intervention group had their feet examined ($p<0.001$), received footcare education ($p<0.001$) and found the education useful ($p=0.03$). Moreover, health professionals' knowledge scores also improved in the intervention group ($p<0.001$), compared with no change in the control group ($p=0.008$). Appropriate referrals from the intervention group to the specialised foot clinic increased significantly ($p=0.046$) compared with the control group ($p=0.14$).

Corbett et al (2003) tested the effectiveness of an educational intervention in 40 people with diabetes who were randomised to the intervention group (n=20) or the control group (n=20). There were no group differences in footcare knowledge or self-care practice at baseline. At the 6-week assessment, the intervention group showed improvements in foot care knowledge ($p=0.007$), patients' confidence ($p=0.014$), and footcare practices ($p=0.003$), while there was little change in the control group. At 12 weeks, people in the intervention group still had improvements in knowledge ($p=0.029$) and reported foot selfcare practices ($p=0.007$), but not confidence ($p=0.29$) compared with people in the control group.

To test the hypothesis that a motivational brochure will increase the number of Medicare eligible people with diabetes making therapeutic footwear claims, LeMaster et al (2003) randomly recruited 5,872 people from three states in the U.S who were aged 65 years or older and had Medicare claims related to diabetic foot problems (callus formation, history of foot ulcer, foot deformity, previous complete or partial amputation, or poor circulation) in the past two years. The motivational brochures describing the Medicare diabetes-related therapeutic footwear benefit were mailed to all 5,872 Medicare beneficiaries. During the 18-month study period, 2,602 people (60%) made at least one claim in the intervention states compared with 1,761 people (40%) in the comparison states where the mailing did not occur. In the month after the first mailing, the number of persons/month making claims increased to 13 persons per month (CI 11-15) in the intervention states; while it stayed the same (0.5 persons per month, CI -3.5 to 1.1) in the comparison states (p<0.001).

Footcare education for people with diabetes may prevent serious foot lesions and amputation

The Valk et al (2002) systematic review also assessed 2 RCTs which evaluated the impact of educational programmes on the incidence of ulcer, amputation and/or infection (Ronnemaa et al, 1997; Malone et al, 1989). In one, the reduction in ulcer incidence (OR: 0.28 (0.13,0.59)) and amputation rate (OR: 0.32 (0.14,0.71)) were both statistically significant at 1 year follow-up with no effect on the incidence of infection (Malone et al, 1989). This study compared footcare education with no footcare education in 203 people with diabetes. The patients in this RCT were at high risk of foot ulceration as they had been referred to podiatry or vascular surgery due to foot infection, ulceration or prior amputation. The education intervention consisted of viewing slides of infected feet and amputated limbs and the provision of simple foot self care instructions. There were significantly more ulcers (15% v 5%, p<0.005) and amputations (12 v 4%, p<0.025) in the group which did not receive education compared with the education group during a 1-26 month follow up period. The other RCT (described above) that reported amputation rate and ulcer prevalence at 7 year follow-up did not find a difference between intervention and control groups with regard to either outcome (Ronnemaa et al, 1997). Because of the large difference in baseline risk of foot ulceration of the patient populations in these RCTs, the results of these 2 RCTs were not pooled.

Litzelman et al (1993) assessed the effect of a multifaceted intervention in a general practice setting in 395 people with Type 2 diabetes. The 12-month intervention included a footcare session with 1 to 4 people conducted by nurse clinicians which covered footcare behaviours and proper footwear, and follow-up by telephone and postcards reminding people of self footcare. At the end of 12 months, the intervention group had less serious foot lesions than the control group (OR 0.41 CI 0.16-1.00, p=0.05) and only 1 amputation had been performed in this group compared with 4 in the control group (no p value). Although not fully described in the publication, these subjects did not appear to be at particularly increased risk of foot problems.

Patout et al (2000) reported on a 1-year prospective study of a comprehensive preventive foot care programme. 197 people categorised as having either low or high risk feet participated in the programme and received foot care education and assistance in selection of footwear according to their foot risk category. Compared with before the programme, after 1-year of the footcare programme, there were significant reductions in foot-related ulcer days (-49%, p<0.01), foot operations (-87%, p<0.01), lower-extremity amputations (-79%, p<0.01), hospitalisations (-89%, p<0.01), hospital days (-90%, p<0.01), emergency room visit (-81%, p<0.01), antibiotic prescriptions (-57%, p<0.01), and missed workdays (-70%, p<0.01).

Horswell et al (2003) compared a staged diabetes foot management programme with standard care in a retrospective study. All subjects had diabetes and foot ulcers, of whom 45 received the staged foot care that consisted of selfcare education, devices to offload pressure, and custom-fabricated orthoses and footwear after healing, while 169 subjects received standard foot care. Baseline characteristics were similar in both groups. In the 1-year follow-up period, the staged foot care group had a lower foot-related hospitalisation rate than did the standard care group (0.09 v 0.50 admissions per person, p=0.002), lower foot-related inpatient days (0.91 v 3.97 days per person, p=0.03), and fewer amputation-related hospitalisation (0.04 v 0.19 per person, p=0.035). There were also fewer emergency visits (0.60 v 1.22 visits, p=0.004) in the staged foot care group compared with the standard care group.

A 2-year cohort study conducted by Carrington et al (2001a) showed that a footcare programme produced no significant effect in preventing second amputation in 143 people with diabetes and unilateral amputation. The footcare programme included education, podiatry service and follow up three monthly by a footcare nurse, a rehabilitation nurse and a podiatrist. At baseline, 27% of people had an ulcer on the remaining foot. During follow-up, 22 people had a contralateral amputation. There was no difference in foot care knowledge and mean neuropathy scores between this group and the group which remained as unilateral amputees. However, mean ankle-brachial pressure index was significantly lower for the bilateral amputees (0.75±0.04) compared with the unilateral amputees (0.90±0.03) (p<0.05). Overall, the footcare programme did not have an impact on contralateral limb amputation (22 of 143, 15.4%) compared with matched people not attending the programme (21 of 148, 14%) over the two-year period.

Calle-Pascual et al (2002) assessed the effect of a preventative foot care programme in 308 people (mean age 72.3 years) with diabetic neuropathy in this cohort study. The programme consisted of four 120 min sessions over 1 week which covered callus care, foot hygiene, the use of foot care products and the methods of foot and shoes inspection. Of all people, 124 with a VPT <25 V were defined as a low risk group, while 184 with a VPT ≥25 V as a high risk group. During the 4.6-year follow-up, the cumulative foot ulcer rate was 7.2% in the low risk group, and 13.0% in the high risk group (p<0.05). However, the incidence of foot ulcer was significantly lower in people who were compliant with the programme than in people who were noncompliant (1.1 v 26.7% in the low risk group, p<0.001; 3.9 v 32.7% in the high risk group, p<0.01). Similarly compliant people had a lower incidence of first ulcer than people who were noncompliant (0.2 [0-1.0] v 4.4 [0-9.3], p<0.01 in the low risk group; 0.5 [0-1.2] v 4.3 [1.7-6.9], p<0.01 in the high risk group).

Summary – Patient Education and Foot Disease

- Interpretation of available studies on the effects of footcare education is hampered by inconsistent interventions, the use of different endpoints and the generally short duration of follow up

- Overall studies suggest that education can improve knowledge and may improve self care behaviour

- Some, but not all studies, have reported improved foot outcomes with less ulcers and amputation after programmes which include an educational component, but more research is required to fully address this question

- The ideal content, nature and frequency of education necessary to achieve improved outcomes is unknown

Evidence Table: Section 8

Effect of patient education

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Barth R (1991) (Adults – Australia)	II	RCT	Medium	High +	High
Bloomgarden ZT (1987) (Adults – US: majority African American and Hispanic)	II	RCT	Medium	High +	Low
Calle-Pascual AL (2002) **(**Adults – Spain)	III-2	Cohort	High	High +	High
Carrington AL (2001a) (Adults – UK)	III-2	Cohort	High	Low	High
Corbett CF (2003) (Adults – US)	II	RCT	Medium	High +	High
Donohoe ME (2000) (Adults – UK)	II	RCT	High	High +	High
Horswell RL (2003) (Adults – US)	III-2	Cohort	Medium	High +	High
Kruger S (1992) (Adults – US)	II	RCT	Medium	Low	High
LeMaster JW (2003) (Adults – US)	III-2	Cohort	Medium	High +	High
Litzelman DK (1993) (Adults – US)	II	RCT	High	High +	Low
Malone JM (1989) (Adults – US)	II	RCT	Medium	High +	High
Mason J (1999)	I	Systematic review	High	Medium +	High
Mazzuca SA (1986) (Adults – US)	II	RCT	Medium	Low	High
Patout Jr CA (2000) **(Adults – US)**	III-2	Cohort	Medium	High +	Low
Pieber TR (1995) (Adults – Austria)	III-2	Cohort	Medium	High +	High
Rettig BA (1986) (Adults – US)	II	RCT	Low	High +	High
Ronnemaa T (1997) **(**Adults & children – Finland)	II	RCT	High	High +	High
Valk GD (2002)	I	Systematic review	Medium	Medium +	High
Ward A (1999) (Adults – US)	III-2	Cohort	Medium	High +	High

For magnitude rating:
+ indicates positive effect of patient education on diabetic foot disease. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 9: Diabetes Foot Problems

Issue

Does improved glycaemic control decrease the development or progression of peripheral neuropathy?

Recommendation

Aim to achieve the best possible glycaemic control in people with Type 2 diabetes in order to prevent or reduce the development of peripheral neuropathy which is a major risk factor for foot ulceration and amputation.

Evidence Statements

- The development and severity of peripheral neuropathy in Type 2 diabetes is related to the long-term glycaemic control
  Evidence Level I

- Improved glycaemic control can prevent or reduce the development of peripheral neuropathy in people with Type 2 diabetes
  Evidence Level II

Background - Glycaemic Control and Peripheral Neuropathy

The strong correlation between better glycaemic control and a lower incidence of diabetic complications has been known for a long time (Pirart, 1978). There is also a strong relationship between the level of impaired glycaemic control and the severity of diabetic peripheral sensorimotor polyneuropathy (Tkac & Bril, 1998).

As reviewed in Section 1, peripheral neuropathy is a major predisposing factor for ulceration and amputation in people with diabetes. The question arises as to whether achievement of near normal blood glucose levels prevents or reduces the development of peripheral neuropathy.

The Diabetes Control and Complications Trial (DCCT) in people with Type 1 diabetes clearly demonstrated that intensive treatment which improved diabetes control could delay the onset or slow the progression of peripheral neuropathy compared with conventional therapy (DCCT, 1993). The risk of developing peripheral neuropathy was reduced by 69% in those without neuropathy and progression was reduced by 67% in those who already had other microvascular complications.

This section addresses the question of whether a similar effect can be achieved in people with Type 2 diabetes with improved diabetes control.

Evidence – Glycaemic Control and Peripheral Neuropathy

The development and severity of peripheral neuropathy in Type 2 diabetes is related to the long-term glycaemic control

In 1998, prior to the United Kingdom Prospective Diabetes Study (UKPDS), Gaster & Hirsh (1998) reported the results of a systematic review of 20 prospective observational English language studies published since 1970 which examined the association between hyperglycaemia and microvascular complications and neuropathy. This review pointed out the similarity of microvascular and neuropathic complications in both Type 1 and Type 2 diabetes when adjusted for level of hyperglycaemia and identified a strong association between hyperglycaemia and complication rate, although only 2 studies included measurements for neuropathy (Gaster & Hirsh, 1998).

The Wisconsin Epidemiological Study of Diabetic Retinopathy studied people receiving primary care in an 11 county area of southern Wisconsin (Klein et al, 1996). This sample included a younger onset group in which almost all had Type 1 diabetes (n=1,210) and an older onset group (n=1,780) in which 824 were taking insulin and 956 were not taking insulin. After 10 years, data were available for 43% of the original cohort and showed an exponential relationship between the extent of complications and poorer glycaemic control (Klein et al, 1996). There was a similar relationship between young and mature onset people with diabetes for any given level of hyperglycaemia. In the older onset group, a trend of increasing 10-year incidence of loss of tactile sensation or temperature sensitivity associated with increasing HbA_{1c} level at baseline (with HbA_{1c} at 5.4 to 8.5%, 8.6 to 10.0%, 10.1 to 11.5%, and 11.6 to 20.8%) was observed in those taking insulin ($p<0.05$; $p<0.005$, respectively) and those not taking insulin ($p<0.0001$; $p=0.16$, respectively). This relationship was remarkably similar to that of the DCCT trial for retinopathy, proteinuria and neuropathy (Klein & Moss, 1995; Klein et al, 1996).

