Diabetic foot problems

Review protocol

	Details	Notes & Status
Review question 1 (CG119)	*What are the key components and organisations of hospital care to ensure optimal management of people with diabetic foot problems?*	
Objectives	To identify best practice and organisation of hospital care for diabetic foot problems.	
Language	*English only*	
Study design	*No restrictions.*	Any studies that addressed service delivery issues.
Status	*Published papers (full papers only)*	
Population & Healthcare setting	Inclusion: • Adults (18 and older) with or at a particular high risk of diabetic foot problems. Setting: • Secondary and tertiary care	
Intervention	• Key components of hospital care for diabetic foot problems • Service organisations and delivery of hospital care, from hospital admission to discharge planning, for diabetic foot problems.	
Comparisons	N/A	
Outcomes	• Rates and extent of amputation (major or minor) • Length of hospital stay • Rates of hospital readmission • Mortality • Health related quality of life (QoL) • Complications • Patient's satisfaction	
Other criteria for inclusion/ exclusion of studies	*Exclusion:* • *Studies on children (younger than 18)* • *Studies on key components and organizations of primary care.* • *Studies on key components and organizations of hospital care in different healthcare systems that were not applicable to the NHS.* • *Studies on care standards for general management of diabetes, comorbidities and complications of diabetes (other than diabetic foot problems).* • *Studies on key components and organizations of hospital care of other foot diseases (other than diabetic foot problems).*	
Search strategies	Please see previous section.	
Review strategies	• *Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies.*	

This review protocol underpins section 4.1 of the full guideline which is from 2011 and has not been updated by an evidence review

	• *Data on all included studies will be extracted into evidence tables.* • *Where statistically possible, a meta-analytic approach will be used to give an overall summary effect.* • *All key outcomes from evidence will be presented in GRADE profiles, or modified evidence profiles, and further summarised in evidence statements.*	

	Details	Additional comments
Review question 2	In UK current practice, are there existing definitions and compositional models (including skills and specialism) for the foot protection team and the multidisciplinary foot care team?	
Objectives	To determine the different service arrangements (including types of team member) of foot protection teams and multidisciplinary foot care teams currently providing services in the UK	
Type of review	Narrative review	
Language	English only	
Study design	No restrictions	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Intervention	Effective service arrangements of foot protection and multidisciplinary foot care teams, including team member composition.	
Comparator	Not applicable	
Outcomes	• Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes. • Resource use and costs. • Rates of hospital admission for foot problems resulting from diabetes. • Length of hospital stay.	
Other criteria for inclusion / exclusion of studies	Exclusion: • Criteria for referral to foot protection teams or multidisciplinary foot care teams. • Non-UK based studies • Papers published before 2000	
Search strategies	To be developed	
Review strategies	Not applicable – narrative review	
Identified papers	None	

	Details	Additional comments
Review question 3	When and with what criteria should people with diabetes be referred to the foot protection team or the multidisciplinary foot care team?	
Objectives	To establish the situations when it is appropriate and effective to refer people with diabetes to foot protection teams or multidisciplinary foot care teams	
Type of review	Prognostic	
Language	English only	
Study design	Systematic review Prospective or retrospective cohort study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes	
Prognostic factor	Varying criteria for referral of people with diabetes to foot protection and multidisciplinary foot care teams	The current review could not find studies that compared different criteria for referral to either of these teams. As a result evidence was presented for studies showing the effectiveness of a protocol/referral pathway for use of these teams or studies showing the effect of the establishment of a multidisciplinary team in a specific population group.
Comparator	Not applicable	
Outcomes	• Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes • Resource use and costs (including referral rates) • Rates of hospital admission for foot problems resulting from diabetes. • Length of hospital stay • Health-related quality of life	
Other criteria for inclusion / exclusion of studies	Exclusion: • Configuration of foot protection teams or multidisciplinary foot care teams providing care for children and young people with diabetes) admitted to hospital who have foot problems. • Examination of service arrangements and composition of foot protection teams and multidisciplinary foot care teams in the UK.	
Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements.	

