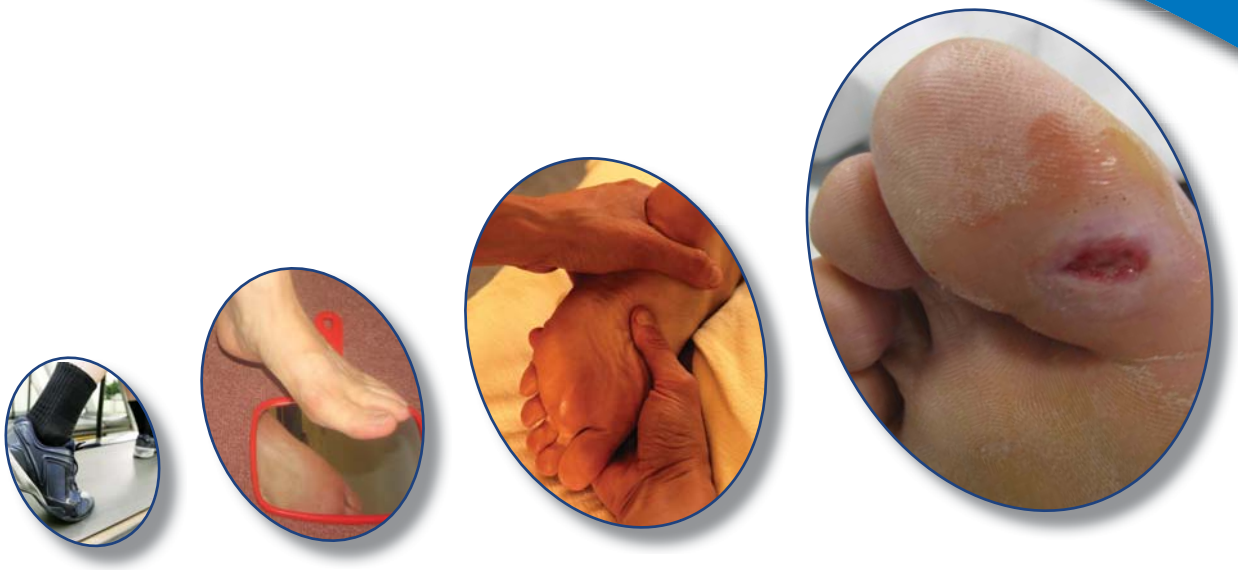
National Evidence-Based Guideline

Prevention, Identification and Management of Foot Complications in Diabetes



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AHTA Adelaide Health Technology Assessment

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Disclaimer

This document is a general guide to appropriate practice, to be followed subject to the circumstances, clinician's judgement and patient's preferences in each individual case. The guidelines are designed to provide information to assist decision making. Recommendations contained herein are based upon the best available evidence published up to 1 November 2009 through to 10 December 2009 for the last question searched. The relevance and appropriateness of the information and recommendations in this document depend on the individual circumstances. Moreover, the recommendations and guidelines are subject to change over time. Copies of the guideline can be downloaded through the Baker IDI Heart & Diabetes website: www.bakeridi.edu.au or the Type 2 diabetes guideline website: http://t2dgr.bakeridi.edu.au

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Publication approval

Australian Government

National Health and Medical Research Council

These guidelines were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on *6 April 2011*, under Section 14A of the *National Health and Medical Research Council Act 1992*. In approving these guidelines the NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of 5 years.

NHMRC is satisfied that they are based on the systematic identification and synthesis of the best available scientific evidence and make clear recommendations for health professionals practising in an Australian health care setting. The NHMRC expects that all guidelines will be reviewed no less than once every five years.

This publication reflects the views of the authors and not necessarily the views of the Australian Government.

Contents

Summary of Evidence-Based Recommendations and Expert Opinions

EBR	Evidence-based recommendation formulated after a systematic review of the literature
EO	Expert opinion – where evidence was absent or unreliable and advice was formulated based on the clinical judgement and experience of experts in the field

Recommendations and Expert Opinions Relevant to Primary Care Settings

Assessing and defining risk

EBR 1	**Assess all people** with diabetes and stratify their risk of developing foot complications.[1]	Grade C	p19
EO 1	Any suitably trained healthcare professional may perform the risk assessment.	EO	p19
EBR 2	Assess risk stratification by **inquiring about previous foot ulceration and amputation, visually inspecting** the feet for structural abnormalities and ulceration, **assessing for neuropathy** using **either the Neuropathy Disability Score or a 10g monofilament** and **palpating foot pulses**.[1]	Grade C	p19
EBR 3	Stratify foot risk in the following manner: • "low risk"- people with no risk factors and no previous history of foot ulcer/amputation • "intermediate risk"- people with one risk factor (neuropathy, peripheral arterial disease or foot deformity) and no previous history of foot ulcer/amputation • "high risk" - people with two or more risk factors (neuropathy, peripheral arterial disease or foot deformity) and/or a previous history of foot ulcer/amputation[1]	Grade C	p19
EO 2	Until adequately assessed all **Aboriginal and Torres Strait Islander people** with diabetes are considered to be **at high risk** of developing foot complications and therefore will require fo**ot checks at every clinical encounter** and **active follow-up**.	EO	p19

Frequency of risk assessment

EO 3	In people stratified as having **low-risk feet** (where no risk factors or previous foot complications have been identified), **foot examination** should occur **annually**.	EO	p20
EO 4	In people stratified as having **intermediate-risk or high-risk feet** (without current foot ulceration), **foot examination** should occur at least **every 3 to 6 months**.	EO	p20

Prevention of foot complications

EBR 4	People assessed as having **"intermediate risk"** or **"high risk"** feet should be offered a **foot protection program**. A foot protection program includes foot care education, podiatry review and appropriate footwear.[1]	Grade C	p22
EO 5	**Podiatry review** is an important component of a foot protection program. However, in settings where this is not possible, a suitably trained health care worker may undertake a review of the feet.	EO	p22
EO 6	**Foot care education** should be provided to all people with diabetes to assist with prevention of foot complications.	EO	p22

Management of Foot Complications in Primary Care Settings

Predicting outcomes from foot ulcer

EO 7	**A foot ulcer is serious** and needs to be **managed immediately**.	EO	p23

Tools for grading of foot ulcer severity

EBR 5	**Foot ulcer severity can be graded** on the basis of wound depth, presence of infection (local, systemic or bone) and presence of peripheral arterial disease. Ulcer grading helps determine the degree of risk to the person and limb.[2,3] **The University of Texas (UT) wound classification system** is the most useful tool for grading foot ulcers.[4,5]	Grade C	p24

Interventions for ulcer management

Wound debridement

EO 8	Local sharp **debridement of non-ischaemic wounds should be performed** as it improves ulcer healing.	EO	p26
EBR 6	**Topical hydrogel dressings** may be considered for autolytic debridement to assist the management of non-ischaemic, non-healing ulcers with dry, non-viable tissue.[6-9]	Grade B	p26

Wound dressings and other topical treatments

EO 9	There is insufficient evidence to demonstrate the superiority of any one wound dressing over another in management of ulcers. This means that the dressing plan will need to be tailored to the specific characteristics of the wound. In **non-ischaemic ulcers**, create a moist wound environment. In **ischaemic ulcers** maintain a dry wound environment using a dry, non-adherent dressing, until the wound has been reviewed by someone with experience in peripheral arterial disease.	EO	p26

Pressure reduction, redistribution of pressure or offloading of the wound

EBR 7	**Pressure reduction**, otherwise referred to as redistribution of pressure or offloading, is required to optimise the healing of plantar foot ulcers.[10]	Grade B	p27
EBR 8	Offloading of the wound can be achieved with the use of a **total contact cast or other device rendered irremovable**.[10]	Grade B	p27
EO 10	Other **removable offloading devices** may be considered in particular settings (e.g. wounds that require more regular debridement and dressing changes) or where patient factors (e.g. significant risk of falls) do not allow the use of an irremovable device.	EO	p27

Types of care

EBR 9	People with diabetes-related foot ulceration are best managed by a **multi-disciplinary foot care team**[11-14]	Grade C	p28
EO 11	The following factors should always precipitate **referral** to a multi-disciplinary foot care team: • deep ulcers (probe to tendon, joint or bone) • ulcers not reducing in size after 4 weeks despite appropriate treatment • the absence of foot pulses • ascending cellulitis and • suspected Charcot's neuroarthropathy (e.g. unilateral, red, hot, swollen, possibly aching foot) If access to a multi-disciplinary foot care team is limited, foot ulceration or foot complications other than those above should be managed by a GP together with a podiatrist and/or wound care nurse.	EO	p28
EBR 10	**Remote expert consultation with digital imaging** should be made available to people with diabetic foot ulceration living in remote areas who are unable to attend a multi-disciplinary foot care team/service for management.[15]	Grade C	p28

Recommendations and Expert Opinions Relevant to Specialist Settings

Management in specialist settings

The following may be considered for foot ulcers in specialist centres, as part of a comprehensive wound management program:

EBR 11	**Topical negative pressure therapy**[16-22]	Grade B	p30
EBR 12	**Hyperbaric oxygen therapy**[23-30]	Grade B	p30
EBR 13	**Larval therapy**[31-33]	Grade C	p31
EBR 14	**Skin replacement therapies** • **Cultured skin equivalents**[34-43] • **Skin grafting**[44]	 Grade B Grade D	p31

Project Outline

Scope and Purpose of the Guideline

This guideline is part of an overall set of recommendations for the prevention, diagnosis and management of type 2 diabetes. The other components of the type 2 diabetes guidelines include:

- Primary Prevention
- Case Detection and Diagnosis
- Patient Education
- Blood Glucose Control
- Diagnosis, Prevention, and Management of Chronic Kidney Disease
- Management of Diabetic Retinopathy
- Blood Pressure and Control
- Lipid Control
- Prevention and Detection of Macrovascular Disease

A guideline on primary prevention of vascular disease for people with and without diabetes is also currently being completed by the National Vascular Disease Prevention Alliance (NVDPA).

This national evidence-based guideline addresses: **Prevention, identification and management of foot complications in diabetes,** and is equally relevant for type 1 and type 2 diabetes.

This guideline will update and replace the section of the national evidence-based guidelines for the management of type 2 diabetes mellitus, namely: Part 6 detection and prevention of foot problems in type 2 diabetes (last updated 2005).

The purpose of this guideline is to inform a broad range of health professionals and health care workers of best practice to prevent, identify and manage foot complications in adults with type 1 or 2 diabetes in both urban and rural/remote primary care and in specialist foot centres.

The scope of this revised guideline was primarily driven by the scope of the original guideline (2005) with adjustments made by the panel of experts drawn together to assess the recent evidence. There is one notable gap in the previous and current version of the guideline; recommendations or information on assessment and management of **osteomyelitis**. The expert panel recognises the need for a systematic examination of this area in the next revision of the guideline.