Dyck et al (1999) found that chronic hyperglycaemia exposure was associated with severity of diabetic polyneuropathy (DPN). In a cohort study of 264 people (mean age 62.8 years) with Type 1 or 2 diabetes, the Neuropathy Impairment Score of Lower Limbs plus 7 tests which combined major sensory, autonomic, and motor weakness impairment was used to assess the severity of DPN during a 7-year follow-up. 36% of participants had DPN, and only 9.5% were symptomatic. In the multivariate analysis, the independent risk associated with the severity of DPN for people with Type 1 diabetes was HbA_{1c} × duration of diabetes ($p<0.001$); for people with Type 2 diabetes was mean HbA_{1c} ($p<0.001$); and for people with Type 1 or Type 2 diabetes combined, the risk factors were HbA_{1c} × duration of diabetes ($p<0.001$), mean HbA_{1c} ($p<0.001$), and type of diabetes ($p=0.002$).

Van de Poll-Franse et al (2002) evaluated risk factors for severity of DPN assessed by a clinical neurological examination (CNE) in a prospective cohort study of 486 elderly people (mean age 65.4 years) with Type 2 diabetes. 31.7% of people were classified as having DPN (with a CNE score >4) at baseline. The mean CNE score increased significantly during the 4-year follow-up for those with two, three or four CNE measurements (7.5±1.05 to 8.7±1.07 in people with DPN; 2.2±1.04 to 4.2±1.06 in people without DPN; p for trend <0.001). The percentage of people with CNE >4 also increased, and 21.3% of people without DPN (CNE ≤4) at baseline progressed to a CNE score >4 after 3 years of follow-up. The multivariate analysis showed that the change of CNE was best predicted by age ($p<0.05$), diabetes duration ($p<0.05$) and HbA_{1c} level ($p<0.05$), with HbA_{1c} being the strongest predictor.

Improved glycaemic control can prevent or reduce the development of peripheral neuropathy in people with Type 2 diabetes

The UKPDS compared intensive treatment with diet or medications and less intensive control in 5,102 people with newly diagnosed Type 2 diabetes who were followed for at least 10 years. The percentage of people at entry to the study with a VPT >25 V assessed with the biothesiometer was similar in the conventional and intensive group (11.4% and 11.8% respectively). The median HbA_{1c} over 10 years in the intensive policy group was 7% compared with 7.9% in the conventionally treated group. Significantly less people in the intensive policy group had an impaired vibration sensory threshold (31.2% v 51.7%, $p=0.005$) after 15 years of follow up (UKPDS 33, 1998). However it should be noted that differences between the control and intensively treated groups did not reach statistical significance at earlier time points.

The Kumamoto study randomised 110 Japanese people with Type 2 diabetes who were non-obese (body mass index 16.4-23.5 kg/m^2) (Ohkubo et al, 1995) to receive intensive therapy with multiple insulin injections or conventional insulin therapy. The study included both primary and secondary prevention groups. After 6 years HbA_{1c} levels were 7.1% in the intensively treated group which was significantly lower than 9.4% in the conventionally treated group. Neuropathy, assessed by lower extremity vibration threshold was observed in 12.8% of the intensively treated group compared with 64% in the conventionally treated group ($p<0.05$).

In a previous Japanese randomised study of intensified glycaemic control with multiple insulin injections in 50 people, 9 with Type 1 and 41 with Type 2 diabetes, Hotta et al (1993) demonstrated that improving HbA_{1c} from approximately 10% to 8% with multiple insulin injections achieved a significant improvement in impaired motor nerve conduction velocity over a 4 year period (at 1, 2, 3 and 4 years v baseline value, all $p<0.05$). However there was no direct evidence of an effect on clinical neuropathy since VPT did not change in either group.

There are little data on whether diabetic neuropathy can be reversed by improving glycaemic control in people with Type 2 diabetes. In a 1-year intervention, 34 elderly Swedish people with Type 2 diabetes (mean age 75.2 years) were randomised to treatment with insulin or sulphonylureas. Neuropathy was present in 56% at entry to the study and did not alter over one year despite a reduction in HbA_{1c} from 9.2 ± 1.4% to 7.3 ± 1.1% ($p<0.001$) in the insulin treated group (n=18). The sulphonylurea treated group (n=16) had an initial HbA_{1c} of 9.1 ± 1.2% and did not change significantly throughout the study period. The 1-year duration of study could be inadequate to detect any significant change of neuropathy (Tovi et al, 1998).

Another study has also reported that optimal glycaemic control did not decrease the overall prevalence of peripheral neuropathy in Type 2 diabetes (Azad et al, 1999). Neuropathy was diagnosed clincially by a comprehensive neurologic history and physical examintion working from a standard form. 153 men with Type 2 diabetes were randomised to receive intensive treatment (INT) which used a four-step strategy to maintain HbA_{1c} between 4.0 and 6.1% or standard treatment (STD) for two years. At baseline, the prevalence of peripheral neuropathy was 48% in the INT and 53% in the STD group. Although glycaemic control significantly improved in the INT group (mean HbA_{1c} 9.3 to <7.3%) compared with the STD group (mean HbA_{1c} 9.5% through the study period) after 24 months ($p<0.001$ for HbA_{1c} and FPG), the prevalence of peripheral neuropathy increased to 64% in the INT group (v baseline, p=0.008) and to 69% in the STD group (v baseline, p=0.005), and there was no difference between the two groups. However, the score for abnormalities in upper extremity touch sensation decreased (indicating improving) in the INT group (34±14% to 7±5%), but increased in the STD group (3±3% to 14±11%) (INT v STD, p=0.03), and the difference between the groups in the cranial neuropathy score was borderline significant (19±14% to 49±23% in STD v 39±22% to 0 in INT, p=0.053).

Summary - Glycaemic Control and Peripheral Neuropathy

- There is a direct relationship between worsening glycaemic control and the development of peripheral neuropathy in people with Type 2 diabetes

- There is strong evidence that improvement in glycaemic control is effective in reducing the risk of the development and progression of neuropathy in Type 2 diabetes

- There is no evidence that established neuropathy can be reversed by improving diabetes control

Evidence Table: Section 9

Glycaemic control and peripheral neuropathy

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Azad N (1999) (Adults – US)	II	RCT	High	Medium +	High
Dyck PJ (1999) (Adults – US)	III-2	Cohort	High	High +	High
Gaster B (1998)	I	Systematic Review	High	High +	High
Hotta N (1993) (Adults – Japan)	II	RCT	Medium	High +	Low
Klein R (1995) (Adults – US)	III-2	Cohort	High	High +	High
Klein R (1996) (Adults – US)	III-2	Cohort	High	High +	High
Ohkubo Y (1995) (Adults – Japan)	II	RCT	Medium	High +	Low
Tovi J (1998) (Adults – Sweden)	II	RCT	Medium	Low	High
UKPDS 33 (1998) (Adults – UK)	II	RCT	High	High +	High
van de Poll-Franse LV (2002) (Adults – The Netherlands)	III-2	Cohort	High	High +	High

For magnitude rating:
+ indicates positive effect of glycaemic control on diabetic foot disease. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 10: Diabetes Foot Problems

Issue

Does appropriate footwear reduce ulceration and amputation?

Recommendations

People with diabetes should be encouraged to wear properly fitted, cushioned footwear and padded socks.

People with diabetes with high risk feet require special attention to footwear.

Evidence Statements

- Therapeutic footwear reduces the risk of ulcer recurrence
  Evidence Level I

- Therapeutic footwear combined with podiatry care reduces the risk of amputation in high risk individuals
  Evidence Level II

- Plantar foot pressures are influenced by footwear
  Evidence Level III-2

- Callus formation can be reduced by certain footwear
  Evidence Level II

- Padded socks reduce plantar pressure
  Evidence Level III-2

Background - Footwear to Reduce Ulceration and Amputation

A pivotal or initiating event commonly precedes the development of a foot ulcer or leads to an amputation (Pecoraro et al, 1990). This may be an acute traumatic event, such as stepping on a tack, or the result of abnormal pressure on the foot, such as wearing new or ill fitting shoes or socks. Pressure ulcers, also called stress ulcers or mal perforans, frequently result from repetitive low-pressure stress of walking on an unprotected neuropathic foot, resulting in repeated friction over prominences such as a plantar callus. In addition they may result from ingrown toenails or from immobilisation in a bed or chair. This initiating event superimposed on an at risk foot (eg insensate or with vascular insufficiency) is often the critical factor which may ultimately lead to amputation (Mayfield et al, 1996).

Apelqvist et al (1990) studied 314 consecutive people with diabetes and a foot ulcer and identified an acute traumatic precipitating event in 18%, ill fitting shoes or socks in 39%, mal perforans in 12%, paronychia in 6%, decubitus pressure in 5%, and no obvious precipitating event in 16%. In another study shoe trauma preceded ulceration in 47% of 386 ulcers in 239 people (Edmonds et al, 1986).

Mayfield et al (1996) in a retrospective study of 61 diabetic Pima Indians with diabetes who underwent an amputation identified trauma as the pivotal event in 44% (shoe trauma 8% of total) and new onset ulcer without trauma, many of which were probably mal perforans, in 39%.

Elevated plantar pressure is causally related to the occurrence of foot ulcers in people with diabetes with neuropathy (Veves et al, 1992). As well as exposing the foot to injury, barefoot walking is associated with higher foot pressures than wearing shoes. In addition the type of footwear also has a significant influence on plantar pressures **(**Lavery et al, 1997; Kastenbauer et al, 1998).

Tovey (1984) has detailed the desirable characteristics of appropriate diabetic footwear aiming to reduce shock and shear, and accommodate, stabilise and support deformities.

- width to accommodate the first metatarsophalangeal joint
- length should allow about 1cm between the end of the shoe and the longest toe
- depth to allow sufficient room in the toe area and instep
- laces to adjust for oedema and deformities
- snug fit of heel without undue motion
- wide low heels to improve stability

Wearing of inappropriate footwear is common in people with diabetes. Reiber et al (2002b) studied footwear in people with diabetes and a history of foot ulcer. A total of 400 people (mean age 62 years) with diabetes and a history of healed full-thickness foot lesion, no foot deformities requiring a custom shoe, and ability to walk one block and climb one flight of stairs daily were included in this cross-sectional study. 58% of subjects were insensate to the 10g monofilament. In general, women spent an average of 51% of their time in dangerous shoes defined as those with shallow or narrow toe box, no laces, open toes or heels, and a heel height placing extra pressure on the ball of the foot than men who spent 27% of their time wearing dangerous shoes. Both men and women spent nearly 30% of their time in slippers, stockings and barefoot for their regular activities.

Custom made orthopaedic footwear is expensive, costing considerably more than manufactured footwear. In addition, acceptance and use of custom made orthopaedic footwear is poor. A survey of 62,170 people with diabetes who were Medicare beneficiaries in 3 American states found low utilisation of therapeutic footwear. Of the 13% who fell into the “high risk” group, only 2.9% claimed for footwear and of the 14% with possibly increased risk, claims were made by only 0.7% (Sugarman et al, 1998). Other authors also report low levels of compliance with therapeutic footwear, often related to the appearance of the footwear (Chantelau & Haage, 1994; McCabe et al, 1998). In contrast, specially designed, extra depth, extra width shoes with a rocker bottom were well accepted by 24 male Veterans with 88% compliance (Reiber et al, 1997).

The studies reviewed in this Section have used a variety of footwear and/or insoles and/or socks. The term “therapeutic footwear” has mostly been used in studies to refer to the use of specially manufactured shoes or to the use of casts (total or half, removable or non-removable). A variety of insoles, either customised or not, and made of a variety of materials have been studied.