	Sub-analysis will be undertaken by age group where possible	
Identified papers	None identified	

	Details	Additional comments
Review question 4	What are the clinical utilities of assessment and risk stratification tools for examining the feet of people with diabetes and classifying risk of foot problems?	
Objectives	To establish the risks, benefits and accuracy of assessment and risk stratification tools for examining feet and classifying the risk of people with diabetes developing foot problems.	
Type of review	Prognostic	
Language	English only	
Study design	Systematic review Test and treat RCT If insufficient evidence is available progress to: Cohort study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Prognostic factor	Assessment and stratification tools for risk of foot problems in people with diabetes.	Tools for examining feet include: 10g monofilament Tuning fork Neurothesiometer Biothesiometer Tendon hammer Achilles hammer LDI flare test QST devices Neuropad Ipswich touch test Neurotip Hot or cold rods Risk stratification tools could include: Scottish (Graham Leese) NICE guideline
Comparator	Clinical examination and NICE guidance classification system	
Outcomes	1. Rates of foot ulceration/ infection 2. Rates of gangrene resulting from diabetes. 3. Rates of amputation (major and minor) 4. Rates of A&E / hospital admission for foot problems resulting from diabetes 5. Resource use and costs	
Other criteria for inclusion / exclusion of studies	Inclusion: • Multivariate analysis. Exclusion: • Tools for classification of foot ulcer severity or diagnosis of foot infection.	

Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by risk classification and age group where possible	
Identified papers	<u>Systematic reviews</u> Monteiro-Soares,Vaz-Carneiro,Sampaio et al (2012) Validation and comparison of currently available stratification systems for patients with diabetes by risk of foot ulcer development. European Journal of Endocrinology, 09 2012, vol./is. 167/3(401-7), 0804-4643;1479-683X (2012 Sep) <u>Studies (Medline search [diabet* and (foot or feet) and risk])</u> Sibbald, Ayello, Ostrow et al (2012) Screening for the high-risk diabetic foot: a 60 second tool. Advances in Skin & Wound Care, 10 2012, vol./is. 25/10(465-76; quiz 477-8), 1527-7941;1538-8654 (2012 Oct) Baker (2012) An alternative to a 10g monofilament or tuning fork? Two new, simple, easy to use screening tests for determining foot ulcer risk in people with diabetes. Diabetic Medicine, 12 2012, vol./is. 29/12(1477-9), 0742-3071;1464-5491 (2012 Dec) Raymen, Vas, Baker et al (2011) The Ipswich Touch Test: a simple and novel method to identify inpatients with diabetes at risk of foot ulceration. Diabetes Care, 07 2011, vol./is. 34/7(1517-8), 0149-5992;1935-5548 (2011 Jul) Bower and Hobbs (2009) Validation of the basic foot screening checklist: a population screening tool for identifying foot ulcer risk in people with diabetes mellitus. Journal of the American Podiatric Medical Association, 07-08 2009, vol./is. 99/4(339-47), 8750-7315;1930-8264 Mugambi-Nturibi, Otieno, Kwasa et al (2009) Stratification of persons with diabetes into risk categories for foot ulceration. East African Medical Journal, 05 2009, vol./is. 86/5(233-9), 0012-835X;0012-835X (2009 May) Lavery, Peters, Williams et al (2008) Re-evaluating the way we classify the diabetic foot: restructuring the diabetic foot risk classification system of the International Working Group on the Diabetic Foot. Diabetes Care, 01 2008, vol./is. 31/1(154-6), 0149-5992;1935-5548 (2008 Jan)	

	Details	Additional comments
Review question 5	How often should people with diabetes at risk of developing foot problems be reviewed?	
Objectives	To determine the appropriate review frequency for people with diabetes according to the risk of developing foot problems.	
Type of review	Intervention	
Language	English only	
Study design	Systematic review Randomised controlled trials If insufficient evidence is available progress to: Non-randomised controlled trials Cohort study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Intervention	Review schedules of varying frequency	
Comparator	Standard care based on risk category	
Outcomes	1. Rates of foot ulceration/ infection 2. Rates of gangrene resulting from diabetes. 3. Rates of amputation (major and minor) 4. Rates of A&E / hospital admission for foot problems resulting from diabetes 5. Resource use and costs	
Other criteria for inclusion / exclusion of studies	Exclusion: • Children, young people and adults with diabetes with foot problems who are admitted to hospital.	
Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by risk classification and age group where possible	
Identified papers		