The recommendations and expert opinion-based statements in this guideline apply equally to Aboriginal and Torres Strait Islander people and non-Indigenous Australians. Specific guidance, however, has been provided in regard to the frequency of screening for foot complications for Aboriginal and Torres Strait Islander people. Further, special consideration has been given to targeting this high risk population in the implementation plan for this guideline. Education, services and programs for people with particular needs will need to be delivered in culturally appropriate and sensitive ways.

Structure of the Guideline

Clinical questions† were developed by a panel of foot experts (see Appendix 3) and used to structure the guideline into the following parts:

- **Part A** gives a **general overview of foot complications in diabetes**, including a discussion of foot problems in the context of type 1 and 2 diabetes, the significance of this problem, and key issues in diagnosing and treating people with foot complications
- **Part B** reviews the evidence in relation to **assessment of risk** of developing foot complications and assessment of severity of foot ulcers
- **Part C** discusses **prevention** of foot complications from diabetes
- **Part D** summarises the evidence for **healing of foot ulcers and management of foot complications** in relation to therapeutic and educational interventions, as well as to organisation of care
- **Part E** discusses **future research and development**
- **Part F** discusses **implementation**
- **Appendices** provide additional information and resources on Charcot's neuroarthropathy and provide detail of the team that prepared the guideline.

Guideline Development Process and Life of the Guideline

Baker IDI Heart and Diabetes Institute, The George Institute for Global Health and Adelaide Health Technology Assessment convened an expert panel and guidelines advisory committee (GAC) in 2009 to review the 2005 national evidence-based guideline for the management of type 2 diabetes mellitus, Part 6 detection and prevention of foot problems in type 2 diabetes. The process involved reviewing and rewriting the original questions. From the questions a protocol was developed that guided the systematic literature review. Searches for evidence were conducted in relevant databases, bibliographies of identified relevant studies, guidelines and websites of relevant peak bodies between 1 November 2009 and 10 December 2009. The Foot Expert Panel and GAC meet regularly throughout 2009/2010 to review and approve the questions, protocol and drafted recommendations/guideline. The drafted guideline then underwent a 30 day consultation period.

A list of committee members, expert panel members and the project executive are outlined in Appendix 3, 4 and 5. Their declaration of competing interests can be found at **http://t2dgr.bakeridi.edu.au** under the conflict of interest quick links.

This guideline should be fully reviewed within 5 years from date of release; however the guideline developers strongly recommend annual re-running of the literature searches to identify new evidence for consideration as to whether the recommendations or expert opinions should be revised.

The guideline developers also strongly recommend that a systematic review of the literature on assessment and management of **osteomyelitis** should be undertaken during a future revision of the guideline.

† *All clinical questions and methodological detail in the accompanying technical report*

Grading Method

Each recommendation was formulated using evidence-based methods and graded using the NHMRC grades of recommendations.

Definition of NHMRC grades of recommendations[45]

Grade of recommendation	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

To develop these graded recommendations, the body of evidence addressing each of the clinical questions was rated according to the criteria outlined in Table 1, using an Evidence Statement Form (ESF). This allows explicit and transparent formulation of the recommendation on the basis of the available evidence.

When the evidence was of sufficient strength (generally Grade C or above), applicable to the Australian context, consistent with usual practice and/or with positive cost effectiveness data, the expert panel formulated an evidence-based recommendation. The recommendations operationalised the evidence-based statements which were developed as part of the systematic review process. These evidence-based recommendations are designed to be practical, clear and action-oriented in order to assist with clinical decision making. Evidence-based recommendations are identified in the text by the use of the acronym EBR.

Expert Opinion (EO) is a consensus statement from experts to inform clinical practice. These are provided to guide clinical practice in the following circumstances:

- where evidence is of poor quality and not considered reliable enough for an evidence-based recommendation to be formulated;
- in the absence of evidence that directly answers the clinical question (evidence gaps found through the systematic literature review); and/or
- to supplement a graded recommendation by providing suggestions as to how the recommendation may be implemented in clinical practice.

Expert opinions were initially formulated by the Foot Expert Panel, ratified by the Guideline Advisory Committee and then an online survey was conducted to determine wider expert agreement with the statements.

Table 1 Components of body of evidence considered when grading each recommendation[45]

Component	A	B	C	D
	Excellent	**Good**	**Satisfactory**	**Poor**
Evidence base† ‡	one or more level I studies with a low risk of bias or several level II studies with a low risk of bias	one or two level II studies with a low risk of bias or a SR/several level III studies with a low risk of bias	one or two level III studies with a low risk of bias, or level I or II studies with a moderate risk of bias	level IV studies, or level I to III studies/SRs with a high risk of bias
Consistency§	all studies consistent	most studies consistent and inconsistency may be explained	some inconsistency reflecting genuine uncertainty around clinical question	evidence is inconsistent
Clinical impact	very large	substantial	moderate	slight or restricted
Generalisability	population/s studied in body of evidence are the same as the target population for the guideline	population/s studied in the body of evidence are similar to the target population for the guideline	population/s studied in body of evidence differ to target population for guideline but it is clinically sensible to apply this evidence to target population¶	population/s studied in body of evidence differ to target population and hard to judge whether it is sensible to generalise to target population
Applicability	directly applicable to Australian healthcare context	applicable to Australian healthcare context with few caveats	probably applicable to Australian healthcare context with some caveats	not applicable to Australian healthcare context

SR = systematic review; several = more than two studies

† *Level of evidence determined from the NHMRC evidence hierarchy – see Table 2*

‡ *Risk of bias was defined by the quality of the individual study. A rating of low, moderate or high risk of bias was assigned to studies of high, average and low quality, respectively.*

§ *If there is only one study, rank this component as 'not applicable'*

¶ *For example, results in adults that are clinically sensible to apply to children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer.*

Table 2 NHMRC levels of evidence[45,46]

Level	Intervention	Diagnostic Accuracy	Prognosis
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive persons with a defined clinical presentation	A prospective cohort study
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive persons with a defined clinical presentation	All or none
III-2	A comparative study with concurrent controls: • Non-randomised, experimental trial • Cohort study • Case-control study • Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial
III-3	A comparative study without concurrent controls: • Historical control study • Two or more single arm • Interrupted time series without a parallel control group	Diagnostic case-control study	A retrospective cohort study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of persons at different stages of disease

Technical Report

The full findings of the systematic literature review are available at **http://t2dgr.bakeridi.edu.au/**

Part A: Overview

This part of the guideline gives a general overview of foot complications in diabetes, based on recent review articles, international guidelines and information from Australian surveys and data collections.

A1 Foot Complications in Diabetes – Rationale for a National Evidence-Based Guideline

To date, considerable effort and research has been directed towards primary prevention of foot complications in patients with diabetes. In 1998, the National Diabetes Strategy[47] identified foot care as a major issue and recommended implementation of a National Diabetic Foot Disease Management Program. The aims of the program included a 50% reduction in lower limb amputation by 2005 and an 80% level of screening for risk factors for diabetes-related foot complications each year. However, for this to be achieved, health professionals require knowledge and resources that enable them to appropriately identify those at risk and to implement strategies to prevent adverse outcomes.

In Australia the prevalence of type 2 diabetes has increased dramatically over the past two decades and continues to rise, with a current prevalence of approximately 7%.[48] This translates to an ever-increasing population of people who are at risk of developing foot complications. It is estimated that 15% of people with diabetes will develop a foot ulcer during their lifetime.

The spectrum of diabetes-related complications that affect the foot includes ulceration, deformity, ischaemia, infection (including osteomyelitis), and Charcot's neuroarthropathy (CNA)†. The pathophysiology of foot ulceration is complex and multi-factorial. Peripheral neuropathy, peripheral arterial disease, foot deformity, trauma, infection, impaired healing and limited self-care may all contribute to foot ulceration or failure of healing of ulceration. Failure of foot ulcers to heal can lead to amputation.

A2 Epidemiology of Foot Complications in Diabetes

Peripheral neuropathy, foot deformity, external trauma, peripheral arterial disease and peripheral oedema are all common causes of foot ulceration with the first three listed identified as being the most common.[49] A study by Tapp et al found that in a population-based sample of Australian adults aged 25 years or older (the Australian Diabetes, Obesity, and Lifestyle Study) the prevalence of peripheral neuropathy was 13.1% in those with previously diagnosed diabetes and 7.1% in those with newly diagnosed diabetes.[50] The prevalence of peripheral arterial disease (PAD) was 13.9% in those with previously diagnosed diabetes and 6.9% in those with newly diagnosed diabetes. A substantial proportion of people with diabetes (19.6%) were at risk of foot ulceration.

Foot ulceration is a leading cause of hospitalisation for people with diabetes. The Australian Institute of Health and Welfare (AIHW) reports that diabetes-related foot ulceration resulted in 9,900 hospitalisations for years 2004-2005.[51]

In Australia, diabetes is acknowledged to be the most common cause of non-traumatic lower-limb amputation.[52] In 2000 the incidence of lower limb amputation in people with diabetes was estimated at 0.8% per year[53] with recent reports suggesting this rate to be increasing. In 2004-2005, approximately

† *Charcot's neuroarthropathy is considered an important complication for people with diabetes, however, it fell outside of the scope of the systematic literature review for this guideline. In light of its clinical importance, material has been developed from key literature as a reference for health professionals. See Appendix 2.*

3,400 diabetes-related lower limb amputations were reported by the Australian Institute of Health and Welfare[51] as compared to approximately 2,600 for each year between 1995 and 1998.

Of all lower limb amputations, about half are classified as major (below or above knee) while the other half are classified as minor (distal to the ankle). Of those who have an amputation, about half will experience a subsequent amputation of the other limb.[54] Five-year survival for those who have had limb amputation is poor, with mortality rates ranging from 39 to 80%.[55] Diabetes related foot complications are more prevalent in the elderly, which suggests a further increase in this condition as the population ages and diabetes prevalence increases.

A3 Economic Consequences of Foot Complications in Diabetes

In Australia in 2004-2005, the average length of hospital stay for people with diabetes requiring lower limb amputations was 26 days.[51]

A recent study estimated the cost of lower extremity amputations in Australia to be $A26,700 per person. Estimated costs for other countries were $A24,660 for Canada; $A46,064 for France; $A31,809 for Germany; $A14,650 for Italy; and $A21,287 for Spain.[56] Other direct and indirect economic costs of foot complications, not included in the above data, include the costs of rehabilitation, purchase and fitting of orthotics/prostheses, and time lost from work.

A4 Cost Effectiveness of Assessment, Prevention and Management of Foot Complications

A number of cost-effectiveness systematic reviews[57,58] or health economic evaluations of a variety of strategies for the prevention, diagnosis and management of foot complications in people with diabetes have been conducted.

Those strategies determined to be cost-effective or have cost-utility (and possibly be cost saving) include:

- Preventative strategies such as prevention programs, optimal foot care, regular foot examinations, intense glycaemic control and patient education
- Proper management and early institution of antibacterial therapy
- MRI for diagnosing osteomyelitis in patients with diabetic foot ulcers (but at higher cost)
- Novel therapies such as bio-engineered live skin equivalents and hyperbaric oxygen therapy (HBOT)

None of these evaluations considered the Australian context and some had methodological issues such that some of the results may be overstated and need to be interpreted with caution. The authors of the studies conclude that more quality economic studies are needed in this area, and need to consider appropriate sample sizes with adequate power, study design, study duration, blinding of outcome assessors and appropriate selection of endpoints and outcomes.