Evidence – Footwear to Reduce Ulceration and Amputation

Therapeutic footwear reduces the risk of ulcer recurrence

Mason et al (1999) performed a systematic review of diabetic foot ulcer prevention strategies and identified only 1 randomised trial (Uccioli et al, 1995) on the effect of therapeutic footwear. Although this study showed a beneficial effect, Mason et al (1999) recommended confirmatory studies on larger numbers of people with diabetes with comparisons of ‘optimised’ normal shoes and special therapeutic shoes to confirm the relative effectiveness and cost-effectiveness of wearing therapeutic shoes.

The study by Uccioli et al (1995) was a multicentre, RCT which assessed therapeutic footwear and ulcer recurrence in people with previous foot ulcers. Manufactured therapeutic shoes were designed according to Tovey’s guidelines as previously described. Customised insoles were also provided. Foot ulcer relapses were significantly lower in the group of 33 wearing therapeutic shoes compared with the control group of 36 wearing their own shoes (27.7% v 58.3%, OR 0.26, CI 0.2-1.54; p=0.0009). In multiple regression analysis adjusted for severity of disease, age and sex, the use of therapeutic shoes was negatively associated with foot ulcer relapse (coefficient of variation - 0.32, CI -0.54 to -0.08; p=0.009).

A cohort of 51 people with diabetes were provided with protective footwear, cushioned with insoles after healing of a neuropathic foot ulcer and followed for up to 4 years (Chantelau & Haage, 1994). In those who wore the protective footwear for >60% of daytime hours, ulcer recurrence was reduced by 50% (p=0.0002) compared with those who wore their footwear less frequently. After 2 years, the protective effect wore off, suggesting that footwear needed adaptation and renewal within this time period. In addition people without ulcer relapses had a significantly increased frequency of attending for footcare including callus removal and nail cutting ($p<0.05$).

In a 31-month prospective cohort study, Busch & Chantelau (2003) assessed the effects of a particular stock 'diabetic' shoe (SDS) on the rate of foot ulcer relapse in high risk diabetic people (mean age 63 years) with healed foot ulcer. Of a total of 92 people, 87 had polyneuropathy and 24 suffered from PVD. 60 people wore the SDS, while 32 people were asked to use their normal footwear. There were no differences regarding to age, gender, type and duration of diabetes, and prevalence of polyneuropathy and PVD between the two groups. In the first year of follow-up, 19 people (60%) without SDS experienced an ulcer relapse, compared with 9 (15%) with SDS. The absolute risk reduction by the SDS treatment in the first year was 45% (CI 26-64%). The overall cumulative ulcer-free survival was significantly greater in people with SDS ($p<0.0001$).

While therapeutic footwear reduces ulcer recurrence, some studies have shown differences in this effect between different footwear. In a study of 50 people with neuropathic plantar ulcers (Caravaggi et al, 2000), 24 were randomised to receive a therapeutic shoe and 26 to receive fibreglass off-bearing cast treatment. At the end of 30 days of treatment, 8.3% of people (2/24) assigned to the shoe group presented with an increase in ulcer size, whereas no one in the cast group showed an increase. The reduction of the ulcer area was faster in the cast group ($p=0.0004$). The ulcer completely healed in 5 people in the shoe group, compared with 13 in the cast group ($p=0.032$). Patient acceptance of treatment was high in both groups and there was no difference between groups. No side effects were observed in either group.

The effectiveness of three different therapeutic footwear on ulcer healing was evaluated in 63 people with noninfected, nonischaemic diabetic plantar ulcers: total-contact cast (TCC, n=19), removable cast walkers (RCW, n=20) and half-shoe cast (n=24) in a 12-week study (Armstrong et al, 2001). The proportions of ulcer healing were 89.5% for people treated with TCC, 65.0% with RCW, and 58.3% with half-shoe. At 12 week, the proportion of healing was significantly higher in the TCC group compared with the other two groups (89.5 v 61.4%, $p=0.026$, OR 5.4, 95% CI 1.1-26.1). The mean time to ulcer healing was significantly shorter in the TCC group than in the half-shoe group (33.5 ± 5.9 v 61.0 ± 6.5 days, $p=0.005$), but not shorter than in RCW group (50.4 ± 7.2 days, $p=0.07$). The TCC seemed to heal a higher proportion of ulcers in a shorter amount of time than two other footwear.

In a nonrandomised prospective study, Ha Van et al (2003) compared the effectiveness and safety of a nonremovable fiberglass cast boot (n=42) and off-loading shoes (n=51) in 93 people with diabetes (most Type 2 diabetes) who had a noninfected, nonischaemic plantar ulcer. During follow-up, the healing rate was higher with the cast boot group than with the off-loading shoe group (81 v 70%, $p=0.017$), with the mean time to healing of 68.6 ± 35.1 and 134.2 ± 133 days, respectively. The age-adjusted hazard ratio for healing in people treated with a cast boot was 1.68 (CI 1.04-2.70, $p=0.017$), compared with the off-loading shoe. Complete compliance was better in the cast boot group (98 v 10%, $p=0.0001$). Overall, 8 people failed treatment in the cast group due to an ulcer caused by fiberglass in 5 people, osteomyelitis in 2 and a toe fracture in 1 person. In comparison, no new ulcers developed in the off-loading shoe group, but 15 people failed treatment, including 2 people who did not achieve healing at the end of the study and 13 people had an osteomyelitis during the follow-up. Secondary osteomyelitis developed in 3 patients in the cast boot group (7%) and 13 patients in the off-loading shoe group (25%) ($p=0.026$).

However, not all studies have had positive outcomes. Reiber et al (2002a) studied 400 people (mean age 62 years) who were randomly assigned to receive 3 pairs of therapeutic shoes with cork inserts, or 3 pairs of therapeutic shoes with prefabricated inserts, or assigned to wear their usual footwear for 2 years. At baseline, 58% of people were insensitive to the 10g monofilament and 32% had moderate foot deformity. A total of 95 reulcerations occurred during the 2-year follow-up. The cumulative reulceration incidence across the 3 groups was similar: 15% in the cork-insert group, 14% in the prefabricated-insert group, and 17% in the control group. People assigned to therapeutic shoes did not have a significantly lower risk of reulceration compared with controls - RR was 0.88 (95% CI 0.51-1.52) for the cork-insert group, and 0.85 (95% CI 0.48-1.48) for the prefabricated-insert group.

A cohort of 352 people with Type 2 diabetes were followed over 12 months to assess the impact of footwear on the development of foot wounds (Litzelman et al, 1997b). At examination at 12 months 63 feet (53 people) had either a blister or wound. Contrary to expectation, a recommendation to wear special footwear was associated with increased risk of foot wounds at follow up (OR 2.19, CI 1.07-4.49; $p=0.03$). However the study group was not provided with therapeutic footwear or better access to therapeutic footwear and in fact only one person actually wore the special footwear.

Edmonds et al (1986) reported the 3-year outcomes of a specialised foot clinic for people with diabetes and foot ulcers. 239 people with diabetes and foot ulcers were divided into two groups: 148 with palpable pulses in the neuropathic group and 91 without foot pulses in the ischaemic group. After initial healing, 121 people in the neuropathic group were observed further, 22 of the 86 people (26%) wearing specially fitted shoes developed ulceration compared with 29 of the 35 people (83%) wearing their own shoes (Edmonds et al, 1986).

Therapeutic footwear combined with podiatry care reduces the risk of amputation in high risk individuals

Protective footwear was offered to a group of high risk people with neuropathy, previous ulceration, vascular insufficiency (ABI ≤ 0.75) and/or foot deformity, in a RCT of a diabetic foot screening and protection programme (McCabe et al, 1998). A total of 2,001 people with diabetes were included in this study and were randomly allocated to the index group (n=1,001) or the control group (n=1,000). 128 people with a high risk of ulceration in the index group were recruited to a protection programme which provided podiatry sevices and protective footwear. At 2-year follow-up, there were 24 ulcers in the index group compared with 35 ulcers in the control group. Moreover, less ulcers progressed to amputation in the index group (7, 1 major and 6 minor) compared with 23 amputations in the control gropu (12 major and 11 minor). The difference in the total number of amputations between the two groups was significant ($p<0.04$) and the difference in major amputation was also significant ($p<0.01$).

Plantar foot pressures are influenced by footwear

Comparisons of in-shoe foot pressure were made between 44 people with Type 1 or 2 diabetes and 65 healthy controls (Sarnow et al, 1994). In those with diabetes, pressures were significantly higher than controls when only socks were worn (8.77±4.67 v 7.23±2.95 kg/cm^2, $p<0.02$) as would be expected since 50% had peripheral neuropathy. When shoes were worn, in-shoe foot pressures were significantly lower in both groups (5.28±2.22 kg/cm^2 for the diabetic group; 4.77±1.87 kg/cm^2 for the control group) than those measured when walking only in socks. There were no differences in foot pressures between the two groups when wearing shoes indicating that the wearing of shoes resulted in a greater degree of pressure reduction in people with diabetes. This study confirms that well fitting shoes have a cushioning effect and reduce foot pressures in people with diabetes.

Inexpensive running shoes were tested in a group of 13 non diabetic controls, 13 people with diabetes without neuropathy and 13 people with neuropathy (Perry et al, 1995). There were no significant differences between the groups for age, weight or duration of diabetes. Foot pressures while wearing Oxford style shoes were similar to wearing socks. Plantar pressures were reduced while wearing running shoes by 31±9.1% at the forefoot and heel regions and 44% at the second metatarsal head, the commonest site for diabetic ulceration. The strongest correlation between the initial plantar pressure and pressure reduction was for the second metatarsal head (absolute reduction, r= -0.96; percentage reduction, r= -0.77). Pressure reduction was similar in all groups although people with diabetic neuropathy had higher pressures at the metatarsal heads initially (p=0.008).

The effectiveness in reducing plantar pressures of commercially available shoes, comfort and cross trainers, were compared with traditional extra-depth therapeutic shoes (Lavery et al, 1997). Each shoe was tested in 32 people with diabetes and current or recently healed neuropathic foot ulcers. All shoes reduced pressures compared to a standard inexpensive, rubber-soled, canvas Oxford shoe ($p<0.05$). The comfort shoes provided significantly lower pressures than cross trainers and extra-depth therapeutic shoes for ulcers under the first and lesser metatarsals ($p<0.05$). For each shoe the addition of a visceroplastic insole provided a further significant reduction in pressures compared with no insole ($p<0.05$); and reduced pressures an additional 5.4-20.1% at ulcer sites compared with a standard insole.

In-shoe plantar pressures were measured in 13 people with diabetes, comparing a leather-soled Oxford shoe, a custom-made insole in an extra depth shoe and a specially designed running shoe (Kastenbauer et al, 1998). The running shoe was designed for maximal pressure relief at the forefoot area. Compared with the Oxford shoe, the running shoe reduced mean peak plantar pressures (MPP) by 32% in the great toe area ($p<0.01$), 29% at the first metatarsal head ($p<0.05$) and 47% at the second and third metatarsal heads ($p<0.05$). The extra depth shoe with the custom made insole resulted in the greatest MPP reduction of 50% at the metatarsal heads and under heels ($p<0.01$). Inexpensive running shoes were found to halve plantar pressures at the MTHs and the use of custom-made insoles reduced pressures at the MTHs by a similar amount (Kastenbauer et al, 1998).

Raspovic et al (2000) evaluated the effect of customised insoles on vertical plantar pressures in 8 people with diabetes and a history of neuropathic ulceration (four with unilateral ulceration and four with bilateral ulceration). The insoles used were of the non-cast type. The plantar pressure, which was measured by the F-Scan in-shoe pressure measurement system, was examined in a total of 12 previously ulcerated feet. A significant reduction in peak plantar pressure was observed between using and not using the insole ($p<0.01$), with a large range of pressure reduction varying from 0.2 to 7.5 kg/cm^2.