	Details	Additional comments
Review question 6	What is the effectiveness of different prevention strategies for people with diabetes at risk of developing foot problems? This includes information, advice and education about self-monitoring and preventing foot problems, appropriate footwear, provision of foot orthoses, and skin and nail care.	
Objectives	To determine the effectiveness of strategies to prevent foot problems in people with diabetes, including information, advice and education about looking after your own feet, appropriate types of footwear, provision of orthoses, and provision of skin and nail care treatments.	
Type of review	Intervention	
Language	English only	
Study design	Systematic review Randomised controlled trials If insufficient evidence is available progress to: Non-randomised controlled trials Cohort study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Intervention	• Information, advice and education on self-monitoring and skin and nail care • Information, advice and education about foot wear • Provision of foot orthoses • Provision of skin and nail care treatment • Other preventive and management strategies • Education for healthcare professionals	To include education and information about smoking cessation.
Comparator	Standard care	
Outcomes	• Rates of foot ulceration/ infection • Rates of gangrene resulting from diabetes. • Rates of amputation (major and minor) • Rates of A&E / hospital admission for foot problems resulting from diabetes • Resource use and costs	
Other criteria for inclusion / exclusion of studies	Exclusion: • Strategies for management of current foot problems in people with diabetes. • Strategies for prevention of foot problems in people without diabetes.	
Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an	

	overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by risk classification and age group where possible	
Identified papers	Systematic reviews Dorrensteijn, Kriegsman, Assendelft et al (2012) Patient education for preventing diabetic foot ulceration. Cochrane Database of Systematic Reviews 2012, issue 10. Paton, Bruce, Jones et al (2011) Effectiveness of insoles used for the prevention of ulceration in the neuropathic diabetic foot: a systematic review (structured abstract) Journal of Diabetes and its Complications.2011;25(1):52-62 Arad Y, Fonseca V, Peters A et al. (2011) Beyond the monofilament for the insensate diabetic foot. Diabetes Care 34: 1041–6 Dorrensteijn, Kriegsman, Valk (2010) Complex interventions for preventing diabetic foot ulceration. Cochrane Database of Systematic Reviews 2010, Issue 1. Morrell, Booth and Akehurst (1998) The prevention and treatment of diabetic foot ulcers: a review of clinical effectiveness studies (structured abstract). Journal of Clinical Effectiveness.1998;3(3):99-104.	

	Details	Additional comments
Review question 7	What are the clinical utilities and accuracy of tools for assessing and diagnosing: • foot ulcers (including severity) • soft tissue infections • osteomyelitis • gangrene?	
Objectives	To establish the risks, benefits and accuracy of tools to assess and diagnose: • foot ulcers (including severity) • soft tissue infections • osteomyelitis • gangrene?	This will include classification of foot ulcer
Type of review	Diagnostic	
Language	English only	
Study design	Systematic review Test and treat RCT Cross-sectional study If insufficient evidence is available progress to: Case control study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Diagnostic test	Any tool for assessing and diagnosing: • foot ulcers (including severity) • soft tissue infections • osteomyelitis • gangrene	GDG suggested test for diagnosis of: osteomyelitis could be probe to bone test Systems for classification of severity include: European pressure ulcer advisory panel system University of Texas Wagner S(AD) SAD SINBAD
Comparator	Standard care Clinical judgement	Reference standards confirmed with GDG: Foot ulcer – clinical examination Soft tissue infection – Clinical examination, swab tests and deep tissue biopsy Osteomyelitis – Bone biopsy Dry gangrene – Clinical examination Wet gangrene – clinical examination, tissue swab
Outcomes	a) Clinical utility or diagnostic test accuracy (if available) including: • Test validity such as face validity, content validity, construct validity, concurrent validity, criterion validity;	