These promising cost-effectiveness analyses from other countries provide ample justification for similar analyses that consider Australian data and resource use.

Many individual drugs and some MBS funded procedures will already have been assessed in terms of their cost effectiveness in Australia. However, strategies that involve team care and a range of procedures are not routinely assessed for cost effectiveness.

A5 Aboriginal and Torres Strait Islander people and Diabetic Foot Complications

In 2006 it was reported that Aboriginal and Torres Strait Islander people were more than three times as likely to have diabetes as non-Indigenous Australians. Aboriginal and Torres Strait Islander people living in remote areas are more likely to have diabetes than those living in non-remote areas. The prevalence of diabetes amongst Aboriginal and Torres Strait Islander people over 55 years of age is over 30%.[59] McDermott et al reported the incidence of diabetes in remote community Aboriginal and Torres Strait Islander populations in far north Queensland to be nearly 4 times higher than the non-indigenous populations and 50% higher than the incidence reported 10 years ago in Australian Aboriginals.[60]

Diabetes-related foot complications are also prevalent in Aboriginal and Torres Strait Islander people. Aboriginal and Torres Strait Islander people also experience the greatest risk of amputation. Trends in amputations for arterial disease or diabetes-related complications in Western Australia for the period 2000-2008 show that among those aged 25-49 with diabetes, minor amputations were 27 times more likely, and major amputations 38 times more likely, in Aboriginal and Torres Strait Islander people than in non-indigenous Australians. Nearly all (98%) amputations were related to diabetes.[61]

A6 Access to Care and Education

The Fremantle Diabetes Study found that “subjects who were older, whose schooling was limited, who were not fluent in English and/or who were from Southern European or Indigenous Australian ethnic groups had significantly lower knowledge (of diabetes) scores and were less likely to have received diabetes education, dietetic advice or to perform self monitoring of blood glucose (SMBG)”.[62] The authors concluded that these populations experienced barriers to access or utilisation of contemporary diabetes education and were likely to benefit from specialised programs.

Culturally sensitive diabetes education for Indigenous people in North America has been associated with better outcomes.[63,64] Long-term studies in Nauru have demonstrated the importance of education and health promotion for reducing the incidence of amputation (50% reduction in the incidence of first lower extremity amputations).[65] Such strategies are also likely to improve the foot outcomes of Aboriginal and Torres Strait Islander populations.

The issue of access to services can be experienced in remote, regional and some urban areas by both Aboriginal and Torres Strait Islander people and non-Indigenous people with diabetes.

Aboriginal and Torres Strait Islander people, and those from other disadvantaged groups require particular attention in regard to screening, early intervention and monitoring to improve clinical outcomes.

A7 Clinical Questions for the Systematic Literature Review and Background Questions

The following clinical questions were used to conduct a systematic review of the literature:

Question Number	Questions	EBR or Expert Opinion number
Assessment		
1	Which assessments lead to improved foot-related clinical outcomes in people with diabetes?	EBR 1 - 4, EO 1 and EO 2
2	Which clinical assessments best predict foot ulcer and/ or amputation in people with diabetes? (*In the absence of evidence for Q1, this question would then be answered*)	See Question 1 above.
3	Which assessments best predict foot ulcer severity and outcomes in people with foot ulcer? (*In the absence of evidence for Q1, this question would then be answered*)	EBR 5, EO 7
4	How often, and by whom, should foot assessments be carried out in people with or without foot ulcer?	EO 3-5
5	When should a patient be referred to a high risk foot clinic? (*What are the risk factors for a poor foot related outcome for people in a primary care setting?*)	EO 11
Intervention		
6	Which interventions improve foot related clinical outcomes – a) For people without foot ulceration? b) For people with foot ulcer?	EBR 6-14, EO 6, EO 8-10
7	Under what circumstances are antibiotics effective in the treatment of foot ulceration?	No recommendation See Section D1

Background questions†

Question Number	Questions	Location
Assessment		
Background Question 1	What clinical signs indicate the presence of Charcot neuroarthropathy?	See Appendix 2
Response to Treatment		
Background Question 2	How is the effectiveness of interventions for ulceration monitored?	Section D3
Economics		
Background Question 3	What are the economic consequences of diabetes foot problems?	Section A3
Background Question 4	What are the socioeconomic factors associated with diabetes foot problems?	Section A5-6

† *Background questions were still the subject of a literature review, but not a systematic review*

Part B: Assessments for Foot Complications in Diabetes

This part of the guideline describes the clinical assessments for foot complications in diabetes.

Part B provides evidence from the systematic literature review and details recommendations and expert opinions (in the absence of evidence) on the following:

- upstream causes and risk factors for foot complications;
- tools for identifying and defining risks of foot complications and amputation; and
- the frequency of monitoring for foot complications in diabetes.

Assessing Risk of Developing Foot Complications

Risk factors

Preventing foot complications begins with identifying those at risk. The risk of foot ulceration and amputation is increased in patients with the following four risk factors:

- **Previous Foot Ulceration or Previous Amputation**
- **Peripheral Neuropathy**
  - Peripheral neuropathy can be easily identified using ordinary bedside clinical tools. The best evidence for identifying the risk of neuropathic ulceration supports use of the 10g monofilament or the Neuropathy Disability Score (NDS). The NDS is a score based on vibration perception, pin-prick sensation, temperature perception, as well as ankle (Achilles) reflexes. It requires the use of a tuning fork (for both vibration and temperature sensation), neurological pin and tendon hammer. Refer Box 1 for the NDS ‘score sheet’.
- **Peripheral Arterial Disease**
  - The best clinical guide to the presence of peripheral arterial disease is palpation of foot pulses, which has been shown to predict foot ulceration and amputation. Although claudication can be a useful symptom, peripheral arterial disease is commonly asymptomatic in people with diabetes. The ankle-brachial pressure index (ABPI or ABI), using Doppler ultrasound is a useful adjunct to assess foot perfusion. The results of this investigation can be falsely elevated in the presence of arterial calcification in people with diabetes. The toe-brachial pressure index or toe pressures (using photoplethysmography) are useful adjuncts for assessing foot perfusion if the ABPI is falsely elevated.
- **Foot Deformity**
  - This includes, but is not limited, to such conditions as: hallux deformity, hammer/claw toe, callus, previous amputation, excessively flat or high arched feet, abnormally wide feet and Charcot’s neuroarthropathy.

Box 2 provides an overview of the tools for assessing neuropathy, circulation and foot deformity.

There is also evidence to suggest that the following factors increase risk of foot complications:

- visual impairment
- kidney disease
- poor glycaemic control
- ill-fitting footwear
- socio-economic disadvantage

Whilst the presence of peripheral neuropathy is the leading risk factor for foot ulceration, a pivotal event, such as trauma from footwear, is also needed for most ulcers to occur.[66] Rubbing from footwear was identified as the definite cause of 35% of foot ulcers reviewed as part of a prospective study conducted in the United Kingdom.[67] Furthermore, the follow-up of 472 patients at The Royal Prince Alfred Hospital Diabetes Centre (NSW, Australia) identified that 50% of all foot ulcers that developed in this group, could be directly attributed to trauma from footwear.[68]

Box 1 Modified Neuropathy Disability Score[69]

Neuropathy Disability Score (NDS)			
		Right	Left
Vibration Perception Threshold 128-Hz tuning fork; apex of big toe: normal = can distinguish vibrating/ not vibrating	Normal = 0 Abnormal = 1		
Temperature perception on Dorsum of the Foot Use tuning fork with beaker of ice/ warm water			
Pin Prick Apply pin proximally to big toe nail just enough to deform the skin; Trial pair: sharp, blunt; Normal= can distinguish sharp/ not sharp			
Achilles Reflex	Present = 0 Present with reinforcement = 1 Absent = 2		
NDS Total out of 10			

Identifying Those at Risk of Foot Complications

One large randomised trial examined the effects of a 2-stage foot screening program followed by a foot protection program for those classified as high risk for foot ulceration compared to standard care. Patients randomised to screening were classified as high or low risk for foot ulceration. Those classified as high risk were entered into a foot protection program that included foot care (podiatry and hygiene maintenance), support hosiery and protective shoes. Those classified as low risk received no

further special treatment. A significant reduction in major and total amputation was demonstrated in the intervention group and there was a trend to increased ulcer healing†.[1]

The foot screening program was also shown to be cost-effective in a UK setting.[1] Taking into account the cost of the screening and protection program, and comparing it to the cost of an avoided amputation, a net cost saving was calculated for the amputations prevented out of the 1,001 patients in the intervention arm of the study.

Other, non-randomised, observational studies have shown that a range of other commonly used clinical assessments (see Box 2) are effective in predicting foot ulceration and/or amputation.[70-72] These single assessments and combined assessments are outlined in more detail in the technical report. The combined assessment within the Neuropathy Disability Score (NDS) appeared to perform better at predicting foot ulceration and lower extremity amputation than did single assessments but no direct comparison has been reported.

EBR 1	**Assess all people** with diabetes and stratify their risk of developing foot complications.[1]	Grade C
EO 1	Any suitably trained healthcare professional may perform the risk assessment.	EO
EBR 2	Assess risk stratification by **inquiring about previous foot ulceration and amputation, visually inspecting** the feet for structural abnormalities and ulceration, **assessing for neuropathy** using **either the Neuropathy Disability Score or a 10g monofilament** and **palpating foot pulses**.[1]	Grade C

Defining Risk of Foot Complications and Amputation

EBR 3	Stratify foot risk in the following manner: • "low risk"- people with no risk factors and no previous history of foot ulcer/amputation • "intermediate risk"- people with one risk factor (neuropathy, peripheral arterial disease or foot deformity) and no previous history of foot ulcer/amputation • "high risk" - people with two or more risk factors (neuropathy, peripheral arterial disease or foot deformity) and/or a previous history of foot ulcer/amputation[1]	Grade C
EO 2	Until adequately assessed all **Aboriginal and Torres Strait Islander people** with diabetes are considered to be **at high risk** of developing foot complications and therefore will require **foot checks at every clinical encounter** and **active follow-up**.	EO

† *Refer technical report, Question 1, Table 2 for information on number needed to treat*

Frequency of Risk Assessment

There were no studies providing evidence for the optimal frequency of foot assessment in people with and without foot ulceration. Expert opinion therefore suggests the following frequencies.

EO 3	In people stratified as having **low-risk feet** (where no risk factors or previous foot complications have been identified), **foot examination** should occur **annually**.	EO
EO 4	In people stratified as having **intermediate-risk or high-risk feet** (without current foot ulceration), **foot examination** should occur at least **every 3 to 6 months**.	EO

The main aim of the more frequent assessment of those at intermediate or high risk is to reassess for new risk factors and for other more rapidly-developing problems, such as tinea, gangrene, ulcers, and Charcot's neuroarthropathy, which may need immediate intervention.