In a 1-year cohort study (Lobmann et al, 2001) of 81 people with Type 2 diabetes, 18 people with increased plantar foot pressure were provided with specially manufactured insole support, while the remaining 63 people received conventional footwear. At baseline, the maximum peak pressure (MPP) of the foot was significantly higher in the treatment group than in the control group (474.4±183.0 v 367.7±157.0 kPa, p=0.003). A 32.6% reduction of the total foot MPP immediately after insole support (290±106 kPa, p<0.001), and a 28% reduction (324±127 kPa, p=0.001) after 6 months were observed in the treatment group. However, the total foot MPP increased again after 6 months, and at 1 year, the total foot MPP was 380±190 kPa in the treatment group. In contrast, the MPP of the heel region and metatarsal region increased significantly (263.1±127 v 328.4±137 kPa, p=0.005; 339.9±171 v 407.6±161 kPa, p=0.001, respectively) in the control group. There was also a trend towards higher total foot MPP at 1 year (baseline 367.7±157.0 v 437.4±161 kPa, p=0.152) in the control group.

Praet et al (2003) examined the effect of shoe design on the plantar pressure in 10 people (mean age 63 years) with diabetic neuropathy during walking. Three shoe design categories were tested - category A "over-the-counter" leather shoes, category B semi-orthopaedic Xtra Depth shoes, and category C fully individualised, plaster cast-based, soft leather rocker-bottom shoes. Compared with shoes from categories A and B, category C shoes showed peak pressure reductions of 50% in the central forefoot (18±2 N/cm^2 in C v 31±2 N/cm^2 in A, p<0.05; v 30±2 N/cm^2 in B, p<0.05). Total contact area surface increased significantly (3.4-7.3 cm^2) in all three shoe categories when an insole was used, but this did not result in a significant reduction underneath the forefoot. Pressure underneath the heel and medial forefoot on average showed no significant differences among the three different shoes with a cushioning insole. This study confirmed that a shoe with a rocker sole reduces forefoot pressure more than an extra depth shoe.

Callus formation can be reduced by certain footwear

A RCT assessed the effectiveness of orthotics in reducing callus compared with routine debridement by a podiatrist performed every 3 months (Colagiuri et al, 1995). The orthotic was a custom-made rigid plastic insert worn inside running shoes. At baseline there was no difference in the study population between the intervention or control groups in age 63±10 years v 69±6 years, duration of diabetes 10.7±7.6 years v 7.9±6.6 years, number of calluses 2.4±1.0 v 2.9±1.4 or mean callus grade 1.9 v 1.6. At 1 year, callus grade improved in 16 of the 22 calluses and remained unchanged in the other six in the orthotic treated group (n=9). In contrast, only two of the calluses improved, 23 remained unchanged and seven deteriorated in the podiatry treated group (n=11) (p<0.02). There were no adverse events in people wearing the orthotic device.

The rate of plantar callus formation and the need for debridement can be reduced by athletic running shoes (Soulier et al, 1987). In a pre and post test case series 78 people with a mean age of 55 years wore running shoes for a minimum of 9 months. The participants had the size of their calluses assessed monthly and it was found that there was a significant change in the average size of the callus after 10 months ($t=-3.32$, $p=0.001$ and the need to have calluses trimmed was also decreased.).

Padded socks reduce plantar pressure

Plantar pressures can also be influenced by socks. The effects of experimental padded hosiery was studied in 10 people with diabetes and clinical neuropathy and compared with commercially available sports socks in another 16 people with diabetes. Experimental padded hosiery reduced plantar pressures by 31.3% ($p<0.05$) at baseline and 17.6% ($p<0.01$) at 6 months, confirming that the protective effect can be maintained over time (Veves et al, 1990). Although the commercially available sports socks provided significant pressure reductions, 10.4% ($p<0.01$) with medium and 17.4% ($p<0.01$) with high density padding, this reduction was 27% less effective in pressure reduction compared with the experimental socks ($p<0.05$).

Summary - Footwear to Reduce Ulceration and Amputation

- Shoe trauma is frequently the pivotal event which precedes ulceration or amputation
- Therapeutic shoes and customised insoles have been shown to reduce ulcer recurrence and the severity of callus
- Therapeutic shoes in combination with podiatry care decrease amputation
- Plantar pressures are influenced by barefoot walking and type of footwear
- Plantar pressure can be reduced with moderately priced commercially available running shoes and cross trainers
- Plantar pressures can be further reduced by insoles, especially if custom-made
- Padded experimental hosiery has been shown to reduce plantar pressures
- People with diabetes and high risk feet require special attention to footwear which should be professionally fitted

Evidence Table: Section 10

Foot wear and effect on ulceration and amputation

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Armstrong DG (2001) (Adults – US)	II	RCT	High	High $^{U+}$	High
Busch K (2003) (Adults – Germany)	III-2	Cohort	High	High $^{U+}$	High
Caravaggi C (2000) (Adults – Italy)	II	RCT	High	High $^{U+}$	High
Chantelau E (1994) (Adults – Germany)	III-2	Cohort	Low	High $^{F+}$	High
Colagiuri S (1995) (Adults – Australia)	II	RCT	High	High $^{C+}$	High
Edmonds ME (1986) (Adults – UK)	III-2	Cohort	Low	High $^{A+ U+}$	High
Ha Van G (2003) (Adults – France)	III-2	Cohort	High	High $^{F+}$	High
Kastenbauer T (1998) (Adults – Austria)	III-2	Case-control	High	High $^{P+}$	High
Lavery LA (1997) (Adults – US)	III-2	Case-control	High	High $^{P+}$	High
Litzelman DK (1997b) (Adults – US, African American)	III-2	Cohort	Low	Low	Low
Lobmann R (2001) (Adults – Germany)	III-2	Cohort	High	High $^{P+}$	High
Mason J (1999)	I	Systematic review	High	High $^{U+}$	High
McCabe CJ (1998) (Adults – UK)	II	RCT	High	High $^{U+, A+}$	High
Perry JE (1995) (Adults – US)	III-2	Case-control	Medium	High $^{P+}$	High
Praet SFE (2003) (Adults – The Netherlands)	III-2	Cross-sectional	Medium	High^{+}	High
Raspovic A (2000) (Adults – Australia)	III-2	Cross-sectional	Medium	High $^{P+}$	High
Reiber GE (2002a) (Adults- US)	II	RCT	High	Low	High
Sarnow MR (1994) (Adults – US)	III-2	Case-control	High	High $^{P+}$	High
Soulier SM (1987) (Adults – US)	III-2	Cohort	Medium	High $^{C+}$	High
Uccioli L (1995) (Adults – Italy)	II	RCT	High	High $^{U+}$	High
Veves A (1990) (Adults – UK)	III-2	Cohort	Medium	High $^{P+}$	High

For magnitude rating:
$^{+}$ indicates that appropriate footwear may reduce the risk of ulceration and amputation; High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.
P= plantar foot pressure; C= callus formation; F= foot lesions; U= ulcer; A= amputations.

Section 11: Diabetes Foot Problems

Issue

Do specialist foot clinics and multi-disciplinary teams decrease amputation?

Recommendation

People with diabetes who have foot ulcers or with high risk feet should be cared for by a multi-disciplinary service which should include a physician and podiatrist and have ready access to a specialist nurse, orthotist and surgeon.

Evidence Statements

- A multi-disciplinary specialist footcare team can reduce ulceration and amputation in people with high risk feet
  Evidence Level III-2

- The multi-disciplinary footcare team commonly includes a physician, podiatrist, specialist nurse, orthotist and surgeon
  Evidence Level III-2

Background - Foot Clinics and Multi-disciplinary Teams

Recommendations to prevent amputation in people with diabetes and high risk feet include regular foot examination, education, suitable footwear and orthotics, podiatry services, and early ulcer treatment including surgery where indicated (Mason et al, 1999). Implementation of these recommendations cannot be achieved easily by one category of health provider and are best achieved with a multi-disciplinary team approach. Providing this recommended care requires the services of a physician, podiatrist, diabetes educator and vascular or orthopaedic surgeon (Bild et al, 1989). Unfortunately multi-disciplinary diabetes foot clinics are not common in Australia and most people receive their care in different sites and some have geographical difficulty in accessing a complete range of services.

Because of cost implications and geographic considerations it is important to evaluate whether a multi-disciplinary team approach can reduce amputation in high risk people. Even if this can be demonstrated, the provision of such services will still remain a challenge in many parts of Australia.

Evidence - Foot Clinics and Multi-disciplinary Teams

A multi-disciplinary specialist footcare team can reduce ulceration and amputation in people with high risk feet

The studies identified are difficult to compare because there is no universal definition of multi-disciplinary care and the settings in which such care is offered vary from primary care to hospital specialist referral clinics. Studies have been either retrospective or prospective cohort studies and true randomisation of high risk subjects to routine care or specialised clinic is virtually impossible and probably unethical.

In Manchester, UK, a weekly diabetic foot clinic with a multi-disciplinary team was established at the district hospital to which people with diabetes and foot lesions were referred from a wide range of sources (Thomson et al, 1991). The diabetic foot clinic was staffed by a diabetologist, chiropodist, specialist foot nurse and orthotist. Subjects were discharged from the clinic once adequate provision for follow up podiatry care had been made. Of 260 subjects who were referred to the clinic, 112 (73%) had Type 2 diabetes, and 153 (59%) had a new foot ulcer. Ulcer healing was obtained in 96 cases among 119 subjects available for follow-up. The annual amputations in people with diabetes in the subsequent 3 years were reduced by 42% compared to prior years (Thomson et al, 1991).

A predominantly descriptive report from Italy detailed the effects of setting up of a multi-disciplinary hospital foot clinic which provided intensive management of ulcers with patient education, surgery and detailed follow up of foot lesions (Ghirlanda et al, 1997). People attending the clinic had underlying neuropathy and presented with plantar ulcers (66%), soft tissue infections (30%), necrosis of at least one toe (24%) and osteomyelitis (10%). In the 250 people evaluated over the initial 3-year period, no amputation were performed. 98% of people with neuropathy had healing of their lesion, 10% had ulcer recurrence at the primary site, 4% at a different site and 5% had osteomyelitis at other locations (Ghirlanda et al, 1997).

A Swedish retrospective study reported the changes in diabetes related amputation following the implementation in 1983 of a multi-disciplinary footcare team programme for prevention and treatment of diabetic foot ulcers (Larsson et al, 1995). The team consisted of a diabetologist, orthopaedic surgeon, diabetes nurse, podiatrist and orthotist. From 1982 to 1993, 294 people with diabetes (mean age 77 years) had 387 major (above the ankle) or minor (through or below ankle) amputations which represented 48% of all lower extremity amputations. During this period the annual number of amputations at all levels decreased from 38 to 21, equalling a decrease in incidence from 19.1 to 9.4/100,000 people ($p=0.001$); and the incidence of major amputations decreased by 78% from 16 to 3.6/100,000 inhabitants ($p<0.001$). Calculated per 1,000 people with diabetes, the total incidence of amputation decreased from 7.9 to 4.1 and of major amputation from 6.7 to 1.5. The total reamputation rate decreased from 36 to 22% between the first and last 3-year period ($p<0.05$). These findings indicate that a multi-disciplinary approach plays an important role in reducing major amputations in people with diabetes (Larsson et al, 1995).

Edmonds et al (1986) reported the 3-year outcomes of a specialised foot clinic for people with diabetes and foot ulcers which was attended by a podiatrist, shoe-fitter, nurse, physician and surgeon. This multi-disciplinary approach achieved an 86% healing rate in neuropathic ulcers (204 out of 238) and a 72% healing in ischaemic ulcers (107 out of 148) among 239 people with diabetes. There were 19 amputations over the 3 years compared with 23 in 2 years before the establishment of the clinic (Edmonds et al, 1986).

Another prospective cohort study highlighted the importance of podiatry and vascular surgery collaboration in managing foot ulceration in a mixed group with and without diabetes who attended a high risk foot clinic in Arizona, US (Van Gils et al, 1999). Among the 124 high risk subjects of whom 90 had diabetes, only 18 (15%) had a major lower extremity amputation within an average follow-up period of 55 months, demonstrating an 85% limb salvage rate after primary ulcer occurred. The survival analysis showed an 86.5% probability of surviving up to 30 months without a lower extremity amputation and 83% at 70 months (Van Gils et al, 1999).