	• Test reliability such as internal reliability/consistency, test-retest reliability, inter-rater reliability. • Sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios, diagnostic odds ratio and area under the ROC analyses. b) • Rates of infection and gangrene. • Rates of hospital admission for foot problems associated with diabetes. • Rates and extent of amputation (major or minor)	
Other criteria for inclusion / exclusion of studies	Exclusion: • Assessment or diagnostic tools for foot ulcers or infection in people without diabetes.	
Search strategies	To be developed	
Review strategies	QUADAS-2 tool will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by age group where possible	
Identified papers	Systematic reviews Karthikesalingam A, Holt PJE, Moxey P et al. (2010) A systematic review of scoring systems for diabetic foot ulcers. Diabetic Medicine 27: 544–9 Kapoor, Page, LaValley et al (2007) Magnetic resonance imaging for diagnosing foot osteomyelitis: a meta-analysis (structured abstract). Archives of Internal Medicine.2007;167:125-132 Nelson, O'Meara, Craig et al (2006) A series of systematic reviews to inform a decision analysis for sampling and treating infected diabetic foot ulcers (structured abstract). Health Technology Assessment.2006;10(12):1-238	

	Details	Additional comments
Review question 8	How often should people with diabetes who have foot ulcers, soft tissue infections, osteomyelitis or gangrene be reviewed?	
Objectives	To determine the appropriate review frequency for people with diabetes who have foot ulcers, soft tissue infections, osteomyelitis or gangrene.	
Type of review	Intervention	
Language	English only	
Study design	Systematic review Randomised controlled trials If insufficient evidence is available progress to: Non-randomised controlled trials Cohort study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Intervention	Review schedules of varying frequency	
Comparator	Standard care based on different risk category	
Outcomes	1. Rates and extent of amputation (major or minor) 1. Rates of healing / cure 1. Time to further ulceration 2. Rates of foot ulceration, infection and gangrene resulting from diabetes 3. Resource use and costs 4. Rates of A&E/hospital admission for foot problems resulting from diabetes 5. Mortality 6. Time to healing / cure	Top three equal weight
Other criteria for inclusion / exclusion of studies	Exclusion: • Children, young people and adults with diabetes with foot problems who are admitted to hospital.	
Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by risk classification and age group where possible	
Identified papers	None identified	

	Details	Additional comments
Review question 9	What is the effectiveness of different management strategies for people with diabetes who have foot ulcers, soft tissue infections, osteomyelitis or gangrene? This includes information, advice and education about self-monitoring and preventing further foot problems, blood glucose management, and skin and nail care.	
Objectives	To determine the effectiveness of strategies to manage foot ulcers, soft tissue infections, osteomyelitis or gangrene in people with diabetes, including information, advice and education about looking after your own feet, appropriate types of footwear, blood glucose management provision of orthoses, and provision of skin and nail care treatments.	Please note provision of footwear and foot orthoses will be covered in full in review question I (as part of the section relating to off-loading), therefore will not be covered in this review question
Type of review	Intervention	
Language	English only	
Study design	Systematic review Randomised controlled trials If insufficient evidence is available progress to: Non-randomised controlled trials Cohort study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	Subgroup: people with visual impairment
Intervention	• Information, advice and education on self-monitoring and skin and nail care • Information, advice and education about foot wear • Blood glucose management • Provision of foot orthoses • Provision of skin and nail care treatment • Other management strategies	Cardiovascular risk management (however this may be a cross referral to the PAD guidance)
Comparator	Standard care	
Outcomes	1. Rates and extent of amputation (major or minor) 1. Rates of healing / cure 1. Time to further ulceration 2. Rates of foot ulceration, infection and gangrene resulting from diabetes 3. Resource use and costs 4. Rates of A&E/hospital admission for foot problems resulting from diabetes 5. Mortality 6. Time to healing / cure	Top three equal weight
Other criteria for inclusion / exclusion of studies	Exclusion: • Strategies for management of foot problems in people without diabetes.	
Search strategies	To be developed	
Review	Appropriate NICE Methodology Checklists,	

strategies	depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by risk classification and age group where possible	
Identified papers	Systematic reviews None identified.	