Box 2 Tools for assessing neuropathy, circulation and foot deformity[70-72]

- **Neuropathy**
  - 10g monofilament sensitivity
  - Vibration perception (tuning fork or biothesiometer)
  - Neuropathy Disability Score – ankle (Achilles) reflexes and the sensory modalities of pinprick, vibration and temperature perception
- **Circulation**
  - Palpation of peripheral pulses
  - Ankle-brachial pressure index (ABPI)
  - Toe-brachial pressure index
- **Foot Deformity Score**

  6 point scale (1 point for each characteristic)
  - small muscle wasting
  - Charcot foot deformity
  - bony prominence
  - prominent metatarsal heads
  - hammer or claw toes
  - limited joint mobility

  Score of 3 or above indicates foot deformity

Part C: Prevention of Foot Complications in Diabetes

A number of interventions have been studied for their ability to prevent foot complications.

Foot Protection Program

One large, good quality trial examined the effectiveness of a foot protection program for people with intermediate to high risk feet (see below for definition).[1] A significant reduction in major and total amputation was demonstrated.

Foot Protection Program[1]

A Foot Protection Program aims to prevent foot complications in people with diabetes, and includes the following components:

- Podiatry;
- Hygiene maintenance – advice to inspect and wash feet daily;
- Appropriate footwear and hosiery;
- Protective shoes – avoid constrictive footwear; and
- Clinic contact initiated by patient if concerned.

Therapeutic Footwear

There was insufficient evidence to determine the effectiveness of therapeutic footwear (2 average quality trials) for the prevention of foot complications. The trials demonstrated a trend towards benefit of therapeutic footwear with cork or prefabricated insoles over usual footwear. One other small trial also studied the effects of rigid orthotic devices on plantar callus formation. A significant improvement in the grade of callus was demonstrated.

Educational Programs

The evidence for educational programmes for the prevention of ulcer recurrence and amputation was equivocal. Two trials (one good and one average quality) compared brief education with usual care for the prevention of ulcer recurrence and amputation. One indicated no effect[73] and the other indicated a large positive effect.[74] One trial and one controlled study (both average quality) compared an education program consisting of multiple sessions with usual care for the prevention of foot complications. The randomised trial indicated no effect on the incidence of foot lesions or requirement for hospitalisation. The study indicated less callus, mycosis and fissures with the education program. One large trial (good quality) compared education targeting the patient and doctor with usual care for the prevention of foot complications and reported a significant reduction in serious foot lesions, ingrown toenails and dry or cracked skin. No significant reduction in amputation was demonstrated.[75] One large trial (average quality) compared home education to usual care for the prevention of foot complications and reported no effect on foot appearance or hospitalisation rates.[76] Two trials

(average quality) compared intensive education involving one-on-one teaching by a podiatrist with brief education for the prevention of foot complications. One trial indicated reduced callus after one year and ingrown toenails after seven years and the other trial indicated a significant reduction in foot complications during the program, which did not remain after the program had ceased.[77,78] A meta-analysis of three trials comparing the addition of any education to usual care alone was also conducted and found a non- significant reduction in the risk of amputation (refer to the Technical Report, Figure 15: Meta-analysis of education interventions for the prevention of amputation).

Despite the inconsistent nature of the evidence of educational programmes for prevention of ulcer recurrence and amputation, foot education was considered by the Expert Panel to be important for preventing foot complications.

Cost-Effectiveness of Prevention Strategies

There is evidence, from Europe, of cost effectiveness, lower costs and a gain in quality adjusted life years (QALY's) in patients receiving optimal foot care alone and those receiving optimal foot care and intensive glycaemic control together to prevent foot complications.[57] In an analysis of prevention strategies, cost effectiveness was only found when preventive care was provided to people classified as high risk. Preventive care for low risk patients was not found to be cost effective.

EBR 4	People assessed as having **"intermediate risk"** or **"high risk" feet** should be offered a **foot protection program**. A foot protection program includes foot care education, podiatry review and appropriate footwear.[1]	Grade C
EO 5	**Podiatry review** is an important component of a foot protection program. However, in settings where this is not possible, a suitably trained health care worker may undertake a review of the feet.	EO
EO 6	**Foot care education** should be provided to all people with diabetes to assist with prevention of foot complications.	EO

Part D: Management of Foot Complications in Diabetes

This part of the guideline discusses the clinical care of foot complications, mostly related to foot ulceration, in patients with diabetes, in whom early assessment and appropriate intervention are required to restore optimal functioning, followed by continuing care to prevent recurrence and/or need for amputation. Early intensive intervention to resolve foot ulcers and other complications in people with diabetes should be relentlessly pursued to avoid costly future interventions such as amputation or hospitalisation.

Section D1 provides a summary of current evidence on the treatment of foot ulceration and management of foot complications in primary care settings from the systematic literature review undertaken for the guideline, and gives evidence-based recommendations on physical interventions, pharmacological interventions and combined therapies.

Section D2 provides a summary of current evidence on the treatment of foot ulceration in specialist settings from the systematic literature review undertaken for the guideline.

Section D3 outlines monitoring of response to treatment and prevention of ulcer recurrence.

D1 Treatment of Diabetes-Related Foot Ulceration in Primary Care Settings

Predicting outcomes from foot ulcer

Foot ulcers can be classified as ischaemic, neuropathic, or neuroischaemic and then further staged or graded according to a wound classification system. Wound classification systems and other clinical/ laboratory assessments have been studied for their ability to predict foot ulcer severity and outcomes. A number of clinical or laboratory assessments (Box 3) were found to assist with predicting foot ulcer outcomes, although the application of many may be restricted to specialist or research centres.

EO 7	**A foot ulcer is serious** and needs to be **managed immediately**.	EO

Box 3 Tools for predicting foot ulcer outcomes

Assessment	Outcome
Transcutaneous oxygen saturation (TcPO2) on dorsum of foot and toe pressure	TcPO2 >25mmHg and toe pressure >45mmHg indicating ulcers more likely to improve or heal
X-ray and bone/leukocyte nuclear scans	Presence of osteomyelitis indicating increased risk of amputation
Ankle peak systolic velocity measurements using Duplex ultrasound	Low velocities indicating increased risk of ulcer non-healing
Skin perfusion pressure using a radioisotope clearance method	Lower skin pressures indicating increased risk of ulcer non-healing
Capillary perfusion using macro aggregated albumin scanning	Poor circulation associated with ulcer non-healing, good circulation associated with ulcer healing
Hyperspectral imaging of oxyhaemoglobin and deoxyhaemoglobin	Positive index indicating greater healing than negative index
Plasma fibrinogen	Fibrinogen >300 mg/dl indicating greater risk of amputation

Source: Technical report p11-61

Tools for grading of foot ulcer severity

The use of an ulcer grading system and score provides a standardised approach to the documentation of ulcer severity and assists communication between health care providers.

A number of ulcer grading systems or scores (see Appendix 1) were found to predict foot ulcer healing and amputation risk. Of these, the University of Texas Wound Grading System and the Wagner Wound Grade System were considered to have the best discrimination for predicting ulcer healing. When compared, the University of Texas Wound Grading System was found to be more useful in grading foot ulcers (see Box 4).

EBR 5	**Foot ulcer severity can be graded** on the basis of wound depth, presence of infection (local, systemic or bone) and presence of peripheral arterial disease. Ulcer grading helps determine the degree of risk to the person and limb.[2,3] **The University of Texas (UT) wound classification system** is the most useful tool for grading foot ulcers.[4,5]	Grade C

Box 4 University of Texas Wound Grading System[5,79]

Grade/depth: "How deep is the wound?"					
	Depth	**Grade**			
		0	I	II	III
Stage/ Comorbidities: "Is the wound infected, ischemic, or both?"	A	Pre- or post-ulcerative lesion completely epithelialized	Superficial wound not involving tendon, capsule or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
	B	Pre- or post-ulcerative lesion completely epithelialized with infection	Superficial wound not involving tendon, capsule or bone with infection	Wound penetrating to tendon or capsule with infection	Wound penetrating to bone or joint with infection
	C	Pre- or post-ulcerative lesion completely epithelialized with ischemia	Superficial wound not involving tendon, capsule or bone with ischemia	Wound penetrating to tendon or capsule with ischemia	Wound penetrating to bone or joint with ischemia
	D	Pre- or post-ulcerative lesion completely epithelialized with infection and ischemia	Superficial wound not involving tendon, capsule or bone with infection and ischemia	Wound penetrating to tendon or capsule with infection and ischemia	Wound penetrating to bone or joint with infection and ischemia

Armstrong et al 1998[5]

Interventions for ulcer management

Wound debridement

The first priority of management of foot ulceration is to prepare the surface and edges of a wound to facilitate healing. If foot pulses are present, non-viable tissue should be removed from the wound bed and surrounding callus removed. If foot pulses are absent, assessment and management of the peripheral vasculature is mandatory before removal of non-viable or necrotic tissue is considered. Referral to a vascular surgeon and/or multidisciplinary team is suggested in this situation.

Removal of non-viable tissue can be quickly and effectively accomplished by local sharp debridement. Other forms of debridement include mechanical, e.g. the wet to dry method of soaking the wound with a wet gauze and then removing non-viable tissue that has dried onto it; autolytic, e.g. using hydrogels that when applied to a dry wound complement the body's natural debridement process; and sterile larvae (maggot) therapy.

Evidence on the preferred form, frequency and extent of debridement was reviewed and proved insufficient to draw any conclusions. One small trial investigated the effectiveness of surgical debridement that included conic ulcerectomy compared to standard wound care that included local sharp debridement. Surgical debridement significantly reduced the time to ulcer healing however the number of ulcers healed was not increased.[80] One systematic review (good quality) of three trials (of varying quality) assessed the use of hydrogels for wound debridement in addition to standard wound

care compared with standard wound care alone. Hydrogel dressings significantly increased the number of ulcers healed and were associated with fewer adverse events than standard wound care.[7]

Clinical experience suggests that local sharp debridement should be considered first followed by one or more of the other modalities, depending on the clinical presentation or response of a wound. Debridement should be repeated as often as required to remove all non-viable tissue.

Newer forms of mechanical debridement (e.g. acoustic energy or ultrasonic sound waves and high-pressure jet of sterile saline) are increasingly available and popular for use in practice, however there was no high quality evidence found to support their use.

EO 8	Local sharp **debridement of non-ischaemic wounds should be performed** as it improves ulcer healing.	EO
EBR 6	T**opical hydrogel dressings** may be considered for autolytic debridement to assist the management of non-ischaemic, non-healing ulcers with dry, non-viable tissue.[6-9]	Grade B

Wound dressings and other topical treatments

All foot ulcers require regular inspection, cleansing and dressing. Dressings need to provide a warm and moist wound environment, absorb excess exudate and protect the wound for optimal healing. The exception to this being when there is inadequate blood supply to allow wound healing to occur. In this case, the dressing plan should aim to keep the wound dry until assessed by a multidisciplinary team.