In a rural primary care setting a prospective study of American Indians evaluated the outcomes of foot care at three periods. During the standard care phase people received foot care at the discretion of the primary care provider; in the public health period people received screening and education together with protective footwear, and in the third phase comprehensive guidelines for foot management were adapted by the primary care clinicians for their practices. 639 individuals (mean age 54 years and duration of diabetes 8-9 years) were involved in the 3 periods of observation. During the first phase the incidence of lower extremity amputation was 29/1,000 diabetic person years, declined to 21/1,000 during the second phase and was further reduction to 15/1,000 during the final period; with an overall 48% reduction ($p=0.016$). The incidence of a first amputation declined from 21 to 6/1,000 person years ($p<0.001$). The provision of education, footwear and the implementation of customised practice guidelines with a footcare team reduced amputation in a rural primary care setting (Rith-Najarian et al, 1998).

A prospective non randomised controlled study from Lithuania has assessed a multi-disciplinary approach to diabetic footcare on recurrent ulceration and amputation (Dargis et al, 1999). 145 people with diabetes and a past history of neuropathic foot ulcers but no evidence of PVD were studied. All received baseline assessment and footcare education. People in the intervention group (n=56) were followed in a special clinic by a multi-disciplinary team of physicians, nurses and podiatrists and received regular podiatry and re-education every 3 months and provision of special footwear as required. Scotch casting was also available to aid ulcer healing. The standard treatment group was followed in their local clinic every 3 months for routine care. Subjects in the two groups had a similar mean age of 59 years and had a similar incidence of neuropathy. Two of the intervention group and 8 of the standard treatment group were hospitalised with ulcers. The intervention group had significantly fewer recurrent ulcers during the two years compared with the standard group (30.4% v 58.4% respectively; OR 0.31 [CI 0.14-0.67], $p<0.0001$) and fewer amputations (7% [3 minor, 1 major] v 13.7% [8 minor, 4 major], p=NS) (Dargis et al, 1999).

Willoughby and Burroughs (2001) used a 21-item multiple choice questionnaire to compare the characteristics and behaviour of 48 people with diabetes who attended a footcare clinic regularly and 15 subjects with diabetes who did not attend such a clinic. In this footcare clinic, the clinical nurse specialist with advanced education worked closely with rehabilitation services, the outpatient wound care clinic, as well as with the patient’s primary care provider. There were no differences in age, gender, duration of diabetes, or number of primary care visits per year. Those attending the clinic were more likely to report having corns, calluses, or other non-ulcer pathology (69 v 40%, $p=0.045$), to see healthcare professional after discovering foot problem (92 v 66%, $p=0.001$) and to have special shoes related to their diabetes (57% v 0, $p=0.001$). In terms of footcare behaviours, those not attending the clinic were more likely to go barefoot (60 v 25%, $p=0.036$), and to treat foot problem themselves or just wait for it to get better (20 v 2%, $p=0.001$).

A retrospective incidence study (Van Houtum et al, 2004) was conducted for all hospital lower-extremity amputations in the years 1991-2000. Over these years the incidence of diabetes-related lower extremity amputation in the Netherlands decreased in both men and women with diabetes. The overall incidence of patients who underwent lower-extremity amputation decreased over the years from 55% to 36% per 10,000 patients with diabetes ($p<0.05$). A significant decrease was observed in both men (72% v 46% $p<0.05$) and women 45% v 28%, $p<0.05$) with diabetes. A possible explanation for the decrease in amputations may reflect increased attention to diabetic foot problems in the Netherlands. The number of Dutch hospitals with a podiatrist increased from 32% in 1995 to 72% in 2000 and the number of hospitals with multidisciplinary foot clinics increased from 16% to 40%.

The multi-disciplinary specialist footcare team commonly includes a physician, podiatrist, specialist nurse, orthotist and surgeon

The studies reviewed above have used different combinations of personnel in their multi-disciplinary teams. In Manchester the multi-disciplinary team comprised a diabetologist, podiatrist, specialist nurse and orthotist and had ready access to vascular and orthopaedic surgeons (Thomson et al, 1991). In the Italian study the team included a diabetologist, nurse specialist, orthopaedic surgeon, podiatrist, vascular surgeon and radiologist (Ghirlanda et al, 1997). In the Swedish study the team comprised a diabetologist, orthopaedic surgeon, diabetes nurse, podiatrist and orthotist (Larsson et al, 1995). In the London specialised foot clinic the team included a podiatrist, shoe-fitter, nurse, physician and surgeon (Edmonds et al, 1986). In the prospective Lithuanian study the team included a diabetologist, rehabilitation physician, podiatrist, orthopaedic surgeon and shoe makers (Dargis et al, 1999).

In summary, the common components of the specialist multi-disciplinary team have been a physician and podiatrist. Most have also included a specialist nurse and orthotist and all have involved or had ready access to a surgeon.

The podiatrist is an essential member of the multi-disciplinary team. Plank et al (2003) evaluated the impact of regular podiatric care on the recurrence rate of diabetic foot ulcers among 91 people (mean age 65 years) with diabetes and healed foot ulcers. 47 people were randomly assigned to the intervention group in which people received monthly chiropodist care, while 44 were assigned to the control group in which podiatric care was not recommended. During the median follow-up of 386 days, 18 people in the intervention group suffered from ulceration compared with 25 people in the control group (HR 0.60, CI 0.32-1.09; p=0.09). However, there were fewer feet affected in the intervention group than in the control group (20 feet v 32 feet, RR 0.52, CI 0.29-0.93; p=0.03). There was no significant difference in the location of ulcers between the two groups. Minor amputation was performed in two people in the intervention group and one person in the control group. At the end of follow-up, there was a significant reduction in overall events of ulceration, amputation and death in the podiatric care group (18 v 29 events, HR 0.54, CI 0.30-0.96; p=0.03).

Further research is required to define the core services in multi-disciplinary care which are essential in improving outcomes by reducing the incidence of ulcer or amputation in people with diabetes with high risk feet (Pinzur et al, 1996).

Summary - Foot Clinics and Multi-disciplinary Teams

- A multi-disciplinary footcare team can improve the rate of ulcer healing and reduce ulcer recurrence rate and the rate of amputation in people with diabetes and high risk feet

- The common components of the specialist multi-disciplinary team have been a physician and podiatrist. Most have also included a specialist nurse and orthotist and have involved or had ready access to a surgeon

- Further research is required to define the core services in multi-disciplinary care which are essential in improving outcomes by reducing the incidence of

Evidence Table: Section 11

Foot clinics and multi-disciplinary teams

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Dargis V (1999) (Adults – Lithuania)	III-2	Cohort	High	High [EPSHF+]	High
Edmonds ME (1986) (Adults – UK)	III-2	Cohort	Low	Medium [EPSNF+]	High
Ghirlanda G (1997) (Adults – US)	III-2	Cohort	Low	Medium [EPSNOR+]	High
Larsson J (1995) (Adults – Sweden)	III-2	Cohort	Medium	High [EPSNO+]	High
Pinzur MS (1996) (Adults – US)	III-2	Cohort	Medium	Medium [PS+]	Medium
Plank J (2003) (Adults – Austria)	II	RCT	High	High[P+]	High
Rith-Najarian S (1998) (Adults – US: Chippewa Indians)	III-2	Cohort	Medium	High [PNED+]	Low
Thomson FJ (1991) (Adults – UK)	III-2	Cohort	Low	High [EPSNO+]	High
Van Gils CC (1999) (Adults – US)	III-2	Cohort	Medium	High [SNED+]	High
van Houtum WH (2004) (Adults – The Netherlands)	III-2	Cohort	Medium	High [+]	High
Willoughby D (2001) (Adults – US)	III-2	Case-control	Medium	High [FNH+]	High

For magnitude rating:
[+] indicates positive effect of glycaemic control on diabetic foot disease . High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.
E = endocrinologist, P = podiatrist, S = vascular or orthopaedic surgeon, N = specialist nurse, O = orthotist, H = rehabilitation physician, R = radiologist, F = shoe-fitter, D = Dietitian

Section 12: Diabetes Foot Problems

Issue

What are the economic consequences of diabetes foot problems?

Recommendation

The cost effectiveness of intensified interventions should be considered in the prevention and management of diabetes foot problems

Evidence Statements

- Foot problems in people with diabetes are costly
  Evidence Level III-2

- Intensified foot care prevention and management strategies are cost effective
  Evidence Level III-2

Background - Economic considerations

Diabetic foot problems are a major cost to the health care system. The most common reason for hospital admission for diabetes is a diabetic foot complication (Young et al, 1993a). The DiabCost Australia study (Colagiuri et al, 2003) showed that hospitalisation and complications were the major cost drivers in people with Type 2 diabetes.

People with diabetes are 3-7 fold more likely to have an amputation than those without diabetes (Reiber, 1993). About half of the lower extremity amputations are “major” (below or above knee), while the other half involving the foot or toes are designated “minor”. The direct cost of an amputation in the UK in 1996 was $A 27,600 for a major amputation and $A 6,900 for a minor amputation (Connor, 1997) and are estimated to be similar in Australia. In Australia there are at least 2600 diabetes-related lower limb amputations each year (Payne, 2000). Applying these costs to the 2600 amputations which are performed each year in Australia gives a total direct cost of approximately $A 44 million each year. A 50% reduction in LEA would result in an annual saving of $A 22 million. However, there is little evidence to support a reduction and the trend may be in the other direction. For example, during 1992 to 1997, hospital separations in Central Australia for diabetes foot problems increased 3-fold (Eward et al, 2001).

Evidence - Economic considerations

Foot problems in people with diabetes are costly

Girod et al (2003) evaluated the cost of foot ulcers in people with diabetes. Among 239 subjects (mean age 65.5 years, 72.8% with Type 2 diabetes), 79.5% had neuropathy, and 59% had previously suffered from one or more foot ulcers and 38.5% had already had an amputatation. At the time of inclusion in this study, patient’s main lesion had been present for an average of 13.5 months. Lesions were most commonly found on the toes (50.5%) or the sole of the foot (24.3%). Lesions were considered severe in 28% of subjects - grade 3, 4 or 5 according to the Wagner classification at the study inclusion consultation. The average monthly costs related to the treatment of foot ulcers per person were $A 1190 for outpatient care and $A 2660 for hospitalisation. The grade of the lesion was a significant cost determinant of both outpatient (p=0.0403) and hospital care (p=0.0001). The average monthly cost for a patient with a grade 4/5 lesion was 2.5 times higher than for a grade 1 lesion ($A 4690 v $A 1925).

An Australia study also found a considerable difference between hospital and outpatient costs of treating foot ulcers. The average cost of hospitalisation for treatment of a diabetic foot ulcer was $A 12,474 in 1994. By comparison outpatient treatment by a specialist foot care team dthis cost by 85% (Hoskins, 1994).

In a study by Benotmane et al (2001), 163 out of 1,779 hospital admissions for diabetes were related to a foot lesion during a 5-year period. The lesions were allocated to one of the following groups: I - superficial or deep ulcer; II - deep abscess and/or osteomyelitis; III - fore-foot gangrene or foot gangrene. The average length of hospitalisation was 26.9±20.9 days, 48.3±31.6 days, and 57.1±43.2 days per episode, respectively in the 3 groups (p<0.001). Total costs, which included hospitalisation (80%), laboratory tests (3%), medical treatment (10%) and surgeons' and anesthetists' fees (7%), were $A 272,000, $A 222,000, and $A 770,000, respectively. By the end of the study, primary healing occurred in 59% of subjects (n=78), 17% (n=23) required major amputation and 14% (n=19) had a minor amputation. 12 subjects died. 118 people took a time off from work for a total of 3,780 days.

In a Belgium study (Van Acker et al, 2000), 151 people with diabetic foot problems referred to a diabetic foot clinic during July 1992 to June 1993 were follow for one year. The health resource utilisation included medications, ambulatory care, diagnostic tests, hospitalisations, topical treatments, orthopaedic therapy, and surgery. These direct cost were converted to expenditures at the market prices for 1993. The indirect cost included lost productivity and missed days at work. A total of 63 people were hospitalised, and the mean length of hospital stay was 24 days for people without amputation (n=47) and 43 days for people having an amputation (n=16). Total cost for treatment during the study period was $A 1.7 million and the total cost increased with the level of the Wagner classification, ranging from $A 60,800 for grade 0 to $A 443,600 for grade IV. The average cost of preventive care (n=47 without ulcers at entry) was $A 1220, while curative care cases (n=120 ulcers at entry or during the study) including diagnostic tests, wound dressings, antibiotic therapy, and off loading techniques resulted in a mean cost of $A 7260 per ulcer. The 16 cases requiring amputation had a mean cost of $A 44,050.