	Details	Additional comments
Review question 10	What is the clinical effectiveness of surgical or non-surgical debridement, wound dressings and off-loading?	
Objectives	To identify the most effectiveness wound management for diabetic foot problems.	
Type of review	Intervention	
Language	English only	
Study design	RCT only.	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes and foot ulcer (with or without soft tissue infection, osteomyelitis or gangrene)	
Intervention	• Surgical or non-surgical debridement • Wound dressing • off-loading • footwear	GDG suggested the following search terms: Surgical off-loading, orthopaedics, osteotomy
Comparator	Standard care Head to head comparison	
Outcomes	• Rates and extent of amputation (major or minor) • Length of hospital stay • Rates of hospital readmission • Mortality • Health related quality of life (QoL) • Complications • [or other diabetic foot related outcomes] • Re-ulceration	The GDG agreed the 3 critical outcomes should be prioritised as: Cure rates of foot ulcer resulting from diabetes Rates and extent of amputation Length of stay
Other criteria for inclusion / exclusion of studies	Include: • Studies in which people with diabetes and foot ulcer are a subset of people with chronic wounds and data is presented separately. Exclusion: • Non-randomised trials • RCTs with < 10 study sample • Crossover studies with no washout period and no carry over effects analysis • Studies on other wound management (other than those listed in section 7) • Studies on wound management for other conditions/diseases (other than diabetic foot problems)	
Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect.	

	All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by age group where possible	
Identified papers		

	Details	Additional comments
Review question 11	What is the clinical effectiveness of different antibiotic regimens and antimicrobial therapies for foot infection (with or without osteomyelitis) in people with diabetes?	
Objectives	To determine the most effective antibiotic and antimicrobial treatments for foot infection in people with diabetes	
Type of review	Intervention	
Language	English only	
Study design	Systematic review Randomised controlled trials	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes and foot ulcer with soft tissue infection (with or without osteomyelitis or gangrene)	
Intervention	Any antibiotic regimen or antimicrobial therapy	GDG to prioritise which types of treatment the review should examine.
Comparator	• Standard care • Placebo • No treatment • Head to head comparison • Topical antibiotics	The GDG suggested it may be appropriate to consider the following treatment comparisons: IV vs. Orals Single agent & combined therapy Empirical therapy vs. culture target regimes Duration of regimes (divided by type of infection/ depth of infection/ location of infection)
Outcomes	• Cure rates of foot infection in people with diabetes • Rates and extent of amputation (major or minor) • Adverse events (treatment failure, healthcare assoc. infections, side effects of antibiotics, mortality, sepsis) • Length of stay • Health-related quality of life	The GDG agreed the following 3 critical outcomes should be prioritised as critical: Cure rates of foot infection in people with diabetes Rates and extent of amputation (major or minor) Adverse events (treatment failure, healthcare assoc. infections, side effects of antibiotics, mortality, sepsis) In looking at outcomes GDG suggested it may be appropriate to stratify by setting – inpatient vs outpatient
Other criteria for inclusion / exclusion of studies	Include: • Studies in which people with diabetes are a subset of the people with foot infection and data is presented separately. Exclusion: • Studies on antibiotic regimens and antimicrobial therapies for people with diabetes and infection in a site other than the foot. • Studies in which people with foot infection is not a subset of the population or where data is not presented separately.	

Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by presence of osteomyelitis where possible Sub-analysis will be undertaken by age group where possible	
Identified papers	Systematic reviews Crouzet, Lavigne, Richard et al (2011) Diabetic foot infection: a critical review of recent randomized clinical trials on antibiotic therapy. International Journal of Infectious Diseases, 09 2011, vol./is. 15/9(e601-10), 1201-9712;1878-3511 (2011 Sep) Nelson, O'Meara, Craig et al (2006) A series of systematic reviews to inform a decision analysis for sampling and treating infected diabetic foot ulcers (structured abstract). Health Technology Assessment.2006;10(12):1-238 O'Meara, Cullum, Kajid et al (2000) Systematic revi0ews of wound management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration (Structured abstract). Health Technology Assessment 2000;4(21):1-237 O'Keefe, Hutchinson, McIntosh et al (1999) A systematic review of foot ulcer in patients with type 2 diabetes mellitus – II: treatment (structured abstract). Diabetic Medicine.1999;16(11):889-909 Morrell, Booth and Akehurst (1998) The prevention and treatment of diabetic foot ulcers: a review of clinical effectiveness studies (structured abstract). Journal of Clinical Effectiveness.1998;3(3):99-104.	