Six average quality studies examined advanced moist wound dressings: Aquacel (hydrofibre), Fibrocol (collagen-alginate), Polymem (starch co-polymer) and Algosteril/Sorbsan (calcium alginate) and compared them to debridement plus gauze conventional dressings (dry, saline and greasy). Advanced moist wound dressings did not improve ulcer healing when compared to standard wound care. No trials comparing silver or other topical antimicrobial dressings to conventional dressings were found.

EO 9	There is insufficient evidence to demonstrate the superiority of any one wound dressing over another in management of ulcers. This means that the dressing plan will need to be tailored to the specific characteristics of the wound. In **non-ischaemic ulcers**, create a moist wound environment. In **ischaemic ulcers** maintain a dry wound environment using a dry, non-adherent dressing, until the wound has been reviewed by someone with experience in peripheral arterial disease.	EO

Pressure reduction, redistribution of pressure or offloading of the wound

An important reason for failure of an ulcer to heal is continued trauma to the bed of the wound. This generally occurs because the foot is insensate and the individual continues to bear weight through the wound. The wound can however be protected by using an offloading device to reduce the pressure through it. A number of offloading devices are currently available for use. These include total contact casts, removable prefabricated devices, e.g. Controlled Ankle Movement (CAM) walkers, half shoes and therapeutic shoes.

Two average quality trials examined the effectiveness of pressure reduction or wound offloading in people with plantar foot ulcers. One trial compared total contact cast offloading[10] and the other felt foam offloading to standard wound care.[81] Total contact casts increased the number of ulcers healed, reduced healing time and reduced amputation rates. Felt foam dressing/padding and half shoe reduced ulcer size and healing time. Pooling the effects of these offloading interventions indicated a significant reduction in the time to ulcer healing.

Two average quality trials compared total contact casts with other prefabricated offloading devices rendered irremovable for the treatment of plantar foot ulcers.[82,83] No significant differences in the

proportion of ulcers healed or time to ulcer healing were reported. Three average quality controlled trials and one average quality prospective non-randomised study compared irremovable devices with removable devices for the treatment of plantar foot ulcers. The irremovable devices increased the number of ulcers healed and reduced ulcer healing time. However, it was noted that peri-wound maceration was also increased with the irremovable devices.[84]

EBR 7	**Pressure reduction**, otherwise referred to as redistribution of pressure or offloading, is required to optimise the healing of plantar foot ulcers.[10]	Grade B
EBR 8	Offloading of the wound can be achieved with the use of a **total contact cast or other device rendered irremovable**.[10]	Grade B
EO 10	Other **removable offloading devices** may be considered in particular settings (e.g. wounds that require more regular debridement and dressing changes) or where patient factors (e.g. significant risk of falls) do not allow the use of an irremovable device.	EO

Types of care

Multi-disciplinary care of diabetes-related foot complications

Best-practice management of diabetes-related foot ulceration requires coordinated and expert multi-disciplinary input in both the inpatient and outpatient settings. Multi-disciplinary teams consist of medical, surgical, nursing, podiatry and allied health professionals – with the appropriate skills and knowledge needed to manage this group of individuals. Some multi-disciplinary teams also include an infectious disease specialist or microbiologist. The integrated approach acknowledges that no one specialist possesses all the abilities and knowledge to manage the patient. In Australia, there is no agreed definition for the composition of a Multi-Disciplinary Foot Care Team. The Scottish Intercollegiate Guideline Network (SIGN) definition is used as a reference point (see Box 5 for definition and explanation).

Box 5 Definition of Multi-Disciplinary Foot Care Team/Service

Multi-Disciplinary Foot Care Team/Service

Based on the advice of the Scottish Intercollegiate Guidelines Network (SIGN)[85] and from other studies, a multi-disciplinary foot (MDF) care team/service would ideally include:

- Podiatrist
- Diabetes physician
- Diabetes nurse specialist
- Vascular surgeon
- Orthopaedic surgeon
- Radiologist
- Wound care nurse
- Footwear technician

MDF care teams/services provide evidence-based staged management of diabetic foot ulcers is implemented via detailed algorithms according to guidelines for both assessment and treatment, which provide standardised treatment protocols for each risk category. The various components of the team do not need to operate at a single location.

Box 6 Team Skills for Reducing Amputation Rates

Seven Essential Skills for Targeted Limb Salvage

Fitzgerald et al have identified seven essential skills that necessarily enable a limb salvage team to appropriately manage the most common presenting problems in patients with diabetes, including vasculopathy, infection, and deformity.[86] These include:

(1) perform hemodynamic and anatomic vascular assessment with revascularization, as necessary;

(2) perform neurologic workup;

(3) perform site-appropriate culture technique;

(4) perform wound assessment and staging/grading of infection and ischemia;

(5) perform site-specific bedside and intraoperative incision and debridement;

(6) initiate and modify culture-specific and patient-appropriate antibiotic therapy; and

(7) perform appropriate postoperative monitoring to reduce risk of reulceration and infection.

Three large, average quality studies (controlled or cohort) compared the multi-disciplinary staged care of foot ulcers to standard care.[11-14] The multi-disciplinary care approach was associated with substantially reduced amputation rates, foot related hospitalisation and length of hospital stay.

One randomised trial of average quality examined the effectiveness of digital imaging (digital photographs of wounds and measurements) and a remote expert consultant compared to digital imaging and standard care by the local physician in the treatment of lower extremity ulcers. Remote expert advice with digital imaging improved ulcer healing rates (reduction in ulcer size per week) and reduced amputation rates.

EBR 9	People with diabetes-related foot ulceration are best managed by a **multi-disciplinary foot care team**[11-14]	Grade C
EO 11	The following factors should always precipitate **referral** to a multi-disciplinary foot care team: • deep ulcers (probe to tendon, joint or bone) • ulcers not reducing in size after 4 weeks despite appropriate treatment • the absence of foot pulses • ascending cellulitis and • suspected Charcot's neuroarthropathy (e.g. unilateral, red, hot, swollen, possibly aching foot) If access to a multi-disciplinary foot care team is limited, foot ulceration or foot complications other than those above should be managed by a GP together with a podiatrist and/or wound care nurse.	EO
EBR 10	**Remote expert consultation with digital imaging** should be made available to people with diabetic foot ulceration living in remote areas who are unable to attend a multi-disciplinary foot care team/service for management.[15]	Grade C

Systemic drug interventions

Antimicrobials for non-infected ulcers

The need for antimicrobial therapy in the management of foot ulcers will depend on the presence or absence of clinical evidence of infection.

Infected ulcers should be treated with antimicrobial therapy according to published antibiotic guidelines†.[87] In the setting of clinical infection it is appropriate for cultures to be collected for identification of microbiological organism/s and antibiotic sensitivities. There is no role in culturing clinically uninfected ulcers as colonising organisms will always be detected. Similarly, cultures should not be taken to determine the need for antibiotics. The need for antibiotics should be determined on clinical grounds. The most appropriate tissue samples for microbiological evaluation are either deep tissue swabs after debridement or tissue/bone biopsies.[54]

There is no consistent evidence that the use of an antimicrobial is indicated in the management of non-infected ulceration. One good quality trial[88] and one average quality cohort study[89] assessed the effects of antibiotics compared to placebo in addition to standard care. No significant effects on ulcer healing or ulcer size were reported.

Lipid modifying agents

One good quality trial evaluated the use of fenofibrate for reducing amputations (a pre-specified tertiary outcome) in people with type 2 diabetes.[90] After a median follow up of 5 years, fenofibrate significantly reduced all amputations. This was primarily due to a significant reduction in minor amputations in people without large vessel disease. No significant effects on major or minor amputations in people with large vessel disease were observed.

Although this study suggests that fenofibrate may have a promising role in preventing minor amputation due to microvascular disease in people with type 2 diabetes, the expert panel considered that the data were insufficient to make a recommendation at this time, because of the inconsistency of the results (benefits only seen in people free of large vessel disease). Further trials examining a broader range of pre-specified foot outcomes (including amputation and ulcer healing) are required to confirm any likely beneficial effects and the types of patients likely to benefit.

Agents for the improvement of microvascular blood flow and improving immune function

Studies have been conducted on the following therapies, but there was insufficient evidence to make a recommendation for any of them:

- Angipars -Herbal extract
- Low molecular weight heparin
- Illoprost
- Ketanserin
- Pentoxyfyline
- Pycnogenol
- Tinospora cordifolia

† *The antibiotic guideline referenced here is commonly referred to by clinicians in their everyday practice however it does not meet the criteria set by NHMRC for an evidence based guideline.*

Nutritional supplements

People with foot complications may experience a number of nutritional deficiencies.

Two small studies examined the effect of herbal[91] or nutritional supplements[92] on ulcer healing or amputation in patients with foot ulceration. No significant effects were demonstrated. It therefore remains unknown whether any treatment for nutritional deficiencies improves ulcer healing or reduces amputation rates.

D2 Treatment of Diabetic Foot Ulceration in Specialist Settings

Topical negative pressure therapy

Topical negative pressure therapy is non-invasive and creates a localised, controlled sub-atmospheric pressure environment that promotes faster wound healing.[17] The exact mechanism for enhancing wound healing is unclear but is thought to involve increasing local blood flow, encouraging the formation of granulation tissue, decreasing bacterial colonisation, enhancing cell migration across the wound bed, and reducing oedema.[19]

Six studies (two good quality[17,22] and four average quality[16,18-21]) examined the effectiveness of topical negative pressure therapy in addition to standard wound care (including aggressive debridement and dressings) compared to standard care alone in treating diabetic foot ulceration. Topical negative pressure therapy significantly reduced ulcer size, improved the number of ulcers healed and reduced the need for minor amputation.

EBR 11	**Topical negative pressure therapy** may be considered for foot ulcers in specialist centres, as part of a comprehensive wound management program.[16-22]	Grade B

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy (HBOT) involves the administration of oxygen at 2-3 times the sea-level atmospheric pressure and produces tissue oxygen levels that are ten-fold greater than normal and sufficient to meet resting cellular oxygen requirements independent of circulating haemoglobin. This requires the patient to be confined within an airtight vessel and given 100 percent oxygen for respiration. Sessions usually take between 45 and 120 minutes and are administered once or twice daily depending on the setting.[30]

One good quality systematic review (of four average quality studies) examined the effectiveness of HBOT compared to standard care for the treatment of non-healing diabetic foot ulceration (present for at least six weeks).[30] HBOT healed ulcers faster and reduced the risk of major amputation.

A cost utility analysis of adjunctive HBOT in the treatment of diabetic ulcers suggests that HBOT is cost effective if used long-term.[57] However this was based on US data and further research is warranted before adopting adjunctive long-term HBOT.