A database analysis was performed of 8,905 people with Type 1 or Type 2 diabetes (mean age of 65.8 years) participating in a health maintenance organisation from 1993-1995 (Ramsey et al, 1999). The cumulative incidence of foot ulcers over 3 years was 5.8%. Of these 15.6% required amputation, and a similar proportion (15%) developed osteomyelitis, of whom 36% had a lower extremity amputation during the follow up. The attributable cost for a foot ulcer was $A 38,900 in the 2 years after development of an ulcer (Ramsey et al, 1999).

Gordois et al (2004) used a prevalence based model to estimate the annual costs in the US of diabetic peripheral neuropathy and its complications (ulcer, osteomyelitis and amputation) in people with Type 2 diabetes. The estimated total annual cost ranged from $A 6 billion to 17.6 billion with an average of $A 14 billion, which accounted for 27% of the total direct medical costs of diabetes.

Intensified foot care prevention and management strategies are cost effective

Kantor et al (2001) conducted a cost-effectiveness analysis using data from published clinical trials and a meta-analysis, as well as from a database created by Curative Health Services, an administrative and clinical database of more than 26,000 diabetic people seen in wound care clinics. Only people with diabetic neuropathic ulcers of at least 8 weeks were included (n=20,136). Data for the standard care arm were taken from the published metaanalysis. Four available treatment options were considered - standard care (SC) which was used by most primary care physicians, specilised wound care centres (WCC), becaplermin, a recombinant growth factor preparation, and the use of platelet releasate (PR). Since becaplermin and platelet-releasate are not widely used in Australia, only the data comparing SC and WCC are considered here. The total costs for 20 weeks were $A 2446 for SC and $A 2330 for WCC. The rates of ulcers healed were 30.9% (95% CI 26.6-35.0%) for SC and 35.6% (CI 34.8-36.4%) for WCC. Although cost were similar outcomes were better for the WCC. However this study is limited by the database used and the probably that people attending wound care clinics had more severe lesions than people receiving standard care.

Horswell et al (2003) compared a staged diabetes foot management programme with standard care on health care cost and utilisation in a retrospective study. All subjects had diabetes and foot ulcers, of whom 45 received staged foot care that consisted of selfcare education, devices to offload pressure, and custom-fabricated orthoses and footwear after healing, while 169 subjects received standard foot care which consisted of uncoordinated treatment including wound care, antibiotics and self care education. Baseline characteristics were similar in both groups. In the 1-year follow-up period, the staged foot care group had a lower foot-related hospitalisation rate than the standard care group (0.09 v 0.50 admissions per person, p=0.002), lower foot-related inpatient days (0.91 v 3.97 days per person, p=0.03), and fewer amputation-related hospitalisation (0.04 v 0.19 per person, p=0.035). There were also fewer emergency visits (0.60 v 1.22 visits, p=0.004) and lower emergency department charges ($104 v $208, p=0.006) in the staged foot care group compared with the standard care group. Overall the total cost was significantly lower in the staged foot care group than in the standard care group ($A 6,630 v $A 13,060, p=0.014).

Ortegon et al (2004) performed a cost-effectiveness analysis of prevention and treatment of diabetes foot disease in the Netherlands. A Markov model was developed to simulate the health and economic outcomes of optimal care of the diabetic foot in a cohort of 10,000 people (mean age 61 years) with newly diagnosed Type 2 diabetes who were followed through the model over their lifetime. Diabetic foot risk (DFR), based on the classification system of the International Diabetic Foot Working Group, was defined as: DFR1 - no neuropathy; DFR2 - sensory neuropathy, and DFR3 - sensory neuropathy and deformity or PVD. Costs used in the model were expressed as 1999 dollars. Compared with current standard care, the mean total lifetime costs of a person receiving guideline-based care (intensive glycaemic control (IGC) or optimal foot care (OFC)) ranged from $A 5,680 to $A 6,090. For people receiving IGC and OFC, the costs resulted in <$A 35,000 per QALY gained, even for levels of preventive foot care as low as 10%. OFC resulted in a greater reduction in ulcer and amputation rate than IGC (11.2 v 0.56%; 9.4 v 4.4%, respectively). People receiving both IGC and OFC showed approximately the same ulcer and amputation reduction rate as people receiving OFC alone (11.2%; 10.5%, respectively). The cost-effectiveness varied depending on the level of foot ulcer reduction attained.

Summary - Economic consequences

- Diabetic foot problems are a major cost to the health care system and are the most common reason for hospital admissions for diabetes
- The annual total direct cost for amputations in Australia is approximately $A 44 million
- Peripheral neuropathy and its complications (ulcer, osteomyelitis and amputation) account for 27% of the total direct medical costs of diabetes
- The average cost of hospitalisation for treatment of a diabetic foot ulcer was $A 12,474 in 1994
- In a Belgium study the average cost of preventive care was $A 1,220 compared with $A 7,260 for treatment of an ulcer
- Intensified foot care prevention and management strategies, such as staged foot care, are cost effective
- The total cost for staged foot care was $A 6,630 compared with $A 13,060 for standard care

Evidence Table: Section 12

Economic Considerations

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Benotmane A (2001) (Adults – France)	III-2	Cohort	High	High +	High
Girod I (2003) (Adults – France)	III-2	Cross-sectional	High	High +	High
Gordois (2004) (Adults – US)	III-2	Cross-sectional	High	High	High
Horswell RL (2003) (Adults – US)	III-2	Cohort	Medium	High +	High
Hoskins (1994) (Adults – Australia)	III-2	Cohort	Medium	High	High
Kantor J (2001) (Adults – US)	III-2	Cohort	Medium	Medium	Medium
Ortegon MM (2004) (Adults – The Netherlands)	III-2	Cohort	Medium	High +	High
Ramsey SD (1999) (Adults – US)	III-2	Cohort	High	High +	High
Van Acker K (2000) (Adults – Belgium)	III-2	Cohort	High	High	High

For magnitude rating:
+ indicates negative effect (or impact) of lower socioeconomic status on diabetic foot disease. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Section 13: Diabetes Foot Problems

Issue

What are the socioeconomic influences on diabetes foot problems?

Recommendation

The influence of socioeconomic factors should be considered in the prevention and management of diabetes foot problems

Evidence Statements

- Socioeconomic factors influence the occurrence of diabetes foot problems
  Evidence Level III-2

Background - Socioeconomic considerations

Diabetic foot problems are a major cost to the health care system. The most common reason for hospital admission for diabetes is a diabetic foot complication (Young et al, 1993a). The DiabCost Australia study (Colagiuri et al, 2003) showed that hospitalisation and complications were the major cost drivers in people with Type 2 diabetes.

Socioeconomic factors are important barriers to diabetes care. Factors which may interfere with self care include financial difficulties, priorities resulting from an individual with diabetes having family caretaker role and responsibilities, housing and family problems. While these may apply to any person with diabetes, they are more likely to apply to a person with a lower socioeconomic status. These barriers have been shown to result in reduced physical and social functioning, and reduced physical and mental health in people with diabetes (Hill-Briggs et al, 2002). Also the greater the number of socioeconomic barriers the greater the effect (Hill-Briggs et al, 2002). While these barriers can have a direct effect on diabetes care eg not being able to afford medications or attend services, they may also operate through an indirect effect. One study showed that when significant socioeconomic barriers were present, 77% of intervention visits were used to address these non-diabetes specific issues, which reduced the focus on diabetes care as a priority (Batts et al, 2001).

Evidence - Socioeconomic considerations

Socioeconomic factors influence the occurrence of diabetes foot problems

Few studies were identified which specifically addressed this issue in relation to foot problems in people with diabetes and further research is required in this area. Some indirect information is contained in the following studies.

Weng et al (2000) examined environmental factors which affect diabetes outcome. A cohort of 610 people living within the Greater London boundary and having their first diabetes clinic visit at St Thomas hospital in 1982-85 was analysed in 1995. Out of 610 people, 186 had died, 332 were re-examined in the clinic and 92 were unable to be traced. Social deprivation was ranked according to the Jarman ‘under-privileged area’ (UPA) score. People were allocated according to the UPA score - >30 was classified as a deprived area and a score <10 to a prosperous area, while a score of 10-30 was classified an intermediate deprived area. Compared with people from prosperous areas (n=59), people from deprived areas (n=182) were older (61.3 v 58.6 years, p=0.014) and had a shorter duration of diabetes (14.2 v 19.6 years, p=0.002). Overall, people from deprived areas had a significantly higher mean HbA_{1c} than people from prosperous areas (n=59) (10.5% [CI 10.1-10.9] v 9.1% [CI 8.2-10.0], p=0.003) and more diabetes complications: neuropathy (51.5 v 20.0%, p<0.001); ulcer/amputation (16.2 v 7.3%, p<0.001). The age-adjusted mortality rate was significantly higher in deprived than prosperous areas (2.66 v 1.91 per 100 person-year, no p value reported).

Some ethnic groups are associated with lower socioeconomic status and some studies have examined foot problems in relation to ethnicity. In a 2-year cohort of 1,666 people (mean age 69 years; 52.0% Mexican American, 44.0% non-Hispanic whites, 4.0% other ethnic group) with Type 2 diabetes (Lavery et al, 2003b), the incidence of ulceration, infection, amputation, and lower-extremity bypass was 68.4, 36.5, 5.9, and 7.7 per 1,000 persons per year. The prevalence of peripheral sensory neuropathy with loss of protective sensation was 40.9% in Mexican Americans and 42.2% in non-Hispanic whites. Amputation incidence was higher in Mexican Americans than in non-Hispanic whites (7.4/1,000 v 4.1/1,000; OR 1.8, CI 1.2-2.7, p=0.003), while there was no significant difference in the incidence of ulceration (p=0.1), foot infection (p=0.9) and lower-extremity bypass (p=0.3) between ethnic groups. Mexican Americans were 3.8 times more likely to have a failed bypass which leaded to an amputation than non-Hispanic whites (75.0 v 44.0%; OR 3.8, CI 1.2-11.8, p=0.01).

Young et al (2003) reported that individuals from certain ethnic minority groups had an increased risk of LEA. Among 429,918 people with diabetes (mean age 64 years, 97.4% male) who received primary care within the Veterans Affairs Health Care System, 3,289 people had an LEA during the study period (1 Oct 1997 to 10 Sept 1998). Compared with people without amputation, amputees were more likely to belong to a minority group and to have more comorbid conditions. Native Americans had the highest risk of amputation (RR 1.74, CI 1.39-2.18), followed by African Americans (RR 1.41, CI 1.34-1.48) and Hispanics (RR 1.28, CI 1.20-1.38) compared with whites. Asians were more likely to have toe amputations and Native Americans were more likely to have below-knee amputations compared with whites or other ethnicities.

Karter et al (2002) reported diabetic complication rates in an ethnically diverse population (n=62,432) with diabetes which included Asians (12%), blacks (14%), Latinos (10), and whites (64%) in a 4-year observational study. Latinos were least likely (35%), followed by blacks (55%), to have more than a high school education. At baseline, self-reported peripheral neuropathy was 19% in Asians, 31% in Latinos and 32% in blacks and 32% in whites, respectively. From January 1995 to December 1998, there were 574 hospitalisations for nontraumatic LEA procedures. The age- and sex-adjusted incidence rate was 10.7 (CI 9.2-12.3) per 1,000 person-years in blacks, 9.2 (CI 8.6-9.9) in whites, 6.3 (CI 5.0-7.8) in Latinos and 5.9 (CI 4.7-7.2) in Asians. The incidence of LEA procedures was significantly lower in Asians than in whites, with a HR of 0.40 (CI .028-0.62); while there was no statistically significant black-white and Latino-white difference for LEA (HR 0.84, CI 0.65-1.08, p=0.16; HR 0.85, CI 0.63-1.14, p=0.27).

Australia's Aboriginal and Torres Strait Islander peoples, a socioeconomically disadvantaged group, are especially likely to suffer many foot problems related to diabetes. Unfortunately there are no specific data relating to the management of diabetes related foot problems among socioeconomically disadvantaged people, and research in this area is urgently needed.