	Details	Additional comments
Review question 12	What is the clinical effectiveness of adjunctive treatments in treating diabetic foot problems, for example, dermal or skin substitutes, growth factors, hyperbaric oxygen therapy, bio-debridement, topical negative pressure therapy and electrical stimulation?	
Objectives	To identify the most cost-effective adjunctive treatment for diabetic foot problems.	
Type of review	Intervention	
Language	English only	
Study design	RCT only	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes and foot ulcer (with or without soft tissue infection, osteomyelitis or gangrene)	
Intervention	• dermal or skin substitutes • skin grafts • growth factors • hyperbaric oxygen therapy • hydro-debridement • topical negative pressure therapy • electrical stimulation • ultrasonic simulation • laser therapy • surgical intervention (offloading / biomechanical healing) • leucopatch	GDG suggested the following search terms: Platelet rich plasma, growth factor containing dressing, integra (skin substitutes), orthotics
Comparator	Standard care without adjunctive treatment	
Outcomes	• Cure rates of foot ulcer resulting from diabetes 1 • Rates and extent of amputation (major or minor) 2 • Length of stay 3 • Health-related quality of life • Adverse events	
Other criteria for inclusion / exclusion of studies	Include: • Studies in which people with diabetes and foot ulcer are a subset of people with chronic wounds and data is presented separately. • People with Charcot arthropathy Exclusion: • Non-randomised trials • RCTs with < 10 study sample • Crossover studies with no washout period and no carry over effects analysis • Studies on adjunctive therapies for other conditions/diseases (other than diabetic foot problems)	
Search strategies	To be developed	
Review	Appropriate NICE Methodology Checklists,	

strategies	depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub-analysis will be undertaken by age group where possible	
Identified papers		

	Details	Additional comments
Review question 13	What signs and symptoms or risk factors should prompt healthcare professionals to suspect Charcot arthropathy?	
Objectives	To establish what signs and/or symptoms might raise suspicions about Charcot arthropathy (bony swelling or deformity as a result of circulation or nerve problems) (restriction of blood flow in the lower limbs)?	
Type of review	Diagnostic	
Language	English only	
Study design	Systematic review Controlled trial test and treat Diagnostic cross-sectional study If insufficient evidence is available progress to: Case control study	
Status	Published papers only (full text)	
Population	Adults with type 1 or type 2 diabetes	
Intervention	Signs and symptoms of Charcot arthropathy, including but not limited to: • deformity • inflammation • loss of sensation • pain • redness • warmth • fractures	Suggested signs and symptoms to be developed by the GDG.
Comparator	Confirmed diagnosis	
Outcomes	• Accuracy metrics (Sen, Spec, PPV, NPV, +LR, -LR, etc.) • Predictive measures from adjusted regression model • Rates of hospital admission for foot problems resulting from diabetes. • Rates and extent of amputation (major or minor)	
Other criteria for inclusion / exclusion of studies	Include • Studies in which people with diabetes are a subset of people with suspected Charcot arthropathy. Exclusion • Treatment or management of Charcot arthropathy and lower limb ischemia. • Studies in which people with diabetes are not a subset of people with suspected Charcot arthropathy.	
Search strategies	To be developed	

Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements.	
Identified papers	<u>Studies</u> Wu, Chen, Chen et al (2012) Doppler spectrum analysis: a potentially useful diagnostic tool for planning the treatment of patients with Charcot arthropathy of the foot? Journal of Bone & Joint Surgery - British Volume, 03 2012, vol./is. 94/3(344-7), 0301-620X;0301-620X (2012 Mar) Aerden D, Massaad D, von Kemp K et al. (2011) The ankle–brachial index and the diabetic foot: a troublesome marriage. Annals of Vascular Surgery 25: 770–7 Rozziango, Tagliani, Vittorini (2009) Role of magnetic resonance imaging in the evaluation of diabetic foot with suspected osteomyelitis. Radiologia Medica, 02 2009, vol./is. 114/1(121-32), 0033-8362;0033-8362 (2009 Feb) Rogers and Bevilacqua (2008) The diagnosis of Charcot foot. Clinics in Podiatric Medicine & Surgery, 01 2008, vol./is. 25/1(43-51, vi), 0891-8422;0891-8422 (2008 Jan)	