EBR 12	**Hyperbaric oxygen therapy** may be considered for foot ulcers in specialist centres, as part of a comprehensive wound management program.[23-30]	Grade B

Larval therapy

In addition to local sharp debridement of wounds, sterile larvae may be applied to assist with debridement. Three studies (one controlled[32] and two observational studies of average quality[31,33])

compared the effect of sterile larval therapy with standard wound care or surgical debridement. One study reported reduced ulcer healing time and reduced amputations,[31] one reported greater reduction in ulcer size but no effect on ulcer healing time or amputation[33] and one reported reduced hospital stay but no effect on the number of ulcers healed or amputation.[32]

EBR 13	**Larval therapy** may be considered for foot ulcers in specialist centres, as part of a comprehensive wound management program.[31-33]	Grade C

Skin replacement therapies

Skin/epidermal grafting or application of bioengineered skin equivalents to a clean wound may accelerate wound healing where there is adequate limb perfusion. Skin equivalents comprise cultured sheets of living fibroblast or fibroblast and keratinocyte cells combined with matrix proteins, cytokines and growth factors.

Two studies investigated the use of skin grafting (split-skin grafting and grafting epidermal sheets from suction blisters); one trial used meshed skin grafting; two trials used cultured keratinocytes, one with autologous cells and the other with allogenic cells; and one controlled study used cultured allogenic fibroblasts.

Skin grafting improved ulcer healing time, reduced the risk of amputation and reduced the length of hospital stay in patients with chronic foot ulcers.[93] Meshed skin grafting appeared equivalent to split skin grafting.[44]

One systematic review and nine trials examined the use of cultured skin equivalents; three trials used acellular dermal tissue matrixes; and one trial compared a cultured skin equivalent compared to an acellular dermal tissue matrix. Cultured skin equivalents combined with standard wound care improved the number of ulcers healed in patients with chronic foot ulcers.[34-43]

A systematic economic evaluation[58] of some growth factors and tissue-engineered artificial skin products (all from the United States, Canada and Europe except for one Australian study) found a favourable cost effectiveness ratio in patients with chronic wounds. The review concluded that despite their high initial costs, tissue-engineered wound care products were cost effective or even cost saving if their use was restricted to chronic, non-healing ulcers.

EBR 14	**Skin replacement therapies** • **Cultured skin equivalents**[34-43] • **Skin grafting**[44] may be considered for foot ulcers in specialist centres, as part of a comprehensive wound management program.	 Grade B Grade D

Heat or electrical stimulation therapy

The use of heat or electrical stimulation therapy in the healing of foot ulcers is an emerging field.

Three small, average quality trials examined application of a warmed, wound chamber after standard wound debridement and cleansing, and found it to be more effective in healing foot ulcers than standard wound care alone. Increased skin maceration was however reported.[94-96] One small, average quality trial examined local heat application with an infrared lamp or global heat in a warmed room in addition to electrical stimulation and standard wound care. Increased ulcer healing was demonstrated compared to standard wound care alone.[97] Three trials examined electric stimulation in addition to standard wound care.[98-100] All studies were underpowered. No significant effects were demonstrated.

Larger trials are required to confirm any likely beneficial effects and determine the types of ulcers that may benefit from these therapies.

Growth factors

Gel-based topical or parenteral recombinant growth factors have been investigated for their potential role in the treatment of chronic non-healing foot ulcers.

Twenty-two studies examined the effects of human growth factors in various forms or blood products including recombinant human epidermal growth factor (rhEGF), recombinant human platelet-derived growth factor (rhPDGF), recombinant human granulocyte-colony stimulating factor (rhG-CSF), recombinant human vascular endothelial growth factor (rh VEGF), platelet rich plasma gel/releasate, recombinant human transforming growth factor β2 (rhTGF) and basic fibroblast growth factor (bFGF).

Recombinant human epidermal growth factor and human platelet derived growth factor have shown the greatest promise for improving ulcer healing but further studies are necessary. However the findings may not be generally applicable, due to lack of availability of these products in Australia and high cost.

Box 7 Diagnosis and Treatment of Osteomyelitis

The diagnosis and treatment of osteomyelitis was not within the scope of the revision of the guideline. The guideline developers have recommended that a full systematic review of the area be done as a matter of urgency so evidence-based clinical advice can be provided. In the absence of any current evidence-based guideline, clinicians may refer to the International Working Group on the Diabetic Foot (IWGDF) advice on diagnosis and management of osteomyelitis.[101]

The recommendations on diagnosis are based on clinical opinion, however the guidance on the management of osteomyelitis in the diabetic foot is evidence-based (from a systematic review).

In summary, the IWGDF concluded that there was no evidence that surgical debridement of the infected bone is routinely necessary. Despite the lack of evidence, however, many experts feel that arrest of bone infection is facilitated by appropriate debridement of necrotic bone. Culture and sensitivity of isolates from bone biopsy may assist in selecting properly targeted antibiotic regimens, but empirical regimens should include agents active against staphylococci, administered either intravenously or orally (with a highly bioavailable agent). There are no data to support the superiority of any particular route of delivery of systemic antibiotics or to inform the optimal duration of antibiotic therapy. No available evidence supports the use of any adjunctive therapies, such as hyperbaric oxygen, granulocyte-colony stimulating factor or larvae.

The IWGDF urged caution before the conclusions that were drawn in this review were extrapolated into practice due to the weakness of the available evidence. The quality of published work is poor, with few controlled studies, unclear reporting and small or heterogeneous populations. The lack of standardization of diagnostic criteria and of consensus on the choice of outcome measures pose particular difficulties.

The IWGDF counselled that decisions concerning clinical care should be based on individual circumstances, taking into account the needs and desires of each patient, local resources, expertise and trends in antimicrobial resistance. While they found no evidence of differences in the effectiveness of various treatment strategies, this may not mean that such differences do not exist, and the important differences in both effectiveness and cost effectiveness may yet emerge from adequately powered studies that use appropriate definitions and outcome measures.

D3 Monitoring of Response to Treatment and Prevention of Ulcer Recurrence

When monitoring the response of an ulcer to treatment, it is important to review the characteristics of the ulcer and any vascular or infective complications. Further damage can occur in people with neuropathy due to unrecognised trauma.

Ulcer evaluation should include regular documentation of the wound location, size, shape, depth, wound bed, peri-wound tissue, wound edge, odour and exudate quantity, colour and viscosity. The documentation system used should allow comparison of ulcer characteristics over time to determine progress.[102]

Signs of infection, such as the presence of erythema, increasing heat, swelling, odour, or purulent discharge, should be documented and aerobic and anaerobic cultures performed. Superficial swabs are likely to identify colonising organisms and may not identify the relevant infecting organism/s. Appropriate samples include post debridement swabs or tissue samples. A sterile probe is useful in assessing the presence of sinus tracts and determining whether a wound extends to a tendon, joint, or bone. Any wound extending to tendon, joint or bone will require further assessment with imaging to investigate for osteomyelitis and deep abscess.[103]

Techniques to assess ulcer size include: direct measurement with a disposable ruler, tracing the ulcer edge onto a clear film or wound tracing grid (which can be stored in the patient record or transferred onto graph paper) or photography including a scale strip to allow an estimation of the area.[54] Care should be taken to replicate patient positioning to ensure the accuracy of the results. Systems that allow computerised calculation of ulcer area from a tracing or digital photograph may also be considered. Photography has significantly less inter-observer variation than traditional techniques (such as using a ruler) and has high patient satisfaction because it avoids the pain of direct contact.[104]

Part E: Future Research

Most of the studies reviewed by the systematic literature review lacked statistical power to detect a real treatment effect or suffered from other methodological weaknesses. Good quality, large-scale studies are urgently required to inform clinical care of people with diabetes-related foot complications. Future studies need to consider all of the following key areas of good clinical trial design: adequate sample size, clear inclusion criteria, true randomisation, blinded outcome assessment, clear and consistent outcome definitions, comparisons of baseline characteristics, intention-to-treat analyses, detailed reporting of withdrawals, concomitant use of interventions and adverse effects.

Particular areas for further research include:

- Use of fenofibrate for prevention of amputation
- Prevention, assessment and management of osteomyelitis
- The form, frequency and extent of debridement needed
- The effectiveness of antibiotic therapy compared to standard wound care on ulcer healing for management of uncomplicated foot ulceration
- Drugs for the improvement of microvascular blood flow
- Recombinant human epidermal growth factor and human platelet derived growth factor applied outside of highly specialised unit settings
- The effect of herbal or nutritional supplements on ulcer healing or amputation
- Thermal wound therapy in addition to standard wound care
- Educational programmes for the prevention of ulcer recurrence and amputation
- Comparative assessments of wound dressings

Part F: Implementation

Introduction

An Implementation Working Group was established to specifically consider issues for implementation of the recommendations and advice contained in the guideline.

During the consultation period, the guideline developers invited organisations, health professionals, other health workers and people with diabetes to explicitly comment on matters that were pertinent to the guideline's implementation. An on-line survey asked individuals and organisations to provide views on whether evidence-based recommendations and expert opinions were current practice and what they saw as the possible barriers to implementation.

Deliberations by the Implementation Working Group, the Expert Panel and the Guidelines Advisory Committee, were combined with feedback from the consultation to identify implementation issues, priorities and ideas for consideration by policymakers, consumer and professional organisations.

Relationship of the Guideline to Current Practice

The feedback from the consultation and the Implementation Working Group highlighted that most of the recommendations were usual practice at least some of the time within the broad medical and allied health community. However, on balance, nine of the fourteen evidence-based recommendations included in the draft guideline were considered to represent a change to usual practice in primary care, at least for some practitioners (EBR 1-5, EBR 7-10).

The guideline developers concluded that although the EBR 6 (topical hydrogel dressings) and EBR 11-14 (management strategies in specialist settings) were not likely to be usual practice amongst primary care practitioners, they were likely to be usual practice for specialist clinicians and nurses and other health professionals working in specialist settings. It is therefore considered that they would require limited attention in implementation:

- Topical hydrogel dressings (EBR 6)
- Negative pressure therapy (EBR 11)
- Hyperbaric oxygen (EBR 12)
- Larval therapy (EBR 13)
- Skin replacement therapies (EBR 14)

Of the 11 expert opinions included in the guideline, all appear to represent usual practice except podiatry review (EO 6). However, where expert opinion supports evidence-based recommendations they have been referenced in the discussion below on implementation of practices that may not currently be usual.

An Approach to Implementation

In making suggestions for implementation of the foot complications in diabetes guideline, what is increasingly understood is that one strategy on its own will not result in uptake of evidence-based guidelines. An overview of systematic reviews on changing practitioner behaviour concluded that

there were some promising results from strategies such as educational outreach (for prescribing) and reminders.[105] However, they also concluded that multifaceted interventions targeting different barriers to change are more likely to be effective than single interventions.[105] It is essential that the focus should not be entirely on practitioner behaviour and individual preferences or attitudes, but that system issues such as resourcing, organisational behaviour and institutional approaches need to be included in any strategy to change behaviour.[106,107]

It is the strong view of the guideline developers that unless there is full integration of the guideline recommendations into the broad framework of current practice, then the guideline will fail to be implemented. The impact of producing written material disseminated in hard copy or electronically, is likely to be very limited. A co-ordinated, national, multifaceted, systems approach for implementation is considered essential by the guideline developers.