Summary - Socioeconomic consequences

- Diabetic foot problems are a major burden on the health care system and are the most common reason for hospital admissions for diabetes

- Socioeconomic factors influence the occurrence of diabetes foot problems, although few studies have addressed this issue and further research is required in this area

Evidence Table: Section 13

Socioeconomic Considerations

Author	Evidence				
	Level of Evidence		*Quality Rating*	*Magnitude Rating*	*Relevance Rating*
	Level	*Study Type*			
Karter AJ (2002) (Adults – US)	III-2	Cohort	High	High[+]	Medium
Lavery LA (2003b) (Adults – US)	III-2	Cohort	High	High[+]	Medium
Weng C (2000) (Adults – UK)	III-2	Cohort	High	High[+]	Medium
Young BA (2003) (Adults – US)	III-2	Cohort	High	High[+]	Medium

For magnitude rating:
[+] indicates negative effect (or impact) of lower socioeconomic status on diabetic foot disease. High = clinically important & statistically significant; Medium = small clinical importance & statistically significant; Low = no statistically significant effect.
Criteria for Quality and Relevance ratings are detailed in Appendix 9.

Diabetes Foot Problems: Evidence References

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2.6 Diabetes Foot Problem Guideline Search Strategy and Yield

Electronic Databases Searched:

Medline
CINAHL
EMBASE
Cochrane

Terms used to search the databases:

Detailed within the table below.

Search Inclusion Criteria:

Where possible the searches were limited by the English language and human research. The databases were searched for the following years of publication: Medline 1966-2004; CINAHL 1982-2004; EMBASE 1988-2004; Cochrane 1993-2004; Unless other year ranges are specified. PsycInfo and Sociological Abstracts were searched for the following years of publication of socioeconomic issues: 1994-2004.

Other searching:

Reference lists at the end of review articles of particular relevance were hand searched.
Relevant articles were solicited from expert colleagues and organisations.
Local and international clinical practice guidelines were reviewed for relevant references.

Abbreviations:

The database searched has been indicated next to each set of keywords using the following abbreviations. M = Medline, CI = CINAHL, EM = EMBASE and CO = Cochrane. All EMBASE and Medline searches were done using English language (En.La) and human as a limit. The symbol / after a word indicates that it is a MeSH term and any article found by this method has been allocated to this subject heading used in the database; .mp indicates that that word was searched as a keyword in the database. Other abbreviations used were: NIDDM = non-insulin-dependent diabetes mellitus; RCT = randomised controlled trial; CVD = cardiovascular diseases; PVD = peripheral vascular diseases; IC = intermittent claudication; CBD = cerebrovascular disorders; bl = blood; cl = classification; co = complications; dh = diet therapy; di = diagnosis; dm = disease management; dt = drug therapy; ep = epidemiology; et = etiology; mo = mortality; nu = nursing; pa = pathology; pc = prevention and control; pp = pathophysiology; px = psychology; rh = rehabilitation; si = side effects; th = therapy.

Identified = number of articles which matched the MeSH terms listed or contained the text terms in each particular database.
Relevant = those articles considered relevant to the questions being asked after viewing titles or abstracts.
Articles Identified by Other Strategies = articles identified by hand searching, other searches for other questions, or from colleagues.
Total for Review = relevant articles for each question identified through searches or other strategies and met the following criteria.

Criteria used to determine the suitability of articles for review

In assessing the evidence the following criteria were used to determine the suitability of studies:

1. Papers or editorials that present original data.
2. Appropriate population for question being addressed.
3. Article in the English language.
4. Study conducted in humans.
5. Articles were obtained from journals able to be accessed within our library or ordered through an interlibrary loan.

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
1.	**Is peripheral neuropathy a risk factor for ulceration or amputation?**	**Total for Question 1**	**2000**	**363**	**53**	**131**	**2**	**4**	**32**	**3**	**41**	**I**
		Diabetic neuropathies/ AND (skin ulcer/ OR amputation/ OR callus/) M 66-99, CI 82-04	154 (M) 44 (CI)	36 (M) 7 (CI)								
		Diabetic neuropathies/ AND (skin ulcer/ OR amputation/ OR callus.mp) M 99-03	50									
		Diabetic neuropathies/ AND (skin ulcer/ OR amputation/ OR Bony callus/ M 03-04	11	1								
		Diabetic neuropathies/ AND (skin ulcer/ OR callus/ OR amputation/ OR diabetic foot/) M 66-99, CI 82-04	344 (M) 290 (CI)	73 (M) 42 (CI)								
		Diabetic neuropathies/ AND (skin ulcer/ OR amputation/ OR callus.mp OR diabetic foot/) M 99-03	136	53								
		Diabetic neuropathies/ AND (skin ulcer/ OR amputation/ OR Bony callus/ OR diabetic foot/) M 03-04	35	1								
		Risk factors/ AND diabetic foot/ M 66-04, CI 82-04	450 (M) 115 (CI)	66 (M) 33 (CI)								
		Diabetic neuropathy/ co,dm,rh,si,ep AND (amputation/ OR skin ulcer/ pc,co,rh,di,si,ep,th,et OR below knee amputation/ OR callus/ et,co, pc,di,th,ep OR limb amputation/) EM 88-99	182	29								
		Diabetes mellitus/co,rh,si,ep AND Risk factors/ep,co,et,di,pc, si EM	5	0								
		Diabetic neuropathy/ AND Risk factors/ EM 99-04	159	20								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
1.	**Is peripheral neuropathy a risk factor for ulceration or amputation?**	Diabetic neuropathy/ co,dm, rh,si,ep AND (diabetic foot/ et,co,pc,di,rh,dm,ep,th OR skin ulcer/ pc,co,rh,di,si,ep,th, et OR amputation/ OR below knee amputation/ OR foot deformities, acquired/ OR foot amputation/ OR keratosis.mp OR limb amputation/) EM 88-99	171	26								
		Diabetic neuropathy/ co,dm, rh,si,ep AND (diabetic foot/ et,co,pc,di,rh,dm,ep,th OR skin ulcer/ pc,co,rh,di,si,ep,th, et OR below knee amputation/ OR foot amputation/ OR keratosis.mp OR limb amputation/) EM 99-03	169	32								
		Diabetic foot/ AND diabetic neuropathies/ CO	21	6								
		Diabetic foot/ AND risk factors/ CO	12	6								
		Diabetes mellitus/ AND risk factors/ CO	64	2								
2.	**Is peripheral vascular disease a risk factor for ulceration or amputation?**	**Total for Question 2**	**1743**	**185**	**64**	**106**	**1**	**3**	**22**	**5**	**31**	**I**
		PVD/ AND (skin ulcer/ OR callus/ OR amputation/ OR diabetic foot/) M, CI	54 (M) 57 (CI)	1(M) 17 (CI)								
		PVD/ AND (skin ulcer/ OR foot deformities, acquired/ OR keratosis/ OR amputation/ OR diabetic foot/) M 66-99, CI	117 (M) 57 (CI)	6 (M) 10 (CI)								
		PVD/ AND (skin ulcer/ OR callus.mp OR amputation/ OR diabetic foot/ OR keratosis/ OR foot deformities, acquired/) M 99-02	76	11+								
		PVD/ AND (skin ulcer/ OR bony callus/ OR amputation/ OR diabetic foot/ OR keratosis/ OR foot deformities, acquired/) M 03-04	21	1								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
2.	**Is peripheral vascular disease a risk factor for ulceration or amputation?**	PVD/ AND (skin ulcer/ OR callus/ amputation/ OR diabetic foot/ OR foot deformities, acquired/ OR keratosis/) CI 99-04	54	11								
		Risk factors/ AND diabetic foot/ M 66-04, CI 82-04	402 (M) 114 (CI)	61 (M) 30 (CI)								
		PVD/co,pc,rh,si,ep,et, AND (skin ulcer/pc,co,rh,di,si,ep,th,et OR keratosis.mp OR below knee amputation/ OR foot deformities acquired/ OR amputation/ OR diabetic foot/ OR limb amputation/) EM	679	23								
		Risk factors/ep,co,et,di,pc,si AND diabetes mellitus/ co, rh,si,ep EM	60	10								
		Peripheral vascular disease/ AND (amputation/ OR foot amputation/ OR below knee amputation/ OR leg amputation/ OR foot ulcer/ OR skin ulcer/ OR keratosis/ OR diabetic foot/) EM 99-04	196	8								
		Diabetic foot/ AND risk factors/ CO	12	6								
		Diabetes mellitus/ AND risk factors/ CO	149	13								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
3.	**Is foot deformity or a previous amputation a risk factor for ulceration or amputation?**	**Total for Question 3**	**936**	**128**	**73**	**86**	**1**	**5**	**30**	**3**	**39**	**I**
		Foot deformities/ AND (skin ulcer/ OR amputation/ OR keratosis/) M 66-04, CI 82-04	10 (M) 6 (CI)	5 (M) 2 (CI)								
		Risk factors/ AND diabetic foot/ M 66-04, CI 82-04	402 (M) 114 (CI)	61 (M) 30 (CI)								
		Risk factors/ep,co,et,di,pc,si AND diabetes mellitus/co,rh,si,ep EM	69	9								
		(Foot malformation/ OR callus/ OR keratosis/) AND risk factors/ AND (amputation/ OE foot amputation/ OR below knee amputation/ OR leg amputation/) EM 99-04	6	4								
		Foot malformation/et,co,pc,di,rh, ep,th AND (skin ulcer/ pc,co,rh, di,si,ep,th,et OR amputation/ OR below knee amputation/ OR limb amputation/ OR foot amputation/) EM	53	15								
		Diabetic foot/ AND risk factors/ CO	13	8								
		Diabetes mellitus/ AND risk factors/ CO	63	0								
		NIDDM.mp AND (deformity.mp OR amputation.mp OR callus.mp OR foot ulceration.mp) CO	378	4								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
4.	**Is a current or previous ulcer a risk factor for amputation?**	**Total for Question 4**	**1172**	**138**	**35**	**62**	**0**	**2**	**12**	**2**	**16**	**II**
		Amputation/ AND (keratosis/ OR skin ulcer/) M, CI	49 (M) 9 (CI)	4 (M) 0 (CI)								
		Risk factors/ AND diabetic foot/ M, CI	264 (M) 75 (CI)	53 (M) 28 (CI)								
		(Foot amputation/ OR below knee amputation/ OR limb amputation/ OR amputation/) AND (callus/ et,co,pc,th,ep OR skin ulcer/ pc,co,rh,di,si, ep,th,et) EM	258	35								
		Risk factors/ep,co,et,di,pc,si AND diabetes mellitus/co,rh, si,ep EM	5	1								
		(amputation/ OR foot amputation/ OR below knee amputation/ OR leg amputation/) AND risk factors/ AND diabetic foot/ EM 99-02	59	10								
		Diabetic foot/ AND Risk factors/ CO	63	0								
		Diabetes mellitus/ AND risk factors/ CO	12	5								
		NIDDM.mp AND (deformity.mp OR amputation.mp OR callus.mp OR foot ulceration.mp) CO	378	2								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
5.	**What is the most practical method for detecting loss of protective foot sensation in the primary care setting?**	**Total for Question 5**	**1216**	**73**	**12**	**17**	**2**	**2**	**13**	**0**	**17**	**I**
		Diabetes mellitus/ AND monofilament.mp/ M, CI	33 (M) 9 (CI)	14 (M) 3 (CI)								
		Diabetic neuropathies/ AND clinical assessment tools/ CI	6	3								
		(Monofilament.mp OR screening test/) AND (diabetic neuropathy/co, dm,rh,si,ep OR diabetic foot/et,co,pc,di,rh,dm,ep,th) EM	958	15								
		(diabetic neuropathy/ OR diabetic foot/) AND (monofilament.mp OR screening test/) EM 99-02	62	25								
		Monofilament.mp CO	74	8								
		Risk factors/ AND: Diabetic foot/ Diabetes mellitus/ CO	12	5								
		Diabetes mellitus/ AND risk factors/ CO	63	0								
6.	**How should peripheral vascular disease be assessed clinically?**	**Total for Question 6**	**908**	**62**	**2**	**30**	**1**	**6**	**18**	**0**	**25**	**I**
		NIDDM/ AND PVD/ AND symptoms.mp/ M, CI	5 (M) 0 (CI)	3 (M) 0 (CI)								
		IC.mp/ AND PVD/:	261 (M) 41 (CI)	9 (M) 5 (CI)								
		AND NIDDM/ M, CI	4 (M) 2 (CI)	1 (M) 0 (CI)								
		PVD/ AND NIDDM/ AND risk factors/ M, CI	28 (M) 3 (CI)	8 (M) 2 (CI)								
		IC/ AND PVD/ EM	187	10								
		PVD.mp AND (IC.mp OR pedal pulses.mp) CO	137	3								
		Pedal pulse.mp AND NIDDM/ M	22	7								
		Foot pulses.mp/ M	33	1								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
6.	**How should peripheral vascular disease be assessed clinically?**	Foot pulses.mp M 99-02 Pulse/ AND NIDDM/ M, CI Pedal pulses.mp/ CI, EM NIDDM/ AND pulse rate/ EM 99-04 PVD.mp AND (IC.mp OR pedal pulses.mp) CO	7 30 (M) 14 (CI) 11 (CI) 25 (EM) 13 96	1 5 (M) 1 (CI) 2 (CI) 2 (EM) 1 1								
7.	**What should be the frequency of foot assessment?**	**Total for Question 7** Diabetic foot/ AND (clinical assessment.mp OR assessment.mp/) M, CI Risk assessment/ AND diabetic foot/ M, CI Diabetic foot/et,co,pc,di,rh,dm, ep,th AND Risk assessment/ EM Diabetic foot/et,co,pc,di,rh,dm, ep,th AND (assessment.mp OR clinical assessment.mp) EM Diabetic foot.mp AND clinical assessment.mp CO	**514** 155 (M) 110 (CI) 26 (M) 22 (CI) 70 93 38	**103** 31 (M) 26 (CI) 8 (M) 9 (CI) 19 6 4	**4**	**10**	**4**	**0**	**0**	**0**	**4**	**I**
8.	**Does patient education improve footcare and outcomes?**	**Total for Question 8** Diabetic foot/ AND (education/ OR patient education/) M, CI Diabetic foot/et,co,pc,di,rh,dm, ep,th AND (education/ OR patient education.mp/) EM Diabetic foot.mp AND (education.mp OR patient education.mp) CO	**432** 168 (M) 95 (CI) 131 38	**130** 47 (M) 25 (CI) 46 12	**13**	**19**	**1**	**6**	**7**	**2**	**16**	**I**