	Details	Additional comments
Review question 14	What are the indicators for referral to specialist services such as investigative or interventional radiology, orthopaedic or vascular services, specialist pain management and specialist orthotics?	Includes indications for referral because of Charcot foot
Objectives	To establish the situations when it is appropriate and effective to refer people with diabetes who have foot problems to specialist services	To establish when you should be referred from within a diabetes multidisciplinary foot care team to one of the listed services. Criteria may include: depth of the ulcer/ placement of the ulcer Example: Should fractures in the presence of peripheral neuropathy stay in the fracture service or referred to a specialist foot team The current review could not find studies that compared different criteria for referral to these specialist teams. As a result evidence was presented for studies showing the effectiveness of a protocol/referral pathway for use of these teams or studies showing the effect of a referral to a specialist team in a specific population group.
Type of review	Prognostic	
Language	English only	
Study design	No restriction	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Prognostic factor	Varying criteria for referral of people with diabetes to specialist services such as investigative or interventional radiology, orthopaedic or vascular services, specialist pain management and specialist orthotics.	
Comparator	Not applicable	
Outcomes	• Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes. • Rates of hospital admission for foot problems resulting from diabetes. • Rates and extent of amputation (major or minor) • Health-related quality of life	
Other criteria for inclusion / exclusion of studies	Exclusion: • Examination of service arrangements of specialist services. • Examination of the different types of team members of specialist services.	
Search strategies	To be developed	
Review	Appropriate NICE Methodology Checklists,	

strategies	depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements. Sub group analysis will be undertaken by age group where possible.	
Identified papers	None identified	

	Details	**Additional comments**
Review question 15	What are the clinical utilities and accuracy of tools for assessment and diagnosis of Charcot arthropathy in people with diabetes?	
Objectives	To establish the risks, benefits and accuracy of tools to assess and diagnose Charcot arthropathy	
Type of review	Diagnostic	
Language	English only	
Study design	Systematic review Test and treat RCT Cross-sectional study If insufficient evidence is available progress to: Case control study	
Status	Published papers only (full text)	
Population	Children, young people and adults with type 1 or type 2 diabetes.	
Diagnostic test		GDG suggested the following interventions should be looked at: MRI Bone scans, with neuropathy and primary fracture Clinical suspicion and deformity Temperature difference in the foot
Comparator		x-ray
Outcomes	a) Clinical utility or diagnostic test accuracy (if available) including: •Test validity such as face validity, content validity, construct validity, concurrent validity, criterion validity; •Test reliability such as internal reliability/consistency, test-retest reliability, inter-rater reliability. •Sensitivity, specificity, positive predictive value,	

	negative predictive value, likelihood ratios, diagnostic odds ratio and area under the ROC analyses.	
Other criteria for inclusion / exclusion of studies		Exclusion: People without diabetes
Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements.	
Identified papers		

	Details	**Additional comments**
Review question 16	What is the clinical effectiveness of surgical interventions, adjunctive treatment, off-loading or orthoses for managing Charcot arthropathy?	
Objectives	To determine the most effective methods of surgical interventions, adjunctive treatment, off-loading and orthoses for managing Charcot arthropathy	
Type of review	Intervention	
Language	English only	
Study design	Systematic review Randomised controlled trials If insufficient evidence is available progress to: Non-randomised controlled trials Cohort study	
Status	Published full text only	
Population	People with diabetes and diagnosed Charcot arthropathy	
Intervention	• surgical interventions • adjunctive treatment • off-loading • orthoses	The GDG suggested the following interventions should be considered:Contact casting Removable boot device (Crow device) Bisphosphanates (oral and intravenously) Early orthopaedic intervention
Comparator	Surgical gold standard:	GDG advice needed.

	Non-surgical gold standard:	
Outcomes	Amputation Mortality Ulceration Time to remission	The GDG suggested the following outcomes should be considered: Rates and extent of amputation Deformity
Other criteria for inclusion / exclusion of studies		Exclusion: People without diabetes
Search strategies	To be developed	
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key outcomes from evidence will be presented in GRADE profiles and further summarised in evidence statements.	
Identified papers		