Integration of the Guideline into Daily Practice

Many of the suggestions from the consultation reinforced the view that the most effective method of implementation of evidence-based guidelines is via integration into everyday clinical practice. In most cases this means readily available prompts and tools at the clinical interface. For most medical practitioners, this means medical software that indicates the need for particular actions when a patient is in front of them, or that produces reminder notices for recalling the patient for monitoring, assessment or management activities.

Electronic decision support tools are available and in current use for some practitioners. They do, however, remain incomplete (diabetes is not yet one of the conditions included) and not fully integrated into the current medical software programs that are in widespread use. The use of “sidebars”, although highly effective when used, still relies on the practitioner choosing to load the program in addition to their usual medical records and prescribing software. This currently represents a significant barrier to practicing evidence-based care.

Allied health professionals are currently less likely than general practitioners or medical specialists to use electronic records software in their clinical encounters. Therefore other means of delivering the recommendations on assessment and care for foot complications in people with diabetes is imperative to explore with their professional representative bodies.

Aboriginal Community Controlled Health Services currently have access to electronic clinical medical record tools and can increasingly integrate guidelines into their activities through organisational policy and procedures. Encouragement to implement the recommendations of the foot complications in diabetes guidelines will be important. Awareness of the revised guideline amongst the network of Aboriginal Community Controlled Health Organisations would facilitate the uptake into practice.

A solution to the current impasse on integration of decision support tools into medical software is needed urgently.

Access and Resourcing

While access to timely advice at the coalface of clinical care is important, access to health services and care in general, and specialist services in particular, for people with high risk feet and those with current complications is equally a high priority in terms of this guideline.

The workforce issues are particularly relevant here, in terms of the recruitment, skills and training of nurses, aboriginal health workers and podiatrists to undertake many of the recommended practices in the guideline. Increased availability of practice nurses in GP clinics was supported. It may be possible

for nurses to do some of the assessment and monitoring work that cannot be accommodated in the timeframe of the usual GP consultation.

A very practical approach to resourcing and access especially for rural or remote areas may be the provision of kits that contain all the necessary equipment for foot examination (e.g. vibration fork, sterile stick for pinprick sensation or monofilament) and associated instruction materials. The provision of such practical resources to Aboriginal Health Workers and Aboriginal Community Controlled Health Services for example may be a small cost; however the support may be enough to see greater implementation of a key recommendation in a high risk group.

The strong evidence to support the intervention of multi-disciplinary teams in cases where people have high risk or current complications should encourage both professional bodies and governments at the State/Territory and Commonwealth level to ensure that there is access to such teams in each jurisdiction. The avoidance of amputation, disability and/or loss of mobility for people with diabetes and foot complications is possible if access is available, either close by, or by remote consultation supported by digital imaging.

Consideration of policy development and funding of multi-disciplinary foot clinics for people with diabetes at high risk of foot complication or with non-healing ulcers or Charcot's neuroarthropathy is a high priority. The guideline developers consider that at a minimum, all people with diabetes should have reasonable access to a high-risk foot clinic that is adequately funded to cope with demand, and with the facilities to deliver remote support to regional and remote centres via digital imaging.

Awareness, Education and Training

As expected, there was a call from those who responded to the consultation for more training, education and general awareness to be put in place for this guideline. This is the case for practitioners as well as people with diabetes. There is limited evidence to show that education activities increase uptake of guidelines, especially when done in isolation from other more system approaches. However there could be positive encouragement by professional bodies to make their members aware of the revised guideline via notices in journals and newsletters, on websites and via any other means possible such as conferences. Educational and skill development programs could be developed and conducted as widely as possible by professional bodies.

Training and skill development of allied health workers in assessment of risk, wound debridement, appropriate use of dressings for ulcers, and appropriate implementation of pressure reduction of wounds were particularly raised by many respondents.

For people with diabetes, awareness of the self-care activities they could be undertaking as well as the expectations they should have of their health care providers and the health system generally would be useful in assisting with implementation of the guideline. Vehicles such as the NDSS and Diabetes Australia (and its State counterparts) are obvious mechanisms for disseminating the information about evidence-based assessment, prevention and management of foot complications in people with diabetes.

Part G: Related International Guidelines and Resources

A number of international guidelines exist in this area that may assist clinicians in the management of foot-related complications from diabetes. This guideline is based upon more recent evidence. The guideline developers are confident that the recommendations developed for this guideline are consistent with international guidelines. The minor variations are considered to be justified by the evidence.

International Working Group on the Diabetic Foot

Practical guidelines on the management and prevention of the diabetic foot (Based upon the International Consensus on the Diabetic Foot) (2007). **http://www.iwgdf.org/index.php?option=com_content&task=view&id=27&Itemid=29**

These guidelines are based on both evidence and consensus, and cover all aspects of prevention and management, including a section on management of osteomyelitis.

National Institute for Clinical Excellence (NICE) - UK

Type 2 diabetes: prevention and management of foot problems **http://guidance.nice.org.uk/**

This is a clinical guideline on the inpatient management of diabetic foot problems.

Diabetic Foot Disorders: A Clinical Practice Guideline (US)

This guideline was developed by the Clinical Practice Guideline Diabetes Panel of the American College of Foot and Ankle Surgeons. See *J Foot Ankle Surg*. 2006 Sep-Oct; **45**(5 Suppl):S1-66.

This guideline is a very comprehensive and detailed set of advice about all aspects of foot risk, assessment, prevention, pathology, ulcer evaluation and treatment, advanced wound care, infections, Charcot and surgical management.

Management of Diabetes - A national clinical guideline – Management of Diabetic Foot Disease (Scotland)

This guideline covers all aspects of foot complications from diabetes. **http://sign.ac.uk/guidelines/fulltext/116/index.html**

Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association

This guideline covers risk assessment in some detail. It is also endorsed by the American Association of Clinical Endocrinologists. See Boulton AJ, Armstrong DG, Albert SF, et al. Comprehensive Foot Examination and Risk Assessment. *Diabetes Care*. Aug 2008;**31**(8):1679-1685.

Appendix 1: Grading Foot Ulcer Severity – Additional Tools

Wagner wound grade[79]

Grade	Clinical assessment
1	Superficial wound
2	Deep wound involving tendons and capsules but not bone
3	Bony involvement
4	Localised gangrene
5	Generalised gangrene

DEPA scoring system[108]

DEPA score	**Score**		
	1	**2**	**3**
Depth of the ulcer	Skin	Soft tissue	Bone
Extent of bacterial colonisation	Contamination	Infection	Necrotising infection[a]
Phase of ulcer	Granulating[b]	Inflammatory[c]	Nonhealing[d]
Associated etiology	Neuropathy	Bone deformity	Ischaemia[e]

a Infected ulcer with surrounding cellulitis or fasciitis;
b evidence of granulation tissue formation;
c hyperaemic ulcer with no granulation tissue < 2 weeks duration;
d nongranulating ulcer > 2 weeks duration;
e clinical signs and symptoms of chronic lower-limb ischaemia.

Grading of ulcers based on DEPA score

Grade of ulcer	**DEPA score**
Low	< 6
Moderate	7–9
High	10–12 or ulcer in association with wet gangrene

S(AD)SAD system[3]

Grading of ulcers by S(AD)SAD system

Grade	Area	Deep	Sepsis	Arteriopathy	Denervation
0	Skin intact	Skin intact	–	Pedal pulses present	Intact
1	Lesion < 1cm2	Superficial (skin and subcutaneous tissue)	No infected lesions	Pedal pulses reduced or one missing	Reduced
2	Lesion 1–3cm2	Lesion penetrating to tendon, periosteum and joint capsule	Cellulitis-associated lesions	Absence of both pedal pulses	Absent
3	Lesion > 3cm2	Lesion in bones or joint space	Lesions with osteomyelitis	Gangrene	Charcot joint

Curative Health Services classification[109,110]

Curative Health Center classification of foot ulcers

Grade	Criteria
1	Partial thickness involving only dermis and epidermis
2	Full thickness and subcutaneous tissues
3	Grade 2 plus exposed tendons, ligament, and/or joint
4	Grade 3 plus abscess and/or osteomyelitis
5	Grade 3 plus necrotic tissue in wound
6	Grade 3 plus gangrene in the wound and surrounding tissue

International Working Group on the Diabetic Foot

Criteria for wound classification

Perfusion	Depth of wound	Infection	Sensation
Grade 1 No symptoms or signs of ischaemia, palpable pedal pulses, 0.9 < ABI < 1.1	**Grade 1** Superficial ulcers not penetrating any structure below the dermis	**Grade 1** No signs or symptoms of infection	**Grade 1** No loss of sensation of the affected foot
Grade 2 Signs and symptoms of intermittent claudication, or ABI <0.9 with ankle pressure >50 mmHg	**Grade 2** Deep ulcers penetrating down to subcutaneous structures, fascia, muscles, and tendons.	**Grade 2** Infection involving skin and subcutaneous tissues without systemic signs: Local swelling and induration; erythaema >0.5–2 cm around ulcer; local tenderness or pain; local warmth; purulent discharge	**Grade 2** No pressure sensation with a 10g monofilament on two or three sites on the plantar side of the foot. No vibration sense with a 128 Hz tuning fork on both sides of the hallux.
Grade 3 Critical limb ischaemia defined by systolic ankle pressure <50mmHg	**Grade 3** Deep ulcers penetrating down to the bone and/or joint.	**Grade 3** Erythaema >2cm Deep abscess; osteomyelitis; septic arthritis and fasciitis.	
		Grade 4 Any foot infection associated with systemic inflammatory response syndrome. Temperature >38°C or <36°C; heart rate >90 beats/min; respiratory rate >20 breaths/min; total white cell count >12,000 or <4000/cm	

ABI = ankle-brachial index also known as ankle-brachial pressure index (ABPI)

Appendix 2: Charcot's Neuroarthropathy

What is Charcot's neuroarthropathy?

Charcot's neuroarthropathy (hereafter referred to as CNA) is a non-infectious, degenerative disease of the bones and joints, particularly weight-bearing joints such as the foot and ankle. In developed countries diabetic neuropathy is the most common cause. It is characterised by joint dislocation, fractures and deformities and in extreme cases may significantly disrupt the bony architecture of the affected joint.

What are the causes of CNA?

CNA is caused by sensory or autonomic neuropathy. There are several theories proposed to explain its aetiology.

- Neurotraumatic theory: This proposes that peripheral neuropathy impairs proprioception causing overuse injuries of insensate joints, either from repetitive microtrauma or a single traumatic event. The loss of protective mechanisms results in the initial injury or injuries.
- Neurovascular theory: This suggests that autonomic dysfunction leads to increased blood flow (via arterio-venous shunting), an imbalance of bone destruction and synthesis, and subsequent bone resorption and weakening (osteopenia)
- Involvement of inflammatory cytokines (e.g. tumour necrosis factor-α and interleukin-1), which result in the stimulation of osteoclast formation.

Who gets CNA?