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
9.	**Does improved glycaemic control decrease the development or progression of peripheral neuropathy?**	**Total for Question 9**	**1720**	**165**	**16**	**45**	**1**	**5**	**6**	**0**	**12**	**I**
		NIDDM/ AND neuropathy.mp AND (glycaemic control.mp OR glycemic control.mp) M	127	45								
		NIDDM/bl,mo,nu,cl,pa,co,pc,dh, pp,di,dt,px,rh,ep,et,th AND (CBD/ OR macrovascular.mp OR retinopathy.mp OR neuropathies/ OR nephropathy.mp/ OR vascular disease/ OR coronary disease/ OR diabetic nephropathies/ OR CVD/ OR diabetic microvascular.mp/ OR diabetic angiopathies/ OR neuropathy.mp. OR diabetic neuropathy/ OR stroke.mp OR PVD.mp/) LIMIT TO (controlled clinical trial OR clinical trial OR multicentre study OR RCT OR clinical trial, [phase i – iv] OR meta analysis) M	410	17								
		Diabetes mellitus/bl, co, pc, dh, dt, th, et AND (glycemic control.mp OR glycaemic control.mp OR diabetes control.mp) AND (neuropathy.mp OR neuropathies.mp OR diabetic neuropathies/) M 99-04	53	5								
		Risk factors/ AND diabetic foot/ M, CI	264 (M) 75(CI)	46 (M) 21 (CI)								
		NIDDM/co,dh,pa,dt,pp,ed,ss,ep, et,th AND (glycemic control/ OR diabetic neuropathies/ OR blood glucose monitoring/ OR vascular diseases/ OR neuropathy.mp/ OR diabetic neuropathies/ OR risk factors/ OR retinopathy/ OR diet/ OR diabetic angiopathies/ OR nephropathy.mp/ OR CVD/ OR retinopathy.mp/ OR glycemic control.mp OR macrovascular.mp OR microvascular.mp OR diabetes control.mp) CI	44	2								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
9.	**Does improved glycaemic control decrease the development or progression of peripheral neuropathy?**	NIDDM/bl,co,pc,dh,dt,et,th AND (neuropathy.mp OR neuropathies.mp OR diabetic neuropathies/) AND glycaemic control.mp OR glycemic control.mp/ OR diabetic control.mp) CI 99-04	6	0								
		(Glycosylated hemoglobin/ OR hemoglobinA1c/ OR HbA1c.mp/) AND Diabetes mellitus/ EM	450	16								
		(Glycaemic control.mp OR glycaemic control.mp OR diabetes control/) and NIDDM/ AND (peripheral neuropathy/ OR diabetic neuropathy/ OR neuropathies) EM 99-04	71	6								
		Diabetes mellitus/co,rh,si,ep AND Risk factors/ep,co,et,di,pc, si EM	5	0								
		NIDDM.mp AND (glycemic control.mp OR neuropathy.mp) CO	174	4								
		Neuropathy.mp AND glycemic control.mp CO	41	5								
10.	**Does appropriate footwear reduce ulceration and amputation?**	**Total for Question 10**	**982**	**252**	**53**	**64**	**2**	**4**	**16**	**0**	**22**	**I**
		(Orthopedic footwear/ OR shoes/ OR footwear.mp) AND skin ulcer/ AND diabetes mellitus/ M, CI	26 (M) 15 (CI)	2 (M) 1 (CI)								
		(Orthopedic footwear/ OR shoes/ OR footwear.mp) AND diabetic foot/ M, CI	221 (M) 162 (CI)	64 (M) 51 (CI)								
		(Orthopedic footwear/ OR shoes/ OR footwear.mp) AND amputation/ M, CI	90 (M) 67 (CI)	10 (M) 15 (CI)								
		(Shoe/ OR footwear.mp) AND skin ulcer/pc,co,rh,di, si,ep,th,et AND diabetes mellitus/co,rh,si,ep EM	53	7								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
10.	**Does appropriate footwear reduce ulceration and amputation?**	(Shoe/ OR footwear.mp)AND diabetic foot/et,co,pc,di,rh,dm, ep,th EM	140	51								
		(Shoe/ OR footwear.mp) AND (amputation/ OR below knee amputation/ OR foot amputation/OR limb amputation/) EM	52	27								
		Footwear.mp CO	54	12								
		Diabetes.mp AND (ulceration.mp OR amputation.mp) AND foot.mp CO	102	13								
11.	**Do specialist foot clinics or multidisciplinary teams decrease amputation?**	**Total for Question 11**	**808**	**133**	**21**	**45**	**1**	**2**	**12**	**0**	**15**	**I**
		(Outpatient clinics, hospital/ OR multidisciplinary.mp OR patient care team/ OR clinic.mp) AND diabetic foot/ M, CI	192 (M) 43 (CI)	62 (M) 13 (CI)								
		diabetic foot/ AND (clinics.mp OR multidisciplinary care team/ OR patient care team.mp)) CI 99-04	53	23								
		Diabetic foot/et,co,pc,di,rh,dm, ep, th EM	413	11								
		Diabetic foot/ AND (outpatient clinics, hospital.mp OR multidisciplinary team.mp OR patient care/ OR clinics.mp) EM 99-02	93	20								
		Diabetic foot.mp AND (high risk foot clinic.mp OR outpatients clinic.mp) CO	14	4								

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
12.	**What are the economic consequences and socioeconomic influences of diabetes foot problems?**	**Total for Question 12** (diabetic foot/ OR diabetic foot problems.mp OR diabetic neuropathies/ OR amputation/ OR foot ulceration.mp) AND (cross-sectional studies/ OR cohort studies/ OR prospective studies/ OR systematic review.mp OR meta-analysis/) AND (socioeconomic status.mp OR social class/ OR sociodemographic.mp OR social environment/ OR social determinants.mp OR income/ OR income.mp OR poverty/ OR wealth.mp OR education/ OR educational status/ OR employment statsu.mp OR employment/ OR unemployment/ OR insurance/ OR ethnic groups/ OR ethnicity.mp OR culture/ OR continental population groups/ OR indigenous.mp OR aboriginal.mp OR housing/ OR leasing, property/ OR tenant.mp OR regional variation.mp OR urban differential.mp OR geographical.mp OR rural.mp OR remote.mp OR smoking/ OR marriage/ OR spouses/ OR nutrition/ OR physical activity.mp OR exercise/ OR alcohols/ OR obesity/ OR overweight.mp OR drugs.mp OR pharmaceutical preparation/ OR gender identity/ OR sex/ OR occupations/ OR equity.mp OR access.mp) M, CI, EM, PsycInfo 94-04 (niddm.mp OR diabetic foot problems.mp OR diabetic foot diseases.mp OR diabetic neuropathy.mp OR foot ulcer.mp OR amputation.mp) AND (socioeconomic status.mp OR socioeconomic position.mp OR socioeconomic factors.mp OR social class	**340** 78 (M) 21 (CI) 44 (EM) 1 (Psyc) 144	**32**	**0**	**21**	**1**			**0**	**15**	

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
12.	**What are the economic consequences and socioeconomic influences of diabetes foot problems?**	OR social determinants.mp OR sociodemographic.mp OR income.mp OR poverty.mp OR insurance.mp OR wealth.mp OR education.mp OR educational status.mp OR employment.mp OR employment status.mp OR unemployment.mp OR occupation.mp OR ethnic groups.mp OR ethnicity.mp OR culture.mp OR continental population groupsmp OR indigenous.mp OR aboriginal.mp OR housing.mp OR leasing property.mp OR tenantmp OR regional variation.mp OR urban differential.mp OR geographical.mp OR rural.mp OR remote.mp OR smoking.mp OR drugs.mp OR marriage.mp OR spouses.mp OR nutrition.mp OR physical activity.mp OR exercise.mp OR alcohol.mp OR obesity.mp OR overweight.mp OR gender.mp OR sex.mp OR equity.mp OR access.mp) AND (cross-sectional study.mp OR cohort study.mp OR prospective study.mp OR systematic review.mp OR meta-analysis.mp) CO 99-04										
		(type 2 diabetes.mp OR foot ulcer.mp OR amputation.mp) AND (social class.mp OR social determinants.mp OR socioeconomic position.mp OR socioeconomic factors.mp OR socioeconomic status.mp OR income.mp OR poverty.mp OR wealth.mp OR insurance.mp OR education.mp OR educational status.mp OR literacy.mp OR occupations.mp OR employment.mp OR employment status.mp OR unemployment.mp OR racial.mp OR ethnic difference.mp OR ethnicity.mp OR culture.mp	11									

QUESTIONS		KEY WORDS	NO. ARTICLES IDENTIFIED	NO. RELEVANT ARTICLES	ARTICLES IDENTIFIED BY OTHER STRATEGIES	TOTAL FOR REVIEW	LEVEL I	LEVEL II	LEVEL III	LEVEL IV	TOTAL NO. REVIEWED & GRADED	HIGHEST LEVEL OF EVIDENCE
12.	**What are the economic consequences and socioeconomic influences of diabetes foot problems?**	OR indigenous.mp OR aboriginal.mp OR housing.mp OR tenant.mp OR leasing property.mp OR remote.mp OR rural.mp OR urban differential.mp OR regional difference.mp OR geographical.mp OR smoking.mp OR drugs.mp OR marriage.mp OR spouse.mp OR nutrition.mp OR physical activity.mp OR exercise.mp OR equity.mp OR access.mp) Sociologial 94-04 (Diabetic neuropathies/ OR diabetic foot/ OR diabetic peripheral neuropathymp OR diabetic foot complications.mp OR amputation/ OR foot ulcer/) AND treatment.mp (cost and cost analysis/ OR cost effectiveness.mp OR cost-benefit/) M, CI 99-04	 30 (M) 11 (CI)									