CNA typically manifests in patients with long-standing diabetes and peripheral neuropathy.[111]

The annual incidence of CNA among those with diabetes has been estimated to be between 0.1% and 1.4%. Over recent years the incidence and/or diagnosis of CNA has been reported to be increasing.[112]

What are the symptoms and signs of CNA?

The commonest symptoms of CNA are redness, swelling, changing foot shape and new onset of pain or discomfort. About half of patients with CNA experience some pain, however the severity of the pain may be less than clinical signs and symptoms would seem to indicate. The pain may be described as a "deep" aching pain.

Specific clinical signs indicating the presence of CNA include:

- In all cases - neuropathy and pounding pulses
- Early cases - may only have erythema and swelling
- Advanced cases - more swelling, effusions and change in foot shape
- Unilateral swelling and joint deformity varies within a wide range depending on the stage of the disease
- Increase in local skin temperature is generally about 3^{o}C higher in the affected extremity

- There may be absence of sweating (indicating neuropathy) and an insensate foot
- Instability, loss of joint function and concomitant ulceration may also be evident

People in the acute stages of CNA usually have signs of inflammation in the affected area. This inflammation is often reported as having developed over a few days. There may be no history of a traumatic event (or at least an event that is recalled) or only a history of a very minor traumatic event some weeks before the onset of symptoms. X-rays may appear normal early on in the course. However, as the condition progresses there will be joint dislocation, bone and joint destruction, and these signs will be evident on X-ray. Even if the x-ray is normal, if there is a high degree of clinical suspicion, then proceed to an MRI.

Stages of CNA

Several classification systems have been proposed to assist in the diagnosis of CNA. The most prevalent is the one devised by Eichenholtz in 1966,[113] which has since been modified slightly by subsequent investigators.[111] The stages and associated markers of this revised classification system are:

Stage 0 normal radiographs, loss of protective sensation, swelling and erythema, clinical instability, (disorder may be misdiagnosed as a deep infection or cellulitis)

Stage I (fragmentation, dissolution or development stage) – osteopenia, periarticular fragmentation, fracture, subluxation of joints, warm oedematous foot, laxity of ligaments

Stage II (coalescence stage) – healing phase, less oedema and warmth, absorption of debris, fusion of bony fragments, early sclerosis

Stage III (reconstruction or remodelling stage) – absence of inflammation, more stable but deformed foot, osteophytes, subchondral sclerosis, narrowing of joint spaces

Distinguishing between CNA and Osteomyelitis

The symptoms and signs of CNA and osteomyelitis may be similar. In the acute stage, differentiating CNA from osteomyelitis can be difficult. Both conditions often present as a hot, swollen, erythematous foot with either normal or non-distinguishing changes on plain radiographs. However pedal osteomyelitis is almost always associated with an ulcer (initiating event). In CNA, ulceration occurs sometimes but is a secondary event.

As it is often difficult to establish the diagnosis of osteomyelitis with microbiological sampling of affected bone, MRI has emerged as the investigative modality of choice to distinguish osteomyelitis from acute CNA.[54] Diagnosis of osteomyelitis with MRI is based on identification of altered bone marrow signal intensity (loss of normal fatty marrow signal intensity on T1-weighted images, with oedema on T2-weighted images and enhancement on post-contrast gadolinium enhanced T1 weighted images). CNA may alter the marrow signal similarly so other radiological signs, such as pattern and location of signal intensity, should be used to help distinguish the two processes. CNA most commonly affects the tarsal-metatarsal and tarsal joints while osteomyelitis is almost exclusively from contiguous infections and occurs most frequently around the fifth and first metatarso-phalangeal joints, the first distal phalanx and the calcaneus. Associated findings in the adjacent bone, joint or soft tissue should also be considered when making a diagnosis.

Aim of treatment

The aim of treatment of CNA is to prevent progression of the disease. Complications that may arise from inadequate or delayed treatment include foot deformity, chronic ulceration and infection (including osteomyelitis).

Management

Suspected acute CNA of the foot is considered an **emergency** and should prompt **immediate referral** to a dedicated multi-disciplinary foot care service. Early management aims to eliminate further trauma or stress to the foot by preventing weight bearing. Offloading with a total contact cast has been shown to protect the foot, reduce foot temperature and reduce bone activity. Offloading is widely accepted as the most effective treatment for patients with acute CNA. Surgical intervention to fix the joint in order to produce a stable foot and to correct deformity is required in some cases. Bisphosphonates have also been studied for their potential to decrease bone resorption. However, further studies are required to determine the role of these agents in the management of CNA.

Management should also consider protection of the other (non CNA-affected) foot as it will be taking extra weight.

Appendix 3: Foot Expert Panel

Expert Panels

The expert panels proposed the initial clinical questions to the Guidelines Advisory Committee (GAC) to be answered by the updated guideline and provided input on the scope and format of the current guideline. The Expert Panels provided guidance to the technical team at Adelaide Health Technology Assessment (AHTA) regarding strategic research and reviews that may have been done in recent times and assisted in ensuring the draft protocol for the systematic review was appropriate prior to sign off by the GAC. During the search and review process for the systematic review, individual experts were called upon to provide advice or interpretation of the evidence as required.

Expert Foot Panel	Membership	Personnel / Speciality
Foot complications	Australian and overseas experts in foot complications	Professor Peter Colman (Chair) – Endocrinologist Dr Sara Jones – Podiatry Academic Professor Andrew Boulton* - Physician Foot Disease Specialist Dr Rob Fitridge – Vascular Surgeon Dr Paul Wraight – Endocrinologist, Diabetic Foot Unit Director Ms Sue Templeton – Nurse Practitioner Wound Management
Overall diabetes care	Australian experts in clinical care of people with type 2 diabetes	A/Professor Jonathan Shaw (Chair) - Diabetologist Professor Paul Zimmet - Diabetologist Dr Pat Phillips - Diabetologist Professor Tim Davis – Professor of Medicine Dr Lynn Weekes – Quality use of Medicines
Diabetes in Indigenous Communities	Australian experts in care of indigenous people with diabetes	Dr Alex Brown (Chair) A/Professor Ashim Sinha

** International expert*

Systematic Reviewers, Adelaide Health Technology Assessment (AHTA)

The technical report underpinning this guideline was completed by the team listed below.

- Elizabeth Buckley
- Stynke Docter
- Judy Morona
- Edith Reddin
- Vineet Juneja
- David Tamblyn
- George Mnatzaganian
- Benjamin Ellery
- Samuel Lehman
- Tracy Merlin

The report is available at: **http://t2dgr.bakeridi.edu.au** as is the declaration of competing interests of every team member.

Appendix 4: Project Executive

The key management structure associated with the project was the Project Executive. The Project Executive consisted of representatives of the key organisations collaborating on this project: The Baker IDI Heart and Diabetes Institute, The University of Adelaide's Adelaide Health Technology Assessment (AHTA), and the George Institute for Global Health.

Name	Organisation	Perspective/ Background	Role
Associate Professor Jonathan Shaw	Baker IDI	Clinician, diabetologist, epidemiologist	Project Leader
Professor Paul Zimmet	Baker IDI	Clinician, diabetologist, epidemiologist	Specialist Adviser
Ms Tracy Merlin	AHTA	Specialist systematic review methodologist, public health	Guidelines Adviser Oversight of systematic review and guidelines methodology
Ms Kathy Mott	Baker IDI	Management, primary care policy and practice, consumer participation and advocacy	Project Manager
Professor Bruce Neal	George Institute for Global Health	Clinician, hypertension expert, researcher	Deputy Project Leader
Dr Sophia Zoungas	George Institute for Global Health	Clinician, endocrinologist, researcher	Oversight of Guideline Writing

The competing interest of every team member can be found at: **http://t2dgr.bakeridi.edu.au**

Appendix 5: Guidelines Advisory Committee

The Guidelines Advisory Committee (GAC) was responsible for overseeing the review and update of the guideline, their specific role included but was not limited to:

- Reviewing the current guideline and defining clinical questions to guide the updating process
- Signing off on the final review protocol prior to the systematic review of the literature
- Reviewing the draft guidelines and providing feedback prior to release for consultation
- Assisting with consultation amongst peers and with stakeholder organisations
- Reviewing the feedback from the stakeholder consultation, and
- Signing off on the final guideline prior to submission to NHMRC for endorsement.

Professor Hugh Taylor was appointed as an independent chair responsible for managing and leading the Guidelines Advisory Committee.

Nominating Organisation	Perspective/Interests Represented	Nominee
Diabetes Australia Ltd	People with diabetes	Dr I White / Professor G Johnson
Australian Diabetes Society	Specialist clinicians	A/Professor N W Cheung
Australian Diabetes Educators Association	Diabetes educators and nurses	Ms C Matthews
Dietitians Association of Australia	Dietitians and Nutritionists	Dr M Vale
Consumers' Health Forum	People with diabetes and carers	Ms H Mikolaj Mr T Benson
Royal Australian College of General Practitioners	General practitioners Practice nurses	Professor M Harris
An appropriate indigenous health organisation – Aboriginal Health Council (SA)	Indigenous health workers	Ms S Wilson
Pharmaceutical Society of Australia	Community and hospital pharmacists	Dr L Bereznicki
Public Health Association of Australia	Health promotion and prevention	A/Professor R Colagiuri
National Heart Foundation of Australia	Cardiovascular health	Professor J Tatoulis
National Vascular Disease Prevention Alliance	Cardiovascular absolute risk	Dr E Lalor
Australasian Podiatry Council	Podiatrists	Mr P Lazzarini
Department of Health and Ageing	Health policy	Ms L Cotton

The competing interest of every team member can be found at: **http://t2dgr.bakeridi.edu.au**

Appendix 6: Glossary of Acronyms/ Terms

ABPI	Ankle-brachial pressure index (also referred to as ABI, Ankle-brachial index)
AIHW	Australian Institute of Health and Welfare
AusDiab	Australian Diabetes, Obesity and Lifestyle Study
CNA	Charcot's neuroarthropathy
EBR	Evidenced-based recommendation
EO	Expert Opinion
GAC	Guidelines Advisory Committee
HBOT	Hyperbaric oxygen therapy
IDF	International Diabetes Federation
IWGDF	International Working Group on the Diabetic Foot
MBS	Medicare Benefits Scheme
MDF	Multi-Disciplinary Foot (clinic/service)
MRI	Magnetic Resonance Imaging
NDS	Neuropathy Disability Score
NHMRC	National Health and Medical Research Council
NVDPA	National Vascular Disease Prevention Alliance
PAD	Peripheral arterial disease (also known as peripheral vascular disease- PVD)
QALY's	Quality adjusted life years
RCT	Randomised controlled trial
SIGN	Scottish Intercollegiate Guidelines Network
Study	Non randomised or observational study
TcPO2	Transcutaneous oxygen saturation
UT	University of Texas
VAC	Vacuum Assisted Closure

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† *This list only includes references that are specifically referred to in the text and includes additional references to those found in the systematic review of literature. The full list of references that were used to formulate the evidence-based recommendations is included in the Technical Report that accompanies the guideline.*

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